Abstract N°: 160

Buschke-Fischer-Brauer Disease: A Plantar Wart Simulator

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Introduction:

Palmoplantar keratodermas (PPKs) are a group of rare, heterogeneous disorders characterized by hyperkeratosis of the palms and soles, which can often be painful and debilitating. These conditions may be hereditary or acquired and typically present in diffuse, focal, or punctate patterns. Punctate PPKs are particularly uncommon and are classified into three morphological types based on clinical presentation: Buschke-Fischer-Brauer disease, spiny keratoderma, and acrokeratoelastoidosis.

Case Presentation:

A 75-year-old woman with a history of kidney transplant due to IgA nephropathy presented with a 20-year history of a disseminated dermatosis affecting palms and soles, characterized by multiple, hyperkeratotic papules ranging from millimeters to 3 cm, yellowish, round, some simulating pits, accompanied by a cutaneous horn on the fifth toe of the left foot. The patient reported mild pain when walking or applying pressure to the lesions and had previously been treated for presumed plantar warts. Her family history was significant for similar lesions in her mother and one sister. Skin biopsies were obtained from the cutaneous horn and one of the smaller papules. Histopathology revealed compact hyperkeratosis, orthokeratosis, and hypergranulosis overlying cup-shaped acanthosis, without evidence of papillomatosis or koilocytosis. Based on the clinical presentation, histopathological findings, and family history, a diagnosis of Buschke-Fischer-Brauer disease was established. The patient was started on 40% urea ointment with minimal improvement.

Discussion:

Buschke-Fischer-Brauer disease, also known as type 1 punctate PPK, is a rare genodermatosis with a prevalence of 1.17 per 100,000 individuals. It follows an autosomal dominant inheritance pattern and has been linked to at least 38 mutations of the AAGAB gene, which encodes alpha and gamma adaptin binding protein responsible for stabilizing AP2 complexes during endocytosis. These mutations impair endocytosis of EGFR, resulting in sustained receptor activation and subsequent hyperproliferative hyperkeratosis. Unlike other genodermatosis, this condition typically presents later in life, with some patients developing symptoms as late as 35 years of age. It is often asymptomatic or causes only mild discomfort with pressure which contrasts with other forms of PPK, which can be debilitating and significantly impact mobility and manual labor. Although some reports have suggested a possible association with malignancy, larger studies have not demonstrated an increased risk compared to the general population. Therefore, routine cancer screening should follow standard guidelines. The disease generally has a favorable prognosis, remaining stable for years or progressing gradually, primarily at pressure sites. Treatment options include keratolytics, PUVA therapy, and topical or systemic retinoids, although these often yield limited efficacy and are frequently followed by relapse upon discontinuation.

Conclusion:

Buschke-Fischer-Brauer disease is a rare genetic disorder that is often misdiagnosed as more common conditions such as plantar warts, resulting in unnecessary and sometimes aggressive treatments. Despite its chronic nature, the prognosis is generally favorable, with no reported systemic or malignant associations. This condition should be considered in the differential diagnosis of palmoplantar keratotic lesions that are unresponsive to standard therapies.

Abstract N°: 174

An Unusual Coexistence of Keratitis-Ichthyosis-Deafness Syndrome and Hidradenitis Suppurativa

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Introduction & Objectives:

Keratitis-ichthyosis-deafness (KID) syndrome is a rare congenital genodermatosis associated with GJB2 gene mutation characterized by keratitis, sensorineural hearing loss and ichthyosiform skin involvement. Hidradenitis suppurativa (HS) is a chronic inflammatory condition of follicular occlusion, presenting with painful, deep-seated nodules, abscesses, sinus tracts, typically located in intertriginous areas. Although HS does not commonly accompany KID, few cases have been reported. We present a patient diagnosed with both conditions, highlighting the diagnostic and therapeutic challenges of this unusual overlap.

Materials & Methods:

An 18-year-old patient with cognitive impairment, hyperkeratotic scaling, bilateral sensorineural hearing loss, and keratitis was admitted to the Dermatology Department for evaluation of painful lesions affecting the scalp, axillae, anogenital, perineal and suprapubic area. She has previously received systemic beta-lactam antibiotics and undergone several surgical interventions with temporary improvement. At birth, facial dysmorphism, hyperkeratotic skin, limb contractures, and bilateral conjunctivitis were noted. Neonatal MRI revealed cerebellar vermis agenesis and cerebellar hypoplasia consistent with Dandy-Walker malformation. Genetic testing confirmed a *GJB2* mutation. Congenital bilateral sensorineural hearing loss was diagnosed, and cochlear implantation was performed in early childhood. The physical examination revealed nodular lesions with sinus tract formation with yellowish scale on the scalp, nodules and abscesses with purulent discharge in intertriginous regions, generalized follicular hyperkeratosis, palmoplantar keratoderma, dental dysplasia, absence of body hair, erythematous plaques with follicular accentuation on the face. Ophthalmological examination confirmed neovascularizing keratitis. Based on clinical presentation and medical history she was diagnosed with KID syndrome with overlapping HS. She was treated with oral clindamycin and topical antiseptics, followed by combination of clindamycin and rifampicin, both at a dose 300 mg twice daily over a 12-week period. On her follow-up visit, an initial improvement in her skin condition was witnessed, although chronic disease activity persisted.

Results:

We present an extremely rare combination of Keratitis-ichthyosis-deafness syndrome and Hidradenitis suppurativa. Despite distinct etiologies, both disorders may present overlapping pathogenic mechanisms particularly follicular occlusion and epidermal barrier dysfunction. In our patient, typical lesions of HS and dissecting cellulitis were observed alongside manifestations of KID. Given the chronic nature, relapsing characteristics of her condition and limited response to conventional therapies, a biological treatment is planned as the next step. She will be evaluated for eligibility to initiate an IL-17A inhibitor, which is approved for HS, although its efficacy in keratinization disorders has yet to be fully established.

Conclusion:

The association of KID syndrome and HS is extremely rare and poses significant diagnostic and therapeutic challenges. A multidisciplinary approach is essential, and biological treatment may be a promising therapeutic option, especially in cases resistant to conventional treatments. Further research into this overlap is needed to

optimize therapeutic strategies.

Abstract N°: 188

Improvement in Hailey Hailey patient undergoing Baricitinib therapy

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Introduction & Objectives:

A 42-year-old female patient was admitted in our outpatient clinic for the first time in 2012 with bilateral axillary and intermammary erosions and plaques. Pemphigus chronicus benignus familiaris (Hailey-Hailey) had been known for several years at that time. In addition, the patient was diagnosed with multiple sclerosis in 2011, which was treated with Afatumumab 20 mg s.c. once/month.

Materials & Methods:

The histopathology performed in our outpatient clinic showed a suprabasal acantholysis and confirmed a Hailey-Hailey disease. The previous treatment with Neotigason for 1 year showed no improvement. Subsequently, dermabrasion was performed several times, sometimes over large areas, which only showed a short-term improvement. After new plaques appeared on the right axilla and left submammary region, an unsuccessful ablative laser treatment was attempted. Also an unsuccessful treatment with doxycycline and Botox injections followed. Further treatments with Dapsone, Otezla and Bimekizumab were discontinued due to lack of effect or side effects. Topical therapies with class II and III steroids and multiple antiseptic therapies did not lead to any improvement.

Results:

In consultation with the neurologists, an off-label therapy with baricitinib 4 mg/day was initiated. There was a rapid and significant skin improvement during therapy. The erosions and plaques healed and the itching and pain improved considerably.

Conclusion:

Hailey-Hailey disease is a rare genodermatosis with an autosomal dominant inheritance pattern, characterized by compromised adhesion between epidermal keratinocytes. It has an estimated prevalence of 1/50,000 and it results from a heterozygous mutation in the ATP2C1 gene, which causes changes in the synthesis of junctional proteins, leading to acantholysis. It usually begins in adulthood. Chronic lesions may form vegetative or verrucous plaques. Pruritus and pain are common. The diagnosis is based on clinical and histopathological criteria like a suprabasal acantholysis, loosely joined keratinocytes, with a few dyskeratotic cells. Direct immunofluorescence is negative. There is no cure and the treatment is challenging. Topical medications (corticosteroids, calcineurin inhibitors, antibiotics), systemic medications (antibiotics, corticosteroids, immunosuppressants, retinoids and immunobiologicals) and procedures such as botulinum toxin, laser and surgery are often ineffective.

Baricitinib is an orally administered, potent, selective and reversible Janus kinase inhibitor (JAKi)1/JAKi2. They work by inhibiting enzymes involved in the transmission of information from receptors located in the cell membrane to the cell interior, specifically to the cell nucleus, thus disrupting the JAK-STAT pathway. This pathway plays a role in key cellular processes such as the immune response. Baricitinib is, among others, already approved for atopic dermatitis, rheumatoid arthritis and alopecia areata. Studies are underway to use JAKi in the treatment of several other dermatoses and represent a promising class of drugs for the treatment of skin diseases refractory

to conventional therapy.

Abstract N°: 220

Pachydermoperiostosis, A rare hereditary disorder associated with ulcerative colitis and ankylosing spondylitis case report and review

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Introduction & Objectives:

Pachydermoperiostosis (PDP) or primary hypertrophic osteoarthropathy (HOA) is a rare osteo-cutaneous disorder which inherited in AR manner and characterized by skin thickening (pachydermia), finger and toes clubbing (Acropathy), hyperhidrosis, bone formation and joint pain and swelling.

This case report highlights the clinical cutaneous manifestations of PDP including skin thickening of face, fingers clubbing and internal diseases presentations and joint pain in a 27-year-old male.

Materials & Methods:

This gentleman referred to our clinic from Internal ward where he had been admitted to manage his underlying diseases including Ulcerative colitis (UC) and Ankylosing spondylitis (AS)

His characteristic clinical features during physical examination were compatible with PDP.

All presented data were collected by Direct physical exam, Paraclincal investigations and etc…

Confirmatory laboratory tests including prior GI endoscopy and imaging showed UC and AS.

Results:

Pachydermoperiostosis, is an Oseteocutaneous disorder with specific skin changes including increasing skin stiffness, forrowing and aged face, also digital and toes enlargement called clubbing are characteristic which both were present in our case.

On the other hand, association of PDP with inflammatory bowel diseases and rheumatologic diseases is quite intersting.

Most of reports, highlighted the association between PDP and crohn disease, but our research showed association between pachydermperiostosis and Ulcerative colitis and ankylosing spondylitis simultaneously.

Conclusion:

Pachydermoperiostosis is a rare disorder and some features of the disorder mimicks physiologic and pathologic conditions.

For exmaple its aged appearance in facial area may be confused with normal aging process

And because of the burden the disease and associations as mentioned earlier, become more familiar with the disorder seem reasonable.

Abstract N°: 343

B-VEC Gene Therapy for Dystrophic Epidermolysis Bullosa: Real-world data from the treatment of 9 patients

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Introduction & Objectives: Dystrophic epidermolysis bullosa (DEB) is a rare inherited skin blistering disorder caused by mutations in the COL7A1 gene, which encodes the alpha-1 chain of type VII collagen. This collagen is essential for anchoring fibrils at the dermal-epidermal junction of the skin and mucosae. Patients with severe recessive DEB (RDEB) suffer from lifelong blistering, recurrent and chronic wounds, leading to severe cutaneous and systemic complications such as infections, scarring, squamous cell carcinoma, and failure to thrive.

Beremagene geperpavec (B-VEC) is a topical gene therapy designed for treating wounds in patients with DEB. It consists of two copies of the COL7A1 coding sequence, encapsulated within a modified herpes simplex virus type 1 (HSV-1) vector. Once inside the cell, the HSV-1 viral DNA is transcribed and translated into collagen VII, which is then secreted into the extracellular space to facilitate the assembly of anchoring fibrils.

Materials & Methods: Since January 2024, 8 patients with severe recessive DEB and 1 with intermediate RDEB were treated with B-VEC, with ages ranging from 9 months to 44 years in the early access program. The duration of treatment ranged from 1 to 10 months (median: 6 months). B-VEC was applied weekly to all wounds and blisters, as labeled by the FDA. Here, we report the real-world experience after treating these patients.

Results: The patients tolerated the treatment well, reporting no discomfort or side effects, except for one adult with severe RDEB and large wound areas who found the procedure exhausting and decided to discontinue the treatment after 6 months. Chronic wounds required more treatment sessions to heal, whereas acute wounds healed within 7-14 days with minimal or no visible scarring. While most healed wounds remained closed, recurrences were common in high-friction areas (head, legs, arms) or pruritic regions prone to scratching. Interestingly, in two patients, some chronic wounds did not heal after 6 and 7 months, respectively, suggesting that additional factors, such as preexisting scarring, chronic inflammation and repeated scratching, may influence wound healing. Regarding treatment adherence to the weekly administration, most patients missed doses due to holidays, non-treatment-related illnesses, or difficulties in reaching the treatment center. However, seven patients successfully continued treatment at home after their wound care team received proper training.

Conclusion: B-VEC is a well-tolerated therapy that has shown promising results in reducing wound area in this case series. However, multiple factors influence treatment success. Chronic wounds—particularly those on scarred background—require longer treatment durations, whereas acute wounds tend to heal fast and remain closed. Patient compliance, general condition, pre-existing scarring, and wound manipulation influence the outcomes. To improve adherence, caregivers should be trained to administer treatment at home, reducing the burden of travel for patients. Further research is needed to explore the pathogenic factors in chronic wounds and refine strategies for maximizing therapeutic benefits.

Table 1: List of the 9 patients treated with B-VEC at our center. The months in which each patient was treated are highlighted in green.

				Treatment Duration (months)									
Patient	**B-VEC Start**	**Age at start (years)**	**Gender**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
1	Jan 24	9 months	M										
2	March 25	1	F										
3	Nov 24	5	M										
4	Nov 24	5	F										
5	March 25	5	F										
6	March 25	7	M										
7	Aug 24	20	F										
8	May 24	25	F										
9	Aug 24	44	M										

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Abstract N°: 396

Vitamin D status in children with epidermolysis bullosa.

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Introduction & Objectives: Paediatric patients with epidermolysis bullosa (EB) are at risk of vitamin D deficiency due to impaired nutritional intake, lack of sunlight and limited mobility. Vitamin D plays an important role in the body, and its deficiency can lead to disruptions in phosphorus-calcium metabolism, as well as the development of osteopenia and osteoporosis.

Materials & Methods: In total, 99 children with EB were examined. All paediatric patients were assessment using the Birmingham Epidermolysis Bullosa Severity (BEBS) score and their vitamin D level.

Results: The study included 22 patients with simple EB (EBS), 10 patients with junctional EB (JEB), and 67 patients with dystrophic EB (DEB). The severity of EB is determined by BEBS, where a range of 0-20 points corresponds to mild severity, 21-45 points indicates moderate severity and more than 46 points to severe severity. The course of simplex EB is often limited to skin only. The median BEBS score was 2.5 points [2; 7,3] which corresponds to mild severity. In children with junctional EB, the median BEBS score was 12 points [9.2; 13.5], also indicating a mild course. The median BEBS score may be increased by mucosal involvement and possible malnutrition. Assessment of vitamin D levels (Me 33,04 [22,89; 38,15]) in patients with junctional EB revealed a decreases, insufficiency and deficiency of vitamin D found in 3 (30%) and 2 (20%) patients, respectively. In patients with dystrophic EB, the median BEBS score was 33 points [24,8; 38,7], indicating moderate severity of the disease. When studying vitamin D levels (Me 27,85 [15,6; 37,87]), insufficiency of vitamin D was observed in 9 individuals (13,4%), deficiency in 22 (32,83%) individuals, and severe deficiency was noted in 6 (8,9%) individuals. Total BEBS scores of 0-20 were observed in 9 patients, scores of 21-45 in 50 patients, and scores higher than 46 in 8 patients.

The study of vitamin D levels revealed the presence of insufficiency and deficiency in both junctional EB and dystrophic EB. Insufficiency was diagnosed in 3 patients with junctional EB and in 9 individuals with dystrophic EB, while deficiency was observed in 2 patients with junctional EB and in 22 individuals with dystrophic EB. Severe deficiency was found in 6 patients with dystrophic EB.

Conclusion: The conducted study showed a low level of vitamin D provision for patients with various types of EB. Data on vitamin D levels in children with different types of EB are necessary to optimize therapeutic strategies for managing this severe category of patients. This work confirms the necessity of research on osteotropic nutrients for timely diagnosis, prevention and treatment of osteopenia and osteoporosis in various types of EB.

Abstract N°: 587

Lymphangioma Circumscriptum in a Patient with Cowden Syndrome

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Introduction & Objectives:

Cowden Syndrome (CS) is a rare genetic condition with an increased risk of tumor formation. It is diagnosed based on clinical criteria and genetic testing. Here, we report a young female patient who met the clinical diagnostic criteria of CS, but unexpectedly, the APC gene mutation was verified by genetic testing instead of the usual PTEN gene mutation. She met more than two major and three minor criteria of the clinical criteria. Also, she had lymphangioma circumscriptum, which is seldom reported in the literature as related to the APC mutation, the CS, and a side effect of radiotherapy.

Conclusion:

Taking into consideration the rarity of both lymphangioma induced after radiation therapy as well as CS and the APC mutation and the limited published data about its cutaneous manifestations, we postulate that LC could be one of the clinical manifestations of CS. This case encourages more research and studies on the genetic basis and clinical manifestations of Cowden syndrome.

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Abstract N°: 694

Late Diagnosis of Neurofibromatosis Type 1 Revealed by Upper Eyelid Ptosis Caused by a Giant Plexiform Neurofibroma: A Case Report

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Introduction & Objectives:

Plexiform neurofibroma is a benign nerve tumor that predominantly affects the head and neck region due to its rich innervation. Its occurrence in the upper eyelid area has been reported and can, on its own, be a reason for consultation, sometimes leading to the late diagnosis of neurofibromatosis type 1 (NF1).

Materials & Methods:

We present the case of a 38-year-old woman, who presented with a painless upper eyelid mass that completely obstructed the visual field on the left side.

Clinical examination revealed café-au-lait spots and diffuse lentigines on the body, with a Crowe's sign, as well as two neurofibromas on the thighs. Ophthalmological evaluation identified Lisch nodules. A head scan was performed to evaluate the tumor's extent, assess vascular involvement, and determine its resectability. The diagnosis of neurofibromatosis type 1 was made, and the patient was referred to surgeons for the excision of the plexiform neurofibroma.

Results:

Neurofibromatoses are hereditary disorders with autosomal dominant transmission. Ophthalmological manifestations are primarily dominated by optic pathway gliomas and iris hamartomas.

Plexiform neurofibromas, initially subtle at birth, progressively enlarge during childhood and adolescence before stabilizing. The tumor predominantly affects the upper eyelid, often causing ptosis due to infiltration of the levator palpebrae muscle. Associated findings may include moderate myopia, astigmatism, ectropion, dry eye syndrome, spheno-orbital dysplasia, or congenital glaucoma.

Imaging is crucial for determining the location, extent, and complications of the tumor. Sarcomatous transformation is rare.

Although there is no specific curative treatment for this condition, management primarily involves surgical intervention. The lesions can have significant aesthetic and psychological impacts, which often motivate consultation and justify surgical management. The aesthetic outcome largely depends on the initial tumor size, though the risk of recurrence remains a constant concern.

Conclusion:

Neurofibromatosis, still underdiagnosed due to delayed consultations, is a complex genodermatosis requiring tailored management. Regular patient follow-up is essential and often involves collaboration across multiple medical and surgical specialties.

Abstract N°: 1050

Acute Inflammation in Dystrophic Epidermolysis Bullosa: A Meta-Analysis and Longitudinal Cohort Study

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Introduction & Objectives: Dystrophic epidermolysis bullosa (DEB) is a rare inherited skin disorder caused by mutations in the COL7A1 gene, leading to mucocutaneous blistering and chronic wounds. Acute inflammation—mediated by acute-phase reactants, e.g., C-reactive protein (CRP), interleukin (IL)-6, serum amyloid A** (SAA)—plays a significant role in wound-healing, particularly in response to acute injuries and bacterial invasion. However, its role in recessive DEB (RDEB) remains unclear, with only a few observational studies or case reports investigating acute inflammation markers in this condition.

Materials & Methods: To elucidate the complex inflammatory patterns in DEB, we conducted a meta-analysis synthesizing data from studies assessing inflammatory markers in DEB patients. Our analysis compared DEB patients, healthy controls, and individuals with other types of epidermolysis bullosa (EB). We systematically searched MEDLINE for eligible studies published from 01.01.2004-18.03.2024. Of the 37 identified studies, 11 met our inclusion criteria and provided data on 32 inflammatory markers. We performed an exploratory network meta-analysis using random-effects models to compare standardized mean differences (SMDs) in inflammatory marker levels across the three groups. To further elucidate acute inflammation markers association with RDEB clinical characteristics, we extracted data from our patient cohort over five consecutive years (one visit per year, total of 120 visits), involving 45 RDEB patients (22 severe, 22 intermediate; Table 1).

Results: The meta-analysis revealed that IL-6 levels were lower in healthy controls (SMD: -1.03, 95% CI: -2.79; 0.74) and patients with other EB types (SMD: -0.89, 95% CI: -2.41; 0.62). CRP levels were lower in other EB types (SMD: -0.89, 95% CI: -1.54; -0.24). Additionally, SAA and leukocytes were found to be increased in DEB patients compared to both controls and other EB types.**

Across all visits of the RDEB intermediate group of our cohort, IL-6, CRP and SAA are strongly correlated with wound body surface area [WBSA, Spearman rho (rho)=0.75, p<0.001; rho=0.48, p=0.002; rho=0.66, p=0.007, respectively) and show strong positive associations with the presence of squamous cell carcinoma (SCC, rho=0.51, p=0.011; rho=0.73, p<0.001; rho=0.71, p=0.004, respectively). Leukocytes are moderately correlated with mucosal involvement severity (rho=0.51, p=0.001) and negatively weakly correlated with body mass index (BMI, rho=-0.35, p=0.033). In the RDEB severe group, CRP and neutrophil to lymphocyte ratio (NLR) show moderate correlation with WBSA (rho=0.29, p=0.022; rho=0.32, p=0.017, respectively), while IL-6, CRP, SAA and NLR are moderately associated with the presence of SCC (rho=0.42, p=0.009; rho=0.40, p=0.002; rho=0.45, p=0.035; rho=0.33, p=0.015, respectively). Leukocytes were negatively weakly correlated with BMI and presence of SCC (rho=-0.27, p=0.046; rho=-0.26, p=0.047, respectively).

Conclusion: Acute inflammation markers, such as IL-6, SAA, CRP, NLR are significantly correlated with important RDEB clinical features, such as WBSA, mucosal involvement and presence of SCC. Further research is needed to elucidate inflammation trajectories in DEB, particularly its progression with age and disease severity. This may help identify specific inflammatory targets and determine whether a critical window for intervention exists to prevent irreversible systemic complications.

Table 1: Descriptive characteristics of the patient groups.

	Severe RDEB (N=22)	Intermediate RDEB (N=22)
Age at last visit (2024), years (median, IQR)	16.00 (7.25-24.00)	17.00 (11.00-37.00)
Gender (% females)	50.00	54.50
BMI at baseline (2020), median, IQR	14.08 (13.65-16.67)	18.70 (14.58-20.83)
Wound body surface area % at baseline (2020), median, IQR	5.50 (4.00-8.25)	1.00 (0.62-3.50)
Medication during the 5 visits of the study		
Losartan, n (%)	7 (31.8)	6 (27.3)
BVEC, n (%)	3 (13.6)	0
Dupilumab, n (%)	2 (9.1)	1 (4.5)
Colchicine, n (%)	6 (27.3)	1 (4.5)
Number of total visits (2020-2024)	73	47

Abstract N°: 1227

Correlation between clinical and biochemical phenotypes and genotype in patients with congenital erythropoietic porphyria. A case series from a referral hospital

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Introduction & Objectives:

Congenital erythropoietic porphyria (CEP) is an infrequent disorder resulting from a decreased activity of uroporphyrinogen III synthase (UROS), the fourth enzyme in the heme biosynthesis pathway. In most cases, CEP is an autosomal recessive disease caused by biallelic pathogenic variants in the UROS or GATA1 genes. The accumulation of uro and coproporphyrins in erythrocytes, skin, and other organs can lead to hematological and dermatological alterations as the predominant clinical manifestations of this disease, including hemolytic anemia, photosensitivity, skin fragility with blistering and scarring, bone resorption, and limb mutilation. We aim to describe a large series of patients with CEP and to identify the different genotypes and their correlation with clinical and biochemical phenotypes.

Materials & Methods:

We** retrospectively reviewed all CEP patients studied at our center between 2000 and 2024.

Results:

A total of 15 patients were included. Four of them had a late-onset presentation. In three of them, no pathogenic gene variants were detected, but an underlying hematological malignancy was identified. They were diagnosed with acquired erythropoietic uroporphyria. The fourth late-onset patient showed an heterozygous germline mutation in the UROS gene, with a C73R/wild-type genotype. Acquired mosaicism could be the origin of the atypical phenotype. The remaining 11 patients were diagnosed during childhood, and pathogenic variants in the UROS gene were detected in all of them. Seven different genotypes were described, and a good correlation was found between the genotype and the biochemical porphyrin profile. While the C73R and T228M alleles correlated with the most marked elevations in urinary porphyrin levels, the P248Q variant was associated with a milder biochemical profile. Significant differences were observed in the severity of clinical manifestations in unrelated patients who shared the same genotype and biochemical phenotype.

Conclusion:

We present the largest single-center case series of patients with CEP, a very infrequent disorder. Assessing UROS gene variants is important not only for confirming the diagnosis: it facilitates genetic counseling and relatives' screening, allows for personalized recommendations regarding lifestyle and sun-exposure habits, and can help predict the behavior of the disease. We identified different pathogenic variants in our patients, which correlated well with the elevation pattern of urinary porphyrin levels. However, the severity of the clinical manifestations could not always be predicted based on the genetic alteration or biochemical profile. Other environmental or genetic factors may play a role in the clinical expression of CEP.

Abstract N°: 1322

Cutaneous vasculitis leading to the diagnosis of mosaic RASopathy due to KRAS

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Introduction & Objectives:

KRAS is a small guanine nucleotide-binding protein of the RAS family. When bound to GTP, KRAS promotes an increase in ERK phosphorylation, activating the RAS/MAPK pathway, which can modulate cell growth and proliferation.

Mutations in codon 12 of KRAS lead to the loss of normal endothelial cell junctions and actin cytoskeleton disorganization.

Patients with somatic KRAS mutations can present with multiple manifestations, including cranial bone thinning, polycystic kidneys, multifocal tachycardia, hemimegalencephaly and aortic coarctation.

MEK inhibition is currently being studied as a therapeutic strategy for pathogenic KRAS-activating variants. Trametinib is an oral MEK inhibitor that reduces ERK phosphorylation.

Materials & Methods:

We present the case of a 13-year-old girl with a personal history of renovascular hypertension diagnosed at the age of three, with bilateral renal artery stenosis and inferior right polar artery stenosis, for which she received a stent. She also had stenosis of the superior mesenteric artery and the celiac trunk origin. Her treatment included hydralazine, spironolactone, carvedilol, amlodipine, clopidogrel, acetylsalicylic acid and clonidine. Additionally, she had left renal dysplasia and a recent finding of mesangial glomerulonephritis with IgM and IgG deposition. Magnetic resonance imaging performed due to severe scoliosis revealed dorsal extradural cysts. Dermatology was consulted due to recurrent episodes of purpuric skin lesions on the lower limbs over the past few months, associated with ankle edema and pain. Skin biopsy showed small- and medium-vessel cutaneous vasculitis. A comprehensive examination revealed a capillary malformation on the left dorsal region, which was biopsied for genetic analysis.

Results:

Due to the suspicion that both glomerulonephritis and cutaneous vasculitis were induced by hydralazine, antihypertensive treatment was adjusted, replacing hydralazine with losartan, everolimus, and amlodipine, resulting in improvement of both conditions without further relapses and good blood pressure control.

Genetic analysis of the capillary malformation identified a pathogenic variant in the KRAS gene: c.35G>C, p.Gly12Ala (p.G12A), with an allele frequency of 18%. Given previous literature reports linking arterial stenosis, scoliosis, and spinal lesions to KRAS mutations, it was considered that the identified variant could underlie all the patient’s clinical features. Due to the previous poor progression of arterial stenosis, with episodes of stent rejection and restenosis, trametinib therapy was initiated. At present, after six months of trametinib treatment, although it is still early for definitive conclusions, the patient exhibits good blood pressure control and has not

required further interventions for renal arteries.

Conclusion:

This case illustrates how subtle cutaneous stigmata can be the key to diagnosing a complex condition of somatic mosaicism with extracutaneous manifestations. Postzygotic mutations in genes encoding proteins of the RAS/RAF/MAPK pathway are a major cause of sporadic vascular malformations (VMs). The pathogenicity of these variants in BRAF, KRAS and NRAS is well established in other disorders and tissues. This finding has paved the way for the repositioning of targeted medical therapies, initially developed for oncology, in the treatment of VMs.

Abstract N°: 1329

Lipoid Proteinosis: A Rare Genodermatosis Accompanied By Hoarseness

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Introduction & Objectives:

Lipoid Proteinosis (LP), also known as Urbach-Wiethe disease or Hyalinosis cutis et mucosae, is a rare condition characterized by the deposition of hyaline material in the skin, mucous membranes, and internal organs. The genetic basis of LP is linked to mutations in the ECM1 gene located on chromosome 1q21.2, leading to autosomal recessive inheritance.

Materials & Methods:

Case: Lipoid proteinosis (LP) is a rare autosomal recessive genodermatosis, typically characterized by hoarseness, skin fragility, yellow papules or nodules, and neurological and psychiatric symptoms. The condition often manifests during childhood, with the clinical features evolving over time.

The patient, a 37-year-old male, initially presented to our outpatient clinic with persistent hoarseness since childhood, accompanied by thickening of the elbows and yellow, raised lesions on his face. Upon referral, physical examination revealed atrophic scars on the anterior trunk and back, brown papules and plaques on the elbows, yellow nodules on the scrotum, and yellowish translucent papules on the eyelids, consistent with moniliform blepharosis. A cobblestone-like appearance of the oral mucosa and macroglossia were also noted.

Patient's persistent hoarseness led to an otolaryngology consultation, where laryngoscopy showed mucosal deposition on the vocal cords, consistent with the mucosal involvement characteristic of LP.

Histopathological examination of the skin lesions confirmed the diagnosis of LP, revealing amorphous eosinophilic material distributed in an interstitial, periadnexal, and perivascular pattern in the dermis, with PAS staining positive. The patient was initiated on systemic acitretin therapy at a dose of 20 mg/day for 6 months. In the follow-up period, the patient was photographed at the 3rd and 6th months of treatment.

Results:

LP is a rare genetic disorder, typically inherited in an autosomal dominant pattern, and is most often associated with mutations in the EMD gene. This gene mutation leads to abnormal accumulation of hyaluronan and glycosaminoglycans, resulting in collagen deposition across various tissues and organs, which underpins the pathophysiology of the clinical manifestations of LP. The hallmark features of the disorder include skin thickening, particularly around the eyelids, mucosal changes in the oral cavity, and involvement of other organs. The most frequently observed clinical signs include nodular lesions on the skin, thickening of tissues on the eyelids, mucosal thickening in the oral cavity, and voice changes. These mucosal changes may lead to difficulties in swallowing and speaking, significantly impairing the quality of life.

Neurological symptoms such as seizures, ataxia, and psychiatric disturbances, including schizophrenia and anxiety, are commonly observed in patients with LP.

Due to the rarity of the disease, treatment is based on case series and clinical experience. Systemic retinoids, particularly acitretin (0.5 mg/kg/day), are considered the first-line option for alleviating skin and laryngeal

symptoms. Alternative treatment options include topical or intralesional corticosteroids, oral dimethyl sulfoxide, etretinate, and D-penicillamine.

Conclusion:

In conclusion, while LP is a rare disorder, its diverse clinical presentations and treatment challenges have made it a focal point of scientific research.

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Abstract N°: 1392

Excellent clinical response to JAK-1 selective inhibition in two patients with VEXAS syndrome

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Introduction & Objectives:

VEXAS syndrome is an adult-onset autoinflammatory disease caused by somatic mutations in the *UBA1* gene. It is characterized by systemic inflammation, cytopenias, and multi-organ involvement. Diagnosis is challenging due to its phenotypic overlap with autoimmune and hematologic conditions, and the disease carries significant morbidity and mortality. Here we report two genetically confirmed VEXAS patients treated with the JAK-1 selective inhibitor upadacitinib.

Materials & Methods:

We conducted a retrospective chart review of two male patients diagnosed with VEXAS syndrome confirmed with *UBA1* mutation testing. Clinical data including presentation, diagnostic investigations, treatment regimens, and response to upadacitinib were collected and analyzed. Consent was obtained from both patients.

Results:

Patient 1 is a 71-year-old male referred for suspected systemic lupus erythematosus with a positive ANA and systemic symptoms. He had a history of indurated nodules on the trunk and limbs and violaceous plaques and nodules on the chest and forearms. He presented afebrile with a persistently elevated CRP, recurrent infections, suspected deep vein thrombosis, dysphagia, Helicobacter pylori infection, myalgias, and 16 kg of unintentional weight loss. A skin biopsy demonstrated neutrophilic dermatoses, suggestive of Sweet's syndrome (Figure 1). The patient had a limited therapeutic response to colchicine, methotrexate, and dapsone. He later developed cytopenias and interstitial lung disease with ground-glass opacities. Subsequently, cytopenias limited treatment with mycophenolate and he developed meningitis secondary to Listeria monocytogenes infection. The patient also was unable to wean prednisone to less than 25 mg. Due to a strong clinical suspicion of VEXAS syndrome, genetic testing was ordered and upadacitinib was initiated prior to confirmation.

Patient 2 is a 67-year-old male with atypical Sweet's syndrome on pathology, mild inflammatory arthritis, and chondritis. The patient was unable to taper prednisone to less than 10 mg. While diagnostic evaluation was ongoing, suspicion was raised for VEXAS syndrome, genetic testing was initiated, and the patient was treated with upadacitinib prior to confirmation.

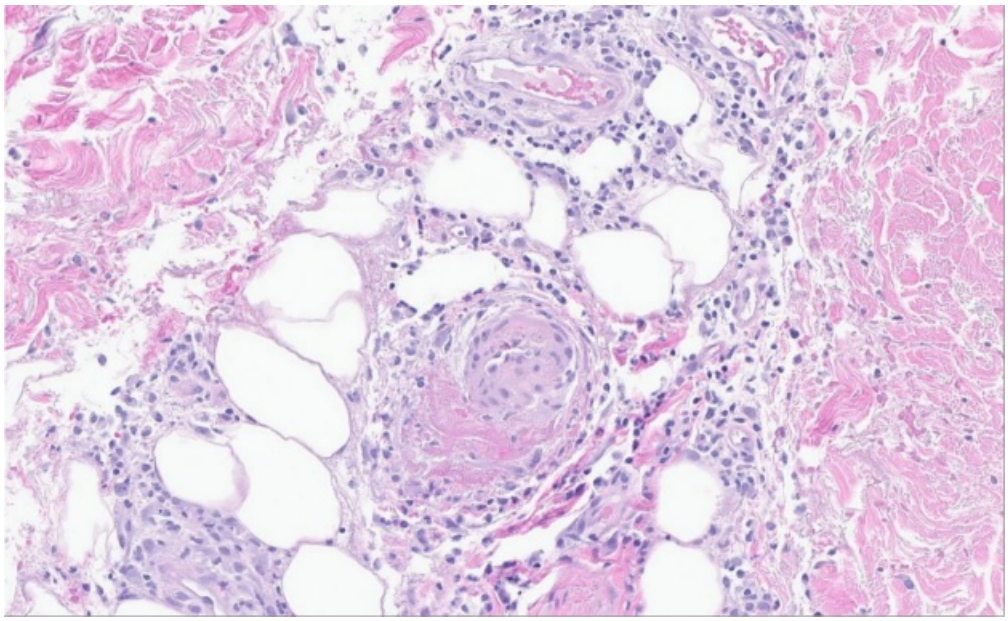
Both patients were confirmed to have VEXAS syndrome via somatic UBA1 mutation testing and responded favorably to upadacitinib, with a reduction in systemic inflammation and steroid burden.

Conclusion:

VEXAS syndrome is an underrecognized but potentially fatal autoinflammatory disease that presents with a spectrum of systemic and cutaneous manifestations. These cases highlight the therapeutic potential of JAK-1 selective inhibitors as steroid-sparing agents in VEXAS syndrome management. Increased awareness and early

genetic testing are essential to identify patients who may benefit from targeted immunomodulation.

Figure 1. Skin biopsy from the left lateral shoulder of Patient 1 demonstrating a moderate perivascular and interstitial mixed inflammatory infiltrate composed of lymphocytes and neutrophils. No evidence of small vessel vasculitis is observed. Periodic acid–Schiff (PAS) stain is negative for fungal organisms. Findings are consistent with Sweet's syndrome.



Abstract N°: 1411

Coexistence of Williams Syndrome and Atopic Dermatitis: A Rare Case and Clinical Implications

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Introduction & Objectives:

Williams syndrome is a rare genetic disorder caused by a microdeletion in the 7q11.23 region, characterized by cardiovascular anomalies, distinctive facial features, and significant neurodevelopmental traits. This report presents a rare case of Williams syndrome coexisting with atopic dermatitis, discussing possible shared pathophysiological mechanisms and emphasizing the importance of a multidisciplinary approach to patient management.

Materials & Methods:

Case Presentation: A 19-year-old female with a confirmed diagnosis of Williams syndrome was referred to the dermatology clinic due to widespread pruritic and exudative eczematous skin lesions. Physical examination revealed pronounced lichenified and excoriated lesions on the flexor surfaces of both upper extremities. Additionally, severe eczematous, exudative plaques were observed in both periorbital regions, along with Dennie-Morgan folds in the bilateral eyelids. The patient's history indicated that similar dermatological findings had been present since childhood. The patient was started on a treatment regimen consisting of topical mometasone furoate oinment, systemic prednisolone (32 mg/d), and regular emollient therapy. She continues to receive multidisciplinary follow-up, including dermatological and genetic counseling.

Results:

Williams syndrome results from a microdeletion in the 7q11.23 region, leading to cardiovascular anomalies, neurodevelopmental differences, and unique phenotypic characteristics. In addition to these features, individuals with Williams syndrome often present with distinct dermatological traits, including soft skin, premature graying of hair (especially after the age of 20), wrinkles, and abnormal scarring. These dermatological features contribute to the syndrome's overall phenotypic profile and are observed in a significant proportion of affected individuals. This genetic deletion particularly affects the ELN, LIMK1, and GTF2I genes, contributing to vascular disease, spatial cognition impairments, and hypersocial behavior patterns.

Atopic dermatitis can be associated with various genetic syndromes. These include Wiskott-Aldrich Syndrome**,** Omenn Syndrome **,** Netherton Syndrome**.** While no definitive data exist on the prevalence of atopic dermatitis in individuals with Williams syndrome, immune system alterations in these patients may contribute to an increased susceptibility to atopic diseases.

The management of Williams syndrome is symptomatic and requires a multidisciplinary approach. Cardiovascular monitoring, neurodevelopmental support, psychiatric interventions, and dermatological management are essential for improving the quality of life of affected individuals. In this case, the treatment of atopic dermatitis followed standard dermatological protocols, with particular consideration given to potential immunological variations in Williams syndrome. However, there is a lack of data regarding the efficacy of new agents used in the treatment of atopic dermatitis in these patients.

Conclusion:

The coexistence of Williams syndrome and atopic dermatitis is a rare clinical occurrence, warranting further studies

to elucidate potential shared pathophysiological mechanisms. Multidisciplinary assessment of such cases may contribute to the development of individualized treatment strategies, optimizing patient management.

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Abstract N°: 1453

When Skin Lesions and Vocal Changes Collide: A rare Case of Lipoid Proteinosis

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Introduction & Objectives:

Lipoid proteinosis (LP), also known as Urbach-Wiethe syndrome or hyalinosis cutis et mucosae, is a rare autosomal recessive disorder caused by mutations in the *ECM1* gene located on chromosome 1q21. It is characterized by the extracellular accumulation of eosinophilic hyaline material in the skin, mucous membranes, and other tissues, leading to variable dermatological and neurological manifestations.

Materials & Methods:

A 9-year-old girl had been presenting with papular and bullous lesions on her forehead and limbs since the age of 4 years. Clinical examination showed multiple atrophic and acneiform scarring lesions on the forehead, upper limbs, and back, along with a few erosions in the lumbosacral region and xerosis on both legs. Ophthalmological examination revealed whitish papules arranged in a beaded pattern along the eyelid margins, consistent with moniliform blepharosis. Additionally, macrocheilitis of the lower lip and a hoarse voice were noted. Nasofibroscopy detected vocal cord abnormalities . A complementary ENT biopsy is currently underway.

A skin biopsy confirmed the presence of hyaline material deposits, which were periodic acid-Schiff (PAS) positive. Based on these findings, a diagnosis of LP was established.

Results:

LP is an extremely rare autosomal recessive disorder characterized by the progressive infiltration of mucocutaneous tissues and various organs with hyaline material. Clinically, it presents with pustules, blisters, and hemorrhagic crusts that heal, leaving varioliform or acneiform scars, primarily on the face and extremities, sometimes accompanied by skin thickening. Laryngeal involvement is the most common and earliest manifestation of the disease, clinically presenting as a hoarse voice. This is due to the infiltration of the vocal cords by hyaline deposits. Moniliform blepharosis, often present from childhood and persisting throughout the course of the disease, is a classic sign and a key diagnostic feature. Systemic involvement is rare in this disease. The most characteristic are neurological complications related to intracranial calcifications. The progression is chronic, and the disease tends to slow down in adulthood. Spontaneous improvement after the age of 50 has been reported. While no curative treatment exists, various approaches including dimethyl sulfoxide, retinoids (etretinate, acitretin), penicillamine, surgical procedures, carbon dioxide laser therapy and dermabrasion have shown variable results in management.

Conclusion:

LP is a rare genetic disorder characterized by distinctive mucocutaneous and laryngeal manifestations. As no curative treatment exists, management remains symptomatic, focusing on controlling complications. Early and accurate diagnosis is crucial for optimizing patient care and improving outcomes.

Abstract N°: 1522

Syndrome de Netherton : quand les cheveux racontent une histoire

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Netherton Syndrome: When Hair Tells the Story

Introduction & Objectives:

Netherton syndrome is a rare autosomal recessive genetic disorder caused by mutations in the SPINK5 gene. It classically presents with congenital ichthyosiform erythroderma, a specific hair shaft dysplasia (trichorrhexis invaginata), and a severe atopic diathesis. Due to its clinical heterogeneity, diagnosis is often delayed. Trichoscopy plays a key role in early identification of characteristic hair abnormalities, while confirmation relies on molecular analysis.

Materials & Methods: none

Results:

A 4-year-old girl was admitted to pediatric nephrology for unexplained acute renal failure requiring hemodialysis. Dermatologic consultation was requested due to diffuse skin lesions, severe atopic features, and abnormal hair. Clinical examination revealed diffuse hypotrichosis with dry, brittle hair, fragile skin with erosive lesions, recurrent infections, and intense pruritus exacerbated by inflammatory flares. She also presented with severe atopic manifestations, including major atopic dermatitis, allergic rhinitis, and multiple food allergies, along with growth retardation suggesting nutritional impairment. Trichoscopy revealed trichorrhexis invaginata (“bamboo hair”), a pathognomonic sign of Netherton syndrome, prompting genetic analysis of SPINK5. This case illustrates an atypical presentation with severe multisystem involvement, including renal impairment, complicating the diagnostic process.

Discussion

The clinical variability of Netherton syndrome often mimics other erythrodermic disorders, including congenital ichthyoses, Sézary syndrome, or severe atopic dermatitis. The presence of a specific hair shaft anomaly remains a major diagnostic clue. Trichoscopy is a valuable non-invasive tool that reveals structural hair abnormalities, particularly trichorrhexis invaginata, characterized by the invagination of one hair segment into another, giving the appearance of a bamboo node. Mutations in SPINK5 result in unregulated epidermal protease activity, leading to severe skin barrier dysfunction, excessive transepidermal water loss, and increased susceptibility to infections and allergens. Management is multidisciplinary and includes intensive skin hydration, allergen avoidance in sensitized patients, infection prevention, and close monitoring of growth and nutrition.

Conclusion:

Netherton syndrome should be suspected in the presence of the triad: erythroderma, hair dysplasia, and severe atopy. This case highlights an unusual renal involvement, adding complexity to management. Trichoscopy is essential for early diagnosis and can help avoid unnecessary diagnostic delays. Early recognition and coordinated multidisciplinary care are crucial to improve outcomes and quality of life in affected patients.

Abstract N°: 1574

Pigmentation Under Scrutiny: Oculocutaneous Albinism in Two Patients with Prader-Willi Syndrome and a Third Case of Ocular Albinism Type 1

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Introduction & Objectives:

Oculocutaneous albinism (OCA) comprises autosomal recessive disorders with reduced or absent pigmentation of the skin, hair, and eyes, due to defects in melanin biosynthesis. The most common subtypes are OCA1 (variants in *TYR*) and OCA2 (*OCA2* gene). Ocular albinism type 1 (OA1), caused by *GPR143* variants, is X-linked and affects only the eyes.

In Prader-Willi cases with a 15q11.2–q13 deletion, one copy of the OCA2 gene is lost. If the remaining copy harbors a pathogenic variant, melanin production is impaired, leading to oculocutaneous albinism type 2. This association accounts for less than 1% of all cases.

This study aims to describe and compare three cases with pigmentary disorders: two with OCA and PWS, and one with OA1.

Materials & Methods:

Three patients evaluated for pigmentary and ophthalmologic abnormalities are presented.

Results:

Case 1. A 5-year-old boy with a clinical and molecular diagnosis of Prader-Willi syndrome, confirmed by FISH. He exhibited hypopigmentation of the skin, hair, and eyes, accompanied by photophobia, nystagmus, and reduced visual acuity. Molecular analysis revealed a heterozygous variant in the *OCA2* gene, c.632C>T (p.Pro211Leu), as well as a complete deletion of the *OCA2* gene on the other allele.

Case 2. A 3-year-old girl with a diagnosis of Prader-Willi syndrome due to a deletion confirmed by FISH. She developed hypopigmentation of the skin, hair, and irises, along with nystagmus. Molecular testing identified biallelic variants in the *TYR* gene, c.1217C>T (p.Pro406Leu).

Case 3. A 7-year-old boy with symptoms beginning at 3 months of age, including ametropia and nystagmus. On physical examination, no hypopigmentation of the skin or hair was observed; however, fundus examination revealed absence of retinal pigmentation and anterior iris hypoplasia. Molecular analysis identified a hemizygous variant in the *GPR143* gene, c.8C>T (p.Ser3Phe). (Table 1).

Conclusion:

This case series illustrates how similar phenotype (such as hypopigmentation and/or nystagmus) can arise from distinct genetic mechanisms, even within the spectrum of albinism, highlighting the diagnostic heterogeneity present in multisystemic conditions or those with overlapping phenotypes.

In the context of Prader-Willi syndrome (PWS), the presence of albinism may be associated with a point variant in the *OCA2* gene. However, it is important to recognize that other forms of albinism, such as OCA1, may coexist. Therefore, hypopigmentation in these patients should not be attributed solely to *OCA2* involvement.

The case of ocular albinism type 1 (OA1), unrelated to PWS or to genes within the 15q region, emphasizes phenotypic differences and underscores the importance of a differential diagnostic approach in patients presenting with hypopigmentation and visual disturbances.

The identification of OA1 in a patient without PWS reinforces the value of a phenotype-driven molecular approach, particularly when ocular signs such as nystagmus or retinal abnormalities are present.

These cases demonstrate how a single clinical feature may arise from different molecular mechanisms, underscoring the need for an individualized, genetics-based diagnostic approach. Moreover, they highlight the relevance of distinguishing between different modes of inheritance (autosomal recessive versus X-linked) which is crucial for appropriate genetic counseling.

Table 1

Case	Syndromic diagnosis	Type of albinism	Gene	Identified variants	Inheritance patten	Cutaneous pigmentation	Alteraciones visuales	15q11-q13 Region altered
1	Prader-Willi	OCA type 2	*OCA2*	Compound heterozygous (c.632C>T + complete deletion of OCA2)	Autosomal recessive, (deletion + variant in trans)	Generalized	Nystagmus, photophobia, ↓ visual acuity	Yes (deletion)
2	Prader-Willi	OCA type 1	*TYR*	c.1217C>T (biallelic)	Autosomal recessive	Generalized	Nystagmus	Yes (deletion)
3	No	OA type 1	*GPR143*	c.8C>T (hemizygous)	X-linked	Preserved	Nystagmus, ocular hypopigmentation	No

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Abstract N°: 1601

CM-AVM syndrome in children: clinical manifestations and genetic testing

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Introduction & Objectives:

Capillary malformation-arteriovenous malformation (CM-AVM) syndrome is an uncommon hereditary disorder due to a heterozygous pathogenic variant in EPHB4 or RASA1. Patients develop cutaneous arteriovenous malformations. Some also have concomitant arteriovenous malformations or fistulas which may involve the central nervous system and are potentially fatal. The main objective of this study is to describe the pertinent clinical and genetic features of children with CM-AVM syndrome in Singapore.

Materials & Methods:

This is a single-centre prospective study involving paediatric patients clinically diagnosed with CM-AVM syndrome at the dermatology clinic at KK Women's and Children's Hospital in Singapore. Genetic testing was done on the patients and their parents to confirm the diagnosis. Genomic DNA was extracted from venous blood or affected tissues and sequencing was performed with a SureSelect custom panel consisting of 52 known genes and run on a MiSeq Sequencer using the Micro flow cell. Sequence data was mapped to the reference and analyzed using SureCall. Candidate variants were validated by Sanger sequencing.

Results:

A total of 5 patients were included. The median age at diagnosis was 5.9 years (IQR 2.5-10.0 years). Most were girls (n=4, 80%), with lesions noted since birth (n=1) or during infancy (n=3). The most common sites of involvement were the face, upper and lower limbs. Other affected sites were the neck, chest, abdomen and back. All patients presented with scattered erythematous macules or patches with positive doppler on examination. Genetic testing from peripheral blood was performed for 4 patients and the parents of all 5 patients. There were 2 cases of RASA1 mutation found amongst the 5 patients. There were also 3 cases of EPHB4 mutation found amongst the same 5 patients. Paternal EPHB4 pathogenic variant was detected in 2 cases, and maternal EPHB4 pathogenic variant in 1 case. As for the 2 cases involving RASA1 mutation, maternal pathogenic variant was detected in 1 case, while the other occurred de-novo. Magnetic resonance imaging and angiography (MRI/MRA) of the brain were performed in 2 patients and were unremarkable.

Conclusion:

CM-AVM syndrome is inherited in an autosomal dominant manner. Clinical manifestations of cutaneous capillary malformations often begin from infancy and usually involve the face and limbs. Serial neurological assessments are recommended due to potential brain and spine AVM formations. Genetic testing can be readily performed for diagnosis and prognostication. **

Abstract N°: 1624

WILD Syndrome: A Very Rare Dermatological Case

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Introduction & Objectives:

WILD syndrome is an extremely rare dermatological condition first described by Kreuter et al. in 2008. The acronym “WILD” stands for its four hallmark features: Warts, Immune deficiency, Primary Lymphedema, and Anogenital Dysplasia. This syndrome involves a germline mutation in the GATA2 gene, which plays a key role in hematopoietic and lymphatic development. GATA2 deficiency also increases susceptibility to viral infections and hematologic malignancies. Along with clinical, histopathological, and genetic evaluations, we assessed systemic inflammatory indices to better understand the patient’s immune-inflammatory profile. Herein, we present a rare case of a 36-year-old male diagnosed with WILD syndrome.

Materials & Methods:

Case Report

A 36-year-old male presented with therapy resistant plantar warts, unilateral lower limb swelling, and bleeding nodular lesions in the anogenital region. His dermatological history dated back to age 20, when the first plantar lesions appeared. A comprehensive evaluation was performed.

Results:

Examination revealed hyperkeratotic plaques on the soles, verrucous lesions on the palms, and hemorrhagic nodules in the genital region. Marked lymphedema was noted in the left lower extremity. Laboratory findings included leukopenia (2.68 $x10^9$/L) and neutropenia (1.52 $x10^9$/L). Flow cytometry revealed normal CD marker ratios, except for B cell dysregulation. Complete blood count showed persistent monocytopenia (0.08 $x10^9$/L), consistent with GATA2-related immune dysfunction. Mild thrombocytopenia (111 $x10^9$/L) and anemia (Hgb: 10.5 g/dL) were also observed.

We calculated several systemic inflammatory markers, which are increasingly recognized in the evaluation of immune dysregulation:

- Neutrophil-to-lymphocyte ratio (NLR): 1.52

- Platelet-to-lymphocyte ratio (PLR): 111.0

- Monocyte-to-lymphocyte ratio (MLR): 0.08

- Systemic immune-inflammation index (SII): 168.72

- Hemoglobin-to-lymphocyte ratio (HLR): 10.5

- Platelet-to-monocyte ratio (PMR): 1387.5

- Hemoglobin-to-platelet ratio (HPR): 0.0946

- Derived NLR (dNLR): 1.31

These findings reflect a low-grade but complex inflammatory and immunosuppressive profile, which is characteristic of GATA2 deficiency.

We started systemic acitretin (50 mg/day) and topical 5% imiquimod applied on alternate days. After six months, the patient showed a 75% regression in wart lesions and 90% improvement in anogenital dysplasia.

Conclusion:

WILD syndrome is a complex genodermatosis characterized by dermatologic, immunologic, and lymphatic abnormalities. Due to its variable and often asynchronous symptom presentation, diagnosis is frequently delayed. This case shows the importance of clinical suspicion in patients with chronic warts, immune dysfunction, and lymphedema. Early diagnosis through genetic analysis and timely multidisciplinary management — particularly in collaboration with immunology — are crucial for improving prognosis and preventing malignencies.

In our case, the use of systemic inflammatory markers such as NLR, PLR, SII, and others provided insight into the subclinical immune and inflammatory dysregulation associated with GATA2 deficiency. Although these indices are non-specific, they may offer useful adjunctive data in cases of complex immunodermatological syndromes, especially where immune status and inflammation are intertwined. Their inclusion could potentially aid in monitoring disease progression or therapeutic response in future cases.

Abstract N°: 1641

Linear porokeratosis: differential diagnosis of linear lesions

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Introduction & Objectives:

Porokeratosis encompasses a group of rare hereditary or acquired dermatoses that share a common disorder of epidermal keratinization. The origin remains uncertain, but it is believed to involve an expansion of abnormal epidermal keratinocyte clones Clinically, it manifests as macules or plaques, annular or linear, with an atrophic center and well-defined hyperkeratotic border. Histopathology shows a “cornoid lamella” with specific characteristics. There is no preference for ethnicity or gender, and it typically appears in childhood or adolescence. The six forms of porokeratosis include Mibelli, Disseminated Superficial Actinic, Linear, Disseminated Superficial, Punctate palmoplantar, and Disseminated palmoplantar. Therefore, this case presentation aims to aid medical education and increase diagnostic suspicion of porokeratosis in the spectrum of linear lesions. **

Materials & Methods:

A 60-year-old female patient of mixed ethnicity, with a history of hypertension and anxiety, sought secondary care for pruritic lesions throughout the right lower limb (RLL), present since age 3. She had not been previously monitored for the lesion and had used unidentified topical medications without improvement. On examination, she presented hyperchromic linear plaques with atrophic center and elevated borders on the right leg, one with a psoriasiform pattern extending to the ipsilateral plantar region, along with residual hyperchromic macules in the proximal portion of the limb. A biopsy performed at 2 points confirmed the diagnosis of porokeratosis with characteristic cornoid lamellae. She was initially treated with a compounded formulation of 4% salicylic acid and 20% urea for topical use but discontinued treatment due to skin irritation and worsening pruritus after a few days of use; therefore, systemic treatment with acitretin 30 mg/day was initiated.

Results:

Linear porokeratosis can start at birth or in adulthood but usually appears in childhood, often unilaterally and and follows Blaschko’s lines, consistent with this case report. It is frequently associated with post-zygotic somatic mutations in genes of the mevalonate biosynthetic pathway, such as PMVK and MVD, resulting in a form of genetic mosaicism. The condition has been noted in patients undergoing immunosuppression, though this was not seen in the patient discussed. Different forms of the disease may appear in the same individual or family, and there is a higher risk of malignant changes, particularly into squamous cell carcinoma. The patient displayed a single variant and showed no signs of malignancy but was advised to have regular follow-ups. Possible alternative diagnoses include linear inflammatory verrucous epidermal nevus and other linear dermatoses. There is no effective and lasting treatment described for porokeratosis; therapeutics aim for a palliative rather than curative approach and seek aesthetic comfort and reduction of malignant progression risk.

Conclusion:

Linear porokeratosis is a rare condition that needs careful diagnosis. Despite its generally benign nature, the potential for malignant transformation demands regular monitoring. Treatment remains a challenge, with various therapeutic options available, but without consistently satisfactory results. Sharing clinical cases, especially rarer

types like the linear form, helps improve medical understanding and management of this condition.

Abstract N°: 1805

Neonatal Epidermolysis Bullosa: A Window into Silent Nephropathy

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Neonatal Epidermolysis Bullosa: A Window into Silent Nephropathy

Introduction & Objectives:

Inherited epidermolysis bullosa (EB) encompasses rare genetic disorders marked by extreme skin and mucosal fragility, leading to blistering after minimal trauma. While cutaneous signs dominate, systemic complications, particularly renal involvement, can occur and worsen the prognosis. Among them, interstitial nephritis—though uncommon—can induce severe electrolyte imbalances such as hyponatremia, hypokalemia, and metabolic alkalosis. These complications may be underrecognized, especially in neonates, where early diagnosis is key to preventing chronic kidney disease. This case illustrates the relevance of prompt multidisciplinary management combining dermatology, nephrology, and nutrition.

Materials & Methods: not applicable

Results:

A two-month-old infant was admitted for lethargy, poor feeding, and signs of severe dehydration, including dry mucous membranes, sunken fontanelle, and cold extremities. Since birth, the child exhibited diffuse blistering and erosions suggestive of severe EB. Laboratory findings showed severe hyponatremia (122 mmol/L), hypokalemia (2.6 mmol/L), metabolic alkalosis (pH 7.50, HCO_3^- 34 mmol/L), hypochloremia (90 mmol/L), and elevated uric acid. Tubular proteinuria was present without albuminuria. Renal ultrasound was normal. Despite appropriate rehydration, correction of electrolyte abnormalities was difficult and required prolonged IV supplementation under close monitoring. This clinical picture raised the suspicion of tubulointerstitial nephropathy in a context of likely dystrophic EB. Genetic analysis is ongoing to identify potential COL7A1 mutations, which have been implicated in systemic complications including kidney involvement. Management combined atraumatic wound care, topical antibiotics, electrolyte correction, enriched nutrition, and close multidisciplinary follow-up.

Renal manifestations in EB are uncommon and likely underdiagnosed. Interstitial nephritis may result from inflammation, chronic dehydration, or genetic factors. COL7A1 mutations, linked to recessive dystrophic EB, have been associated with extracutaneous manifestations in severe phenotypes, though a direct genetic correlation with kidney disease remains unclear. Electrolyte disturbances may stem from transcutaneous sodium loss, tubular dysfunction, and reduced intake. Metabolic alkalosis resembling Gitelman-like syndrome has been reported in similar contexts. This case highlights the importance of routine renal monitoring and comprehensive support in severe neonatal EB.

Conclusion:

This case reveals the potential for silent renal dysfunction in neonatal EB, unveiled by persistent electrolyte imbalance. Early biological assessment and multidisciplinary care are essential. Further genetic insights are needed to clarify the pathophysiology linking EB to renal complications.

Abstract N°: 1877

Papillon-Lefèvre Syndrome: New Approaches in Systemic Therapy

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We report on two male patients diagnosed with Papillon-Lefèvre syndrome (PLS).

The **first case** describes a 49-year-old man with long-standing psoriasiform skin lesions and palmoplantar involvement. Initial treatment with acitretin was insufficient, prompting the addition of secukinumab, which led to marked improvement of the skin. However, therapy was discontinued after the patient developed a *Staphylococcus aureus*-induced liver abscess with subsequent sepsis. Mild palmoplantar erythema and scaly plaques persisted. Due to a family history of psoriasiform skin lesions and early tooth loss in his brother, PLS was suspected and later confirmed through genetic testing, which revealed two heterozygous mutations in the *CTSC* gene. Additionally, a heterozygous mutation in *WNT10* was identified.

The **second case** involved a patient with a confirmed diagnosis of PLS, presenting with palmoplantar keratosis and psoriasiform plaques on the elbows. He was initially treated with acitretin 10 mg daily, but due to limited improvement and a single episode of *Staphylococcus aureus* sepsis, the dose was increased to 30 mg. While palmoplantar hyperkeratosis improved, elbow plaques persisted. Apremilast (30 mg twice daily) was added but discontinued after six months due to lack of further benefit. The patient has remained on acitretin monotherapy (30 mg daily) for four years, with stable plaques on the elbows and mild palmar erythema.

PLS is a rare autosomal recessive disorder caused by mutations in the *CTSC* gene, typically presenting with palmoplantar hyperkeratosis, psoriasiform lesions, and early tooth loss. Patients are also at increased risk for bacterial infections and organ abscesses. The additional *WNT10* mutation identified in the first case raises questions about a possible modifying effect or overlap with ectodermal dysplasias.

These cases highlight the diagnostic challenge of differentiating PLS from chronic inflammatory dermatoses, particularly when psoriasiform lesions and palmoplantar involvement are present. Both patients demonstrated a partial response to retinoids. While retinoids remain the most established systemic therapy in PLS, data on biologics and other immunomodulatory agents are limited. In the first case, secukinumab was highly effective but had to be discontinued due to infectious complications.

Notably, both patients developed sepsis after the initiation of retinoid therapy. However, as sepsis also occurs in PLS patients without systemic treatment, a direct causal link remains unclear. Nevertheless, the potential risk of serious infections must be carefully considered, particularly when using immunosuppressive or immunomodulatory therapies—even though retinoids themselves are not classified as such.

These cases underscore the need for individualized therapeutic strategies in managing rare genetic skin disorders like PLS, balancing treatment efficacy with infection risk.

Abstract N°: 2206

A Rare Case of MIDAS Syndrome

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Introduction & Objectives:

MIDAS is an acronym of the X-linked syndrome characterised by microphthalmia, dermal aplasia and sclerocornea, also now known as microphthalmia with linear skin defects (MLS). Congenital linear skin defects are observed limited to the face and neck. Cardiac, central nervous system and genitourinary tract abnormalities may accompany this syndrome. Herein, we report a case of a newborn with MIDAS syndrome.

Materials & Methods:

The patient's medical history were acquired, and a meticulous search of literature was performed, with the keywords "MIDAS syndrome" and "dermal aplasia".

Results:

A 14-day-old female neonate presented with erythematous patches on the face and neck. Dermatologic examination revealed bilateral reticular erythematous atrophic patches with scattered yellow scales, extending from the upper eyelid and nasal bridge to the cheeks and submandibular region. The patient also had visible microphthalmia. These findings were present at birth. She was born full-term by vaginal delivery to nonconsanguineous parents. There was no related family history. Ophthalmologic examination showed microphthalmia and microcornea of the right eye and microcornea of the left eye. Echocardiography revealed patent foramen ovale. Agenesis of the corpus callosum was found on magnetic resonance imaging. Karyotyping revealed 46, XX, der(x)add(X)(p22.1). To identify the exact origin, chromosomal microarray analysis was planned, displaying 11.8 Mb deletion in arr[GRCh37] Xp22.33p22.2(169786_11939721)x1 encompassing HCCS gene. Karyotyping of the mother revealed a normal chromosomal pattern, meaning the mutation is de novo. Based on these evaluations, the diagnosis was consistent with MIDAS syndrome. During 2-year follow-up, the patient exhibited growth and developmental retardation, hypotonia and was unable to achieve independent ambulation. Face and neck lesions regressed with postinflammatory hyperpigmentation.

Conclusion:

MIDAS syndrome is a rare neurocutaneous condition with female predominance, and mostly fatal in males. It is caused by a vast number of chromosomal aberrations resulting in segmental monosomy of the Xp22.1-3 region, as reported in our patient. Intragenic deletions or point mutations in the HCCS gene is the key element of this syndrome. Our case presented with unique head-neck atrophic skin lesions, micropthalmia and microcornea; providing all components of MIDAS syndrome. Focal dermal hypoplasia, another X-linked syndrome with similar eye and skin abnormalities, may need to be distinguished from MIDAS. Agenesis of the corpus callosum is a common finding in approximately one-third of the cases as was demonstrated in our case. Management of cardiac defects, genitourinary malformations and developmental problems require a multidisciplinary approach. Treatment for the skin defects in MIDAS syndrome is limited, but recognition of this rare syndrome provides genetic counseling to patients and their families.

Abstract N°: 2212

Waardenburg Syndrome with Lentigenes: A rare association with phenotypic heterogeneity in Asian skin

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Introduction & Objectives:

Waardenburg syndrome (WS) is a rare autosomally inherited, genetec disorder of neural crest cell development with variable prevalence around the world. It has distinct cutaneous and facial manifestations like pigment abnormalities, dystopia canthorum, white forelock, broad nasal root and synophrys. The condition can manifest with variable expressivity. Based on the clinical presentations, four subtypes of the disease are recognized. WS1 is characterised by sensorineural hearing loss, heterochromia iridis and dystopia canthorum, which is absent in WS2, while the rarest of all, WS3 has associated limb anomalies like hypoplasia and syndactyly. WS4 is similar to WS1 with the addition of Hirschsprung disease. We describe a case of WS in asian ethnicity to highlight the rare occurence of lentigenes in contrast to the more common depigmented lesions seen among the west.

Materials & Methods:

An 8-year-old south Indian girl, accompanied by her mother presented with pre lingual hearing loss and speech delay. She denied any visual impairment. She was born out of non-consanguineous marriage and a term, non-spontaneous pregnancy through invitro fertilization. She denied any similar features among the family members. A comprehensive neurological, ophthalmological and dermatological examination was performed. She had blue colored iris on the right, broad nasal bridge and mild synophrys. The audiological and neurotological examination consisted of otoscopy, pure-tone audiometry, and Brainstem Evoked Response Audiometry (BERA). The ophthalmological examination included visual acuity measurements, visual field examination, and fundus ophthalmoscopy. She was diagnosed with Waardenburg syndrome according to the criteria proposed by the WS consortium. She underwent cochlear implant and was suggested genetic testing, which the parents refused in view of cost.

Results:

Sensorineural hearing loss is the most common feature of WS2, and is also the main reason motivating patients to visit a physician. Compared to the west, heterochromia iridis is commonly observed in asian population and pigmentary abnormalities are less frequent and hyperpigmented lesions are a rarity. Instead of patchy, depigmented skin, as seen in most western cases, hyperpigmented lesions might be a more common phenotype of skin pigmentary abnormalities in asian popultion.Various gene mutations involving PAX3, MITF, SNAI2, SOX10 and EDNRB genes have been observed. Of these, MITF gene mutations have been found to be more associated with pigment changes and also in asian population.

Conclusion:

There is currently no definitive treatment or cure for WS. Sensorineural deafness, bony abnormalities, and Hirschsprung disease associated with WS are some of the potentially serious conditions that significantly deteriorates the quality of life. From a dermatologist’s point of view, an early diagnosis may aid in the initiation of early treatment, social and vocational training, and rehabilitation of these patients. This case also highlights the importance of preimplantation genetic testing as a screening tool in preventing such occurrences.

Abstract N°: 2458

Generalized Cutaneous Lichen Amyloidosis in MEN2: A novel pathogenic RET Y806C Mutation Expanding the Genotype-Phenotype Spectrum of MEN2. Case report.

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Introduction & Objectives: Cutaneous lichen amyloidosis (CLA) is a rare dermatological condition characterized by amyloid deposits in the skin, presenting as pruritic, hyperkeratotic papules. CLA has been associated with multiple endocrine neoplasia type 2 (MEN2), a hereditary syndrome caused by germline mutations in the RET proto-oncogene. While MEN2-associated CLA is typically localized and linked to RET mutations in codon 634, generalized forms of CLA in MEN2 are exceedingly rare. We describe the first reported case of generalized CLA associated with MEN2 in a patient carrying a novel RET mutation (Y806C), expanding the genotype-phenotype spectrum of MEN2.

Materials & Methods: We conducted clinical, histopathological, and molecular evaluations of a 57-year-old male presenting with MEN2 and generalized CLA. Genetic testing of the RET proto-oncogene was performed using Sanger sequencing.

Results: The patient exhibited a rare, generalized form of CLA before being diagnosed with primary hyperparathyroidism (PHPT) and medullary thyroid carcinoma (MTC). Histopathology confirmed amyloid deposition in the skin. Genetic testing identified an ultra-rare heterozygous mutation (Y806C) in exon 14 of the RET proto-oncogene, previously associated with MEN3 but not MEN2. This case represents the first documented association of MEN2-CLA and PHPT with a RET mutation outside codon 634.

Conclusion: This report highlights a novel RET mutation (Y806C) associated with generalized CLA and MEN2, broadening the understanding of genotype-phenotype correlations. CLA may serve as an early clinical marker of MEN2, underscoring the importance of molecular testing and vigilant follow-up in affected individuals. Early recognition of CLA in MEN2 can facilitate timely diagnosis and management, reducing the risk of diagnostic delays.

Abstract N°: 2693

A phenotypic-genotypic observational analysis of the International dystrophic epidermolysis bullosa registry

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Introduction & Objectives:

Dystrophic epidermolysis bullosa (DEB) is a heritable blistering disorder that is caused by mutations in the COL7A1 gene encoding type VII collagen and can be inherited either dominantly or recessively. Accurate estimation of different subtypes of DEB along with genotypic analysis is essential for further clinical trials and for the care of these individuals. The objective of this study was to conduct an analysis of inherited DEB patients stratified by subtype enrolled in the International DEB register.

Materials & Methods:

The study was an observational cross-sectional study. Data were obtained from 1039 patients consecutively enrolled in the International DEB Register which is the result of the collaboration between the International Dystrophic Epidermolysis Bullosa Patient Registry and the *COL7A1* Variant Database. Entries were made from the year 1990 to 2022. Participants were patients of all ages with DEB. Clinical, laboratory and genetic data were collected on patients who were subclassified on the basis of EB classification given by Fine et al in 2008.

Results:

Recessive DEB (RDEB) generalized severe type was overall the most common subtype of DEB (around 35 %) followed by RDEB, generalized other (17%) whereas the most common type of dominant DEB (DDEB) seen was unknown (5.87 %) followed by generalized type was 4.72% .The most common cDNA change seen was c.6127G>A (2.5 %) followed by c.2471dup (1.83 %) and c.425A>G (1.54%). Genotype-phenotype correlation showed the most common mutations seen in RDEB generalized severe type was c.6527dup and c.425A>G, in RDEB generalized other type was c.2471dup and c.4448G>A. c.6127G>A was the most common mutation seen in different subtypes of DDEB. Data on ethnicity was not reported in majority of patients, however in the data available Spanish and polish population were the most common (4.62 % and 3.95 % respectively)

Conclusion:

Prevalence of different subtypes of DEB differ with a predominance towards recessive subtype. There also seems to be significant correlation between different genotypes and phenotypes which might help in prediction of specific clinical variants based on genetic analysis. This should assist investigators in choosing which subtypes are amenable to properly designed, large-scale, clinical trials.

Abstract N°: 2731

Systemic complications in JEB intermediate: a case series

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Introduction & Objectives:

Junctional epidermolysis bullosa (JEB) comprises genetically heterogeneous rare blistering disorders with skin cleavage within the basement membrane. Our cohort consists of 21 patients (12 males and 9 females, median age 31.3 years) with intermediate JEB with pathogenic variants in the genes encoding laminin 332 (12) and type XVII collagen (9). The aim of this retrospective analysis is to identify systemic complications in intermediate JEB patients.

Materials & Methods:

Laboratory diagnostics, skin biopsy and histopathology, wound surface area documentation, clinical follow-up visits, as well as specialist internist and oncology consultations were performed.

Results:

Our patients show multiple complications including chronic anemia, elevated inflammatory parameters, impaired kidney function and cutaneous tumors. The wound body surface area (wBSA) was measured during regular follow-up visits: 13 patients had more than 2% wBSA, 3 patients had 10% and 20% wBSA, respectively. Anemia was present in 11/21 patients. Inflammatory parameters are commonly elevated in JEB patients with chronic wounds. Ten/21 patients had more than two-fold elevation of the inflammatory parameter CRP (max. fold change 15.2) and 10/21 patients had increased values for interleukin-6 (max. fold change 9.27). The leucocytes count was increased (max. value 16 Tsd/µl) in 10/21 patients. Chronic wounds were colonized with multiple bacterial strains: staphylococcus aureus, streptococcus pyogenes and dysgalactiae/canis, pseudomonas aeruginosa, proteus mirabilis. Impaired kidney function is more common in dystrophic EB-patients, nevertheless four patients (mean age 41.5 years, *LAMC2*, *LAMB3* and two patients with *COL17A1* mutations) had elevated cystatin C, from which one patient had albuminuria, and one urethra stricture. Interestingly there was another patient in our cohort, which developed chronic relapsing urethra strictures but showed normal renal parameters. Serum amyloid is commonly elevated in conditions with chronic inflammation, which is the case in DEB patients. Six JEB patients demonstrated more than two-fold serum amyloid elevation (>10 mg/l), two of them having impaired kidney function. In addition, three patients developed squamous cell carcinomas (median age 49.3, localization: one on the upper back, two on the lower leg) and one dermatofibrosarcoma protuberans. All complications were present in patients with large wBSA, most of them adults (median age 32.9, all JEB genes).

Conclusion:

There is a clear correlation between the affected wBSA, elevated inflammatory parameters (CRP and IL-6), presence of anemia, but also development of impaired kidney function and cutaneous tumors in our cohort. Hence, all four JEB patients with impaired kidney function had severe wound burden (3 patients with 20% and one with 10% BSA with wounds), elevated inflammatory parameters, anemia and two of these patients developed squamous skin carcinoma. Two patients with *LAMB3*-mutations also had urethral involvement. These findings suggest that wound burden and chronic inflammation may cause early manifestation of systemic complications in JEB patients. Therefore, regular laboratory and clinical follow up-examinations are essential for early diagnosis and

treatment of systemic complications.

Abstract N°: 2768

Sjogren Larson Syndrome: Recurring Genetic Variants in Endogamous Indian Populations.

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Introduction & Objectives: Syndromic ichthyoses (excluding XLRI) constitute a small fraction of inherited ichthyoses. But they are important to identify because the involvement of other organ systems significantly affect management , prognosis and genetic counselling. Majority of these are inherited in an autosomal recessive manner.

Sjogren Larson syndrome is characterised by the triad of ichthyosis, intellectual disability, and spastic diplegia. It is a 100% penetrant disease with onset of neurological symptoms within the first 2 years of life.

Materials & Methods: Whole exome sequencing was done for 2 unrelated families with a total of 3 affected children with Sjogren Larson Syndrome from the same state in India. In both families, there was no history of consanguinity.

A literature review was done for genetic variants associated with Sjogren Larson syndrome in Indian patients.

Results: The same genetic variant in the ALDH3A2 gene causing a splice site loss was identified in both the families in a homozygous state.

In the literature review, another recurring mutation affecting the amino acid at the 48th position of fatty aldehyde dehydrogenase was found in a homozygous state in 2 other affected families.

A search of the 10,000 genome India database is awaited to identify pathogenic variants in the ALDH3A2 gene that may be prevalent in Indian populations.

Conclusion: Strict endogamy in many populations in India lead to increased incidence of recessive disorders resulting from founder events. Even when consanguinity is not reported by families of affected individuals, the likelihood of recessive disorders is higher in these populations. The IBD (identity-by-descent) scores have been reported to be higher in various Indian populations.

Abstract N°: 2856

Bullous Darier Disease: An Uncommon Clinical Presentation

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Introduction & Objectives: Darier disease is an autosomal dominant acantholytic dermatosis. It typically manifests around puberty with brownish keratotic papules in skin folds and seborrheic areas. We report a rare case of the bullous variant of Darier disease.

Materials & Methods:

Results:

A 54-year-old woman with a history of Darier disease since the age of 16, treated with acitretin (25 mg/day) but with poor adherence, presented with a generalized, pruritic vesiculobullous eruption evolving over six days. Dermatological examination revealed the presence of multiple brownish follicular keratotic papules, vesicles, and confluent post-vesicular erosions on the trunk and limbs, as well as palmoplantar keratoderma. Examination of the mucous membranes showed a fissured tongue covered with a weakly adherent whitish coating and erythematous papules on the palatine mucosa. Examination of the nails revealed subungual hyperkeratosis with longitudinal striations on all fingernails. The diagnosis of Kaposi-Juliusberg syndrome, complicating Darier disease, was suspected. Acyclovir (10 mg/kg every 8 hours) was initiated. In the absence of clinical improvement after five days of treatment, a biopsy of a vesiculobullous lesion was performed. Pathological examination revealed focal hyperkeratotic epidermis, the site of intra-epidermal detachment with supra-basal acantholysis and no signs of herpetic superinfection. Direct immunofluorescence (DIF) was negative. The diagnosis of bullous Darier disease was made. Treatment with acitretin (25 mg/day) was resumed with good clinical progression.

Conclusion:

Various atypical presentations of Darier disease have been reported, including vesiculobullous, hypertrophic, hyperkeratotic, comedonal, hemorrhagic, and dyschromic forms. The vesiculobullous variant is characterized by small blisters, often occurring on affected areas but sometimes appearing on healthy skin. These bullous lesions can be predominant, and their rupture leads to weeping, crusted, circinate-bordered erosive plaques, primarily affecting the neck and major skin folds. The differential diagnosis includes Hailey-Hailey disease, pemphigus, and Kaposi-Juliusberg syndrome. Histologically, these bullae are a major expression of acantholytic clefts. Treatment is based on retinoids combined with local care to prevent superinfection. Emerging therapeutic perspectives include IL-17 inhibitors.

Abstract N°: 2933

An Uncommon Presentation of Giant Congenital Nevus in an Adult: Case Report and Literature Review

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Introduction & Objectives:

Giant congenital nevus is a rare benign melanocytic tumor present at birth. It may lead to serious complications, both somatic and psychosocial, particularly when it is extensive or located in a visible area. We report the case of a 22-year-old female patient presenting with an extensive dorsal giant congenital nevus, associated with satellite lesions and a significant psychosocial impact.

Materials & Methods:

A 22-year-old woman, with no significant family history and no parental consanguinity, consulting for evaluation of a congenital pigmented nevus covering a large portion of her back. She reported significant aesthetic discomfort particularly with lesions witch are located in exposed areas, along with occasional episodes of pruritus and skin irritation.

On clinical examination, the nevus measured approximately 35 cm along its longest axis, located on the dorsal region, extending from the nape to the lumbar area. It appeared as a dark brown to black pigmented plaque, with an irregular, thickened surface, partially verrucous, and marked hypertrichosis. Numerous satellite nevi were observed on the shoulders, upper limbs, and lower limbs.

Brain and spinal MRI was performed to investigate potential neurocutaneous melanosis and returned normal. A skin biopsy confirmed the benign nature of the lesion, with no signs of malignant transformation.

CO_2 laser treatment was performed on nevi located in exposed areas. By the third session, a noticeable reduction in pigmentation was observed, accompanied by a high level of patient satisfaction with the aesthetic results.

Results:

Giant congenital nevus is defined as a pigmented lesion present at birth measuring more than 20 cm in adulthood. It affects approximately 1 in 20,000 live births and can reach impressive dimensions, with a predilection for the trunk, scalp, and limbs. Its surface may be flat, verrucous, or cerebriform, and it is often associated with hypertrichosis. The “bathing trunk” type is among the most recognized topographic variants, but isolated dorsal forms, as in our case, are also common.

The main long-term risk is malignant transformation into melanoma, estimated between 0.7% and 10%, depending on the size and depth of the lesion. This risk increases with lesions larger than 40 cm or the presence of numerous satellite nevi (>20). Another potential complication is neurocutaneous melanosis, characterized by meningeal infiltration of melanocytes. Although often asymptomatic, it can lead to hydrocephalus, intracranial hypertension, or seizures. Systematic MRI screening is recommended in such cases.

Psychologically, the impact can be significant, particularly in young adults. Issues related to self-esteem, social anxiety, and body image disturbances are frequently reported. A multidisciplinary approach, including dermatology, plastic surgery, psychological or even psychiatric support, is often necessary.

Conclusion:

Giant congenital nevus is a rare condition with multiple clinical and psychosocial implications. Management should be individualized, addressing both medical risks and aesthetic and psychological concerns. Regular follow-up, patient education, and access to appropriate psychological support are essential components of effective, comprehensive care.

includes psychological support, in order to improve the well-being of individuals living with visible scars.

Abstract N°: 3262

Clinical, Histopathological, and Genetic Features of Amyloidosis Cutis Dyschromica: A Case Series of Eight Filipino Patients from a Single Pedigree

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Introduction & Objectives:

Amyloidosis cutis dyschromica (ACD) is an un uncommon type of primary localized cutaneous amyloidosis. It typically presents with prepubertal onset of reticulated hyperpigmented and hypopigmented macules due to amyloid deposition in the papillary dermis. Autosomal recessive ACD has been linked to truncating mutations in Glycoprotein non-metastatic melanoma protein B (GPNMB) gene, encoding for the GPNMB protein which plays a role in melanosome differentiation. Based on this Filipino pedigree, a semidominant inheritance pattern has been hypothesized. We describe eight members of a single family who have a range of ACD manifestations and related GPNMB mutations.

Materials & Methods:

Clinical, histopathologic, and genetic assessment of eight individuals with ACD was done. Sanger sequencing was performed on available family members. Dermoscopy and immunofluorescence studies were also carried out.

Results:

Eight Filipino patients (6 females, 2 males; aged 3–58 years) from a single pedigree were evaluated. Classic presentation of ACD with generalized hypopigmented and hyperpigmented macules was observed in three individuals with homozygous GPNMB mutations. Among the three homozygotes, one presented with an unusual hyperpigmented patch, while another had vesicular lesions at onset.

Patients with heterozygous GPNMB mutations exhibited milder phenotypes, wherein a female displayed lichen amyloidosis-like plaques and two other females presented with linear patches in addition to hypopigmented and hyperpigmented macules, suggestive of koebnerization. One male with heterozygous GPNMB mutation was unaffected. One individual with a lichen amyloidosis-like phenotype declined genetic testing.

Histopathology confirmed dermal amyloid deposits in all biopsied cases. Dermoscopy patterns differed between phenotypes. Immunofluorescence revealed decreased GPNMB expression and reduced basal melanocytes in lesional skin.

Conclusion:

This case series expands the inheritance pattern of ACD to include semidominant transmission. Heterozygotes may present with a spectrum of findings, ranging from milder forms of skin dyschromia with hypo- and hyperpigmented macules, to lichen amyloidosis-like plaques, or may remain clinically unaffected. Recognition of the inheritance patterns of this condition is important for early diagnosis, family screening, and genetic

counseling.

Abstract N°: 3483

Natural History of Hand and Foot Deformities in Dystrophic Epidermolysis Bullosa: A Descriptive Analysis of 30 Pediatric Patients

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Introduction & Objectives:

Recessive dystrophic epidermolysis bullosa (RDEB) is characterized by progressive pseudosyndactyly (PSD), loss of grip function, and mutilating deformities that severely impact quality of life. While these complications are well-recognized, detailed data on their temporal progression remain limited. This descriptive study analyzes a cohort of 30 DEB patients to identify: mean ages at key functional milestones including PSD onset, grip loss, and first mutilation; disease progression in RDEB severe and intermediate subtypes; potential gender differences in disease manifestation; surgical intervention patterns and outcomes.

Materials & Methods:

We conducted a longitudinal retrospective review of 30 genetically confirmed RDEB patients under the age of 10 followed-up at the Freiburg EB Center. Using standardized data extraction, we recorded ages (in decimal years) at: first documented PSD (hands and feet separately); complete loss of grip function; first mutilation (defined as any degree of autoamputation); surgical interventions (web space release, syndactyly correction). Analysis focused on descriptive statistics (mean ± standard deviation) for all milestones. Subgroup comparisons were made between: RDEB severe (n=20) *vs* intermediate (n=10); male (n=18) vs female (n=12) patients; ≤5 years (n=20) vs 6 to 10 years (n=10). Observational data on surgical outcomes were included where available.

Results:

Disease Milestones (mean age ± SD in years): hand PSD onset: 2.0 ± 1.7 (range 0.4-4.4); foot PSD onset: 3.1 ± 3.3 (range 0.3-9.2); grip loss: 5.1 ± 1.2 (range 3.2-6.6); foot mutilation: 1.8 ± 2.1 (range 0.2-6.2); hand mutilation: 6.2 ± 0.6 (range 5.4-6.6); by the age of 10 one fifth has lost grip function secondary to PSD and contractures; the loss of grip is four times more present after the age of 5.

Subtype Analysis: RDEB severe patients had five times more foot PSD compared to intermediate patients. No intermediate RDEB patients showed PSD of the hand, loss of grip or hand mutilation. One third of severe RDEB had PSD of the hand and Loss of Grip, while one sixth showed mutilation of the hand. One tenth of the severe RDEB patients underwent hand surgery.**

Gender Observations: No significant difference in milestone timing.

Surgical Outcomes (n=3): Two patients hand surgeries: one preserved grip function at last follow-up one year later; one foot surgery: subsequent mutilation within one year.

Conclusion:

This comprehensive analysis documents the natural history of functional decline in RDEB in this cohort, demonstrating:

- RDEB severe subtype progresses more rapidly, with grip loss typically occurring by age of five.
- Foot mutilation precedes grip loss and hand mutilation in most cases.
- Surgical outcomes remain variable, warranting further study.

These findings emphasize the need for standardized functional assessments and early intervention strategies in DEB management. The established milestone timelines will serve as valuable benchmarks for future studies.

Abstract N°: 3531

Reed syndrome as the beginning of screening of associated neoplasms

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Introduction & Objectives:

Reed syndrome is characterized by the presence of cutaneous leiomyomas of pillar origin, uterine leiomyomas in women and, in some cases, is associated with malignant neoplasms. Dominant autosomal inheritance entity. It can be associated with renal carcinomas and other neoplasms such as bladder or breast cancer. Histopathologically, it presents as bundles of smooth muscle fibers interwoven with collagen fibers, arranged in a fusiform and irregular pattern within the dermis, while sparing the epidermis. The nuclei are blunt-ended or “cigar-shaped,” with no nuclear atypia, mitotic figures, or pleomorphism.

Materials & Methods:

We present two clinical cases.

Results:

The first case corresponds to a 41-year-old female patient, with a history of rheumatoid arthritis, myomatosis hysterectomy and a family history of 1º degree of cutaneous leiomyomas. She consulted for an 11-year table of evolution of skin lesions located on the anterior face of the left hemithorax, erythematous papules type, some confluent forming plates, of zosteriform distribution, painful on palpation. Blood analysis was performed without alterations, histopathological and immunohistochemical study that reported smooth muscle hamartoma, arriving at the diagnosis of multiple leiomyomatosis. The second clinical case corresponds to a 48-year-old female patient, with a history of myomatosis hysterectomy and currently being treated with tamoxifen for breast cancer. She consulted for lesions of more than 10 years of evolution, like papules and painful nodules on palpation, of hard elastic consistency, some normochromic, others erythematous, located on the anterior face of the right hemithorax, with extension towards the homolateral back, adopting zosteriform disposition. Blood analysis was performed without alterations and histopathological study whose diagnosis was piloleiomyoma.

Conclusion:

The importance of researching the associations described in the presence of multiple leiomyomas is highlighted, given the consequences of their evolution without timely treatment.

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Abstract N°: 3551

When Alopecia Meets Rare Genetic Syndrome: A Case Study of Tricho-Rhino-Phalangeal Syndrome

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Introduction & Objectives: **

Tricho-rhino-phalangeal syndrome (TRF) is a rare genetic disorder characterized by progressive alopecia, phalangeal malformations, and facial anomalies such as nasal prominence. This autosomal dominant condition has an extremely low prevalence, making diagnosis and management challenging. There are two types of TRF: type 1, associated with bone dysplasias and facial features, and type 2, which also involves premature aging. Despite some published studies and case reports, TRF remains a complex diagnosis due to overlapping symptoms with other common conditions, such as androgenetic alopecia and seborrheic dermatitis. The lack of effective therapeutic responses to conventional treatments like minoxidil emphasizes the importance of identifying and appropriately managing this rare condition.

Materials & Methods: A 14-year-old female presented with a history of progressive diffuse hair loss on the scalp, which had been occurring since the age of 10. The patient also reported irregular hair growth and thinning areas. Her medical history included Perthes disease, obesity, irregular menstrual cycles, and allergies to dust mites. Despite numerous treatments, including topical minoxidil and antifungal medications, the patient showed no significant improvement. Physical examination revealed thinning hair with areas of finer, brittle hair on the scalp, and signs of seborrheic dermatitis with erythema and greasy scales. Nails showed mild alterations, and the nose was slightly more prominent than usual, a hallmark feature of TRF. The patient was diagnosed with TRF type 1, also known as Giedion syndrome, a rare autosomal dominant disorder caused by mutations in the TRPS1 gene. This gene encodes a transcription factor involved in the development of structures such as the phalanges, hair, and nose.

Results:

Clinical features such as short or malformed phalanges, nasal prominence, and progressive alopecia, manifesting since childhood, were consistent with TRF type 1. Despite the overlap with common dermatological conditions such as androgenetic alopecia and seborrheic dermatitis, a thorough clinical evaluation and genetic testing led to the correct diagnosis. The diagnosis was further confirmed by histopathological and genetic studies, which identified mutations in the TRPS1 gene. The patient’s lack of response to conventional therapies and the distinctive features of TRF pointed to the need for a more in-depth diagnostic approach.

Conclusion: This clinical case emphasizes the importance of considering Tricho-Rhino-Phalangeal Syndrome in the differential diagnosis when encountering diffuse alopecia and seborrheic dermatitis that do not respond to standard treatment. The combination of dermatological and skeletal manifestations makes TRF challenging to diagnose, especially when common conditions, such as androgenetic alopecia or seborrheic dermatitis, obscure the symptoms. This case highlights the need for deeper histopathological and genetic investigations and underscores the significance of early recognition of rare diseases in dermatological practice. Understanding these conditions will help develop more targeted management strategies for patients with rare syndromes like TRF.

Abstract N°: 3589

Unusual Autosomal Dominant Inheritance of Oculocutaneous Albinism Type 4 (OCA-4): Clinical and Functional Features from A Chinese Family

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Unusual Autosomal Dominant Inheritance of Oculocutaneous Albinism Type 4 (OCA-4): Clinical and Functional Features from A Chinese Family

Introduction & Objectives:

Oculocutaneous albinism (OCA) is a complex genetic disorder characterized by reduced or absent pigmentation in the skin, hair, and eyes. Among the eight known OCA subtypes, OCA-4 is caused by mutation in *SLC45A2* gene, which plays a crucial role in melanin biosynthesis. While autosomal recessive inheritance is the typical and most common pattern for all OCA subtypes, there have been extremely rare cases reported with dominant inheritance.

Materials & Methods:

We report three patients from a Chinese family exhibiting autosomal dominant OCA-4. Clinical assessments were conducted to evaluate pigmentation and ocular features in the affected family members. Genetic analysis was performed using next-generation sequencing to identify potential pathogenic variants. Functional studies in MNT-1 cells were performed to explore the impact of the variant.

Results:

Clinically, these patients exhibited mild hypopigmentation and foveal hypoplasia, consistent with the OCA-4 phenotype. We identified a pathogenic variant of c.208T>C (p.Tyr70His) in *SLC45A2* gene in affected individuals from this family. Functional studies demonstrated that this variant led to retention of the protein in the endoplasmic reticulum, resulting in reduced melanin production. This family represents the first documented cases of autosomal dominant OCA-4 in the Chinese population and only the second reported cases worldwide.

Conclusion:

Our findings confirm that the p.Tyr70His variant causes autosomal dominant OCA-4. This study is helpful for our understanding of the genetic mechanisms underlying OCA-4 and increases the complexity of its inheritance patterns in genetic counseling.

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Abstract N°: 3632

building bridges and beyond: learning from patient and carer experiences on perceived healthcare barriers in rare skin disease epidermolytic ichthyosis

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Introduction & Objectives:

Rare genetic skin diseases like Epidermolytic Ichthyosis (EI) can be hard to recognize and even more challenging to manage. It is widely acknowledged that in the case of very rare skin diseases that expert patients can offer healthcare professionals (HCPs) a great deal of insight regarding the barriers that patients face when trying to access appropriate care, and offer advice on how to mitigate the risks. Patient advocacy group, EI Cure Project and the associated online EI Support Group raise awareness of EI and help to provide educational resources for patients, carers, and HCPs alike to improve the quality of care around the world.

Materials & Methods:

The EI Support Group, managed by the EI Cure Project, is a group of over 200 families affected by EI from all over the world. The group was asked to privately share their thoughts on the existence of healthcare barriers when seeking support for their rare skin disease. Qualitative methods were used to explore the emerging themes from the group, and clinical case studies were then used to describe each theme in more depth. In the event that images were considered helpful for case studies, group members were invited to complete a consent form and were made aware that these images would be used for educational purposes.

Results:

The following seven themes emerged from the data: 1) lack of disease awareness and expertise; 2) misdiagnoses and inappropriate treatments; 3) lack of care guidelines or protocols; 4) limited evidence to support treatments; 5) inability to overcome therapeutic inertia (with specific reference to recognizing and managing skin infections); 6) lack of trust due to past traumatic events; and 7) discrimination and inability to see past EI. These themes were explored in more depth in order to develop a plan to better support HCPs in future.

Conclusion:

Despite advances in genetic testing, EI remains a challenging diagnosis. The EI Cure Project and EI Support Group recognize the difficulties faced by HCPs when they are presented with limited resources. This study can be used to provide HCPs, patients, and carers with the necessary educational resources to facilitate more effective patient-professional interactions, with the aim of achieving better outcomes for patients. The first EI Global Symposium will be hosted by the EI Cure Project in March 2026 and will present an opportunity for HCPs to learn more about the diagnosis, and for a Steering Committee to be gathered to finalise much-needed Consortium Care Guidelines for babies, children, and adults, in addition to specific guidelines for the management of skin infections.

Abstract N°: 3826

Identification of 4 novel uroporphyrinogen decarboxylase gene mutations in 4 different families with familial porphyria cutanea tarda

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Identification of 4 novel uroporphyrinogen decarboxylase gene mutations in 4 different families with familial porphyria cutanea tarda

Introduction & Objectives:

Porphyrias are a group of diseases caused by disturbances in heme biosynthesis. Porphyria cutanea tarda (PCT; OMIM 176100) is the most common form and is due to a deficiency of uroporphyrinogen decarboxylase (UROD), which is the fifth enzyme of the heme synthesis pathway. To the date, two variants of the disease exist, type I and II. Type I is the most common form (sporadic PCT, S-PCT) and in it, UROD deficiency is restricted to the liver. Type II (familial PCT, F-PCT) is transmitted in an autosomal dominant manner, mutations in *UROD (NM_000374.5)* gene are present and the activity of the enzyme is reduced in all tissues. F-PCT presents variable clinical expression and usually does not trigger an active phenotype in the absence of aggravating factors.

Here, we report 4 new mutations in the *UROD (NM_000374.5)* gene described in 4 different families with F-PCT.

Materials & Methods:

We studied 4 patients from 4 different families with suspected PCT who were referred to our Dermatology Unit for diagnosis or follow-up. A diagnosis of PCT was established on clinical grounds and confirmed by biochemical analysis of urine and feces. Genomic DNA was extracted from whole blood and the coding regions and intron/exon boundaries of the *UROD (NM_000374.5)* gene was analyzed by Sanger Sequencing.

Results:

We identified 4 novel mutations, each on each one of these families. The first one, named c.787A>T, caused an alteration in p.Lys263* and the patient was a female who presented at the age of 23 with hypertrichosis and skin fragility following the use of oral contraceptives. The second one, named c.235G>T, caused the aminoacid change p.Asp79Tyr, and the third one, c.473C>T, caused the substitution p.Pro158Leu. Both were female patients who presented with skin fragility following the use of oral contraceptives. The fourth one, p.Ala209Thr, was a man who presented with skin fragility, with associated factors being positive for HCV and a significant alcohol consumer.

Conclusion:

In this study, we identified four previously undescribed mutations in the *UROD (*NM_000374.5) gene in four unrelated families diagnosed with F-PCT. These findings expand the mutational spectrum associated with F-PCT and reinforce the role of genetic analysis in confirming the diagnosis, especially in familial cases with atypical or

variable clinical presentation. Early identification of pathogenic variants not only facilitates adequate genetic counseling but also allows for timely detection of at-risk family members who may benefit from preventive measures to avoid triggering factors. Further functional studies are warranted to better understand the impact of these mutations on UROD enzymatic activity and their contribution to disease pathogenesis.

Abstract N°: 3843

Late-Onset Autosomal Recessive Dystrophic Epidermolysis Bullosa: A Case Report

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Introduction & Objectives: Epidermolysis Bullosa (EB) is a rare group of genodermatoses. There are four major subtypes of EB including EB simplex, junctional EB, dystrophic EB, and Kindler syndrome. Dystrophic epidermolysis bullosa (DEB) typically presents at birth and affects skin and nails. It is divided into two main forms: autosomal recessive (RDEB) and autosomal dominant (DDEB). In this case report, we aimed to present the diagnosis, differential diagnosis, and treatment of a late-onset RDEB patient complicated by drug eruption.

Materials & Methods: A 73-year-old female patient with a 3-day history of widespread skin eruption and pruritus that started after a seven-day use of betahistine dihydrochloride 24 mg, oral vitamin D3, and Ginkgo biloba prescribed for tinnitus. The rash first started on the upper trunk, which then spread to her extremities.The patient had a history of trauma-induced bullous lesions on acral sites since her thirties but experienced widespread blistering for the first time in her life. Dermatological examination revealed tense bullae and erosions on an erythematous base over the trunk and extremities as well as nail dystrophy and anonychia on the toes. A punch biopsy was taken from the back. The pathology report suggested a clinicopathologic correlation for a possible drug eruption. Due to suspicion of EB, the patient was referred to the Department of Medical Genetics. Whole exome sequencing (WES) revealed a homozygous missense variant, c.6022C>T in COL7A1 classified as pathogenic according to the standards of the American College of Medical Genetics and The Association for Clinical Genomic Science.

The patient was diagnosed with RDEB complicated by a drug eruption. The patient received oral methylprednisolone, and eroded lesions were treated topically. With treatment, new lesions stopped appearing, and eroded areas began to heal.

Results: Dystrophic epidermolysis bullosa is the second most common EB subtype, accounting for approximately 30% of all cases. RDEB and DDEB result from mutations in the *COL7A1* gene, which encodes the α1 chain of type VII collagen. Compared to DDEB, RDEB presents with a more severe clinical phenotype, often involving chronic, persistent, and treatment-resistant wounds.

The presence of late-onset RDEB cases suggests that the clinical spectrum of RDEB might be broader than initially thought, and different *COL7A1* mutations can lead to varying phenotypes and times of onset. Although homozygous mutations such as c.6022C>T (p.Arg2008Cys) in the *COL7A1* gene are typically associated with early-onset and severe clinical phenotypes, the manifestation of symptoms in midlife following drug exposure in this patient suggests a relatively mild disease course and underscores the potential influence of environmental factors on phenotypic expression.

Conclusion: The absence of symptoms in the patient's parents and the presence in both the patient and her siblings confirm autosomal recessive inheritance, with both parents likely being carriers. The late-onset presentation in this patient is noteworthy, as it may reflect a milder phenotype associated with this specific mutation. The triggering of symptoms following medication use, absence of oral mucosal involvement, and overlapping drug eruption contribute to the atypical clinical presentation of this patient.

Abstract N°: 3934

Facing the Uncommon: A Case Report of Restrictive Dermopathy in a Neonate

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Introduction & Objectives: Restrictive Dermopathy (RD), also known as Lethal Tight Skin Contracture Syndrome, is a rare and fatal autosomal recessive genodermatosis caused by mutations in the *ZMPSTE24* or *LMNA/C* genes. These mutations disrupt nuclear envelope function, leading to tight, rigid skin, facial dysmorphisms, joint contractures, and severe pulmonary hypoplasia. First described in 1986, RD remains one of the most severe congenital skin disorders, with fewer than 120 reported cases globally. This report presents a genetically confirmed case of RD, focusing on its distinctive clinical features and the genetic origins underlying the condition.

Materials & Methods: A preterm female neonate was delivered at 30 weeks and 6 days of gestation via emergency cesarean section due to breech presentation. The parents were first-degree relatives, with no known family history of congenital anomalies or neonatal deaths. The neonate, weighing 1 kg at birth, presented with immediate respiratory distress and an APGAR score of 3 at 1 minute. She was intubated and admitted to the neonatal intensive care unit (NICU). A detailed physical examination and supportive investigations were performed, followed by a skin biopsy and whole exome sequencing for genetic analysis.

Results: The neonate exhibited classic features of RD, including tight, shiny skin, restricted limb movement, ectropion, absent eyelashes, a beak-shaped nose, micrognathia, an “O”-shaped mouth, and visible subcutaneous veins. She also had mobile neonatal teeth and long nails with tapering fingers. Despite supportive care, she developed respiratory acidosis, anemia, and hypothermia. Imaging studies were unremarkable. On day 30 of life, the infant deteriorated and, despite intensive resuscitation efforts, was declared deceased. Genetic testing revealed a homozygous variant of uncertain significance in the *ZMPSTE24* gene, supporting the diagnosis of RD in the context of the clinical findings.

Conclusion: Restrictive Dermopathy is a rare and lethal congenital disorder with distinct clinical features, severe respiratory compromise, and poor prognosis. This case underscores the importance of early recognition, especially in consanguineous populations, and highlights the role of genetic testing in confirming the diagnosis. While management is palliative, prompt identification is critical for guiding clinical care, providing appropriate counseling, and considering genetic testing in future pregnancies. Awareness of RD’s characteristic presentation can improve diagnosis and inform prenatal counseling in affected families

Abstract N°: 3962

Lamellar Ichthyosis in a 3-Year-Old Child: A Case Report

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Introduction & Objectives:

Lamellar ichthyosis is a genodermatosis caused by a keratinization disorder that results from mutations in proteins that are essential for the formation of the epidermal barrier. It manifests as thick, dark scales covering the entire body, with little to no associated erythroderma. In addition, eclabium, nasal and auricular cartilage hypoplasia may occur, often associated with nail dystrophies and alopecia. The main ocular finding is palpebral ectropion. As it is a rare disease, we consider it relevant to report a case of lamellar ichthyosis with ocular complications managed in our service.

Materials & Methods:

The information contained in this work was obtained through a review of the patient's medical record and an interview with the patient's guardian, his adoptive mother.

Results:

A 3-year-old male patient with a prior diagnosis of lamellar ichthyosis, currently undergoing both topical and systemic treatment, is being cared for by his adoptive family for the past year, with no known history of previous medical conditions. He is under joint follow-up with the oculoplastic department, having already undergone palpebral reconstruction, and is presently using an dexpanthenol ophthalmic gel. The patient's guardian reported that, since the adoption, the patient has exhibited xerotic and scaly skin, accompanied by intense pruritus. The bathing routine consists of two daily baths using regular bar soap and a luffa sponge. A moisturizer combined with vegetable oil is applied as needed, in addition to a 3% urea cream following baths. On the scalp, ketoconazole shampoo 20 mg/mL is used on alternate days. The patient has been receiving acitretin at a dose of approximately 0,9 mg/kg/day, along with a first-generation oral antihistamine (hydroxyzine hydrochloride, syrup). On clinical examination, the patient presented with diffusely xerotic and desquamative skin, exhibiting hyperchromic, flattened, thick scales in an ichthyosis-like pattern, involving even the flexural areas. Additionally, palmoplantar keratoderma and nasal cartilage hypoplasia were observed. Moreover, bilateral bipalpebral madarosis and cicatricial ectropion were present, along with right lagophthalmos and corneal ulceration. We recommended discontinuing the use of ketoconazole shampoo and advised shorter baths, without the use of a loofah, substituting regular bar soap with a Syndet cleanser. Furthermore, we maintained the use of the 3% urea cream post-bath and prescribed a moisturizer with technology that targets epidermal barrier restoration, reduction of inflammation and neuronal hyperreactivity, and skin microbiota rebalancing, to be used twice daily. We also replaced the first-generation antihistamine with a second-generation alternative that has fewer sedative properties.** The systemic retinoid therapy was continued. During the follow-up visit, subsequent to the implementation of behavioral measures and the prescription of topical therapy, it was stated a substantial reduction in the perception of pruritus, with no significant improvement in the signs of xerosis and scaling.

Conclusion:

Lamellar ichthyosis is a challenging condition for the healthcare team during the neonatal period, requiring

intensive care. As there is no cure, it is essential to provide multidisciplinary follow-up, focusing on dermatology, pediatrics, and ophthalmology. Genetic counseling is important, as well as fostering a good physician-patient-family relationship.

Abstract N°: 3970

Integrating molecular diagnostics in the practice of dermatology: A perspective from the Philippines

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Introduction & Objectives:

Molecular diagnostics is gaining wider use in dermatology, particularly in dermato-oncology, infectious diseases, inflammatory conditions, and genodermatoses. It enables more accurate diagnosis, prognostication, treatment monitoring, and the potential for targeted symptomatic or gene therapy. In the Philippines, the application of whole exome and transcriptome sequencing is a relatively young field. The project aims to establish a strong collaboration among three institutions to pioneer the use of molecular diagnostics and generate baseline clinical and molecular profiles of epidermolysis bullosa (EB) and other genodermatoses in the Philippines.

Materials & Methods:

A unit for molecular dermatology was newly established in a tertiary hospital in the country. Collaboration was done with a local omics facility and a hospital with genetic center in Taiwan for the ongoing research on baseline profiling of Filipino patients with EB and other genodermatoses (Registry ID: PHRR231002-006183). Patients aged 1 day to 80 years who are suspected to have EB or other genodermatoses – either through clinical evaluation or traditional diagnostics – are recruited into the study, along with two of their family members for trio testing. Following informed consent, demographic and clinical information are collected through interviews. Skin specimens from affected participants are submitted for routine diagnostics, including hematoxylin and eosin staining. Blood and skin tissue samples are sent to the collaborating laboratories for whole exome sequencing (WES), RNA sequencing, and Sanger sequencing. The project also includes training of local personnel to build institutional capacity in performing molecular diagnostics for genodermatoses.

Results:

A collaborative partnership between our hospital and a local omics facility has been established, with the international partner committed to transferring technical expertise to its Filipino counterparts through this initiative. In the first year of project implementation, two patients with EB and six with other genodermatoses, along with 13 family members, were successfully enrolled in the study. Patient ages ranged from 11 days to 19 years. Four patients were referred from the institution's dermatology outpatient clinic, two from the pediatrics department, and the remaining two from private dermatology clinics. Blood and skin tissue specimens were successfully sent to collaborating laboratories. Capacity-building activities for Filipino dermatologists and laboratory technicians will also be carried out as part of this project.

Conclusion:

This project underscores the critical role of inter-institutional collaboration in advancing the application of molecular diagnostics for rare dermatologic conditions in the Philippines. By integrating clinical, academic, and international expertise, the initiative lays the foundation for more accurate diagnoses, improved patient care, and strengthened local capacity in molecular dermatology. The establishment of the molecular dermatology unit, along with ongoing partnerships, marks a promising step toward a more personalized and precise approach to dermatologic care in the country.

Abstract N°: 4179

mucinous breast carcinoma in a patient with neurofibromatosis type 1 : a rare association with prognostic implications highlighting the importance of early screening

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Introduction & Objectives:

Neurofibromatosis type 1 (NF1), is a heterogeneous multisystemic genetic disorder of highly variable severity, caused by a mutation in the NF1 gene and combining neurocutaneous abnormalities marked by brown "café-au-lait" spots and neurofibromas. The lifetime risk of developing cancer for an NF1 patient is 4 to 5 times higher than that of the general population, primarily for malignant peripheral nerve sheath tumor, but also an increased risk of breast cancer has been reported. Mucinous breast carcinoma is a rare histological subtype of breast cancer, representing approximately 2% of invasive breast carcinomas, and typically occurs in women over the age of 62. Despite being invasive, this cancer is often described as a benign-like nodule, both clinically and on imaging and generally has a better prognosis. However, its association with NF1 is rarely reported.

We report a case of mucinous breast carcinoma in a patient with NF1, highlighting how NF1 may influence its prognosis.

Materials & Methods:

We report a case of a female patient with neurofibromatosis type 1 who was diagnosed with mucinous breast carcinoma, hospitalized in the dermatology department. The diagnosis was revealed by the anatomopathological examination and immunohistochemistry in addition to imiging and biological analysis.

Results:

A 69-year-old female patient, with NF1 since childhood, without medical follow-up, presented with a tumoral proliferation on the anterior thoracic wall, following a neglected deep second-degree burn that occurred two months prior to her admission.

Clinical findings included:

- NF1 signs: Multiple neurofibromas, café-au-lait spots (>6), facial melasma and lumbar scoliosis.

- Soft tissue infiltration of the thoraco-abdominal wall with destruction of mammary glands.

- Bilateral cervical and axillary lymphadenopathy.

- Fluid syndrome.

Biological findings included : Normochromic normocytic anemia, lymphocytopenia, cholestasis, inflammatory syndrome, elevated CA-125.

Histopathological and immunohistochemical analysis revealed a mucinous adenocarcinoma with the following profile: CK7+, CK20-, GATA+, CDX2-, ER: 80%, PR: 90%, HER2: positive (score 3), and Ki67 proliferation index: 30%, indicating a breast origin.

Metastatic involvement included clustered axillary and cervical lymphadenopathies, pleural effusion with pulmonary nodules.

The proposed treatment plan consisted of dual HER2 blockade (Trastuzumab-Pertuzumab), with Paclitaxel-based chemotherapy. Hormonal therapy was under discussion.

Due to the advanced stage, the rapid tumor progression, and the occurrence of cardiorespiratory complications, the patient passed away before anticancer treatment could be initiated.

Conclusion:

This rare case of an association between NF1 and mucinous breast carcinoma exhibited an unusually aggressive tumor profile, likely influenced by NF1. HER2 overexpression and high proliferation index contrast with the classical features of this histological type. It underscores the importance of early screening and closer monitoring in NF1 patients, due to the risk of breast cancers with atypical biological profiles and unpredictable progression.

Abstract N°: 4193

Facial angiofibromas in a Tuberous Sclerosis child: Clinical outcome after CO2 LASER ablation

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Introduction & Objectives:

Tuberous Sclerosis or Tuberous Sclerosis Complex (TSC) is a multi-system clinical entity with a genetic background, caused by inherited or sporadic mutations in the TSC1 or TSC2 gene. TSC may affect almost all organs, but most commonly has cutaneous, renal, cardiac, ocular and pulmonary manifestations. The cutaneous clinical findings of the disease typically include hypomelanotic "ash leaf" and confetti macules, facial angiofibromas, ungual fibromas, fibrous cephalic plaques and shagreen patches. We present a case of TSC with multiple facial angiofibromas exhibiting no response to topical sirolimus and significant clinical improvement after ablative CO2 LASER sessions.

Materials & Methods:

A 12-year old male patient presented to our clinic with a confirmed TSC diagnosis (point mutations in intronic loci of the TSC2 gene). Hypomelanotic macules were present at birth, whereas spasms, cerebral hamartomas and arrhythmogenic cardiac rhabdomyomas appeared in infancy. Later, he developed renal angiomyolipomas, a SubEpendymal Giant cell Astrocytoma (SEGA), epilepsy and facial angiofibromas. He had a 3-year neurodevelopmental deficit. Clinically, he presented with diffuse hemispheric papules around the nose and cheeks, in keeping with angiofibromas, distributed on the face, neck, torso and thighs. Periungual fibromas (Koenen tumours) were found on the right thumb and the left index finger. There were longitudinal fissures on both hallux nail plates indicative of subclinical fibromas, while hypomelanotic macules were present on the scalp, torso, upper limbs, thighs and the most sizeable on both gluteal areas. The facial angiofibromas caused negative psychological impact and were thus treated with 0.2% topical sirolimus in petrolatum twice daily for 12 weeks with no response. Subsequent treatment with 12 ablative CO2 LASER sessions every 2 weeks yielded marked clinical improvement.

Results:

Facial angiofibromas, usually appear as round papules during the first decade of life. The most common, non-invasive therapeutic options include topical and oral mTOR inhibitors with reported improvement that may reach 90% when topical sirolimus 0.2% is applied. In our case, this modality was used with poor results. Various invasive modalities have been used to treat angiofibromas, such as dermabrasion, surgical excision, electrocautery, IPL (Intense Pulsed Light) and LASER ablation. In our case, CO2 LASER was selected on the grounds of superior efficacy on fibrous exophytic lesions as in our patient, and resulted in significant improvement that reached 70%.

Conclusion:

Although the clinical outcome of facial angiofibromas in our patient is encouraging, TSC is associated with detrimental effects on patients' psychosocial evolution, clinical status and life expectancy.

Timely diagnosis and efficient preventative and therapeutic strategies with an unyielding commitment to improve children 's quality of life must be an absolute priority. CO2 LASER should be considered as a treatment option in

patients who do not respond to topical treatment.

Abstract N°: 4288

Genotype-Phenotype Relationship in Cutaneous Manifestations of Neurofibromatosis Type 1 in Pediatric Patients from a Tertiary Care Center in Mexico

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Introduction & Objectives: Neurofibromatosis type 1 (NF1) is an autosomal dominant genetic disorder caused by mutations in the NF1 gene. It is characterized by wide clinical variability, including cutaneous manifestations such as café-au-lait spots, neurofibromas, and freckling, as well as extracutaneous features such as Lisch nodules and optic gliomas. Despite being a monogenic disease, phenotypic variability suggests the influence of additional genetic and environmental factors.

To analyze the genotype-phenotype correlation in the cutaneous manifestations of pediatric patients with NF1.

Materials & Methods: An observational, cross-sectional, and ambispective study was conducted based on a historical cohort of pediatric patients diagnosed with Neurofibromatosis Type 1 (NF1) treated at a tertiary care center in Mexico between 2010 and 2024. Clinical and genetic data were collected from medical records meeting inclusion criteria, excluding cases with incomplete data, unconfirmed diagnoses, or genetic alterations unrelated to NF1. The variables analyzed included demographic characteristics, genetic mutations, cutaneous and extracutaneous manifestations, and treatment with selumetinib and its adverse effects. Statistical analysis involved descriptive methods and inferential tests, with significance defined at $p \leq 0.05$.

Results: The sample included 84 patients, 52.4% of whom were female and 47.6% male, with a median age of 9.5 years. The most common mutations were nonsense (28.6%), frameshift (22.6%), and missense (21.4%), with 69% being de novo. All patients presented café-au-lait spots, with an average size of 6 mm. Axillary or inguinal freckling was observed in 96.4% of patients, while cutaneous neurofibromas were present in 41.7% and plexiform neurofibromas in 29.8%. Among extracutaneous manifestations, 25% presented Lisch nodules, and 8.3% had optic gliomas.

Conclusion: This study did not find a significant association between mutation types and cutaneous manifestations in patients with Neurofibromatosis Type 1, suggesting that lesions such as café-au-lait spots and freckling are independent of genotype. The most frequent mutations were nonsense, frameshift deletions (Del FS), and missense. Selumetinib proved to be an effective and safe option for managing unresectable plexiform neurofibromas. These findings emphasize the need to investigate epigenetic and environmental factors to better understand the disease, providing relevant evidence for clinical and therapeutic management.

Abstract N°: 4362

A Diagnostic Challenge in Dermatology: Coexistence of IL17RA and CYP1B1 Mutations in a Pediatric Patient with Chronic Skin Lesions

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Introduction & Objectives:

Primary immunodeficiencies (PIDs) often present with dermatological manifestations that can precede other systemic symptoms. We present a unique pediatric case with chronic cutaneous lesions and dual genetic findings: a homozygous IL17RA mutation and a heterozygous CYP1B1 mutation. This case underscores the importance of interdisciplinary diagnostics in patients with atypical dermatologic phenotypes.

Materials & Methods:

A 16-year-old male presented with follicular papules and pustules from infancy, localized to the mid-axillary line, back, chest, buttocks, and pubic area. Violaceous-red nodular and lichenified lesions were noted on the lower legs. A skin biopsy from the right axilla was performed, followed by histopathological, immunohistochemical, and genetic testing. The patient was evaluated by a multidisciplinary team, including dermatology, immunology, and endocrinology.

Results:

Histopathology showed hyperkeratosis, an intraepidermal neutrophilic blister, and a dermal infiltrate predominantly composed of CD3+, CD4+, CD8-/+ T lymphocytes with sparse CD20+ B cells and CD138+ plasma cells. Fungal infection was excluded. Genetic analysis revealed a homozygous c.441C>A (p.Tyr147*) mutation in the IL17RA gene, associated with autosomal recessive immunodeficiency type 51 (OMIM 613953), typically characterized by chronic mucocutaneous infections. Surprisingly, the patient lacked classical immunological symptoms. Additionally, a heterozygous c.1334G>A (p.Arg448His) mutation in the CYP1B1 gene was identified, associated with congenital adrenal hyperplasia, but without endocrine manifestations in this patient.

Conclusion:

This case highlights an atypical dermatological manifestation of a primary immunodeficiency caused by an IL17RA mutation, compounded by an incidental CYP1B1 mutation. The absence of classical systemic features emphasizes the diagnostic complexity and the necessity for genetic screening in persistent, treatment-resistant skin diseases of unclear etiology.

Abstract N°: 4451

Facial features revealing Muir-Torre Syndrome Associated with Heterozygous MUTYH Mutations

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Introduction & Objectives:

Muir-Torre syndrome (MTS) is characterized by sebaceous skin tumors and internal malignancies, especially colorectal cancer. It is typically autosomal dominant, linked to mismatch repair gene mutations (MLH1, MSH2, MSH6, PMS2). A subset of autosomal recessive cases, termed MTS type II, involves defects in the base excision repair gene MUTYH and accounts for up to 35% of cases. These do not show microsatellite instability.

Materials & Methods:

Case report.

Results:

A 72-year-old male with a personal history of MUTYH-associated polyposis, was referred by oncogenetic consultation to dermatology. Genetic testing revealed heterozygous variants in the MUTYH gene: c.347-1G>C and c.1145G>A (p.Gly382Asp). His medical history included subtotal colectomy for multiple colonic polyps in 2013 and stage II mucinous adenocarcinoma of the jejunum treated with segmental enterectomy in 2020. Family history was significant for colorectal carcinoma affecting his father and sister, and hemicolectomy in another brother due to multiple colonic polyps.

On physical examination, numerous sebaceous hyperplasias were observed on the face, evolving for more than 30 years. A crusted, bleeding lesion in the left frontal region raised suspicion of sebaceous carcinoma or basal cell carcinoma, but excisional biopsy revealed a sebaceous adenoma. He underwent CO_2 laser treatment for multiple facial sebaceous hyperplasias.

Based on the presence of multiple histologically confirmed sebaceous adenomas in conjunction with MUTYH-associated polyposis, a diagnosis of autosomal recessive Muir-Torre syndrome type II was established.

Conclusion:

This case illustrates the typical facial features of Muir-Torre syndrome caused by MUTYH mutations, contributing to the expanding spectrum of phenotypic presentations and highlighting the importance of multidisciplinary surveillance in hereditary cancer syndromes.

Abstract N°: 4454

Quantifying the Increased Risk of Atopic Disorders in Patients with Ectodermal Dysplasias: A Nationwide Registry-Based Study

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Introduction & Objectives:

Ectodermal dysplasias (EDs) have been associated with an increased risk of atopic disorders in surveys and small case series. However, population-based studies on complications and long-term prognosis of patients with ED are lacking. This study aimed to investigate the risk of atopic disorders in a large nationwide cohort of ED patients.

Materials & Methods:

We included a validated nationwide population-based cohort of Danish patients with ED (n=396) and comparators matched by age, sex, and municipality (n=3960). We conducted both case-control and cohort analyses to estimate the risk of hospital-diagnosed atopic disorders before and after ED diagnosis. Secondary analyses utilized dispensed prescriptions from community pharmacies as a proxy for atopic diseases treated outside the hospital setting.

Results:

ED was associated with an increased risk of hospital-diagnosed atopic disorders both before (odds ratio (OR) 2.32, 95% CI 1.62–3.31) and after (hazard ratio (HR) 3.21, 95% CI 2.38–4.34) ED diagnosis. The association was particularly strong for atopic dermatitis (OR 4.68, 95% CI 2.39-9.14; HR 11.33, 95% CI 6.57-19.56). In subgroup analyses, patients with hypohidrotic ED had a particularly high risk of atopic disorders (HR 5.96, 95% CI 3.80-9.34), especially atopic dermatitis (HR 26.74, 95% CI 11.90-60.07). This increased risk for atopic disorders in hypohidrotic ED was further confirmed in secondary analyses using prescription data.

Conclusion:

Patients with hypohidrotic ED have an increased risk of atopic disorders, including atopic dermatitis, asthma, and allergic rhinitis. These results emphasize the importance of optimising care to limit atopic morbidity and improve well-being in this population.

Abstract N°: 4513

A genetic and rare hair shaft abnormality: a case of monilethrix diagnosed dermatoscopically and microscopically with genetic study

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Introduction & Objectives:

The name Monilethrix comes from the monile (Latin for necklace) and thrix (Greek for hair). It is a rare hair shaft abnormality with autosomal dominant involvement.It is usually associated with mutations in type II hair keratin genes located on chromosome 12q13 (KRT81, KRT83 or KRT86). In addition, mutations in Desmoglein 4 have been found in autosomal recessive forms.

In trichoscopy, a dermoscopy method, elliptical nodes and a beaded appearance with regular interval constrictions are seen in the hair shaft. Hair breakage is observed at these constrictions. Hairs may be affected in isolation or may be associated with syndactyly, dental abnormalities, nail abnormalities, keratosis pilaris, and cataracts.

Materials & Methods:

We report a 2-year-old girl who came to our dermatology clinic with hair loss.There was no history of consanguineous marriage in her parents; no hair abnormalities were observed in her mother, father or siblings. In her physical examination, hypotrichosis and broken hairs were observed, predominantly in the vertex and occipital area; there was dryness and brittleness in the hair shafts of the scalp.

Results:

In trichoscopic examination, regular expansions (nodes) and contractions (internodes) were seen in all scalp hair shafts; fractures were seen in the contractions. There was no hair medulla in the internodes. Breakages and extra short hairs were mostly seen in the occipital region, while hyperkeratotic follicular papules were observed in these areas. In microscopic examination of the hair, there were hairs resembling rosary beads, nodes and constrictions. The patient’s laboratory parameters were within normal limits, there were no nail-tooth abnormalities, eye examination was normal, no other skin findings were observed. With these findings, our patient was diagnosed with monilethrix. In the genetic study, a clinical echo panel was performed first and a missense variant heterozygous mutation of (NM_001320198.2):c.1237G>A, p.(Glu413Lys) rs121909129 was observed in the KRT86 gene. The detected variant was studied with single gene point mutation analysis for confirmation and the variant KRT86(NM_001320198.2):c.1237G>A, p.(Glu413Lys) rs121909129 was detected in heterozygous form. After diagnosis, we used topical minoxidil in the patient’s treatment.

Conclusion:

Moniletrix is a rare autosomal dominant genetic hair abnormality with variable expression.

Hair is usually normal at birth but is replaced by abnormal hair in the first few months of life.Clinically, it presents with extremely short, brittle hair, especially in the occipital region, with split ends emerging from keratotic follicular papules; in severe cases, eyelashes, eyebrows, axillary and pubic hair are also affected. The fragility of the hair shaft causes it to fail to reach a normal length.Diagnosis is made by trichoscopy and microscopy.

Monilethrix typically occurs in early childhood and can sometimes resolve spontaneously in adolescence. Treatment may include protection from mechanical damage, topical-oral minoxidil and oral acitretin. Genetic studies and counseling can be provided.

Abstract N°: 4529

Epidermodysplasia verruciformis pityriasis versicolor-like : two new family cases

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Introduction & Objectives: Epidermodysplasia verruciformis (EDV) , or Lutz-Lewandowski syndrome, is a rare genodermatosis generally presenting in childhood, characterized by an abnormal susceptibility to infection by some twenty related group B human papillomaviruses (HPVs). We report two new familial cases of epidermodysplasia verruciformis.

Materials & Methods: Case 1: Patient aged 45, from a 1st degree consanguineous marriage; followed up for EDV having started at the age of 15 with the appearance of multiple flesh-coloured papules associated with hypopigmented macular PV like lesions located on the face and limbs, Recently, there has been an extension of these lesions to the rest of the integument

2nd case: The 40-year-old sister of the first patient presents with EDV that began at the age of 18 with the appearance of hyperperpigmented PV like macules. In addition, there was an ulcerated lesion on the face that had been evolving for several months, and whose biopsy excision was consistent with basal cell carcinoma.

Treatment with Acitretin 1 mg/kg/d with photoprotection measures was initiated, resulting in stabilization of the disease.

Results: Epidermodysplasia verruciformis is a multifactorial disease involving genetic, immunological and environmental factors in addition to specific viruses. The mode of transmission of epidermodysplasia verruciformis is usually autosomal recessive. Felix Lewandowsky and Wilhelm Lutz first described the condition clinically. The most frequently observed skin lesion is a macular rash similar to that seen in pityriasis versicolor, accompanied by scaly, verrucous papules. The risk of transformation, particularly into squamous cell carcinoma, is high. Several treatments have been tried (retinoids, interferon, cimetidine) with little or no reproducible success. The most important thing is sun protection, assiduous clinical monitoring and rapid excision of any lesions on the verge of carcinomatous degeneration**.**

Conclusion: This case highlights the importance of early diagnosis and management of EDV, including photoprotection and regular monitoring of precancerous lesions. Treatment options, ranging from pharmacological interventions to surgical excision, aim to reduce the risk of malignant transformation.

Abstract N°: 4736

The Price of Exposure: Xeroderma Pigmentosum and Skin Cancer

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Introduction & Objectives:

Xeroderma Pigmentosum (XP) is a rare autosomal recessive genodermatosis characterized by a defect in the nucleotide excision repair pathway of DNA. This condition leads to extreme photosensitivity, pigmentary changes, premature aging and increased risk of UV-induced skin and mucous membrane neoplasms.We report a case of squamous cell carcinoma in a 55-year-old female with XP. ### **Case Report** A 55-year-old female presented with a single asymptomatic skin lesion on left cheek that developed over the past two years. Examination revealed a well-defined, round to oval black raised nodulo-plaque, with a central adherent crust and raised superior margin. Histopathological examination revealed an invasive tumor arising from hyperplastic and dysplastic squamous epithelium with cytokeratin positivity.

Discussion

XP presents significant clinical challenges due to its severe photosensitivity and the associated risk of developing multiple skin cancers at a young age which highlights the necessity for ongoing research into effective treatments and preventive strategies. Genetic counseling can play a vital role for families, enabling them to understand the implications for future generations. Increased awareness can help improve the quality of life and reduce the incidence of associated malignancies.

Abstract N°: 4766

Optimizing photoprotection and patient education in xeroderma pigmentosum: A two-year follow-up study in Nepal

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Introduction & Objectives:

Xeroderma pigmentosum (XP) is frequent in Nepal. In a first study, we found that nearly all patients had a XPC mutation resulting from the specific homozygous mutation c.1243 C > T, p.R415X, with a severe phenotypic profile in most cases (1). We thereafter highlighted that the frequency of ocular and cutaneous malignancies widely resulted from an inadequate understanding of disease etiology and photoprotection measures (2). Given the critical role of patient education in preventing skin tumors (3), this study revisited and extended the XP cohort from 2 years ago (2) to reassess their prevention habits and evaluate the impact of recent educational measures.

Materials & Methods:

Among 30 previously enrolled patients in 2022 (median age 16 years), 1/3 were lost to follow-up. The remaining 20 and 13 additional ones were (re-)assessed in 2024 using the same standardized questionnaire concerning access to information, sun protection and dermatological care.

Results:

Some 15 patients (75%) from the previous cohort stated being aware of clinical signs warranting dermatological consultation, but only 8 (40%) had been seen by a dermatologist in the meantime; 8 underwent surgical excision of tumors; 8 reported having received new information about XP; 7 expressed a desire for further details about the origins of skin lesions; 10 felt adequately informed, although only 1 was aware of all sources of UV radiation, including indirect exposure via windows and artificial light. Photoprotection practices showed modest improvements: 9 patients reported having enhanced protection measures; however, only 6 used full-body covering clothing (long sleeves, pants, gloves and hat), and 7 did not protect effectively their face or hands. About half reported using sunglasses, though many were basic tinted lenses without effective UV filtering. A dedicated sun protection mask was available for 4 patients, but only 2 wore it systematically, 1 occasionally, and 1 avoided it due to discomfort. The number of patients using daily sunscreen doubled from 6 to 12, often reflecting gift of product during previous consultations.

Data from 13 newly enrolled patients (median age 11.5 years) showed even less favorable results. Despite some regular follow-up, many lacked a comprehensive understanding of UV risks: 4 were unaware of the role of UV in tumor development, and half did not know the risk related to indirect exposure. Full adherence to protective measures was low, with only 1 patient systematically covering the entire body and a minority using accessories such as gloves or proper headgear.

Conclusion:

These findings highlight persistent gaps in both knowledge and photoprotection practices, emphasizing the need for intensified educational initiatives, culturally appropriate communication strategies, and improved access to effective photoprotection tools. A multifaceted approach, including regular follow-up, is essential to reduce XP-related morbidity and mortality in Nepal.

1 - Espi P et al. Clinical and genetic characteristics of xeroderma pigmentosum in Nepal. JEADV 2018 ;32:832-9.

2 - Fournier M et al. Access to information, sun protection and dermatological care in patients with xeroderma pigmentosum in Nepal. JEADV Clin Pract. Août 2024; jvc2.494.

3 - Morgan M et al. The influence of perceived medical risks and psychosocial concerns on photoprotection behaviours among adults with xeroderma pigmentosum: a qualitative interview study in the UK. BMJ Open 2019 Feb.

Abstract N°: 4800

A rare genodermatosis: Dowling Degos Disease

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A rare genodermatosis: Dowling Degos Disease

Introduction

Dowling-Degos disease (DDD) is a rare autosomal dominant genodermatosis characterized by acquired reticular hyperpigmentation, typically affecting flexural areas such as the axillae, groin, face, neck, arms, and trunk. Mutations in various genes, including KRT5, POFUT1, POGLUT1, and recently PSENEN, have been implicated in its pathogenesis, affecting melanosome trafficking and interactions between melanocytes and keratinocytes. Clinically, patients present with symmetrical hyperpigmented macules, comedo-like lesions, and acneiform scars. Dermoscopy aids diagnosis, showing characteristic patterns such as reticulated pigmentation, comedo-like openings, and follicular pigmentation.

Case Presentation

This report describes a 53-year-old female patient presenting with a decade-long history of reticular hyperpigmented macules and pinpoint papules with keratin plugs in bilateral axillae. Additional clinical manifestations included dark brown lesions on the labia majora, nodular and pustule-associated lesions in inguinal areas, and an abscess-like lesion on the right breast. Dermoscopic examination revealed brown, star-like areas with irregular projections and hypopigmented centers on a brownish background. Histopathological analysis from an axillary biopsy demonstrated hyperkeratosis, thin branching hyperpigmented epithelial strands extending into the dermis, follicular plugging, and horn cysts, findings consistent with Dowling-Degos disease.

Genetic analysis via peripheral blood sampling, screening known DDD-related genes including KRT5, POFUT1, POGLUT1, PSENEN revealed no significant mutations. This result highlights potential unknown genetic contributors, suggesting a sporadic case and emphasizing the need for further genetic research.

Differential diagnoses considered included acanthosis nigricans, reticulate acropigmentation of Kitamura, dyschromatosis universalis hereditaria, dyschromatosis symmetrica hereditaria, and Galli-Galli disease. Clinical and histopathological features effectively excluded these entities, reinforcing the definitive diagnosis of DDD.

Notably, DDD is frequently associated with hidradenitis suppurativa (HS), a chronic inflammatory condition manifesting as nodules, abscesses, sinus tracts, and fibrotic scars predominantly in intertriginous areas. Despite the atypical presentation, the patient's clinical picture suggested concurrent HS, aligning with established associations described in the literature.

Conclusion

In conclusion, recognizing Dowling-Degos disease is vital for accurate diagnosis and differentiation from other pigmentary disorders. Comprehensive evaluation, encompassing clinical, dermoscopic, histopathological, and genetic analyses, is essential. This case underscores the variability of genetic mutations involved and highlights the importance of considering DDD-associated conditions such as hidradenitis suppurativa. Increased awareness and detailed reporting of cases contribute significantly to understanding the disease spectrum and facilitating prompt diagnosis and management.

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Abstract N°: 4833

Lipoid proteinosis in twin sisters: Clinical, histopathological, and dermoscopical findings of a rare genodermatosis

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Introduction & Objectives: Lipoid proteinosis (LP), or Urbach-Wiethe disease, is a rare autosomal recessive disorder caused by mutations in the ECM1 gene, leading to the accumulation of hyaline-like material in the skin, mucous membranes, and various internal organs. Clinically, it presents with hoarseness from infancy, vesiculobullous and keratotic skin lesions, atrophic scarring, and moniliform blepharosis (beaded eyelid papules). First described in 1929, LP has an estimated 500 reported cases worldwide and is more prevalent in regions with high rates of consanguinity, such as Turkey.

This report aims to present the clinical, dermoscopic, and histopathological findings in twin sisters with lipoid proteinosis, and to emphasize the importance of early diagnosis, site-specific dermoscopy, and the potential role of isotretinoin in treatment.

Materials & Methods: Two 20-year-old identical twin sisters presented with hoarseness and progressive skin lesions. Dermatological examination revealed multiple hyperkeratotic papules and plaques on the elbows, eyelid margins, and hands, along with atrophic scars on the face and extremities. Eye examination showed characteristic beaded papules on both upper and lower eyelids.

Dermoscopy with a polarized Dermlite DL4 revealed pale, structureless areas with sulci and gyri on the elbows, pinkish-white "pulpy" clumps on the extremities, and beaded papules with distichiasis on the eyelids. Laboratory tests showed elevated anti-TPO and anti-TG levels in one twin, with mild elevations in the other; other parameters were normal.Histopathological examination of a skin biopsy confirmed the diagnosis by showing hyperkeratosis, focal epidermal atrophy, and deposition of eosinophilic hyaline material surrounding dermal vessels, along with chronic perivascular inflammation.

Genetic testing revealed a pathogenic ECM1 mutation. Laryngoscopy revealed normal vocal cord movement, but glottic closure defect and thick sublingual frenulum. Both patients had developmental dysplasia of the hip (DDH), with a history of pelvic osteotomy. Radiographs showed Crowe type III/II in one and IV/I in the other.

Treatment with oral isotretinoin (20 mg/day) was initiated for both patients.

Results: Both patients displayed classic mucocutaneous findings of LP. Dermoscopic findings were consistent with previous literature and proved helpful in supporting the diagnosis. Histopathological and genetic analyses confirmed the condition.

Thyroid autoantibodies were elevated, although patients were euthyroid. Systemic examination ruled out neurological and gastrointestinal involvement.

Following one month of oral isotretinoin therapy, a partial response was observed, particularly in the reduction of hyperkeratotic lesions. The drug was well tolerated with no adverse effects reported.

Conclusion: LP is a rare genetic disorder that often presents in early life with progressive mucocutaneous involvement. In high-risk populations, early clinical suspicion, supported by dermoscopy and confirmed through biopsy and genetic testing, is essential. Systemic retinoids like isotretinoin may offer partial clinical benefit. As no curative treatment exists, patient education and genetic counseling are crucial for long-term management and family planning.

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Abstract N°: 4871

Mosaic Incontinentia Pigmenti in a Male Infant with Extensive Cutaneous Disease, Bilateral Retinopathy, and Neurologic Abnormalities

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Introduction & Objectives: Incontinentia Pigmenti (IP) is an X-linked dominant disease, typically seen exclusively in females because most affected males die in utero. IP is caused by a mutation in the Inhibitor of Nuclear Factor-κB Kinase Regulatory Subunit Gamma (*IKBKG)/* Nuclear Factor-κB Essential Modulator *(NEMO)* gene, typically presenting at birth or within the first few weeks of life and progressing through four stages of skin lesions: vesicular (birth-4 months), verrucous (2-24 months), hyperpigmented (6 months-adolescence), and hypopigmented/atrophic (adolescence-adulthood). Herein, we present a rare case of IP in a male infant with extensive cutaneous disease, bilateral retinopathy, and evidence of neurologic abnormalities.

Materials & Methods: A 12-day-old male was referred for evaluation of skin changes present since birth. He was born at 40 weeks and 3 days via a vacuum-assisted vaginal delivery and uneventful pregnancy. He was otherwise growing well with no other health concerns. He had four older healthy siblings (two females and two males) with no history of congenital skin disease in the extended family. Parents denied consanguinity and prior history of miscarriages. Mother reported no changes to her skin, hair, teeth, or sweating. A full skin examination revealed scattered vesicles with raised violaceous-to-brown verrucous papules and plaques extensively distributed in linear Blaschkoid streaks over the upper and lower extremities and trunk. No nail changes, hair abnormalities, or oral lesions were identified. A 3-mm skin punch biopsy obtained from a representative lesion on his right anterolateral thigh revealed epidermal acanthosis and hyperkeratosis with scattered dyskeratotic keratinocytes and pigment incontinence. In addition, a superficial perivascular inflammatory infiltrate with scattered eosinophils was noted. A complete blood count returned peripheral eosinophilia.

Results: Our case had characteristic clinical and pathological features of IP. Therefore, referrals were placed for ophthalmology, neurology and clinical genomics consultations. He was found to have significant bilateral retinopathy with peripheral avascular retina requiring serial panretinal photocoagulations. Brain MRI revealed a focal area of hyperintense T2 signal in the right inferior temporal lobe gyrus, representing an area of chronic gliosis potentially related to a small remote infarct. Reassuringly, his neurologic exam remains normal and he is achieving appripriate developmental milestones as expected at 11 weeks. For skin-directed management, he was recommend to apply petroleum jelly daily. Chromosomal microarray demonstrated normal XY karyotype and an Xq25 deletion of uncertain significance which did not involve the *IKBKG/NEMO* gene location located on chromosome Xq28, ruling out XXY/Klinefelter Syndrome. This points to our case having a post-zygotic somatic mutation in the *IKBKG/NEMO* gene.

Conclusion: Most patients with IP who are affected by somatic mutations in the*IKBKG/NEMO* gene tend to have milder and limited phenotypes of disease. However, our patient had extensive cutaneous involvement as well as notable retinal and neurologic extracutaneous manifestations. This case underscores the importance of screening for extracutaneous manifestations of IP even in male infants with somatic disease, especially if the skin involvement is extensive.

Abstract N°: 4941

Successful treatment of epidermolysis bullosa pruriginosa with Tofacitinib- A case report

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Introduction & Objectives: Epidermolysis bullosa (EB) pruriginosa is a rare and distinctive clinical subset of dystrophic EB. It is characterized by marked itching and nodular prurigo-like lichenified lesions predominantly over legs, occasional trauma-induced blistering, excoriations, nail dystrophy and albo-papuloid lesions. Skin manifestations may present at birth or occur as later. The diagnosis is based on characteristic clinical features, alteration in the number and ultrastructure of anchoring fibrils and mutation analysis involving type VII collagen. The inheritance can be autosomal dominant, recessive or sporadic in nature. There are no standard treatment guidelines for the management of this rare disease. We present a case of EB pruriginosa that was successfully treated by us with the use of tofacitinib.

Materials & Methods: A 22-year-old lady came with itching, blistering, erosions & scarring on the legs, forearms & nail dystrophy. She gave history of her nails being dystrophic since birth or not growing normally. The skin lesions began at the age of 10. But became more severe for the last 3 years. A skin biopsy done for histopathology was suggestive of EB pruriginosa. Her younger brother & aunt were having nail dystrophy but no skin lesions. She was treated with multiple drugs in the past like dapsone, colchicine, methotrexate, prednisolone, cyclosporine, ketotifen, antihistamines, topical steroids, etc. There was no improvement. When she came to us for the first time, we started her on mycophenolate mofetil to which there was partial improvement. It was changed to Apremilast. But there was no response to it. Thus, we put her on tofacitinib 5 mg twice daily.

Results: The skin lesions began to heal by 1 month & there was complete healing as well as subsidence of itching by 4 months. The drug has been continued till date. The side effect of weight gain and hyperlipidemia has happened at the end of 10 months.

Conclusion: This rare condition of epidermolysis bullosa pruriginosa was successfully treated with tofacitinib.

Abstract N°: 4998

Neurofibromatosis Noonan Syndrome : A Rare Case Report and Clinical Insights

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Introduction & Objectives:

Noonan-Neurofibromatosis Syndrome (NNFS) is a rare RASopathy syndrome. Affected patients exhibit a combination of clinical features typical of both Neurofibromatosis Type 1 (NF1) and Noonan Syndrome.

Our case report explores Noonan-Neurofibromatosis Syndrome (NNFS), highlighting its clinical and genetic features, and discussing the diagnostic challenges and management strategies associated with this rare RASopathy.

Materials & Methods:

In this report, we detail the case of a patient diagnosed with Noonan-Neurofibromatosis Syndrome (NNFS)

Results:

We report the case of a 16-year-old boy with a family history of Behcet's disease on the mother's side and café-au-lait spots on the father's side. He presented with cervical and trunk masses that had been evolving since birth.

Clinical examination revealed multiple soft, poorly defined masses, some topped with erythematous plaques and pustules. Café-au-lait spots were located on the trunk and limbs, with numerous lentigines in the axillary and inguinal regions. Additionally, there was a painless soft swelling of the left buccal mucosa, dento-maxillary disharmony, and left parotidomegaly. Ophthalmologic examination revealed a single Lisch nodule in the right iris. The patient also had growth retardation, thoracolumbar scoliosis, hypertelorism, a pterygium colli, and low-set, posteriorly rotated ears.

A cervical MRI showed diffuse infiltration of the soft tissues of the left cervicofacial and right cervical regions. Further paraclinical investigations to screen for malformations did not reveal any abnormalities.

Surgical excision was performed, and histopathological findings confirmed the presence of nodular and plexiform neurofibromas.

The diagnosis of NNFS was established based on the diagnostic criteria corresponding to both Noonan Syndrome and NF1. In our patient, the criteria for Noonan Syndrome included growth retardation, hypertelorism, pterygium colli, and low-set posteriorly rotated ears. For NF1, the patient presented with more than six café-au-lait spots larger than 15 mm, lentigines, nodular and plexiform neurofibromas, and scoliosis.

Conclusion:

NNFS can present with a wide range of symptoms and clinical signs in affected patients. Regular follow-up with a dermatologist, cardiologist, and ophthalmologist, as well as orthopedic monitoring, is essential to ensure close surveillance and to detect any complications related to the disease.

Abstract N°: 5012

Dupilumab as a therapeutic alternative in severe and refractory erosive Darier disease: a case report

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Introduction & Objectives:

Darier disease (DD) is a rare autosomal dominant genodermatosis caused by mutations in the *ATP2A2* gene, which encodes the SERCA2b calcium pump. The impaired calcium homeostasis leads to defective keratinocyte adhesion and differentiation. Erosive lesions are common in DD, especially in intertriginous areas, lower legs, and feet; however, their formation may be influenced by specific mutant genotypes alongside environmental triggers. Treatment is challenging, particularly in erosive or intertriginous forms, where oral retinoids may exacerbate lesions. There are currently no therapeutic guidelines for DD, highlighting the need for standardized therapies, especially for patients unresponsive to first-line treatments or who have contraindications.

Materials & Methods:

Case report and literature review.

Results:

We present the case of a 55-year-old man with a history of DD spanning over 20 years, previously treated with acitretin, isotretinoin, doxycycline, systemic and topical corticosteroids, cyclosporine, CO_2 laser therapy, and botulinum toxin. Despite multiple therapies, disease control remained suboptimal. He was admitted with a severe flare involving 60% of his body surface area, presenting with extensive erosive and macerated lesions on the occipital scalp, posterior neck, back, flanks, groin, and inner thighs. Laboratory results showed renal dysfunction, electrolyte imbalance, hypoalbuminemia, and liver profile abnormalities—findings consistent with a systemic inflammatory response resembling that seen in patients with extensive burns. Bacterial and viral superinfection were ruled out upon admission.

Initial treatment included intravenous methylprednisolone pulses and secukinumab, with no significant improvement after five weeks. Therapy was then switched to dupilumab, leading to clinical improvement, enhanced mobility, and the onset of re-epithelialization. Oral acitretin was later added due to the emergence of new crusted lesions. After six months of combined dupilumab and acitretin therapy, the patient remained stable, with sustained improvement and erosions affecting less than 1% of his body surface.

Conclusion:

To our knowledge, only one previous case of DD treated with dupilumab has been reported. The drug has shown efficacy in genodermatoses with pathophysiologic similarities to DD, such as Hailey-Hailey disease. A proposed mechanism for dupilumab's effectiveness in DD involves IL-13 inhibition, which may enhance calcium influx into keratinocytes, thereby improving adhesion and differentiation. Additionally, we suggest that downregulation of Th2-mediated inflammation may contribute to reduced skin inflammation and lesion severity.

This case supports the potential role of dupilumab as a promising therapeutic option in severe or treatment-refractory DD, particularly in erosive and intertriginous forms. Further studies are warranted to explore the efficacy and safety of targeted biologics in genodermatoses such as DD.

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Abstract N°: 5272

Localized Darier Disease: A Rare Case of Exclusive Nasal Involvement

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Introduction & Objectives:

Darier disease (DD) is a rare autosomal dominant acantholytic dermatosis with an estimated prevalence of 1 in 30,000–100,000. It is characterized by keratotic papules, focal loss of adhesion, and abnormal keratinization, predominantly in seborrheic areas, usually beginning after puberty. Both sexes are equally affected. A localized form of DD, first described by Kreibich in 1906, accounts for approximately 10% of cases. Several clinical variants have been reported, including unilateral, linear, segmental, and zosteriform forms. Predominant nasal involvement is uncommon. We report a sporadic case of DD with lesions strictly localized to the nose.

Materials & Methods:

J.F.M., a 60-year-old man, presented with a 20-year history of a persistent erythematous, hyperkeratotic, pruritic, scaly, and friable lesion on the nasal dorsum, with recurrent bleeding and significant impact on quality of life. He had been previously misdiagnosed with pemphigus foliaceus and treated with oral prednisone and topical mometasone, without improvement. Due to the lack of response, a new biopsy was performed, revealing: "Skin fragment showing epidermis with irregular foci of acanthosis and spongiosis, columns of parakeratosis with marked dyskeratosis, presence of corps ronds, and suprabasal clefting — findings consistent with Darier disease." Systemic isotretinoin therapy was initiated, resulting in good initial response and marked improvement in quality of life. The patient, previously ashamed of the lesion, no longer needed to cover his face with a mask in public.

Results:

Darier disease, first described by Prince Marrow in 1886 and later by Darier and White in 1889, is caused by mutations in the ATP2A2 gene on chromosome 12q23–12q24. This gene encodes the sarco/endoplasmic reticulum Ca^{2+} ATPase type 2 (SERCA2). Its dysfunction leads to calcium imbalance, loss of cellular adhesion, and characteristic histological features such as acantholysis and dyskeratosis. Localized DD is rare, and segmental forms have been described. Triggering factors include sun exposure, heat, sweat, and occlusion. Secondary infections are common. Associated conditions may include neuropsychiatric disorders and squamous cell carcinoma. Treatment remains challenging, as no curative option is available. First-line therapy includes topical corticosteroids or retinoids, while systemic retinoids are reserved for extensive or refractory cases.

Conclusion:

Darier disease is a rare and often underdiagnosed dermatologic condition with heterogeneous clinical manifestations. Nasal-localized presentation is exceptional and may delay diagnosis. Histopathological confirmation is essential for accurate diagnosis and appropriate treatment. Although several therapies have been described, clinical effectiveness remains limited.

Abstract N°: 5299

Multiplexed Assays of Variant Effect and Re-classification of TYR Variants in Chinese Oculocutaneous Albinism Patients

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Introduction & Objectives: Oculocutaneous albinism type 1 (OCA-1), caused by mutations in the tyrosinase (TYR) gene, is the most common form of albinism worldwide. Due to the variants of uncertain significance (VUS) classified by The American College of Medical Genetics and Genomics (ACMG) guidelines, patients who carry these VUS do not receive a definitive molecular diagnosis. In order to clarify the pathogenicity of the VUS variants, we conducted multiplexed assays of variant effect (MAVEs) to re-classify the TYR VUS variants.

Materials & Methods: Protein expression, melanin production, enzyme activity, and subcellular localization were applied to 46 selected variants: 27 VUS from 1243 albinism patients, 14 pathogenic/likely pathogenic (P/LP) and 5 benign/likely benign (B/LB) control variants. OddsPath values were calculated as recommended by Brnich et al (2019).

Results: By conducting MAVEs, PS3_moderate or PS3_supporting evidence was applied. 25 out of 27 VUS were re-classified as LP, 3 out of 11 LP variants as P by following the ACMG guidelines. Therefore, 19 out of 20 (95%) previously undiagnosed patients had a molecular diagnosis of OCA-1. In addition, the pathogenic

mechanisms of TYR have been elucidated and categorized.

Conclusion: These comprehensive MAVEs provide a robust approach for curating TYR VUS. This study advocates MAVEs for validating

an accurate genotype-phenotype relationship.

Abstract N°: 5310

Genotype-phenotype spectrum and correlations in Chinese patients with keratinocytic epidermal naevus: A retrospective study of 22 cases

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Introduction & Objectives:

Keratinocytic epidermal naevus is characterised by hyperkeratotic lesions arranged along Blaschko's lines. So far, multiple genes have been implicated, but there is no detailed data or genotype-phenotype correlation studies of keratinocytic epidermal naevi in Chinese patients. We aim to evaluate the clinical, histopathological and genetic features, genotype-phenotype correlations of keratinocytic epidermal naevus in the Chinese population.

Materials & Methods:

A retrospective study of patients with keratinocytic epidermal naevi referred to the Department of Dermatology, West China Hospital, in the last four years. Medical history, clinical data, histopathological characteristics, and evidence of genetic mutations were collected from 22 unrelated Chinese patients with this problem.

Results:

The distribution of the keratinocytic epidermal naevi exhibited right-side dominance. Non-epidermolytic epidermis naevus was much more common. Eight reported missense mutations were found in this study, which were detected in five genes, including *HRAS, KRT10, FGFR3, GJB2,* and *PIK3CA*. *HRAS* was the most commonly affected gene (9/22, 40.91%) in this study, with the c.37G>C (6/22, 27.27%) substitution representing a possible hotspot mutation. Mutation allele loads were higher in the affected lesions than blood samples. Epidermolytic epidermal naevus was found in three patients exclusively carrying *KRT10* mutations. Inflammatory epidermal naevi were caused by mutations of *KRT10* and *PIK3CA*. Most of the mosaic mutations detected in keratinocytic epidermal naevi patients were the same as germline mutations identified in systemic diseases caused by these genes.

Conclusion:

Our findings reveal the genotype-phenotype spectrum and their correlation amongst Chinese patients with keratinocytic epidermal naevi. In addition, our data underscores the importance of genetic testing in lesional skin to help characterise and categorise keratinocytic epidermal naevi, decide on a therapeutic strategy, and offer genetic counselling and prenatal diagnosis.

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Abstract N°: 5338

Mosaic pachyonychia congenita caused by postzygotic KRT6A mutation: clinical manifestations and genetic implications

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Mosaic pachyonychia congenita caused by postzygotic *KRT6A* mutation: clinical manifestations and genetic implications

Introduction & Objectives:

Pachyonychia Congenita (PC) is a rare genodermatosis caused by keratin gene mutations and characterized by hypertrophic nail dystrophy, palmoplantar hyperkeratosis, follicular keratosis, and oral leukokeratosis. Until now, all reported PC cases exclusively resulted from germline mutations. This report presents a case of mosaic PC caused by a postzygotic *KRT6A* mutation, aiming to explore its distinctive clinical manifestations and its implications for intergenerational genetic risk assessment.

Materials & Methods:

Following institutional ethics approval and informed consent, blood samples from the proband and unaffected parents were analyzed via whole-exome and Sanger sequencing.

Results:

The proband exhibited onychodystrophy and bilateral plantar hyperkeratosis progressing over two decades. Nail involvement manifested as marked thickening and dystrophy affecting multiple toenails along with the 2nd, 3rd, 5th fingernails of the left hand. The remaining nail plates exhibited fragility with a tendency to fracture (Fig. 1a-b). Bilateral plantar focal hyperkeratosis predominantly affected the forefoot and heel, accompanied by punctate hyperkeratosis along the lateral borders without hand involvement (Fig. 1c). Oral leukokeratosis was observed on bilateral buccal mucosa (Fig. 1d). Genetic testing identified a heterozygous c.516_518del (p.Asn172del) mutation in the *KRT6A* gene with a mutation allele load of 28.2627%.

Conclusion:

To the best of our knowledge, we reported the first case of mosaic PC and revealed its distinctive clinical manifestations. Notably, the generalized nail dystrophy with bilateral plantar hyperkeratosis observed in this case deviated from the classic segmental distribution patterns of mosaic dermatoses. Moreover, the varying severity of involvement in different nail units and plantar regions contrasted with the uniform manifestations characteristic of germline mutations. These distinct phenotypic patterns suggest that generalized yet regionally heterogeneous manifestations may represent a distinctive characteristic of mosaic PC. Importantly, two published cases documented asymptomatic parental *KRT6A* mosaicism transmitting PC through germline transmission1, 2, suggesting the gene’s intrinsic predisposition to mosaicism and highlighting the need for prioritizing genetic risk assessment to prevent intergenerational transmission of pathogenic variants.

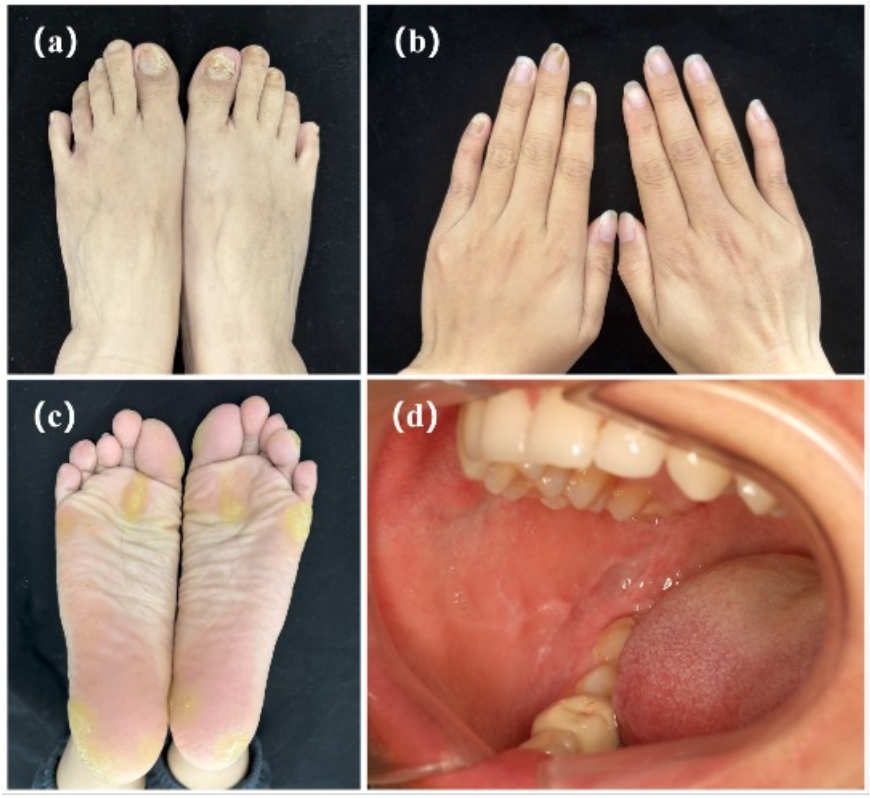

Figure 1. (a-b) Pachyonychia affecting the hands and feet. (c) Bilateral plantar focal and punctate hyperkeratosis. (d) Oral leukokeratosis.

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Abstract N°: 5439

Transforming mechanical stress into therapeutic power: Activation of Piezo1 and TRPV4 counteracts mechano-induced damage of cellular junctions in Hailey Hailey disease

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Introduction & Objectives:

Hailey-Hailey disease (HHD) is characterized by impaired intracellular calcium transport due to ATP2C1 mutations, leading to defective interkeratinocyte adhesion and acantholysis, especially under mechanical stimulation, which exacerbates the disease. Despite the clinical consensus on the link between mechanical stimulation and HHD progression, effective therapeutic strategies targeting the mechanical aspects of the disease remain unexplored. The aim of this study is to introduce a novel mechanotherapeutic approach that leverages the overactivation of mechanosensitive calcium channels, transforming destructive mechanical forces into therapeutic power.

Materials & Methods:

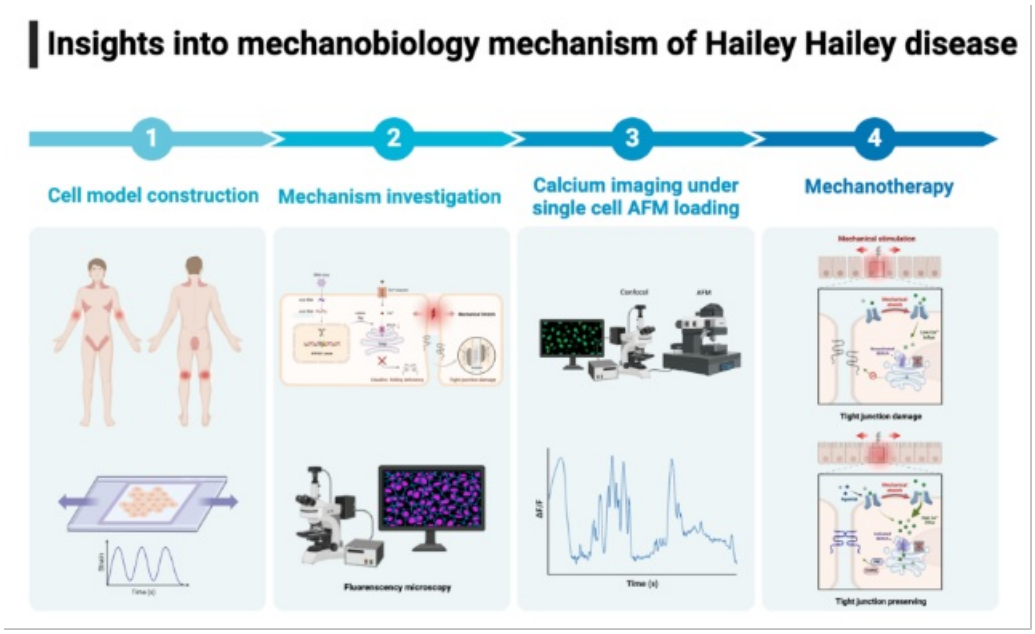
First, we collected tissue specimens from HHD patients and normal controls (with ethical approval and signed informed consent forms in person) to explore the changes in intercellular junction proteins and mechanically sensitive ion channels. Then we employed an experimental design involving ATP2C1 knockdown HaCaT cells to assess the effects of mechanical stretching on intercellular junctions. We compared the protective effects of high-calcium environments and tested specific agonists for mechanosensitive calcium channels by calcium imaging under AFM single-cell mechanical loading, specifically Piezo1 and TRPV4, to evaluate their ability to restore junction integrity under mechanical stress.

Results:

Our findings revealed that mechanical stretching significantly disrupted intercellular junctions in ATP2C1 knockdown cells, while high-calcium environments offered limited protective effects. Remarkably, agonists of Piezo1 and TRPV4 fully restored junction integrity during mechanical stress without necessitating additional calcium supplementation. This effect was not observed with non-mechanosensitive calcium channel agonists like TRPA1 and TRPV1. Additionally, atomic force microscopy and molecular analyses demonstrated that Piezo1 and TRPV4 agonists accelerate calcium uptake during mechanical stimulation, with calcium being transported via SERCA channels to stabilize intercellular junctions.

Conclusion:

These findings highlight a potential paradigm shift in treating blistering diseases by utilizing mechanical stimulation and mechanosensitive pathways to restore cellular function.


Insights into mechanobiology mechanism of Hailey Hailey disease
1
2
3
4
Cell model construction
Mechanism investigation
Calcium imaging under single cell AFM loading
Mechanotherapy
Confocal
AFM
Fluorescency microscopy
Time (s)
Tight junction damage
Tight junction preserving

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Abstract N°: 5527

Effectiveness of Treatment with Anti-IL-4Rα for Recalcitrant, Generalized Eczema Complicated with Hypohidrotic Ectodermal Dysplasia

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Introduction & Objectives:

Hypohidrotic ectodermal dysplasia (HED) is a rare genodermatosis characterized by faulty development of the ectodermal structures, causing symptoms including hypohidrosis, hypotrichosis, and hypodontia. Genetic variants render HED patients with increased epidermal permeability and decreased dermcidin expression, putting them at greater risk for eczema. However, optimal treatment and prognosis of this condition remain underexplored.

Materials & Methods:

We documented the treatment responses of anti-IL-4Rα in two cases of HED with refractory, generalized eczema.

Results:

A 33-year-old male presented with generalized, relapsing eczematous dermatitis, tooth agenesis, sparse hair, and little sweating since childhood. The itchy skin condition had been refractory to topical steroids, methotrexate, azathioprine, cyclosporin, and phototherapy, constituting a total eczema area and severity index (EASI) score of 35.8. Whole exome sequencing identified a nonsynonymous variant in *WNT10A* (c.G637A) and a novel stop gain variant in *EDA1* (c.C120A), both predicted to be disease-causing. Skin biopsy of lesional skin showed findings compatible with HED complicated with severe eczema. Laboratory workup revealed elevated serum levels of immunoglobulin E (IgE), and Th2 -dominated inflammatory markers, including interleukin (IL)-31, thymic stromal lymphopoietin (TSLP), C-C motif chemokine 22 (CCL22), pulmonary and activation-regulated chemokine (PARC), and thymus- and activation-regulated chemokine (TARC). After informed consent, standard treatment of anti-IL-4Rα was initiated, which started from a loading dose of 600mg followed by a 300mg injection every two weeks. The skin lesions improved gradually without encountering any adverse events, and eventually reached an EASI score of 19.5 at 12-month-followup. Additionally, both serum IgE level and Th2-skewed inflammatory markers gradually improved during the anti-IL-4Rα treatment (Figure 1).

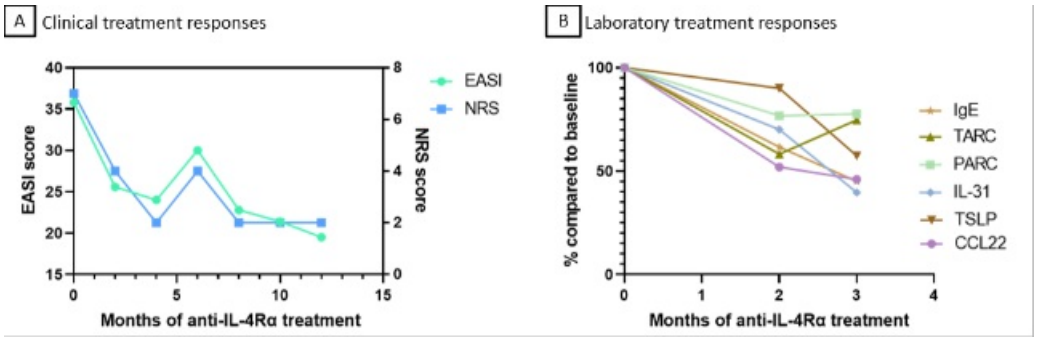
Another 12-year-old male patient diagnosed with HED with a family history and atopy, was referred to our clinic for scattered eczematous lesions on multiple body parts for long, constituting an EASI score of 12.6 with markedly elevated IgE level upon examinatio. Previous workup revealed a nonsynonymous variant in *EDA1* (c.C466T), which has been considered causative for X-linked HED. Similarly, the itchy skin rash could not be controlled by topical agents. After informed consent, standard treatment of anti-IL-4Rα was provided along with topical agent use. After 2 months of treatment, improvements in redness, edema, scratching, and lichenification could already be note, with a gradual reduction in serum IgE levels. After 12 months of anti-IL-4Rα use, further improvements in skin condition and an amelioration in EASI score to 5.5 could be appreciated. Besides mild conjunctivitis, there was no other adverse effect or complication throughout the treatment course.

Conclusion:

Our findings suggest that the presence of severe eczema in HED patients could be stably and safely managed with

anti-IL-4Rα, warranting further investigation.

Figure 1. Clinical and laboratory treatment responses of anti-IL-4Rα in the first case.



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Abstract N°: 5611

Rare Genodermatosis Unveiled: A Case Series of Erythrokeratodermia Variabilis

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Introduction & Objectives:

Erythrokeratodermia variabilis (EKV) is a rare, heterogeneous skin disorder and a subtype of a broader group of skin diseases known as erythrokeratodermias. It is characterized by migratory erythema and fixed hyperkeratotic plaques. The aim of this study is to report a series of seven cases of this rare dermatological condition, with limited descriptions in the medical literature.

Case series

We report seven cases of the same dermatological condition occurring within a single family. The index case was identified in 2008, when the family matriarch presented to the dermatology service with erythematous lesions, thickened skin accompanied by pruritus, some with scaling, which had first appeared in childhood. The anatomopathological examination (APE) showed moderate irregular acanthosis and a mild perivascular inflammatory infiltrate. When asked about similar lesions in family members, the patient reported that her three children had exhibited lesions with the same clinical pattern since early childhood. They were subsequently invited for evaluation. One of the sons, a 49-year-old, reported having similar lesions since the age of 6 months. His APE showed hyperkeratosis and papillomatosis, in addition to hypergranulosis and a mild perivascular lymphocytic infiltrate in the papillary dermis. All seven affected individuals displayed the same lesion pattern. In the case of the patient's granddaughters—aged 1 year and 12 years—biopsy was not performed due to clinical findings consistent with EKV and the patients' young ages and the risk of unaesthetic scarring due the procedure. All patients are currently being managed with skin hydration. Only one of the patients was prescribed acitretin due to progressive thickening of lesions and pruritus, with improvement of the condition.

Discussion:

EKV is a rare form of autosomal dominant inheritance with incomplete penetrance and variable expressivity. Erythrokeratodermias are genodermatoses belonging to the group of ichthyosiform disorders and present in three distinct clinical forms: cocard genodermatosis, progressive symmetric erythrokeratodermia, and the variable type, also known as erythrokeratodermia variabilis. Classical EKV, first described by Mendes da Costa, is characterized by two distinct morphological components: one transient and the other fixed. The transient lesions are erythematous with mild keratosis, while the fixed lesions appear as rough, well-demarcated plaques, predominantly located on extensor surfaces and the face. APE findings are not specific; however, the presence of hyperkeratosis with focal parakeratosis, preserved granular layer, acanthosis, and a superficial perivascular inflammatory infiltrate may support the diagnosis of EKV. Treatment usually involves use of topical keratolytics and emollients resulting in some improvement in hyperkeratosis. Low-dose systemic retinoid may be beneficial.

Conclusion

We conclude that EKV cases should be reported in order to expand the understanding of this rare condition.

Abstract N°: 5710

Xeroderma Pigmentosum in Nepal: a pilot experience in preventive education

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[2]Hospital Center University De Rouen, Rouen, France
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[4]Teaching hospital maharjgunj, Kathmandu, Nepal
[5]CH Valence, Valence, France
[6]University of Poitiers, GRESCO, Poitiers, France

Introduction & Objectives:

Xeroderma pigmentosum (XP) in Nepal is characterized by a specific XPC c.1243 C>T, p.R415X, mutation, and a high severity of disease. The severe phenotypic profile in most cases is associated with lack of information, poor understanding of the condition, and limited access to photoprotection and healthcare. Therapeutic education is not developed in Nepal, and patients typically only seek medical care for tumor excision. This led us to implement two initiatives: 1 - Preventive Education Consultations (PEC) at a reference center. 2 - Home Visits (HV) to patients and families.

Materials & Methods:

\1) Preventive Education Consultations (PEC): Out of 72 known patients, 37 were contacted, and 12 were seen in consultation. Each PEC was conducted in a quiet environment, attended by a French dermatology resident and a Nepali nurse and/or translator. The consultation included an oral educational session supported by visual teaching aids, followed by an interactive session using the PICTURES and DRESS-ME educational games depending on the patient’s age. A 44-item knowledge questionnaire was completed at the beginning and end of each session. The mean duration of each session was 40 minutes, contrasting with 5 to 10 minutes for a standard dermatological consultation.

\2) Home Visits (HV): Ten patients (and their families) were selected based on home accessibility in two locations (Kathmandu and Butwal, at nine-hour drive by jeep). The visits were conducted by the dermatology resident, a French mother involved with the “Enfants de la Lune” association, and a Nepali translator. Each family was visited for one full day, allowing for a comprehensive assessment, educational exchange, and distribution of photoprotection equipment.

Results:

\1) PEC**:** The 12 patients were 8 males and 4 females, with a median age of 14 years. Minor patients were accompanied by parents. All showed strong interest in the sessions. The median number of incorrect answers was 17 at initial evaluation. Main incorrect answered concerned the source of UV light, the origin of tumors (sometimes attributed to cold temperatures or sunscreens), and the physical signs of tumors. The median number of incorrect answers decreased to 1 following the educational consultation.

\2) HV: The 10 patients were 8 males and 2 females, with a median age of 12 years. Some 4/10 had previously attended the PEC sessions and 4/10 were equipped with French photoprotective masks; however, despite the knowledge acquired, none of the patients wore their masks daily.

Conclusion:

PEC sessions resulted in significant short-term knowledge acquisition. However, this will have to be reassessed over time, along with additional material and educational support. Expansion of PEC sessions to reach more patients is necessary. Home visits highlighted the need for repeated educational sessions and adaptation of photoprotection equipment to ensure better acceptance, taking into account cultural and climatic environment.

Abstract N°: 5783

“Glioblastoma on Neurofibromatosis Type 1 in Adults: A Rare Occurrence”

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Introduction & Objectives:

Neurofibromatosis type 1 (NF1) is a familial tumor syndrome with autosomal dominant transmission. Benign brain tumors, such as pilocytic astrocytomas and hypothalamic optic gliomas, constitute the majority of intracranial neoplasms in NF1. However, glioblastoma remains rare. We report a rare occurrence of a malignant glioblastoma in a patient with NF1.

Cas report :

The patient is A.I., a 30-year-old with a family history of NF1, presenting with a moderately altered general condition with a history of progressive headache. The cutaneous examination shows multiple café au lait spots and neurofibromas on the thorax, abdomen, back, and arms. With an erythematous mass on the scalp, a skin biopsy suggests a sarcoma. A cerebral MRI detected a massively necrotic, edematous tumor lesion in the right internal temporo-occipital region, displacing and compressing the temporo-occipital horn of the right lateral ventricle, suggesting a glioblastoma. The patient underwent surgery; the histopathological study confirmed the diagnosis of a glioblastoma; chemotherapy regimens were subsequently initiated.

Discussion :

Neurofibromatosis type 1 (NF1) is a familial tumor syndrome with autosomal dominant transmission. The majority of intracranial tumors associated with NF1 are pilocytic astrocytomas and optic gliomas, considered to be of low pathological grade. However, there is an increased risk of developing malignant tumors of the central and peripheral nervous system. Glioblastoma is a common malignant brain tumor in adults, but glioblastoma in patients with NF1 is rare. Until 2010, 12 cases of NF1 associated with glioblastoma had been reported. Among these cases, four occurred in adults. In adults, glioblastoma is the most frequent and most aggressive primary brain tumor. The methylation status of the MGMT gene promoter is currently a promising molecular prognostic marker. Huttner et al. reported that children with NF1 may be at risk of glioblastoma and that the prognosis of glioblastoma in children with NF1 may be better than in those without NF1. However, in adults, information on cases of glioblastoma with NF1 is limited.

Conclusion:

Glioblastoma is an exceptional entity in patients with NF1. This case illustrates the importance of not ruling out the possibility of a high-grade malignant tumor in the presence of any atypical brain lesion. Close neuro-radiological monitoring and multidisciplinary management are essential for early detection and appropriate treatment.

Abstract N°: 5928

Congenital Milia and Multiple Malformations in an Infant: A Case of Oral-Facial-Digital Syndrome Type 1

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Introduction & Objectives:

Oral-facial-digital syndrome type 1 (OFD1) is the most common subtype of a heterogeneous group of disorders affecting the oral cavity, face, and digits, with at least 16 subtypes identified based on inheritance patterns and associated abnormalities in various organs. OFD1 is inherited in an X-linked dominant manner, leading to lethality in males, although over 70% of cases are sporadic. It is characterized by congenital milia, hypotrichosis, craniofacial and digital malformations, and may involve the central nervous system and visceral organs in females, with an estimated incidence of 1 in 50,000 to 250,000 live births.

Materials & Methods:

We report a rare case of OFD1 syndrome, in which the diagnosis was guided by the presence of congenital milia.

Results:

Our case involved a female infant presenting with signs of OFD syndrome, with no family history suggesting a genetic disorder. She was born to non-consanguineous parents. At 11 months old, she was assessed in our pediatric dermatology consultation, where numerous milia measuring 1–3 mm were observed on her malar cheeks, forehead, and both helices. She also had multiple open comedones, pitted scars, and wiry hair with occipital partial alopecia. Facial dysmorphia was noted, including hypertelorism, a broad, depressed nasal bridge, and a prominent frontal bone.

Oral examination revealed a cleft soft palate, cleft tongue, an accessory frenulum, and multiple soft hamartomas on the tongue, buccal mucosa, and gums. Digital abnormalities included clinodactyly and brachydactyly.

Head CT imaging showed intracerebral cysts and agenesis of the corpus callosum. Based on these findings, the child was clinically diagnosed with OFD1. She underwent frenulectomy and surgical removal of the oral hamartomas. A topical retinoid was prescribed to manage the congenital milia

Conclusion:

Because overlap of the clinical features between subtypes is common, classification of a specific patient can be difficult. However, OFD1 can be distinguished from other types by its characteristic milia. Observed in about 30% of patients with OFD1. It is caused by heterogeneous mutations, a centrosomal protein, which causes dysfunction of cilia in affected individuals. It is characterized by craniofacial abnormalities; multiple large milia-like cysts of the face, scalp, ears, and back of the hands; xerosis; cleft lip and palate; and other oral and digital defects. Although milia formation tends to decrease with age, scarring may result.

Congenital milia can be managed with topical retinoids such as tretinoin or adapalene to promote skin turnover. In resistant cases, manual extraction can be performed using a sterile needle, or advanced treatments like laser therapy or cryotherapy may be considered. Most cases require only observation, with parents advised to keep the skin clean and avoid manipulation to prevent irritation or infection.

Abstract N°: 5966

Osler-Weber-Rendu syndrome: A diagnostic challenge with a successful therapeutic response to Thalidomide

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Introduction & Objectives:

Osler-Weber-Rendu syndrome (OWRS), a rare genetic disorder affecting approximately 1 in 10,000 individuals, is characterized by vascular abnormalities, primarily telangiectasias, which can lead to severe complications. We present the case of a patient with recurrent epistaxis for twenty years without an initial clear diagnosis, illustrating the diagnostic and therapeutic challenges of this syndrome.

Materials & Methods:

NA

Results:

A 75-year-old female, followed for chronic iron-deficiency anemia requiring transfusions, presented with recurrent epistaxis for 20 years, resistant to conventional treatments. She had consulted for cutaneous and mucosal telangiectasias since the age of 40, mainly located on the nose and lower lip. Her brother and son exhibited similar symptoms. Clinical examination and the Curaçao criteria led to the suspicion of OWRS, confirmed by complementary tests. A thoraco-abdomino-pelvic CT scan revealed hepatic arteriovenous shunts without signs of portal hypertension. Severe anemia (Hb 7.1 g/dL) prompted treatment with 100 mg/day of thalidomide. After one month, the number of episodes of epistaxis decreased from four times per day to twice per week, and hemoglobin increased to 10.5 g/dL.

Conclusion:

OWRS is diagnosed clinically using the Curaçao criteria, which include recurrent epistaxis, mucocutaneous telangiectasias, visceral arteriovenous malformations, and a family history of the disease. Therapeutic management of OWRS, particularly chronic epistaxis, remains challenging. Thalidomide, an immunomodulatory and antiangiogenic agent, has emerged as a promising treatment option. Its mechanism of action involves inhibition of vascular endothelial growth factor (VEGF), a key mediator in the pathogenesis of telangiectasias. In this case, thalidomide significantly reduced epistaxis frequency and improved hemoglobin levels, demonstrating its dual benefit in controlling bleeding and addressing anemia. These findings align with previous studies showing thalidomide’s efficacy in reducing bleeding episodes and improving quality of life in OWRS patients.

In conclusion, this case illustrates the diagnostic challenges and therapeutic potential of thalidomide in managing chronic epistaxis in OWRS. Thalidomide represents a promising therapeutic option for refractory epistaxis, as evidenced by the marked clinical improvement in this patient. However, its use must be balanced against potential risks, and further research is needed to optimize treatment strategies. This case contributes to the growing evidence supporting thalidomide’s role in OWRS management and highlights the importance of personalized therapeutic approaches in rare diseases.

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Abstract N°: 6117

Disseminated Granulomatous Infections in a Child: A Diagnostic Challenge of MSMD

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Introduction & Objectives:

Mendelian susceptibility to mycobacterial disease (MSMD) is a rare, inherited primary immunodeficiency characterized by increased susceptibility to weakly virulent mycobacteria in otherwise healthy individuals due to impaired interleukin-12/23-interferon-gamma (IL-12/23-IFN-γ) immunity. Affected individuals may also be prone to infections by other pathogens, including Salmonella, Listeria, Histoplasma, Toxoplasma, and certain viruses. While at least 19 genes have been implicated in MSMD, most affect IFN-γ-mediated immunity. Clinical presentation varies from severe, life-threatening infections in early childhood to milder, later-onset, or even asymptomatic forms.

Materials & Methods:

We present the case of a 12-year-old female whose persistent, disseminated granulomatous infections of diverse etiologies and progressive, treatment-refractory course ultimately led to a diagnosis of Mendelian susceptibility to mycobacterial disease (MSMD), highlighting the diagnostic challenges in such complex presentations.

Results:

A 12-year-old female presented at age 4 with progressively developing, thick, erythematous to violaceous infiltrated plaques on the chest, left flank, and left leg, without systemic involvement. By age 8, biopsies revealed mixed cellular granulomas throughout the dermis, including multinucleated giant cells, neutrophils, and eosinophils. Gene Xpert PCR for acid-fast bacilli was negative, but PAS staining was positive, and Histoplasma capsulatum was cultured. Initial treatment with intravenous liposomal Amphotericin B, Terbinafine, Itraconazole, and Potassium Iodide for six months yielded only moderate improvement. Subsequent development of facial lesions prompted the addition of intralesional Fluconazole. After a year of loss to follow-up, she returned with exacerbated plaques and a large, coalescing facial lesion. Voriconazole was added due to persistent lack of response over six months.

Repeat biopsies of the facial lesion demonstrated a diffuse dermal granulomatous infiltrate with multinucleated giant cells and plasma cells. Tissue culture grew Mycobacterium abscessus, wound culture yielded MRSA, and urine culture was positive for Escherichia coli. The patient’s history of recurrent granulomatous infections from diverse microorganisms, a chronic course, and treatment refractoriness strongly suggested Mendelian susceptibility to mycobacterial disease (MSMD), although genetic testing was pending. Based on culture sensitivities, a regimen of Rifampicin, Ethambutol, Amikacin, and Azithromycin was initiated, resulting in significant improvement of the plaques within two months, with reduced thickness and residual scarring.

Conclusion:

This case of MSMD in a young patient underscores the critical importance of considering this rare immunodeficiency in the differential diagnosis of persistent, treatment-refractory granulomatous infections of diverse etiologies. Early recognition is crucial for implementing targeted therapies, improving patient outcomes, and mitigating potential complications.

Abstract N°: 6236

Increased Prevalence of Renal Cysts in Hereditary Leiomyomatosis and Renal Cell Cancer Syndrome: A Cross-Sectional MRI Based Study

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Introduction & Objectives:

Hereditary Leiomyomatosis and Renal Cell Cancer (HLRCC) is a genetic syndrome caused by pathogenic variants in the *fumarate hydratase* (*FH*) gene. Clinically, it is characterized by cutaneous leiomyomas, uterine leiomyomas, and aggressive renal cell carcinoma (RCC). While renal cysts are not formally part of the HLRCC phenotype, emerging evidence suggests increased prevalence in this patient population. We aimed to quantify the prevalence and features of renal cysts in a large genetically confirmed HLRCC cohort.

Materials & Methods:

We conducted a cross-sectional analysis of prospectively collected magnetic resonance imaging (MRI) data from HLRCC patients followed at our OncoGenodermatology clinic (December 2022-January 2025). MRI reports were analyzed for renal cyst features. Demographics and HLRCC characteristics were additionally recorded. Renal cyst prevalence was stratified by sex and decade. Prevalence ratios (95% confidence interval [CI]) compared HLRCC to published general population estimates from a European MRI-based cohort. Multivariate logistic regression analyzed predictors of cyst presence, using adjusted odds ratios (aORs) and 95% CIs.

Results:

A total of 72 HLRCC patients were included (68.06% female, 98.61% White, median age: 44.5 years [interquartile range: 36, 55]). Renal cysts were present in 59.72%, significantly higher than the 27% prevalence reported in the MRI-based general population study (p <0.0001), with a prevalence ratio of 2.18 (95% CI 1.78-2.67). Cysts were more frequent in males (65.22%) and older patients (30.00% in patients <30 years vs 100.00% in ≥70). Increasing age was independently associated with renal cysts (aOR per year: 1.07; 95% CI 1.03–1.12). No associations were observed with *FH* variant type, CL, UL, or RCC history. Among cyst-positive patients, 67.44% had multiple cysts and 53.49% had bilateral involvement. Cyst diameter ranged from 0.20-5.70 centimeters. Of 19 with available data, 36.84% had Bosniak II cysts, with 26.32% having both Bosniak I and II types.

Conclusion:

Our study identified renal cysts in nearly 60% of HLRCC patients, approximately double the rate reported in the general population, suggesting that renal cysts may be an under-recognized feature of HLRCC. Given that early HLRCC-associated RCC can arise from cystic lesions, close follow-up may be warranted, particularly for complex cysts, highlighting the utility of MRI surveillance for early intervention. Longitudinal studies are needed to define the natural history of HLRCC-associated renal cysts and evaluate their potential as RCC precursors.

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Abstract N°: 6240

Multiple rapidly growing cutaneous lesions in Muir-Torre syndrome: A rare case report

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Introduction & Objectives:

Muir-Torre Syndrome (MTS) is a phenotypic variant of Lynch syndrome (known as hereditary nonpolyposis colorectal carcinoma, HNPCC), which is mainly associated with sebaceous tumors (sebaceous adenomas, sebaceous epitheliomas, sebaceous carcinomas, and cystic sebaceous tumors) and/or keratoacanthomas. Cutaneous squamous cell carcinomas (cSCCs) and basal cell carcinomas (cBCCs), may also occur, though their link with the syndrome is unclear. HNPCC is well known for its association with visceral malignancies, particularly colorectal (CRC), endometrial, ovarian, urothelial, and prostate cancers. In MTS, additional cancers have been reported, including breast, pancreatic, hepatobiliary, gastric, lung, brain, and hematologic malignancies. Two-thirds of MTS cases are caused by germline mutations in mismatch repair (MMR) genes-most commonly MSH2, but also MSH3, MSH6, MLH1, and PMS2-leading to microsatellite instability (MSI), which follow an autosomal dominant inheritance pattern. The remaining one-third of cases result from biallelic germline mutations in the base excision repair gene MUTYH, which are inherited in an autosomal recessive manner.

Materials & Methods:

Our 51-year-old patient, with a confirmed diagnosis of HNPCC (carrying mutations in both MLH1 and MSH2), has a history of two CRC resections at the ages of 46 and 48, along with a positive two-generation family history of related cancers. He was recently hospitalized for evaluation and management of three rapidly growing skin lesions located on the nose, right supraclavicular area, and left zygomatic region. These lesions developed within a two-week period, with the most recent one appearing just a week prior to admission and were surgically excised during hospitalization. Remarkably, two days postoperatively, the patient noticed the development of a new lesion at the surgical site in the left zygomatic area, specifically onto the sutures. Additionally, the patient's forehead showed multiple sebaceous adenomas, as was indicated by the histopathology report of similar lesions three years ago. However, they seemed to reappear in a greater number than before.

Family history

Father	Died of lung cancer at the age 32
Mother	Died of endometrial cancer at the age 60
Brother	Died of colon cancer at the age 45
Sister	She is 56 years old, healthy, and has undergone a prophylactic hysterectomy with bilateral salpingo-oophorectomy

Results:

Our patient exhibits a characteristic phenotype of MTS according to the Mayo Muir-Torre risk score system and Amsterdam criteria, even though he had not previously been aware of it. Histopathological examination of the excised skin lesions revealed that one lesion exhibited features consistent with keratoacanthoma, while the other two with cSCCs. Notably, the new lesion at the site of the sutures has continued to enlarge even after suture removal, either as a part of residual disease or as a part of a newly developing lesion. Given these possibilities, surgical excision of the lesion is planned in the coming days to determine its nature and guide further

management.

Conclusion:

In light of the above findings, surveillance of patients with MTS must be close, not only for visceral cancers risk, but also in order to identify any new skin findings, given the fact that specific guidelines for the skin are lacking. In some cases, cutaneous manifestations may precede the onset of internal cancers, and their simultaneous appearance can be an alarming sign for genetic testing. The interesting part of this case was the rapid growth of both the keratoacanthoma and cSCCs, as well as the emergence of a new lesion at the suture site. Furthermore the surveillance and/or the screening of family members would be essential.

Abstract N°: 6271

Evaluation of Artificial Intelligence Chatbots in Assisting Genetic Counselors in Genodermatology

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Introduction & Objectives:

Genetic counseling is vital in the management of patients with inherited skin disorders, but it remains resource-intensive and time-constrained. AI-driven chatbots can support healthcare professionals by synthesizing complex information and improving patient communication. To date, the integration of AI into specialized fields such as genodermatology has not been systematically evaluated. This study aimed to assess the performance, reliability, and user-friendliness of five contemporary chatbots in addressing genetic counseling scenarios in genodermatology.

Materials & Methods:

Based on cases seen at our Genodermatology clinic (June 2024-February 2025), twenty de-identified clinical vignettes were generated and input into ChatGPT 4o mini, Gemini, Bing AI, DeepSeek, and OpenEvidence. Each chatbot received identical standardized prompts. Responses were independently graded by a board-certified dermatologist and a medical geneticist using the modified DISCERN (mDISCERN) tool and a 5-point Likert misinformation scale to assess information quality and misinformation, respectively. The Patient Education Materials Assessment Tool (PEMAT) and the Health Literacy Editor were used to assess actionability and understandability, respectively. Statistical analyses were performed using Kruskal-Wallis tests with Dunn's post-hoc comparisons.

Results:

A total of 100 responses were evaluated. Agreement between graders for quality and misinformation was strong (Cohen's *Kappa* range: 0.602-0.960). OpenEvidence scored highest in terms of information quality ($p < 0.05$); however, mDISCERN scores for chabots were severely impacted by lack of cited references, limited acknowledgment of the sources of information, and failure to mention additional sources of uncertainty. Misinformation across all chatbots was low (median 1 [range 1, 4]) with no significant difference between chatbots ($p > 0.999$). Of 100 prompts, content deviation (i.e., moderate or major misinformation) was only observed in three across all chatbots. The median actionability score was 40 [0, 60], with ChatGPT 4o mini performing the best ($p < 0.05$). The median understandability score was 15.25 [12.6, 22.9], with Gemini performing the best (13.55 [12.6, 15.7]; $p < 0.001$) and ChatGPT 4o mini and OpenEvidence ranking lowest. As well, we created prompts to overcome pitfalls identified and created a trained custom chatbot.

Conclusion:

Our study highlights that AI chatbots can generate high-quality genetic counseling responses in genodermatology with factual accuracy and minimal misinformation. Chatbots, particularly those like OpenEvidence that are literature-based, have the potential to streamline genetic counseling workflows and allow the reallocation of time toward interpretation, emotional support, and shared decision-making. OpenEvidence could serve as a starting point to automate information synthesis although targeted improvements are warranted.

Abstract N°: 6409

Neural Crest Lineage in Disease: Coexistence of NF1, Parkinson's Disease, and Multiple Cutaneous Melanomas

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Introduction & Objectives: We present the case of an 84-year-old retired engineer with a background of Neurofibromatosis Type 1 (NF1), recently diagnosed Parkinson's disease (PD), and conservatively managed plasmablastic lymphoma. Despite his comorbidities, he remains clinically stable. His dermatologic history is notable for a long-standing and extensive pattern of cutaneous malignancy, under the care of dermatology and plastic surgery services since 2001, following the excision of his first melanoma. Over the past two decades, he has undergone multiple excisions, including 10 superficial spreading malignant melanomas (SSMM), 4 melanomas in situ (M-is), and 3 dysplastic nevi (DN), all managed surgically at early stages with primary and wide local excisions.** A CT head, neck, thorax, abdomen, and pelvis (HNTAP) performed in March 2022 ruled out internal metastatic disease. He continues to receive regular follow-up and comprehensive skin surveillance.

This case offers a compelling intersection of multiple neural crest–derived pathologies. NF1 is a genetic disorder primarily affecting neural crest-derived Schwann cells. Melanocytes, the origin of this patient's numerous melanomas and dysplastic nevi, are also neural crest derivatives. Furthermore, recent studies have implicated neural crest–related pathways and alpha-synuclein expression in the peripheral tissues of patients with Parkinson's disease (PD), which is another diagnosis relevant to this patient.

Materials & Methods: This report was assembled through a retrospective chart review and direct clinical observation of an 84-year-old male patient receiving long-term dermatologic and multidisciplinary care. Clinical data were collected from hospital records spanning from 2001 to 2024, including histopathology reports, surgical notes, imaging studies, and outpatient follow-up documentation. All cutaneous lesions were evaluated and managed by board-certified dermatologists.

Results: The findings of multiple melanomas, NF1, and PD represent a rare intersection of neural crest–derived pathologies. No family history of melanoma or PD was reported. The recurrence of melanomas exclusively in early-stage form suggests an intrinsic predisposition to melanocyte dysregulation, possibly modulated by atypical neural crest cell biology rather than environmental factors or immunosuppression.

Conclusion: This case spotlights a rare clinical convergence of three distinct yet developmentally related conditions, namely, Neurofibromatosis Type 1 (NF1), Parkinson's disease (PD), and multiple primary cutaneous melanomas, which are all derived from neural crest cell lineages. The patient's perennial history of early-stage melanomas, compounded with NF1 and newly diagnosed PD, suggests that dysregulation of neural crest development or maintenance may fortify a shared pathogenic mechanism. While the coexistence of these conditions may be coincidental, their neural crest origin renders the possibility of a unifying developmental vulnerability that merits further investigation. Recognition of such patterns in clinical practice may prompt earlier surveillance strategies and support future studies exploring neural crest biology as a common thread in multi-system disease presentations.

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Abstract N°: 6653

A Case of Mal de Meleda Diagnosed in Late Adulthood

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Introduction & Objectives: Mal de Meleda (MDM) is a type of autosomal recessive palmoplantar keratoderma, marked by hyperkeratosis on both palms and soles and it is often associated with hyperhidrosis, perioral erythema, lichenoid plaques, nail anomalies and digital anomalies [1,2]. Hyperkeratosis can be complicated by hyperhidrosis, with subsequent microbial infection leading to malodorous and painful lesions [2]. The disease usually begins in infancy and progresses slowly throughout adulthood. Pathogenic variants in the *SLURP1* gene were established as the molecular basis of MDM [3]. SLURP-1 regulates keratinocyte apoptosis and its dysfunction in MDM impairs apoptosis, leading to hyperkeratosis [2]. We present a case of Mal de Meleda diagnosed in late adulthood, highlighting the importance of considering this rare genodermatosis in the differential diagnosis of hereditary palmoplantar keratodermas.

Materials & Methods: The clinical records of a late-diagnosed Mal de Meleda patient were reviewed.

Results: A 76-year-old male patient presented to our clinic with complaints of thickening, erythema and hyperhidrosis of the palms and soles, which had been present since the age of 4–5 years. Dermatological examination revealed generalized hyperkeratotic thick yellow-white plaques on both palms and soles, brachydactyly of the right fifth finger and oligodactyly of the left hand. Maceration was observed between the toes and on the plantar surfaces of both feet, accompanied by hyperhidrosis and malodor. No dental or hair anomalies were observed. There was no family history. Laboratory tests were unremarkable. Skin biopsy demonstrated hyperkeratosis, regular epidermal hyperplasia, focal lymphocytic exocytosis in the epidermis, focal hypergranulosis, and spongiosis. Tissue culture obtained from the plantar surface of the foot yielded *Aspergillus niger*. Genetic analysis identified a pathogenic variant in the*SLURP-1* gene, which was associated with the acrokeratoderma Mal de Meleda phenotype. The patient was started on oral acitretin 20 mg and systemic itraconazole. During follow-up, the acitretin dose was increased to 35 mg, topical keratolytic therapy was added, and the patient received systemic and topical antifungal treatments as needed due to fungal infections. The patient was enrolled in a physical therapy program to address movement limitations caused by hyperkeratosis. During follow-up, the patient showed marked clinical improvement.

Conclusion: MDM is a rare autosomal recessive disorder caused by a mutation in the SLURP-1 protein and should be considered in the differential diagnosis of patients with early-onset, progressive, and transgredient palmoplantar keratoderma. Standard treatment involves topical keratolytics, anti-inflammatories, and management of secondary infections, with oral retinoids as the main systemic option [4]. Genetic testing is advised for definitive diagnosis and to inform genetic counseling, facilitating effective patient and family management [2]. In conclusion, this rare case highlights the importance of considering MDM in the differential diagnosis of hereditary palmoplantar keratoderma. Despite early-onset symptoms and digital anomalies, our patient was not referred for dermatological evaluation or genetic counseling until late adulthood, leading to a delayed diagnosis. The absence of systemic involvement likely contributed to the lack of suspicion and timely referral.

Abstract N°: 6768

The Unseen Burden: Unraveling the Layers of Pachyonychia Congenita and Its Inherited Legacy

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Introduction & Objectives: Pachyonychia congenita (PC) is a rare, autosomal dominantly inherited keratinization disorder marked by a constellation of cutaneous and mucosal manifestations, most notably hypertrophic nail dystrophy, painful palmoplantar keratoderma, and oral leukokeratosis. Despite its low global prevalence, the clinical burden is considerable, frequently leading to significant functional limitation and psychological distress. In regions with limited access to genetic diagnostics, recognition of phenotypic hallmarks and detailed family history remains crucial for diagnosis and management.

Materials & Methods: A 52-year-old man, previously diagnosed with PC in a Medical Genetics Clinic based on clinical features and family history, was admitted to the dermatology department due to worsening cutaneous symptoms. Genetic testing had not been performed, as it remains unavailable in Romania.

Results: The patient was referred for evaluation and management of painful, disabling palmoplantar hyperkeratosis with deep fissures, foul odor, and marked functional impairment. Dermatological examination revealed hypertrophic, dystrophic nails with subungual hyperkeratosis and dark discoloration of both fingernails and toenails, consistent with pachyonychia. Hyperkeratotic plaques were also present on the elbows and knees. Oral examination identified thickened, white plaques on the tongue, clinically consistent with leukokeratosis. Family history revealed he is the sixth child of healthy, non-consanguineous parents, with no known genetic disorders. Of his four children, two—a 16-year-old daughter and an 11-year-old son—exhibit similar symptoms, supporting autosomal dominant inheritance. During hospitalization, comprehensive clinical evaluation, laboratory testing, and internal medicine consultation were conducted to assess systemic involvement and comorbidities. Oral swab testing was positive for Candida spp., while plantar fissure cultures confirmed Escherichia coli superinfection. Routine inpatient assessments also revealed previously undiagnosed stage 2 hypertension, requiring initiation of antihypertensive therapy based on cardiology guidance.The diagnosis of PC was reaffirmed based on characteristic clinical findings and the familial pattern. Treatment included topical emollients, antifungals, and antibiotics. A multidisciplinary approach with continued dermatologic, cardiologic, and genetic follow-up was recommended. Genetic counseling addressed recurrence risk, inheritance, and long-term management.

Conclusion: This case highlights the complex, disabling phenotype of PC, marked by extensive mucocutaneous involvement and functional impairment extending beyond dermatologic care. In the absence of genetic confirmation, the multigenerational transmission underscores the enduring value of clinical evaluation and detailed family history in diagnosing rare genodermatoses. The presence of oral leukokeratosis, secondary infections, and debilitating keratoderma reflects the systemic burden of PC and the necessity of coordinated, long-term multidisciplinary care. Documenting such cases with high clinical fidelity contributes to global efforts in refining diagnostic algorithms and improving patient outcomes.

Abstract N°: 6820

Imiquimod in Xeroderma Pigmentosum Variant: a Therapy for Managing the Tumors and the Field

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Introduction & Objectives:

Xeroderma pigmentosum (XP) is a rare genodermatosis characterized by the development of early onset skin cancers resulting from ultraviolet radiation exposure. It is caused by defective DNA repair mechanisms. XP variant represents a milder phenotype still carries a significant morbidity.

Imiquimod, a topical immunomodulator approved for actinic keratoses, superficial basal cell carcinomas and genital warts, has been in use for patients with basal cell carcinomas and actinic keratoses. A few case reports have addressed imiquimod treatment in XP patients. Hereby we present a case of XP variant treated with imiquimod.

Materials & Methods:

We report a case of a young female, who presented in five years ago at around the age of 17 with multiple non-melanoma skin cancers over the face. The cancers were excised by the plastic surgery and she needed regular follow up. On examination, she had a few scars around the nose and cheeks, with multiple actinic keratoses overlying actinic damage. She received multiple sessions of cryotherapy for superficial lesions and actinic keratoses with moderate results. Larger papules and nodules were excised as needed. She had no similar family history, dysmorphic features, or comorbidities. The patient was clinically diagnosed as XP variant based on the history, presentation, and the mild course of the disease. Topical imiquimod 5% cream was prescribed for the patient to use on superficial lesions and as a field therapy. The application was for eight hours every other day as tolerated for three months. She responded well with minimal side effects and clearance of her skin. During follow up of the patient she was given a second course of imiquimod as a field therapy. The patient remains under care and has a manageable disease course.

Results:

The treatment of XP variant in our patient was well-tolerated and effective in reducing the background actinic damage and precancerous lesions.

Conclusion:

XP variant can carry significant morbidity with propensity to develop skin cancers. Imiquimod, a topical immunomodulator, was used in our patient as a well-tolerated and a safe option in the treatment of XP variant, both as a therapeutic option for the use on the tumors, and as a preventive therapy on areas with field cancerization.

Abstract N°: 6824

Severe Generalized Darier Disease Presenting with Leonine Facies: A Rare Clinical Variant

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Introduction & Objectives:

Darier disease (keratosis follicularis) is a rare, autosomal dominantly inherited genodermatosis caused by ATP2A2 gene mutations. It typically manifests as keratotic papules in seborrheic areas and may involve mucosa and nails. Although most cases are mild, generalized forms with extensive facial involvement—especially leonine facies—are exceedingly rare and pose diagnostic challenges.

This report presents the case of a patient with a severe flare of Darier disease, notably involving leonine facies, with the objective of contributing to the limited literature on this rare clinical variant and emphasizing the importance of early recognition and treatment.

Materials & Methods:

We report the case of a 67-year-old male with a family history of similar skin lesions who presented with a severe flare of Darier disease. The patient exhibited widespread hyperkeratotic papules over the trunk, scalp, and limbs. Notably, his facial involvement included thick, verrucous plaques with exudative fissures, leading to a leonine appearance. Mucosal examination revealed cobblestone-like depressions on the hard palate. Nail and palmoplantar involvement were absent.

Laboratory findings showed leukocytosis, hyperlipidemia, and mildly elevated liver enzymes. Histopathology from both facial and forearm lesions confirmed suprabasal acantholysis with dyskeratosis, consistent with Darier disease. Differential diagnoses included mycosis fungoides, Sézary syndrome, sarcoidosis, and amyloidosis.

The patient was treated with oral acitretin (20 mg/day), topical keratolytics, and antiseptics, with follow-up in an outpatient setting.

Results:

The clinical presentation involved widespread hyperkeratotic papules on the trunk, scalp, and limbs. Facial lesions were characterized by thick, verrucous plaques with exudative fissures that produced a leonine facies. The oral mucosa showed cobblestone-like depressions on the hard palate, while nail and palmoplantar areas were unaffected.

Laboratory investigations revealed leukocytosis, hyperlipidemia, and mildly elevated liver enzymes. Histopathologic examination of facial and forearm skin lesions demonstrated suprabasal acantholysis with dyskeratosis—hallmarks of Darier disease.

Differential diagnoses including mycosis fungoides, Sézary syndrome, sarcoidosis, and amyloidosis were considered but ruled out based on clinical and histopathologic findings. The patient showed clinical improvement with a regimen of oral acitretin, topical keratolytics, and antiseptics.

Conclusion:

Leonine facies is rarely associated with Darier disease, with few cases documented in the literature. This presentation may mimic cutaneous lymphomas or granulomatous conditions, warranting histological confirmation. Our case emphasizes the need for awareness of such variants and highlights the value of early systemic retinoid therapy and skin hygiene in managing severe forms.

Clinicians should consider Darier disease in patients with generalized hyperkeratosis and facial thickening. Prompt histopathologic diagnosis is key to avoiding misdiagnosis and initiating appropriate therapy.

Abstract N°: 6827

Neurofibromatosis type 1 or not: reveal from the genetic test

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Introduction & Objectives:

Neurofibromatosis type 1 (NF1) is a multisystem disorder characterized by multiple café-au-lait macules (CALMs), intertriginous freckling, multiple cutaneous neurofibromas, and learning disabilities or behavioral problems. According to current diagnostic criteria, genetic testing is optional; however, in some cases presenting with multiple CALMs and freckling, genetic analysis can reveal alternative diagnoses.

Results:

We report three cases that presented with multiple CALMs.

The first case was a 30-year-old male with over ten CALMs (>15 mm in diameter), multiple intertriginous freckles, and cutaneous neurofibromas. Although the clinical features were highly suggestive of NF1, ophthalmologic examination and brain MRI showed no abnormalities. Family history was unremarkable. Genetic testing for NF1 revealed no pathogenic variants. Subsequently, whole genome sequencing identified a mutation in the PMS2 gene which was extremely rare and associated with Lynch syndrome and constitutional mismatch repair deficiency syndrome (CMMRD). Colonoscopy showed no abnormalities at the time. Due to insufficient clinical evidence, a definitive diagnosis of Lynch syndrome or CMMRD could not be made; however, regular surveillance with colonoscopy every 2–3 years was recommended.

The second case was a 7-year-old female presenting with 12 CALMs and multiple intertriginous freckles. No other cutaneous lesions were detected. Family history was noncontributory, and ophthalmologic examination was normal. Suspecting NF1, genetic testing was performed and revealed a heterozygous variant in the NF1 gene. Although neurological symptoms were absent, a brain MRI was conducted, revealing scattered foci of abnormal signal intensity requiring follow-up.

The third case involved a 26-year-old female with multiple CALMs and freckles. Family history was unavailable due to adoption. Ophthalmologic and brain MRI findings were normal. Genetic testing confirmed a heterozygous NF1 variant.

Conclusion:

These cases show that while multiple café-au-lait macules (CALMs) often point toward neurofibromatosis type 1, genetic testing can sometimes reveal other unexpected conditions, highlighting its important role in patient care and follow-up planning.

Abstract N°: 6931

Atypical Gorlin Syndrome Revealed by Flexural BCCs and Distinctive Dermoscopy: A Case Report

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Introduction & Objectives:

Gorlin-Goltz Syndrome (GGS) is a rare autosomal dominant disorder with highly variable manifestations. Its prevalence in the general population ranges from 1 in 57,000 to 1 in 256,000. It is characterized by multisystem involvement, including a predisposition to cysts, neoplasms, and various developmental abnormalities.

Materials & Methods:

We report a rare case of Gorlin-Goltz Syndrome (GGS) in a young male patient with an atypical presentation, characterized by multiple basal cell carcinomas (BCCs) predominantly in intertriginous areas (axillary, umbilical, inguinal folds, and flanks), which is quite unusual.

Results:

A 42-year-old patient consulted our dermatology department for the assessment of progressively appearing pigmented lesions, which had been evolving over the past three decades. The patient had no family history of similar conditions. Clinical examination revealed multiple erythematous-pigmented papules, plaques, and tumors with an infiltrated base, ranging in size from a few millimeters to 8 cm. The lesions were symmetricaly distributed in photo exposed area as face and nek but the majoryty of the leasons were located in intertriginous areas as axillary, umbilical, inguinal folds.

Dermoscopy findings revealed typical patterns of BCC in some lesions, including ovoid nests, blue-gray dots, arborizing vessels, and chrysalis formations. However, other lesions exhibit other patterns, like brown dot and globules. prompting us to perform multiple biopsies, especially for those with an atypical dermoscopic presentation, raising suspicion for other diagnoses such as trichoblastoma, adnexal tumors or seborrehic keratosis. Ultimately, all biopsies confirmed the diagnosis of nodular BCC.

Given the clinical suspicion of Gorlin syndrome, further investigations were conducted. A panoramic dental X-ray revealed radiolucent cystic-like lesions, consistent with odontogenic keratocysts. A chest X-ray showed the presence of bifid ribs.

Based on the identification of three major criteria (multiple BCCs, odontogenic keratocysts, and bifid ribs), the diagnosis of Gorlin syndrome was confirmed. The patient was referred for multidisciplinary management, including dermatologic, dental, and genetic counseling.

Conclusion:

Gorlin-Goltz Syndrome (GGS) results from a mutation in the *PTCH1* gene, located on the long arm of chromosome 9. It is primarily inherited in an autosomal dominant pattern, although 35% to 50% of cases arise from spontaneous mutations with no family history. In Gorlin syndrome, basal cell carcinomas (BCCs) can develop in both sun-exposed and sun-protected areas, often appearing at an early age, sometimes even during childhood or adolescence. Patients typically present with multiple BCCs, which may vary in size, pigmentation, and

histological subtype, with nodular and superficial forms being the most common.

The peculiarity in our patient lies in the predominance of lesions located in skin folds. Previous investigators have suggested that local factors—such as chronic friction and humidity—combined with the effect of ultraviolet radiation on distant sun-exposed sites, may contribute to the tumorigenesis of BCCs in these hidden areas

Abstract N°: 7092

Epidemiology and Clinical Characteristics of Harlequin Ichthyosis: A Systematic Review and Meta-Analysis of Case Reports

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Introduction & Objectives:

Harlequin Ichthyosis (HI) is considered one of the rarest and severe congenital disorders that is characterized by the development of thick, plate-like scales, ectropion, eclabium, and multi-system complications that mainly cause high neonatal death.

Objectives: The current systematic review and meta-analysis aimed to assess the epidemiology of the condition as well as the clinical features, genetic findings, and the outcomes of different management strategies.

Materials & Methods:

A comprehensive search across different databases, depending on using different predefined terms, was conducted, and only case reports and case series in English were included in this review.

Results:

The review was conducted among 56 case studies and case series, including 68 cases that revealed that 64.7 % of them had an unspecified genetic mutation, while 30.9 % carried an ABCA 12 mutation. The clinical manifestations among the patients were severe, including thick scales reported in 79.4 % of the patients, ectropion, which was reported in 80.9 % of them, and eclabium, which was reported in 79.4 % of the patients. Despite the supportive care received by the patients, the mortality rate among the patients was as high as 60.3 %, with an average age of death of 47.19 days. Treatment response varied among the patients, where only 30.9 % of them had shown clinical improvement.

Conclusion:

Our review highlights the significantly high morbidity and mortality rates associated with a diagnosis of HI, indicating the need for early diagnosis, genetic counseling, and improvement of the management strategies.

Abstract N°: 7119

McCune-Albright Syndrome: An Atypical Presentation of a Rare Disease

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McCune-Albright Syndrome: An Atypical Presentation of a Rare Disease

Introduction & Objectives:

McCune-Albright syndrome (MAS, also known as fibrous dysplasia) is a rare genetic disorder originally recognized by the triad of: café-au-lait macules, polyostotic fibrous dysplasia and endocrine hyperfunction.

The disease is a rare mosaic disorder, the result of an embryonic missense mutation of the GNAS gene which encodes the G-signaling complex. Since the latter is ubiquitous in the body, the mutation can affect multiple tissues. Therefore, the phenotype of the disease can vary significantly, leading to diagnostic challenges, especially when presentations are incomplete or atypical. Skin manifestations may provide crucial early clues. This case highlights the role of dermatologic findings in identifying MAS in a patient with unexpected autoimmune and endocrine comorbidities.

Materials & Methods: ** We present the case of a young 35-year-old female, previously diagnosed with idiopathic juvenile arthritis (at 14-years-old), reffered to dermatology for evaluation and treatment of a purpuric leukocytoclastic vasculitis confirmed by skin biopsy. Cutaneous examination revealed an extensive unilateral sharply demarcated café-au-lait macule, with midline demarcation, localised on the left hemiabdomen. The large geographical pattern of the spot resembling "the coast of Maine" was a characteristic clue of a potentially McCune-Albright syndrome. Notably, the patient reported joints pain localized to the same (left) side, raising further suspicion of segmental involvment. The acral enlargmenet suggestive of acromegaly and palpable goiter were clinical findings which prompted an extensive diagnostic workup.

Results: ** The patient was reffered to endocrinology where elevated ATPO antibodies were detected, establishing the diagnosis of autoimmune thyroiditis with hypothyroidism- an atypical finding for MAS, where hyperthyroidism is more common. Hormonal analysis confirmed acromegaly and blood tests revealed low serum levels of 25-hydroxivitamin D and phosphorus- usual elements of bone fybrosis. The rheumatologic evaluation established a diagnosis of double-seropositive rheumatoid arthritis with high disease activity DAS28=6.03, likely evolving from the juvenile arthritis. DXA scans of the femoral neck and lumbar spine were normal. However, plain radiographs of the feet revealed evidence of old, healed fractures of the left metatarsal bones, suggesting possible subclinical fibrous dysplasia. Although a genetic testing for GNAS mutation could have brought light to the case, it could not be performed due to patient's financial constrains.

Conclusion: ** This case emphasizes the critical importance of recognizing subtle dermatological signs as potential indicators of rare genetic syndroms. Although the patient did not fulfill the classical diagnostic triad of McCune-Albright syndrome, the combination of café-au-lait macule morphology, lateralized symptoms, endocrine abnormalities and occult skeletal findings supported a clinical suspicion of MAS. Clinicians should maintain a high index of suspicion and consider atypical or incomplete presentations when evaluating patients with multisystemic involvement. Multidisciplinarity is key in managing such complex cases, especially when resource limitations exist.

Abstract N°: 7190

Use of epidermal growth factor receptor inhibitor erlotinib in the treatment of Olmsted syndrome caused by TRPV3 mutation

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Introduction & Objectives:

Olmsted syndrome (OS) is an extremely debilitating and rare genodermatosis that results from pathogenic variants of *TRPV3* gene. *TRPV3* activation is associated with epidermal growth factor receptor (EGFR) signaling through a process of transactivation. EGFR activation lowers the *TRPV3* activation threshold.

OS is characterized by painful, mutilating, inflammatory and diffuse palmoplantar keratoderma (PPK) which progresses and leads to flexion contractures and pseudoainhum. Erythema and warty hyperkeratosis develop in the periorificial and intertriginous sites.

Materials & Methods:

We present an 11-year-old Caucasian girl with OS manifestations since her first year of life on her toes and since her sixth year of age on her palms. Genetic analysis found mutation in the *TRPV3* gene. First, she was treated with topical corticosteroids and keratolytics without significant therapeutic effect. At the age of seven, acitretin at 0.85 mg/kg/day was introduced. The therapy resulted in complete resolution of hyperkeratosis, decrease of erythema and disappearance of itching and pain. Acitretin dose has been corrected according to the clinical presentation: from maximal 0.9 to minimal of 0.5 mg/kg/day. After 3.5 years of acitretin therapy, she developed side effects in the form of severe telogen effluvium and cheilitis. Dose reduction resulted in worsening and redevelopment of painful keratoderma on the palms and especially the soles.

Results:

Clinical examination showed diffuse palmar and plantar erythema, partial plantar keratoderma in the form of very painful yellowish hyperkeratosis, as well as flexion contractures of the fingers. There was significant diffuse hair loss and cheilitis with fissures and hyperkeratosis in the corners of the lips. Acitretin dose was gradually tapered and discontinued, while erlotinib was introduced at a dose of 75 mg/day (70 mg/m^2). After 2 months of therapy there was a significant reduction of palmar and plantar hyperkeratosis, as well as a reduction of lesions on and around the lips. The pain and pruritus were absent. Afrer 7 months of erlotinib therapy, she has mild plantar hyperkeratosis and no pain.

Conclusion:

Mutations in *TRPV3* result in activation of transient receptor potential vanilloid 3, leading to increased EGFR signaling, palmoplantar epidermal hyperproliferation and severe lesional pain.

Up to 2023, 82 OS cases have been reported worldwide. No effective treatment is available and patients' quality of life is very poor. Topical keratolyticsand retinoids, oral retinoids and sirolimus have been used in the treatment of PPK with initial improvement and partial benefit. Use of EGFR inhibitors was first reported in 2010. Erlotinib is a tyrosine kinase inhibitor of EGFR. The purpose of using an EGFR inhibitor was to break the vicious cycle of

reciprocal *TRPV3*/EGFR activation initiated by constitutive activation of mutated *TRPV3*. The erlotinib-induced complete remission in patients confirmed EGFR's role as an important mediator of *TRPV3* activity.

Reported studies, as well as our patient, have confirmed the effectiveness of erlotinib in the treatment of PPK in OS, improvement of itch and pain and substantial improvement in life quality. No severe adverse effects were reported. Erlotinib may be a promising, life-changing treatment for children with OS.

Abstract N°: 7319

Mainstreaming melanoma genetic testing: Comparable participant outcomes between dermatologists and genetic counsellors

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Introduction & Objectives: Approximately 10% of melanoma cases have a positive family history and 1-2% have familial melanoma. Variants in melanoma genes explain 20-40% of familial cases and increase lifetime risk by 52-84%. Genetic testing can promote early detection, facilitate personalised screening, and improve preventative behaviours without causing psychological harm. However, access to melanoma genomic testing is currently limited by the high prevalence of melanoma in Australia and finite capacity of clinical genetics services. Thus, alternate models-of-care are needed.

Materials & Methods: High-risk melanoma participants were pseudo-randomised to receive genetic testing from an upskilled dermatologically-trained doctor or a genetic counsellor embedded within a melanoma clinic. We evaluated whether participants' satisfaction and psychological wellbeing varied depending on provider type. Participant reported outcomes were assessed using questionnaires at four timepoints: i) baseline, ii) following pre-test counselling iii) 2-weeks post-result disclosure and iv) 3-months post-result disclosure.

Results: Questionnaires were completed by 148, 138, 117 and 115 participants, at timepoints i) to iv) respectively. Hospital anxiety and depression scores indicated mild-moderate distress at all timepoints with no change over time, or differences according to provider type. Melanoma-specific distress was elevated, but unchanged between baseline and follow up, which is consistent with 82% (n=120/148) of participants having a personal history of melanoma. However, melanoma-specific distress was not associated with provider type. Satisfaction was high at both timepoints, with modestly higher levels detected in the genetic counsellor group following pre-test counselling (p=0.032), and no difference following result disclosure.

Conclusion: These findings confirm our hypothesis that melanoma genetic testing was associated with comparable participant reported outcomes when provided by dermatologically-trained clinicians and genetic counsellors. If replicated, these results support the mainstreaming of melanoma genetic testing in dermatology clinics. To our knowledge, this is the first study to directly evaluate participant outcomes in groups receiving testing from genetic counsellors and non-genetics doctors.

Abstract N°: 7357

Exploring Predictors of Cutaneous Leiomyoma Severity in Hereditary Leiomyomatosis and Renal Cell Cancer Syndrome: An Observational Study

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Introduction & Objectives:

Hereditary Leiomyomatosis and Renal Cell Cancer (HLRCC) is an autosomal dominant syndrome caused by germline pathogenic variants (GPVs) in the *fumarate hydratase* (*FH*) gene. HLRCC is characterized by cutaneous leiomyomas (CLs), uterine leiomyomas (ULs), and ~15% lifetime risk of aggressive renal cell carcinoma (RCC). CLs are often the earliest sign and can be painful, numerous, and visibly disfiguring, potentially leading to significant health-related quality-of-life (QoL) impairment. Yet, predictors of CL severity remain unknown. This study aimed to identify factors associated with CL severity, focusing on lesion number, pain and QoL impact.

Materials & Methods:

This cross-sectional study included HLRCC patients referred to our OncoGenodermatology clinic (December 2022 - April 2025). All patients underwent a total body skin exam by a single dermatologist. Demographics (e.g., age, sex), CL characteristics (e.g., pain level on a scale of 0-10, pain triggers, Dermatology Life Quality Index [DLQI] score), and other HLRCC characteristics (e.g., GPV type) were collected. Negative binomial and logistic regression models (ordinal and binary where appropriate) analyzed predictors of CL severity outcomes: age, sex, and GPV type for **lesion number**; age, sex, GPV type, and body location for **pain**; age, sex, GPV type, and presence of pain for **QoL** as measured by the DLQI score.

Results:

A total of 78 patients with HLRCC were included. 72 (92.3%) had CLs (median lesional number: 15.0; range 0-112). The trunk (88.9%) and upper limbs (77.8%) were most frequently involved. Age was the only significant predictor of total number of CLs, with count increasing by 17% per decade (rate ratio [RR] 1.17, 95% confidence interval [CI]

1.02-1.35; *p*= 0.0291).

Pain (>0) was reported by 43 (59.7%) patients. Of these, 41.9% experienced moderate-to-severe pain (median 3 [range 1-10]). Touch was the most common pain trigger (35.9%), followed by trauma (23.1%), cold (19.5%), and heat (15.3%). While no associations were observed with age, sex or GPV type, CLs on the head and neck were more likely to be painful than those located elsewhere on the body (odds ratio [OR] 4.02, 95% CI 1.03 – 15.74; *p*= 0.0455).

QoL impairment (DLQI >0) was reported by 35 (48.6%) patients, with 17.1% of these reporting moderate impact (median 2 [range 1,9]). QoL impairment related to CLs was independent of age, sex or GPV type. However, presence of pain was a significant predictor of reduced QoL (OR 7.94, 95% CI 2.64 – 23.90; *p*= 0.0002).

Conclusion:

Our findings demonstrate that CLs are common, often painful, and impact QoL. Lesion number increased with age, head and neck location predicted pain, and pain strongly predicted QoL impairment. CL-related burden remains a major unmet need in HLRCC, highlighting the need for early recognition and targeted management strategies.

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Abstract N°: 7387

Beyond Photosensitivity: Long-term survival in Xeroderma Pigmentosum

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Introduction & Objectives:

Xeroderma Pigmentosum variant type (XP-V) is a rare autosomal recessive disorder caused by mutations in the POLH gene, involved in post-transcriptional DNA repair. Unlike other XP types, XP-V retains nearly complete DNA repair capacity, resulting in lower UV sensitivity and longer life expectancy despite a high incidence of skin cancer. Understanding the differences in post-UV damage repair mechanisms is essential, as they directly impact the phenotype and prognosis. This case highlights the importance of early genetic and molecular diagnosis to optimize clinical management and guide future personalized therapies.

Materials & Methods:

A 69-year-old woman (Fitzpatrick phototype III) with no relevant family history (Figure 1) presented with over 30 excised skin tumors, including 24 basal cell carcinomas and 9 squamous cell carcinomas. She showed early signs of XP in preschool, was diagnosed at 22, and developed her first skin cancer at 25. Ophthalmologic findings included ocular melanosis, xerophthalmia, and photophobia. She exhibited widespread dermatosis in sun-exposed areas, with multiple pigmented lesions suggestive of basal cell carcinoma, and marked actinic damage. Cognitive, neurological, and motor functions were normal. Genetic testing revealed a homozygous pathogenic POLH variant (NM_006502.2:c.490G>T), confirming XP-V.

Results:

XP is a group of autosomal recessive genodermatoses with DNA repair defects, mainly involving the nucleotide excision pathway. XP-V, caused by POLH mutations, affects the translesion synthesis process. While other XP types have significantly reduced repair capacity and early-onset malignancies, XP-V typically presents later, with less severe symptoms and no neurological impairment. The phenotype depends on sun exposure and residual repair ability. Differential diagnosis includes types A, D, and E, each with distinct repair capacities. XP-V patients often reach adulthood with functional lives. Though no curative treatments exist, regular skin exams, lesion excision, and potentially immunotherapy are key. Experimental gene-editing therapies may offer future solutions.

Conclusion:

XP-V is a rare XP subtype with preserved DNA repair capacity, leading to milder clinical manifestations and extended life expectancy. Genotype-phenotype correlation is vital for prognosis and management. Early and precise diagnosis enables better clinical outcomes and the possibility of personalized treatments, shifting the outlook from one of early morbidity to a functional, long-term life.

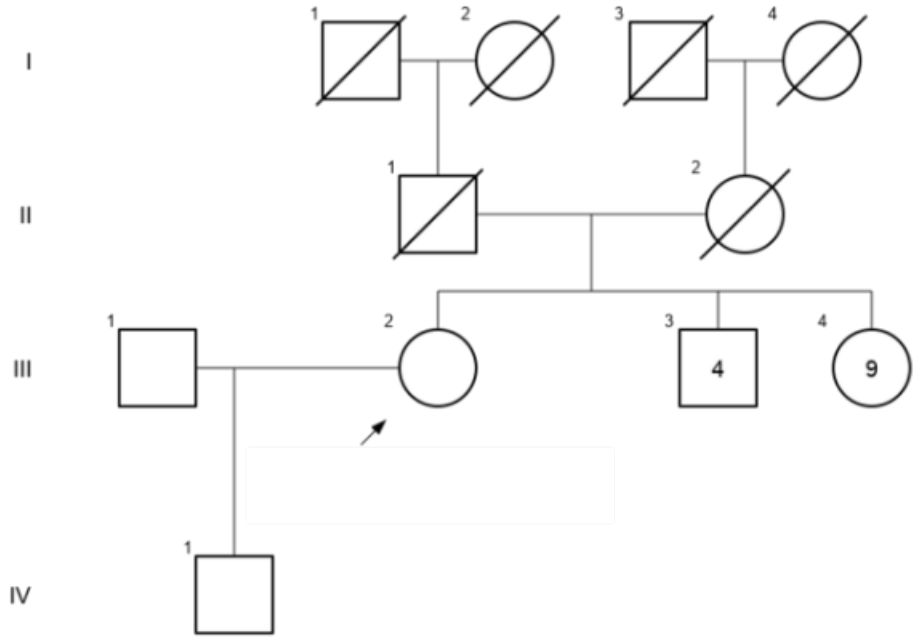

Figure 1. Pedigree of the patient

Abstract N°: 7403

Acrokeratoelastoidosis of Oswaldo Costa: a rare autosomal-dominant genodermatosis

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Introduction: Acroceratoelastoidosis is a type of palmoplantar keratoderma, originally described by dermatologist Oswaldo Gonçalves Costa. It is a rare autosomal dominant genodermatosis, which can also occur sporadically.

Case report: A 72-year-old woman reported that she began experiencing peeling on her hands and feet during adolescence, without associated symptoms. She denies any comorbidities and use of medications. On dermatological examination, she presented with an eruptive papular and hyperkeratotic linear lesion in margins of the hands and feet, with skin thickening over the metacarpophalangeal and proximal interphalangeal joints. A histopathological examination revealed prominent hyperkeratosis and acanthosis, with a normal appearance of the collagen bundle distribution. Staining with orcein showed a reduction in elastic fibers, which were irregular and fragmented. Therefore, a diagnosis of acroceratoelastoidosis by Oswaldo Costa was made. Treatment was initiated with Acitretin 25mg/day and emollient and keratolytic creams, resulting in a partially satisfactory response.

Conclusion: In acroceratoelastoidosis, the clinical is characterized by multiple yellowish papules, sometimes translucent and keratotic, located on the lateral margins of the hands and feet, symmetrically. The most common histopathological findings are hyperkeratosis, mild acanthosis, and changes in elastic fibers in the dermis. Due to the asymptomatic nature of the lesions and their lack of association with morbidity, no treatment is necessary. However, for aesthetic reasons, topical and systemic treatments may be employed, often with unsatisfactory responses. Acitretin appears to demonstrate greater efficacy, although recurrence is common after its discontinuation.

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Abstract N°: 7465

Dermatofibroma- Keloidal Presentation

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Introduction & Objectives: Dermatofibroma is a cutaneous condition that is typically localised in the dermis of the skin.(1) It occurs more often in middle-aged people and is slightly more common in women.(2) Diagnosing dermatofibromas can be challenging due to their diverse range of clinicopathological variations. Here, we present a case of Keloidal Dermatofibroma. Trauma being a potential cause of dermatofibroma may be supported by the results of keloidal transformation in dermatofibromas.

Materials & Methods: Dermatology with multiple, asymptomatic exophytic lesions located at the lateral aspect of the left upper arm and back for last 2 years. The lesions are progressive in nature and insidious in onset. Patient has a history of local trauma on affected site. Furthermore, the family history of the patient is non-significant. On examination, three, well-defined exophytic tumour-like lesions of size varying from 3cm to 6 cm in diameter with shiny, hyperpigmented, smooth surface were present over the back. They are rubbery on palpation, without apparent adhesion to deeper layers . A solitary, well defined, skin coloured growth of similar morphology, of size 2 cm in diameter presented over the left upper arm. Upon palpation, it was firm and non-tender. Dimpling sign could be elicited over these lesions. Dermoscopic findings revealed central reddish brown patch with peripheral dark brown network. Few lesions exhibited linear or arborizing telangiectasia. The biopsy was taken from the sites of lesions to confirm the diagnosis.The histological findings revealed poorly defined proliferation of fibro-histiocytic cells within the dermis, with overlying sparing of the grenz zone. At the periphery of the lesion, entrapment of collagen fibre was noted. The overlying epidermis is acanthotic and showed increased basal layer pigmentation. This thus confirmed the diagnosis of dermatofibroma.

Results: Dermatofibroma accounts for approximately 3% of skin biopsy samples, which are received by dermatopathology laboratories.(2) Dermatofibromas typically present clinically as hard, reddish-brown nodules, whereas keloidal dermatofibromas typically manifest as hard, erythematous papules.(4) Upon histopathological analysis, in the superficial part of the tumour in keloidal dermatofibromas, bounded, keloid-like patches made of thick, highly eosinophilic collagen fibres which are placed erratically can be seen. Additionally, round keloidal collagenous fibres can be seen. Furthermore, keloidal dermatofibromas lack elastic fibres which is a similar morphology as of keloidal scars.(5)

Conclusion: To the best of our knowledge, only a small number of cases of keloidal dermatofibroma have been documented since its initial description in 1998. The existence of keloidal dermatofibroma has been proposed to support the injury theory of dermatofibroma genesis, since keloids are caused by skin injuries.(6)
The hypothesis that trauma may be a potential cause of dermatofibroma may be supported by the finding of keloidal transformation to dermatofibromas. Researchers have discovered this variation to be important because Asians are at greater risk of developing keloids.(5)

Abstract N°: 7540

Age in a furrow: Forehead rhytidectomy in a 27-year old male with pachydermoperiostosis

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Introduction & Objectives:

Pachydermoperiostosis or primary hypertrophic osteoarthropathy is a rare, genetic syndrome with familial and idiopathic forms characterized by progressive joint effusion associated with pachydermia, periostosal proliferation of the long bones, and finger clubbing. This condition presents with distinctive thickening and furrowing of the skin of the scalp, forehead and cheeks, enlargement of the distal parts of the extremities, excessive sweating, and severe seborrhea of the scalp and face.

Materials & Methods:

This is a case of a 27-year old male with a 10-year history of acne, seborrhea, joint pains, enlargement of the wrists, fingers, knees and ankles, and palmoplantar hyperhidrosis. Cutaneous examination showed thickened, furrowed, greasy skin on the face with accentuation of facial folds on the cheeks, chin and forehead. The scalp is grooved and thickened* with minimal scales. Multiple papules, pustules, nodules over the face and chest as well as enlarged distal tips of the fingers and toes, wrists and knees, could also be observed. Histopathology results were consistent with pachydermoperiostosis.

Results:

The patient responded well to oral isotretinoin at a dose of 0.5mg/kg/day. He also underwent forehead rhytidectomy under the plastic surgery service, with noted improvement of the furrows on his forehead. He is maintained on oral retinoids.

Conclusion:

The typical course of pachydermoperiostosis is self-limited as it appears in adolescence, progresses for a number of years, and stabilizes, without diminishing life expectancy. However, once disease has stabilized, patients are left with significant cosmetic morbidity. As physicians it is always our aim to improve the patient's quality of life. In cooperation with other subspecialties, I believe that it is possible to address the varying issues of our patients. In our case, treatment has been mainly focused on the control of sebum production and cosmetic improvement by plastic surgery.

Abstract N°: 7634

GWAS Meta-Analysis in Europeans Identifies Novel Psoriatic Arthritis Risk Loci and Fine-Maps Effector Genes and Cell Types

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Introduction & Objectives:

Psoriatic arthritis (PsA) is a complex immune-mediated systemic disease with strong genetic underpinnings. Despite advances in PsA genetics, the cellular and molecular mechanisms linking risk loci to disease remain incompletely understood. In this work, we aimed to (1) identify new PsA risk loci through a large-scale GWAS meta-analysis in Europeans, (2) fine-map candidate causal genes using transcriptomic integration, and (3) explore the cellular context of disease-associated eQTLs through deconvolution and single-cell-informed approaches.

Materials & Methods:

We meta-analyzed summary statistics from European PsA GWAS datasets (10,425 cases, 265,019 controls) including Finnish (ICD L40.5), UK, Spanish, and North American cohorts, confirming minimal population stratification ($\lambda = 1.032$). Genome-wide significant loci ($P < 5\times10^{-8}$) were functionally mapped using FUMA. Fine-mapping employed the FIZZI-FOCUS pipeline combining GWAS, GTEx eQTLs (blood, spleen to prioritize candidate genes. Colocalization and SMR analyses incorporated eQTL, pQTL, and mQTL data to assess causal gene expression effects. Finally, we applied in silico single-cell deconvolution using the ENIGMA framework on 917 individuals from the OneK1K cohort, leveraging healthy and PsA-specific scRNA-seq references.

Results:

We identified 31 independent genome-wide significant loci, including 12 novel associations across chromosomes 1, 5, 6, 8, 10, 11, 15, 16, 17, and 20. FUMA-based enrichment implicated blood and spleen tissues. TWAS fine-mapping prioritized genes such as ERAP1, TYK2, KAT5, and UBE2L3, while colocalization highlighted overlapping signals in blood and spleen. SMR analyses identified genes with potential causal roles, including IL23R, IL12B, and NFKBIA. In cellular fine-mapping, we identified genome-wide significant QTLs influencing CD4+ and CD8+ memory T cell, Treg, and CD16+ monocyte frequencies, although replication in the PsA context was limited, underscoring the need for bulk RNA-seq from PsA patients to enhance decon-eQTL discovery.

Conclusion:

Our study delivers the largest PsA GWAS meta-analysis to date in Europeans, revealing novel risk loci and pinpointing putative effector genes and immune cell types. Integrating genomics with transcriptomics and cellular deconvolution offers a promising path toward unraveling the mechanisms linking genetic risk to PsA pathogenesis.

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Abstract N°: 7744

annular epidermolytic ichthyosis type 2 and pitted keratolysis

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Introduction & Objectives: Genodermatoses are diseases that affect the skin due to a genomic alteration. Addressing them is essential for providing a timely diagnosis and appropriate treatment. The objective of this study is to provide tools for both the clinical suspicion and the diagnostic pathway for annular epidermolytic ichthyosis type 2

Materials & Methods: A case report and literature review of annular epidermolytic ichthyosis type 2. The PubMed databases were used for the literature search.

Results: A 13-year-old patient presented with a 2-year history of scaly, polycyclic plaques on the body, which changed in size and were migratory. He also presented with permanent plaques with pigmented hyperkeratotic borders and skin folds accentuation in horizontal parallel hyperkeratotic lines in the antecubital folds. The condition began as a newborn with erythroderma and blisters on the cheeks and trunk that improved with age. At 3 months of age, he began with diffuse palmoplantar keratoderma and localized hyperkeratosis areas. Skin's Histopathological results from the lateral neck were diagnosed with epidermolytic ichthyosis/disseminated epidermal nevus. It was decided to take 2 new biopsies on the palm and arcuate plaques of the abdomen, resulting in an epidermolytic hyperkeratosis. Annular epidermolytic ichthyosis was suspected. During a check-up, the presence of cavities and an accentuated bitter odor was noticed in the palms of the hands, for which reason pitted keratolysis was suspected, and topical antibiotics were started. Medical genetics performed a genetic panel by next-generation sequencing, with the finding of a Pathogenic heterozygous variant of the KRT1 gene: 1436C>T p.Ile479Thr, which is compatible with annular epidermolytic ichthyosis type 2 (OMIM: 620148). The patient's palmar cavities improved. Once the diagnosis of annular epidermolytic ichthyosis was confirmed, management with topical retinoids on the palms and soles and 40% urea on the lesions of the trunk and extremities was initiated, with adequate improvement.

Conclusion:annular epidermolytic ichthyosis is a rare, autosomal dominant genodermatosis, first clinically described by Dr. Sahn in 1992. It is a cornification disease characterized by a bullous congenital ichthyosiform erythroderma phenotype and subsequent intermittent episodes of polycyclic, erythematous, scaly plaques on the trunk and extremities. In addition, the presence of bacterial colonization and hyperhidrosis has been described in the form of diffuse palmoplantar keratoderma. The annular form is considered a less severe subtype of epidermolytic ichthyosis. The annular subtype differs from classic epidermolytic ichthyosis at the genetic level in that it does not present mutations in the start or end zones of the alpha helix, but rather in unit 1A or 2B, which would explain a less severe clinical form, like that of the patient. There are 2 types of annular ichthyosis described: type 1 due to a mutation in the KRT10 gene and type 2 with an alteration in the KRT1 gene, with acral lesions like the one presented by this patient, which clinically differentiates it from type 1. This case is presented because it has annular epidermolytic ichthyosis type 2 (OMIM: 620148), an entity described in the literature in 23 patients, and because it is the second case in South America, and the concomitant presence of a pitted keratolysis.

Abstract N°: 7842

Clinical patterns of pruritus in epidermolysis bullosa: an observational study

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Introduction & Objectives:

Pruritus is a major cause of morbidity in patients with epidermolysis bullosa (EB), particularly in dystrophic EB (DEB). Various therapies have been explored, from topical agents to systemic antihistamines and immunomodulators, with dupilumab emerging as a promising new option. However, managing pruritus remains challenging, with limited evidence to guide treatment.

The clinical patterns of pruritus in EB are not well understood. The occurrence and severity of pruritus are known to vary in different EB subtypes. It may also be influenced by factors involving the patient (such as age and infection) or the environment (e.g. ambient temperature). Identifying these factors may enhance our understanding of the pathogenesis of pruritus in EB and contribute to the development of more effective treatment strategies.

Our primary objective was to understand the clinical patterns of pruritus and the factors affecting it in our group of EB patients.

Materials & Methods:

This retrospective observational study included all patients with a clinical diagnosis of EB over an 18-month period. Detailed clinical assessments were performed during a single visit, and past medical records were reviewed. Data collected included pruritus characteristics (severity, sites, variation with age and weather, response to therapy), EB subtype, genotype, disease severity scores, and other clinical features such as scarring, milia, and nail changes. Pruritus intensity was measured using a visual analogue scale (VAS), with parental VAS for infants and young children.

Results:

The study included 12 patients: 6 with DEB, 3 with junctional EB (JEB), and 3 with EB simplex (EBS). Pruritus was reported in all cases except one adult with localised EBS and a 1-month-old with recessive DEB-intermediate (RDEB-I).

Pruritus most commonly began in late infancy (6–7 months), with the earliest onset at 3 months in a DEB case. In most cases, pruritus improved after the first two years of life and became more localised, particularly to acral or scarred areas. Predictable summer exacerbations were also a frequent finding. Episodes of severe itch associated with extensive blistering were reported in 3 cases: RDEB-I (1-year-old), JEB-I (1-year-old) and EB pruriginosa (12-year-old).

All patients were managed with cool compresses/ wet wraps, topical steroids/ tacrolimus, and antihistamines (cetirizine/ hydroxyzine).

Additional systemic agents were required in 3 cases and resulted in marked reduction in itch (and blistering) in all.

1. **Low-dose cyclosporine (3mg/kg/day for 6 weeks) in a 1-year-old RDEB-I (pruritus VAS score reduced from 9/10 to 2/10).**
2. **Dapsone (1mg/kg/day for 4 weeks) in a 12-year-old EB pruriginosa (VAS 8/10 to 2/10).**
3. **Dapsone (1mg/kg/day for 4 weeks) in a 4-year-old with EBS-I with itchy annular lesions (VAS 6/10 to 0).**

Conclusion:

Significant pruritus was reported in nearly all EB cases, regardless of subtype. Itch typically began in late infancy and improved in older children. Summer exacerbations were common. Recognising these patterns may help guide optimal and proactive treatment strategies for itch in EB. Systemic agents such as cyclosporine and dapsone can provide interim relief in selected cases with severe pruritus, particularly when newer therapies are unavailable.

Abstract N°: 7847

Secondary genetic findings in epidermal differentiation disorders: insights from a Polish cohort.

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Introduction & Objectives:

Epidermal differentiation disorders (EDDs) are heterogenous inherited conditions characterized by abnormal epidermal differentiation. EDDs are monogenic diseases caused by pathogenic variants in over 100 distinct genes. Genetic analysis is currently the integral part of diagnostic process and according to novel classification, the name of the causative gene is a central part of disease nomenclature. Identification of causative variants is important in terms of treatment, as well as for the genetic counseling purposes. The genetic analysis process is mostly based on Next Generation Sequencing (NGS), which enable analysis of multigenic panels. This enables rapid detection of causative genetic defects, but also may identify the presence of the other (secondary) defects in the EDDs genes. Whether this secondary findings have any clinical impact on patients phenotype remains unknown. Also the number of patients, in whom such variants were reported is unavailable, as in majority of articles this aspect is not mentioned.

The aim of the study was to retrospectively reanalyze the cohort EEDs patients of Polish origin in order to identify secondary findings (SF) in the other genes involved in epidermal barrier formation.

Materials & Methods:

A cohort of 262 EEDs patients were included to the study. All of them had established molecular cause of their disease using panel NGS analysis. In order to detect secondary variants, the raw data were re-analyzed and annotated using ClinVar and HGMD data. Novel variants were scored according to Consensus Recommendation of the American College of Medical Genetics and Genomics (ACMG).

Results:

In 28 patients (10,7%) secondary variants were identified. Most of the variants were known pathogenic/likely pathogenic ones, notably 3 were novel truncating mutations. In majority of patients (12) variants in *FLG* gene were detected. Other patients had variants in *ABCA12, ALOX12B, ALOXE3, DSP, ERCC3, GTF2H5, NIPAL4, SPINK5, STS, SUMF1, TGM1, VPS33B* and *WNT10A* genes. In a single case two additional variants in two different genes were found.

Conclusion:

Secondary findings are detected in over 10% of patients, which make it an important issue in the context of genetic counselling. Importantly, *FLG* variants were detected in 12 cases. The *FLG* gene defects are causative for an autosomal semidominant ichthyosis vulgaris (IV) and atopic dermatitis. It has already been reported in few studies that *FLG* variant exaggerated the symptoms of X-linked (*STS*) ichthyosis.

Nevertheless, the majority of SF are detected in the genes connected with autosomal recessive disorders. It cannot be excluded that disruption of a single allele may influence, otherwise impaired, cellular protein-lipid epidermal homeostasis, as well as phenotype. The aspect of presence and significance of SF in epidermal differentiation disorders requires further investigation on a larger number of patients in future.

Abstract N°: 7860

Copy Number Variants significantly contribute to the genetic landscape of Epidermal Differentiation Disorders.

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Introduction & Objectives:

Epidermal Differentiation Disorders, EDD, formerly referred to as Mendelian Disorders of Cornification (MeDOC), are a large group of genetically determined diseases with abnormal epidermal differentiation and are inherited in an autosomal recessive, dominant or sex-linked manner. To date, pathogenic variants in over 100 genes are known to be causative for EDDs. In majority of genes, with the exception of *STS*, single nucleotide variants are identified and larger rearrangements are rarely found. The Next Generation Sequencing (NGS) dedicated panels allows determining the molecular cause of EDDs in around 80%-90% of patients across various populations. Although NGS based diagnostics was introduced around 10 years ago, the bioinformatic algorithms enabling detection of large rearrangements - copy number variations (CNVs) were gradually developed. The aim of this study was to perform retrospective analysis to identify the copy number variations (CNVs) in EDDs patients without full molecular diagnosis after performing NGS panel.

Materials & Methods:

The study included 48 patients with EDDs, in whom a panel (self-designed NGS panel) sequencing of 69 genes was previously performed and no molecular pathology was determined or only one pathogenic variant in autosomal recessive disease was found. CNVs *in-silico* analysis was performed based on raw data from NGS using dedicated algorithms: CODEX, CoNIFER, cn.mops, ExomeDepth and XHMM. The presence of CNVs was confirmed with certified methods: RT-qPCR, direct sequencing of breakpoints and/or PCR.

Results:

Potential copy number variations were detected in 17 out of 48 patients. Most prevalent CNV was duplication of exons 10-14 in the *TGM1* gene (9 patients). Next were deletions of exons 1-16 in *SPINK5* gene (3 patients), deletions of exons 1-5 in *SPINK5* gene (2 patients), deletion of exons 4-5 in *CERS3* gene (1 patient), deletion of exons 12 in *CERS3* gene (1 patient) and exon 10 deletion in *JUP* gene (1 patient). In 16 out of 17 patients, CNV analysis enabled determination of the full genotype.

Conclusion:

Copy number variations are an important cause in the pathogenesis of EDD. CNV analysis should be introduced into the routine molecular diagnostics algorithm.

Abstract N°: 7942

Recurrent cutaneous myoepithelioma in upper limb: a case report

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Introduction & Objectives:

Myoepitheliomas are rare myoepithelial cell tumors, more common in salivary glands, but can occur cutaneously. They show heterogeneous histology (spindle, epithelioid, hyaline) and benign behavior similar to chondroid syringoma. Cutaneous myoepithelioma is rare, with few reports. We present a recurrent case since childhood.

Materials & Methods:

21-year-old male with recurrent forearm nodules since age 4, no lymphadenopathy. Initial MRI showed well-defined subcutaneous nodule (1.9cm). Excisions in 2006 and 2010, with proximal recurrence. New axillary lesion with same features. First nodule (age 4): oval, firm, white, 1.7x1.5x0.8cm. Histology: myoepithelioma. Immunohistochemistry: S100+, cytokeratin+, smooth muscle actin+. Recurrences: S100+, EMA focal+, GFAP focal+, desmin-, CD34-, pan-CK-, smooth muscle actin-. Chest/abdomen CT/MRI unremarkable. Watchful waiting chosen.

Results:

Cutaneous myoepithelioma is rare; definitive diagnosis is by histopathology and immunohistochemistry. Local recurrences are common in benign forms. Differential includes epithelioid sarcoma and chondroid syringoma. Treatment not standardized.

Conclusion:

Rare cutaneous tumor case report, important for differential diagnosis of skin nodules and documenting therapeutic approaches, given lack of standardization. More reports will enrich the literature.

Abstract N°: 7978

H Syndrome Presenting with Bilateral Cheek Enlargement and a SLC29A3 Gene Variant

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Introduction & Objectives: H syndrome (OMIM #602782) is a rare autosomal recessive genodermatosis caused by *SLC29A3* gene mutations. The term was first coined in 2008 since most of the clinical features observed in affected patients start with the letter 'H'. We present a case of an adolescent female with hyperpigmentation, hypertrichosis, and 'H' symptoms consistent with H syndrome. In addition, she also had bilateral cheek enlargement, an uncommon presentation of the syndrome, as well as a variant of *SLC29A3* gene mutation detected in her genetic studies.

Materials & Methods: An adolescent female, the second child of a non-consanguineous marriage, presented with symmetric, diffuse, indurated hyperpigmented plaques and patches with overlying hypertrichosis, associated with warmth and tenderness on the hypogastric and sacral area, and bilateral lower extremities, sparing the knees. The patient also had bilateral cheek enlargement, sensorineural hearing loss on pure tone audiometry, low height (below 3rd percentile), facial telangiectasias, mild hepatosplenomegaly on abdominal CT scan, and symptoms of hypogonadism including amenorrhea and delayed development of secondary sexual characteristics.

Results: Five-millimeter skin punch biopsies of the hyperpigmented lesions and a core-needle biopsy of the enlarged cheeks both revealed fibrohistiocytic proliferation with lobular panniculitis, with CD68 and S100 positive and CD1a negative staining patterns. Craniofacial MRI revealed symmetric hypertrophy with focal fatty infiltration of the facial muscles, temporalis, and masseter. Genetic testing showed a homozygous frameshift mutation in the *SLC29A3* gene, a mutation that has also been observed in individuals with clinical features of*SLC29A3*-related conditions. The patient was managed by a multidisciplinary team with nonsteroidal antiinflammatory drugs for fibrosis, hormone replacement for amenorrhea, and Neodymium-doped Yttrium Aluminum Garnet laser for hair reduction.

Conclusion: H syndrome is a rare disorder and it is important to consider this condition in patients presenting with hyperpigmentation and hypertrichosis in the setting of multisystemic involvement. H syndrome patients do not usually manifest with bilateral cheek enlargement but the authors believe that the mechanism of developing this feature is similar to that of the other skin changes due to similar histopathologic findings of both the skin and cheek biopsies. Genetic testing is the gold standard of diagnosis but mutations involving unique exon and codons in the *SLC29A3* gene may result in a different phenotype. While there is no definitive management, multidisciplinary care and regular monitoring must be instituted to better manage symptoms and complications.

Abstract N°: 8051

Treatment of keratosis pilaris by Pinhole technique using 10,600 nm carbon dioxide (CO2) laser

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Introduction & Objectives:

Introduction: Keratosis pilaris (KP) is a common hereditary disorder of keratinisation that affects 50-80% of adolescents worldwide. Follicular hyperkeratosis leads to formation of multiple, small, folliculocentric papules with perifollicular erythema predominantly on the extensor aspects of arms, thighs and buttocks. While KP is often asymptomatic, it can be cosmetically disfiguring and may lead to psychosocial distress among patients. Various treatment modalities for keratosis pilaris have been tried with limited success. With the Pinhole method of CO2 laser, multiple small holes are created in targeted skin lesions through which laser energy can be delivered to achieve destruction of deep dermal tissues as well as thermal stimulation of surrounding collagen bundles.

Objectives: To evaluate the therapeutic efficacy and tolerability of Pinhole technique of an ablative 10,600-nm Carbon dioxide (CO2) laser using Ultra pulse mode in the treatment of Keratosis pilaris.

Materials & Methods:

A total of 24 patients with keratosis pilaris were treated with two sessions of CO2 laser treatment using the pinhole method. Patients received two consecutive treatments at 4-week intervals on the KP lesions. Laser fluences were delivered under Ultra pulse mode with the following settings: pulse duration of 100 ms, frequency of 50 Hz, power 30 Watts. Standardized clinical photographs were obtained at each visit. Clinical improvement was evaluated 1 month after the last treatment, using the photographic data. Two non treating dermatologists, evaluated the clinical improvement grades by comparing pre- and post-treatment clinical photographs using physicians' global

assessment on two main criteria: skin texture (keratotic papules) and dyspigmentation (hyperpigmentation and erythema). Patients' satisfaction and side effects were assessed at baseline and at 1 month after the last treatment

Results:

Evaluation of the clinical results at 1 month after the second treatment session

demonstrated marked clinical improvement (51~75%) in sixteen out of the twenty-four

patients (66.6%) in skin texture and dyspigmentation of keratosis pilaris lesions,

respectively according to physicians' global assessment ($p < 0.05$). Four patients (16.66%) showed near total (>75%) improvement in the skin texture whereas five patients (20.83%) showed near total improvement in dyspigmentation. Surveys for overall patient satisfaction with pinhole Co2 laser treatment revealed that 14 of the 24 patients (58.33%) were satisfied, 8 (33.33%) were extremely satisfied and two (8.33%) were fairly satisfied. Post treatment side effects -erythema, burning sensation, mild pain and crusting were noted in the laser treated lesions resolving rapidly within the study period. Post therapy transient pigmentary alteration was observed in 6 patients. However, no severe adverse effects like bleeding, oozing, scarring, secondary bacterial infections or blister formation were reported.

Conclusion:

Application of the pinhole method of CO2 laser exerts positive therapeutic effects by

accurately aiming at KP lesions and delivering high laser energy using an ultrapulse char-

free mode offering the ability to target deep dermal tissue without significant risk for

adverse sequelae makes it a viable treatment modality for Keratosis pilaris.

Abstract N°: 8056

Recessive Dystrophic Epidermolysis Bullosa: Clinical, Genetic and Multisystemic Characterization of Two Familial Cases

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Introduction & Objectives:

Recessive dystrophic epidermolysis bullosa (RDEB) is a severe inherited skin disorder caused by mutations in the COL7A1 gene, leading to defective or absent type VII collagen and resulting in sublamina densa blistering after minor trauma. With an incidence of up to 49 per million and RDEB prevalence at 1.35 per million live births, the disease presents with significant clinical and systemic involvement. This report describes two siblings with RDEB to highlight the importance of early diagnosis, genetic testing, and multidisciplinary care.

Materials & Methods:

We evaluated two affected siblings from a consanguineous family (Figure 1). Both developed blisters within two weeks of life. Histopathology revealed subepidermal blistering. The genetic study of sequencing of the complete exome of the female patient was performed and the results are still pending.

Brother (26 years): Presented with extensive erosive and hemorrhagic lesions, non-healing ulcers, pruritus, malnutrition, dysphagia, pseudosyndactyly, microstomia, and partial anonychia.

Sister (24 years): Displayed similar findings with added cicatricial alopecia and more severe disease progression. Both had dental hypoplasia and cutaneous fragility. Each has a clinically unaffected child.

Results:

Type VII collagen deficiency contributes to impaired wound healing, tumorigenesis, and systemic involvement. RDEB's phenotype varies, influenced by genetic mutations, their combinations, and environmental factors. Although ideally confirmed through electron microscopy, immunohistochemistry, or genetic testing, diagnosis often remains clinical. In this case, whole-exome sequencing was initiated for the female patient, though results are pending. The consanguineous background supports a recessive inheritance pattern and reflects trends seen in up to 92% of RDEB cases.

RDEB complications include pseudosyndactyly, esophageal strictures, joint contractures, and aggressive squamous cell carcinomas—often the leading cause of early death (41%). Cardiomyopathy and heart failure account for another 30% of mortality. Multisystem involvement includes ocular, gastrointestinal, and genitourinary complications, among others. Despite increased pregnancy risks, childbirth is possible with appropriate management.

Conclusion:

RDEB severely affects quality of life due to progressive cutaneous and systemic complications. Limited access to molecular diagnostics and specialized care hampers effective management. Broader availability of genetic testing, early intervention, and coordinated care are essential. Further research into population genetics and emerging therapies such as gene or cell-based treatments holds promise for altering disease progression and improving

patient outcomes.

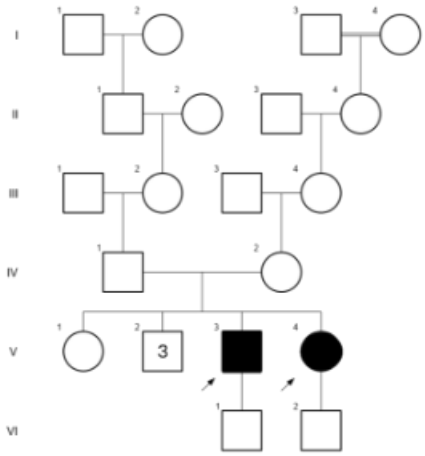

Figure 1. Pedigree of the affected patients.

Abstract N°: 8118

Prevalence and Severity of Anemia in Patients with Recessive Dystrophic Epidermolysis Bullosa in Uzbekistan

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Introduction & Objectives:

Anemia in epidermolysis bullosa (EB) is multifactorial and varies by subtype. Poor nutritional intake due to painful mucosal lesions, along with chronic blood and protein loss from non-healing wounds and frequent infections, contributes significantly. Severe anemia is most common in junctional EB and recessive dystrophic EB, where extensive skin damage leads to substantial iron loss, making chronic cutaneous bleeding a major cause of iron deficiency. To date, there has been no comprehensive data on the prevalence of anemia in EB patients specifically characterized in Uzbekistan. Our aim was to assess and describe the prevalence of anemia in the Uzbekistan population with recessive dystrophic epidermolysis bullosa (RDEB) through a retrospective cross-sectional study.

Materials & Methods:

A review was conducted on 38 RDEB patients registered in the Uzbekistan Epidermolysis Bullosa Registry who received inpatient care in 2023, with the aim of assessing evidence of anemia. The patients were grouped into pediatric (<18 years) and adult (≥18 years) categories, further subdivided by sex.

Results:

Of the 38 patients included in the analysis, the sex distribution was equal, with 19 males (50.0%) and 19 females (50.0%). Patient age ranged from 3 to 30 years, with a mean age of 16.5 years. The mean hemoglobin level for pediatric patients (n = 26) was 102.92 ± 20.75. The mean hemoglobin level for adult female patients (n = 6) was 105.5 ± 9.19 g/dL. The mean hemoglobin level for adult male patients (n = 6) was 94 ± 31.2 g/dL. The overall prevalence of anemia in RDEB patients (*n* = 38) was 78.9%. (*n* = 30/38). Anemia was classified according to the World Health Organization (WHO) criteria. Among 38 patients with recessive dystrophic epidermolysis bullosa (RDEB), the distribution of anemia severity varied by age and sex. In pediatric patients aged 0–5 years (n = 4), 50% (n = 2) had moderate anemia (hemoglobin 70–99 g/L), and 50% (n = 2) had normal hemoglobin levels (≥110 g/L). Among children aged 5–12 years (n = 14), 57.14% (n = 8) had moderate anemia (80–109 g/L), 14.29% (n = 2) had mild anemia (110–114 g/L), and 28.57% (n = 4) had normal hemoglobin levels (≥115 g/L). In adolescents aged 12–14 years (n = 4), 50% (n = 2) had severe anemia (hemoglobin <80 g/L), while the remaining 50% (n = 2) had moderate anemia (80–109 g/L). Among females older than 15 years (n = 6), 66.67% (n = 4) had moderate anemia (80–109 g/L), and 33.33% (n = 2) had mild anemia (110–119 g/L). In males older than 15 years (n = 6), 66.67% (n = 4) had severe anemia (hemoglobin <80 g/L), while 33.33% (n = 2) had normal hemoglobin levels (≥130 g/L).

Conclusion:

In conclusion, the study found a high overall prevalence of anemia (77.78%) in Uzbek RDEB population. Anemia severity varied by age and sex, with pediatric patients mostly having moderate anemia, while adolescents and adults, particularly males, experienced more severe forms.

Abstract N°: 8121

Pachyonychia Congenita: A Rare Diagnosis to Keep in Mind in Infants with Thick Yellow Nails

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Introduction & Objectives:

Pachyonychia congenita is a rare autosomal dominant disorder characterized by severe, painful palmoplantar keratoderma, nail dystrophy, and oral leukokeratosis. Its etiology is attributed to mutations in keratin genes.

Materials & Methods:

Herein, we report an infant presenting with nail dystrophy who was diagnosed with pachyonychia congenita based on clinical and genetic findings, including a de novo heterozygous variant in the *KRT6A* gene.

Results:

A male infant born at 36+6 weeks of gestation via spontaneous vaginal delivery to a 38-year-old mother presented with thickened, yellow discoloration of fingernails and toenails. Progressive nail changes were noted over the following months, prompting further evaluation in collaboration with the dermatology department. His medical history included hospitalization in the neonatal intensive care unit with an early diagnosis of sepsis. The patient had an unremarkable family history. Dermatological examination revealed discolored, thickened, and wedge-shaped fingernails and toenails. Leukokeratotic plaques were observed on the dorsum of the tongue and hard palate mucosa, first noted during the third month of life. Based on nails and oral mucosa findings, a preliminary diagnosis of congenital pachyonychia was considered. After obtaining informed consent from his parents, genomic DNA was extracted from peripheral blood. Whole exome sequencing (Qiagen, Hilden, Germany) detected a de novo heterozygous variant in the *KRT6A* gene [NM_005554.4:c.513C>A (p.N171K)]. Segregation analysis confirmed that both biological parents were homozygous for the wild-type allele, verifying the variant as de novo. The diagnosis of pachyonychia congenita was confirmed by the identification of a pathogenic genetic mutation. The patient was treated with 10% urea cream, resulting in visible nail smoothening during follow-up. Oral hygiene was also recommended.

Conclusion:

Pachyonychia congenita typically manifests within the first three years of life with a triad of nail dystrophy, plantar pain, and plantar keratoderma. Although mutations in the *KRT6A, KRT6B, KRT6C, KRT16,* and *KRT17* genes are implicated in its pathogenesis, *KRT6A* mutations, which encodes keratins expressed in the palmoplantar epidermis, nails, and mucosa, are the most frequently encountered.

Among *KRT6A* mutations, toenail dystrophy is the most common finding, tends to be more severe, and has a significantly increased likelihood of involvement of all toenails. Subungual thickening leading to a V-shaped curvature of both fingernails and toenails is characteristic. Plantar keratoderma appears with onset of walking, typically at the heels, and plantar pain leads to walking difficulties. Oral leukokeratosis generally appears by the third week of life, most commonly affecting the tongue, and may cause snoring. Other frequent findings include

follicular hyperkeratosis, hyperhidrosis, and cysts. Diagnosis relies on clinical, genetic, and family history assessments.

In this case report, we presented an infant with nail dystrophy who was diagnosed with pachyonychia congenita due to a *KRT6A* mutation. This case highlights the importance of a detailed dermatological examination, including the oral mucosa, in infants presenting with thick yellow nails. Pachyonychia congenita should be considered among the differential diagnoses, even in the absence of a family history, due to the possibility of de novo mutations.

Abstract N°: 8131

Autosomal recessive congenital ichthyosis caused by a novel variant in cornifelin gene: A case report

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Introduction & Objectives:

Autosomal recessive congenital ichthyosis (ARCI) is a genetically heterogeneous disorder of keratinization. While over a dozen genes are implicated, the role of the CNFN (cornifelin) gene has not previously been linked to a confirmed clinical phenotype. We present two brothers with nonsyndromic ichthyosis carrying a novel homozygous CNFN splice site variant, adding to the emerging understanding of cornified envelope dysfunction in ARCI.

Materials & Methods:

Two male siblings, aged 12 and 5, born to consanguineous parents, presented with generalized polygonal brown scales involving the trunk and limbs, sparing the face, palms, soles, and flexures. There was no collodal membrane at birth, and no mucosal, hair, or nail abnormalities were noted. Systemic examination was unremarkable apart from retractile testes in one child and early dental caries in the other. Growth and development were age-appropriate.

Whole exome sequencing revealed a novel homozygous CNFN variant: c.113-1G>T (NM_032488.4), located at the splice acceptor site of intron 1. This variant was classified as “likely pathogenic” per ACMG guidelines (PVS1) and absent from population databases (gnomAD, HGMD). Carrier testing confirmed parental heterozygosity. In silico predictors (SpliceAI, dbscSNV, Varsome) supported the variant’s deleterious impact on splicing. Clinical management included topical emollients, urea-based keratolytics, and regular dermatologic follow-up. Both patients exhibited stable disease without progression or new findings over several years.

Results:

This is the first report linking a CNFN splice site variant to a phenotype consistent with autosomal recessive congenital ichthyosis. The absence of systemic involvement and the consistent dermatologic findings in both siblings support a nonsyndromic ARCI presentation. CNFN encodes cornifelin, a cornified envelope protein involved in terminal keratinocyte differentiation. Its dysfunction likely disrupts epidermal barrier integrity, manifesting as ichthyosis. Previous models have demonstrated reduced loricrin and increased involucrin expression in CNFN-overexpressing mice; however, no definitive link to ichthyosis had been established until this report.

Conclusion:

This case expands the genotypic spectrum of ARCI by implicating a novel pathogenic splice site variant in CNFN. It emphasizes the role of cornifelin in cutaneous barrier formation and highlights the importance of considering rare genes in the evaluation of congenital ichthyosis, especially in consanguineous populations. Genetic confirmation of such cases not only informs prognosis and recurrence risk but may also pave the way for future gene-targeted therapies. Further studies are needed to validate CNFN’s role and explore its interactions within the cornified envelope protein network.

Abstract N°: 8243

Harlequin Ichthyosis: Two New Case With Fatal Outcomes

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Introduction & Objectives:

Harlequin ichthyosis is the most severe and often fatal form of congenital ichthyoses, with an estimated incidence of approximately 1 in 300,000 live births. It is inherited in an autosomal recessive manner, caused by mutations in the ABCA12 gene. Clinically, the condition presents at birth with skin encased in thick, yellowish scales separated by deep, red fissures.

Our study aims to report two new cases and describe their clinical features, with emphasis on the diagnostic and prognostic implications of this severe congenital disorder.

Case report:

Case 1: A female newborn, first child of first-degree consanguineous parents, was evaluated on day 1 of life. The mother was 20 years old with no notable medical history. The pregnancy was poorly monitored and delivered at 32 weeks of gestation. The infectious workup was negative. There was no medication, toxic exposure, or similar familial cases reported. The baby was delivered vaginally, with an Apgar score of 8/10 and a birth weight of 1400 grams.

Dermatological examination revealed shiny, taut, varnished skin resembling a collodion membrane with areas of fissuring. Thick ichthyosiform scales in a "fish-scale" pattern were present on the dorsal arms and upper back. The face exhibited large, yellowish scales separated by deep red fissures, with ectropion, eclabion, eversion of the ears and nose, wrinkled auricle, swollen extremities without palmar or plantar creases, tapered, gloved fingers, and short, curved toes. The evolution was rapidly fatal.

Case 2: A male newborn evaluated at 6 hours of life, born to first-degree consanguineous parents. The 24-year-old mother had a history of miscarriage and a poorly monitored pregnancy delivered at 34 weeks via cesarean section due to fetal heart rate abnormalities. The Apgar score at birth was 7/10 and birth weight was 1500 grams.

Dermatological examination showed thick, rigid, yellowish plaques forming a true armor-like shell, separated by deep, bright red fissures resembling a mosaic pattern. There was marked ectropion, nasal eversion, eclabion, and auricles adhered to the scalp, creating a characteristic "frog-like" facial appearance. The extremities were swollen with gloved fingers and short, curved toes. The course was rapidly fatal.

Conclusion:

Harlequin ichthyosis represents the most severe form of congenital ichthyosis, often leading to death due to dehydration and infections. Neonatal management includes 100% humidity, topical emollients, and oral retinoids such as acitretin (0.5–1 mg/kg/day). Despite these interventions, mortality remains high, highlighting the importance of early discussions regarding palliative care or medical termination of pregnancy (MTP) in confirmed antenatal diagnoses.

Therapeutic decisions must be multidisciplinary, considering the extremely poor prognosis and impact on quality of life. Family support is essential in managing this devastating condition.

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Abstract N°: 8251

A Case of Plexiform Neurofibroma Associated with a Pathogenic NF1 Variant: Multisystem Evaluation and Dermatologic Clues

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Introduction & Objectives: Neurofibromatosis type 1 (NF1) is an autosomal dominant genetic disorder caused by pathogenic variants in the NF1 gene. It is characterized by cutaneous, neurological, and systemic manifestations. Plexiform neurofibromas are complex, often congenital tumors involving multiple nerve fascicles and are considered pathognomonic for NF1. Dermatologic manifestations such as café-au-lait macules, axillary freckling, and cutaneous neurofibromas often appear before systemic symptoms, emphasizing the key role of dermatologists in early identification.

Case Report: A 26-year-old female presented with a congenital, soft, hyperpigmented mass located in the right hypochondriac and right infrascapular regions The lesion was soft, compressible, and poorly circumscribed on palpation. Skin examination revealed two café-au-lait macules on the back and axillary freckling. No Lisch nodules were detected on ophthalmologic examination. Cardiology consultation, including echocardiography, revealed normal left ventricular systolic function, normal right heart chambers, and mild tricuspid regurgitation with a maximal TR velocity of 2.0 m/s. Neurological examination was unremarkable. A biopsy was performed from the soft masses, and histopathological examination revealed a plexiform growth pattern. Histopathology confirmed the diagnosis of plexiform neurofibroma. Genetic testing demonstrated a pathogenic mutation in NF1, meeting NIH diagnostic criteria for neurofibromatosis type 1. No optic pathway gliomas or other systemic complications were identified. The multidisciplinary evaluation ruled out organ dysfunction.

Discussion: Plexiform neurofibromas can be clinically diagnosed, although histopathologic confirmation remains essential, especially in congenital soft tissue masses of uncertain origin. In this patient, the presence of only two café-au-lait macules might have been overlooked if not for the clinician’s awareness of the significance of the mass and axillary freckling.

Given their potential for malignant transformation into malignant peripheral nerve sheath tumors, plexiform neurofibromas warrant close clinical monitoring and long-term surveillance, even in the absence of current systemic involvement.

This case also illustrates the importance of integrating dermatologic, genetic, and multisystem evaluation to guide diagnosis and follow-up in suspected NF1 cases

Conclusion: This case highlights the role of dermatologists as frontline clinicians in recognizing hereditary tumor syndromes. Early identification enables for comprehensive multisystem evaluation, patient education, genetic counseling, and ongoing surveillance for complications such as optic pathway gliomas, learning disabilities, skeletal abnormalities, and malignant transformation.

Abstract N°: 8285

Mucinous Carcinoma in NF1: Raising Awareness for Atypical Malignancies in Genetic Disorders

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Introduction & Objectives:

Mucinous carcinoma is a rare form of adenocarcinoma characterized by abundant extracellular mucin production, commonly affecting the breast, colon, and ovary. Neurofibromatosis type 1 (NF1) is a genetic disorder predisposing individuals to benign and malignant tumors. While NF1 is primarily associated with neurofibromas and malignant peripheral nerve sheath tumors, an increased risk of breast cancer has been reported.

Observation:

We report the case of a 69-year-old female with a history of NF1, diagnosed with mucinous adenocarcinoma of mammary origin following a neglected deep second-degree burn on the anterior chest wall. Clinical findings included:

• Cutaneous and systemic signs of NF1: Multiple neurofibromas, café-au-lait spots (>6), and soft tissue infiltration of the thoraco-abdominal wall.

• Histological and immunohistochemical analysis: CK7+, CK20-, GATA3+, CDX2-, ER 80%, PR 90%, HER2 3+ (positive), and Ki67:

30%, confirming a breast origin.

• Metastatic involvement: Axillary, cervical, and inguinal lymph nodes; pleural effusion with pulmonary nodules.

Treatment with dual HER2 blockade (Trastuzumab-Pertuzumab) and chemotherapy (Paclitaxel) was considered, but the patient died before treatment was initiated due to rapid disease progression and cardio-respiratory complications.

Discussion:

NF1, is a heterogeneous multisystem disease of genetic origin of highly variable severity, associating neuro-cutaneous anomalies and caused by mutation of the NF1 gene. Mucinous breast cancer, also known as colloid or gelatinous carcinoma, is in particular a rare histological entity of breast cancer, accounting for around 2% of invasive breast carcinomas, and generally occurs in women over the age of 62. Mucinous breast carcinoma classically expresses ER, whereas less than 70% express RP. The extent of cellularity is a poor prognostic factor. Indeed, these tumours are often of low histological grade, with rare vascular or nerve invasion and less frequent lymph node infiltration. Immunohistochemically, mucinous breast carcinomas are characterized by a high expression of hormone receptors, noted in 87% of cases. Moreover, tumour cells are most often Her 2 negative (score 0, 1 or 2 non-amplified). Regarding the proliferation index, Ki67 levels are low in most cases (below 14%). In contrast to our case, HER2 overexpression (Score 3+) and a high proliferative index (Ki at 30%) were noted, which is rare in pure mucinous carcinomas and could explain the exceptionally remarkable tumor aggressiveness in our patient. The presence of chronic inflammation from a burn injury may have contributed to local carcinogenesis. The patient was considered metastatic and was initiated on trastuzumab-pertuzumab with paclitaxel

chemotherapy. Hormonal therapy is under discussion. This case highlights the need for early screening in NF1 patients, particularly for aggressive HER2-positive breast cancers, and emphasizes the role of inflammatory triggers in tumor development.

Conclusion:

This case illustrates the unusually aggressive behavior of a mucinous breast carcinoma in the context of NF1, characterized by HER2 overexpression and elevated Ki67. This unexpected evolution suggests a possible influence of the NF1 mutation on tumor biology. The rarity of this association highlights the need for early screening of NF1 patients, and raises questions about the impact of this pathology on breast cancer prognosis.

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Abstract N°: 8314

CYLD Cutaneous Syndrome Presenting with Multiple Trichoepitheliomas

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Introduction & Objectives:

CYLD cutaneous syndrome (CCS) encompasses a spectrum of inherited adnexal tumor syndromes including Brooke-Spiegler syndrome (BSS), multiple familial trichoepithelioma (MFT), and familial cylindromatosis, all associated with germline mutations in the CYLD gene. These syndromes were historically defined by tumor type and inheritance patterns, but recent studies support a shared pathogenesis with overlapping phenotypes. Trichoepitheliomas, benign adnexal tumors, may be the sole clinical finding, especially in MFT-like presentations. However, sporadic cases without family history have challenged the conventional classification. We present a case of CCS with multiple trichoepitheliomas and a novel CYLD mutation in the absence of familial involvement.

Materials & Methods:

Results:

A 27-year-old female presented with multiple asymptomatic papules on the face and scalp, first noted at age 14. Lesions were distributed over the nose, nasolabial folds, forehead, and occipital scalp. Some had been previously excised with recurrence. Excision of two lesions revealed dermal tumors composed of basaloid cell nodules with keratin horn cysts and fibrous stroma, consistent with trichoepithelioma, without features of cylindroma or spiradenoma. Genetic analysis identified a previously unreported heterozygous pathogenic mutation in CYLD (c.864del, p.Phe288Leufs*23) via SNV indel analysis. The patient had no personal or family history of similar lesions or systemic disease.

Conclusion:

This case exemplifies the phenotypic variability of CCS, illustrating a sporadic MFT-like phenotype with histologically confirmed trichoepitheliomas and a novel CYLD mutation. While the absence of cylindromas and spiradenomas favors MFT, the lack of family history and confirmed pathogenic mutation underscore the limitations of rigid phenotypic classification. Sporadic cases with de novo CYLD mutations likely reflect the same pathogenic mechanism and warrant similar clinical vigilance.

To date, over 100 pathogenic CYLD mutations have been described; the novel variant in this case expands the known mutational spectrum. Surgical excision remains the mainstay of treatment, though recurrence is common. Alternative therapies targeting the NF-κB pathway are under investigation. Given the small but significant risk of malignant transformation, long-term dermatological surveillance is essential. Genetic counseling and regular follow-up are recommended for individuals with CYLD mutations, even in the absence of a family history, to monitor for disease progression and potential malignancy. This case highlights the diagnostic ambiguity within CCS and supports the view that it represents a continuum of phenotypes rather than strictly distinct syndromes. The identification of a previously unreported CYLD mutation (c.864del, p.Phe288Leufs*23) expands the known genetic spectrum and underscores the need for a more flexible classification system that accommodates both familial and sporadic presentations. As genotype–phenotype correlations become clearer, future studies should aim to refine diagnostic criteria and explore targeted therapies to improve long-term outcomes in affected

patients.

Abstract N°: 8448

Harlequin-type ichthyosis

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Introduction & Objectives:

Harlequin-type ichthyosis (HI) is a rare genetic disorder inherited in an autosomal recessive pattern, characterized by profound disruptions in skin keratinization. It is primarily caused by mutations in the ABCA12 gene, which impair lipid transport within the epidermis, leading to a severely compromised skin barrier. Without early recognition and intervention, the condition is frequently fatal in the neonatal period. This study aims to deliver an in-depth review of HI, examining its clinical features, genetic etiology, therapeutic approaches, and prognostic indicators to support timely diagnosis and enhanced patient outcomes.

Materials & Methods:

This work compiles findings from peer-reviewed sources, including individual case reports, clinical studies, and expert recommendations pertaining to HI. Data were gathered from platforms such as PubMed and Scopus using terms like “Harlequin ichthyosis,” “ABCA12 mutations,” “congenital ichthyosis,” and “retinoid treatment.” Priority was given to literature addressing clinical manifestations, genetic testing, treatment methodologies, and outcomes over extended follow-up periods.

Results:

Newborns with HI exhibit thickened, armor-like skin plates separated by deep fissures, frequently accompanied by ectropion, eclabium, and restricted joint movement. The majority of cases are linked to homozygous or compound heterozygous mutations in ABCA12, confirmed via molecular diagnostics. Improvements in neonatal care, particularly the early use of systemic retinoids like isotretinoin or acitretin, have led to markedly better survival rates. Nevertheless, patients continue to face persistent dermatological complications that demand ongoing, multidisciplinary care. Prenatal identification through procedures such as chorionic villus sampling or amniocentesis is now available for families at risk.

Conclusion:

Once uniformly lethal, Harlequin ichthyosis now has a significantly better outlook thanks to advances in early detection and therapeutic interventions. Timely genetic diagnosis and the introduction of systemic retinoid therapy are pivotal in reducing infant mortality and enhancing quality of life. Continued investigation into targeted treatments and comprehensive care plans remains vital to further improving prognosis in this challenging condition.

Abstract N°: 8530

H Syndrome: 02 cases

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Introduction & Objectives:

H syndrome is a rare genodermatosis, mainly characterized by cutaneous findings. To date, around 100 cases have been reported in the literature. We herein present **two** clinically and histologically confirmed cases of H syndrome.

Materials & Methods:

Case 1: A two-and-a-half-year-old child presented with indurated, hyperpigmented, and hypertrichotic cutaneous plaques affecting the trunk and limbs, along with bilateral inguinal lymphadenopathies, bilateral exophthalmos, scrotal hypertrophy, and a micropenis. A CT scan revealed hepatosplenomegaly. Cardiac ultrasound objectified a dilated-phase hypertrophic cardiomyopathy. Histopathological analysis of a skin biopsy revealed a non-Langerhans cell histiocytosis. The patient died two months after his discharge, due to heart failure.

Case 2: A 42-year-old male presented with indurated, hyperpigmented, and hypertrichotic plaques on the thighs and legs, evolving since the age of 5. Clinical and paraclinical exams also objectified bilateral hearing loss, hallux valgus, gynecomastia, and hypergonadotropic hypogonadism. CT imaging revealed retroperitoneal fibrosis and diffuse lymphadenopathies. No cardiac abnormalities were detected. Lymph node biopsy confirmed non-Langerhans cell histiocytosis. The patient had previously undergone a left subtotal thyroidectomy due to a compressive goiter, which later recurred on the contralateral side.

Results:

The diagnosis of H syndrome was retained for both patients, based on clinical and histological elements. H syndrome is a rare autosomal recessive genodermatosis, caused by mutations in the *SLC29A3* gene. It is a non-Langerhans cell histiocytosis that manifests primarily as indurated, hyperpigmented, and hypertrichotic plaques typically located on the lower limbs, along with a great variety of systemic manifestations secondary to organ infiltration, mainly hepatosplenomegaly, heart abnormalities, and endocrinopathies. H syndrome represents a clinical, genetic, histological and immunohistochemical overlap within the group of non-Langerhans cell histiocytosis linked to *SLC29A3* mutations. The broader designation "Histiocytosis-Lymphadenopathy Plus Syndrome" (PHID) is thus now favored. Cardiac involvement, as seen in the first case, appears to be a key prognostic factor. The second case underscores the importance of long-term monitoring for endocrine and lymphoproliferative complications. The association with goiter in this patient constitutes, to our best knowledge, a novel finding in the clinical spectrum of H syndrome.

Conclusion:

Although rare, H syndrome should be suspected in patients presenting with characteristic cutaneous findings, particularly indurated, hyperpigmented, and hypertrichotic plaques. Early diagnosis is crucial for identifying systemic involvement, guiding appropriate multidisciplinary management, and improving outcomes.

Abstract N°: 8531

Rapid response and sustained remission of Hailey-Hailey disease under IL-13 inhibition with tralokinumab

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Introduction & Objectives:

Familial benign chronic pemphigus, commonly referred to as Hailey-Hailey disease (HHD), is a rare hereditary acantholytic genodermatosis characterized by erosions and flaccid vesicles in intertriginous body regions. As the vegetating lesions arising in the course of the disease frequently ooze and are colonized by microbes, patients' quality of life is severely impaired not only by severe itching and pain, but often also by a malodour emanating from the lesions.

As there is no specific therapy for HHD, various treatments with varying and often only moderate success are reported in the literature. However, recently dupilumab, which inhibits the signaling of IL-4 and IL-13 by blocking the IL-4 receptor, has been described as an effective and safe therapy in several case reports. We therefore wondered whether blockade of IL-13 alone could achieve improvement of symptoms and treated a patient with refractory HHD with the IL-13 antagonist tralokinumab.

Materials & Methods:

A 68-years-old female presented to our department with painful erythematous to livid, erosive, plaques-like, partially exudative lesions with fissures in the axillae, groins and submammary region. She had been diagnosed with HHD 37 years ago and had been treated unsuccessfully with local and systemic corticosteroids, acitretin and isotretinoin, CO2-laser ablation, and, due to recurrent bacterial and herpes infections, with local antiseptics, various antibiotics and antiviral drugs, respectively.

When her skin condition deteriorated significantly again and she had to be admitted to hospital due to severe erosions and intense pain, we started treatment with the IL-13 inhibitor tralokinumab, initially at a dose of 600 mg, which was continued at 300 mg every 14 days.

Results:

Already one month after the first application, the lesions had improved significantly and the patient was considerably less afflicted by the disease, which was reflected in a decrease in the Dermatological Quality of Life Index (DLQI) from an initial score of 26/30 to 20/30 points. Treatment was well tolerated throughout, and no side effects occurred.

As the patient had been symptom-free for several months while being treated with the IL-13 inhibitor, we initially extended the treatment interval and then discontinued therapy with tralokinumab. She has meanwhile been symptom-free for more than six months and has resumed Nordic walking, swimming, and cycling. At the last consultation, her DLQI score was 1/30.

Conclusion:

This case suggests that IL-13 inhibition alone is sufficient to achieve significant improvement or even remission in patients with HHD. Furthermore, in our patient, tralokinumab proved to be just as effective in terms of onset of action and just as well tolerated in terms of side effects as dupilumab.

Abstract N°: 8564

Late onset Darier's disease

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Late onset Darier´s disease – a case report

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Late onset Darier´s disease – a case report

Introduction & Objectives:

Darier´s disease is an autosomal dominant genodermatosis caused by mutations in ATP2A2 gene. Usually it is presented with hyperkeratotic papules and plaques on seborrheic areas and intertriginous areas with nail abnormalities [1,4]. Disease typically manifests during adolescence (2,3). We would like to report a case of late onset of Darier´s disease with clinicopathological correlation.

Materials & Methods:

We would like to present a case of a 54-year-old male patient who came to our dermatology out-patient department with complaints of multiple erythematous papulous lesions with pronounced itching presented over face, neck and upper chest with for more than a year. In the past 3 months lesions spread throughout the rest of his trunk and groins. Patient complained of aggravation of lesions in summer. So far he has been treated with methotrexate and topical corticosteroids without any significant improvement. It is important to add that his mother had similar complaints from her adolescent age but never visited a dermatologist.

Histopathological examination was done from the excisional biopsy taken from the lesion on the chest which showed dyskeratotic keratinocytes- corps ronds in the malphigian layers of the epidermis and grains and suprabasal separation.

Results:

We administered acitretin to our patient, to which he quickly received an excellent therapeutic response and gradually there was a clinical regression of skin changes and pruritus.

Conclusion:

We believe that this is a clinically and scientifically interesting case considering it`s presentation in adult age, without symptoms of skin changes in earlier age. Despite the fact that Darier's disease is a rare keratinization disorder with clinical presentation mainly in the adolescent population we should be aware that this disease can rarely be present in the adult population, so we should think about it in such atypical clinical presentations.

References:

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Abstract N°: 8659

Buschke-Fischer-Brauer Disease Revealed by Severe Plantar Disability: A Case Report

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Introduction & Objectives:

Punctate palmoplantar keratoderma (PPPK) type I, also known as Buschke-Fischer-Brauer disease, is a rare hereditary disorder characterized by multiple hyperkeratotic papules and plaques affecting the palms and soles. Inherited in an autosomal dominant pattern, it usually manifests between the second and fourth decades. Though benign, it can cause significant discomfort and functional disability. We report a late-diagnosed case of hereditary PPPK type I in a neurologically impaired elderly patient, highlighting the clinical and therapeutic challenges.

Materials & Methods:

A 69-year-old man with insulin-dependent diabetes, hypertension, and post-ischemic stroke hemiplegia presented with painful, progressive palmoplantar keratoderma evolving since the age of 38. He reported a similar history in his father. Clinical examination revealed multiple verrucous, yellowish-brown keratotic nodules and plaques distributed over weight-bearing areas of the soles and palmar surfaces, sparing the nails and mucosae. The lesions were disabling, both functionally and aesthetically. A clinical diagnosis of PPPK type I was made. Histology and genetic testing were not performed due to patient frailty. No signs of internal malignancy or systemic disease were noted.

Results:

PPPK type I has been linked to mutations in the *AAGAB* gene, involved in epidermal proliferation control. Although the diagnosis is typically made earlier in life, underdiagnosis or misattribution of symptoms may delay recognition, particularly in comorbid patients. This case highlights the disease's progressive nature and its impact on mobility and quality of life. Management remains symptomatic, including keratolytics, emollients, and in selected cases, systemic retinoids—though these may be contraindicated in elderly patients. Differential diagnoses include punctate porokeratosis, spiny keratoderma, arsenical keratoses, and acquired palmoplantar keratodermas. While some PPPK variants may be associated with malignancy, no such features were present in this case.

Conclusion:

Hereditary PPPK type I can present with disabling lesions in elderly patients, particularly when comorbidities delay diagnosis. Awareness of this condition is essential for prompt recognition and functional management. Clinical evaluation and family history remain key diagnostic tools, especially when histology or genetic testing is not feasible.

Abstract N°: 8693

Epidermodysplasia verruciformis associated with multiple squamous cell carcinomas

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Introduction & Objectives: Epidermodysplasia verruciformis (EV) is a rare genodermatosis characterized by increased susceptibility to beta-HPV infections. It is associated with a high risk of malignant transformation into squamous cell carcinoma (SCC). We present a familial case with multiple SCC**.**

Materials & Methods:

NA

Results: A 34-year-old male patient presented with warty lesions on the forehead. His medical history includes a sister who has been diagnosed with epidermodysplasia verruciformis.

Clinical examination revealed multiple verrucous lesions in the forehead and retro auricular area. Additional lesions characteristic of EV were also observed, including flat wart-like (PV-like) lesions on the abdomen and flat, keratotic papules on the upper back.

Histopathological analysis confirmed the diagnosis of multiple squamous cell carcinomas (SCCs). Complementary investigations including liver, renal, thyroid, and lipid panels, were all within normal limits.

Discussion : Epidermodysplasia verruciformis (EV) is a rare genodermatosis characterized by an abnormal susceptibility to specific types of human papillomavirus (HPV), particularly types 5, 8, and other beta-HPVs. These viruses lead to the development of disseminated, persistent, wart-like lesions, often beginning in childhood or adolescence. The condition follows an autosomal recessive inheritance pattern in most cases, although sporadic forms exist. The clinical presentation of our patient, in association with a positive family history (affected sister), strongly supports the diagnosis of familial EV. A major concern in EV is its well-established association with the development of non-melanoma skin cancers, especially squamous cell carcinoma (SCC), often occurring on sun-exposed areas. These malignancies typically appear in the third to fourth decade of life, as seen in our patient.

The normal results of liver, renal, thyroid, and lipid panels suggest the absence of systemic involvement. However, given the severity and recurrence of malignant lesions, a multidisciplinary follow-up is imperative. Management includes strict photoprotection, regular dermatologic examinations, early biopsy of suspicious lesions, and consideration of systemic retinoids in selected cases. Genetic counseling is also essential, especially in familial forms, to screen relatives and discuss the implications of inheritance .

Conclusion: This case highlights the clinical complexity and oncogenic potential of epidermodysplasia verruciformis, particularly in its familial form. The early onset and recurrence of squamous cell carcinomas in our patient underscore the critical need for timely diagnosis, patient education, and rigorous dermatologic follow-up.

Abstract N°: 8698

Cutaneous Clues to a Multisystemic Disorder: A Case of Tuberous Sclerosis in Adolescence

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Introduction & Objectives: Tuberous sclerosis complex (TSC) is a rare genetic disorder characterized by the formation of hamartomas in multiple organs. It is caused by mutations in the TSC1 or TSC2 genes and frequently presents with cutaneous, neurological, and renal manifestations. Dermatological findings are often diagnostic clues. We present a classic case of TSC in an adolescent with well-defined cutaneous and neuroimaging features.

Materials & Methods: A 17-year-old female diagnosed with TSC in early childhood presented with multiple facial angiofibromas, fibrous plaques on the forehead, hypopigmented macules, and a Shagreen patch on the lower back. She had a history of epilepsy with infantile onset, well-controlled with carbamazepine. Imaging showed subependymal nodules and renal angiomyolipomas. The patient previously used topical sirolimus with good results but discontinued due to cost. She is currently receiving dermatologic care with dermabrasion for facial lesions and multidisciplinary follow-up is being re-established.

Results: The patient exhibited classical cutaneous findings of TSC, including bilateral angiofibromas, a Shagreen patch, and ash leaf macules. Neuroimaging confirmed subependymal calcifications, and abdominal ultrasound revealed renal angiomyolipomas. Topical sirolimus had demonstrated significant improvement, though interrupted due to access barriers. Dermoabrasion has provided partial improvement in facial lesions. Seizures remain controlled with antiepileptic medication, and no current signs of disease progression in other organ systems were noted.

Conclusion: This case exemplifies a classic multisystemic presentation of tuberous sclerosis complex with stable neurological status and prominent cutaneous findings. Cutaneous lesions in TSC not only guide diagnosis but also offer visible therapeutic targets. Topical mTOR inhibitors remain effective, although access may be limited. Early diagnosis and continued multidisciplinary management are essential for optimal outcomes.

Abstract N°: 8823

Multiple scalp and neck lesions in an 80-year-old man

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Introduction and Objectives: Mosaic CYLD cutaneous syndrome (CCS) is a rare disorder marked by multiple benign adnexal skin tumours, such as cylindromas. While CCS is typically associated with germline CYLD mutations and presents in early adulthood with autosomal dominant inheritance, late-onset cases without a family history may reflect somatic mosaicism. We report a rare case of late-onset mosaic CCS in an elderly patient, aiming to highlight its clinical, histological, and genetic features, and to emphasise the importance of recognising mosaic presentations in atypical contexts.

Materials and Methods: An 80-year-old male with no personal or family history of skin disease presented with a five-year history of over 20 asymptomatic papules and nodules on the scalp and neck. Lesions varied in size (2 mm to 3 cm) and colour (skin-coloured to pink). Dermoscopic examination revealed arborising telangiectasia with background structureless pink colour. Five anatomically distinct lesions were biopsied and examined histologically using haematoxylin and eosin staining. Genetic testing on peripheral blood was performed using next-generation sequencing (NGS) with whole-exome enrichment.

Results: Histopathology of all five biopsies revealed basaloid neoplasms with prominent basement membranes arranged in a characteristic "jigsaw" pattern, consistent with a diagnosis of multiple cylindromas. Genetic testing detected a pathogenic variant in the CYLD gene in a mosaic state, confirming a diagnosis of mosaic CYLD cutaneous syndrome (CCS). A low level of mosaicism was detected (minor allele frequency <0.01%) in DNA from peripheral blood, which may explain why the patient developed signs and symptoms much later in life than typically occurs. The patient's five children, aged 40 to 60 years, showed no signs of disease. Clinical management included regular monitoring due to the risk of recurrence and malignant transformation.

Conclusion: This case illustrates a rare presentation of mosaic CCS in late life, confirmed by genetic testing. It highlights the importance of understanding the genetic basis and clinical variability of CYLD mutation syndromes, which is crucial for accurate diagnosis, risk assessment, management, and genetic counselling. It also emphasises the need for detailed genetic and histopathological evaluations to distinguish mosaic from hereditary forms, particularly in atypical late-onset cases.

Abstract N°: 8836

HIV positive in xeroderma pigmentosum XPC young patient successful treated with pembrolizumab

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Introduction & Objectives: Xeroderma pigmentosum (XP) is an autosomal recessive condition associated with a increase in the development of malignancies. HIV causes immunodeficiency that alters appropriate responses in the context of care for patients with neoplasms; low CD4 levels and high viral load correlate with the presence of neoplasms.

We report a very rare and complex case of a XP patient infected with HIV successful treated with pembrolizumab.

Materials & Methods: Case report.

Results: A 8 years-old African boy, phototype V, presented black macules in sun-exposed areas since the age of 2. Since the age of 4, the nodules and papules were excised. Due to a growth and local bleeding of a tumor, he received a transfusion during which he contracted HIV.

An ulcerated tumor in the region of the left lower lip that extended to the chin drew attention, distorting the anatomy and impede feeding, which caused malnutrition (figure 1). He also had bilateral corneal opacity and visual loss.

A hypothesis of DNA repair disorder was made. Systemic involvement was ruled out. Biopsies showed that the tumor were a squamous cell carcinomas at the lower lip (figure 2) and at the eye (figure 3). The patient was staged with positron emission tomography/computed tomography and magnetic resonance (figure 4).

We perform a genetic analysis, by sequencing, to confirm molecularly our hypothesis. Ilumina® Platform, the preparation of the library was carried out with Kit Nextera DNA Flex, capture with xGen-V.2 IDT of NGS, sequencing performed for exome with Novaseq 6000 and reference genome: Hg38. This test was carried out in a scientific research protocol approved by the ICB Research Ethics Committee. The classification and interpretation of the alterations found in this test are based on the evidence available in the databases of changes and pathogenicity prediction programs consulted at the time of the preparation of this report.

A homozygous pathogenic variant was identified in the XPC gene, c.2251-1G>C, altering the splicing processing of the mRNA, and leading to a deficiency or absence of this protein. This pathogenic variant is gone previously described by Cartault et al. 2011 and is recorded as a pathogenic variant dbSNP (Short Genetic Variations) rs754673606 and Clinvar ID: 190213 databases data from the National Library of Medicine, having been identified in other patients with other regions of the world, associated with XP, which reinforces the diagnosis.

Previous studies show the action of pembrulizumab in HIV reservoirs and improved response in this context. Due to this, antiretroviral treatment, pembrulizumab, acitretin and enteral nutrition via gastrostomy were initiated.

The patient showed an excellent response after 6 cycles of pembrulizumab and in follow-up for more than one year without tumor recurrence, combined with good retroviral control and nutritional improvement (figure 5 and 6).

This case is relevant not only because of its rarity, but also because it raises the possibility of using

prembrulizumab in the context of XP and immunodeficiencies. And it draws attention to the need for a better understanding of immunological pathways in XP.

Conclusion: This case is relevant not only because of its rarity, but also because it raises the possibility of using prembrulizumab in the context of XP and immunodeficiencies. And it draws attention to the need for a better understanding of immunological pathways in XP.