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EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

Abstract N°: 14

Exploring the involvement of Innate Lymphoid Cells in Hailey-Hailey disease through multicolor immunofluorescence analysis in situ

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Introduction & Objectives:

Hailey-Hailey disease is a rare genetic skin disorder that affects the adhesion between skin cells. It is caused by mutations in the ATP2C1 gene, which can result in the breakdown of desmosomes, the structures responsible for cell adhesion, causing the characteristic skin blistering and peeling. Therefore, Calcium regulation plays a crucial role in maintaining the stability and functionality of desmosomes. Innate lymphoid cells (ILCs) play a crucial role in skin immunity and have been linked to the development or exacerbation of inflammatory skin conditions characterized by desmosome disruption. Cytokines produced by ILCs can influence keratinocyte proliferation, differentiation, and barrier function, which are closely related to desmosome dynamics and skin integrity. ILCs interplay closely with other leukocyte populations, thus resulting in inflammation or down regulation of inflammation, depending on which ILC subset is involved. Understanding the complex interplay between immune cells, cytokines, and epithelial structures like desmosomes in HHD could offer insights into the disease mechanisms and potential therapeutic targets. The goal of this project is to investigate the topographical relationship between ILCs and desmosome disruption in HHD. For this end, we intend to characterize and quantify in situ ILCs in the skin of patients with Hailey-Hailey disease using multicolor immunofluorescence.

Materials & Methods:

Paraffin-embedded skin samples from Healthy controls (HC) will be compared to samples from Hailey-Hailey disease (HHD) patients. First, samples are deparaffinized, and antigen retrieval is performed. ILCs are defined as Lineage (CD16, CD94, CD3, CD4, CD20, CD1a, CD11c, CD14, CD34, CD15, CD123 and CD203c) negative cells. Furthermore, transcription factors will be used to determine the subset of ILC (Tbet, GATA3, RORC, and AHR). Images will be acquired using the Confocal Stelaris 8 Leica microscope.

Results:

Conclusion:

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Abstract N°: 74

Dyskeratoses Congenita

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Introduction & Objectives:

- **Dyskeratosis congenita, a rare genetic disorder with three modes of inheritance, i.e. X linked recessive, autosomal dominant, autosomal recessive due to defective DKC1 (dyskerin) gene, hTERC, NOP10, NHP2, respectively is estimated to occur in 1 in 1 million people. The disease is characterised by a classic triad: nail dystrophy, reticulate skin pigmentation, and oral leukoplakia. It has various modes of transmission. Several genes have been mapped to the cause of this disease. Early mortality is often associated with bone marrow failure, infections, fatal pulmonary complications, or malignancy. More than 200 individuals have been reported in the literature with dyskeratosis congenita**

Materials & Methods:

- **An 18 year old male presented with generalized weakness and discoloration of eyes. On examination, he had reticulate pigmentation all over the body including tongue.**
- **There was evidence of nail dystrophy**
- **Laboratory investigations showed haemoglobin-4.1gm%, total cell count- 1870/cmm with neutrophilia of 80%, reticulocyte count- 1.2%, red blood cell- 1.7 million/cmm, random blood sugar-90gm/dl. Peripheral blood smear examination revealed pancytopenia with anemia of dimorphic type. USG abdomen showed mild splenomegaly and multiple collateral at splenic hilum, mildly prominent splenic vein with minimal inter bowel free fluid. Bone marrow examination showed a hypocellular marrow. Skin biopsy showed mild hyperkeratosis and increased melanin pigment in basal layer of epidermis with melanin incontinence and collagenisation of dermis.**

Results:

- **The minimal clinical criteria for diagnosis of DC include the presence of at least 2 of the 4 major features (abnormal skin pigmentation, nail dystrophy, leukoplakia, and BM failure) and 2 or more of the other somatic features (epiphora, learning difficulties/developmental delay, mental retardation, pulmonary disease, short stature, extensive dental caries/loss, esophageal stricture, premature hair loss/greying/sparse eyelashes, hyperhiderosis, malignancy, intrauterine growth retardation, liver disease/peptic ulceration, ataxia/cerebellar hypoplasia, hypogonadism/undescended testes, microcephaly, urethral stricture/phimosis, osteoporosis/aseptic necrosis/scoliosis and deafness.**
- **Our patient had skin pigmentation and nail dystrophy as described in literature along with deranged liver functions, thus presenting with yellowness of sclera and hypo/hyper pigmentation of eye lids.**
- **DC predisposes to early onset of variety of malignancies like myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), esophageal or head and neck cancer.**
- **These patients are treated with blood transfusion, Antibiotic, anabolic steroids, granulocyte colony stimulating factor and erythropoietin; however, definitive treatment is bone marrow transplantation only.**
- **Unfortunately, prognosis remains poor in full blown case and most of the patient's die of some or the**

other complication.

Conclusion:

- **We want to highlight the unusual manifestation of the syndrome and recommend close multidisciplinary follow-up of such cases for progression to malignancies of blood through regular blood count, & bone marrow biopsy as necessary. Genetic counselling in a family with known case is of prime importance.**

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Abstract N°: 558

Results from the BEACON Trial: A Phase 2, Randomized, Open-label Trial of Bitopertin in Erythropoietic Protoporphyria

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Introduction & Objectives: Erythropoietic protoporphyria (EPP) and X-linked protoporphyria (XLP) are associated with accumulation of photoreactive protoporphyrin IX (PPIX) in the skin and other organs, causing debilitating phototoxic skin reactions following exposure to sunlight, and potentially life-threatening hepatopathy in some patients. Reduction of PPIX is associated with amelioration of disease in the settings of hematopoietic stem cell transplant, pregnancy, and extracorporeal photoinactivation.

Glycine transporter 1 (GlyT1) supplies extracellular glycine for the initial step of heme biosynthesis in erythroid cells. Bitopertin is an investigational, orally administered inhibitor of GlyT1. It is hypothesized that GlyT1 inhibition can decrease heme pathway intermediates, including PPIX, and can improve light tolerance.

Materials & Methods: BEACON is a Phase 2, randomized, open-label trial (ACTRN12622000799752) of 22 participants who receive oral, once-daily administration of 20 mg or 60 mg of bitopertin for 24 weeks. The trial includes participants ≥12 years of age with a confirmed diagnosis of EPP or XLP. The primary endpoint is percent change from baseline in whole-blood metal-free PPIX. Additional endpoints include patient-reported outcomes of light tolerance and quality of life, as well as safety.

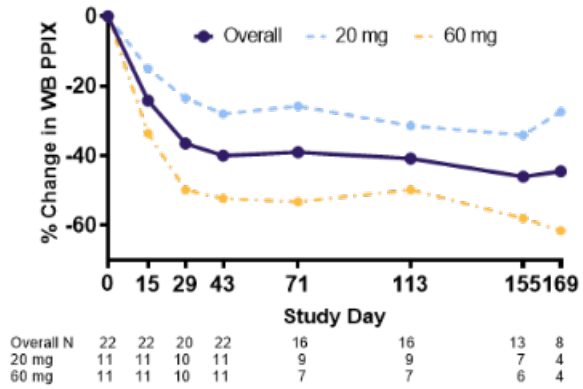
Results: As of data cutoff (20 October 2023), a total of 22 adults had been enrolled. For the primary endpoint, treatment with bitopertin resulted in significant and sustained reductions in PPIX levels; mean reduction >40% ($p<0.001$ versus baseline; Figure 1). For the key secondary endpoint, the mean (± SD) cumulative total time in light observed over the 6-month treatment period on days without pain (precedented pivotal endpoint) was 222.6 ± 129.3 hours, which represents approximately a 3-fold increase with bitopertin treatment relative to historical control.

Bitopertin improved other measures of light tolerance: time to prodrome reported during weekly sun exposure challenges increased 3-fold relative to baseline ($p<0.001$) and patient-reported phototoxic reactions decreased by 92% while on treatment compared to baseline. This functional benefit was also associated with improvements in quality of life, and nearly all participants who completed treatment (12/13) reported in the Patient Global Impression of Change their EPP was much better or a little better at the end of the study.

Bitopertin was generally well tolerated at both dose levels with no serious adverse events, stable mean hemoglobin levels, and no anemia adverse events (AEs) reported. The most common AEs (reported in >1 participant) were dizziness, lightheadedness, headache, and nausea.

Conclusion: By reducing PPIX levels, bitopertin targets the underlying pathophysiology of EPP, resulting in improvements in multiple measures of light tolerance and quality of life. Bitopertin has been well tolerated to date. Final adult results from the study will be presented at the meeting.

Figure 1. Percent Changes in Whole-Blood (WB) Metal-Free Protoporphyrin IX (PPIX) with Bitopertin


Overall
20 mg
60 mg
% Change in WB PPIX
0
-20
-40
-60
0 15 29 43 71 113 155169
Study Day
Overall N 22 22 20 22 16 16 13 8
20 mg 11 11 10 11 9 9 7 4
60 mg 11 11 10 11 7 7 6 4

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Abstract N°: 561

Topline Results of the AURORA Trial: A Phase 2, Randomized, Double-blind, Placebo-controlled Trial of Bitopertin in Erythropoietic Protoporphyria

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Introduction & Objectives: Erythropoietic protoporphyria (EPP) and X-linked protoporphyria (XLP) are caused by pathogenic variants in the ferrochelatase (*FECH*) or 5-aminolevulinate synthase 2 (*ALAS2*) genes, respectively, resulting in accumulation of photoreactive protoporphyrin IX (PPIX). In the protoporphyrias, elevated levels of PPIX cause debilitating phototoxic skin reactions following exposure to sunlight and may lead to potentially life-threatening protoporphyric hepatopathy in some patients. Reduction of PPIX is associated with amelioration of disease in the settings of hematopoietic stem cell transplant, pregnancy, and extracorporeal photoinactivation.

Glycine transporter 1 (GlyT1) supplies extracellular glycine for the initial step of heme biosynthesis in erythroid cells. Bitopertin is an investigational small molecule inhibitor of GlyT1. It is hypothesized that GlyT1 inhibition leads to a decrease in heme pathway intermediates, including PPIX, and can improve light tolerance. Initial data from an open-label study of bitopertin in 22 adults with EPP or XLP (BEACON; ACTRN12622000799752) showed that treatment with bitopertin resulted in mean reductions in PPIX >40 % ($p<0.001$), which translated to meaningful improvements in sunlight tolerance and improvements in patient reported quality of life.

These data, combined with a favorable safety profile observed in prior clinical studies of bitopertin with cumulative enrollment of >4000 participants, provided rationale for AURORA.

Materials & Methods: AURORA is a Phase 2, randomized, double-blind, placebo-controlled trial (NCT05308472) that randomized 75 participants (1:1:1) to receive oral, once-daily administration of 20 mg, 60 mg bitopertin, or placebo for 17 weeks. Participants ≥18 years of age with a confirmed diagnosis of EPP by PPIX analysis and/or genetic testing were enrolled. Exclusion criteria included concurrent treatment with afamelanotide or dersimelagon. Randomization was stratified by baseline light tolerance (time to prodrome < or ≥30 minutes), as assessed during a 2week screening period.

The primary endpoint is percent change from baseline in whole blood metal-free PPIX in participants randomized to bitopertin compared to placebo. The key secondary endpoint is the total hours of sunlight exposure to skin on days with no pain from 10:00 to 18:00 hours. Upon completion of the double-blind treatment period, participants may continue in an open-label extension study.

Results: Unblinded topline safety and efficacy data, including changes from baseline in wholeblood metal-free PPIX and measures of light tolerance, will be presented.

Conclusion: Bitopertin has been shown to significantly reduce PPIX levels in prior clinical and nonclinical studies

of EPP. The AURORA trial evaluates whether reductions in PPIX with bitopertin can improve measures of light tolerance in adults with EPP. Topline safety and efficacy data will be presented.

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Abstract N°: 576

Case series of Dowling-Degos Disease: Discussion and review of the literature

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Introduction & Objectives:

Dowling-Degos Disease, also known as reticulate pigmented anomaly of flexures, is a rare genodermatosis with autosomal dominant inheritance and unknown epidemiology. Clinically, it is characterized by reticular hyperpigmentation with variable hyperkeratosis in intertriginous areas, comedo-like lesions on the face and trunk, as well as scars, with a variable but progressive clinical onset ranging from childhood to adulthood. Cases have been observed in association with other pathologies, such as hidradenitis suppurativa and multiple epidermal cysts, suggesting a common pathophysiological mechanism related to follicular occlusion. The objective of this study is to present six cases of patients with Dowling-Degos Disease, analyze their clinical and histopathological findings, and their association with other diseases.

Materials & Methods:

We analyzed the clinical, histopathological findings, and association with different diseases of six patients diagnosed with Dowling-Degos Disease who were evaluated at the Dominican Dermatology Institute "Dr. Huberto Bogaert Díaz" in 2023.

Results:

All six patients were female, with the onset of the pathology in adolescence, and with a familial association in all cases. In addition to the reticular hyperpigmented macules, comedo-like lesions, and depressed scars on the face and/or flexural regions found in all six patients, two patients had concurrent hidradenitis suppurativa, and two patients showed epidermal cysts.

Conclusion:

Dowling-Degos Disease is characterized by pigmented lesions, comedo-like lesiones, and scars caused by mutations in the KRT5 gene in up to 50% of cases, a gene involved in cell adhesion and melanosome function. However, other mutations have been identified in clinical variants of this condition; in non-flexural variants, the POFUT1 and POGLUT1 genes; and in variants associated with hidradenitis suppurativa, the PSENEN gene. These genes are involved in the Notch signaling pathway, important in skin differentiation and homeostasis, mediating the interaction between melanocytes and keratinocytes.

Currently, there are no curative treatments for this disease. Topical retinoids and laser therapy have been used with variable results. While this disease does not limit the patient's life expectancy, it can significantly impact their quality of life due to its progressive nature and poor response to treatment. Providing timely diagnosis, identifying concomitant pathologies, and offering adequate patient education can be useful in managing and preserving quality of life.

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Abstract N°: 600

Disseminated familial comedones without diskeratosis: a case report.

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Introduction

Disseminated familial comedones without diskeratosis is an autosomal dominant genodermatosis that presents with widespread and extensive involvement of comedones on the skin surface, distinguished by specific histopathological findings such as dilated follicles filled with laminar keratin and filiform extensions of basaloid cells in the outer root sheath without acantholysis or diskeratosis. It constitutes a very rare dermatosis, with only 67 individuals in 4 families previously reported in the literature.

Case report

We present the case of a 39-year-old female who presented to the clinic with nodules and comedonic lesions that initiated at 14 years of age. Upon physical examination, a polymorphic dermatosis was observed, disseminated in the face, back, and axillary and inguinal folds characterized by numerous comedones of 1-4 mm in diameter, mostly covered by a central dark brown keratotic plug; multiple erythematous-violaceous painful nodules were also found, varying in size from 1 to 3 cm, with follicular openings and dark brown keratotic plugs on their surface, some covered by hematic crust, few hypertrophic and retractile scars, numerous pinpoint depressions, and multiple light brown postinflammatory macules. The dermatosis had a clear predominance to the back with minimal involvement of the intertriginous areas. The rest of the physical examination was normal.

A notable finding in her family history was that several family members, spanning three generations, had similar cutaneous lesions that began in adolescence and varied in severity.

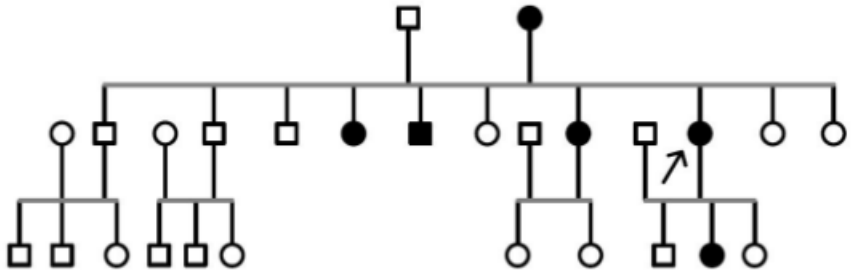
Skin biopsies taken from the patient´s comedones showed histopathological findings consistent with this disease.

The patient has been on oral isotretinoin treatment at a dose of 30 mg/day for 1 year, observing improvement only in the nodular lesions.

Conclusion

The genealogical study of our patient allows us to confirm an autosomal dominant inheritance pattern, we will continue to follow up the patient and its family to characterize this behavior. Two affected members have yet to birth offspring, and three family members of the third generation are still in the age range of 6 to 15 years, so it is possible that they will present distinctive cutaneous manifestations in the future. To make an accurate diagnosis, a thorough evaluation of other clinical information such as age of onset, corollary signs and symptoms, and a biopsy was needed to rule out other differential diagnosis that may present with comedones including Familial comedones with diskeratosis (histopathological findings with diskeratosis), chloracne (no history of exposure to pesticides or herbicides), Darier’s disease (lack of characteristic keratotic papules in sun-exposed areas), etc. Although there is currently no curative treatment, oral isotretinoin has been shown to decrease morbidity by controlling inflammatory lesions and associated symptoms. Long-term monitoring is important, considering the

association with squamous neoplasms observed in other cases.



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Abstract N°: 881

Segmental type 1 Darier disease: a case series

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Introduction & Objectives: Darier's disease (DD) is a dermatosis with autosomal dominant inheritance due to mutations in the ATP2A2 gene. Clinically, it is characterized by multiple erythematous to brownish hyperkeratotic papules. Additionally, DD is associated with neuropsychiatric diseases. About 10% of patients have a segmental form of DD due to mosaicism. If the postzygotic mutation occurs in a healthy embryo, it is a segmental DD type 1 (SDD1), and if it occurs in a heterozygous embryo with DD, it is a segmental DD type 2. SDD1 is clinically and histologically identical to DD but is distinguished by the linear, segmental, or zosteriform distribution of the lesions. It appears later than DD, around 30 to 50 years of age. There is no family history, and it is not usually associated with nail, palmar, or mucosal involvement. It should be distinguished from herpes zoster, lichen striatus, ILVEN, Hailey-Hailey disease, or linear Grover's disease. Diagnosis is clinicopathological, but in case of doubt, it can be confirmed genetically. Treatment is similar to DD. Topical options include emollients, retinoids, 5-FU, calcineurin inhibitors, synthetic vitamin D3, diclofenac and short corticosteroid regimens during flares. As these are localized lesions, surgery, CO2 laser ablation or photodynamic therapy may be attempted. In extensive cases, oral retinoids are the treatment option with the most evidence.

Materials & Methods: We performed a retrospective review and identified 5 cases of SDD1 in our service. We summarized the clinical, histological characteristics, and treatment response of these patients.

Results: We present a series of 5 patients (Table 1) with SDD1. The diagnosis of SDD1 was made between 26 and 59 years of age; all presented with erythematous-brownish papules and pruritus exacerbated by heat and sweating. The patients also reported asymptomatic periods between flares. The distribution of lesions was blaschkoid (2), zosteriform (1) and segmental (2). The affected sites were hemiabdomen (5), back (4), hemithorax (3), leg (1), and arm (1). The percentage of skin affected ranged from 3 to 14% (mean 7.4%). One patient had nail involvement in the form of longitudinal erythronychia. None had a family history. 2 had associated psychiatric comorbidities (depression and attention-deficit/hyperactivity disorder); and 2 also had psoriasis, although this association has not been described. Histology in all of them showed acantholytic dyskeratosis. All had used topical corticosteroids during the flares, and 1 patient used topical retinoids that were discontinued due to irritation. 3 patients abandoned treatment with acitretin due to poor tolerance, while the patient treated with isotretinoin 20mg presented complete remission and tolerates maintenance with 5mg every 48h.

Conclusion: SDD1 is a rare condition with about 40 cases reported in literature. We present a series of 5 patients with SDD1, the second-largest series reported to our knowledge. All patients had similar clinical features, so it is important to consider SDD1 in patients with erythematous-brownish papules that follow a linear, zosteriform or segmental distribution. In addition, these patients may also present psychiatric comorbidities and nail involvement despite localized DD. Due to the small extent of the lesions, symptoms are mild and 4/5 patients are not currently undergoing any treatment. However, one of our patients shows remission of the disease and good tolerance with systemic retinoids.

TABLE 1

Patient number	1	2	3	4	5
Age and sex	81 / male	71 / male	75 / male	34 / male	30 / female
Duration of illness and age at diagnosis	30 (diagnosis at 59)	41 (diagnosis at 30)	26 (diagnosis at 49)	19 (diagnosis at 15)	4 (diagnosis at 26)
Symptoms	Pruritus	Pruritus	Pruritus	None or mild pruritus in summer	Pruritus
Precipitating or aggravating factors	Hospital admissions, heat	-	Heat, sweat	Heat, sweat, sun exposure, friction, acute illnesses with fever	Sun exposure, heat, sweat
Affected areas	Hemiabdomen	Left anterior hemithorax and hemiabdomen. Left back. Anterior and posterior left leg.	Right anterior hemithorax and hemiabdomen. Right back.	Left anterior hemithorax and hemiabdomen. Left back. Left arm.	Left anterior hemiabdomen. Left back.
Body surface area affected in %	3	8	7	14	5
Distribution	Zosteriform	Linear	Segmental	Linear	Segmental
Clinical features	Brownish and erythematous papules	Brownish and erythematous papules	Brownish and erythematous papules. Hypopigmented macules.	Brownish and erythematous papules	Brownish and erythematous papules
Affectation of nails, mucosa, hands or scalp	No	No	2 nails with longitudinal eritronychia	No	No
Previous diagnosis	Psoriasis	-	Grover disease	No	Pilaris keratosis, Residual hyperpigmentation
Family history	No	-	No	No	No
Associated comorbidities	No	No	Anxious-depressive syndrome	No	ADHD, Depressive Disorder

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Abstract N°: 933

Dermatophytic disease: failure of griseofulvin, ketoconazle and itraconazole. Requires correction of immunodeficient terrain, combined with antifungals could be the best therapy

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Introduction & Objectives:

Dermatophytic disease (MD) is a rare and serious condition caused by common dermatophytes. A genetically predisposed condition could explain the frequent failure of antifungal therapies.

A 28-year-old man with MD is reported. Despite 2 years of griseofulvin, then 23 months of ketonconazle and 8 months of itraconazole, the therapeutic failure is obvious: Dermatophytia of the glabrous skin, papulo-nodules, vegetating plaques, ulcerations, superficial and deep lymphadenopathy, brain damage and deterioration of the general condition.

Materials & Methods:

Dermatophytes are ubiquitous, weakly virulent filamentous fungi, usually responsible for benign superficial infections of the skin (circinate herpes), nails (onychomycosis) and scalp (ringworm). At the house of In some people, dermatophytes can invade the deep layers of the skin (the dermis and hypodermis), spread to the lymph nodes, and occasionally the bones, the intestine and/or the brain, leading to a disease that can involve the vital prognosis: deep dermatophytosis.

Results:

the researchers were able to demonstrate the involvement of the CARD9 gene in the development of this pathology. Indeed, two homozygous mutations (Q289X and R101C) of CARD9 were identified in these patients. These mutations, carried by the two alleles, induce a loss of function of the protein. Familial segregation shows autosomal recessive inheritance with complete clinical penetrance. this discovery broadens the spectrum of fungal infections associated with CARD9 deficiency. It also strengthens the hypothesis that infectious diseases can be monogenic hereditary diseases of the immune response.

Conclusion:

This work opens up new diagnostic and probably therapeutic possibilities for the pathology. They allow early genetic diagnosis leading to prophylactic antifungal treatment to limit the progression of the disease, but also the provision of genetic counseling to patients' families.

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Abstract N°: 947

Pachyonychia Congenita: A Case Report

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Introduction & Objectives:

Pachyonychia Congenita is a rare, hereditary, autosomal dominant disorder associated with mutations in one of the keratin genes. It is characterized by the triad of palmoplantar keratoderma, plantar pain, and dystrophic nails. In this report, we present a case of Pachyonychia Congenita with clinical manifestations consistent with the condition, confirmed through genetic testing.

Materials & Methods:

A 3-month-old female patient, with no known comorbidities, presented to the dermatology service with onychodystrophy, hyperkeratosis of all twenty nails, blisters, palmoplantar hyperkeratosis, and asymptomatic oral leukokeratosis since birth. Clinical suspicion of Pachyonychia Congenita was raised and confirmed through genetic analysis, revealing a mutation in the KRT16 keratin gene, responsible for Pachyonychia Congenita type PC K16. Symptomatic treatment with moisturizers and emollients was advised, along with multidisciplinary follow-up.

Results:

Pachyonychia Congenita is a rare, autosomal dominant hereditary disorder affecting the skin and nails, attributed to mutations in one of the five keratin genes: KRT6A, KRT6B, KRT6C, KRT16, and KRT17. Its most common manifestation is painful plantar keratoderma, often accompanied by vesicles, blisters, hyperhidrosis, and pruritus. Nail dystrophy can affect from one to twenty nails, making the diagnosis challenging. Other manifestations include oral leukokeratosis, dental alterations, follicular hyperkeratosis, follicular cysts, and steatocystomas.

The disease has been classified into five subtypes: PC-K16, PC-K17, PC-K6a, PC-K6b, and PC-K6c, based on genetic mutations. PC-K17 and PC-K6a appear to exhibit an earlier onset of nail involvement, while PC-K16 and PC-K6b present a broader range of nail symptoms. PC-K6c may be associated with milder clinical manifestations, although the correlation is not well-established at this time.

Diagnosis is initially clinical and confirmed through genetic testing. Differential diagnoses include Olmsted syndrome, Clouston syndrome, simple epidermolysis bullosa, congenital dyskeratosis, among others.

Treatment involves symptomatic measures, including topical use of keratolytics, emollients, and moisturizers. Oral retinoids (such as low-dose acitretin), botulinum toxin, sirolimus, and rosuvastatin may also play a therapeutic role. EGFR oral inhibitors like Erlotinib have been described in treatment, and a topical selective TRPV3 antagonist is under study, awaiting further evidence.

Conclusion:

Pachyonychia Congenita is a rare and debilitating disease. Early diagnosis, genetic counseling, and multidisciplinary follow-up are essential. Specific treatment options are still limited, and the use of keratolytics, moisturizers, and emollients should be employed.

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Abstract N°: 960

An uncommon association of Phakomatosis pigmentovascularis, Sturge Weber syndrome and Klippel Trenaunay syndrome

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[1]University hospital of constantine , dermatology and venereology , Algeria

An uncommon association of Phakomatosis pigmentovascularis, Sturge Weber syndrome and Klippel Trenaunay syndrome.

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Introduction:

Phakomatosis pigmentovascularis (PPV) is an uncommon congenital condition characterized by the association of a vascular malformation and pigmentary nevus. It has been classified into 4 subtypes by Happle either associated or not to systemic involvement. Rarely, the association of PPV to Sturge Weber syndrome (SWS) and / or Klippel Trenaunay syndrome (KTS) have been reported. We report a new case of PPV associated to both SWS and KTS.

Observation:

A 13-year-old girl, born to non-consanguineous Algerian parents, was referred to dermatology ward for evaluation of skin lesions that were present since birth. The patient's history was marked by glaucoma of the left eye and epilepsy since eight years of age, but she had a normal psychomotor development. Skin examination revealed bilateral port-wine stain (PWS) distributed over the trigeminal nerves (including the V1), neck, trunk and limbs, an extensive livedoid anemic nevus on the neck and trunk and Bilateral ocular melanosis. We noted also a hypertrophy of the left hemibody and lower lip, with lower limb length inequality. Her intercritical electroencephalogram showed low voltage activity over the left cerebral hemisphere. Cerebral CT scan showed hypertrophy of the choroid plexus of the left lateral ventricle .The lower extremity arteriovenous Doppler ultrasound was normal and her biological tests were within normal ranges. Thus, our patient fulfilled several criteria of unclassifiable type of PPV as well as those of SWS and KTS.

Discussion:

In our case, the association of PWS, nevus anemicus and ocular melanosis correspond to unclassifiable type of PPV. This rare disease has been firstly described by Ota and al. in 1947 as the association of capillary anomalies and dermal melanosis, with or without systemic manifestations. In 2005, Happle proposed a new classification of PPV into 4 types: cesioflammea (aberrant mongoloid spots and PWS); spilorosea (nevus spilus and PWS); cesiomarmorata (aberrant mongoloid spots and cutis marmorata telangiectatica congenita) and unclassifiable PPV. Other skin features may include nevus anemicus and café-au-lait spots. Most cases could be explained by a somatic mutation in the GNA11 or GNAQ gene. Interestingly, a sporadic somatic mutation of the GNAQ gene has been recognized as the etiology for SWS as well as SW and KT overlap syndrome. Indeed, the combination of neurological (epilepsy; hypertrophy of the choroid plexus of the left lateral ventricle) and ophthalmological (glaucoma) involvement with PWS over the trigeminal area correspond to the triad which defined SWS and the association of extensive PWS of the hemibody with ipsilateral soft tissue hypertrophy would likely correspond to KTS. This triple association, although previously reported, remains extremely exceptional.

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Abstract N°: 1010

Bourneville-Pringle Disease - a case report

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Introduction & Objectives:

Materials & Methods:

Results: Bourneville disease or Tuberous sclerosis complex is an autosomal dominant genetic disorder caused by a mutation in either the TSC1 or the TSC2 gene. De novo mutations can explain the apparently nonfamilial cases. Clinically, it is characterized by pleomorphic features, with a variety of benign tumors involving the kidney, brain, eyes, heart, liver, lung and skin. Cognitive deficits, learning disabilities, epilepsy are the disease's associated neuropsychiatric disorders (TAND). The most common skin lesions are: angiofibromas (usually on the malar regions of the face), hypopigmented macules, fibrous forehead plaques and shagreen patches (most commonly on the lower back). Bourneville disease is very well known for its variability in expression regarding the number and severity of manifestations.

The clinical features and/or genetic testing form the diagnosis. Further testing should focus on detecting significant manifestations that can be treatable and prevent complications.

The management of the patients depends on the clinical findings. Electrosurgery, dermabrasion and lasers provide a small benefit for the skin lesions, such as facial angiofibromas.

We report the case of an anxious 22 year-old man who presented for clinical picture consisting of asymptomatic multiple papules located on the malar regions of the face, nose and chin. Clinical examination revealed multiple erythematous papules on the chin, nose and cheeks as well as 2 red brown plaques (4/2,5 cm and 2,5/3 cm in diameter) involving the forehead and submandibular area evolving for approximately 15 years prior to the consultation.

The lesions were interpreted as tuberous sclerosis and a 4 mm punch biopsy from a lesion located on the nasolabial fold was performed.

Histopathological findings were compatible with the diagnosis of tuberous sclerosis, revealing irregular proliferation of fibrous tissue with slightly atrophic epidermis and collagenous stroma with increased fibroblasts and dilated blood vessels.

Interdisciplinary consultations revealed no other organ implications. Due to the progressive character of the disorder, the patient was advised to have periodic examinations.

The facial lesions weren't a cosmetic concern for the patient. Instead, he was highly anxious about the cognitive deficits he read about on the internet. The patient was then advised that the severity of the disease can vary substantially among affected individuals.

We particularly want to highlight the importance of an effective therapeutic doctor-patient relationship based on trust and communication. The physician must translate medical statistics into meaningful personalized information

for a patient that is constantly navigating the troubled waters of medical knowledge.

Conclusion:

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Abstract N°: 1060

xeroderma pigmentosa; a challenging condition.

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Introduction & Objectives:

Xeroderma Pigmentosa, also called DeSanctis-Cacchione syndrome, is a rare autosomal recessive genodermatosis that results from a defect in the nucleotide excision repair system. Xeroderma Pigmentosa patients are susceptible to sunlight, premature skin ageing, and an increased risk of skin cancers. This report highlights the challenges faced by individuals with XP, particularly in resource-limited settings, where awareness and understanding of the disease may be lacking.

Materials & Methods:

We present an 8-year-old male with a four-year history of nodules on the scalp and cheek. Despite seeking medical attention at various health centres, definitive management was only achieved once the patient visited our centre. Clinical examination revealed freckling poikiloderma, xerosis, a fungating mass on the left parotid area, an extensive tumour on the scalp, and cervical lymphadenopathy. Ophthalmological findings included photophobia and decreased visual acuity in both eyes. MRI of the head confirmed left parotid Squamous Cell Carcinoma with left frontal bone metastasis, leading to a diagnosis of Xeroderma Pigmentosa with metastatic Squamous Cell Carcinoma. Excision biopsy and debulking were performed, but complete excision was hindered by tumour infiltration into underlying muscles.

Results:

Three months later, the patient received a donation of Cemipilimab, a promising therapeutic agent. Monthly follow-up assessments were initiated to monitor the patient’s response and overall condition.

Conclusion:

Living in a stigmatised community, Xeroderma Pigmentosa remains a misunderstood and feared disease. This case underscores the importance of early diagnosis and multidisciplinary management, even in resource-limited settings, to enhance the survival prospects of individuals with Xeroderma Pigmentosa. Increased awareness and collaboration among healthcare providers are crucial in improving outcomes for these patients.

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Abstract N°: 1180

Chronic Granulomatous Disease in a Filipino Patient: A Case Report

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Introduction & Objectives:

Chronic granulomatous disease is a primary immunodeficiency due to a defect in 1 of 6 subunits that make up the nicotinamide adenine dinucleotide phosphate oxidase complex. The clinical presentations are predominantly infectious or inflammatory, with suppurative adenitis, pneumonia, liver and lung abscesses as the most common infectious presentations. Diagnosis can be made by the absent or significantly decreased respiratory burst in stimulated neutrophils by nitroblue tetrazolium test, dihydrorhodamine-123, or 2'7'-dichlorofluorescein diacetate test done at least twice.

Materials & Methods:

None

Results:

This is a case of a four-year-old Filipino male presenting with generalized, erythematous, well-defined papules and pustules on an erythematous base, mostly with yellow crusts, some with dry white scales, with onychodystrophy and subungual hyperkeratosis (Figure 1), since 2 years of age. History of present illness started at neonatal period with diagnoses of pneumonia, recurrent fungal infection, tuberculous meningitis, and osteomyelitis with axillary lymphadenopathy. Histopathologic examination revealed subacute spongiotic dermatitis. Tests for combined antibody and T-cell deficiencies were normal. A diagnosis of chronic granulomatous disease was confirmed with a low nitroblue tetrazolium test and dihydrorhodamine-123. Trimethoprim-sulfamethoxazole 5 mg/kg/day, Zinc pyrithione+Betamethasone scalp solution, Tacrolimus 0.03% ointment for the face and intertriginous areas, Hydrocortisone 1% lotion and ureacontaining lotion for the body, were started. Currently, with good tolerability and no adverse events were reported. Patient is for bone marrow transplantation.

Conclusion:

Given the rare occurrence of this disease, makes this an important emerging field of study. This case report will add to the minimal data we have about CGD, particularly in the Philippines.

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Abstract N°: 1230

A Unique Presentation of Osler-Weber-Rendu Syndrome: Nail Involvement and Coexistence with Sjogren's Syndrome

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Introduction & Objectives: Osler-Weber-Rendu syndrome, also known as hereditary hemorrhagic telangiectasia (HHT), is a rare autosomal dominant disorder characterized by abnormal blood vessel formation. Clinical diagnosis relies on the Curacao criteria, incorporating features such as recurrent epistaxis, mucocutaneous telangiectasias, visceral organ involvement, and family history. We present a case of HHT with a rare manifestation of hemorrhages affecting all nail plates, along with coexisting Sjogren's syndrome, highlighting the importance of recognizing atypical presentations of HHT, especially in the context of concurrent autoimmune diseases.

Materials & Methods: A 51-year-old female presented with a 5-year history of nail changes involving all fingers and toes. Initial physical examination revealed multiple globular nail hemorrhages affecting all nail plates. The patient had a significant medical history of Sjogren's syndrome with glandular and extraglandular involvement and was under rheumatology care, which attributed the findings to this syndrome. However, a more complete physical examination revealed telangiectasias in the soft palate mucosa, and the medical history showed additional symptoms, including recurrent epistaxis (3 episodes per week), gastrointestinal bleeding, and chronic migraine. The endoscopic evaluation identified angioectasias throughout the entire small intestine, while a bilateral rhinoscopy revealed septal varices in zones II-III. Additionally, a brain CT scan showed cavernous angiomas. Given the clinical suspicion and the review of these collective symptoms, genetic evaluation for Hereditary Hemorrhagic Telangiectasia (HHT) was initiated.

Results: The patient fulfilled 3 of the 4 Curacao criteria for HHT, leading to a diagnosis of the syndrome. However, the unique presentation of nail hemorrhages involving all digits, in conjunction with Sjogren's syndrome, posed diagnostic challenges and underscored the need for a comprehensive approach to investigate potential underlying genetic and autoimmune factors contributing to the patient's complex clinical phenotype.

Conclusion: This case highlights a rare presentation of Osler-Weber-Rendu syndrome with a unique nail involvement and concurrent Sjogren's syndrome, emphasizing the importance of considering HHT in patients with unexplained bleeding manifestations, particularly in the presence of autoimmune diseases. The coexistence of these conditions further complicates diagnosis and management, justifying multidisciplinary study and genetic evaluation to optimize patient care.

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Abstract N°: 1264

The Role of Steroidal Hormones on the Cutaneous Manifestations in Neurofibromatosis Type 1 (NF1): A Systematic Review

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Introduction & Objectives: Neurofibromatosis type 1 (NF1) is an autosomal dominant disorder resulting from pathogenic variants in the NF1 gene. The cutaneous manifestations of NF1, including Café au Lait Macules (CALMs) and plexiform neurofibromas (PNs), exhibit an age-dependent progression, with CALMs and PNs appearing at birth, body fold freckling during school age, and cutaneous/subcutaneous neurofibromas (NFs) emerging in puberty. While it is presumed that these manifestations worsen during hormonally mediated life events, evidence supporting this is lacking. Thus, we conducted a systematic review following PRISMA guidelines to explore changes in NF1 skin features during hormonal variability and iatrogenic hormonal therapy. Our objectives include investigating hormonal influences on NF1 cutaneous features through a systematic review, focusing on CALMs, PNs, and NFs, exploring the impact of puberty and pregnancy on NF1 skin changes, emphasizing gender-based variations and pregnancy-associated NF development and evaluating iatrogenic hormonal therapy effects on NF size and number in females with NF1, highlighting the need for control groups and clinical implications.

Materials & Methods: A search of PubMed, Web of Science, and OVID/Medline databases yielded 23 relevant studies, comprising 6 observational studies and 17 case reports/case series. Most studies focused on NFs, indicating an increase in size and/or number during puberty, pregnancy, and systemic hormonal contraceptive use.

Results: Adolescence saw NF growth associated with female sex and a higher risk of having over 100 NFs in adulthood. Pregnancy resulted in more than 8% of women reporting new or enlarged NFs, with some experiencing size reduction post-partum. Limited data were available for other NF1 cutaneous features, with PNs showing no significant change during puberty, while CALMs increased in size during pregnancy.

Conclusion: However, there is a dearth of information on the evolution of NF1 skin changes during menopause, andropause, or iatrogenic hormonal therapy beyond contraception. Furthermore, data on additional cutaneous features in NF1, such as axillary freckling and nevus anemicus, are lacking. The existing literature suggests hormonal life events may influence NFs, but comprehensive, prospective studies incorporating objective measures and age-sex matched NF1 control groups are needed to confirm these findings.

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Abstract N°: 1303

Itch in Ichthyosis: a prospective studyof 20 Tunisian patients

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Introduction & Objectives: Itch is the main symptom of ichthyosis. However, only a few studies were interested in this subject.

Materials & Methods: We conducted a single-center prospective study to measure the burden of itch in patients with ichthyosis.

Results: Twenty ichthyosis patients were included in a questionnaire-based study. All patients completed the Leuven Itch Scale, a multidimensional instrument to measure all aspects of itch: frequency, duration, severity, distress, consequences, and surface area. There were: 8 congenital ichthyosiform erythroderma (CIE), 5 Netherton's Ichthyoses (NI), 1 reverse ichthyosis, 2 lamellar ichthyoses (LI), 1 bathing suit ichthyosis (BSI), 1 Sjögren-Larsson syndrome (SLS), 1 keratinopathic type, and 1 ichthyosis vulgaris. The patients were 11 women and 9 men. The average age was 21.6 years old. Itch occurred in 85 % of patients. Sixty percent of patients reported itch in the last month among which 35% reported that it was sometimes and 15% always present. Almost all episodes (87 %) were short (less than 30 minutes). However, two patients (Netherton's Ichthyoses) reported that itching lasted more than two hours. Patients reported that itch flared in a hot environment (45%), cold weather, or during a change in weather (in respectively 10 %), when sweating (15 %), stress or contact with air (in respectively 5 %). Itch score of severity in NI was the highest. Principals' consequences of itching were difficulty falling asleep, lesions from scratching, reduced quality of life, and social contact. Data on the genetics was obtained for 10 patients with a mutation in the gene TGM1 (3 CIE, 1 BSI), in the CYP4F22 (1 LI), PNLPA1 (2 CIE), SPINK 5 (3 NI), ALDH4 (1 SLS).

Conclusion: Our study demonstrated that itch is a major problem in ichthyosis. Itch should be considered when treating these patients to improve their quality of life.

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Abstract N°: 1366

Dyskeratosis congenita in a 20-year-old male: a case report

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Introduction & Objectives:

Dyskeratosis congenita (DC) is a condition caused by defects in telomere biology that presents with bone marrow failure and cancer predisposition.

Materials & Methods:

A 20-year old male presented with a 13-year history of generalized reticular hyperpigmentation and nail dystrophy. He eventually developed oral leukoplakia, dental caries, hair loss, palmoplantar hyperkeratosis, adermatoglyphia, and hyperhidrosis. Three days prior, he had episodes of black tarry stools associated with dizziness.

Mucosal examination revealed multiple well-defined white to erythematous patches with erosions and petechiae on the tongue, palate, and gingivae. Dermatologic examination showed multiple well-defined brown macules with lacy reticular pigmentation and areas of hypopigmentation. Nail findings include micronychia, anonychia, and pterygium formation.

Results:

Dermoscopy revealed pigmented lines, brown dots and globules in a netlike pattern with hypopigmented holes in between. Histopathologic examination showed marked compact hyperkeratosis with an intact granular layer, epidermal atrophy, basal layer hyperpigmentation, and melanophages in the dermis. Complete blood count revealed pancytopenia and fecal occult blood test was positive. Bone marrow aspiration showed markedly hypocellular bone marrow for age. Chest CT scan suggested the possibility of interstitial lung disease.

Conclusion:

Dyskeratosis congenita is a multisystem disease that requires a multidisciplinary approach. Routine surveillance is very important in managing patients with DC.

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Abstract N°: 1473

Systemic anti-inflammatory therapy in congenital ichthyosis: real-world experience in a series of 22 cases

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Systemic anti-inflammatory therapy in congenital ichthyosis: real-world experience in a series of 22 cases

Introduction & Objectives:

A paradigm change took place in the therapeutic management of congenital ichthyosis, as targetable patterns of inflammation have been recognized. Reported cases showed variable responses to anti-inflammatory drugs. Up to date, it remains unclear which type of inflammation should be therapeutically targeted and which outcomes should be expected. These questions are addressed in this study.

Materials & Methods:

Patients with ichthyosis treated with systemic anti-inflammatory therapy between 2018 and 2023 were included in this single center retrospective study. Indications for systemic anti-inflammatory therapy were erythroderma, itch, and dermatitis with or without atopy.

Results:

Eighty-one % of the patients or caregivers perceived a benefit, and the investigator's global assessment and itch decreased. Patients/caregivers' assessment regarding therapeutic response guided the decision on the treatment. Drugs against type 2 inflammation performed better against itch in patients with severe atopy, while drugs against type 3 inflammation reduced erythema and scaling. IL-17A expression by immunohistochemistry predicted the response to drugs against type 3 inflammation

Conclusion:

The results suggest that** systemic anti-inflammatory drugs** may alleviate disease severity in patients with congenital ichthyoses. Although the benefit seems modest compared to common inflammatory dermatoses, it is highly relevant for patients with intractable genodermatoses. The design of clinical trials should consider that the expected outcomes are lower than in common inflammatory disorders. Further research is needed to establish biomarkers for the stratification of the patients for therapies and characterize genotypes, age groups, and stages of diseases, in a personalized manner.

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Abstract N°: 1795

H syndrome in a child: a new form of non-Langerhansian histiocytosis

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Introduction :
H syndrome is an autosomal recessive genodermatosis characterized by cutaneous and systemic manifestations.

It is caused by mutations in the SLC29A3 gene, leading to histiocytic infiltration of several organs.

Case presentation :
A 2-and-a-half-year-old child from a non-consanguineous marriage presented for 2 years with sclerotic pigmented plaques on the legs, associated with hypertrichosis, bilateral inguinal adenopathy, hepatosplenomegaly, exophthalmos and scrotal hypertrophy. The lesions spread to the thighs, back and upper limbs, sparing the knees. About 1 month ago, the patient presented with respiratory distress.

On examination, hyperpigmented, brownish, sclerotic or indurated patches and plaques were found on the limbs, trunk, inguinal folds and scrotum, and bilateral, white, firm, non-decubitating oedema on the feet. Skin biopsy of the plaques showed cutaneous histiocytosis, biology showed microcytic hypochromic anaemia, positive inflammatory syndrome, abdomino-pelvic ultrasound showed slight micronodular hepatosplenomegaly, Chest CT showed no evidence of diffuse interstitial lung disease, echocardiogram showed probable overload cardiomyopathy, good left ventricular function, dilatation of left cavities, pulmonary arterial hypertension, left ventricular hypertrophy, minimal pleuropericardial effusion. Given the skin involvement associating hyperpigmentation, sclerosis and hypertrichosis, hepatosplenomegaly, inguinal adenopathies and PAH, the diagnosis of H syndrome was evoked and confirmed by skin biopsy.

Discussion:

Syndrome H is a form of non-Langerhansian histiocytosis secondary to a mutation in the SLC29A3 gene encoding the nucleotide transport protein hENT3. 100 cases have been reported in the literature, the majority of them in adults, making our case unique.

It is characterized by hyperpigmented, sclerodermiform skin patches surmounted by hypertrichosis (68% of cases), located preferentially on the lower limbs, typically sparing the knees. Isolated hypertrichosis, telangiectasia and hypopigmentation have also been reported. Systemic symptoms include hepatosplenomegaly, skeletal abnormalities, exophthalmos, diabetes, hypogonadism, oedema, hypoacusis, cardiac involvement and biological abnormalities such as aregenerative anaemia and inflammatory syndrome. Cardiac involvement is a major prognostic factor, and can be life-threatening, leading to heart failure and death, as in our patient's case. As far as treatment is concerned, tocilizumab (anti-IL-6) has shown the most promising results. Other molecules, such as methotrexate, azathioprine, oral corticosteroids and TNF drugs, have been proposed, but their efficacy has been inconsistent.

Conclusion :

Hyperpigmented patches with hypertrichosis should prompt us to consider the diagnosis of H syndrome, and to look for systemic damage, including cardiac damage, which may be life-threatening and require strict monitoring.

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Abstract N°: 1901

Leukocyte adhesion defect (LAD): An uncommon yet important cause of skin ulceration

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Introduction & Objectives: Leukocyte adhesion defect (LAD) is an autosomal recessive primary immunodeficiency disorder (PID) with defect in integrins. Chemotaxis, adhesion, rolling, of leukocytes to the vessel wall endothelium and their migration to extravascular space is defective. Neutrophilic leucocytosis, non-healing ulcers with absence of pus formation at the site of infection is the hallmark presentation.

Materials & Methods: In this series we describe 3 cases of LAD, all infants presenting with single or multiple ulcers without pus formation. History of consanguinity was present in two patients and one patient gave history of delayed umbilical cord separation. Two cases had perianal and oral ulcers while the third patient had multiple ulcers over abdomen and upper limb with sepsis. On investigations, in all cases TLC was markedly raised, in range of 80,000 to 200,000/cu.mm with neutrophilic predominance, hemoglobin was low and one case had decreased platelet count as well. Flow cytometry analysis showed reduced neutrophil expression of CD18,11a in all the cases.

Results: Based on clinical presentation of ulcers without pus in children with suspected sepsis, markedly increased leucocyte count with neutrophilic predominance, anemia and reduced CD18,11a, diagnosis of LAD was made and the patients were treated with antibiotics and supportive care. Prognosis and further management options were explained to the parents including advice for allogeneic hematopoietic stem cell transplant (HSCT).

Conclusion: LAD is a rare immunodeficiency disorder and has four variants LAD1,2,3 &4. In all the variants, the clinical presentation and inheritance remains the same. It is frequently misdiagnosed with differentials as leukaemia, sepsis, congenital syphilis etc. they present with recurrent skin and systemic infections. In severe cases, it is usually fatal by two years of age. Timely diagnosis, genetic evaluation and management can reduce the morbidity and will have better future outcomes for child and family.

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Abstract N°: 1939

Effect of Triterpene Extract on Skin Cohesion in Epidermolysis Bullosa

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Effect of Triterpene Extract on Skin Cohesion in Epidermolysis Bullosa

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Introduction & Objectives:

Epidermolysis bullosa (EB) is a rare, debilitating condition characterized by chronic skin fragility and high wound burden. Triterpene Extract (Birch triterpenes, TE) in the Oleogel-S10 formulation has been shown to accelerate healing of wounds in people with Junctional and Dystrophic EB (JEB and DEB). Given these clinical results, and the previously demonstrated preclinical effects of TE on wound healing processes, here we explore the effect of TE on epidermal to dermal cohesion, a key aspect dysregulated in the pathophysiology of EB.

Materials & Methods:

Healthy, laminin-332-deficient JEB and DEB donor-derived keratinocytes and fibroblasts were employed (n=3 per condition). Adhesion of keratinocytes to laminin-332 and collagen I to microtiter plates after vehicle or TE treatment was measured. To explore the effects in a skin-relevant 3D model, human skin equivalents (HSEs) composed of healthy, JEB and DEB keratinocytes and fibroblasts were treated with vehicle or TE and immunohistologically assessed for epidermal differentiation, and skin barrier, blister and dermal-epidermal junction (DEJ) formation.

Results:

Adhesion of healthy donor keratinocytes to collagen I and laminin-332 substrates was not affected by TE. However, TE treatment significantly reduced adhesion of DEB-donor keratinocytes on both substrates, whilst for JEB keratinocytes, TE exposure reduced adhesion to collagen I but not laminin-332. This suggested a differential effect of TE on JEB and DEB keratinocytes. To explore this in a skin-relevant 3D model, we performed long-term TE treatment of HSEs. TE exposure from the cell seeding to epidermal stratification phases (up to 21 days) did not alter markers linked to terminal epidermal differentiation (loricrin) or barrier formation (NileRed) in HSEs derived from all donors. Nevertheless, analyses indicated significantly reduced processing-induced blister formation in treated JEB HSEs. Given the effect observed on adhesion to different substrates, we reasoned that the effect could be explained by altered integrin activity. Toward this end, we performed molecular characterization of the DEJ. This revealed that TE treatment in JEB HSEs promoted basal localization of molecular complexes involved in cell-matrix adhesion, including integrin a6b4 and keratin-14 with variable changes observed in healthy and DEB HSEs.

Conclusion:

Collectively, our data suggest potential context-dependent skin stabilizing properties of TE in JEB and DEB. TE in JEB evokes, basal localization of cell-matrix adhesion complexes adhesion strength, which may account for the improved epidermal to dermal cohesion observed in TE-treated JEB HSEs. This finding, coupled with other pre-clinical studies, further supports the clinically demonstrated wound healing properties of Oleogel-S10 specifically in JEB and DEB.

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Abstract N°: 2010

Focal facial dermal dysplasia (FFDD) type III due to triplication in the chromosomal region 1p36.23-p36.22

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Introduction & Objectives:

Focal facial dermal dysplasia (FFDD) type III due to triplication in the chromosomal region 1p36.23-p36.22

Materials & Methods:

We documented a case of FFDD type III attributed to triplication within chromosomal region 1p36.23-p36.22, in a 5-month-old female.

Results:

A 5-month-old female, originally from a non-consanguineous family but from an endogamous locality, presented with a localized dermatosis on her head, specifically in the temporal region, characterized by bilateral and symmetrical scar-like lesions. She exhibited redundant facial soft tissues, sparse lateral and upslanting eyebrows, upper distichiasis, periorbital puffiness, flattened nasal bridge, bulbous nasal tip, and prominent upper lip, micrognathia. She had history of congenital hypothyroidism. She was the only child of non-consanguineous parents, both without visible congenital defects upon physical examination.The approach was complemented with neurofisiology and documented right superficial hypoacusis and the echocardiographic study showed an atrial septal defect, pulmonary valve stenosis and pulmonary hypertension. Skin biopsy reports findings consistent with aplasia cutis. Exome sequencing was performed, which revealed a triplication in the region 1p36.23-p36.22 (3.04 Mb, 60 genes). These results led to the diagnosis of FFDD type III (Setleis syndrome).

FFFD, a group of developmental syndromes, characterized by bitemporal (FFDD Types I-III) or peri-auricular (FFDD-IV) scar-like depressions resembling forceps marks or cutis aplasia. FFDD type III (OMIM # 227260) presents bitemporal scar-like lesions as well as other facial manifestations listed in Table 1. This disease results from alterations of a single gene, monogenic, or an alteration in the structure of chromosomes, with *TWIST2* biallelic variants resulting in loss of function and pathogenic variants in *CYP26C1* the most described etiologies. Chromosomal alterations including duplications and triplication, are associated with severe phenotypes, involving delayed neurodevelopment and cardiac abnormalities. Genetic heterogeneity is evident in FFDD-III with some cases showing duplication in 1p36.22 without *TWIST2* variants. Other studies contrast triplications and duplications, showing smallest region of overlap (SRO) with an overlap of 14 morbid genes, suggesting their contribution to the phenotype in individuals with gain in 1p36. The hypothesis may be the production of a gene product that interferes with *TWIST2* activity, contributing to the development of the phenotype in this syndrome. Studies suggest that *DRAXIN* inhibits the WNT signaling pathway, affecting neural crest cell delamination and epithelial-mesenchymal transition (EMT). Further research on *DRAXIN* is needed to understand its role in facial dermal structure development and EMT, clarifying the mechanism behind 1p36.22 copy number variants in Setleis syndrome. In cases of duplication and triplication, they converge at a locus with dosage-sensitive genes that may explain the FFDD-III phenotype. However, the involvement of other genes is not ruled out.

Conclusion:

In conclusion, our case report underscores the importance of comprehensive genetic evaluation in patients with FFDD, elucidating potential genetic mechanisms and contributing to our understanding of the disorder's etiology and clinical spectrum. Further studies within this SRO on 1p36.22 may shed light on the pathogenesis of Setleis syndrome.

Table 1. Facial findings of FFDD type III
Low frontal hairline
Sparse lateral and upslanting eyebrows
Multiple rows of eyelashes on the upper eyelid (distichiasis)
Absence of eyelashes on the lower eyelid
Periorbital puffiness
Flattened nasal bridge
Bulbous nasal tip
Prominent upper lip Redundant skin
Epicanthal folds
Slanting palpebral fissures
Short palpebral fisures
Septum below alae nasi
Horizontal chin furrow
Vertical chin cleft
Linear grooves on forehead
Low-set/dysplastic ears

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Abstract N°: 2026

Assessment of Growth Hormone and Insulin-like Growth Factor 1 in Children with Epidermolysis Bullosa Dystrophica

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Introduction & Objectives:

Epidermolysis bullosa dystrophica (EBD) is characterized by muco-cutaneous fragility with blistering, scarring and severe growth retardation attributed to many factors.

Materials & Methods:

This cross-sectional study included 51 patients aged 1-12 years with EBD. Weight and height were measured, with the calculation of weight standard deviation score (SDS), height SDS, and body mass index (BMI), followed by plotting them on Egyptian growth curves. Serum levels of basal growth hormone (GH), insulin like growth factor 1 (IGF-1), hemoglobin (HB) level, erythrocyte sedimentation rate (ESR), and thyroid functions (TSH and T4) were measured. Growth hormone stimulation test was performed in 10 patients.

Results:

Weight SDS and height SDS were significantly lower than normal measurements ($P < 0.05$*). Growth hormone, growth hormone stimulation, and IGF-1 were significantly lower than the normal range ($P < 0.05$*). HB levels were significantly lower than normal, while ESR levels were significantly elevated ($P < 0.001$*). A negative correlation was found between ESR and basal GH, and a positive correlation between ESR and IGF1.

Conclusion:

In conclusion, children with generalized DEB have poor growth and low circulating GH and IGF-1 levels, likely due to malnutrition, anemia, and inflammation that suppresses GH/IGF-1 axis. Future treatments targeting the correction of GH and IGF1 levels and anti-inflammatory treatment should be considered.

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Abstract N°: 2103

More Than Meets The Eye

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Introduction & Objectives:

Lipoid proteinosis is a rare multisystemic autosomal recessive genodermatoses caused by mutations in the extracellular matrix 1 gene (ECM1). It is characterized by deposition of amorphous hyaline material in the skin, mucus membranes and other internal organs. The aim of this report is to highlight the telltale signs of lipoid proteinosis to facilitate early disease detection.

Materials & Methods:

We report a 20-year-old Malay girl, who first presented to the dental team with chronic oral ulcers, eyelid papules and difficulty swallowing since her early teens. She was treated for oral pemphigus vulgaris with azathioprine and tapering doses of oral prednisolone to which she showed poor response. Further evaluations by the otorhinolaryngology and opthalmology teams were inconclusive. Her symptoms progressively worsened, and she was subsequently referred to the dermatology team. Further examination revealed classical features of lipoid proteinosis. She had yellow waxy papules and plaques with generalized skin thickening over the extensor surfaces, back and forehead, beaded eyelid papules, diffuse alopecia, cobblestone appearance of the oral mucosa, thickened sublingual frenulum resulting in mild dysarthria, and hoarseness of voice since childhood. Her developmental milestones were appropriate with age

with no cognitive disability. She was of non-consanguineous marriage and family history was unremarkable. Histopathological examination of the cutaneous lesions revealed multiple deposits of amorphous eosinophilic acellular hyaline material at the level of the papillary dermis which stained positive for PAS and PAS+D. She was then commenced on oral acitretin. Subsequent clinic review showed improvement in her skin lesions.

Results:

-

Conclusion:

A comprehensive approach is required in this case to detect a rare disease with multisystem involvement. Oral mucosal manifestations of lipoid proteinosis may resemble several other cutaneous and systemic diseases. Histopathological examination as well as genetic analysis and counselling should be carried out. As there is no curative treatment, efforts to assist and support the patient to alleviate her symptoms as well as quality of life are equally important.

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Abstract N°: 2107

A case of Schöpf-Schulz-Passarge syndrome with facial erythema and telangiectasia and review of the literature

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Introduction & Objectives: Schöpf-Schulz-Passarge syndrome (SSPS) is a rare type of ectodermal dysplasia, characterized by palmoplantar keratoderma, hypodontia, hypotrichosis, nail dystrophy, and multiple periocular and eyelid apocrine hidrocystomas. The aim of this case report is to describe a patient with SSPS presenting with facial erythema and telangiectasia.

Materials & Methods: A 40-year-old female patient presented to our clinic with a 20-year history of erythema and thickening of her palms and soles with excessive sweating. She also had a cyst at the eyelid margin and facial erythema/telangiectasias. Before experiencing these skin changes, she had dull and sparse hair, permanent teeth loss, and toenail dystrophy. The parents are not consanguineous. Her brother also had facial erythema, telangiectasia, and palmoplantar keratoderma. Her other siblings and parents had no similar complaints.

Results: Laboratory analysis was within the normal range. Histopathological examination of the plantar skin biopsy showed orthokeratosis and hypergranulosis in the epidermis with suprapapillary thickening. After obtaining informed consent, the genetic analysis of peripheral blood was conducted using the Next-Generation Targeted Sequencing method. The WNT10A sequencing (Wingless related integration site) identified a homozygous single nucleotide transversion C>T at position c.321 in exon2 (c.321C>A; p.Cys107*). According to standards and guidelines developed by American College of Medical Genetics and Genomics and the Association for Molecular Pathology, the patient was diagnosed as SSPS. Oral acitretin and topical emollients were prescribed as symptomatic treatment.

WNT signalling is crucial for various aspects of embryogenesis, organ development, tissue regeneration, and homeostatic self-renewal in many adult tissues, such as skin and teeth. Odonto-onychodermal dysplasia (OODD) and SSPS are two diseases caused by a mutation in the WNT10A gene. SSPS is characterized by the presence of multiple hidrocystomas in the periocular and eyelid areas. In addition to other clinical findings, the patient's eyelid presented with an apocrine hidrocystoma, which prompted us to conduct a genetic analysis.

The literature search for other SSPS cases revealed 50 patients in total. Out of all the reported cases, 7 patients had homozygous mutation in exon 2 (c.321C>A ; p.Cys107*) of the WNT10A gene. In patients with the c.321 C>A p.Cys107* mutation, rosacea-like facial erythema and telangiectasia were previously reported in only one case. In all cases described in the literature, the hallmark feature was the presence of eyelid apocrine hidrocystoma. Unlike our patient, who had normal fingernails, those with toenail dystrophy also exhibited dystrophy in their fingernails. Sex, age at diagnosis, clinical features and type of mutation are summarised in Table 1.

Conclusion: Rosacea is a common condition, and there is scant evidence to support its association with SSPS. WNT signaling has an important place in follicular cells and sebocytes in embryological development. This gene mutation may cause differences in these cell groups, predisposing to rosacea. In conclusion, when rosacea and apocrine hidrocystoma co-occur, it's advisable to check for dental anomalies and hyperkeratosis to consider the possibility of SSPS. Genetic analysis should be performed for diagnosis.

Table-1

Author	Patient Age/Gender	Clinical Features	Mutation
Schöpf et al, 1971	68 years/Female	Palmoplantar hyperkeratosis, nail dystrophy, hypotrichosis, abnormal dentition, eyelid cysts, rosacea	Not available
Burket et al., 1984	35 years/Male	Palmoplantar hyperkeratosis, nail dystrophy, hypotrichosis, abnormal dentition, eyelid cysts, rosacea, follicular infundibulum tumour,	Not available
Font et al., 1986	67 years/Male	Palmoplantar hyperkeratosis, nail dystrophy, hypotrichosis, abnormal dentition, eyelid cysts, basal cell carcinoma, milia, photophobia, vitreous degeneration	Not available
Nordin et al., 1988	80 years/Female	Palmoplantar hyperkeratosis and hyperhidrosis, nail dystrophy, abnormal dentition, eyelid cysts, eccrine poroma, rosacea	Not available
	75 years/Male	Palmoplantar hyperkeratosis, nail dystrophy, hypotrichosis, abnormal dentition, eyelid cysts, eccrine poroma, rosacea	Not available
	83 years/Male	Palmoplantar hyperkeratosis, nail dystrophy, eyelid cysts, basal cell carcinoma	Not available
Perret, 1989	75 years/Male	Palmoplantar hyperkeratosis, hypotrichosis, abnormal dentition, eyelid cysts, squamous cell carcinoma	Not available
Monk et al., 1992	62 years/Female	Palmoplantar hyperkeratosis, nail dystrophy, hypotrichosis, abnormal dentition, eyelid cysts, basal cell carcinoma, bird-like facies, hypernephroma	Not available

	58 years/Male	Abnormal dentition, eyelid cysts, bird-like facies	Not available
	51 years/Male	Palmoplantar hyperkeratosis, nail dystrophy, hypotrichosis, abnormal dentition, eyelid cysts, bird-like facies	Not available
Küster&Hammerstein, 1992	43 years/Female	Palmoplantar hyperkeratosis, nail dystrophy, hypotrichosis, abnormal dentition, eyelid cysts, benign acanthoma	Not available
Craigen et al., 1997	56 years/Male	Palmoplantar hyperkeratosis, nail dystrophy, hypotrichosis, abnormal dentition, eyelid cysts	Not available
Starink, 1997	78 years/Female	Palmoplantar hyperkeratosis, nail dystrophy, hypotrichosis, abnormal dentition, eyelid cysts, malignant eccrine syringofibroadenoma	Not available
	59 years/Female	Palmoplantar hyperkeratosis, hypotrichosis, abnormal dentition, eyelid cysts	Not available
	73 years/Female	Palmoplantar hyperkeratosis, nail dystrophy, hypotrichosis, abnormal dentition, eyelid cysts, basal cell carcinoma, breast cancer	Not available
	71 years/Female	Palmoplantar hyperkeratosis, nail dystrophy, hypotrichosis, abnormal dentition, eyelid cysts	Not available
Verplancke et al., 1998	53 years/Male	Palmoplantar hyperkeratosis, nail dystrophy, hypotrichosis, abnormal dentition, eyelid cysts, follicular infundibulum tumour,	Not available

		eccrine poroma, rosacea	
Simpson et al., 1998	64 years/Male	Palmoplantar hyperkeratosis and hyperhidrosis, nail dystrophy, abnormal dentition, eyelid cysts, eccrine hidrocystoma, milia	Not available
	74 years/Male	Palmoplantar hyperkeratosis, nail dystrophy, abnormal dentition, eyelid cysts	Not available
Dot et al., 2000	71 years/Male	Palmoplantar hyperkeratosis and hyperhidrosis, nail dystrophy, hypotrichosis, abnormal dentition, eyelid cysts, basal cell carcinoma, macular degeneration	Not available
Gkolfinopoulos et al., 2001	49 years/Female	Palmoplantar hyperkeratosis, nail dystrophy, hypotrichosis, abnormal dentition, eyelid cysts, bird-like facies	Not available
	56 years/Male	Palmoplantar hyperkeratosis, nail dystrophy, hypotrichosis, abnormal dentition, eyelid cysts, mild diffuse hyperkeratosis	Not available
Hampton et al., 2005	69 years/Male	Palmoplantar hyperkeratosis, nail dystrophy, hypotrichosis, abnormal dentition, eyelid cysts	Not available
Castori et al, 2008	65 years/Female	Palmoplantar hyperkeratosis, sparse and brittle hair, onychodystrophy including longitudinal ridging, splitting, koilonychia, onycholysis, pterygium unguis, eyelid cysts, milia on nasal tip, bird-like facies, oligodontia,	Not available

		hypoplastic nipples and areola, optic atrophy	
	73 years/Male	Palmoplantar hyperkeratosis, onychodystrophy, oligohypotrichosis, rosacea, hypoplastic nipples and areola, eyelid cysts, oligodontia	Not available
Nagy et al., 2010	70 years/Female	Eyelid cysts, nail dystrophy, palmoplantar hyperkeratosis, hyperhidrosis, fine frizzy sparse hair	WNT10A, c.321C>A; p.Cys107*, homozygote
Petrof et al., 2011	59 years/Female	Eyelid cysts, palmoplantar hyperkeratosis, nail dystrophy	WNT10A, c.321C>A; p.Cys107*, homozygote
Wedgeworth et al., 2011	83 years/Male	Eyelid cysts, palmoplantar keratoderma, nail dystrophy, microdontia, oligodontia, hypotrichosis, hyperhidrosis, multiple seborrheic keratosis, eccrine hydrocystomas, malignant melanoma, squamous cell carcinoma, basal cell carcinoma, photophobia, retinal detachment, rosacea	WNT10A, c.321C>A; p.Cys107*, homozygote
Granger et al., 2012	56 years/Male	Eyelid cysts, plantar hyperkeratosis and maceration, eyelid cysts	WNT10A, c.391G > A; homozygote
Tziotzios et al., 2014	58 years/Female	Eyelid cysts, palmoplantar keratoderma, dystrophic fingernails&toenails, hypodontia, hypotrichosis, hyperhidrosis	WNT10A, c.321C>A ; p.Cys107*, homozygote
	50 years/Male	Eyelid cysts, palmoplantar keratoderma, dystrophic fingernails&toenails,	WNT10A, c.1168G>T ;p.Glu390, homozygote

		hypodontia, hypotrichosis, hypohidrosis	
	43 years/Male	Eyelid cysts, palmoplantar keratoderma, dystrophic fingernails&toenails, hypotrichosis, hyperhidrosis, keratoconus	WNT10A, c.321C>A; p.Cys107 c.810C>A; p.Ser270Arg, compound heterozygote
	36 years/Female	Eyelid cysts, palmoplantar keratoderma, hypodontia, hypotrichosis, basal cell carcinoma, hyperhidrosis	WNT10A, c.321C>A; p.Cys107*, homozygote
	57 years/Male	Eyelid cysts, palmoplantar keratoderma, dystrophic fingernails&toenails, hypodontia, basosquamous carcinoma, bird-like facies	WNT10A, c.1084T>C; p.Cys362Arg, homozygote
	28 years/Male	Palmoplantar keratoderma, dystrophic fingernails, hypodontia, hyperhidrosis	WNT10A, c.321C>A; p.Cys107*, homozygote
	49 years/Female	Eyelid cysts, palmoplantar keratoderma, hypodontia	WNT10A, c.321C>A; p.Cys107 c.391G>A; p.Ala131Thr, compound heterozygote
Vilas-Sueiro et al., 2015	70 years/Male	Palmoplantar hyperkeratosis, nail dystrophy with pterygium, hypodontia, eyelid cysts, trichofolliculoma	WNT10A, c.682T>A; p.Phe228Ile, c.831G>T; p.Trp277Cys, homozygote
Painsi et al., 2017	86 years/Female	Sparse scalp hair, short eyelashes, sparse eyebrow, palpebral cysts, nail dystrophy, palmoplantar hyperkeratosis	WNT10A, c.1135C>T; p.Arg379Cys; homozygote
Pauly et al., 2018	59 years/Female	Bilateral eyelid cysts, palmoplantar hyperkeratosis, xerosis of skin and mucous membranes, sparse hair growth, nail dystrophy, hypotrichosis, hypoplastic nipples, hypopigmented areola, hypodontia, hair	WNT10A, c.318C>G ; p.Asn106Lys c.1036T>C; p.Cys346Arg, heterozygote

		thinning in vertex, uterine fibroid, palmoplantar hyperhidrosis, xerosis	
Rambhia et al., 2018	36 years/Male	Papules, nodules and cysts on periocular area, eyelid papules, bird-like facies,ichthyosis, palmoplantar hyperkeratosis, nail dystrophy, hypodontia, loss of papilla on tongue	Not available
Hsu et al., 2018	54 years/Male	Palmoplantar hyperkeratosis, nail dystrophy, eyelid cysts, hair loss in androgenetic pattern	WNT10A, c.310C>T; p.Arg104Cys, homozygote
Ismail et al., 2019	58 years/Female	Bilateral eyelid cysts, palmoplantar keratoderma, nail dystrophy, hypodontia, palmoplantar hyperhidrosis, perifollicular hyperkeratosis on shins, scaling on nose tip, nodular basal cell carcinoma	WNT10A, p.Cys107; p.Arg128, heterozygote
Zimmerman et al., 2019	53 years/Male	Eyelid cysts, palmoplantar hyperkeratosis, nail dystrophy, oligodontia, sparse hair, basal cell carcinoma	WNT10A, c.321C>A; p.Cys107 c.742C>T; p.Arg248
	51 years/Female	Eyelid cysts, palmoplantar keratoderma, oligodontia, nail dystrophy, dry hair, sparse eyebrows and body hair, hypohidrosis, xerostomia	WNT10A, c.321C>A; p.Cys107 c.742C>T; p.Arg248
	46 years/Female	Palmoplantar keratoderma, hypodontia, eyelid cysts	WNT10A, c.742C>T; p.Arg248
	25 years/Female	Mild keratoderma, nail dystrophy, hypodontia,	WNT10A, c.742C>T; p.Arg248
	8 years/Female	Dry hair, hypodontia,	WNT10A, c.742C>T; p.Arg248
Monroig et al., 2020	64 years/Female	Palmoplantar keratoderma, hyperhidrosis, sparse and brittle hair, eyelid cysts, oligodontia	WNT10A, c.18_42del26; p.R7Afs*28
Drakensjö et al., 2021	73 years/Male	Angiomas on tongue, eyelid cysts, palmar erythema and desquamation, hypotrichosis, brittle nails, hypoplastic nipples, pili torti	WNT10A, c.321C>A; p.Cys107* homozygote
Ren et al., 2022	22 years/Female	Toenail dystrophy, permanent teeth agenesis, conical teeth, palmoplantar keratoderma	WNT10A, c.742C>T; p.Arg248* c.376+1G>A, heterozygote
Present Case	40 years/Female	Palmoplantar erythema and desquamation, sparse hair, oligodontia, eyelid cysts, hyperhidrosis, oligodontia, rosacea	WNT10A, c.321C>A; p.Cys107*, homozygote

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Abstract N°: 2113

Dupilumab in the Treatment of Hailey-Hailey Disease: A Case Report

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Introduction: Hailey-Hailey disease is an autosomal dominant genodermatosis, caused by mutations in the ATP2C1 gene, leading to dysregulation of intracellular calcium signaling, thus compromising adhesion between keratinocytes. Clinically, it manifests as painful flaccid blisters and erosions localized in intertriginous areas, significantly impacting quality of life. Treatment is challenging and mostly ineffective, requiring the use of multiple therapeutic approaches. Recently, dupilumab has been successfully used in the treatment of this disease.

Case Description: We describe the case of a 54-year-old male with no relevant personal history, followed in Dermatology clinic for severe Hailey-Hailey disease. He underwent various previous therapies, including multiple cycles of antibiotics, botulinum toxin injection, acitretin, low-dose naltrexone, cyclosporine, topical corticosteroids, and topical calcineurin inhibitors with no significant response. In August 2023, due to a clear worsening of the dermatosis, with the development of extremely painful hyperkeratotic and erosive plaques, on the thoracic, lumbar, pectoral, axillary, and thigh regions (BSA=14%, DLQI=19), treatment with dupilumab 300mg every two weeks was initiated. At the 12-week follow-up, there was still no significant clinical response, but it was decided to continue the therapy. After 6 months of dupilumab therapy, the patient showed marked improvement of the lesions, with only a small lumbar plaque and residual axillary lesions remaining (BSA=3%). He also reported significant improvement in itching and quality of life (DLQI=5).

Conclusion: Dupilumab has demonstrated efficacy in treating Hailey-Hailey disease, as shown in this case. Inhibition of IL-4 and IL-13 by dupilumab appears to modulate intracellular calcium signaling, correcting the defect present in this genodermatosis. Sharing cases like this one is crucial due to the rarity of the disease and the limited treatment options available, potentially expanding the use of dupilumab to other acantholytic disorders.

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Abstract N°: 2185

Trichothiodystrophy: a case series

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Introduction & Objectives:

Trichothiodystrophy is a rare, autosomal recessive disease in which patients have sulfur-deficient brittle hair associated with variable neuroectodermal symptoms which may include ichthyosis, intellectual impairment, short stature, and proneness to infections. Half of the patients affected present photosensitivity caused by defects in DNA repair, damaged by UV light, without presenting further risk to develop skin cancer. Polarization microscopy of the hair allows to observe alternating light and dark bands that confer a “tiger tail” pattern, and genetic findings in those cases that present photosensitivity show pathogenic variants in genes encoding transcription factor IIH, such as GTF2H5.

PURPOSE: Describe epidemiological, clinical, trichoscopy and hair polarized microscopy, and genetic findings of patients with trichothiodystrophy seen at our department.

Materials & Methods:

Descriptive, observational, retrospective study. We reviewed the medical records of patients which presented clinical findings compatible with trichothiodystrophy, “tiger tail” pattern with polarization microscopy of the hair, and with genetic confirmation or genetic findings probably compatible with trichothiodystrophy at the Department of Dermatology of a National Pediatric Referral Center, evaluated during the period from January 2011 to April 2024.

Results:

Three patients were diagnosed with trichothiodystrophy. All were male.

Diagnoses were made at a mid age of 7.6 years. All of them presented skin manifestations at birth: two patients as collodion baby syndrome, and one patient as neonatal

erythroderma. Photosensitivity was found in all cases, as well as ichthyosis. Intellectual impairment, short stature and growth restriction was observed in all patients. Two patients presented hematologic manifestations and ocular abnormalities. Recurrent skin infections were described in two patients and respiratory infections in one patient. Squamous cell carcinoma was found in one patient. Hair structure alterations were found in all patients and polarization microscopy of the hair showed “tiger tail” pattern. In the three cases genetic study showed pathogenic variants in GTF2H5.

Conclusion:

Trichothiodystrophy comprises a heterogeneous group of autosomal recessive entities. Clinical expression is variable and although abnormalities are generally presents at noted from birth, they vary widely in both nature and severity. Patients with trichothiodystrophy should have a thorough exhaustive evaluation for other associated manifestations. Although this disease is not related with an increased risk of skin cancer development, one of our patients presented a squamous cell carcinoma, therefore it is fundamental to encourage strict solar protection.

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Abstract N°: 2307

Ferguson Smith Disease with perineural involvement

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Introduction:

Ferguson Smith Disease (FSD) is a rare genodermatosis, characterized by multiple recurrent skin tumours that clinically and histologically resemble cutaneous well-differentiated squamous cell carcinomas (SCCs) and keratoacanthomas (KAs).

Observation:

We present a case of a 42-year-old Caucasian woman who experienced a non-resolving erythematous, crusty skin lesion on her right cheek for one year. A similar lesion emerged on the dorsum of her nose without any associated trauma. Upon examination, a 10mm indurated plaque with central pitted scar was observed on her right chin along with a 20mm erythematous crusty plaque on the dorsum of her nose. While waiting for excision of both lesions, the lesion on the right cheek spontaneously regressed wheareas the one on her nose quadrupled in size. Multiple biopsies of the nose confirmed well differentiated SCC.

She had a complex medical background of right vestibular schwannoma removed with ventriculoperitoneal shunt in-situ, congenital right blind eye, post-neurosurgical trigeminal neuralgia, and psoriasis. Further investigation revealed that she had Scottish ancestry and both her sister, and two aunts had experienced similar self-limiting skin lesions, all of which were confirmed to be cases of FSD. She had a genetic testing which confirmed FSD with pathogenic variant of TGFBR1 gene. After a multidisciplinary team (MDT) discussion, she underwent screening and was found negative for neurofibromatosis. She continued developing similar lesions on lips, left upper eyelid and right cheek. These were treated conservatively with cryotherapy, imiquimod cream and Acitretin, effectively stabilising the skin lesions.

Her Acitretin was increased to 40mg, and prednisolone was initiated when she developed right infra-orbital swelling and neuropathy on the right face. An MRI of neck and biopsy demonstrated inflammation. Subsequently, she developed left cheek swelling with severe neuropathic pain, necessitating referral to pain team. MRI of neck showed perineural enhancement along the left infraorbital nerve. While prednisolone was continued for inflammation, Acitretin was reduced to 30mg due to side effects. Following numerous MDT discussions, conservative management with imiquimod cream and cryotherapy for active lesions was deemed the best approach. Radiotherapy was not recommended due to risk of recurrence and of blindness.

Discussion:

FSD manifests in an autosomal dominant manner, with many affected families sharing Scottish ancestry. It is caused by a mutation in the transforming growth factor beta receptor 1(TGFBR1) gene, which inhibits normal epithelial cell proliferation. Defects in this gene lead to unrestricted cell growth, increasing the risk of carcinogenesis.

While perineural involvement (PNI) is more commonly associated with SCC, it has rarely reported in cases of FSD. PNI can result in perineural spread, causing pain, dysesthesia, and radiologically detectable infiltration.

Although FSD tumours often regress spontaneously, treatment is crucial to prevent disfigurement from scarring post-resolution. Managing FSD is challenging, but systemic treatment like retinoids (isotretinoin, acitretin) have shown effectiveness. The optimal treatment for FSD should be further evaluated.

Conclusion:

We describe a complex case of FSD involving perineural invasion, which posed challenges in management, requiring numerous regional and national MDTs for treatment planning.

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Abstract N°: 2473

X-inactivation pattern and the gravity of clinical findings in Incontinentia pigmenti

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Introduction & Objectives:

Materials & Methods: Incontinentia pigmenti (IP) is a rare X-linked genodermatosis with an estimated prevalence of 1.2/100.000 (Orphanet report series, 2020). It appears almost exclusively in females and is usually lethal in males (Landy and Donnai, 1993). It is caused by a mutation of the IKBKG gene localized on the X chromosome.

The most prominent clinical manifestations of IP are skin changes, representing major IP diagnostic criteria (Minic et al, 2014, Clin Gen). Dental, ocular and central nervous system (CNS) anomalies are considered as minor criteria (Minic et al, 2014, Clin Gen).

CNS anomalies usually occur from the neonatal period and represent the most important threat to normal life of patients with IP.

The presented case is a proband diagnosed with IP, with severe CNS anomalies since birth. After confirming the IKBKG gene mutation, the X-chromosome inactivation assay showed a random X-chromosome inactivation pattern in the proband.

Magnetic resonance imaging (MRI) of the brain showed Microcephaly, and supratentorial white matter abnormalities with cavity formation and gliotic alterations. In addition, MRI showed hypoplasia of corpus callosum and thalamus, as well as atrophy of truncus cerebri and enlargement of the ventricular space (characteristic for IP). Orbital MRI showed atrophy of the optic nerves, optic tracts and optic chiasm corresponding to the findings of the concurrent ophthalmological examination. Transcranial ultrasonography of the brain showed normal echogenicity in the region of substantia nigra, and no pathological changes in basal ganglia at all.

Further analyses in the form of Next Genome Sequencing (NGS) and Whole Exome Sequencing (WES) revealed a heterozygous GBA gene mutation L444R indicative of

Gaucher disease (GD). The proband did not have GD, but was a carrier for the GBA gene mutation.

According to the literature, both skewed and random X-chromosome inactivation were found in IP patients (Dangouloff-Ros et al, 2017). Dangouloff-Ros et al, found severe neuroimaging anomalies associated with a random X-chromosome inactivation. The authors suggest that a skewed X-chromosome inactivation may protect the brain from damage, while, in the case of a random inactivation, the expression of the mutated IKBKG gene may lead to severe brain lesions. The findings of the examined proband's random X-chromosome inactivation and severe brain anomalies are in accordance with this statement (Dangouloff-Ros et al, 2017).

Results:

Conclusion:

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Abstract N°: 2588

SAM Syndrome: A rare syndrome with pulmonary stenosis

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Introduction & Objectives:

SAM syndrome (Severe Dermatitis, Allergies, and Metabolic Wasting) is a genetic disorder that can result from mutations in DSG1 gene or, in some cases, DSP gene. It follows an autosomal recessive inheritance pattern. Herein, we present a case of a 20-month-old male infant with SAM syndrome who presented with eczema during early neonatal period. The patient also had high eosinophil and IgE levels, resistant diarrhea, cardiac anomaly, and hypernatremia.

Materials & Methods:

A 20-month-old male, the first child of non-consanguineous parents, presented with redness, peeling, and scaling covering his entire body since birth. Upon presentation, he exhibited erythematous scaly plaques on bilateral malar region, scalp, and extensor surfaces of forearms. His medical history revaled that he was admitted to intensive care unit for approximately 15 days due to hypernatremia, feeding disorder as well as persistent pneumonia and diarrhea. During this hospitalisation, a skin biopsy was taken and reported as psoriasiform dermatitis. His total IgE level was 3603 IU/ml, and eosinophil count was 6700/microliter. Due to persistent hypernatremia, resistant diarrhea, persistent infections and severe eczema, genetic testing was performed, the mutation Trp303Cys (c.909>C) was detected in a homozygous state. With those findings, SAM syndrome was diagnosed in this patient. Further investigation for systemic involvement showed pulmonary stenosis in echocardiography. Acitretin 0.5 mg/kg/day was initiated which improved his skin lesions.

Results:

SAM syndrome is reported to manifest with severe erythroderma, failure to thrive, atopic manifestations, recurrent infections, cardiac malformations, hypotrichosis and palmoplantar keratoderma. However, as far as we know, pulmonary stenosis has not been documented before.

Conclusion:

Severe Dermatitis, Allergies, and Metabolic Wasting (SAM) syndrome is a rare genodermatosis however, in cases with early-onset severe atopic dermatitis, food allergy and metabolic disorders it should be considered. In patients diagnosed with this syndrome, investigation for cardiac malformations such as concomitant pulmonary stenosis is recommended.

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Abstract N°: 2592

Comprehensive medical support for children with hereditary skin diseases

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Introduction & Objectives: Genodermatoses are a group of hereditary heterogeneous diseases, the distinctive feature of which is the predominant damage to the skin and its appendages. Genodermatoses are distinguished by their variability, a wide range of complications and concomitant pathology from other organs and systems of the body. For timely diagnosis and prescription of symptomatic therapy, patients with genodermatoses require observation by a multidisciplinary team of specialists.Purpose of the study is present the rationale for an integrated approach to diagnosis, treatment and preventive monitoring for genodermatoses using the example of congenital epidermolysis bullosa and ichthyosis.

Materials & Methods: An analysis of extracutaneous manifestations and complications of such genodermatoses as congenital epidermolysis bullosa and ichthyosis was carried out from foreign and domestic scientific sources. The spectrum of complications and manifestations of internal organs in genodermatoses is described, the topic of symptomatic treatment and management of patients with congenital epidermolysis bullosa and ichthyosis in the neonatal period is highlighted. Recommendations for the symptomatic treatment of skin manifestations and complications of the gastrointestinal tract and musculoskeletal system are described.

Results: Based on the analyzed literary sources and our own clinical experience, it can be argued that with genodermatoses, not only the skin, but also other organs and systems of the body are involved in the pathological process. Timely diagnosis of the disease is extremely important for patients with these diseases, since symptomatic treatment of genodermatoses must begin as early as possible. Congenital epidermolysis bullosa and ichthyosis are serious diseases from the group of genetic skin diseases, characterized by great variability in clinical manifestations and a wide range of extracutaneous complications.

Conclusion: Preventive observation and treatment of patients with genodermatoses is a complex problem and its solution requires the involvement of a multidisciplinary team of specialists, which should include a dermatologist, pediatrician/therapist, geneticist, gastroenterologist, surgeon, ophthalmologist, otorhinolaryngologist, oncologist, dentist, orthopedist, rehabilitation specialist, psychologist, palliative care physician and qualified nurse.

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Abstract N°: 2701

cowden syndrome revealing pheochromocytoma

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Introduction:

Cowden Syndrome (CS) is an uncommon autosomal dominant genodermatosis, associated with various benign or malignant tumors. It is also called "multiple hamartoma" syndrome. Early detection of this syndrome is important to anticipate the development of any malignant tumor. (1) We report a case of CS revealing pheochromocytoma.

Observation:

A 35 year old women, with no particular family history and a personal history of thyroidectomy for papillary carcinoma. She is followed in gynecology for bilateral breast cystic dystrophy, uterine fibroids, uterine leiomyoma and serous cystadenoma of the ovary, in dental surgery for gingival hypertrophy and periodontal disease, which led to the complete avulsion of her teeth. She was referred by her dental surgeon for lesions of the lips and oral mucosa. On clinical examination we find: flesh-colored papular lesions on the nose and the perioral region, corresponding histologically to trichilemmomas. There are also cobblestones shaped lesions on the tongue and lower lip. The patient also presents papillomatous lesions on the neck, inframammary and axillary folds and punctate palmar hyperkeratosis. Thus, the diagnosis of CS was retained according to The International Cowden Syndrome Consortium (2). Thoraco-abdomino-pelvic CT scan revealed a left adrenal myelolipomas as well as a right adrenal tumor mass, for which the patient underwent surgical excision. The histopathology report concluded to pheochromocytoma. A colonoscopy is also scheduled.

Discussion:

Cowden syndrome (CS) is a rare genodermatosis caused by mutation in the Phosphatase and TENsin homolog (PTEN) gene, a tumor suppressor gene (3), located on chromosome 10q23, transmitted in an autosomal dominant mode (4) with a female predominance. Symptoms usually appear between the third and fourth decades. Some diagnosed cases occur sporadically, without a family history of CS (5), the case of our patient. This syndrome is characterized by a wide range of symptoms, including mucocutaneous lesions and involvement of different organs, leading to a massive cumulative risk of cancer over the lifespan. (6) In the maxillofacial region, it is around the mouth, nose and in the periorbital region that papules are found. Corresponding to trichilemmomas or hamartomas derived from hair follicles. Involvement of the gingival and oral mucosa, with the presence of fibromatous papular lesions, is pathognomonic. (5) Cobblestones like oral lesions are encountered in 40% of patients. In our patient, we found: the cobblestones appearance, trichilemmomas and papillomatous lesions. Among the extracutaneous manifestations, the thyroid is the most affected organ after the skin. (5) CS is associated with increased risk of breast, endometrial, gastrointestinal tract, and renal cancers. (4) In our patient we found: papillary thyroid carcinoma, breast cysts, leiomyoma and uterine fibroid. The discovery of a pheochromocytoma in our patient (not being a typical malignancy in CS) is explained by the genetic mutation of the Succinate dehydrogenase enzyme complex (SDHB, SHDC, SDHD) and prompts us to be vigilant regarding the occurrence of a renal tumor, frequently found during this association (CS and pheochromocytoma) (3)

Conclusion:

Our observation highlights the need to look for tumors usually associated with Cowden syndrome, but also

pheochromocytoma, an exceptional association, and encourages us to regularly monitor our patients and their families.

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Abstract N°: 2744

VEXAS Syndrome case report over a 2 years long follow up period

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Introduction & Objectives:

VEXAS syndrome is a newly identified , adult-onset autoinflammatory disease, whose acronym stands for Vacuoles, E1 enzyme, X-linked, Autoinflammatory and Somatic. It was first diagnosed in October 2020 and it is proved to be caused by a somatic mutation of the UBA1 gene. Since the UBA 1 gene is located on the X-chromosome, the disease affects only males, with a median age of onset in the late 50's to mid 60's. The clinical manifestations often overlap between haematological, dermatological and rheumatological diseases.

Materials & Methods:

We are reporting about a case of a 65-year-old male with histopathologically confirmed granuloma annulare and a pre-existing vasculitis, mild pancytopenia, macrocytosis, polyarthralgia and recurrent perichondritis, over a follow up period of 2 years.

Results:

A 65-year-old patient with multiple disseminated and partially confluent, annular, erythematous plaques on the back, chest and neck. The lesions are not painful nor pruritic. There has been a complete resolution in the past while the patient was undergoing a therapy with prednisolone for a bilateral perichondritis, but they recurred every time after the therapy was stopped. A biopsy was performed from an annular lesion on the back and the histopathological finding was conclusive for Granuloma annulare (no presence of neutrophilic infiltrate, no presence of CD163 positive cells). The therapy with topical potent corticosteroids (bethametasone valerate ointment) wasn't providing any improvement. The patient was reporting of a 4 year history of palpable purpura on the both distal extremities, which in the past was clinically diagnosed as a small cell vasculitis, without histopathological confirmation. These lesions have also completely resolved after the perioral therapy with prednisolone.

The laboratory results showed an increase in RF, ESR and GGT, as well as leukopenia 3,0 g/l, thrombocytopenia and ANA 1:320, ENA negative, ANCA negative. Mutation analyse of the UBA-1 gene was performed and there was a heterozygous proof on c.121A>c (pMet41Leu) in the UBA-1 gene, which confirmed the diagnose VEXAS syndrome. A bone marrow biopsy showed presence of cytoplasmic vacuoles.

The patient was given a perioral therapy with prednisolon 60mg daily with a slow reduction of the dosage. Full resolution of the vasculitic lesions was observed as well as almost full resolution of the granuloma annulare lesions. In the follow up period of 1 year (until present), the patient had no new skin manifestations, except of single Morbus Bowen lesion on the trunk, which was suspected not to be related with the other manifestations of VEXAS Syndrome.

Conclusion:

The most common dermatological manifestations of a VEXAS Syndrome are neutrophilic dermatosis that histopathologically show a perivascular neutrophilic infiltrate and CD163 positive cells. In our patient a neutrophilic dermatosis was not present and the skin lesions were histopathologically identical to granuloma

annulare lessions.

A therapy with a JAK inhibitors has been suggested in the literature, with ruxolitinib being the recommended drug as more effective than other JAK inhibitors in a retrospective multi-center study. An extensive research is being performed in this field and we expect a new therapeutic possibilities in near future.

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Abstract N°: 2766

Primary Hypertrophic Osteoarthropathy: the complete form of the syndrome

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Introduction & Objectives:

Primary Hypertrophic Osteoarthropathy (PHO), also known as Pachydermoperiostosis or Touraine-Solente-Gole Syndrome, is a very rare multisystemic autosomal recessive disorder characterized by three main clinical features - digital clubbing, osteoarthropathy, and pachydermia. It is caused by pathogenic variants in the 15-hydroxyprostaglandin dehydrogenase (HPGD) or Solute Carrier Organic Anion Transporter Family Member 2A1 (SLCO2A1).

Materials & Methods:

We describe a complete form of this syndrome in an African male patient with a homozygous variant in the SLCO2A1 gene.

Results:

A 24-year-old man from São Tomé e Príncipe was referred to our tertiary hospital in Portugal with a five-year history of symmetrical painful and swollen hands, knees, ankles, and feet with prolonged morning stiffness, previously diagnosed as Juvenile Idiopathic Arthritis. He also reported since 22-year-old the onset of progressive facial changes and bilateral ptosis. Family history was irrelevant, and parents were non-consanguineous.

On clinical examination, he presented marked skin thickening on the face, most notably on the forehead, with accentuation of the skin folds (cutis verticis gyrata), bilateral ptosis, hypertrophy of the hands and feet, clubbing of the fingers and toes, and swelling of the periarticular tissues of knees and ankles.

Laboratory investigations showed elevated inflammatory markers, without other changes. Plain radiographs of the skull, hands, knees, and feet revealed soft tissue swelling, and periosteal hypertrophy with subperiosteal bone formation. On the skin biopsy performed on the frontal region sebaceous hyperplasia was observed.

Due to the absence of other clinical signs suggesting a secondary cause, after multidisciplinary evaluation PHO was suspected. A genetic study detected a pathogenic variant in the SLCO2A1 gene in homozygosity, thus confirming the diagnosis. The patient started oral etoricoxib with symptomatic improvement and surgical interventions for ptosis are planned.

Conclusion:

While secondary hypertrophic osteoarthropathy is associated with underlying cardiopulmonary diseases and malignancies, the primary form accounts for only 5% of all cases.

PHO typically affects males (male to female ratio of 9:1), begins during childhood or adolescence and may stabilize after 5-20 years, or progress gradually. Currently available therapeutic options are palliative and directed

toward amelioration of the patient’s complaints, including non-steroidal anti-inflammatory drugs.

This case emphasizes the importance of being aware of this syndrome and the role of the dermatologist in helping to diagnose genetic diseases with skin involvement.

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Abstract N°: 2797

Mucocutaneous triad of abnormal skin pigmentation, nail dystrophy & leukoplakia: What is your diagnosis?

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Introduction & Objectives: Collaboration between dermatologists and rheumatologists is often needed to identify patients with autoimmune connective tissue diseases. The bigger picture of the disease emerges only when both fields work together. This collaboration aids in the optimal development of disease diagnostic and classification criteria. They also help diagnose and manage various disease manifestations in the clinical setting. Our objective is to present a clinical case highlighting the importance of collaboration between dermatologists and rheumatologists.

Materials & Methods: A 66-year-old woman presented for evaluation of a 5-month history of progressively worsening, painful skin tightening, swelling of her arms and legs, and inflammatory arthritis. On physical examination, there was symmetric, woody induration of the trunk, arms, and legs, sparing the hands and feet. The involved skin had a dimpled appearance (*peau d'orange*). Elevation of the arms resulted in visible indentations along the course of superficial veins, a finding known as the "groove sign." Joint contractures and tendon retraction were evidenced by the "prayer sign." Laboratory analysis was notable for peripheral eosinophilia, with an absolute eosinophil count of 810 cells/µL, an erythrocyte sedimentation rate of 66 mm/h, ANAs positive titer of 1:160, an elevated aldolase 11.6 U/L, serum electrophoresis showed hypergammaglobulinemia associated with a band in the gamma, and an IgG-lambda monoclonal protein was detected on immunofixation. Bone marrow biopsy and aspiration were normal. Nailfold capillaroscopy showed no changes. Skeletal radiography demonstrated no abnormalities, and magnetic resonance imaging results of the thighs were consistent with fasciitis. An incisional skin biopsy of the right forearm revealed septal panniculitis with infiltration of lymphocytes and plasma cells, with no eosinophils. Therapy was initiated with oral corticosteroids and methotrexate, subsequently improving the induration and stiffness in follow-up consults.

Results: According to *Pinal-Fernandez's* proposed criteria, eosinophilic fasciitis (EF) was diagnosed. Laboratory results showed that the patient had a concomitant monoclonal gammopathy, IgG lambda.

Conclusion: EF is a rare, acquired, fibrosing disease that was first described by Shulman in 1975. Erythema and edema are characteristic features, with subsequent induration of the skin. Peripheral eosinophilia is also considered a classic feature of this disease, although it is not universally present. Other hematologic abnormalities may occur, like in our patient. Systemic sclerosis, morphea, nephrogenic fibrosing dermopathy, and graft-vs-host disease are considered in the differential diagnosis. Notably, sparing of the digits is typically seen in EF. Early diagnosis and prompt, aggressive treatment are essential to prevent permanent fibrosis and joint contracture, which may lead to significant morbidity.

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Abstract N°: 2903

Role of acitretin in cutaneous lesions and hoarseness related to lipoid proteinosis

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Introduction & Objectives:

Lipoid proteinosis (Lp) is a rare autosomal recessive deposition disorder in which hyaline-like material is deposited within multiple organs, including the skin, oral mucosa, larynx and brain. Hoarseness of voice appears as the first clinical manifestation which is followed by various cutaneous findings such as blisters on trauma prone sites, waxy papules, moniliform blepharosis and pock like scar. Acitretin is superior than other retinoids in decreasing hyaline deposition and hence has found its role improvement in the hoarsness of voice and cutaneous findings

Objective: To assess the efficacy of oral acitretin in addressing the hoarseness of voice and improvement of cutaneous lesions in patients of Lp.

Materials & Methods:

A total of 6 patients of clinically diagnosed Lp (excluding pregnant and lactating women) were enrolled in the study done in a tertiary care hospital from January 2021 to December 2022. Capsule acitretin 0.5mg/kg/day was started for 6 months and the patients were followed up at every month till 6 months. Liver function test and lipid profile of the patient were done at every month. Hoarseness of voice was assessed at every month by GRBAS (Grade, Roughness, Breathiness, Asthenia, Strain) scale. The rating scale was 0: normal, 1: slight, 2: moderate, 3: severe. Any side effects occurring during the treatment interval were assessed. The patients were also followed up at 6 months after treatment completion. Acitretin was further continued till improvement in hoarseness of voice and cutaneous lesions

Results:

The mean age of the patients was 14.93±1.82 years with a male: female ratio of 1:1. Of the 6 patients analysed, 50% (n=3) patients achieved mean GRBAS Score from 13 to 10 at the end of 4 months. On further continuing monotherapy with acitretin for 6 months, there was improvement in the severity of disease with 100%(n=6) patients achieving GRBAS Score from 13 to 6 (50% improvement). At the end of 4 months, 33.33% patients (n=2) achieved >50% clinical improvement, while 66.67% patients (n=4) achieved >50% clinical improvement at the end of 6 months. After 6 months mean DLQI score was significantly improved from 17.5 to 8.5 ($p<0.05$). None of the patients experienced any untoward side effect during the therapy.

Conclusion:

Lp has considerable morbidity from birth in the form of dysphonia and cutaneous lesions. Acitretin has demonstrated notable efficacy not only in ameliorating cutaneous manifestations but also in alleviating vocal hoarseness, thereby enhancing overall quality of life.

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Abstract N°: 3072

Case Report of Congenital Ichthyosiform Erythroderma with a Mutation in the KRT1 gene and CARD14 gene

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Introduction & Objectives:

Congenital Ichthyosiform Erythroderma is a genetic disorder characterized by generalized hyperkeratosis. It is a rare pathology which affects about 1/200.000-1/100.000 people. Regarding its etiopathogenesis, mutations in at least nine genes have been found. Its way of inheritance is typically autosomal recessive, though cases with autosomal dominant inheritance have also been described.

Materials & Methods:

We present the case of a 10-year-old feminine patient from Tijuana, Baja California, whose condition began 20 days after birth and included widespread erythroderma and blisters. There are no relevant data on consanguinity or endogamy. Regarding her development, she presented low height and weight for her age and did not have psychomotor disorders or associated comorbidities. As part of the patient's follow-up, ichthyosis gene panels were requested for genetic testing. Heterozygous variants of the KRT1 gene were found, which causes autosomal epidermolytic ichthyosis, Ichthyosis hystrix of Curth-Macklin, and annular epidermolytic ichthyosis. Parents' genetic assessment was also carried out, resulting in the detection of the same heterozygous variant in the father, who does not show this pathology. When expanding its panel of genetic studies, another mutation was found that is a heterozygous variant of the CARD14 gene where the variants of this gene present as pityriasis rubra pilaris and psoriasis; important fact to consider, since it is the first time that a CARD14 gene mutation associated with congenital ichthyosiform erythroderma has been reported. The diagnosis was complemented with a skin biopsy stained with hematoxylin and eosin in which epidermis with parakeratotic lamellar hyperkeratosis was observed. Dailly use emollients and urea-containing creams were indicated as treatment.

Results:

Based on these findings, is the first time that a CARD14 gene mutation associated with congenital ichthyosiform erythroderma has been reported. From this, possible treatments could be proposed, though most options offer poor results. Systemic retinoids could be an exception, but they lead to adverse side effects. Cytokine-directed treatments, including. one with IgG1/κ monoclonal antibody which stands out among the others, have been suggested given IL-17 immunological dominant profile in many ARCI patients.

Conclusion:

Based on the genetic findings and the clinical picture, the diagnosis is congenital ichthyosiform erythroderma due to a genetic alteration of the KRT1 gene with complete penetrance. Congenital Ichthyosiform Erythroderma is a highly disabling disease. Current treatments are based on the improvement of symptoms due to the lack of curative ones. Gene and cellular therapies aimed to correct the functional activity of altered proteins are progressing, but there are still at an early stage. Because the patient shares the mutation of the CARD14 gene

where the variants of this gene present as pityriasis rubra pilaris and psoriasis, she could benefit in the future from being treated with IL 17 inhibitors and improve the dermatosis. Her low weight and early age currently prevent her from being a candidate for that treatment, but once she meets the requirements, indication with strict monitoring will be proposed.

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Abstract N°: 3179

Unveiling a New Dermatological Horizon: Baricitinib in Dystrophic Epidermolysis Bullosa

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Introduction & Objectives:

Dystrophic epidermolysis bullosa (DEB) is a hereditary condition characterized by the development of painful skin blisters and erosions, leading to significant morbidity. A particularly challenging case of DEB and alopecia areata (AA), was observed in a 46-year-old woman with a dominant form of the disease and a family history of DEB. Traditional therapies for AA, including high-dose corticosteroids and SADBE, were ineffective and associated with adverse effects on the DEB side, such as delayed wound healing and exacerbated lesions. The patient's AA condition was recalcitrant until the initiation of treatment with Baricitinib, a selective JAK inhibitor.

Materials & Methods:

Results:

Upon Baricitinib administration, the patient experienced, alongside notable hair regrowth, a marked reduction in skin inflammation, rapid healing of traumatic wounds, and a cessation of spontaneous lesions formation. However, an interruption due to an infectous febrile illness resulted in a rapid reversal of these gains, with a return to severe inflammation, blistering and hair loss. Fourteen days after resuming therapy with Baricitinib, the patient stopped applying dressings for DEB, as there were no more lesions and the previous ones had completely disappeared. Additionally, both the itching and inflammation had also resolved. Resuming Baricitinib led to prompt improvement in both DEB lesions and AA, reaffirming its therapeutic potential.

The effectiveness of JAK inhibitors likely stems from their capacity to inhibit key cytokines involved in DEB pathogenesis such as IL-6 and IL-12. This broad mechanism may help reduce the heightened inflammatory state associated with DEB.

Conclusion:

This case underscores the importance of JAK inhibition in managing the inflammatory and wound aspect of DEB. Baricitinib's capacity to modulate the immune response and inflammation could signify a shift in the treatment paradigm for DEB, offering a benefit for cutaneous lesions. The positive response in this case encourages further investigation into the long-term efficacy and safety of JAK inhibitors for DEB, with a focus on their impact on wound healing and skin integrity.

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Abstract N°: 3242

A genome-wide association study of hand eczema identifies locus 20q13.33 and reveals genetic overlap with atopic dermatitis.

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Introduction & Objectives:

Twin studies revealed that genetic effects play a role in hand eczema (HE), but the responsible genetic factors are unknown. Therefore, the aim of our study is to identify and characterize genetic loci associated with HE and to provide insight into the genetic overlap between HE and atopic dermatitis (AD).

Materials & Methods:

We used questionnaire-derived and genotype data from Lifelines, a European population-based cohort and biobank study. We performed a discovery genome-wide association study (GWAS) of HE (2,879 cases and 16,249 controls) and of AD (1,706 cases and 17,190 controls). We replicated our findings in an independent Lifelines sample for HE (1,188 cases and 6,431 controls) and AD (757 cases and 6,747 controls). Furthermore, we conducted several bioinformatic post-GWAS analyses to identify the most causal variants. Next, we performed genetic correlation analyses between our HE results and independent AD data.

Results:

The GWAS of HE, regardless of adjusting for AD, identified and replicated one independent locus 20q13.33. The signal at this locus is likely driven by a number of potentially causal variants and their affected genes (TNFRSF6B, RTEL1, LIME1, STMN3, ZGPAT, SLC2A4RG, ARFRP1). For the AD GWAS, we replicated a known stop-gained variant rs61816761 at locus 1q21.3 (FLG, FLGAS1). We found a strong genetic correlation ($p<0.01$) between HE and AD ($rg=0.65$), regardless of adjusting for AD ($rg=0.63$).

Conclusion:

Our study identified that locus 20q13.33 is associated with HE, and demonstrated that there is a large genetic overlap between HE and AD.

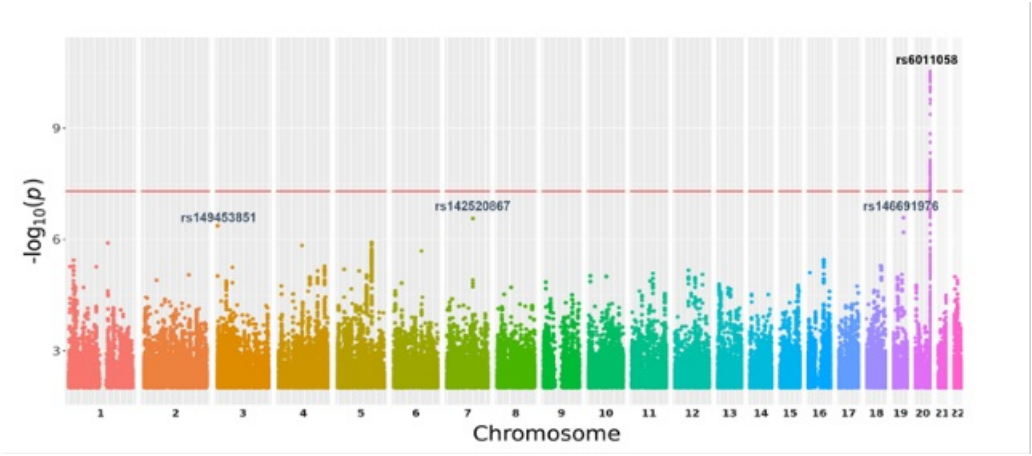

Figure 1. Manhattan plot of the analysis with hand eczema cases versus controls without hand eczema (model 1). Each dot represents a SNP with the genome-wide significant lead SNP indicated. The red horizontal line represents the genome-wide significance threshold (p < 5.0 x 10-8).

Abbreviations: SNP, single-nucleotide polymorphism

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Abstract N°: 3295

Analysis of CARD11 gene variant in a child with Immunodeficiency 11B with atopic dermatitis

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Introduction & Objectives:

To investigate the clinical and genetic characteristics of a case presenting with infantile Immunodeficiency 11B with atopic dermatitis.

Materials & Methods:

A patient with a genetic variant of a known genetic disorder was selected as the study subject, who was admitted to the Department of Dermatology of Hunan Children's Hospital on July 11, 2023. Whole exome sequencing (WES) was performed on the patient, her parents, elder brother and sister, and Sanger sequencing was performed to verify the candidate variants and analyze the pathogenicity.

Results:

The patient was a 7-month-old boy with recurrent pulmonary infection, diarrhea, and atopic dermatitis. The blood IgE level was significantly elevated. Genetic testing showed a heterozygous variant of NM_032415.5: c.286G>A (p.Glu96Lys) in CARD11 gene, which was autosomal dominant and inherited from the father. This variant has not been reported before and was evaluated as a suspected pathogenic variant (PS4_Supporting+PS3_Supporting+PM2_Supporting+PP1_Strong+PP4) according to the relevant guidelines of the American College of Medical Genetics and Genomics (ACMG)

Conclusion:

The NM_032415.5:c.286G>A(p.Glu96Lys) heterozygous variant of CARD11 gene may be the genetic etiology of the patient with immunodeficiency 11B with atopic dermatitis,enriching the variation spectrum of CARD11 gene.

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Abstract N°: 3336

Expanding the Genetic Landscape of Scalp Cylindromas: A Case Report of a Novel CYLD Mutation

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Introduction & Objectives: Cylindromas are rare benign tumors mainly found on the scalp and face, more common in women, often appearing in the second or third decade of life. They can present as single or multiple nodules, the latter linked to CYLD gene mutations, notably in Brooke-Spiegler syndrome. Here, we report a case of a case of a 61-year-old male presenting with multiple scalp cylindromas, which prompted genetic testing revealing a novel mutation in the CYLD gene.

Materials & Methods: We describe the clinical presentation, diagnostic assessment, and genetic testing of a 61-year-old male with a 20-year history of multiple cutaneous tumors on his scalp.

Results:

An otherwise healthy individual presented with multiple asymptomatic, dome-shaped, pink to skin-colored nodules across the scalp. Notably, a family history revealed similar lesions in his mother and sister, beginning around the age 20. Histopathological examination confirmed the diagnosis of cylindroma.

Genetic testing was performed, unveiling a novel heterozygous mutation in the CYLD gene (c.1124G>A, p.(Trp375Ter)), resulting in the substitution of tryptophan with a premature termination codon, previously unreported the literature or databases.

Conclusion:

Identification of this novel CYLD mutation expands our understanding of cylindroma genetics and underscores the importance of genetic testing in patients with multiple adnexal tumors. Such insights facilitate precise diagnosis, risk assessment, genetic counseling, and tailored management strategies. Additionally, patients with specific mutations may qualify for clinical trials exploring non-surgical interventions to halt tumor progression. This case highlights the value of genetic testing in suspected familial cylindromatosis and emphasizes the need for further research in this area.

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Abstract N°: 3416

Gorlin-Goltz Syndrome: a Case Report and literature review

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Introduction & Objectives:

Gorlin-Goltz syndrome (also known as basal cell nevus syndrome or nevoid basal cell syndrome) is a multisystem disorder characterized by skin, eye, dental, and skeletal abnormalities resulting from dysplasia of tissues derived from the mesoectoderm. This study examines a case of Gorlin-Goltz syndrome in Iran.

Materials & Methods:

We studied a patient who was referred to the dermatology clinic at Shahada Hospital in Tehran in 2022. Subsequently, we conducted a review by analyzing similar studies published in the last 10 years in PubMed, Scopus, and Science Direct databases to compare and contrast findings in this field.

Results:

A 24-year-old man visited our dermatology clinic with a complaint of multiple hyperpigmented papules in the scalp area that had been developing for more than 10 years. In the patient's medical history, he underwent cerebellar tumor surgery at the age of 4, which was confirmed to be medulloblastoma in the pathological examination. Additionally, he had a maxillary sinus biopsy and surgery due to a maxillary sinus infection, with a diagnosis of odontogenic keratocyst. Before visiting the dermatology clinic, the patient had undergone excision of a lesion in the head and neck surgery department because of a mass in the left external ear canal. The histopathological examination confirmed Basal Cell Carcinoma. During the examination, the patient measured 152 cm in height and weighed 72 kg. The patient's voice was higher in pitch compared to that of a typical 24-year-old man, and the patient had not experienced the typical growth of beard. Macrocephaly (in relation to height), hypertelorism, frontal prominence, and a large gap between the teeth. were the defining features of the patient's appearance. No pathological findings were observed in the palmoplantar examination.

According to the patient's history and examination, Gorlin syndrome or basal cell nevus syndrome (BCNS) was suggested. Several hyperpigmented lesions on the patient's scalp were removed, and the histopathological examination revealed Basal Cell Carcinoma Pigmented Type in all the excised samples. He had an abnormal lipid profile in the laboratory tests, who had been taking a daily dose of 20 mg atorvastatin for several years to address high triglycerides and cholesterol, all other test results were normal. In the patient's chest x-ray, there were no pathological findings, such as rib deformities or bifurcations. In the ultrasound of the abdomen and pelvis, both testicles of the patient were observed in the inguinal canal with an atrophic appearance, indicating cryptorchidism. In the head and face CT scan, odontogenic keratocyst was observed in the right maxilla, along with falx calcification (see Figure 6), basal ganglia calcification (see Figure 7), and tentorium calcification. According to the patient's medical history and paraclinical tests, the diagnosis of Gorlin-Goltz syndrome was confirmed based on the criteria outlined in various references

Conclusion:

It seems that Gorlin syndrome, in addition to the minor and major criteria mentioned in various references, has many other manifestations that need to be investigated statistically and pathologically.

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Abstract N°: 3470

Reflectance confocal microscopy analysis of epidermolysis bullosa naevi

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Reflectance confocal microscopy analysis of epidermolysis bullosa naevi

Introduction & Objectives: Epidermolysis Bullosa (EB) naevi are acquired asymmetrical melanocytic lesions that develop in areas of former blistering in patients with inherited EB.1

EB nevus may present clinical features of melanoma (MM) and histopathologic features of a benign simulator of MM (compound congenital or persisting nevus).2 The distinctive dermoscopic pattern was previously described with some melanoma-associated dermoscopic criteria.3 Biopsy is recommended in suspicious lesions.

The aim of this study is to evaluate EB naevi with reflectance confocal microscopy (RCM), describing microscopic features of this entity.

Materials & Methods: Lesions diagnosed as EB naevi were evaluated with digital dermoscopy (DD) and RCM analysis. The criteria of ABCD rule of DD (total dermoscopy score – TDS)4,5 and the RCM score6,7 algorithm for melanocytic lesions previously described were applied to distinguish EB naevi from MM.

Results: Thirty-four EB naevi from 22 patients were included. Nine patients had recessive dystrophic EB, 7 dominant dystrophic EB, 4 simplex EB and 2 junctional EB.

DD features (Table 1) associated with MM were: asymmetrical multicomponent pattern (27), irregular dots/globules (21), atypical pigment network (32), irregular pigmentation (33) and structureless areas (28).

On RCM (Table 2), 5 lesions presented atypical honeycomb pattern in the epidermis, while 4 had atypical cobblestone pattern. Pagetoid infiltration was not seen.

At the dermal-epidermal junction (DEJ), non-edged papillae were detected in 5 lesions and the papillary architecture was indistinguishable in 6 due to skin atrophy. The ringed pattern was observed in 7 lesions, the meshwork pattern was seen in 3, the clod pattern in 3 and 15 had a mixed pattern. Junctional nests were observed in 25 lesions. Round to oval cells in the basal layer or within the nests (Figure 1) were identified in 7 lesions, dendritic cells (Figure 2) were seen in 5 and both cells were noticed in 11. Twelve lesions presented monomorphic cells whilst in 11 lesions they were pleomorphic.

The papillary dermis showed melanophages in 19 lesions and dense nests in 13 lesions.

TDS ≥ 5.45 were found in 19 lesions, a result highly suggestive for MM. The RCM score < 3 was found in 33 lesions and the diagnosis of MM was considered in only one (score ≥ 3). This lesion had dendritic cells in the DEJ and mild disarray. Clinically it presented with inflammation and atrophy. (Tables 3 and 4)

Conclusion: RCM features of EB naevi are useful for the distinction between benign and malignant melanocytic lesions whilst DD features could misdiagnose. The RCM score algorithm requires the identification of 6 features, independently correlated with MM diagnosis. Roundish pagetoid cells, widespread pagetoid infiltration, cerebriform nests and nucleated cells in the dermis (atypical melanocytic cells) were absent in all naevi EB

evaluated.

RCM is a viable noninvasive imaging method to evaluate EB naevi and may reduce the need of excisions in this population. No blistering was observed in any of the patients.

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	Dominant Dystrophic EB (12 naevi, 7 patients)	Recessive Dystrophic EB (12 naevi, 9 patients)	Junctional EB (2 naevi, 2 patients)	EB simplex (8 naevi, 4 patients)	Total (34 naevi, 22 patients)
Pattern analysis					
Network	12	11	2	7	32
Structureless areas	9	12	2	5	28
Dots	7	12	1	2	22
Globules	6	9	1	7	23
Streaks	1	0	0	1	2
Atypical pigment network	12	11	2	7	32
Irregular pigmentation	12	12	2	7	33
Irregular dots and globules	7	9	0	5	21
Multicomponent pattern	10	12	0	5	27

Table 1: dermoscopic features

Suprabasal epidermis	
Keratinocytes	Regular: 34 (100%) Atypical: 0 (0%)
Honeycombed pattern	Regular: 29 (85%) Atypical: 5 (15%)
Cobblestone pattern	Regular: 21 (62%) Atypical: 4 (12%) Not observed: 9 (26%)
Roundish pagetoid cells	Present: 0 (0%) Absent: 34 (100%)
Widespread pagetoid infiltration	Present: 0 (0%) Absent: 34 (100%)

Dermal epidermal junction	
Papillae	Edged: 23 (68%) Non-edged: 5 (15%) Not observed: 6 (17%)
Dermal papillae pattern	Rings: 7 (20%) Meshwork: 3 (9%) Clod: 3 (9%) Mixed: 15 (44%) Nonspecific: 6 (17%)
Large cells	Monomorphic: 12 (35%) Pleomorphic: 11 (32%) Absent: 11 (32%)
Shape of large cells	Round to oval: 7 (21%) Dendritic (stellate): 5 (15%) Round and dendritic: 11 (32%) Absent: 11 (32%)
Junctional nests	Present: 25 (74%) Absent: 9 (26%)
Cerebriform nests	Present: 0 (0%) Absent: 34 (100%)
Folliculotropism	Present: 0 (0%) Absent: 34 (100%)
Nests	Dense: 13 (38%) Sparse: 12 (35%) Absent: 9 (27%)

Upper dermis	
Melanophages	Present: 19 (56%) Absent: 15 (44%)
Nests	Dense: 13 (38%) Sparse: 12 (35%) Absent: 9 (27%)
Nucleated cells in the dermis	Present: 0 (0%) Absent: 34 (100%)

Table 2: confocal microscopy features

Diagnostic Criteria	Score	Weight Factor
Asymmetry	0-2	x 1.3
Border pigment pattern	0-8	x 0.1
Color variation	1-6	x 0.5
Different structural components	1-5	x 0.5

Benign melanocytic lesion	< 4.75	6 naevi
Suspicious lesion	4.8 - 5.45	9 naevi
Lesion highly suggestive of melanoma	> 5.45	19 naevi

Table 3: Total Dermoscopic Score (TDS) = 1.3 (A score) + 0.1 (B score) + 0.5 (C score) + 0.5 (D score)

RCM Score Algorithm	Weight Factor	N (naevi)
Non-edged papillae	2	5
Mild to marked cell atypia	2	11
Roundish pagetoid cells	1	0
Widespread pagetoid infiltration	1	0
Cerebriform nests	1	0
Nucleated cells in the dermis	1	0

RCM Score Threshold		
≥ 3	Lesion highly suggestive of melanoma	1 naevi
< 3	Suggestive of benign lesion	33 naevi

Table 4: total RCM score = 2x (non-edged papillae) + 2x (mild to marked cell atypia) + (roundish pagetoid cells) + (widespread pagetoid infiltration) + (cerebriform nests) + (nucleated cells in the dermis)

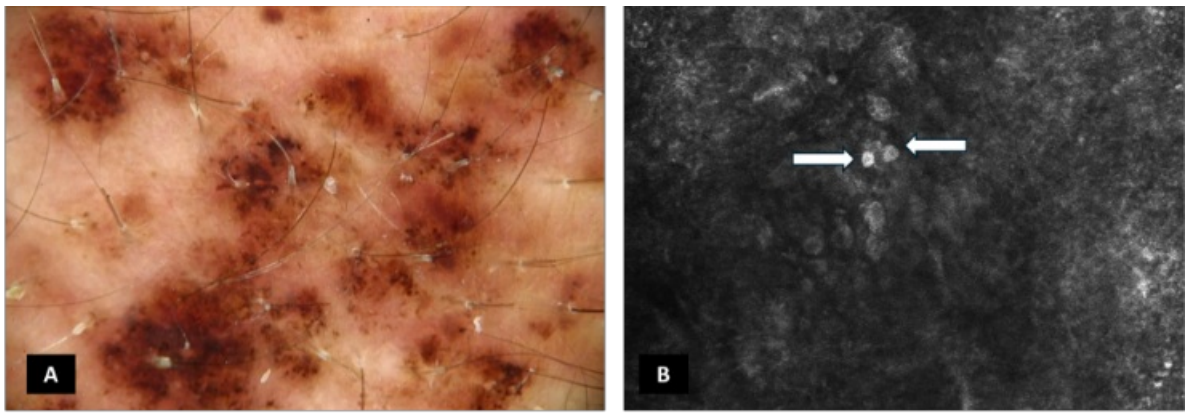

Figure 1: A) dermoscopy image with globular pattern, atypical pigmentation and irregular dots and globules of an EB nevus (female patient, EBDR). B) RCM image with roundish cells (white arrows).

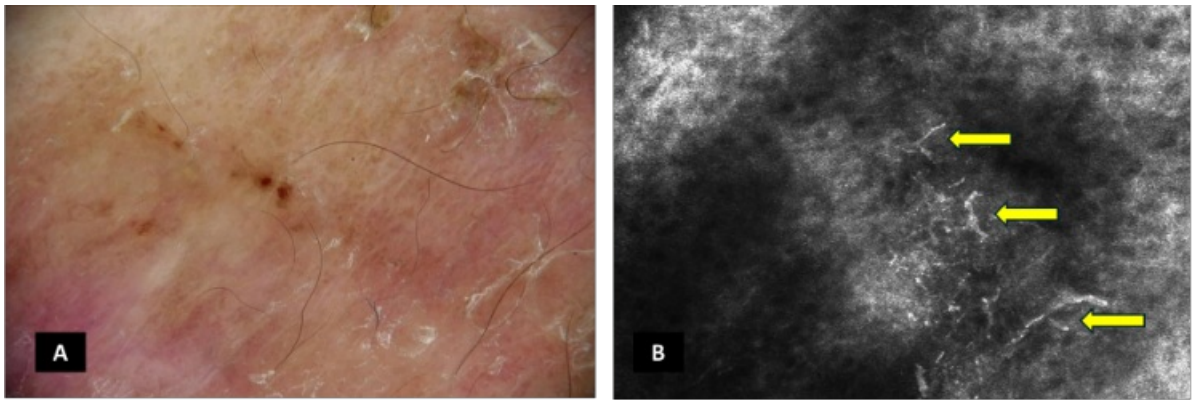

Figure 2: A) dermoscopy image of an EB nevus with atypical pigment network, dots, globules and structureless areas (female patient, EBDR). ; B) RCM image with dentritic cells (yellow arrows).

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Abstract N°: 3535

Targeting Tumors: Sirolimus Therapy in Neurofibromatosis Type 1 - A Case Report

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Introduction & Objectives:

Neurofibromatosis type 1 (NF1) is a genetic disorder characterised by the development of benign nerve sheath tumours known as neurofibromas. There is often a lack of conventional treatment options for these tumours, which makes their management challenging. This case report explores the potential benefits of sirolimus, an inhibitor of mTOR, for treating neurofibromas in a young adult with NF1.

Materials & Methods:

This is a case report of a 19-year-old male with a confirmed diagnosis of NF1 presented with multiple swellings and brown-coloured lesions over his body, progressively increasing in size. The patient's clinical history, sirolimus dosing, and response to treatment were meticulously documented**.**

Results:

After initiating sirolimus treatment, the patient's lesions significantly improved, and new lesions were absent. Sirolimus was well tolerated without any significant adverse effects. This case report suggests that sirolimus may be useful in managing cutaneous neurofibromas associated with NF1. Its inhibition of the mTOR pathway appears to contribute to tumour size reduction and the onset of new lesions. Although further studies are necessary to establish its efficacy more comprehensively, this case underscores the potential benefit of sirolimus in treating challenging cutaneous neurofibromas.

Conclusion:

It was demonstrated that sirolimus is an effective treatment option for treating cutaneous neurofibromas among patients with NF1. This report emphasizes the need for additional research, including larger-scale and longer-term studies, to better define how sirolimus can treat cutaneous neurofibromas.

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Abstract N°: 3588

Topical gabapentin 10% in the treatment of epidermolysis bullosa pruritus: A pilot, double-blind, split-site, randomized controlled trial

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Introduction & Objectives:

Pruritus is a symptom that adversely affects the quality of life of patients with epider- molysis bullosa (EB). Although studies indicate the positive effect of gabapentin on some types of pruritus, its effect on pruritus due to EB remains unexplored. Hence, this study investigated the efficacy of topical gabapentin in treating EB pruritus.

Materials & Methods:

We piloted a 6-week, double-blind, split-site, randomized controlled trial on 14 patients with EB pruritus. In each patient, one pruritic lesion received topical gabapentin and the other a placebo. The items of the Leuven Itch Scale were evaluated before and after therapy; the lesions were photographed, and their appearance (i.e., erythema and excoriation severity, pruritic geometric area) was objectively assessed. Statistical analyses were made using SPSS v. 25. Quantitative data were reported as median (interquartile range) or mean ± standard deviation as appropriate.

Results:

The median age of the 14 patients was 18 years (12–37), and the majority (64.3%) were male. A signifi- cant improvement was seen in the geometric area of the pruritic lesion in the inter- vention group ($p = 0.005$) but not in the control group ($p = 0.054$). Erythema severity, excoriation intensity, pruritus frequency and duration, and symptom-related distress significantly improved in both groups ($p < 0.05$ in all cases), but topical gaba- pentin failed to offer any statistical superiority relative to the placebo in the between-group analysis ($p > 0.05$).

Conclusion:

This study showed no significant difference between topical gabapentin and placebo in erythema severity, excoriation intensity, pruritus frequency and duration, and symptom-related distress among EB patients. However, the lesion area decreased only in the gabapentin group.

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Abstract N°: 3620

Activation of mechanosensitive calcium channels improves the tight junctions of ATP2C1-/- HaCaT cells in Hailey Hailey Disease

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Introduction & Objectives:

Hailey Hailey Disease (HHD) is an autosomal dominant skin disease that occurs in the fold of the skin due to a single gene mutation of ATP2C1. Physical factors such as friction, scratching, and heat can significantly aggravate the disease, leading to achinolysis and disruption of cellular connections. Due to the inevitable mechanical stimulation of the fold site, the clinical treatment effect is not effective enough. However, the biological mechanism of mechanical exacerbation of disease and the treatment of mechanical receptors or signaling pathways have been rarely studied now. So we attempt to explore the effect of mechanical stress on the intercellular junction of HHD keratinocytes and explore the pathological mechanisms and possible mechanically-related therapeutic strategies.

Materials & Methods:

We performed controlled mechanical stretching of ATP2C1 knockout HaCaT cells to simulate in vivo mechanical stimulation. Then we observed and analyzed the destruction of tight junction proteins claudin1, claudin4, as well as the changes of mechanically activated ion channel proteins on cell membrane and intracellular calcium ion concentration. Finally, mechanical stimulation was given in the presence of ion channel agonists to observe the protective effect on keratinocytes junctions.

Results:

We reconstructed the pathological phenomenon of the destruction of HHD cell junction structure in vitro and found a correlation with the expression of mechanical channel proteins, we also verified the protective effect and possible mechanism of interference with mechanical pathways on the intercellular connections.

Conclusion:

The mechanism of mechanical stimulation aggravating HHD disease may be related to the downregulation of intracellular calcium influx caused by insufficient endogenous expression of mechanical ion channel proteins. The use of ion channel agonists may be a possible therapeutic scheme to restore intracellular calcium concentration under mechanical stimuls and relieve the damage of intercellular junctions.

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Abstract N°: 3872

Chronic pancreatitis and tropical sprue with cyclical pigment dilution of hair

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Introduction ** Hypomelanosis of skin and hair can occur due to genetic causes, endocrine disorders, nutritional disorders such as chronic protein deficiency, chronic malabsorption syndrome, vitamin B12 deficiency, copper and selenium deficiency. Acquired pigment dilution of skin and hair was seen in pancreatitic disease of tropics as reported by Klaus et al. We report a case of chronic pancreatitis and tropical sprue who presented with recurrent hypopigmentation of skin and hair.

Case report

A 27 year old man presented with slowly progressive dilution of pigment of hair and skin since 7 months. In addition he also complained of weight loss and gastrocolic reflex. He had developed similar episode 10 years ago wherein he also had ascites and second episode 7 years ago. He developed repigmentation following treatment. On examination, the patient was of average weight and build with diffuse hypopigmentation of hair and skin which was more marked over hands and feet. Investigations revealed normal B12, ferritin and iron levels with negative serology for HIV, HbSAg and HCV. His blood sugars, lipid profile, calcium, parathormone, thyroid function tests were normal. Hair root showed loss of pigment. His serum albumin was 2.5g/dl and stool showed fat globules. USG abdomen suggestive of chronic pancreatitis.

The common causes of chronic pancreatitis include alcohol abuse,Sjogren's syndrome,Renal tubular acidosis,common bile duct obstruction, and genetic mutations.There were no clinical features to suggest the above conditions. The ANA was negative and UGI scopy ruled out pancreatic duct obstruction and it revealed scalloped duodenal folds, biopsy of which showed areas of villous blunting with intraepithelial lymphocytosis. Lamina propria showed increased cellularity and focal Brunner gland extensions. Crypts also showed some intraepithelial lymphocytosis with nucleomegaly. The above features suggested the possibility of tropical sprue and celiac disease. However celiac disease was ruled out since IgA anti-tissue transglutaminase levels normal.

Thus SPINK1 (Serine protease inhibitor Kazal type 1) mutation assay using restriction fragment length polymorphisorm [PCR RFLP] was done and exon 3 of the SPINK gene was amplified which detected heterozygous mutation in the aminoacid sequence at 34th position wherein aminoacid N(Asparagine) was replaced by S(Serine) at exon 3. This confirmed the genetic mutation associated with pancreatitis.

The patient was treated with high protein, low fat diet made of medium chain triglycerides (coconut oil) based diet. He was advised pancreatic lipase supplements three times a day before meals and multivitamins. Following these, partial repigmentation of skin and hair was observed after 20 days followup.

Conclusion: ** The clinical,histological and genetic study confirmed our case. SPINK mutation activation trypsin leading to autodigestion of pancreas resulting in reduced pancreatic enzymes which will present as nutritional deficiency. Klaus et al reported acquired pigment dilution as a sign of pancreatic disease of tropics. DOPA staining, they demonstrated shortened dendrites and reduced production and transfer of pigment and opined that malabsorption induced nutritional deficiency results in diversion of patient's limited protein resources from melanogenesis.We present this case to highlight the dramatic changes in pigmentation observed in a case of genetically induced chronic pancreatitis due to SPINK1 mutation.

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Abstract N°: 3890

Cowden syndrome with diffuse sebaceous gland hyperplasia: an unusual presentation with delayed diagnosis.

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Introduction & Objectives: Cowden syndrome (CS) is an autosomal dominant entity encompassed within the PTEN hamartoma tumor syndrome, which involves a tumor suppressor gene located on chromosome 10q22-23. It is an inherited cancer predisposition syndrome characterized by macrocephaly and benign and malignant tumors of the breast, thyroid, endometrium, and kidney. However, the skin is the most frequently affected organ in CS, with the most common findings being multiple trichilemmomas, acral keratotic papules, and oral papillomas or mucocutaneous neuromas. The presence of diffuse sebaceous gland hyperplasia constitutes an exceptional phenotypic variant in CS and has been scarcely reported in the literature.

Materials & Methods: We present a case of CS in a 51-year-old woman exhibiting diffuse sebaceous gland hyperplasia. The identification of pathogenic PTEN variants was conducted through massive sequencing gene analysis using a blood sample. Pathological examination of two lesions suggestive of sebaceous hyperplasia was performed to confirm the clinical diagnosis. Additionally, a literature review was conducted to assess the current evidence on this subject.

Results: A 51-year-old female patient presented to the Dermatology clinic with numerous sebaceous gland hyperplasias located on the face, anterior cervical area, and both ears. The patient reported that these lesions had been present since early childhood and had been evaluated on multiple occasions previously without a specific clinical diagnosis. Upon reviewing the patient's medical history, we noted a history of luminal breast carcinoma, nodular thyroid hyperplasia, endometrial hyperplasia, and a thymic cyst. With a clinical suspicion of CS, genetic testing for PTEN gene mutations was performed, along with biopsies of two skin lesions suggestive of sebaceous hyperplasia. Subsequently, the pathogenic allelic variant C322_323del, p.Leu108Ter of the PTEN gene was identified, and the anatomopathological study confirmed the diagnosis of sebaceous gland hyperplasia in the biopsied skin lesions.

Conclusion: Diffuse sebaceous gland hyperplasia may represent a phenotypic variant extending beyond the classic cutaneous clinical forms observed in CS. A detailed clinical history is essential for accurate diagnosis within the spectrum of PTEN hamartoma tumor syndromes.

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Abstract N°: 4008

The burden of Netherton syndrome and the current treatment journey: A qualitative summary of interview responses from patients and their caregivers

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Introduction & Objectives:

Netherton syndrome (NS), a rare genetic condition present in 1:200,000 births,1,2 has lifelong consequences. Beyond its physical impacts on the skin, NS can also result in organ system involvement, immune-related conditions, recurrent infections, sleep disorders and failure to thrive.2,3 There are also substantial emotional burdens for patients and their caregivers. Despite this, current literature lacks comprehensive insights into the perspectives of affected individuals. Current therapies aim to reduce symptoms and preserve skin barrier function; however, there is a need for treatments that reduce symptom burden and improve quality of life (QoL). This study summarises the physical, social and emotional burdens, and the treatment journey associated with NS.

Materials & Methods:

Through a 60-minute web-based interview, patients and their caregivers from the US, Germany, France and China discussed their experiences with NS. These results are summarised.

Results:

Ten patients with NS and eight caregivers (mean patient age [including those under care]: 25.6 years; range 4–70 years) reported several NS-related symptoms affecting their daily QoL. The most commonly reported were itching (n=8), inflammation (n=5), dry skin, red skin and flares (n=4).

Respondents also reported a significant emotional burden associated with NS. At birth, caregivers reported feeling scared, helpless and stressed due to NS-associated financial and family challenges. Adolescents and adults with NS reported social and mental health issues, and challenges with intimate relationships and employment. Owing to a perceived lack of awareness by healthcare professionals (HCPs), respondents reported reaching out to social media for information and support.

The treatment journey for a patient with NS is long and complicated, with significant delays in diagnosis and largely ineffective treatments with potential side effects. Topical treatments were commonly reported (n=16); however, these provided short-term relief and were time-consuming to apply. Six respondents reported using biologics and were generally satisfied, observing improvements in symptoms compared with prior treatments*. Issues relating to self-injection (administration) and access (cost, funding and limited availability of a prescription from dermatologists) were generally accepted by the respondents due to their improved symptom control.

Fourteen respondents mentioned using non-prescribed, over-the-counter medications to alleviate symptoms. When asked if they were open to new treatments, many respondents indicated a willingness to try new treatments for longer symptom control whereas some were reluctant and required more information.

Conclusion:

According to patients and caregivers, there is a need for additional emotional support and increased awareness of NS amongst HCPs to facilitate earlier diagnosis and ongoing lifelong care. The unmet treatment needs highlight the urgency for the development of disease-modifying therapies that alleviate the burden of NS and enhance overall QoL.

*Efficacy can vary significantly between individuals. The long-term efficacy of biologics is unclear.

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Abstract N°: 4022

Palmoplantar keratoderma and anhidrotic ectodermal dysplasia: an unusual association

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Introduction & Objectives:

Rapp Hodgkin Syndrome (RHS) is a rare type of ectodermal dysplasia characterized by anhidrotic ectodermal dysplasia, cleft lip, and cleft palate. Other features have been described in literature, but palmoplantar keratoderma is an unusual manifestation. We report the case of a 15-year-old boy who presented with RHS associated with palmoplantar keratoderma.

Materials & Methods:

Results:

A 15-year-old boy with a two-year history of palmoplantar keratoderma was referred to our department. The patient was born from a second-degree consanguineous marriage and has a history of hair loss, heat intolerance, and reduced ability to sweat. He had also dental prostheses due to dental anomalies. A nephrectomy was performed, and a cleft palate was repaired in childhood. On examination, bilateral palmoplantar keratoderma with palmoplantar pits was noted. The patient presented with a thick, honey-coloured crust mainly on the palms, as well as facial dysmorphia, skin xerosis, alopecic scalp with few light-coloured hairs, and dystrophic nails. The patient’s eyebrows and eyelashes were also scarce. Based on the presence of sweating disorders, dental, hair and nail abnormalities, orofacial cleft and genitourinary abnormalities, the diagnosis of hypohidrotic ectodermal dysplasia type RHS was made. Skin biopsy showed hyperkeratosis, acanthosis and papillomatosis in the epidermis. The dermis was fibrotic with diffuse lymphocytic infiltrate. The lesions were initially treated with keratolytics, resulting in a good outcome, but recurred after 04 months.

Conclusion:

Palmoplantar keratoderma is mostly observed in patients with hidrotic ectodermal dysplasia as it could be caused by mutations in junction proteins leading to a reduced desquamation. however, this manifestation in uncommon in patients with anhidrotic ectodermal dysplasia and only a few cases are reported in literature. This could help in the clinical classification of patients.

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Abstract N°: 4174

Two cases of plantar fibromatosis associated with Dupuytren's disease

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Introduction & Objectives: Plantar fibromatosis also known as Ledderhose's disease and palmar fibromatosis or Dupuytren's disease are both rare and benign fibroblastic connective tissue proliferative disorders. These two conditions may coexist in some cases.**

Materials & Methods: Herein we report two cases of plantar fibromatosis associated with palmar fibromatosis.**

Results: Two brothers, aged 19 and 16 years old, born of a consanguineous marriage, were referred to our dermatology department for assessment of plantar lesions. Dermatological examination revealed painful nodules in the central, medial, and lateral plantar aponeurosis, with toe contracture. The size of the nodules ranged from 1 to 4 centimeters. Additionally, both patients exhibited finger contracture due to palmar fibromatosis. A comparable case was identified within the family. Magnetic resonance imaging was conducted, and the diagnosis of plantar fibromatosis was confirmed. Local steroid injections were performed in the nodules and the patients were referred to orthopedic surgery department.**

Conclusion: Plantar fibromatosis is a rare and benign hyperproliferative disorder of the plantar aponeurosis. It typically affects adults in their fourth or fifth decade, but exceptionally children. There may also be a familial inheritance pattern. Clinically, it is characterized by slow-growing nodules, which most commonly affect the central or medial bands of the plantar fascia. The diagnosis of plantar fibromatosis remains clinical, but ultrasound and magnetic resonance imaging are recommended, and biopsy can be performed to rule out malignant tumors. Although plantar fibromatosis is frequently seen as an isolated disease, an association with Dupuytren's disease has been noted in some patients. According to the literature, the prevalence of Ledderhose disease in patients with palmar fibromatosis varies between 3.7% and 19%. The presented cases of plantar fibromatosis have an uncommon presentation because of the occurrence at a young age, the involvement of the lateral part of the aponeurosis and the association with palmar fibromatosis. **

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Abstract N°: 4308

Congenital generalized hypertrichosis associated with juvenile gigantomastia: Association of two rare conditions

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Introduction & Objectives: Hypertrichosis refers to excessive hair growth in areas that are not primarily androgen-dependent. It may be localised or generalised, congenital or acquired. We report a family case of congenital generalized hypertrichosis (CGH) associated with juvenile gigantomastia

Materials & Methods: A 22-year-old woman, born to consanguineous parents, with a family history of CGH associated with gigantomastia (affecting her sister, aunts and cousins on her father's side). She was born with CGH, which worsened with age, forcing her to interrupt her education. At the age of 12, she developed bilateral asymmetric gigantomastia extending to the umbilical region. She subsequently underwent reduction mammoplasty, accompanied by postoperative Tamoxifen treatment. An anatomopathological study of the surgical specimen showed bilateral adenofibromas with florid adenosis on gigantomastia. In view of the recurrence of the gigantomastia, a second mammoplasty was performed at the age of 21, combined with spironolactone, but without improvement.Clinical examination showed a BMI of 22.35 kg/cm2 , and diffuse hypertrichosis consisting of long, thick pigmented terminal hairs, sparing the hands and feet. A coarse face with bushy, dark eyebrows, a broad and thickened lips. Axillary and pubic appeared normal. Both breasts were large, pendulous and asymmetrical. The external genitalia appeared normal. There were no obvious signs of virilisation. Endocrine tests (Cortisol, Prolactin, Testosterone, LH-FSH, OEstradiol and TSH) were normal. Pelvic ultrasound showed a solid latero-uterine nodule. Pelvic MRI is in progress.

Results: CGH is a rare entity. It is most often idiopathic, linked to excessive stimulation of hair follicles with normal androgen levels. Clinical diagnosis is common, but a thorough physical examination is essential to identify potential extra-cutaneous abnormalities, obesity or intellectual disability. Depending on the clinical symptoms, biological tests, bone X-rays, brain MRI, EEG, ECG and psychometric tests may be useful .Juvenile gigantomastia is also a rare condition and its association with several disorders such as liver failure, psychomotor retardation, ataxia, myasthenia gravis, and D-penicillamine treatment, has been reported .However, our patient had none of these associations.Two cases of association of CGH with gigantomastia have been reported in the literature, associated with gingival hypertrophy and cardiomyopathy. This was not the case in our patient.The need for CGH treatment depends on the patient's age, the location and the degree of hypertrichosis as well as the psychosocial impact. Various methods are recommended, including shaving (conventional/electrical), hair removal, electrolysis and laser hair removal. In our patient's case, laser sessions were chosen.

Conclusion: The combination of CGH and gigantomastia is rare. Its socio-psychological impact encourages a better understanding of its pathogenesis and the development of pharmacological treatments aimed at making these anomalies less disabling.

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Abstract N°: 4391

Dyschromatosis symmetrica hereditaria: a case report

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Introduction: Hyperpigmentation disorders are due to increased melanin synthesis and sometimes to an increase in the number of melanocytes. Reticulated pattern hyperpigmentation disorders are rare. It is essential to review the family history and a thorough physical examination for associated abnormalities. They are characterized by hyperpigmented macules that may or may not be associated with hypopigmentation. Each entity has a specific phenotype and different prognosis. Sometimes they overlap and it is difficult to distinguish among them. Reason why, we rely on genetics.

Clinical history: We present a 24-year-old woman from Peru, under follow-up digital dermoscopy for a phenotype compatible with xeroderma pigmentosum (XP). She developed dyschromatosis on her hands from the age of four. Her father, aunt and paternal grandfather also suffer from this condition. On physical examination she presented hyper- and hypopigmented macules on the dorsum of both hands extending to the limbs. XP is an autosomal recessive disorder caused by an alteration in the repair of DNA damage. Affected individuals present extreme photosensitivity with a high risk of developing skin cancer. The family history suggests a dominant inheritance pattern and the fact that none of the affected individuals have presented malignant cutaneous neoplasms casts doubt on the diagnosis of XP. The differential diagnosis with several genodermatoses was raised; among them, reticulated acropigmentation of Kitamura (ARK), hereditary universal dyschromatosis (HUD) and hereditary symmetrical dyschromatosis (HSD). The diagnosis of HSD was established; an autosomal dominant inherited entity caused by mutations in ADAR1, characterized by hyper- and hypopigmented macules on the dorsum of distal extremities. The diagnosis is clinical, although it is based on the study of the mutations described in blood. Two genetic tests were performed in blood that included different genes; among them ADAR1, ADAM10, SASH1 and ABCB6, but the patient did not show pathogenic changes in the studied sequences. However, these studies do not allow us to confirm or rule out the clinical diagnosis.

Discussion: DSH is a genodermatosis of autosomal dominant inheritance with almost complete penetrance, due to mutations in ADAR1, a gene involved in the NOTCH signaling pathway. It appears in childhood with the appearance of hyper- and hypopigmented macules on the dorsum of the hands and feet. Diagnosis is clinical and based on genetics. Current treatments do not provide satisfactory results. It is essential to avoid sun exposure to reduce the contrast between lesions and genetic counseling is recommended.

Conclusion: We present a case of DSH, an infrequent pathology included in the reticulated hyperpigmentation disorders. Its diagnosis is clinical although it relies on genetics. More than 200 different ADAR1 mutations have been described in patients with DSH worldwide, so even if the genetic study is negative, the diagnosis cannot be ruled out.

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Abstract N°: 4416

Extra-cutaneous manifestations of H syndrome : About 9 cases

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Introduction & Objectives:

The H syndrome (HS) is a rare autosomal recessive genodermatosis caused by mutations in the SLC29A3 gene. It is often associated with systemic involvement. The aim of this study is to determine the extra-cutaneous manifestations of HS.

Materials & Methods:

We conducted a descriptive retrospective study of all patients diagnosed with HS in our department.

Results:

Nine patients (7F/2M) were included, among whom 7 had consanguineous parents and 2 had a family history of similar symptoms. The mean age at symptom onset was 11.1 years.

Clinical examination revealed hepatomegaly (n=2), splenomegaly, and inguinal lymphadenopathy in one patient each, hallux valgus, camptodactyly, and gerontoxon in 5 patients each; and subcutaneous tissue infiltration in 3 patients.

Hypoacusis was diagnosed in 5 patients.

One patient was diagnosed with retroperitoneal fibrosis with renal insufficiency, treated with corticosteroids leading to improvement.

One patient presented with azoospermia and unilateral grade 3 varicocele.

One patient had deep vein thrombosis.

The mean CRP level was 92 mg/l, and the erythrocyte sedimentation rate (ESR) was 98 mm/h. Biological signs of hypogonadism were observed in 5 patients. Only 3 cases showed elevated ANA titers. Echocardiography revealed pericardial effusion (n=2), ventricular wall hypertrophy (n=1), and tricuspid regurgitation (n=2). A homozygous mutation in the SLC29A3 gene, c.1088G>A (p.Arg363Gln) in exon 6, was found in 3 families, and c.971C>T (p.P324L) in exon 6 in 2 families. One patient was a compound heterozygote for both mutations. Three families are undergoing further investigation.

Conclusion:

HS is a rare genodermatosis primarily affecting consanguineous Arab families. The H syndrome presents with phenotypic diversity, characterized by distinctive cutaneous manifestations, including bilateral hyperpigmentation, hypertrichosis, and sclerosis. The frequent and varied extracutaneous manifestations emphasize the importance of recognizing these signs to prevent diagnostic errors. Our results are consistent with the literature, highlighting the predominance of osteoarticular manifestations (camptodactyly, hallux valgus) and auditory manifestations (hearing loss) in the diagnosis of HS, especially in the presence of subtle cutaneous signs. Growth delay,

hypogonadism associated with azoospermia, ophthalmological, and cardiac manifestations further support suspicion of HS, corroborating our observations. The retroperitoneal fibrosis observed in one of our patients has been reported only once in the literature. The mutation c.1088G>A (p.Arg363Gln) is a “founder” mutation in the Tunisian population.

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Abstract N°: 4533

Pediatric Pseudoxanthoma Elasticum: A Case Study of Siblings

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Introduction & Objectives: Pseudoxanthoma elasticum (PXE) is a rare hereditary disorder characterized by the progressive mineralization and fragmentation of elastic fibers in various tissues, including the skin, eyes, and cardiovascular system. While PXE primarily manifests in adulthood, its occurrence in pediatric populations, especially within families, presents unique diagnostic and management challenges. This case study delves into the clinical presentation, diagnostic and therapeutic considerations of PXE in two sisters. We aim to shed light on the complexities of managing PXE in pediatric patients, emphasizing the importance of early detection and multidisciplinary care in optimizing outcomes for affected families.

Materials & Methods: This case study followed two sisters diagnosed with pseudoxanthoma elasticum (PXE) through their clinical journey at a tertiary care dermatology clinic. Detailed clinical histories, including family history, presenting symptoms, and previous medical evaluations, were obtained. Physical examinations focused on cutaneous manifestations, ophthalmological assessments, and cardiovascular evaluations as indicated. Diagnostic investigations included skin biopsies with histopathological findings. Imaging studies such as ultrasound and echocardiography were performed to assess vascular involvement. Multidisciplinary consultations with ophthalmologists were integral to the management process. Treatment strategies, including topical therapies and lifestyle modifications, were tailored to individual patient needs and disease severity.

Results: The two sisters, aged 10 and 14 years, presented with cutaneous manifestations suggestive of pseudoxanthoma elasticum (PXE). The older sister first exhibited lesions on her neck, inguinal, and axillary regions over four years ago, while the younger sister developed similar lesions only one month prior, localized solely on her neck. Ophthalmological examination revealed no abnormalities in either sister, with both showing normal findings on fundoscopic examination and an absence of angioid streaks. Physical examination and histopathological analysis of skin biopsies confirmed the diagnosis of PXE, evident from the presence of calcification and fragmentation of elastic fibers. Cardiovascular evaluation showed no significant abnormalities. Management strategies included the use of topical emollients, sun protection measures, and regular dermatological follow-up for monitoring cutaneous findings. Genetic testing was not performed due to the characteristic clinical and histological features of PXE.

Conclusion: This case underscores the importance of considering pseudoxanthoma elasticum (PXE) even in the absence of typical ophthalmological signs, especially in familial cases with characteristic cutaneous findings. Early diagnosis and multidisciplinary management are essential for optimizing care in pediatric patients. Longitudinal follow-up is crucial for monitoring disease progression and guiding therapeutic interventions and genetic counseling.

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Abstract N°: 4699

KLK11 associated erythrokeratoderma in German patient

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Introduction & Objectives:

Genetic disorders of keratinization comprise a broad spectrum of phenotypes. The objective of this study was to determine genetic basis of the erythrokeratodermic phenotype in a German patient.

Materials & Methods:

Clinical evaluation of the patient over the period of six years and whole exome sequencing were performed. Laboratory diagnostics included whole blood count, IgE and routine biochemistry. Histopathology and immunohistochemistry were performed with standard methods.

Results:

We present a case of a 47 years-old women with cutaneous manifestations including generalized skin dryness, scaling, erythema, palmoplantar keratosis and mild ectropium. These features were present at birth and persisted throughout life. There were no affected family members, and the parents were not related.

During the observation period of 6 years, erythroderma and skin thickening dominated the clinical presentation, with islands of normal appearing skin, never reaching more than 2-3% of the body surface area. Palmoplantar keratoderma was diffuse. There were no hair or nail anomalies, or other extracutaneous features. The main symptoms impairing quality of life were reduced ability to sweat and intense pruritus, reaching peaks of 10/10 on a numeric rating scale.

Laboratory investigation were in normal range except of slightly elevated IgE levels (128 KU/L, normal <100). Histopathology demonstrated acanthosis, alternating hyper- and parakeratosis, papillomatosis and an inflammatory infiltrate with lymphocytes, histiocytes and single eosinophils. Follicular plugging suggested retention hyperkeratosis. The number of sweat glands was reduced. Furthermore, there was prominent fillagrin and Lekti-expression in the upper epidermal layers, including stratum corneum.

Previous repeated genetic testing had excluded any pathogenic variants in genes associated with disorders of keratinization, which was very frustrating for the patient. When the association between monoallelic *KLK11* pathogenic variants and an “autosomal-dominant cornification disorder” was published, genetic results were reanalyzed and the *KLK11* p.Gly50Glu variant was identified in our patient. This kallikrein 11 amino acid substitution is associated with the clinical picture of erythrokeratoderma in our patient and was described previously in four patients originating from Asia.

The therapy targeting type 2 inflammation with an IL4/IL13-inhibitor was initiated, but did not influence the pruritus or the cutaneous condition of our patient. Therefore, the treatment was changed to acitretin that had already shown some benefit in the past, as reported by the patient.

Conclusion:

To the best of our knowledge, this report describes the first non-Asian patient with the above-mentioned

mutation in kallikrein 11 and adds to the definition of the phenotype of this new disorder of keratinization. The pathomechanism of itch in this disorder requires further investigation.

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Abstract N°: 4724

Efficiency of Doxycycline in Hailey-Hailey Disease

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Introduction & Objectives:

Hailey–Hailey disease (HHD), or familial benign chronic pemphigus, is a rare blistering dermatosis characterized by recurrent vesicular and erosive lesions involving intertriginous areas. It is an autosomal dominant genodermatosis caused by a mutation of the ATP2C1 gene. Although multiple therapeutic option were reported, management remains challenging. We report the case of HHD in a woman treated by doxycycline with spectacular response.

Materials & Methods:

A 22 years old woman, presented with a 3-year history of erythematous, erosive and fissured lesions located in the inguino-crural, intergluteal and axillary areas which evolved in flare-ups. Skin biopsy revealed intra-epidermal clefting with acantholysis. Direct immunofluorescence was negative. The diagnosis of Hailey-Hailey disease was made. Furthermore, she presented vulvar fibroids resembling to giant pendulum molluscum confirmed by histopathological examination. The patient had been treated with topical corticosteroids with limited response. After a review of therapeutic options with the patient, she accepted to take doxycycline 100 mg/day for 3 months. At the end of treatment, spectacular improvement was noted with disappearance of erythematous plaques and complete healing of the linear fissures. Doxycycline was continued at the same dosage without relapse after 13 months. Regarding her vulvar fibroids, she is scheduled for surgical excision.

Results:

HHD tends to have a chronic relapsing course and recalcitrant to treatment. However, multiple treatments showed some success in case reports and series such topical corticosteroids, dapsone, cyclosporine, methotrexate, photodynamic therapy, botulinum toxin, lasers. Several case reports have shown the effectiveness of doxycycline at a daily dose of 100 mg for at least 3 months, and therefore confirmed its value as monotherapy or in combination (e.g vitamin PP) in HHD. Besides their antibiotic potential, cyclines also have anti-inflammatory properties (through inhibition of leucocyte chemotaxis and activation, and regulation of inflammatory cytokines in keratinocytes) and anti-collagenase activity via inhibition of matrix metalloproteinases, which are normally up-regulated in the event of dermal destruction. Matrix Metalloproteinase 9 and its inhibitor, Tissue Inhibitor of Metalloproteinase 1, have been shown to be involved in HHD. Nevertheless, pathophysiological rationale for cyclines in HHD remains to be determined. Our patient responded spectacularly to doxycycline after 3 months and the effectiveness was maintained throughout a long period. Relapses are sometimes reported when treatment is stopped. However, remission is observed upon resumption of treatment.

Conclusion:

Hailey-Hailey disease is a rare genodermatosis with challenging management. Doxycycline appears to be an interesting therapeutic option, especially since it is inexpensive, well tolerated and easy to manage in routine practice. Large series studies are necessary to evaluate its effectiveness and define precise therapeutic modalities.

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Abstract N°: 4785

Inherited palmar filiform hyperkeratosis: A case report

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Inherited palmar filiform hyperkeratosis: A case report

Introduction & Objectives:

Filiform keratoderma is an uncommon dermatosis consisting of multiple projections located on the palms and soles, with the distinct histopathological feature of a parakeratotic column above a hypogranular epidermis. This entity has been reported under several different names, such as porokeratotic punctate keratoderma, punctate keratoderma, palmar filiform hyperkeratosis and spiny keratoderma of the palms and soles. Most of the cases described are acquired, although there are also familial cases. As this condition is under-diagnosed and under-reported, it is important for dermatologists to keep keratoderma spinosum of the palms and soles in mind. We present a family case of filiform keratoderma and review the literature.

Materials & Methods:

This is a case report of a 70-year-old woman who presented in our department with multiple small hyperkeratotic spicules on the palms and soles.

Results:

The asymptomatic spicules had appeared since a young age. She mentions a similar appearance in her father and sister. She has no respiratory or digestive symptoms consistent with lung or colorectal carcinoma.

She does not smoke. She has not been exposed to arsenic, has not consumed well water and has no other dermatological history. Physical examination revealed multiple, firm, hyperkeratotic, millimetric spicules on the thenar and hypothenar regions, bilaterally on the fingertips and more diffusely on the soles of the feet. The lesions had not been previously treated. The rest of the physical examination was unremarkable. A diagnosis of hereditary filiform palmoplantar keratoderma was made, given the family history and the early age of onset of the lesions. The patient was treated with 10% salicylated Vaseline in occlusion, with moderate improvement.

The hereditary form is autosomal dominant and develops between the ages of 12 and 50. It has no known association with internal malignancies. The acquired form occurs after the age of 50 and, in some cases, has been associated with underlying neoplasia (breast cancer, colorectal cancer, kidney cancer) or systemic diseases such as type IV hyperlipoproteinemia, Darier's disease, asthma, chronic renal failure, myelofibrosis and polycystic kidney disease with hepatic cysts.

There is no clearly established treatment for spiny keratoderma. It has been described as difficult and unsatisfactory. However, there have been recent reports of success with topical tacalcitol 0.002% , 5-fluorouracil 5% , a combination of topical tacalcitol 0.002% and 5-fluorouracil 5% , ammonium lactate 12% , salicylic acid , or retinoids . Mechanical debridement methods, such as dermabrasion or shaving of spicules with a razor blade, have also been documented

Conclusion:

To our knowledge, only a small number of cases of filiform keratoderma of the palms and soles have been reported. This may be explained by the fact that patients do not consult us for keratoderma filiformis because most cases are asymptomatic or cause only minimal discomfort.

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Abstract N°: 4814

Identification of a Novel Missense Variant in DSG1 Associated with Hereditary Striate Palmoplantar Keratoderma Type 1

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Introduction & Objectives:

Hereditary palmoplantar keratodermas (PPK) represent a diverse group of keratinization disorders characterized by thickened skin on the palms and soles, exhibiting both phenotypic and genetic heterogeneity. Among them, Striate PPK (SPPK) is distinguished by linear hyperkeratosis on the palms and fingers, often accompanied by focal plantar keratoderma. Typically, SPPK follows an autosomal dominant inheritance pattern. Mutations in the DSG1 gene, encoding desmoglein 1, are the most common cause of SPPK, though mutations in DSP or KRT1, which encode desmoplakin and keratin 1 respectively, are rare alternate causes. This genetic diversity further categorizes SPPK into types 1, 2, and 3, corresponding to the specific genes affected.

Materials & Methods:

We present a patient with clinically and genetically diagnosed autosomal dominant SPPK 1 with missense variant in DSG1 that has not been previously documented in the literature.

Results:

A 24-year-old male, otherwise healthy, presented to our Dermatovenerology department with a lifelong history of persistent thickening of the palms and soles, accompanied by palmoplantar hyperhidrosis and limited finger mobility. Notably, his father and paternal grandmother also experienced similar symptoms, yet genetic testing had not been pursued until this presentation. The patient had managed his thickened soles with mechanical debridement. Clinical examination revealed striate hyperkeratosis on the palms and focal hyperkeratosis on the soles, primarily localized to pressure areas. Histopathological examination demonstrated epidermal acanthosis with a prominent granular layer and distinct hyperorthokeratosis, consistent with the clinical diagnosis of keratoderma. Molecular genetic analysis unveiled a heterozygous variant, NM_001942.4:c.788A>G, p.(Asn263Ser), in the DSG1 gene, not previously reported in the literature, thus representing an uncertain significance for autosomal dominant SPPK 1. However, given the typical clinical presentation of palmoplantar keratoderma and the identification of a novel mutation in the DSG1 gene, the diagnosis of hereditary SPPK 1 is strongly suggested.

Conclusion:

Desmoglein 1 is a crucial protein component of intercellular desmosome junctions within the epidermis, where it plays a vital role in preserving tissue integrity through its adhesive properties. Consequently, mutations in the DSG1 gene can result in impaired epidermal cell adhesion, leading to compromised structural stability within the skin. Up to date more than 25 mutations in DSG1 have been reported. However, our case report is suggestive of a novel missense variant in DSG1 that hasn’t been previously documented in association with SPPK 1. Further research is needed to confirm its impact and prevalence. This discovery could enhance our understanding of SPPK genetics, aiding in better diagnosis and treatment.

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Abstract N°: 4815

giant plexiform neurofibroma in Von Recklinghausen disease

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Introduction & Objectives:

Plexiform neurofibromas are pathognomonic of NF1. They are usually slow-growing tumors [1]. Their symptomatology is variable depending on their topography. We report the case of a 23-year-old man with a giant gluteal mass.

Clinical case:

it is a 21 years old young man, without pathological history, who consulted for left gluteal mass, progressing for 3 months. The clinical examination revealed a mass in the left gluteal region, with a soft, painless consistency, and without inflammatory signs, measuring 60 *100 cm. Skin examination showed multiple cafe-au-lait spots on the back and limbs (more than 5) associated with lentigines in the axillary fold. Given these clinical features, the diagnosis of neurofibromatosis type 1 was retained, and an MRI was performed, revealing the presence of a lesional process of the thigh and the left gluteal and lumbar regions, with homolateral perineal infiltration along the ischio pubic branch with bone erosion opposite. The anatomo-pathology of the mass showed an aspect of plexiform neurofibroma. In view of this clinical, histological and radiological findings, the diagnosis of a royal tumor of von Recklinghausen's disease was retained, and the patient was referred to plastic surgery for surgery. the intervention consisted of continuous sectioning with an electric scalpel, removing the tumour in a single block,continuous and step-by-step haemostasis with the electric scalpel, followed by lavage and verification of skin closure, and finally dressing, bandaging and fixation.

Discussion:

Neurofibromatosis type 1 (NF1) is an autosomal dominant genetic syndrome caused by mutations in genes coding for neurofibromin. It is one of the most common human genetic diseases [2].

The plexiform neurofibroma is a rare benign tumor of the peripheral nerves. Its non-encapsulated character explains its infiltrating power. Giant neurofibroma is a poorly defined term used to describe a neurofibroma that has grown to a significant but undefined size. There are a number of case reports and series found in the literature discussing giant neurofibromas.

Imaging is of great help in the diagnosis, allowing to characterize the lesions and to search for possible associated lesions, to evaluate the prognosis and to do a follow-up.

PNFs are difficult to manage surgically as they are extensively infiltrative, highly vascularized and tend to recur. Surgical treatment must be decided judiciously and individualized for each patient. The risk of sarcomatous degeneration justifies, whenever technically possible, the removal of the lesion as completely as possible. And clinical and radiological monitoring of these patients, at least annually until the age of ten, and then regularly, in order to evaluate a possible recurrence or malignant transformation [5].

Conclusion:

The giant plexiform neurofibroma of neurofibromatosis type 1, is a very rare manifestation of the disease, requiring a well codified management in order to not miss a malignant transformation.

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Abstract N°: 4829

Promising, but whether almighty? - Botulinum toxin in Hailey-Hailey disease – systematic review

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Introduction & Objectives:

Hailey-Hailey disease, known as familial benign chronic pemphigus, was first described in 1939 by the brothers Howard and Hugh Hailey. It is a rare blistering genodermatosis with autosomal dominant inheritance. Hailey-Hailey usually results from a mutation of the ATP2C1 gene which encodes a calcium- dependent ATPase (hSPCA1). While the hSPCA1 function is to regulate calcium sequestration in the Golgi apparatus, the mutation leads to impaired desmosome function, causing acantholysis of the suprabasal epidermis in the skin. The classic clinical manifestations include vesicles, erosions, fissures, weeping plaques and scales crust symmetrically distributed in intertriginous areas, with the most common areas being the axillae, groin, neck, subpectoral folds and perineum. Symptoms are often aggravated by sweat, heat, clothing friction and minor trauma. Therapeutic options continue to be limited with the antiseptics and topical corticosteroids considered the mainstay of therapy. Additional treatment options include ablative surgical interventions such as dermabrasion and CO2 laser surgery. As sweat is among the exacerbating factors of skin lesions in HHD, treatment with intradermal injections of botulinum toxin is developing into another therapeutic option.

Materials & Methods:

We performed review of literature in EMBASE and MEDLINE databases, including keywords such as “Hailey-Hailey disease”, “pemphigus”, “botulin toxin”. The searching was as broad as possible, including EMTREE and MESH approaches, conducted according to the PRISMA guidelines. The following inclusion criteria were applied: original trials, case reports, case series, with or without any concomitant reported treatment methods, published in English from the database inception until April 2024. 27 results were identified and given further analysis with additional manual research. 18 articles were included in the final analysis.

Results: ### Eighteen articles involving 46 patients described the use of botulinum toxin in HHD. Most patients achieved significant improvement and partial or complete remission of skin symptoms after injection or re-injection of botulinum toxin. Only two patients showed no improvement in target lesions. A combination treatment of botulinum toxin injection with photodynamic therapy and dapsone was also described, which allowed the patient to achieve a clear and definitive improvement better in areas treated with both PDT and BTXA compared to a control area treated with BTXA alone. No side effects were observed.

Conclusion:

Botulinum toxin appears to be a promising but not omnipotent therapeutic alternative in HHD, both as a complementary treatment and as an adjuvant to other forms of therapy, such as PDT. Larger studies are required to confirm its efficacy, long-term effects and also to establish the optimal doses and number of botulinum toxin injections resulting in a standardized treatment regimen.

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Abstract N°: 4832

Unilateral Zosteriform Segmental Darier's Disease, Exacerbated During Influenza: A Case Report and Discussion based on Pathohistological and Dermatoscopic Examinations

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Introduction & Objectives:

Darier's disease is a rare genetic skin disorder with an autosomal dominant type of inheritance. The prevalence of the disease ranges from 1 in 50000 to 1 in 10000. Unilateral zosteriform distributed Darier's disease (DD) is an uncommon form of DD and accounts for 10% of the total number of cases with DD. There have been approximately 40 cases of this form of the disease described so far. Differential diagnosis is complicated and should be carried out with other skin diseases with a zosteriform type of spread.

50-year-old women patient complained about itchy linear spreaded macular-papular rashes in the left supra- and inframammary region, left abdominal part and left groin region. Elements are represented by clearly delineated not merging hyperpigmentary macules ~0.5-1 cm, as well as hyperpigmentary hyperkeratotic papules. In inguinal area rash was on erythematous background and there were also maceration foci.

Rashes existed for more than 30 years. Patient noted exacerbation and spread during influenza, earlier she was diagnosed clinically and laboratory as Herpes Zoster, and according to patient's words, when taking antiviral drugs (Acyclovir) there was a softening of symptoms, but rash was not regressed.

In general, the oral cavity and nails are not affected, and the family history is not degraded by skin diseases. General laboratory indices are within normal limits. Yeast of Candida were identified from groins SWAB.

Materials & Methods:

The patient was diagnosed as segmental form of DD based on clinical, dermatoscopic and pathohistological examinations.

Results:

A dermatoscopic analysis of the rashes was done. Dermatoscopically polygonal, rounded, yellow-brown formations surrounded by thin white ring were revealed. General background hyperemic. There were also dark brown dots and globules, white-yellow keratotic accumulations, as well as point and linearly twisted vascular structures. Yellow-white squamas were also found.

Pathological changes are represented by formation of suprabasal cavities and fissure-shaped spaces in the epidermis, expressed signs of hyper-, ortho-, parakeratosis, as well as formation of local dyskeratotic epidermocytes. Vascular lymphocytic infiltration in upper dermal layer. Suprabasal cavities are filled with blood, cavity walls are formed by rounded epidermocytes.

Conclusion:

The localized pattern was first reported by Kreibich in 1906. Since that time, two main forms of zosteriform segmentar DD have been identified. The first type results from genetic mosaicism due to postzygotic mutations and is characterized by unilateral distribution along Blashko's lines. In the type II segmental variant, there is

generalized DD with a linear form of distribution. Type II mosaicism occurs in patients with heterozygous germline mutations who also have somatic loss of heterozygosity of the wild-type allele in a segmental area, leading to homo- or hemizygosity and therefore increased severity in a linear array.

Patients with DD disease are more susceptible to skin bacterial and viral infections, particularly herpes simplex virus, papillomavirus and poxvirus infections.

In such cases, differential diagnosis of the disease is very complicated, as the absence of typical clinical manifestations of DD, negative family history, unusual spread of rashes. Patohistological results may coincide in case of DD and AVEN, sotheuse of dermatoscopy may be very effective in DDx of skin diseases.

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Abstract N°: 4867

Hereditary palmoplantar punctate keratoderma: 3 affected generations

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Case report

Introduction & Objectives:

Keratoderma palmoplantar punctate type I or Buschke-Fisher-Brauer is a genodermatosis with an autosomal dominant inheritance pattern. The objective of this work is to present a case of this rare disease.

Materials & Methods:

A 61-year-old female patient with no relevant history was consulted for a localized dermatosis on palms and soles of 30 years of evolution. The palmar lesions were painful when lifting heavy objects or exerting pressure on them. She reported that her mother and daughter had similar lesions in the same location. Her mother started at the age of 25 years, and her daughter at the age of 28 years.

Physical examination revealed multiple millimetric pointed keratotic bumps on the palms which were rough to the touch. On the soles, there were keratotic papules with central depression.

A punch biopsy was performed, completely covering one of the palmar lesions. An area of depressed epidermis covered by a hyperkeratotic plug, orthokeratosis and discrete acanthosis with absence of cornoid lamella was observed.

A laboratory, chest X-ray, abdominal ultrasound, mammography, cervicovaginal cytology, and colonoscopy were performed. The examinations were unremarkable.

Results (discussion):

Based on clinical findings, histopathology, and family history, keratoderma palmoplantaris punctata type I was diagnosed.

Treatment was indicated with 40% urea in occlusive emulsion, topical tretinoin 0.05% in the affected areas and emollience.

In three months, the patient evolved with significant improvement of the condition.

This disease has an autosomal dominant inheritance pattern; however, sporadic cases can also be found. The onset of the process is usually in adolescence or after the age of 20.

Regarding its pathophysiology, mutations in the AAGAB gene have recently been identified. This gene encodes the p34 protein; its deficiency causes an increase in the half-life of tyrosine kinase receptors in basal keratinocytes, leading to hyperproliferation and hyperkeratosis. It has also been linked to mutation of the COL14A1 gene.

This entity has been described in association with Darier disease, nail dystrophies, atopy, neoplasms, among others.

Small filiform keratotic bumps on the palms and soles characterize its clinical presentation. Sometimes, the

keratotic centre is eliminated, leaving a central depression. Generally, it is asymptomatic, but it can be painful under pressure or when performing manual labour.

Histologically, it presents compact columns of orthokeratotic hyperkeratosis and hypergranulosis over a well-defined area without cornoid lamellae or parakeratosis, which allows it to be differentiated from porokeratosis punctate palmoplantaris.

As it is an infrequent disease, there are no guidelines for its treatment. Topical keratolytics such as urea, salicylic acid, and topical or systemic retinoids are used with variable results.

Although it is not currently considered a paraneoplastic syndrome, screening for neoplasms is recommended.

Conclusion:

The case's interest lies in presenting a rare genodermatosis and emphasizing the importance of inquiring about the hereditary-familial antecedents. As some cases are related to neoplasias, it is essential to know this entity and to request the pertinent complementary studies.

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Abstract N°: 5024

GOLTZ SYNDROME: A case report

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Introduction:

Goltz syndrome or focal dermal hypoplasia (FDH) is a rare X-linked disorder characterized by thinning of the dermis leading to atrophic Blaschko-linear plaques, fatty hernias and raspberry-like papillomas. This syndrome is also associated with various skeletal, ocular, dental and neurological defects. (3) (5)(6)(8).

We report the case of a 01-year-old girl with Goltz syndrome.

Case report section:

A 01-year-old female child, born at term to non-consanguineous parents, presented from birth with cutaneous and subcutaneous aplasia on the right flank, allowing direct visualization of the liver through the aplasia, hypopigmented atrophic plaques with blaschko-linear patterns, located on the trunk and extremities; multiple flesh-coloured soft nodules distributed along Blaschko's lines on the right lower limb, and a raspberry papilloma under the lower lip.

The child has distinctive facies, with right-sided facial hypoplasia, a broad nasal bridge, a notch in the right nasal wing, and asymmetrical, low-set, protruding ears. The examination also revealed syndactyly on both feet and the right hand, clinodactyly on the left hand and a coccygeal dermal sinus, a left papillary coloboma, bilateral microphthalmia, ptosis, right optic nerve atrophy and agenesis of the corpus callosum.

Discussion:

Focal dermal hypoplasia is a very rare X-linked genodermatosis (1) due to a mutation in the PORCN gene (1)(8).

Characteristic skin involvement is mainly manifested by atrophic Blascko-linear plaques (2)(4). Telangiectasias (3)(6), periorificial raspberry papillomas (2)(4)(2)(6) and fatty hernia manifesting as soft pinkish-yellow to brown nodules (2)(5).

Our little patient presented with all the cutaneous manifestations described above.

Skeletal anomalies are common (7) (12) (our patient presents with syndactyly and clinodactyly).

The presence of a dermal sinus above the sacral region in our little girl remains unusual, having been observed in only one patient in the series by Sudip Kumar Ghosh et al (11).

Ocular involvement is mainly manifested by chorioretinal coloboma and microphthalmia (11). Our patient presented with a coloboma of the right eye, bilateral microphthalmia, ptosis and optic nerve atrophy.

Patients often present with a distinctive facies, including a broad nasal tip and narrow nasal bridge, notched nasal wings, low-set thin ears, often asymmetrical (as observed in our patient). Slight facial hemi hypertrophy (left hemi hypertrophy in our patient).

Reported neurological manifestations include myelomeningocele, Arnold-Chiari malformation, hydrocephalus (11) and agenesis of the corpus callosum (11)(12) (as observed in our patient).

-The particular clinical presentation of Goltz syndrome generally allows the diagnosis to be established, even in the absence of genetic analysis (7), which was the case for our little patient, and Bostwick et al. have proposed criteria for establishing the diagnosis (11). Our patient presented with three typical skin features and two bone anomalies

Conclusion:

Our patient's case highlights the multiple facets of GOLTZ syndrome. Comprehensive management, including targeted surgical interventions and regular follow-up, is essential to optimize quality of life for these patients.

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Abstract N°: 5073

Rare association of sturge weber and klippel trenauney syndrome in a 12-year-old child

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Introduction:

Sturge Weber (SW) syndrome, or encephalo-trijeminal angiomatosis, is a rare congenital neuro-oculo-cutaneous syndrome associating a facial plane angioma located in the territory of the trigeminal nerve,

ipsilateral leptomeningeal angioma, glaucoma, early-onset epileptic seizures, sometimes with neurodevelopmental delay (1).

Klippel-Trenaunay syndrome (KTS) is defined by the triad of planar angioma, bone and/or soft tissue hypertrophy and varicose veins or venous malformations (1).

These two syndromes are rarely associated, but we report the case of a 12-year-old child presenting with both Sturge-Weber and Klippel-Trenaunay syndromes.

observation:

Child B.K, aged 12, from a non-consanguineous marriage, with a history of epilepsy since the age of 03 and mental retardation, was brought to the clinic with a clinical picture consisting of

angiomatous plaques, the first of purplish color occupying the entire left hemiface, the second of pinkish color occupying the scapula and the left upper limb, with bluish varicose veins in the peri

bluish varicose veins in the left periclavicular region. Right hemiparesis was also present.

-Cerebral CT showed left cortical atrophy, and MRI showed leptomeningeal angioma, left hemispheric atrophy and optic nerve atrophy, resulting in blindness of the left eye.

Ophthalmological examination revealed a secondary tumoral glaucoma on the left eye.

This clinical picture, supplemented by paraclinical examinations, led to the diagnosis of Sturge Weber syndrome.

The physical examination revealed, in addition to a plane angioma of the left upper limb, hypertrophy of the latter with a length inequality of 1.5 cm on the x-ray measurement compared with the right upper limb.

A kyphoscoliosis was also found, and the vascular echodoppler revealed no arteriovenous anomalies.

Klippel Trenauney syndrome was therefore diagnosed.

-We were thus able to make the very rare diagnosis of a combination of Sturge Weber syndrome and Klippel Trenauney syndrome in our patient.

discussion:

SW syndrome is a mesodermal phacomatosis. It clinically associates a planar angioma located in the ophthalmic and maxillary distributions of the trigeminal nerve (4), ipsilateral cerebral angioma

leptomeninges, glaucoma, convulsions, contralateral hemiparesis and neurobehavioral developmental delay (4).

Our patient presents with all of the above manifestations corresponding to the complete form of SWS.

KTS is a mesodermal phacomatosis (3), characterized by a triad of limb angiomas, varicose veins and soft tissue and/or bone hyperplasia (5).

Diagnosis is essentially clinical (5) and is accepted if two elements of the triad are present (6) (the clinical triad was complete in our patient).

The association of SWS and KTS is extremely rare (7); to our knowledge, around 40 cases have been described in the literature (6).

This association almost always occurs sporadically (7), but autosomal dominant transmission has already been described (2); in the article by Y Kentab et al, it is suggested that SW syndrome

syndrome could be considered a variant of KT syndrome, since both syndromes present tissue hypertrophy associated with congenital vascular malformation (4).

Conclusion:

We report a new and very rare case of combined Sturge Weber and Klippel Trenauney syndrome in a 12-year-old child, and highlight the need for multidisciplinary

collaboration in these patients.

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Abstract N°: 5075

Encephalocraniocutaneous lipomatosis, a rare neurocutaneous syndrome case report and literature review

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Introduction & Objectives: **

Encephalocraniocutaneous lipomatosis (ECCL) or Haberland Syndrome is an extremely rare congenital neurocutaneous disorder caused by postzygotic activating mutations in the fibroblast growth factor receptor 1 gene (FGFR1).

Patients usually present with clinical presentations in three major organs including skin, eye and central nervous system. Cardinal presentations are cerebral malformations, ipsilateral eye abnormalities and papulonodular skin lesions including lipomas, fibromas and etc.

This case report highlights the clinical manifestations of ECCL including cerebral malformations, eye abnormalities and skin lesions in a 7-year-old boy who was admitted to our clinic.

Materials & Methods:

A 7-year-old boy presented to our dermatology clinic with a history of a large verrucose plaque on the left temporoparietal area since his birth. He also had a previous history of a left eye tumor, the tumor was described as a firm exophytic pedunculated lesion in the left eye which underwent surgical resection. The histological examination of the tumor reported as lipomatous plexiform neurofibroma.

His past medical history was unremarkable and his family had no consanguinity or history of neurocutaneous disease. Patients laboratory tests were in normal ranges.

During examination, the patient exhibited skin lesions were predominantly located on the scalp and orbital region. The scalp lesion was a large yellowish verrucose plaque measuring 8*12 cm on the left temporoparietal area similar to lipoma with alopecia overlying it, known as nevus psiloliparus.

and as mentioned earlier he had a firm exophytic pedunculated lesion in the left eye which had been removed.

There were no significant findings suggestive of lymphadenopathy or systemic involvement.

Magnetic Resonance Imaging (MRI) of the brain was performed to confirm diagnosis and evaluate extent of the disease. The imaging revealed well-demarcated enhancing mass lesions following the course of the trigeminal nerves along the cavernous sinus. additionally, a crescent-shaped epibulbar mass with fatty intensity was observed at the left lateral canthus, supero-lateral to the eyeball and inferolateral to the lacrimal gland.

The MRI findings showed a bright signal on both T1 and T2 weighted images, with signal loss after saturation of the fat signal. Based on these findings, the brain MRI report concluded that the patient had bilateral trigeminal nerve neurofibroma/schwannoma and a left orbital dermolipoma.

Results:

ECCL or Haberland syndrome is an extremely rare disorder featuring by classic triad of Skin, eye and CNS lesions and as it name declares, the major problem in this syndrome is aberrant lipomatosis.

In 2006, By diagnosis of large series of ECCL patients, Hunter proposed major and minor criteria for diagnosis of Haberland syndrome.

Later in 2009, Moog revised these criteria and presented modified items.

Our patient presented with typical triad of clinical presentations of ECCL including scalp lipoma with alopecia overlying known as nevus psiloliparus in skin, left orbital lipomatosis as dermolipoma and Central nervous system defects.

CNS and Brain MRI Imaging confirmed the diagnosis.

Conclusion:

ECCL is a rare disease but clinical suspicion should be done with every patient presented with similar clinical manifestations.

We suggest genetic analyses and further investigations to facilitate the diagnosis, especially in cases with milder symptoms.

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Abstract N°: 5244

Keratitis, Ichthyosis, Deafness syndrome; 10 years followup in Egypt

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Introduction & Objectives: Keratitis–ichthyosis–deafness (KID) syndrome is a rare congenital multisystem disorder, associated with mutations in the connexin 26 gene. Prevalence of less than one per 1,000,000 was reported. To date, approximately 100 cases of KID syndrome have been reported in the literature.

Materials & Methods: 6 years old, boy presented, with generalized, leathery skin. Palms and soles manifested a unique rugose ridge pattern, analogous to heavily grained leather and reminiscent to acanthosis nigricans.

Bilateral hypoacusis and photophobia has been observed during his infancy, by his parents.

The patient's intelligence was normal, within the limit of his handicapped sensory losses (deaf-mutism and blindness). He was able to communicate with me through touch and smell.

Follow up, particularly during hot and humid summertime, demonstrated recurrent episodes of bacterial and fungal infections mainly onychomycosis, along with heat intolerance. The skin becomes thicker. He developed talipes equino-varus and was severly handicapped in terms of senses and motion. Finally he died at the age of 16 years with a long history of pain and misery.

A comparison with another Egyptian KIDs patient will be provided.

Results: Pure tone and speech tone audiograms revealed that he cannot discriminate speech at 65 decibels. Diagnosis of non-progressive neurosensory deafness was established.

Ophthalmology examination revealed marked keratitis along corneal vascularization and opacification. A biopsy of the conjunctiva for H&E denoted the presence of excessive goblet cells, while E/M microscope denoted excessive and disorganized goblet cells.

A skin biopsy denoted, basket weave hyperkeratosis and acanthosis, along few sweat glands and follicular plugging.

Conclusion: Early diagnosis of KID syndrome is mandatory to minimize complete hearing loss. Speech therapy may minimize the impairment of speech development. Visual acuity may improve, after superficial keratectomy in some patients, Lifelong ophthalmology follow up is necessary to avoid corneal damage. Copious amounts of emollient on daily basis, should be provided.

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Abstract N°: 5289

Cutaneos clues to Muir-torre syndrome: a case report and dermatological insights

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Introduction & Objectives:

Muir-Torre Syndrome (MTS) is a rare genodermatosis with an autosomal dominant mode of inheritance, considered a subtype of hereditary nonpolyposis colorectal cancer, also known as Lynch syndrome (2). Diagnosis hinges on the presence of one visceral malignancy and one cutaneous neoplasm of sebaceous differentiation. Typically, MTS manifests between the ages of 50 and 70, with a higher incidence in male patients (5). Skin tumors in MTS often include sebaceous neoplasms and keratoacanthomas, occasionally accompanied by basal or squamous cell carcinomas (2)(4)(6). These lesions commonly appear as painless, slow-growing nodules with pink or yellow hues, often exhibiting ulceration or central umbilication. Tumors in MTS tend to manifest earlier and with a higher incidence of synchronous or metachronous lesions compared to sporadic colorectal cancer (5). Given these characteristics, careful evaluation of sebaceous neoplasms below the neck is imperative to consider the possibility of MTS.

The process of tumorgenesis involves the loss of genomic integrity, marked by mismatches in repetitive DNA sequencies, leading to microsatelities instabilities. (1). MTS shares clinical features with several other syndromes, including Cowden syndrome, Birt-Hogg-Dubé syndrome, Tuberous Sclerosis, Brooke-Spiegler syndrome, and Gorlin syndrome, highlighting the importance of accurate diagnosis. The objective of this report is to underscore the significance of confirming MTS diagnosis promptly to facilitate early identification and surveillance of internal neoplasms.

Materials & Methods:

A 45-year-old male presented with a one-year history of abdominal pain, hematochezia, and fecal thinning, ultimately diagnosed with adenocarcinoma of the ascending colon in October 2021.

Following right colectomy and lymphadenectomy in December, the patient underwent regular follow-up visits at the coloproctology outpatient clinic, where his extensive family history of neoplasms was noted. Post-surgery, a painless nodular lesion measuring 3 centimeters was observed in the dorsal interscapular area during a follow-up visit. Dermatological evaluation was recommended, but the patient failed to follow up. Five months later, the lesion had progressed to 5 centimeters prompting dermatological assessment. Excision with 1cm margins was performed in December 2022, and histopathology revealed a sebaceous adenoma with loss of immunohistochemical expression of repair enzymes MSH-2 and MSH-6, confirming Muir-Torre syndrome.

Results:

After 2 years and 6 months of follow-up at the coloproctology clinic, the patient's CEA levels remained low and downtrending, obviating the need for further surgery. Dermatological follow-up has shown no lesion recurrence to date.

Conclusion:

Muir-Torre syndrome presents diagnostic challenges, particularly as sebaceous adenomas are relatively common.

While routine dermatological monitoring suffices in most cases, vigilance is crucial, especially when lesions occur below the neck or in the presence of a positive family history of multiple cancers. Early screening for internal neoplasms can significantly impact prognosis, highlighting the importance of comprehensive evaluation and timely intervention in Muir-Torre syndrome.

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Abstract N°: 5711

Exploring Fabry's Disease: Insights from Two Sets of Twins

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Introduction & Objectives: Fabry's disease is a recessively inherited sphingolipidosis linked to the X chromosome, characterized by a deficiency in the lysosomal enzyme α-galactosidase A, resulting in the accumulation of undegraded glycosphingolipids in tissues and plasma. This disorder presents with dermatological symptoms as the initial manifestation, followed by the progression of microvascular disease affecting multiple organs, exacerbating the severity of the condition. Here, we report observations from four male patients diagnosed with Fabry's disease.

Materials & Methods/Observations: The four patients, aged between 20 and 27 years, comprising two unrelated sets of brothers, presented to our dermatology clinic with dermatological concerns as their chief complaint. Dermatological evaluations revealed characteristic features of Fabry's disease, including reddish-purple macules and papules distributed across the back, abdomen, genital region, and thighs, resembling angiokeratomas. Additionally, symptoms such as inflammatory polyarthralgia, acroparesthesia exacerbated by heat, and ocular manifestations were noted. Laboratory investigations confirmed normochromic normocytic anemia, thrombocytopenia, and renal insufficiency in two patients, without cardiac involvement. Skin biopsies corroborated the clinical suspicion of Fabry's disease, revealing characteristic histopathological findings. Deficiency in alpha-galactosidase A was confirmed in all patients, establishing the diagnosis of Fabry's disease. Treatment initiation with beta agalsidase at a dose of 1 mg/kg via biweekly infusion was commenced for all patients.

Results/Discussion: Fabry's disease arises from a deficiency in alpha-galactosidase A, leading to the accumulation of globotriaosylceramide in various cellular compartments, manifesting primarily with dermatological symptoms. These symptoms serve as key diagnostic indicators, though their absence can complicate diagnosis. Additionally, systemic involvement in Fabry's disease encompasses cardiac, renal, neurological, and ocular manifestations, contributing to the disease's complexity and severity. Enzyme replacement therapy with recombinant human alpha-galactosidase A has demonstrated efficacy and safety in managing Fabry's disease.

Conclusion: : In conclusion, the presented cases underscore the importance of recognizing dermatological manifestations in diagnosing Fabry's disease and highlight the significance of comprehensive evaluation and management to mitigate systemic complications associated with this disorder. Enzyme replacement therapy remains a cornerstone in the treatment of Fabry's disease, offering significant therapeutic benefits to affected individuals.

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Abstract N°: 5776

A new era of biological treatments for epidermolysis bullosa

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Introduction & Objectives: Genodermatoses are rare genetic diseases that often impact children since the early years of life and, currently, no curative drugs are available for them. Symptomatic therapies are often insufficient in ensuring a good quality of life and alleviating pain and itching. This study has the aim to investigate the clinical impact of epidermolysis bullosa in a group of children referred to our center. Secondary objective of this study is to investigate the efficacy and safety of biologic therapy (dupilumab) in these patients.

Method: Eight patients affected by epidermolysis bullosa were selected based on clinical criteria (extent and duration of the disease, perceived pain and itch, impact on quality of life) and were treated with dupilumab. Patients were evaluated at regular intervals (3, 6, 9, 12 and 18 months) and were asked to complete questionnaires regarding their quality of life, perceived pain, and itch.

Results: In patients with epidermolysis bullosa we observed an improvement in Children's Dermatology Life Quality Index scores ranging from 21,7% at baseline to 42,6% at 12 months. Results about pain and itch also showed an improvement (48,2% and 54,4%, respectively).

Conclusions: Dupilumab appears to be a safe and effective treatment for children with epidermolysis bullosa and ichthyosis. Our study is based on a small group of patients and further large studies are needed to validate our findings.

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Abstract N°: 5797

Novel genetic variant of Dystrophic congenital epidermolysis bullosa in an afroamerican patient,a new phenotype?

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Introduction & Objectives:

Epidermolysis bullosa (EB) comprises a group of genetically inherited rare diseases characterized by mutations in proteins involved in dermoepidermal adhesion. This results in skin and mucosal fragility, primarily manifested by blister formation, skin erosions, and ulcers even with minor trauma. Depending on the affected structural protein at the dermoepidermal level, four main subtypes of EB can be distinguished: simplex (EBS), junctional (EBJ), dystrophic (EBD), and Kindler syndrome. Dystrophic epidermolysis bullosa is transmitted in an autosomal dominant or recessive manner and is caused by mutations in the COL7A1 gene The recessive subtype is the worst shape of EB in which minor friction brings out blisters and severs skin ulcerations.

Materials & Methods:

We present a case of a female Afro-American patient diagnosed with recessive dystrophic epidermolysis bullosa, confirmed via next-generation sequencing (NGS), identifying a previously unreported homozygous variant in the COL7A1 gene, C.8409delC (p.C2804Afs*94), who exhibited a mild phenotype.

Results:

We present the case of a female patient, afroamerican native to the Colombian Pacific coast, with no relevant medical history, born to a 19-year-old mother with negative prenatal screening and noT consanguinity. At birth, vesicles and blisters were present on the back of the hands and the posterior region of the lower extremities, evolving into erosions. The patient was referred to Dermatology department and a skin biopsy was performed, revealing the presence of a subepidermal blister with mild superficial perivascular mononuclear inflammatory infiltrate, findings suggestive of congenital epidermolysis bullosa. A next generation sequencing (NGS) panel for congenital epidermolysis bullosa was requested, identifying a previously unreported homozygous variant in the COL7A1 gene, C.8409delC (p.C2804Afs*94), causing a frameshift deletion. Prediction tools (Polyphen-2, SIFT, and MutationTaster) classified it as pathogenic, consistent with dystrophic epidermolysis bullosa. Treatment was initiated with skin barrier care and prevention of new lesions. During follow-up, sporadic appearance of vesicles predominantly in acral regions and residual milium cysts distributed mainly on the extremities were identified, with no other recurrences of blistering significantly compromising the patient’s life.

Conclusion:

This case exemplifies the variability in the relationship between genotype and phenotypic traits in EB. Severe clinical manifestations would typically be expected in the dystrophic subtype. However, in our patient, such manifestations have been mild. Additionally, it is essential to highlight the role of the dermatologist in documenting clinical findings and conducting complementary molecular genetic tests to achieve accurate characterization, appropriate diagnosis, and optimal clinical management, thereby establishing a solid correlation between genotype and phenotype.

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Abstract N°: 5847

Secukinumab for ichthyosis with confetti - own experience in paediatric patients

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Introduction & Objectives:

Ichthyosis with confetti (IWC) is a rare, overlooked genodermatosis characterized by erythroderma with numerous confetti-like pale spots. Management primarily focuses on symptomatic relief and scale reduction using emollients, keratolytics, and retinoids. Case reports in the literature have demonstrated the use of biologics like secukinumab as an effective treatment option for adults when systemic therapy with acitretin is insufficient. However, information regarding their use in children remains limited.

Materials & Methods:

We conducted an analysis of the medical histories of two children diagnosed with ichthyosis with confetti who were hospitalized at the dermatology department to optimize their treatment.

Results:

\1. A 13-year-old boy was admitted to the dermatological department with erythrodermic ichthyotic and scaling lesions. Clinical examination revealed ectropion, ear deformations, nail dystrophy, and hypohidrosis. He had previously been treated with topical therapy and oral acitretin. Genetic tests identified a mutation in the keratin 10 gene (KRT10). Adding secukinumab to the existing therapy and increasing the dose of acitretin improved the patient’s skin condition and alleviated symptoms.

\2. A 16-year-old boy was admitted with similar symptoms and a mutation in KRT10. He had previously been treated with topical therapy, oral acitretin, and adalimumab. He also suffered from growth disorders treated with growth hormone supplementation. Adding secukinumab to topical therapy and increasing the dose of oral acitretin led to improvement in skin condition as well as other symptoms.

Conclusion:

Both children showed improvement in skin condition and other symptoms with systemic therapy combining oral acitretin and secukinumab. We believe secukinumab may be an effective therapeutic option in cases where acitretin treatment is insufficient, even in children. This case report represents, to our knowledge, the first use of secukinumab in children diagnosed with ichthyosis with confetti.

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Abstract N°: 5928

Patients with Darier disease have an increased risk of keratinocyte carcinoma: A Swedish registry-based nationwide cohort study

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Introduction & Objectives:

Darier disease is a genodermatosis which manifests as hyperkeratotic papules and superficial erosions mainly in seborrheic skin areas. This retrospective registry-based cohort study aimed to estimate the association between Darier disease and basal cell carcinoma, cutaneous squamous cell carcinoma, and cutaneous melanoma.

Materials & Methods:

Patients diagnosed with Darier disease were identified from the patient registry of Sahlgrenska University Hospital (Gothenburg, Sweden) in 2016-2020. The local cohort included 13 patients. National Patient Registry was searched for Darier disease in 2001-2020, Swedish Cancer Registry for cancers and Prescribed Drug Register for medications.

Results:

The national cohort included 770 patients and tenfold matched control cohort. Patients with Darier disease had an increased relative risk of keratinocyte carcinoma (basal cell carcinoma and cutaneous squamous cell carcinoma combined) (HR, 1.6, 95% CI, 1.0-2.5, P=.036). The risk increase was significant for basal cell carcinoma (HR, 1.8, 95% CI, 1.1-2.9, P=.012), whereas there was a trend for cutaneous squamous cell carcinoma, (HR, 1.9, 95% CI, 0.9-4.1, P=.086) and melanoma (HR, 2.4, 95% CI, 0.9-6.2, P=.083). Standardized incidence ratio for keratinocyte cancers was 2.88 (95% CI, 2.42-3.39). Protective function of acitretin could not be demonstrated.

Conclusion:

Using Swedish health registers, this study examined whether patients with Darier disease have an increased risk of keratinocyte carcinomas (basal cell and cutaneous squamous cell carcinomas), and melanoma. The relative risk for basal cell carcinoma was significantly increased, i.e., 1.8-fold, and cutaneous squamous cell carcinoma and melanoma showed trends toward increased risk. The results can help clinicians monitor the patients with Darier disease more effectively and promote early cancer detection. The patients should also be aware of the risk.

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Abstract N°: 6030

Rapid Response of Everolimus on skin lesions: a case of two patients

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Rapid response of Everolimus on skin lesions: a case of two patients

Introduction & Objectives: Tuberous sclerosis complex (TSC) is an autosomal dominant disease with an estimated incidence of 1 in 6000 births. TSC is caused by mutations in either TSC1 or TSC2, with 70–80% of cases resulting from sporadic mutations. These genes encode for the proteins hamartin and tuberin known to inhibit the mammalian target of rapamycin (m-TOR) pathway, which controls cellular growth and metabolism. TSC is characterized by benign tumors in different organs. Epilepsy, neurocognitive deficits, and neuropsychiatric disorders, including autism, and lesions in the brain, skin, kidney, and lungs are common. Dermatological manifestations are detected in all ages and affect more than 90% of TSC patients. Facial angiofibromas often start to appear within the first 2–5 years of life and ultimately occur in approximately 75% of patients.

Materials & Methods: The discovery of mutations in the TSC1 and TSC2 genes and their association with the mechanistic target of the rapamycin (mTOR) pathway have paved the way toward the development of targeted therapy in TSC patients. Few randomized controlled clinical trials with mTOR inhibitors have shown efficacy in the treatment of several clinical organ manifestations of TSC, most importantly in patients with subependymal giant cell astrocytoma (SEGA), seizures (treatment resistant with focal onset), and angiomyolipoma (AML), as well as cutaneous manifestations. However, real-life experiences in the context of clinical dermatology are lacking. Herein we present the retrospective experience of 2 TSC patients treated with everolimus.

Results: The clinical case describes a 44-year-old woman and a 34-year-old man, affected by TSC, genetically diagnosed, followed at a University-Based Dermatologic Rare-Disease Clinic. Both patients presented renal angiomyolipomas and multiple cutaneous angiofibromas on their face. The female patient was also affected by myoclonic epilepsy and subependymal giant cell astrocytomas. Considering the clinic manifestations and the cutaneous involvement with multiple angiofibromas on the face, sites of frequent bleeding and distress for the patient, a therapy with Everolimus was initiated (starting dose 5 ng/ml). After only two months into therapy, both patients experienced a rapid response with significant reduction of the skin lesions. No adverse events were recorded during the follow up period.

Conclusion: The efficacy of everolimus in treating skin lesions has already been documented and validated through two primary trials, EXIST 1 and EXIST 2. These trials demonstrated a four-year complete response in over half of the patients enrolled. Our case aligns with these findings, providing promise for future therapeutic approaches to this complex disease.

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Abstract N°: 6193

Mid-face toddler excoriation syndrome- a comprehensive phenotypic analysis

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Introduction & Objectives: Mid-face toddler excoriation syndrome (MITES) is a rare autosomal recessive genodermatoses characterized by bilaterally symmetrical self-inflicted excoriations and scars on central face- glabella, nose and nasolabial folds. We report a case series of 4 patients highlighting the distinct phenotypic variations, corelating with their genotype.

Materials & Methods: A detailed phenotypic analysis was done for both cutaneous and systemic features. After informed consent, blood samples were sent for whole exome sequencing was done. Samples were taken only from the index case and not the parents because of non-affordability. Routine blood samples including uric acid levels were also sent.**

Results: Two of these patients had a PRDM12 polyalanine tract expansion, the remaining 2 has SCN11A mutation. While the former 2 patients reported decreased sensitivity to pain with episodes of unconscious trauma, the latter cases reported intense facial itching along with increased sweating. Patients with SCN11A mutation also had lichenified plaques besides deep atrophic scars on the central face. Uric acid levels were within normal limits in all our patients.

	PRDM12 polyalanine expansion	**SCN11A mutation**
No. of patients	2	2
Decreased pain sensitivity	Present	Absent
Increased sweating	Absent	Present in 1 patient
Increased itching and lichenified plaques	Absent	Present
Ragged cuticles and dystrophic nails	Absent	Present
Loss of eyebrows and trichoteiromania	Absent	Present in one patient
Attainment of development milestone	Complete	Complete
Cognitive impairment	None	Present in 1 patient
Altered bowel habits	None	None
Light touch and temperature sensation	Sensation to hot temperature impaired in 1 patient, rest intact	All sensations intact

Conclusion: MITES syndrome lies on the same spectrum as congenital insensitivity to pain and hereditary sensory and autonomic neuropathy. It was initially described as a localized skin condition affecting the midface, however

these patients may have variable cutaneous and systemic features, depending on underlying mutation. Decreased sensitivity to pain, and impaired sensation to hot temperature are more suggestive of an underlying PRDM12 muation, while increased itching with lichenified plaques, trichoteiromania, dystrophic nails and ragged cuticles are more commonly seen in patient with an underlying SCN11A mutation.

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Abstract N°: 6303

Kindler's syndrome - A case report of rare genodermatosis

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Introduction:

Kindler's syndrome is a rare inherited skin disease characterized by acral blistering, photosensitivity, progressive poikiloderma & cutaneous atrophy along with different types of mucosal involvement.

Materials : Case Report - A 30-year-old male, born out of a consanguineous marriage presented with skin lesions all over the body since childhood & an ulcer over left foot since 1 year. Patient had recurrent acral blisters, which started in infancy & persisted till 7 years of age. These blisters contained clear fluid which healed with scarring after rupture. Patient had photosensitivity since childhood which improved over time. There was no history of similar complaints in the family. Cutaneous examination revealed generalized xerosis with multiple hypo & hyper pigmented atrophic macules & patches of variable size seen over face, neck, trunk & extremities. A solitary ulcer measuring 2× 2 cm was present over right heel. Mucosal examination revealed gingival swelling &multiple hyperpigmented patches in the oral cavity. Diagnosis of Kindler syndrome was made based on history, clinical examination and histopathological findings.

Results:

We did Gene sequencing of the FERMT-1 gene affected in this disease but did not find a mutation in it

Conclusion:

Kindler's Syndrome has autosomal recessive pattern of transmission, but sporadic cases are not uncommon, with numerous cases reported in consanguineous families. The case is being reported for its rarity and for emphasizing the importance of considering this condition in the differential diagnosis of disorders that may cause blistering, cutaneous atrophy and poikilodermatous skin changes.

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Abstract N°: 6462

Nail-patella syndrome: a case report

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Introduction & Objectives:

Nail-patella syndrome (NPS), also known as hereditary osteo-onychodysplasia, is a rare autosomal dominant disorder that affects tissues of ectodermal and mesodermal origin. It is characterized by distinctive nail and skeletal abnormalities and may also involve the kidneys and eyes. This report presents the case of a 10-year-old child diagnosed with NPS, highlighting the clinical presentation and management considerations.

Materials & Methods:

Results:

A 10-year-old girl was referred for the evaluation of a congenital nail dystrophy. She was born from a non-consanguineous union and had a history of scoliosis and a deformity of the right elbow with flexion contractures. Physical examination revealed bilateral thumb hypoplasia and facial dysmorphic features, including a convex forehead, hypertelorism, low-set ears, and micrognathia. Additionally, she presented with genu valgum and palpably small, hypoplastic patellae. A diagnosis of NPS was established based on these clinical findings. Further investigations were carried out, including a pelvic X-ray for suspected iliac horns, an ophthalmic examination for potential glaucoma, and a renal evaluation for glomerular nephropathy.

Conclusion:

NPS is a genetic disorder caused by a mutation in the LMX1B gene, which is implicated in limb organogenesis and kidney development. Transmission is autosomal dominant, but de novo mutations occur in 10% of cases. The classic tetrad includes nail dysplasia, patellar agenesis or hypoplasia, the presence of iliac horns and elbow deformities. Nail involvement is the most common symptom, typically bilateral and symmetrical. Nail changes consist of absent, hypoplastic or dystrophic fingernails, as well as triangular lunula and discoloured nails. Toenails are rarely affected. Furthermore, there may be a decrease in bone mineral density in the hip and spine, which can increase the risk of fractures and scoliosis. Early ophthalmological screening for glaucoma and ocular hypertension is recommended. Renal complications are reported in 30-60% of cases. Glomerular nephropathy can cause proteinuria, with or without haematuria. This condition may remain asymptomatic or progress to a nephrotic syndrome or even chronic end-stage renal failure. Treatment is symptomatic and multidisciplinary. The aim of treatment for nephropathy is to reduce proteinuria to slow the progression to end-stage renal failure, which typically occurs around the age of 30.

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Abstract N°: 6585

Whorled scarring alopecia: A rare cutaneous finding in incontinentia pigmenti or overlooked phenomenon ? A case report of incontinentia pigmenti with trichoscopic and dermoscopic findings

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Introduction & Objectives:

Incontinentia pigmenti (IP) or Bloch-Sulzberger syndrome (MIM 308310) is a rare genetic disease that frequently affects the skin, hair, nails, teeth, eyes and central nervous system. IP is X-linked dominant inherited genodermatosis, caused by mutations in the NEMO gene (IKK-gamma) on Xq28 locus (1). It is generally recognized by cutaneous findings including linear erythematous, vesicular or bullous rashes in newborns. Cutaneous findings usually occur sequentially and manifest along the Blaschko lines and classically progress in four stages, which may show some overlap (2).

IP can also involve the hair. Hair involvement has been reported in approximately 28% to 38% of patients (3). Scarring alopecia is the most common manifestation of hair involvement (3,4). Whorled scarring alopecia is a reported cutaneous finding in patients with IP, however; there is no certain data on its frequency. Here in we report a 5-year-old girl with whorled scarring alopecia on the vertex with trichoscopical signs and, dermoscopical findings of Stage 3 of IP.

Case:

A five year-old female patient referred to our Dermatology department for hair loss on scalp since birth and hyperpigmented rash on body. The wounds on the body started with birth and were in the form of fluid-filled blisters. These wounds later burst and turned into crusty wounds. After the age of 2, they turned into linear dark lesions in the groin and armpits. In the genetic mlpa-deletion duplication analysis performed, the 4th-10th gene region scanned in the IKBG gene region was repeated twice. A signal pattern compatible with heterozygous deletion was observed in the exons. She was following up by Ophthalmology, Dentistry, Neurology, Hematology and Pediatric cardiology departments. On dermatological examination; there were reticular linear hyperpigmented macules in the axillary and inguinal areas (Fig. 1a), alopecic areas on the scalp (Fig. 1b), and hypoplastic teeth(Fig. 1c).

Discussion:

Hair involvement [alopecia or abnormal hair (sparse hair, wooly hair, anomalies of eyebrows and eyelashes)] is one of the diagnostic criteria of IP (5). Wang et al. investigated 42 patients with IP and reported hair anomalies in 31% (Vertex alopecia in 26%, thin hair in 12%, wiry hair in 5%, coarse hair in 2%) (6).

There are few reports on dermoscopical and trichoscopical findings in IP cases (10,11). On trichoscopical examination of whorled alopecia in IP patient, Razmi et al reported blue-grey pigment dots, empty hair follicles and and black dots (11).

Blashkoid distrubited hyperpigmented lesions include linear and whorled nevoid hypermelanosis, hypomelanosis of Ito and lichen planus pigmentosus; and may be confusing with stage III of IP (12-14). On the other hand, dermoscopy can be a useful diagnostic too in cutaneous lesions of IP. On dermoscopical findings of pigment

stage of IP, Bishnoi et al reported linear brown to gray-brown dots (10,11).

Scarring alopecia tends to be permanent and; in addition to dental findings, it may be the only one of cutaneous findings remaining in IP patients at older ages. However, it is not clear in how many of these patients the alopecia is distrubited in the blashkoid pattern. (8, 15). Dermoscopy and trichoscopy can be used as a useful tool in differentiating cutaneous and hair findings of IP from other diseases. More studies are needed to determine the frequency of whorled scarring alopecia in IP or its relationship with certain genetic mutations.

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Abstract N°: 6589

Successful Treatment of Hailey-Hailey Disease with Photodynamic Therapy: A Case Report

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Introduction & Objectives:

Hailey–Hailey disease (HHD), also known as familial benign chronic pemphigus, is a rare autosomal-dominant blistering disease. There is no specific treatment, hence several topical and systemic treatments have been attempted with varying results. Only a few cases of HHD have been reported to be treated with photodynamic therapy (PDT).

Materials & Methods:

In this report, we present a new case of HHD successfully treated with PDT.

Results:

A 55-year-old woman presented with a 15-year history of recurrent erythematous plaques, evolving in flare-ups, located on axillary, sub-mammary, inguinal, and pubic regions. She had been diagnosed with Hailey-Hailey disease based on skin biopsy results. The patient underwent multiple treatments such as topical and systematic steroids without improvement. We performed PDT treatment in the axillary and left sub-mammary regions following methyl aminolevulinate (Metvixia®) application in a thin layer under occlusion for 3 hours. The treated areas were irradiated with red light emission at a maximum of 633 nm, providing a total light dose of 37 J/cm2 for ten minutes. The pain was tolerable for the patient and did not require a temporary irradiation interruption. A topical steroid was applied for 5 days after the session. Complete healing was observed for the axillary region and partial improvement (50%) for the sub-mammary fold. A second PDT session was performed after one month, resulting in near-complete healing. No recurrence of lesions in the treated areas was observed after 3 months of follow-up.

Conclusion:

Typically, patients with HHD present with flaccid vesicopustules, crusted erosions, macerations, or fissures in friction-prone skin folds. Treatment of HHD is often challenging and disappointing. PDT appears to offer new perspectives in this challenging context. Over the past few years, several publications have focused on evaluating the role of PDT, either alone or in combination with other therapeutic modalities (such as botulinum toxin injection, and ablative CO2 laser), in HHD with promising results. The main photosensitizing agent used is methyl aminolevulinate, as in our case. The mechanism of action, still poorly understood in this indication, is believed to involve the restoration of normal keratinization. The main limitation remains the pain induced by irradiating injured skin, which is, indeed, patient-dependent. According to some authors, this pain could be alleviated by using infrared filters and analgesics before the session. The use of local anesthetics is more controversial. This is because, according to PDT principles, oxygen is essential to photodynamic reaction and topical or intralesional anesthetics cause vasoconstriction.

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Abstract N°: 6682

Between diagnostic obscurity and singularity: Familial annular erythema, a case report

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Introduction & Objectives:

Familial annular erythema is a rare diagnosis, described in 1966 by Beare and colleagues as a dominant autosomal genetic syndrome present in 3 generations of an Irish family. The typical lesion consists of an erythematous and urticarial spot which enlarges and clears in the center leaving a mild and transient brownish pigmentation. Due to the scarcity of reports, clinical knowledge remains uncertain. The objective is reported the management of a familial annular erythema case.

Materials & Methods:

The data presented in this study were collected via medical record review, patient/family members examinations, and photographic documentation. Statistical analysis was not applicable in this case report, as it primarily focused on clinical description and management rather than quantitative data analysis. Informed consent was obtained to inclusion in the study, ensuring confidentiality and voluntary participation.

Results:

N.S.S, 6-years-old girl was admitted with pruritic lesions, that occurred a few days after birth. The manifestations were cyclic, persisting for 3 to 4 days before subsiding and relocating to different areas, rarely present complete remission. Severe itching is the predominant symptom. Family sought medical services, and corticosteroid treatment was prescribed. We observed a disseminated dermatosis characterized by annular rings of erythema, which enlarges and clears in the center. Similarly to Beare's description, characteristic lesions were evident in 3 generations of the patient's family. A biopsy was performed from the border of a lesion. Histology showed a superficial perivascular dermatitis. We elected to administer bilastine therapy considering the presumed diagnosis of familial annular erythema. There was partial improvement with corticosteroids. The patient exhibited consequences resulting from chronic usage.

The first case of familial annular erythema describes an 8-month-old boy with pruritic cutaneous lesions. These lesions may appear anywhere, no predilection for specific parts of the body. There were moments of remission that could last for weeks, and only rarely was the subject entirely free. Williams and colleagues reported a similar case in a 3-year-old patient. In the literature, familial annular erythema is part of the group of figurate erythema's. There are four main differential diagnoses: centrifugal annular erythema, marginate erythema, chronic migratory erythema, and erythema gyratum repens. The absence of familial repetition, streptococcal infection, spirochete infection, and signs of neoplasia make those differential diagnoses unlikely.

Conclusion:

Our case seems to best fit with the original description of familial annular erythema in terms of its clinical presentation and pathological features. There remains much to discover, even about epidemiological characteristics and diagnostic criteria. Additional research is also needed to establish a treatment consensus.**

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Abstract N°: 6718

Have you considered Human Papillomavirus(HPV) vaccine in the treatment of Epidermodysplasia Verruciformis disease?

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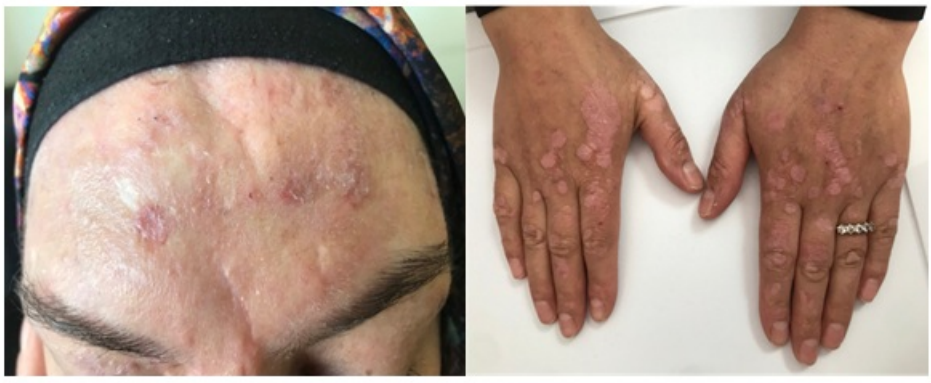
Introduction:

Epidermodysplasia verruciformis(EV) is a rare autosomal recessive disease that usually occurs in early childhood, is characterized by widespread flat verruca-like lesions and skin cancer development, especially in sun-exposed areas[1]. Genetic defects in this disease make the skin susceptible to HPV infection. Squamous cell cancers(SCC) are the most common type of cancer in EV patients. EV therapy includes UV exposure protection, topical imiquimod, oral isotretinoin, and intralesional interferon alfa, but patients are often resistant to these treatments[2]. Some studies suggest that the HPV vaccine may offer a therapeutic option for cutaneous SCC, in addition to its approved use to prevent anogenital HPV infection. Here; we wanted to present the patient who had a significant regression in the lesions and a decrease in the rate of conversion to cancer after vaccination.

Case: A 28-year-old female patient with a diagnosis of EV since the age of 4 was admitted to outpatient clinic in 2015. Her dermatological examination revealed multiple hyperkeratotic, pinkish, flat papules on the face, neck, and hands. Routine blood tests were normal. The patient was started on interferonalpha-2a subcutaneously, 3 million IU 3 times a week, 0.75 mg*kg/day isotretinoin, topical imiquimod 3 x 1 per week. The patient was followed up with this treatment combination for about 3 years. In the follow-ups, actinic keratoses continued to occur and excisions were made from the newly developed suspicious lesions. Despite the current treatment combination, the patient still continued to develop an average of three SCC and one BCC compatible lesions per year. In 2018, the treatments were discontinued due to the patient's thought of becoming pregnant. Before conception, 3 doses of quadrivalent HPV vaccine was recommended, after which lesions were followed up with cryotherapy. At the point we have reached; Although the patient did not receive systemic treatment in the last 3 years, we observed that his lesions regressed significantly. After vaccination, only one malignant tumor excision was required in the last 3 years of follow up. While the number of lesions with malignancy risk and reported as SCC is an average of three per year; Since 2019, only one malignant risk lesion has been observed, excised, and reported as SCC.



Conclusion:

If we refer to the efficacy of the vaccine in cutaneous carcinomas, in a study conducted by Nika et al.in 2015, HPV-32 was isolated in a patient with recurrent squamous cell papilloma resistant to treatments and quadrivalent HPV vaccine was administered, and almost complete regression was observed in the lesions after about three months. The production of cross-protective immunoglobulins and cytotoxic T cells has been considered as a possible mechanism[3]. In a study published by Nichols et al. in 2017, it was observed that the rates of carcinoma development in their routine follow-ups decreased after systemic vaccination in two elderly patients with a history of more than one cutaneous carcinoma[4]. In a study published by the same author in 2018, HPV vaccine was administered systemically and intratumorally and regression was detected in tumors[5]. Thus, it has been shown that vaccination against HPV can also prevent the development of SCCs and BCCs in immunocompetent individuals, possibly through effects on local distribution of the vaccine or on immune-mediated mechanisms.

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Abstract N°: 6866

Type 1 Neurofibromatosis Without Cafe - Au - Lait Macules With Coexistence Renal Angiomyolipoma And Hyperintense Cortical Lesion

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Introduction & Objectives:

Type 1 neurofibromatosis is a genetic disease characterized by the presence of tumors in the nervous system and skin. Patients with NF1 are also at greater risk of experiencing cardiovascular, musculoskeletal, and nervous system disorders. In this study, we reported a case of NF1 with several complications occurring in an adolescent. The patient exhibited pathognomonic features including multiple cutaneous and subcutaneous nodules, as well as abnormalities in the patient's eyes, kidneys, and intracranial region. The patient was treated with various modalities and showed satisfactory outcomes

Materials & Methods:

A 16-year-old female presented with a six-year history of facial nodules. The nodules were skin-colored and non-painful or itchy. Initially, only one nodules, but more appearedover time varying in sizes. The patient also report a history of urinary difficulties, low back pain, and previous kidney removal. Dermatological examination revealed multiple skin-colored nodules on the facial region without hyperpigmented macules (café-au-lait macules). Dermoscopy showed homogeneous pigmented nodules, fingerprint-like areas, and a pigmented network. Histopathological of skin lesion finding schwann cell, fibroblast and mast cell proliferation, multiple polypoid tumor and floret cell were related to Cutaneous NF 1. Head CT scan revealed hyperintense cortical lesions consistent with cortical neurofibroma. Renal histopathological examination showed features of renal epithelioid angiomyolipoma. The patient was treated with topical therapy consisting of 80% TCA application, electrodesiccation, and supportive therapy wich gave good outcome.

Results:

Neurofibromatosis type 1 is an autosomal dominant genetic disease. Nodules typically appear in late childhood or early adulthood and increase in number with age. This patient presented with skin-colored, non-painful, non-itchy nodules of various sizes across her face. Café-au-lait macules are pathognomonic lesion found in 95% of patients with NF 1. NF 1 often involves disorder of other organ systems, including eyes (often optic pathway gliomas), vasculature, musculoskeletal system and nervous system. Notably, this patient lacked café-au-lait macules on her fave and body, which is rare. She experienced visual disturbances likely due to optic pathway glioma, has taste-related autism likely do to intracranial neurofibroma, and underwent kidney removal for renal epitheloid angiomyolipoma. This complication may be linked to malfunction of the tumor suppressor gene NF 1, which can increase the risk of malignancies like nephroblastoma, rhabdomyosarcoma, brain tumors and optic pathway gliomas.

Conclusion:

Neurofibromatosis type 1 is a disorder with potential complications affecting the eyes, nervous system, musculoskeletal system. It can increase the risk of malignancies including nephroblastoma and brain tumors.

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Abstract N°: 6872

Epidermolysis bullosa simplex with migratory circinate erythema: a diagnostic challenge in infancy

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Introduction & Objectives: Epidermolysis bullosa simplex (EBS) is an autosomal dominant inherited disorder, causing distal skin fragility with intraepidermal blisters. EBS with migratory circinate erythema (EBS-migr) is a rare EBS subtype characterized by spreading erythematous patches with marginal blisters that heal with reticular pigmentation. Autoimmune bullous diseases in early childhood may have a similar presentation. Close follow-up of clinical presentation development over time, combined with histopathology, direct immunofluorescence and genetic findings is necessary when making the final diagnosis.

Materials & Methods: A 9-month-old girl was referred to our Clinic with a history of blister formation on hands, legs and feet, starting 5 weeks after birth. At the age of 6 months, pruritic annular lesions bilaterally in her axillar and inguinal regions developed. Her mother and maternal grandmother had occasional blistering over extremities in their childhood, with spontaneous remission at the time of puberty.

Results: On examination, multiple vesicles and bullae with erosions were noted on dorsal sides of hands, fingers and feet. The blisters resolved without scars or milia. Additionally, she had circinate and annular erythema with a trailing edge of vesicles and central healing with hyperpigmentation over axillar and inguinal folds. There were no mucosal or nail changes. Routine laboratory tests were normal. IIF and DIF testing as well as multiple fungal cultures from annular lesions were negative. Biopsy revealed subepidermal cleft with degeneration of basal cells, a finding not typical for EBS, prompting to the genetic testing. Exome sequencing detected a heterozygous deletion in exon 9 (1649delG) of the *KRT5* gene, confirming the diagnosis of EBS-migr. At the last check up, at the age of 20 months, new annular and circinate lesions emerged on the nape of her neck, elbows and knees, with enlargement and central healing of already existing axillar and inguinal lesions.

Conclusion: Diagnosing EBS-migr presents a significant challenge in the setting of its rare occurrencre, as it has been reported in only two cases across Europe. EBS-migr was first** described in 2003, as a milder form of EBS Dowling-Meara, that additionally comprised an unusual migratory circinate pattern on an erythematous background and novel genetic mutation of tail domain in *KRT5 (1649delG)* gene. In the following years, mutations in the *KRT5* tail domain were reported in very few cases, linked to atypical EBS forms like EBS-migr or EBS with mottled pigmentation (EBS-MP), hinting at the domain's involvement in inflammation and pigmentation regulation. Although valuable, light microscopy is not precise enough in determining the level of cleavage. This case underscores the importance of genetic testing in the evaluation of hereditary blistering disorders, particularly in cases with atypical features or inadequate response to initial treatments.

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Abstract N°: 6971

Inflammatory skin and bowel disease linked to ADAM17 deletion – a rare syndrome with a novel mutation

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Introduction & Objectives:

ADAM metallopeptidase domain 17 (ADAM17) is a sheddase belonging to the ADAM family of disintegrins and metalloproteases, responsible for processing large numbers of proteins with a wide variety of ligands such as epidermal growth factor receptor ligands, tumor necrosis factor (TNF)–α, and angiotensin I converting enzyme 2. ADAM17 is crucially involved in various pathological conditions including cancer, inflammation, neurodegeneration, and fibrosis.

inflammatory skin and bowel disease 1 (NISBD1, OMIM # 614328), is characterized by inflammatory features with neonatal-onset, involving the skin, hair, heart and gut with manifestations such as erythroderma, recurrent skin infection and sepsis and prolonged diarrhea.

The skin disease undergoes phases of exacerbation and remission, with recurrent flares of erythema. Gastrointestinal symptoms include malabsorptive diarrhea, which is exacerbated by intercurrent gastrointestinal infections. The hair is short or broken, and eyelashes and eyebrows are wiry and disorganized. Cardiac manifestations described to date involve a report of a fulminant death in a 12 year old female due to parvovirus B19-associated myocarditis whose brother was found to have left ventricular dilation.

Materials & Methods:

We describe a case of a female infant born to consanguineous healthy parents (first degree cousins), that presented since birth with skin rash and recurrent sepsis, eventually leading to her death at the age of 10 months. The pregnancy was uneventful and full term. The birth weight was 2670 g with Apgar index of 6/7/9. The newborn was admitted to intensive care unit because of respiratory distress and generalized skin xerosis. Erythema with yellow crusted scales, similar to those seen in seborrheic dermatitis was seen over the scalp and face. There was also erythema on the neck and xerosis of the abdomen and marked erythema of the perineal area. Topical hydrocortisone was recommended twice daily on the affected regions, except the perineal area, were clotrimazole was applied. Despite these efforts, there was no improvement. On the eight day of life, fever and diarrhea developed, and antibiotherapy was started. A skin biopsy from the erosive dorsal area was obtained, as well as biopsies of the duodenal mucosa because of persistence diarrhea. Genetic evaluation was also requested.

Results:

Skin biopsies indicated focal neutrophilic exocytosis and mild spongiotic dermatitis.

The duodenal biopsy showed villous atrophy without intraepithelial lymphocytosis or signs of activity.

The genetic study identified a novel homozygous mutation in ADAM17. The diagnosis of Inflammatory skin and bowel disease linked to ADAM17 deletion was established.

The infant exhibited severe failure to thrive requiring parenteral nutrition. Off label dupilumab treatment was

attempted for 3 months with no response. Multiple and repeated infections, including sepsis as well as severe heart failure ultimately led to death at the age of 10 months.

Conclusion:

Neonatal inflammatory skin and bowel disease 1 (NISBD1) is rare and has been first reported only recently, with few cases described in the literature. Here we describe a new and severe case, featuring extensive erythema, intractable diarrhea requiring parenteral nutrition, and heart failure with recurrent sepsis resulting in death at a young age and no skin response to dupilumab.

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Abstract N°: 7026

A case series of ARCI: Phenotypes, genotypes and response to high-dose vitamin D therapy

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Introduction & Objectives:

Autosomal recessive congenital ichthyosis (ARCI) is a clinically and genetically heterogeneous condition. Phenotypes include non-bullous ichthyosiform erythroderma (NBIE), lamellar ichthyosis, and harlequin ichthyosis. There is significant variability in the severity of disease as well. Variants of around 14 genes have been implicated in ARCI, with many cases not having an established genetic cause. A clear genotype-phenotype correlation is also not evident in these disorders.

Therapeutic options are limited in severe cases. Acitretin, the current standard of care, has risk of cumulative toxicity with long-term therapy. Few reports have described good response to high-dose vitamin D therapy in ARCI, which merits further evaluation.

Materials & Methods:

Here we describe the phenotypes and genotypes in five cases of ARCI, which presented to our center over the period of a year. High-dose vitamin D3 therapy consisted of 60,000 IU orally every day for 10 days with close monitoring for toxicity. This was administered to two patients with hypovitaminosis D at baseline, after informed consent.

Results:

Three of the cases were associated with homozygous TGM1 mutations (two novel variants). All three cases had severe lamellar phenotype, with complications like ectropion and function-limiting acral keratoderma.

One case presented with NBIE, associated with dark-brown scaling and a unique maserung-like desquamation. Ectropion, deformed ears, and bilateral congenital vertical talus were also observed. Genetic testing revealed a pathogenic homozygous ALOX12B variant.

A novel homozygous LIPN variant was detected in a patient with lamellar ichthyosis, but the phenotype was significantly milder than that of the TGM1-related cases.

Two of the patients with TGM1-related ARCI had low vitamin D3 levels at baseline and were administered high-dose vitamin D3 therapy. The response was noted as desquamation of thick scales and clearing of the facial skin. Though some reduction of scaling and softening of skin were also noted over the trunk and limbs, these changes were not prominent.

Conclusion:

In our series of ARCI, TGM1 mutations (including two novel variants) were most frequently detected; all of which presented with a severe lamellar phenotype. Other cases included ALOX12B- and LIPN-associated

(novel variant) ichthyoses.

We also assessed the response to high-dose vitamin D therapy in two cases of TGM1-related ARCI. Except for clearing observed in facial skin, the response in our cases was suboptimal.

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Abstract N°: 7086

Mutation landscape of inherited palmoplantar keratoderma in an Indian cohort

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Introduction & Objectives: Inherited palmoplantar keratodermas (PPK) present as thickening of palms or soles and may be associated with other cutaneous or systemic features. Morphologically it is classified into diffuse, focal, striate and punctate PPK. While various classifications and distinct syndromes exist, it is often difficult to arrive at a purely clinical diagnosis and molecular analysis is often necessary for an accurate diagnosis. The objective of this study is to characterise the clinical features and genetic mutations in patients of PPK in an attempt to obtain a phenotype-genotype correlation.

Materials & Methods: This was a prospective observational study conducted in a tertiary care centre in India. Consecutive patients who presented with a predominant complaint of PPK were included. Baseline demographic and clinical characteristics were noted. Blood sample was obtained from the patients from which DNA was extracted and a targeted next generation sequencing was performed using a gene panel.

Results: A total of 14 patients were included, amongst whom 11 were male and 3 were female, with a median age of 14.5 years (7.8-36.3). The median duration of disease was 4 years (2-15) and the median age of onset was 7.5 years (3.5-14.3). The morphology was diffuse PPK in 10 patients, striate in two patients, focal in two patients and punctate in one patient. After gene sequencing, a pathogenic mutation was detected in six patients (42.8%). Missense heterozygous mutations were identified in KRT1 gene in patients 1 and 5 who had a clinical diagnosis of Vorner PPK and epidermolytic ichthyosis respectively. A frameshift heterozygous mutation in CYP4F22 gene was detected in patient 2 with a clinical diagnosis of epidermolytic ichthyosis, however the genotype was more consistent with autosomal recessive ichthyosis. A non-sense heterozygous mutation was detected in AAGAB gene in patient 3 with punctate PPK. Patient 4 presented with striate PPK had a missense homozygous mutation in DSG1. A missense heterozygous mutation was detected in patient 6 with focal PPK. Mutations were consistent with the phenotype in all except patient 2. Variant of uncertain significance (VUS) was detected in ATP2A2 gene in patient 1, TRPV3 gene in patient 2 and PKP1 and KRT5 gene in patient 6. VUS was also detected in two other patients in our cohort: KRT6C mutation in a patient with a clinical diagnosis of Bothnia/Nagashima type of PPK and PTPN11 mutation in a patient with a clinical diagnosis of loricrin PPK.

Conclusion: Correlation between genotype and phenotype of inherited PPK was observed in 83.3% cases of pathogenic mutations detected in our cohort. Further analysis with whole-genome sequencing in larger cohorts are needed to completely characterise the genotype of PPK patients in various populations.

Phenotype and genotype details of PPK patients
Pt. No
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Abstract N°: 7095

1-Year Update of Treatment of Hailey-Hailey Disease in a Female Patient Using Once-daily Roflumilast Cream 0.3%

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Introduction & Objectives:

Hailey-Hailey disease (HHD), also known as Benign Familial Pemphigus, is a rare genodermatosis with autosomal dominant inheritance and no current approved treatments. HHD is caused by mutations within the ATP2C1 gene leading to defective keratinocyte activity and barrier defect. The ATP2C1 gene codes for hSPCA1 (human secretory-pathway Ca2+/Mn2+-ATPase isoform 1) and regulates intracellular Ca2+ and Mn2+ concentrations. HHD presents as eroded erythematous plaques with rhagades (fissures in the skin usually in flexural areas) that develop from the rupture of vesicles or bullae, causing chronic pain. Lesions tend to occur in intertriginous locations, such as the neck, axillae, inframammary area, and genitals. Roflumilast cream 0.3% is a potent topical phosphodiesterase 4 (PDE4) inhibitor approved in 2022 by the FDA for the treatment of psoriasis, including intertriginous disease. The structural and mechanistic underpinnings for roflumilast's higher affinity binding to PDE4, relative to other approved PDE4 inhibitors, has been elucidated by applying structural and computational biology techniques.1 Here we report a 1-year update on a case of HHD that was successfully treated with roflumilast cream 0.3% once daily (QD) after 5 weeks.

Materials & Methods:

A 46-year-old female with biopsy proven disease with clinical presentation on approximately 10-15% of her body with erosions on the trunk, inframammary, lower back, and arms. Disease was uncontrolled with exquisitely painful presentation and minimal disease response or improvement with decades of prior treatments. Chronic pain, weeping, and bleeding had a negative impact on QoL which escalated during menses. Past treatments included systemic and topical agents; antibiotics, corticosteroids, calcineurin inhibitors, antifungals, retinoids, and benzoyl peroxide. While completing workup and mandatory 30 day hold prior to starting oral isotretinoin, treatment with roflumilast cream 0.3% QD as monotherapy was started.

Results:

Following 5 weeks of treatment, areas of raw skin had resolved with no weeping erosive plaques, including inframammary erosions. The assessment of overall disease severity improved to 2/10 (mild), which the patient reported to occur after 1 week. Affected skin had re-epithelialized with some post-inflammatory hyperpigmentation. The patient reported improvement in pain associated with HHD symptoms within 1-2 weeks of application, achieving 0/10 (no pain) for the first time since diagnosis. Since then, the patient has had a continued response to roflumilast cream 0.3% QD for the past year resulting in no pain, no swelling, and no redness. The patient continues to be happy with treatment and will continue to use roflumilast for the treatment of her HHD.

Conclusion:

We report the case of a 46-year-old patient with HHD successfully treated with roflumilast cream 0.3% QD monotherapy after prior treatment failure. Improvement in the symptoms of HHD were documented clinically after 5 weeks and have been sustained over a year with roflumilast 0.3% cream QD therapy. This report suggests

reduction of inflammation treatment with a potent topical PDE4 could offer a long-term and well tolerated treatment option for patients with HHD.

1Wang J, Bunick CG. J Investig Dermatol. 2023.143;S194. #1130

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Abstract N°: 7250

Brooke-Spiegler Syndrome – a new genetic variant description causing disease

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Introduction & Objectives:

Brooke Spiegler Syndrome or CYLD cutaneous syndrome is a rare autosomal dominant disease characterized by multiple benign adnexal skin tumors developing mainly in the centrofacial area and rarely at other extrafacial sites. The lesions are usually either cylindromas, spiradenomas or trichoepitheliomas. Histologically lesions may assume hybrid forms intermixing different kinds of lesions.

Materials & Methods:

Case Report.

Results:

A 28-year-old woman, born in Angola, without relevant past medical history other than the onset of multiple centrofacial, monomorphic lesions during her adolescence. She had undergone multiple surgeries in Brazil, South Africa and Namibia but the lesions kept appearing. She also mentioned that a biopsy revealed a trichilemmoma (sic). A skin biopsy was performed and a genetic study focusing on the CYLD gene was requested. Histopathology showed features consistent with a basaloid appendageal tumor with eccrine and piloid differentiation, suggesting a hybrid tumour. Genetic testing identified the variant c.808-1G>C in the CYLD gene (NM_001378743.1) present in heterozygosity and classified as likely pathogenic (PMID:25741868). To the best of our knowledge, this variant was not previously described, namely in population databases, such as genomAD, ClinVar disease database or recent reports. As this variant is located at a canonical splice site, computational predictive models (SpliceAI and CADD) support alteration of the splicing site, potentially resulting in an aberrant protein.

The patient is currently undergoing ablative CO2 laser treatment sessions for the treatment of the most significant tumours. The patient was also referred to genetic consultation.

Conclusion:

A new pathogenic variant causing Brooke Spiegler syndrome is described, emphasizing the need for genetic testing and consultation in the case of certain tumors of the centrofacial location.

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Abstract N°: 7276

Two cases of atopic dermatitis with pigmentary modifications associated with Seckel syndrome: a rare entity

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Introduction & Objectives:

Seckel syndrome is an extremely rare autosomal recessive disorder characterized by pediatric microcephaly. It involves significant intrauterine growth retardation, microcephaly, facial dysmorphia, and intellectual disability. We report two unusual cases of two brothers with Seckel syndrome associated with atopic dermatitis.

Case report:

These are two male siblings aged six and twelve, respectively, born from a first-degree consanguineous marriage, presenting with microcephaly, facial dysmorphia, and psychomotor delay. Clinical examination revealed two conscious but restless children with characteristic facial dysmorphia, including microcephaly, a low and receding forehead, a proportionally larger nose, and small, closely set eyes with blepharophimosis. Dermatological examination of the younger child showed generalized cutaneous xerosis, pruritic eczematous lesions, diffuse hyperpigmentation, fissured cheilitis, palpebral hyperpigmentation associated with blepharitis, and leukonychia of the fingernails and toenails. In the second child, less intense cutaneous xerosis was observed, along with chronic pruritus, pigmentation of the knees, blepharitis, and leukonychia of the nails.

Discussion:

Seckel syndrome, first defined by Seckel in 1960, is a rare autosomal recessive disorder with no gender predilection, with a reported incidence of 1 in 1,000,000 live births. In most cases, the diagnosis of Seckel syndrome is based on key features, including severe intrauterine growth retardation, microcephaly, a characteristic “bird-like head” profile, and intellectual disability. In both presented cases, the diagnosis of Seckel syndrome was established based on the medical history, developmental delay, and clinical and radiological characteristics. To date, three responsible genes are located on chromosome 3 (3q22-q24) for Seckel 1, chromosome 18 (18p11.31-q11) for Seckel 2, and chromosome 14 (14q21-q22) for Seckel 3. This syndrome is associated with skeletal, neurological, ophthalmological, cardiac, and hematological impairments. However, rare cases reported in the literature mention dermatological involvement, as observed in our patients.

Conclusion:

Seckel syndrome is a rare disorder. Its diagnosis is primarily clinical and can be made prenatally, with management predominantly focused on symptomatic treatment.

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Abstract N°: 7434

A Novel Pathogenic Mutation of the POFUT1 Gene in a Turkish Patient with Dowling-Degos Disease

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Introduction & Objectives:

Dowling-Degos disease (DDD) is a rare automosomal dominant genodermatosis characterized by the gradual emergence of reticulated pigmented lesions, primarily affecting flexural regions of the skin. The pathogenesis is linked to mutations in specific genes, including POFUT1.

Materials & Methods:

Here we report a patient with flexural hyperpigmentation who was diagnosed as DDD with novel pathogenic variant of the POFUT1 gene based on clinical, histopathological and genetic findings.

Results:

A 51-year-old Turkish female patient presented with asymptomatic, bilateral pigmented axillary and inguinal lesions that had developed over 10 years. Dermatological examination revealed reticular hyperpigmented macules and patchs on her face, neck, bilateral axillae, arms, hand dorsums, inframammarian folds, intermammarian area and inguinal areas and pits on bilateral palmar regions. Histopathological analysis of hiperpigmented patch from intermammary area showed regular epidermal hyperplasia, keratin cysts in the epidermis, elongation of the rete ridges, focal pigment increase in the tips of rete. Genomic DNA was extracted from the patient's peripheral blood sample. Whole exome DNA sequencing identified a novel heterozygous mutation, NM_015352.2:c.1047dupC NP_056167.1 (p.Phe350LeufsTer34) in POFUT1. The patient was diagnosed with DDD. She was initiated on oral isotretinoin treatment, but discontinued the drug due to its adverse effects.

Conclusion:

DDD is a benign genodermatosis classified as a reticular pigmented dermatosis. The lesions typically manifest in adulthood between the second and fifth decade on flexural sites, presenting as symmetric and progressive macular reticular hyperpigmentation with reddish-brown papules and plaques.

DDD is associated with mutations in the keratin 5, POGLUT1, POFUT1 and PSENEN genes. In 2013, Li et al. identified a POFUT1 gene mutation on chromosome 20q11. The POFUT1 gene encodes the protein O-fucosyltransferase 1, which is related to NOTCH receptors. The results of the functional analysis demonstrated that POFUT1 plays a role in melanin synthesis and transport.

The genetic analysis revealed the presence of a novel pathogenic heterozygous variant, NM_015352.2(POFUT1):c.1047dupC (p.Phe350LeufsTer34), in our patient. This variant has not been previously reported in the databases of the National Center for Biotechnology Information (NCBI), the Database of Single Nucleotide Polymorphisms (dbSNP), the Human Gene Mutation Database (HGMD® Professional 2023.3), or the Clinical Variation Database (ClinVar).

In the literature, a range of clinical findings have been reported in DDD patients associated with different POFUT1 gene mutations. In accordance with the majority of previous reports, the intertriginous regions, face, arms and

hand dorsums were affected in our patient. Furthermore, the presence of palmar pits, which has been reported in a few cases, was also present. A few cases of DDD have been reported in the literature with distinct clinical findings, including an association with HS and multiple seborrheic keratoses. However, our patient did not demonstrate these associations.

This novel mutation, c.1047dupC (p.Phe350LeufsTer34), is reported herewith to contribute to the POFUT1 gene database. Further reports may be helpful in elucidating the relationship between pathogenic variations of the POFUT1 gene and different phenotypes.

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Abstract N°: 7459

h syndrome, a non langerhans histiocytosis to know

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Introduction & Objectives:

Syndrome H is a rare genodermatosis characterized by hyperpigmentation with cutaneous sclerosis overlaid with hypertrichosis and other systemic manifestations overlapping with various other conditions. We report the case of a patient diagnosed with Syndrome H. Through our case, we aim to highlight the uniqueness of Syndrome H, a rare nonLangerhans histiocytosis.

Observation:

We present a 24-year-old patient, born of non-consanguineous parents, with type 1 diabetes since the age of 7, managed with insulin. The patient consulted for the appearance of hyperpigmented sclerotic skin lesions and edema of the lower limbs. Cutaneomucosal examination revealed hyperpigmented sclerotic plaques overlaid with hypertrichosis, located on the lower and upper limbs, lower back, abdomen, and trunk, sparing the knees and popliteal fossae. Joint examination revealed swelling of the knees and ankles, flat feet, bilateral hallux valgus, and joint infiltration. Ophthalmological examination showed moderate exophthalmos, conjunctival hyperemia, bilateral arcus cornealis, and diabetic retinopathy. There was no gynecomastia or hypoacusis, but abdominal examination revealed hepatomegaly without other associated organomegaly. Laboratory investigations showed no anemia on complete blood count, no biological inflammatory syndrome, and no associated cardiac involvement. Hormonal assessment was normal, and erythrocyte sedimentation rate revealed chronic inflammatory syndrome.

Discussion:

Typically, cutaneous involvement of H Syndrome begins to appear during the first or second decade of life. The main clinical manifestations include cutaneous and systemic signs starting with the letter “H,” mainly bilateral and symmetrical hyperpigmentation with induration in 91% of cases and hypertrichosis in 68% of cases. These two signs initially appear on the inner thighs and shins, sparing the knees and popliteal fossae, and the genital organs. Finger flexion contractures may be present in 56% of cases, followed by hepatomegaly in 43% and splenomegaly in 39% of cases. Insulin-dependent diabetes is almost always present, small stature in 49% of cases, hypoacusis or deafness in 53% of patients, cardiac involvement in 34% of cases, hallux valgus in 25%, and hypogonadism. Other characteristics are also frequently described, such as anemia, hypergammaglobulinemia, and diffuse lymphadenopathy present in 24% of cases. Symptoms associated with diffuse organ infiltration have also been described. Indeed, some of these conditions may be absent in 85% of cases. Recent studies have shown that tocilizumab, a humanized monoclonal antibody directed against the IL-6 receptor, has a striking response to treatment by reducing hyperpigmentation and subcutaneous fibrosis, accelerating growth velocity, and improving inflammatory indices, induration, and anemia. Tocilizumab is also highly effective for the treatment of inflammatory manifestations such as arthritis and organ infiltration. It could be a promising treatment for this syndrome. Further studies are needed to better understand the role of IL-6 in the pathogenesis of H syndrome.

Conclusion:

Despite the more in-depth identification and better understanding of the pathophysiology of H syndrome, the

diagnosis remains challenging as its characteristics overlap with many other rheumatological, cutaneous, and genetic diseases. Further research on treatment will be necessary for patient relief.

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Kyrle's disease: a serie of 4 cases

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Introduction & Objectives: Kyrle's disease is a rare acquired perforating dermatosis. We report four observations of this entity in diabetic patients.

Results: Four patients were enrolled, including three men and one woman, aged from 43 to 69 years old. All patients had diabete: type 1 for men and type 2 for the woman. A diabetic nephropathy was found in two cases. Hemodialysis was performed for renal failure in two cases. In addition to diabete, one patient had arterial hypertension and the other gout. All patient presented with a pruritic rash of keratotic papules. The course of the disease was progressive in all patients, ranging from six months to two years. Clinical examination revealed multiple hyperkeratotic papules in all patients, mimicking the appearance of lichen planus. These lesions occurred in the limbs in three cases, the trunk and buttock in one case. Dermoscopy showed in all cases, from center to periphery: a central crust or scale, a grayish white area structureless, a pinkish area structureless, and a peripheral brownish area. Histology revealed a crater-shaped depression filled with keratin lamellae in all cases, associated with a few necrotic keratinocytes in two cases. Treatment included topical corticosteroids and oral antihistamines in all cases. Acitretin was combined with topical treatment in one case.

Conclusion: Kyrle's disease is a rare papulokeratotic dermatosis associated with an underlying disorder such as diabetes mellitus or chronic renal failure, as our cases. Our serie is in line with the literature in terms of male predominance, frequency of pruritus and predilection involvement of the lower limbs. Clinically, the diagnosis can be difficult and may be mistaken for nodular prurigo or hypertrophic lichen planus, as in our patients. The dermoscopic features found are comparable to those described in the literature. This dermoscopic appearance reflects the histological signs: the central crust corresponds to the keratotic material filling the erosion of the epidermis; the greyish structureless zone reflects the thinning of the dermoepidermal junction by invagination of the epidermis; the pinkish structureless zone corresponds to active inflammation with increased vascularization of the dermis. The peripheral hyperpigmented zone is related to melanocytes and increased pigmentation of the basal layer of the epidermis. Treatment is mainly symptomatic, based on emollients and keratolytics. Other options include topical or systemic retinoids, surgery or CO2 laser and phototherapy.

Kyrle's disease is a rare entity, which should be suspected in the presence of pruritic keratotic lesions, particularly in diabetic patients and those suffering from renal failure. Dermoscopy is a non-invasive, valuable technique that can be helpful in the diagnosis of this dermatosis.

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The Use of Multiple Therapeutic Modalities : Topical 80% Trichloroacetic Acid, Electrodessication, And Surgical Excision In Treatment of Cutaneous Type 1 Neurofibromatosis

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Introduction & Objectives:

Type 1 Neurofibromatosis is a genetic disease characterized by the presence of tumors in the nervous system and skin. Therapeutic modalities for type 1 neurofibroma can include surgical excision therapy, electrosurgical therapy, laser therapy, target cell therapy and topical therapy which is currently still in the research stage. We report a case of cutaneous NF1 with several complications that occurred in a teenager who was treated with various modalities, such as topical 80% Trichloroacetic Acid (TCA) surgical excision, and electrodessication which gave good results.

Materials & Methods:

A 16-year-old female presented with complaints of nodules on her face six years. Initially, there was only one lump, but over time, more appeared in various sizes. The nodules were skin-colored non-painful or itchy. The patient had one kidney removed for indications of Renal Ephiteloid Angiomyolipoma. Dermatological examination revealed multiple skin-colored nodules on the facial region without hyperpigmented macules (café-au-lait spots). Dermoscopy showed homogeneous pigmented nodules, fingerprint-like areas, and a pigmented network. Histopathological examination conclusion were neurofibroma type 1. Head CT scan revealed hyperintense cortical lesions consistent with cortical neurofibroma. Patients were treated with various therapeutic modalities such as topical 80 % TCA surgical excision, electrodessication, and supportive therapy.

Results:

In this case, the patient was given several therapeutic modalities, such as surgical excision therapy for large lesions, electrodessication therapy for smaller lesions and other lesions were treated with topical 80% TCA which was carried out every week. Electrodessication is an alternative ablative method performed by dehydrating and denaturing tumors using ablative techniques. In fact, there have been no reports regarding the use of 80% TCA in neurofibromatosis patients, however quite satisfactory results were obtained in this patient. This is related to the TCA mechanism of action with a concentration of 80-90% which works by denatured proteins from tissue, and has a caustic effect which lead to fast coagulation and necrosis effects in superficial tissue.

Conclusion:

Neurofibromatosis type 1 is a disease that presents various complications. Therapy with topical 80% TCA electrodesiccation, surgical excision can provide good outcomes for skin lesion in NF1 patients.

Keyword : Type 1 Neurofibromatosis, 80% Trichloacetic Acid

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Acrokeratosis verruciformis of hopf: fallelic disorder

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Introduction & Objectives:

The relationship between Acrokeratosis verruciformis of Hopf (AVH) and Darier's Disease (DD) has been debated for several years, and even today this association remains controversial (1,2). We present a case of a patient with clinical features of AVH, but with histological changes characteristic of DD.

Materials & Methods:

An 18-year-old female presented with a 7 year history of permanent and asymptomatic lesions on the back of her hands and feet. Over time, the lesions have increased in number. She also mentioned that some family members have similar skin findings in the same locations. A skin biopsy from the back of her left hand was consistent with AVH. However, evidence of dyskeratosis and acantholysis suggestive of DD was also found

Results:

Although both genodermatoses result from genetic defects in the ATP2A2 gene (3), two specific mutations (pro602Leu and A698V) have been associated with the development of AVH, unlike DD which has been linked to a variety of mutations in the same gene (1,2). Overlapping histopathological features between these two dermatoses have been reported in the literature (4), leading to suggestions that they may represent the same entity, with AVH being a milder or initial manifestation of DD (5). However, given the existence of familial cases with exclusive manifestations of AVH (1), as well as distinct histopathological and clinical findings (Table 1), some still consider them as separate diseases (1,2,4).

Acrokeratosis verruciformis of Hopf	Darier's Disease
Papillomatosis Acanthosis Hyperkeratosis Hypergranulosis	Disqueratosis Acantolísis
No mucosal involvement nor seborrheic areas. Pachyonychia	Keratotic papules with seborrheic distribution V-shaped nail notches. White and red longitudinal nail bands. Whitish intraoral papules, especially on hard palate.

Table 1. Differences in clinical and histological features between Acrokeratosis Verruciformis of Hopf and Darier's Disease.

Conclusion:

Despite cases showing histological overlap between these two dermatoses, they are distinct clinical entities. AVH and DD are allelic disorders, and the presence of shared characteristics may indicate a possible progression from AVH to DD. Keywords Darier's Disease Allelic Imbalance Genodermatoses

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Clinical profile and Genetic Analysis of Epidermolysis Bullosa Cases in North Region of India

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Introduction & Objectives: Epidermolysis bullosa (EB) is a rare and heterogeneous hereditary condition affecting the skin and mucous membranes. EB is characterized by skin fragility, leading to blistering and tearing with minimal friction. This study aimed to collect EB patients across north region of India, perform targeted gene panel sequencing, and assess the correlation between genotypic and phenotypic expressions.

Materials & Methods: A single-center, retrospective study in the Department of Dermatology at the Postgraduate Institute of Medical Education and Research (PGIMER) in Chandigarh was conducted. The whole study was conducted after ethical clearance was obtained from the Institutional Review Board and informed consent was obtained from the patients before initiation. A total of 50 patients with a clinical diagnosis of EB were seen between 2019 to 2022, from the Outpatient Department of Dermatology. Baseline demographic data, birth history, family history, collodion membrane presentation, skin manifestation at birth, past medical history, current cutaneous manifestations, and the evolution of the disease were assessed. Genomic DNA was screened for mutations using targeted gene panel sequencing of 23 genes related to EB, and genetic alteration analysis was performed.

Results: In the current study, a total of 50 patients were subjected to targeted gene panel sequencing. Genetic analysis of 50 patients revealed 16 individuals with recessive form of DEB (32%), 12 individuals with junction epidermolysis bullosa (24%), and 10 individuals with epidermolysis bullosa simplex. Eight patients out of all sequenced patients were observed with the condition of dominant dystrophic epidermolysis bullosa (DDEB: 16%), while two were with Kindler EB (4%). The remaining two patients' DNA samples failed to be sequenced. 7 new and 3 previously known mutations were observed in DDEB patients, while RDEB patients revealed 12 new and 4 previously known mutations. Out of 12 RDEB patients, 7 patients (58.33%) revealed compound heterozygous mutations, while 5 patients (41.66%) revealed homozygous alterations in the *COL7A1* gene. The patients with JEB were observed with mutations in the *LAMB3, LAMC2,* and *COL17A1* genes. EBS patients were observed with missense heterozygous mutations in the *KRT5* gene. The patients with Kindler EB revealed heterozygous mutations (one is a splice-site mutation and the other is an insertion mutation) in the *FERTM1* gene.

Conclusion: This study represents the third largest investigation focusing on the clinical and molecular aspects of an epidermolysis bullosa (EB) cohort in India. Our observations indicate a relationship between genotype and phenotype, consistent with earlier studies, revealing the wide range of clinical manifestations and identifying new disease-causing genetic variations. Interestingly, our study yielded different results regarding genotype prevalence compared to existing literature. However, given the rarity of EB and our limited sample size, additional case collections are necessary to establish a robust genotype-phenotype association. In conclusion, our findings provide valuable insights for future clinical assessments and the potential implementation of stratified

management approaches.**

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Phase I study results of a novel immunomodulatory peptide, TCP-25, for treatment of dystrophic epidermolysis bullosa

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Phase I Study Results of a Novel Immunomodulatory Peptide, TCP-25, for Treatment of Dystrophic Epidermolysis Bullosa

Introduction & Objectives: Dystrophic Epidermolysis Bullosa (DEB) is a rare genetic disorder characterized by skin fragility and chronic blistering, leading to wounds prone to bacterial colonization and inflammation. Given the severe wound burden and limited treatment options, novel therapies are urgently needed. Excessive toll-like receptor (TLR)-driven inflammation in DEB patients hinders healing and raises carcinogenesis risk. TCP-25, an immunomodulatory peptide with antimicrobial and anti-inflammatory effects, scavenges bacterial proinflammatory products and disrupts CD14-TLR signaling, showing promise in experimental wound models (Puthia et al., Sci Transl Med 2020).

A TCP-25-containing gel is in development for the treatment of DEB, and we have conducted a three-part Phase I safety study to prepare for its testing in DEB patients. Part I involved 24 healthy volunteers with suction-induced epidermal wounds, while Part II included 6 patients with non-healing leg ulcers, with the main results reported separately. Here, we present the results of Part III, which focuses on assessing the safety, tolerability, and systemic exposure of TCP-25 in DEB patients, along with an exploratory endpoint on wound healing.

Materials & Methods: Part III of the study was an open-label, single-arm, ascending-dose trial. Five DEB patients received TCP-25 gel at 2.9 mg/mL or 8.6 mg/mL, applied three times per week for four weeks. Each patient's primary wound was treated with TCP-25 gel, paired with a similar reference wound treated with standard care. A secondary, non-matching wound also received TCP-25. Patients attended six clinic visits for treatment and follow-up, plus an end-of-study call. Wounds were photographed and sampled during visits, with at-home gel application between visits.

Results: No abnormal local reactions, withdrawals due to adverse effects (AEs), or serious AEs occurred. All AEs were mild to moderate, with 3 DEB patients experiencing wound-related AEs of this intensity. Except for 1 AE possibly linked to gel product adhesion, all AEs were deemed unlikely related to TCP-25. No TCP-25 was detected in plasma. TCP-25 positively impacted wound healing in DEB patients, with mean/median area reductions of 80%/76% for primary wounds and 73%/78% for secondary wounds, compared to 29%/67% for reference wounds.

Conclusion: This Phase I Study established TCP-25 gel as safe and well-tolerated, with no systemic peptide uptake at concentrations up to 8.6 mg/mL. Given its mode of action—scavenging bacterial proinflammatory products and interfering with CD14-TLR signaling—TCP-25 may therefore target the excessive inflammation that hinders wound healing in DEB patients. The observed wound-healing benefits in DEB patients highlight TCP-25's potential as a promising new treatment option for DEB.