EA DV SYMPOSIUM 2026
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Abstract N°: ID-49

Topic: Genetics, inherited skin diseases

Management of Painful Segmental Cutaneous Leiomyoma in HLRCC Syndrome: Efficacy of Topical Calcium-Channel Blockers Validated by Cold-Provocation Test

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Introduction

Cutaneous leiomyomas are benign smooth-muscle tumors that frequently cause paroxysmal, difficult-to-manage pain triggered by cold, pressure, or emotion. The pain mechanism involves calcium-dependent smooth-muscle hypercontractility, providing a rationale for the use of calcium-channel blockers (CCBs). However, systemic CCB therapy is often limited by adverse effects such as hypotension and dizziness. We present a case of segmental cutaneous leiomyoma associated with Hereditary Leiomyomatosis and Renal Cell Cancer (HLRCC) syndrome, successfully managed with a novel approach using topical diltiazem. This report highlights the diagnostic importance of segmental presentation and validates the therapeutic efficacy through a controlled cold-provocation test.

Materials and Methods

A 61-year-old man presented with a 38-year history of multiple painful papulonodules in a segmental distribution on the left abdomen. The pain was severe (Visual Analogue Scale [VAS] 9/10) and impaired daily functioning. Diagnosis was confirmed via histopathological examination (Figure 1). Given the segmental pattern, genetic testing for the fumarate hydratase (*FH*) gene was performed. To objectively assess the efficacy of topical treatment, a standardized cold-provocation test was implemented. This involved controlled ice application with time-series pain recording (VAS) to measure onset, peak intensity, and recovery time before and after the initiation of topical therapy.

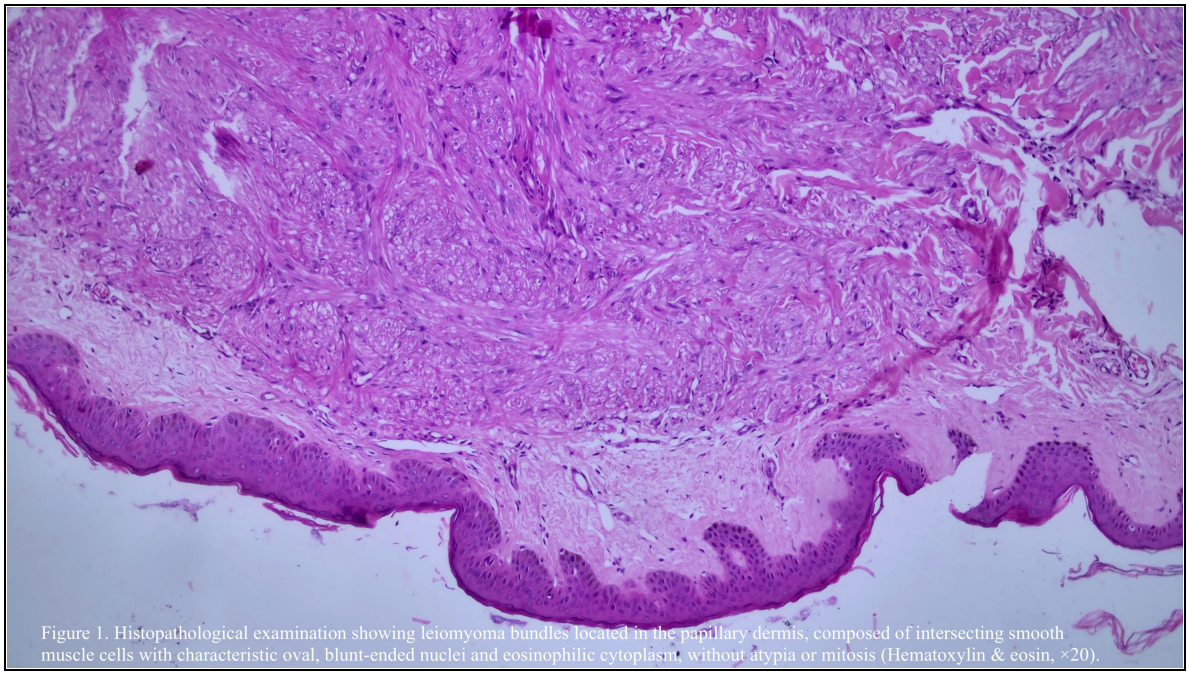

Figure 1. Histopathological examination showing leiomyoma bundles located in the papillary dermis, composed of intersecting smooth muscle cells with characteristic oval, blunt-ended nuclei and eosinophilic cytoplasm, without atypia or mitosis (Hematoxylin & eosin, ×20).

Results

Genetic analysis identified a pathogenic heterozygous splice-site variant (c.1391-2A>G) in the *FH* gene, confirming the diagnosis of HLRCC. Initial treatment with oral amlodipine (5 mg/day) reduced resting pain to VAS 5/10 but dose escalation was prevented by dizziness. The addition of topical diltiazem 2% cream twice daily resulted in a further reduction of resting pain to VAS 2/10 and significant improvement in Brief Pain Inventory (BPI) scores. The cold-provocation test objectively demonstrated that topical diltiazem delayed pain onset, lowered peak pain intensity (from VAS 9.5 to 6.0), and accelerated recovery time compared to baseline (Figure 2). No local irritation or systemic adverse effects were observed during the follow-up.

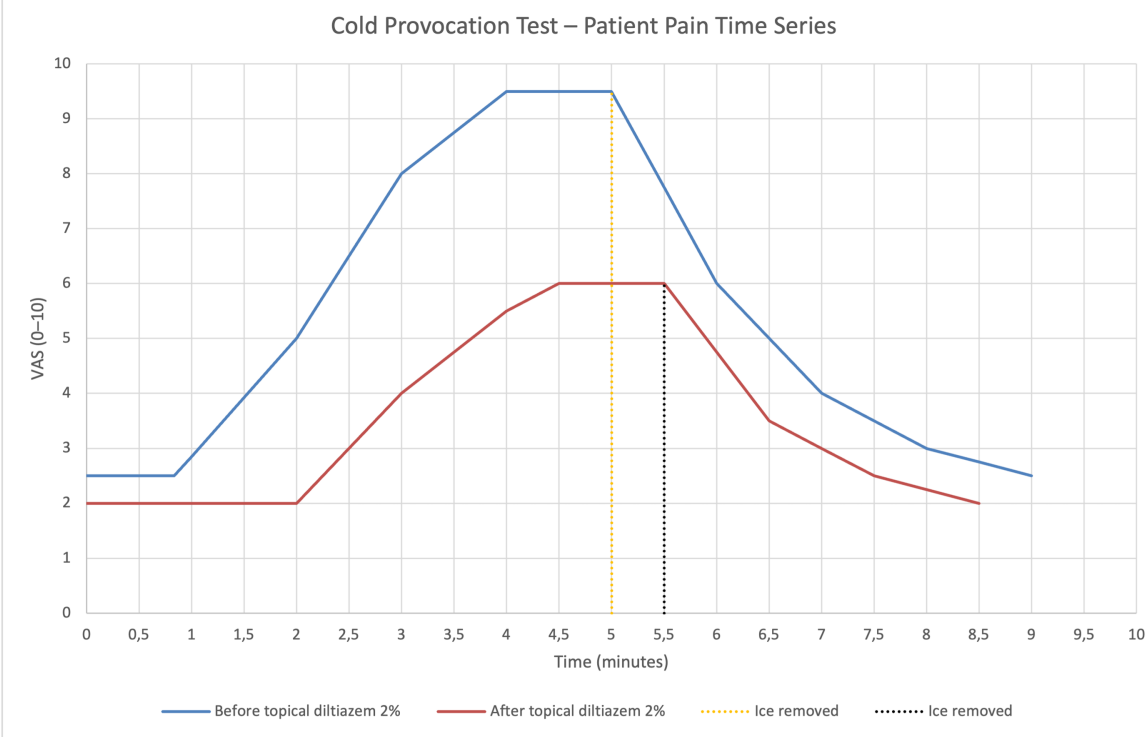

Figure 2. Cold-provocation pain curves before and after topical diltiazem 2%. VAS scores show lower peak and faster recovery after treatment.

Conclusions

This case highlights two critical clinical points. First, segmental cutaneous leiomyomas should prompt genetic evaluation for HLRCC, even in the absence of family history, to enable early renal cancer surveillance. Second, topical diltiazem serves as a mechanistically rational, non-invasive, and well-tolerated treatment for painful leiomyomas in HLRCC patients, particularly when systemic options are limited by adverse effects. Furthermore, the use of a standardized cold-provocation test provided objective evidence of its analgesic efficacy, offering a valuable assessment tool for future studies.

Abstract N°: ID-90

Topic: Genetics, inherited skin diseases

A Case of Neurofibromatosis Type 1 Caused by a Novel NF1 Mutation

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Introduction
Neurofibromatosis type 1 (NF1) is an autosomal dominant disorder caused by pathogenic variants in the *NF1* gene, here we reported a novel *de novo* frameshift insertion (c.7926_7927ins[base]) in the *NF1* gene inducing the phenotype of neurofibromatosis type 1.

Materials and Methods
The patient is a 10-year-old male with a non-contributory family and birth history. His clinical presentation began at approximately 2 years of age with the appearance of multiple café-au-lait macules (CALMs) on the trunk and limbs, which progressed in number and size. At age six, he developed axillary and inguinal freckling, followed by the emergence of multiple, tender, and progressively enlarging subcutaneous nodules on the upper limbs and neck at age seven.Physical examination (Fig.1) revealed numerous well-defined brown macules, 0.5-1.5 cm in diameter, scattered across the body. Over 20 firm, well-defined, and mobile subcutaneous nodules, ranging in size from soybean to red date, were observed on the upper limbs, neck, chest, back, and lumbar region. No iris abnormalities, skeletal deformities, or other systemic diseases were detected.Routine laboratory studies were unremarkable. Brain MRI demonstrated multiple unidentified bright objects (UBOs), characteristic of neurofibromatosis. Whole-body imaging revealed extensive neurofibroma involvement, including multiple small nodules distributed along the spinal axis, peripheral nerves, and a characteristic plexiform neurofibroma(pNF) inferior to the left sacroiliac joint.

Results
Whole-exome sequencing identified a *de novo NF1* variant, c.7926_7927dup (p.Lys2643Ilefs*16), which was confirmed by Sanger sequencing to be absent in both parents (Fig. 2). This variant is unreported in pathogenic mutation databases (e.g., HGMD Pro, ClinVar) and absent from healthy population cohorts (e.g., EXAC, 1000 Genomes), supporting its classification as a novel pathogenic mutation. A novel *de novo* frameshift insertion (c.7926_7927ins[base]) was identified in the *NF1* gene. This mutation alters the reading frame from codon 2643 (p.Lys2643Ile), leading to a premature stop codon 16 residues downstream (p.Lys2643Ilefs*16) and a truncated protein lacking 159 C-terminal amino acids. The mutant transcript is likely subjected to nonsense-mediated mRNA decay, resulting in loss of function. The variant was absent in population databases (PM2_Supporting). Following four months of selumetinib treatment, the patient demonstrated regression of subcutaneous nodules, indicating a clinical benefit, despite no significant change in cutaneous neurofibroma scores on the Nef-ASI scale.

Conclusions
This case, diagnosed via whole-exome sequencing, identifies a novel *NF1* mutation that broadens the spectrum of known pathogenic variants and enhances the understanding of genotype-phenotype correlations. Furthermore, it

corroborates existing evidence that selumetinib can effectively control neurofibroma growth and induce tumor regression with a favorable safety profile.

Abstract N°: ID-165

Topic: Genetics, inherited skin diseases

Arg24Pro is the most common pathogenic CDKN2A detected in an extended cohort of Greek familial and multiple primary melanoma patients

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Introduction
Approximately 5-10% of melanoma cases appear in a familial or mutliple melanoma (MPM) context. In familial melanoma cases, high penetrance genes are implicated including *CDKN2A, CDK4, POT1, TERT, ACD, TERF2IP, MITF* and *BAP,* with *CDKN2A* being the most commonly detected gene. The aim of this study was to investigate the type and frequency of *CDKN2A* variants in a cohort of Greek familial and MPM patients. We also aimed to evaluate the frequency of the most commonly detected variants in the general population.

Materials and Methods
A total number of 147 melanoma families were studied, including 169 affected individuals (86 women and 83 men). We performed targeted sequencing in genetic regions of all known high-penetrance genes implicated in melanoma predisposition. In order to evaluate the frequency of these variants in the general population, we used WES data from 750 unaffected controls.

Results
36/147 (24.5%) families carried pathogenic *CDKN2A* variants. Arg24Pro was the most frequently observed variant in our cohort detected in 20/36 (55.6 %) melanoma families carrying *CDKN2A* mutations, while Trp110* was the second most common variant detected in 10/36 (27.8 %) families. None of these variants were detected in the general population.

Conclusions
Our results show that Arg24Pro is the most common pathogenic variant in Greek familial and MPM patients, suggesting a possible founder effect in our population.

Abstract N°: ID-258

Topic: Genetics, inherited skin diseases

Dermatologic Comorbidities in Patients with Neurofibromatosis Type 1: A Nationwide Population-Based Cohort Study

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Introduction
Neurofibromatosis type 1 (NF1), associated with numerous comorbidities, results in a shorter life expectancy. NF1 frequently affects the skin, contributing to a lower quality of life in patients. However, comprehensive studies on cutaneous comorbidities in NF1 are limited.

Materials and Methods
Patients with a diagnostic code for NF1 between 2009-2023 were 1:3 paired with an age- and birth-year-matched population from the control group, comprising patients with hemangioma of skin and subcutaneous tissue. National insurance data were retrospectively reviewed to assess rate ratios (RR) of cutaneous disorders.

Results
Overall, 28,082 patients with NF1 were matched to 84,246 patients from the control group. Patients with NF1 had significantly elevated risks for several dermatologic conditions, including histiocytosis syndromes (RR 7.36, 95% CI 4.03–13.43), mastocytosis (RR 3.21, 95% CI 1.77–5.84), xanthelasma palpebrarum (RR 3.06, 95% CI 1.93–4.86), radiodermatitis (RR 2.94, 95% CI 1.66–5.20), trichotillomania (RR 2.72, 95% CI 1.05–7.06), decubitus ulcer and pressure area (RR 1.79, 95% CI 1.68–1.92), benign lipomatous neoplasm of skin (RR 1.61, 95% CI 1.53-1.69), and malignant melanoma (RR 1.50, 95% CI 1.03–2.16). Notably, histiocytosis syndromes and mastocytosis predominantly developed during the second year of life. The mean age at diagnosis of non-melanoma skin cancer was significantly lower in the NF1 group compared to controls (61.99 ± 17.46 vs 66.91 ± 16.85 years, p=0.002).

Conditions	NF1 (n = 28,082)	Control (n = 84,246)	RR (95% CI)
Non-neoplastic			
Histiocytosis disorders[a]	36 (0.13)	15 (0.02)	7.36 (4.03, 13.43)
Cutaneous mastocytosis	20 (0.07)	17 (0.02)	3.60 (1.89, 6.88)
Xanthelasma palpebrarum	36 (0.13)	36 (0.04)	3.06 (1.93, 4.86)
Radiodermatitis	23 (0.08)	24 (0.03)	2.94 (1.66, 5.20)
Trichotillomania	8 (0.03)	9 (0.01)	2.72 (1.05, 7.06)
Decubitus ulcer and pressure area	1,317 (4.69)	2,252 (2.67)	1.79 (1.68, 1.92)
Neoplastic			
Benign			
Benign lipomatous neoplasm of skin and subcutaneous tissue	2,544 (9.06)	4,947 (5.87)	1.61 (1.53, 1.69)
Lipomatosis, not elsewhere classified	69 (0.25)	67 (0.08)	3.16 (2.26, 4.42)
Malignant			
Melanoma	42 (0.15)	86 (0.10)	1.50 (1.03, 2.16)

Values are presented as number (%).
[a]Includes xanthogranuloma, reticulohistiocytoma, and sinus histiocytosis with massive lymphadenopathy.
NF1 : neurofibromatosis type 1, RR : rate ratio, 95% CI : 95% confidence interval.

Table 1. Skin comorbidities with increased rate ratio in patients with neurofibromatosis type 1

Conclusions

Several dermatologic comorbidities were significantly associated with NF1. The early onset of juvenile xanthogranuloma and mastocytosis may serve as diagnostic clues in suspected NF1 cases. Given the increased susceptibility to skin malignancies, regular evaluation of newly developed lesions is warranted in this population.

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Abstract N°: ID-262

Topic: Genetics, inherited skin diseases

Steatocystoma multiplex: an inherited skin disorder – a case report

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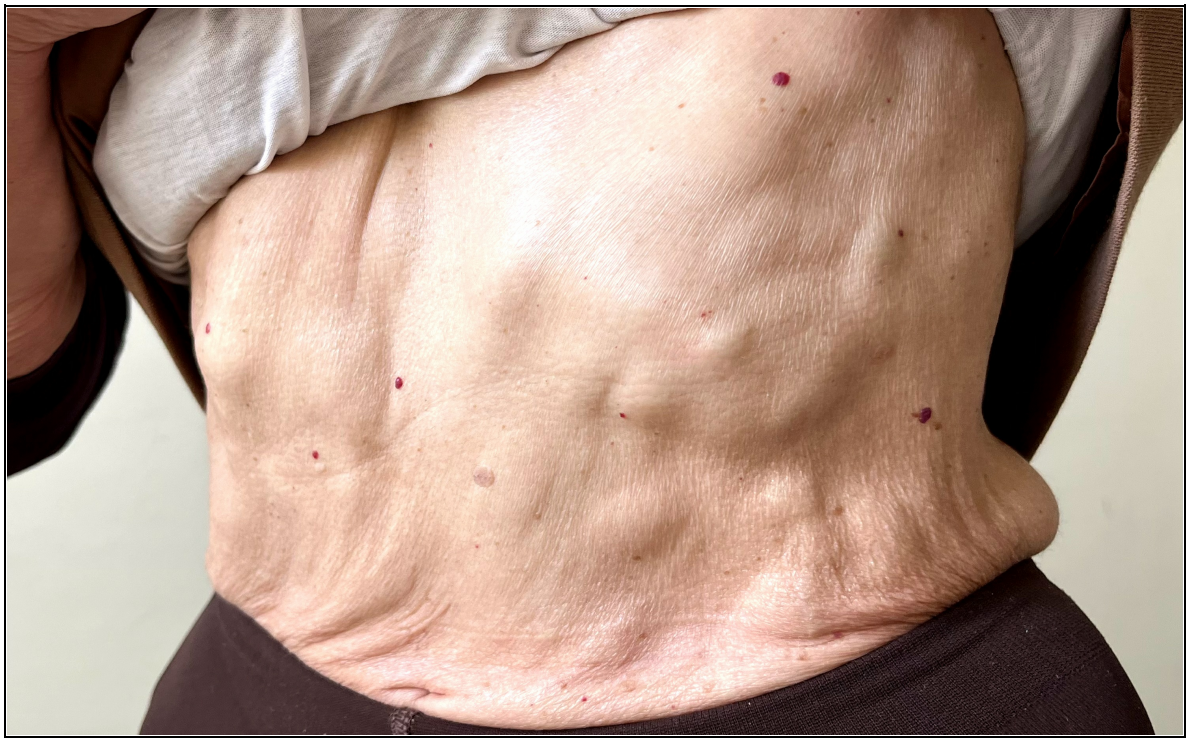
Introduction

Steatocystoma multiplex is a rare, inherited autosomal dominant genodermatosis, characterized by multiple dermal cysts that usually appear in adolescence or early adulthood. It is associated with mutations in the *KRT17* gene. Although benign, the condition may cause significant cosmetic concern and diagnostic difficulty due to its resemblance to other cystic skin disorders.

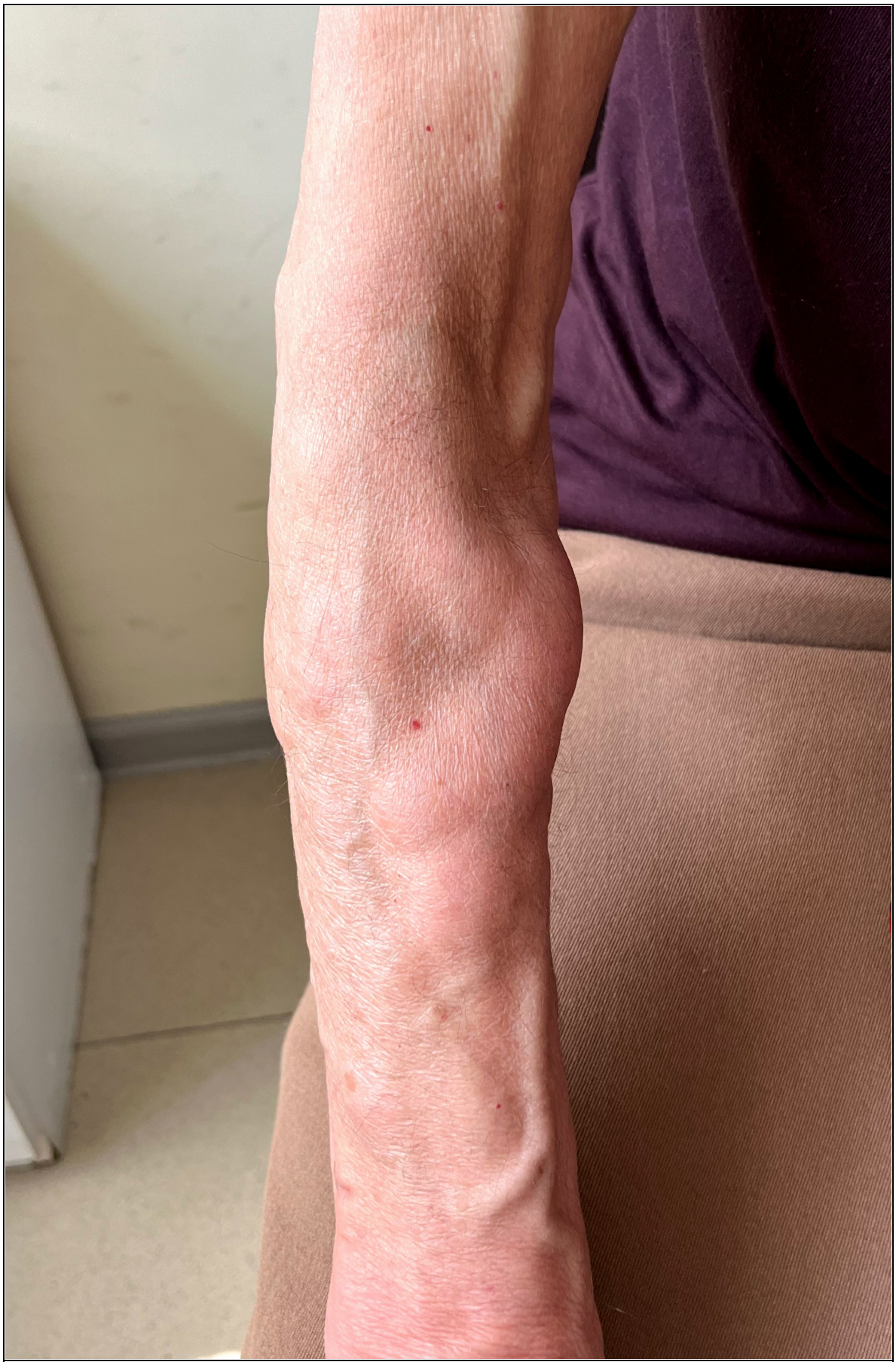


Materials and Methods

A 60-year-old woman was evaluated in our dermatology department. A full clinical examination was performed, including photographic documentation. The diagnosis was confirmed by histopathological examination of a punch biopsy from a representative lesion.

Results

The patient presented with numerous, asymptomatic, skin-colored to yellowish, firm nodules on the chest, back, and proximal upper extremities. Histopathology revealed a dermal cyst lined by stratified squamous epithelium with a characteristic corrugated eosinophilic cuticle and adjacent sebaceous lobules, confirming steatocystoma multiplex. No systemic associations were found.



Conclusions

This case exemplifies the classic presentation of steatocystoma multiplex. It reinforces that precise diagnosis relies on clinicopathological correlation, which is crucial for patient management, alleviating cosmetic concerns, and providing accurate genetic counseling. Dermatologists should consider this entity in the differential diagnosis of multiple cystic cutaneous lesions.

Abstract N°: ID-265

Topic: Genetics, inherited skin diseases

Refractory Warts in a Child Revealing a Rare Genodermatosis

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Introduction

Recalcitrant and extensive cutaneous warts in children should prompt consideration of underlying genetic or immunological disorders. When warts are unusually persistent, widespread, and resistant to conventional therapies, they may represent the first clinical manifestation of a rare genodermatosis. Epidermodysplasia verruciformis (EV) is a rare inherited condition characterized by selective susceptibility to cutaneous human papillomavirus (HPV) infections, resulting in chronic flat warts, pityriasis versicolor–like lesions, and an increased long-term risk of cutaneous squamous cell carcinoma. Although EV typically begins in childhood, it is often misdiagnosed as common viral warts, leading to significant diagnostic delay. We report a familial case of EV in a child presenting with florid, treatment-resistant warts, associated with bilateral iris coloboma, a rare and unusual association.

Materials and Methods

A 5-year-old girl with skin phototype II was referred for diffuse verrucous lesions that had been evolving since the age of 3 years. Dermatological examination revealed multiple flat, wart-like papules predominantly affecting the face, hands, and feet. The lesions were chronic, progressive, and resistant to conventional topical treatments. Prior to referral, the child had consulted several healthcare providers, and a diagnosis of common warts had repeatedly been retained, illustrating frequent diagnostic delay in pediatric EV.

Ophthalmologic examination revealed isolated bilateral iris coloboma, with no additional ocular abnormalities. The child had no significant medical history, normal growth and psychomotor development, no recurrent infections, and no parental consanguinity.

Family investigation revealed a paternal history strongly suggestive of EV, with long-standing verrucous lesions affecting the face and extremities, associated with pityriasis versicolor–like lesions. The father had previously developed a cutaneous squamous cell carcinoma arising on an EV lesion, which was surgically treated. A previous skin biopsy in the father showed a verrucous lesion associated with HPV type 5.

Based on the typical clinical presentation and the familial context, a diagnosis of familial EV was established in the child without skin biopsy. Genetic investigations are currently underway to identify the underlying molecular defect and further characterize this unusual association.

Results

EV results from a defect in cutaneous cell-mediated immunity, leading to impaired control of β-HPV replication, particularly HPV types 5 and 8, which are detected in the majority of EV-associated skin carcinomas. Classical forms are linked to mutations in the EVER1 (TMC6) and EVER2 (TMC8) genes, as well as other less frequently involved genes. These mutations disrupt zinc homeostasis and promote persistent viral replication.

EV typically manifests between 5 and 7 years of age but may appear earlier, particularly in sun-exposed areas. Clinical expression varies within families and is influenced by skin phototype and cumulative ultraviolet exposure, contributing to diagnostic difficulties. The disease course is dominated by a high risk of malignant transformation, estimated at 30–70% in adulthood, mainly in UV-exposed skin.

The association of EV with bilateral iris coloboma is extremely rare. Although no direct pathogenic link has been established, this coexistence raises the possibility of a broader genetic phenotype affecting both cutaneous immunity

and embryonic development. Ongoing genetic analysis may help clarify this relationship.

Conclusions

Recalcitrant, extensive warts in children should prompt consideration of epidermodysplasia verruciformis, particularly in the presence of a family history. Early diagnosis allows for long-term dermatologic surveillance, strict photoprotection, and prevention of malignant complications. The association with bilateral iris coloboma expands the phenotypic spectrum of EV and supports the need for genetic evaluation.

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Abstract N°: ID-310

Topic: Genetics, inherited skin diseases

Multiple Mushroom-like growing cylindromas of the scalp (Turban tumor) in a patient with Brooke-Spiegler Syndrome: unique manifestation in a bulgarian patient

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Introduction

Cutaneous cylindromas are rare, slow-growing adnexal tumors commonly found on the capillitium or face. When located on the capillitium, they can cluster together, forming a headgear-like structure that gives the characteristic "turban" appearance.

Brooke-Spiegler syndrome, an autosomal dominant condition, is typically benign, though malignant transformation can occur.

Materials and Methods

We present a 61-year-old male with a 30-year history of mushroom-like formations, , affecting approximately half of the hairy part of the capillitium. In addition, an erythematous-livid plaque with ulceration and crusting was observed on both left and right lower legs (Fig.1a-d).

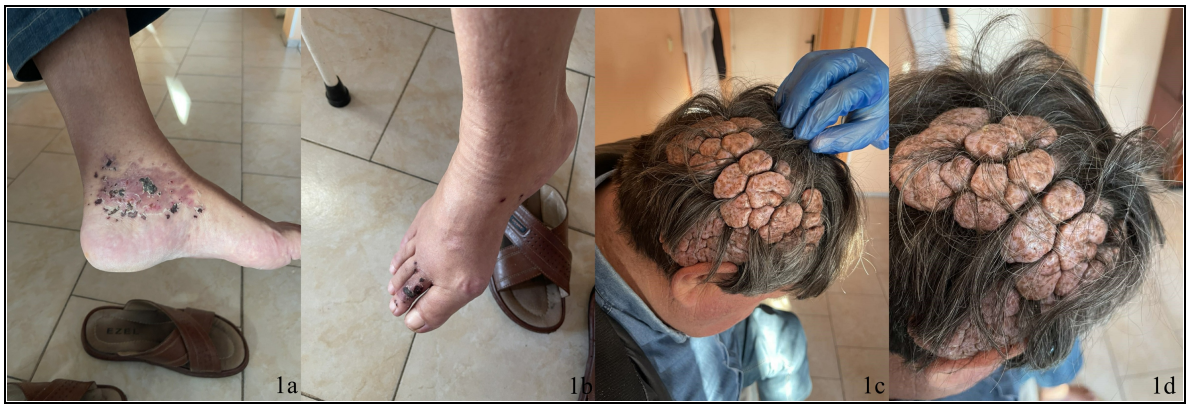

Fig.1a-d: Dermatological examination 1a,b: An erythematous-livid plaque with ulceration and crusting located on the medial surface of the left lower leg and the second toe of the right foot. 1c,d: In the scalp region, exophytic tumor-like formations can be observed, presenting as multiple confluent, monomorphic growths with a gyri-sulci like pattern . These mushroom-like formations clinically resembled cylindromas or spiradenocarcinomas, involving approximately half of the hairy part of the capillitium.

Results

Histopathological examination confirmed the formations as cylindromas (Fig.2a-c). The patient was suspected of having

a sporadic, non-inherited form of Brooke-Spiegler syndrome. Surgical excision of the mushroom-like lesions was recommended.

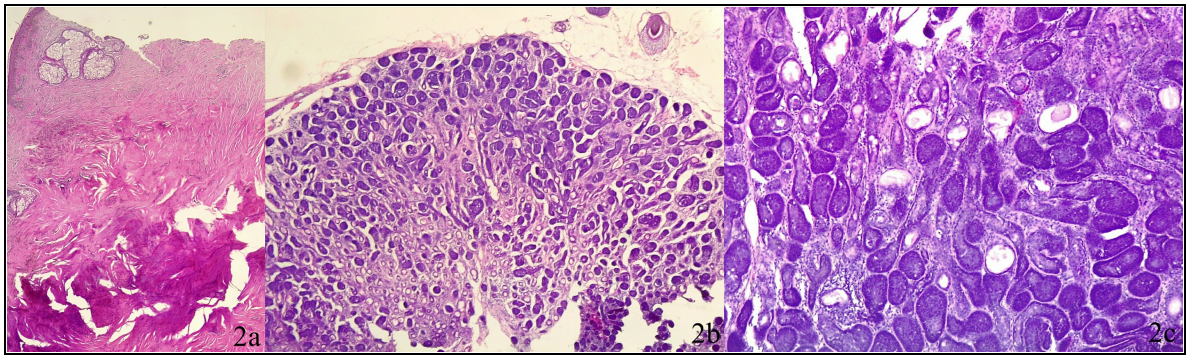

Fig.2a-c: Histopathological findings - Marked ortho- and follicular hyperkeratosis, irregular acanthosis with elongation and owl-like dilatation of the distal parts of the epidermal ridges. The dermal compartment is densely hyalinized, with an underlying proliferation of atypical basaloid keratinocytes forming zig-zag-shaped, multi-caliber nests, surrounded by an eosinophilic periphery and demarcated by mucinous, well-vascularized stroma. 2a: Hyalinized cylindroma x HE x 40 2b: Cylindroma x HE x 40 2c: Cylindroma x HE x 100

Conclusions

In cases of non-inherited forms of Brooke-Spiegler syndrome, early detection and preventative measures are critical. A brief discussion focusing on the management of the condition is provided, emphasizing whether true sporadic cases of Brooke-Spiegler syndrome exist or if they represent another clinically "silent" form of the condition.

Abstract N°: ID-318

Topic: Genetics, inherited skin diseases

Rare case of a Netherton syndrome in a Bulgarian patient: case presentation and focus on new therapeutic horizons

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Introduction

Comel-Netherton syndrome, or Netherton syndrome (NS), is a rare chronic genetic skin condition affecting the daily life of patients, which often results in poorly developed social skills and anxiety. Genetic predisposition plays a key role alongside the clinical findings, and clinicians must be aware of it as it can mimic other well-known skin conditions.

Materials and Methods

Diagnosis is challenging both clinically and histologically. Clinically, it can mimic a severe form of atopic dermatitis, psoriasiform dermatitis overlapping with atopic dermatitis, or erythrokeratodermia variabilis. The difficulties in making histological diagnosis are similar, and it is often necessary to take several biopsies in order to clarify the diagnosis. Although retinoids are used for both psoriasis, erythrokeratodermia variabilis, and other congenital forms of keratodermia, the recommended treatment doses are different. This often results in poor treatment outcome.

Results

We present a case of a 16-year-old patient since childhood with chronic recurrent appearing diffuse erythematous annular maculae, located on the skin of the trunk, upper and lower extremities, face and scalp (Fig.1a-f).

Classical triad manifestations for the Netherton Syndrome were present, combined with a food allergy and diagnosed initially as erythrokeratodermia variabilis and later-on distinguished in an international laboratory for a Ichthyosis linearis circumflexa.

After the reevaluation of the diagnosis a systemic therapy with acitretin 10 mg daily, local pimecrolimus 1%, emollients, and bilastine 20 mg once daily was initiated.

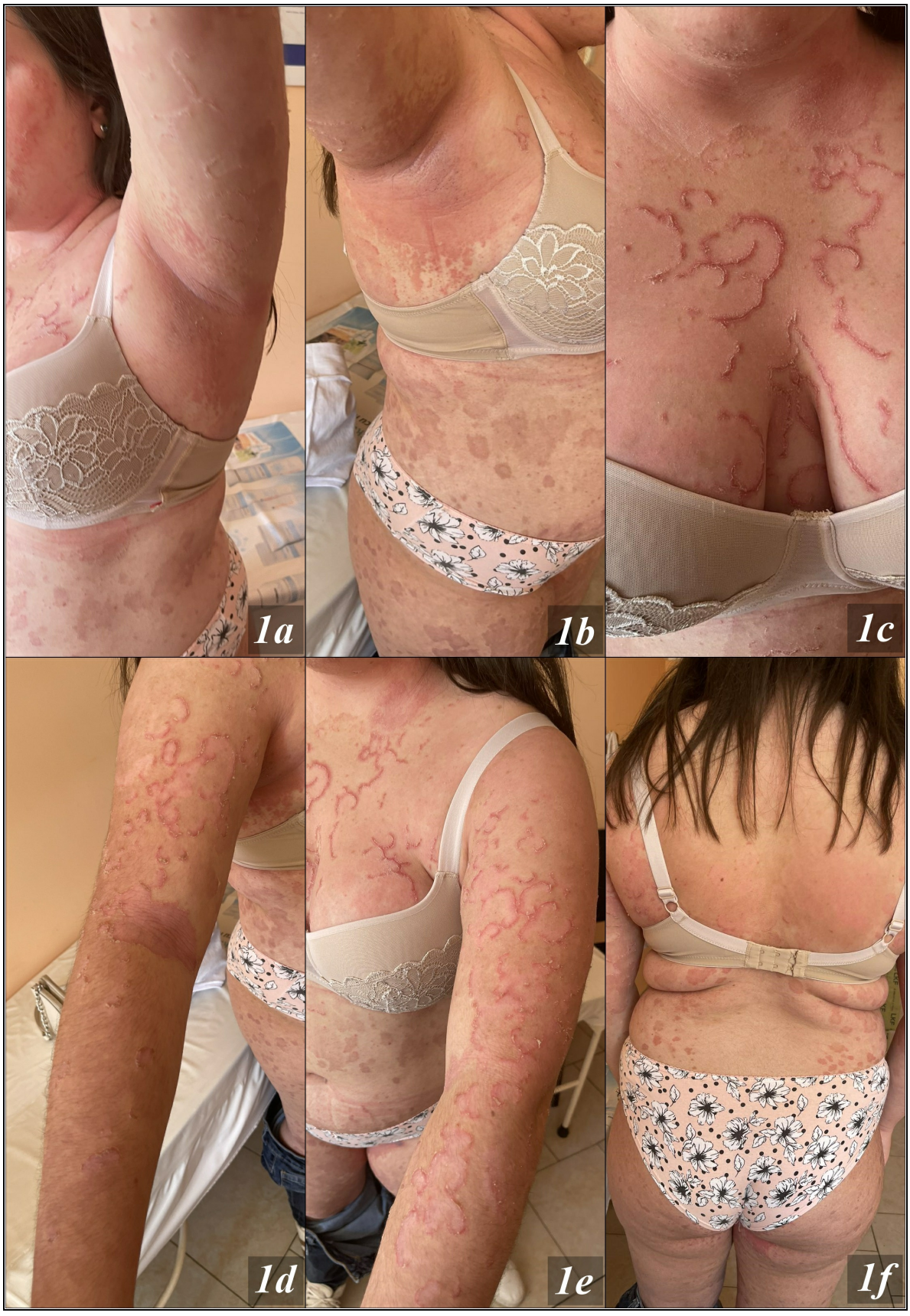

Fig.1a-f: Sparce and bitter hair, with erythematous anullar maculae, in places with confluence into more extensive plaques with double-edged scale, located on the trunk, upper and lower extremities, face and scalp area 1a: Lesions located over the patients whole body with a main focus on the left axillary region 1b: Lesions located over the patients whole body with a main focus on the right axillary region. 1b: Lesions located on the trunk, erythematous plaques can be seen on the lower extremites also 1c: Lesions located on the neck and décolletage 1d: Lesions located on the upper right arm 1e: Lesions located on the upper left arm; The trunk lesions can be spotted 1f: Lesions located on the back

Conclusions

Due to the limited application of retinoids and the difficulties in achieving permanent remission, modern medicine is often faced with the challenge of seeking innovative therapeutic solutions. New hopes are placed on targeted or anti-cytokine therapy, based on inhibiting the inflammatory component of the disease. Innovative therapeutic options, including modern medications such as dupilumab, infliximab, secukinumab, anakinra, omalizumab, and others are the new hope for succesful management of the disease.

Abstract N°: ID-328

Topic: Genetics, inherited skin diseases

Late-Onset, Skin-Limited NLRP3-Associated Autoinflammatory Disease Presenting with Urticaria-Like Lesions: A CAPS Spectrum Case

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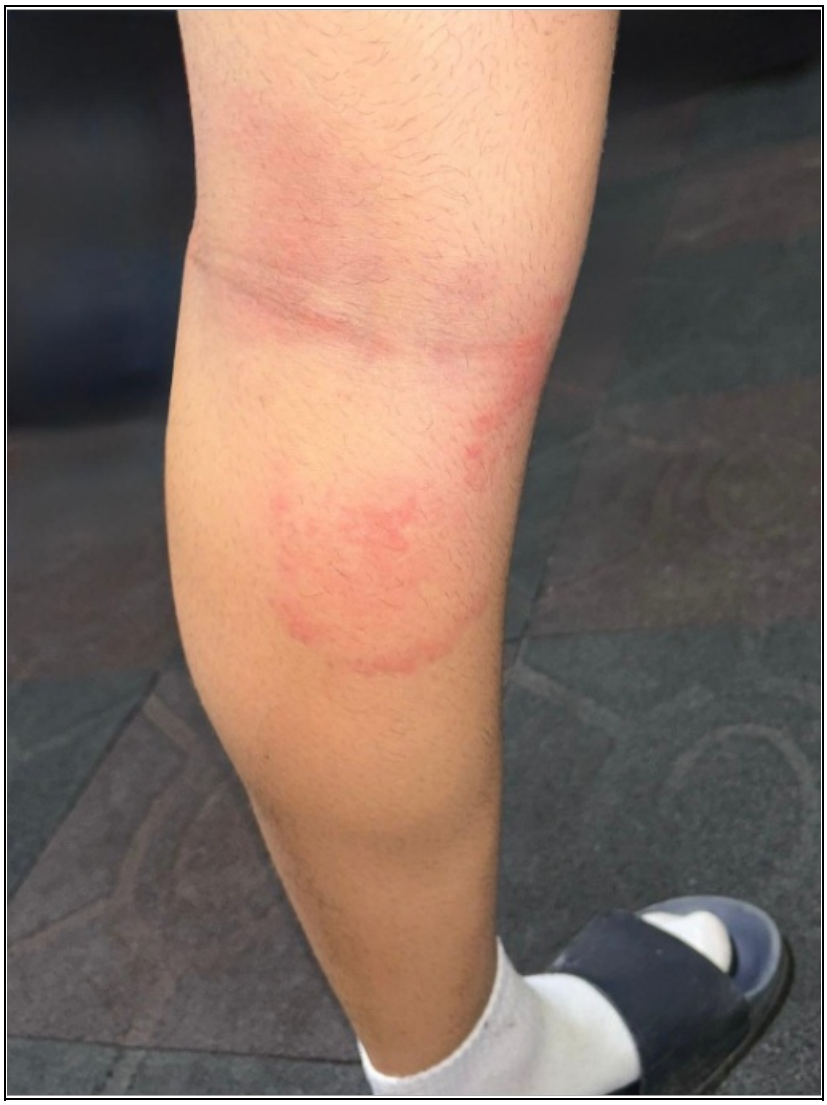
Introduction

Cryopyrin-associated periodic syndromes (CAPS) are a group of rare autoinflammatory disorders caused by gain-of-function mutations in the *NLRP3* gene, leading to dysregulated interleukin-1 (IL-1)–mediated inflammation. Traditionally, CAPS has been classified into three clinical subtypes—familial cold autoinflammatory syndrome, Muckle–Wells syndrome, and neonatal-onset multisystem inflammatory disease—based on age of onset, disease severity, and extent of systemic involvement. However, accumulating evidence indicates that these subtypes represent points along a continuous phenotypic spectrum rather than discrete clinical entities.

Materials and Methods

A 19-year-old male patient presented with a three-month history of recurrent urticaria-like lesions triggered by cold exposure, accompanied by intense pruritus and a burning sensation. He denied systemic symptoms such as fever, arthralgia, myalgia, fatigue, or weight loss, and reported no recent infection, drug exposure, or known allergic triggers. Family history was unremarkable. Physical examination during symptomatic periods revealed erythematous, edematous plaques on the trunk and extremities, resolving spontaneously within 24 hours without residual pigmentary changes. No angioedema was observed.

The patient was initially diagnosed with chronic urticaria; however, despite treatment with second-generation antihistamines at up to four times the standard daily dose, no clinical improvement was achieved.



Ill defined erythematous annular plaques with central clearing on the lower leg , urticaria like plaques

Results

Further diagnostic evaluation revealed neutrophilia and elevated C-reactive protein and serum amyloid A levels during disease flares. Skin biopsy demonstrated perivascular neutrophilic infiltration in the superficial and deep dermis without evidence of vasculitis. Genetic analysis identified a heterozygous pathogenic NLRP3 variant, c.592G>A (p.Val198Met), classified as Class 2 (possible pathogenic, 95–99%), supporting the diagnosis of CAPS.

Treatment with anakinra (100 mg/day, subcutaneous) was initiated, resulting in complete resolution of cutaneous symptoms after two months, with no recurrence of urticarial attacks.

Conclusions

This case illustrates an atypical CAPS presentation with delayed onset and inflammation confined to the skin, highlighting the diagnostic challenges of non-classical phenotypes and supporting a spectrum-based rather than subtype-based classification of CAPS. Accumulating evidence indicates that low-penetrance NLRP3 variants are associated with milder disease courses, later onset, and limited organ involvement, which may delay diagnosis when systemic inflammatory features are absent and cutaneous manifestations predominate.

CAPS pathogenesis is driven by dysregulated NLRP3 inflammasome activation and excessive interleukin-1β production. Lower-intensity or compartmentalized inflammasome activity may preferentially affect the skin, resulting in neutrophilic, antihistamine-resistant urticaria-like lesions. The complete and sustained response to IL-1 blockade in this patient provides functional confirmation of inflammasome-mediated disease activity and supports classification as a skin-limited CAPS phenotype within the broader CAPS spectrum.

Within this framework, the absence of overt systemic inflammatory manifestations should not be viewed as exclusion from the CAPS spectrum but rather as a consequence of variable genetic penetrance and tissue-specific inflammatory expression. The response to IL-1 blockade supports classification of this presentation as a skin-limited CAPS phenotype.

Overall, this case supports an expanded view of CAPS that includes late-onset, skin-restricted phenotypes associated with low-penetrance NLRP3 variant

Abstract N°: ID-425

Topic: Genetics, inherited skin diseases

Topical B-VEC for Epidermolysis Bullosa Wounds: Early Epithelialization in a Pediatric and Adolescent Case Series

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Introduction
Dystrophic epidermolysis bullosa (DEB) is a rare hereditary blistering disorder that is characterised by pathogenic variants in the COL7A1 gene. These variants result in reduced or dysfunctional type VII collagen and impaired anchoring fibrils at the dermal–epidermal junction. The disease is characterised by chronic, painful, non-healing erosions and recurrent blistering, leading to substantial morbidity and impaired quality of life. The prevailing management strategy emphasises wound care and infection prevention, while therapeutic options targeting the underlying molecular defect remain limited.
Beremagene geperpavec (B-VEC) is a redosable, topical HSV-1–based gene therapy designed to deliver functional collagen 7A1 and promote local restoration of type VII collagen. In this study, we present our observations from a clinical trial conducted in a paediatric and adolescent population, employing topical B-VEC treatment for cases exhibiting the EB/DEB phenotype.

Materials and Methods
Three female patients with epidermolysis bullosa (EB), aged 2, 9, and 16 years, received topical beremagene geperpavec (B-VEC) gel administered once weekly to selected active erosions and/or bullae. B-VEC gel was applied directly onto the non-epithelialized wound surface using a standardized dropwise technique. Following administration, treated areas were covered with a hydrophobic dressing and maintained under occlusion for 24 hours. Patients were prospectively monitored for 12 weeks, with weekly clinical evaluations of target lesions focused on epithelialization and clinical wound closure. Longitudinal assessment incorporating caregiver-reported history and physician observation suggested that wound healing exhibited a fluctuating rather than strictly linear trajectory over time. Notably, an apparent acceleration in epithelialization was observed during follow-up, representing a potentially significant improvement in patient morbidity. Safety and tolerability were assessed at each visit through systematic monitoring for local cutaneous reactions and potential systemic adverse events. At the time of reporting, treatment administration remains ongoing.

Results
Topical B-VEC was associated with an early clinical signal of response in all three patients. Treated target areas demonstrated clinically meaningful epithelialization, typically within 1–2 weeks after treatment initiation. In the 2-year-old patient, selected active erosions showed visible improvement and progressive epithelialization during weekly follow-up. In the 9-year-old patient, larger and more chronic erosions demonstrated rapid epithelialization early in the treatment course, with an overall reduction in non-epithelialized wound areas at treated sites. In the 16-year-old patient, epithelialization of recurrent knee/ankle/foot lesions appeared accelerated; preservation of the bulla roof supported wound coverage while healing progressed. No treatment-related systemic adverse events were observed.

Conclusions
In this small pediatric/adolescent EB case series, topical B-VEC was associated with early epithelialization (within 1–2 weeks) and favorable short-term tolerability, supporting its real-world feasibility in EB wound management. Larger cohorts and longer follow-up are warranted to assess durability of response and long-term safety.

Abstract N°: ID-432

Topic: Genetics, inherited skin diseases

Bridging the diagnostic gap in neurofibromatosis type 1: When to consider RNA sequencing

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Introduction
Neurofibromatosis type 1 (NF1) is a common autosomal dominant disorder requiring early diagnosis to enable appropriate surveillance, prognostication, and reproductive counselling. Dermatologists are frequently the first clinicians to assess affected children, as pigmentary features such as café-au-lait macules and intertriginous freckling often represent the earliest manifestations. While genomic DNA (gDNA)-based next-generation sequencing (NGS) panels identify most pathogenic NF1 variants, deep intronic and complex structural variants may be missed, leaving some clinically affected individuals without molecular confirmation. RNA sequencing (RNAseq) enables direct analysis of transcript structure and aberrant splicing and may improve diagnostic yield when standard DNA-based testing is uninformative.

Materials and Methods
Children with clinical features suggestive of NF1 were evaluated using the 2021 diagnostic criteria. Initial molecular testing consisted of gDNA-based NGS panels including NF1 and SPRED1 with copy number analysis. When gDNA testing was negative but clinical suspicion remained high, targeted NF1 RNAseq was undertaken. RNA was extracted from peripheral blood lymphocytes following short-term stimulation, and reverse transcription PCR with complementary DNA amplification was performed to assess abnormal splicing or transcript alterations. RNAseq focused on NF1 transcript analysis rather than whole-transcriptome sequencing. Identified variants were interpreted using established variant classification guidelines.

Results
Five unrelated children with suspected NF1 and negative gDNA-based NGS results underwent RNAseq. At initial assessment, two children fulfilled clinical diagnostic criteria, while three presented with pigmentary features alone. All five subsequently developed additional manifestations consistent with NF1. RNAseq identified clinically informative NF1 variants in all cases (5/5, 100%), including three deep intronic splicing variants, one 5′ untranslated region variant, and one exonic insertion consistent with a complex structural change undetectable by standard gDNA sequencing. Three variants were novel. Four variants demonstrated abnormal-to-normal transcript ratios of approximately 1:1, consistent with complete loss of normal transcript from the affected allele and predicted loss of function. The 5′ untranslated region variant was classified as a variant of uncertain significance but showed familial segregation with NF1 features, supporting its clinical relevance.

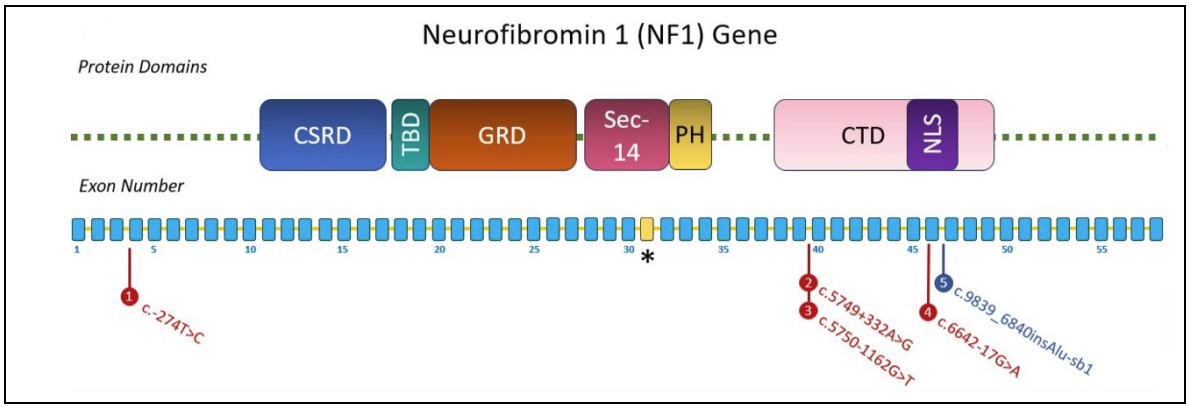

Figure 1: Schematic representation of the NF1 gene showing exon structure and functional domains. RNA sequencing identified three deep intronic splicing variants, one 5′ untranslated region variant, and one exonic insertion undetectable by standard DNA-based sequencing. Four variants demonstrated abnormal-to-normal transcript ratios of approximately 1:1, consistent with loss of function. Variant nomenclature is based on NM_000267.3.

Conclusions

RNA sequencing enabled molecular diagnosis in children with clinically suspected NF1 following negative DNA-based testing, identifying pathogenic variants that would otherwise have remained undetected. These findings support RNAseq as a valuable second-tier diagnostic tool when clinical suspicion of NF1 remains high. Incorporating RNAseq into diagnostic pathways may improve diagnostic accuracy, facilitate appropriate counselling, and support long-term management, particularly in dermatology-led assessment of children with early pigmentary features.

Abstract N°: ID-449

Topic: Genetics, inherited skin diseases

Incontinentia pigmenti in a newborn: the diagnostic value of early skin lesion evolution

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Introduction
Incontinentia pigmenti (Bloch–Sulzberger syndrome) is a rare X-linked genodermatosis caused by pathogenic variants in the *IKBKG* (NEMO) gene. Cutaneous manifestations are often the earliest and most prominent feature, typically evolving through characteristic stages along Blaschko lines. Early recognition of skin findings is crucial for prompt diagnosis and appropriate multidisciplinary management.

Materials and Methods
We report a neonatal case evaluated through detailed clinical observation, microbiological testing, histopathological and immunohistochemical examination of skin biopsies, and confirmatory genetic analysis. Family history was assessed to identify features suggestive of X-linked inheritance.

Results
A female neonate born in 39th week of gestation developed erythematous, papular, and vesiculobullous skin lesions on day 3 after birth. Initially localized on the right lower limb, the lesions subsequently followed Blaschko lines on all extremities, evolving into erosions with yellowish crusts. Empirical antibiotic therapy resulted in only transient improvement. Microbiological investigations were negative, and the general condition remained stable. Over subsequent weeks, partial regression of inflammatory lesions was observed, followed by linear hyperpigmentation and hypopigmentation. Family history revealed similar neonatal skin lesions in the mother, with spontaneous resolution and residual linear pigmentary macules, as well as multiple early miscarriages on the maternal side. Histopathological examination of the infant's skin showed acanthotic epidermis with hyperkeratosis, spongiosis, and intraepidermal vesicles containing inflammatory cells. Immunohistochemistry demonstrated sparse pigment granules positive for S-100 protein and MART-1 expression in isolated basal keratinocytes, consistent with early-stage incontinentia pigmenti. Genetic testing identified a deletion of exons 4–10 in the *IKBKG* (NEMO) gene, confirming the diagnosis.

Conclusions
This case highlights the crucial role of careful observation of evolving neonatal skin lesions in the early diagnosis of incontinentia pigmenti. Recognition of characteristic cutaneous patterns, combined with family history and confirmatory histopathological and genetic testing, enables timely diagnosis and initiation of appropriate multidisciplinary surveillance, particularly for ophthalmologic and neurologic complications.

Abstract N°: ID-485

Topic: Genetics, inherited skin diseases

From adolescence to old age: delayed diagnosis of Brooke–Spiegler syndrome

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Introduction

Brooke–Spiegler syndrome is a rare autosomal dominant genodermatosis caused by mutations in the *CYLD* tumor suppressor gene, characterized by multiple benign adnexal tumors, including cylindromas, spiradenomas, and trichoepitheliomas. Lesions typically appear in adolescence and progress slowly, often leading to delayed diagnosis, particularly in elderly patients presenting with late complications.

Materials and Methods

An 86-year-old woman presented with multiple slowly progressive cutaneous nodules, one of which was complicated by active bleeding. Her medical history included bronchopulmonary carcinoma treated several years earlier, with no evidence of active disease.

Clinical examination revealed numerous nodules and tumors predominantly involving the frontoparietal scalp, some of which were confluent and partially covered with hemorrhagic crusts. A frontal lesion, traumatised during routine hair grooming, was tender and responsible for the bleeding episode. Additional sessile nodules were observed on the face, ears, and limbs. Lesions were mostly asymptomatic, firm to elastic, and variable in size, ranging from a few millimeters to several centimeters, with coloration varying from flesh-colored and pink to violaceous. The patient's general condition was preserved, and no peripheral lymphadenopathy was detected.

Dermoscopy of the facial lesions showed a heterogeneous vascular pattern, characterized by either erythematous or violaceous backgrounds associated with fine linear and branching telangiectatic vessels over a largely structureless background.

Medical history revealed that the first lesions had appeared during adolescence, with gradual multiplication over decades. Two of the patient's three children presented similar but fewer and smaller lesions affecting the scalp and face.

Histopathological examination of a biopsied scalp lesion in the index patient demonstrated features consistent with a cylindroma, supporting the diagnosis of Brooke–Spiegler syndrome. One daughter was subsequently evaluated, and biopsy of a scalp lesion revealed a spiradenoma. Genetic testing performed in the patient identified a pathogenic mutation in the *CYLD* gene, thereby confirming the diagnosis.

Results

Brooke–Spiegler syndrome is a rare autosomal dominant genodermatosis caused by germline mutations in the *CYLD* tumor suppressor gene. It is characterized by the development of multiple benign adnexal tumors, most commonly cylindromas, spiradenomas, and trichoepitheliomas. Lesions typically appear during adolescence or early adulthood and slowly increase in number and size over time.

The present case illustrates a classic but late presentation of Brooke–Spiegler syndrome, with extensive scalp involvement and tumor confluence in an elderly patient. The long-standing evolution, onset during adolescence, and familial aggregation were key diagnostic clues. The coexistence of different adnexal tumor types within the same family, as observed in our patient (cylindroma) and her daughter (spiradenoma), is well described in the literature and reflects the phenotypic heterogeneity of the disease.

Although lesions are benign, progressive tumor burden may lead to complications such as bleeding, pain, secondary infection, and significant cosmetic or psychological impact. In addition, rare cases of malignant transformation have been reported, justifying long-term dermatological follow-up. Dermoscopy, while not diagnostic, may provide supportive information by revealing nonspecific vascular patterns in adnexal tumors and can help guide biopsy of representative lesions.

Conclusions

This case highlights the importance of considering Brooke–Spiegler syndrome in patients presenting with multiple, long-standing cutaneous nodules, particularly when lesions begin early in life and show familial aggregation. Recognition of this rare genodermatosis allows appropriate histological confirmation, genetic counseling, and long-term surveillance to prevent complications and delayed diagnosis.

Abstract N°: ID-519

Topic: Genetics, inherited skin diseases

ERYTHROKERATODERMA VARIABILIS IN A CHILD SUCCESSFULLY TREATED WITH LOW-DOSE ISOTRETINOIN

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Introduction

Erythrokeratoderma variabilis (EKV) is a rare inherited disorder of keratinization characterized by transient, migratory erythematous patches and relatively fixed hyperkeratotic plaques, typically presenting in early childhood. The disease shows marked clinical variability and is often exacerbated by environmental factors such as heat, infections, and psychological stress. Mutations in connexin-encoding genes have been implicated in its pathogenesis, leading to impaired epidermal differentiation.Clinically, EKV manifests as erythematous lesions with changing morphology and distribution, frequently accompanied by pruritus, while histopathological findings are generally nonspecific but supportive in the appropriate clinical context.

Materials and Methods

An 8-year-old boy, born to consanguineous parents, presented with recurrent, migratory, and intensely pruritic skin lesions that had been present since early infancy. The lesions first appeared at 2 months of age as erythematous patches on the face and subsequently spread to various body areas. Over time, the lesions demonstrated a migratory course and frequently assumed annular, polycyclic, and rosette-like configurations, accompanied by marked erythema and pruritus. There was no family history of a similar dermatological condition. The patient's medical history was otherwise unremarkable, and both hearing and visual assessments were within normal limits.Dermatological examination revealed asymmetrically distributed erythematous to brownish plaques with variable degrees of hyperkeratosis involving the neck, trunk, axillary regions, gluteal area, and extensor surfaces of the extremities. Several lesions exhibited annular morphology with central clearing, while others appeared as irregular, geographic erythematous patches Figure 1(a,b). . Post-inflammatory hypopigmented macules were noted in previously affected areas. The palms, soles, scalp, nails, and mucous membranes were not involved.At 2 years of age, a 4-mm punch biopsy obtained from an active lesion demonstrated focal parakeratosis, hyperkeratosis, follicular plugging, papillomatosis, mild acanthosis, and homogenization of collagen in the upper dermis, findings consistent with erythrokeratoderma variabilis. Baseline laboratory investigations were within normal limits. The patient had previously been treated with topical corticosteroids with minimal clinical response, and topical retinoid therapy was discontinued due to local irritation.Given the extent of disease and insufficient response to topical therapies, low-dose oral isotretinoin was initiated at a dose of 10 mg/day (approximately 0.3 mg/kg/day). After three months of treatment, a marked regression of active erythematous and hyperkeratotic lesions was observed, with residual post-inflammatory hypopigmentation only Figure 2(a,b). . The treatment was well tolerated, and no isotretinoin-related adverse effects were detected during follow-up.

Results

Management of EKV remains challenging, particularly in pediatric patients, as topical therapies often provide limited benefit. Although systemic retinoids have demonstrated efficacy, their use in children is restricted by safety concerns. We report a pediatric case of EKV successfully treated with low-dose oral isotretinoin, highlighting its potential as a safe and effective therapeutic option.

Conclusions

This case highlights low-dose oral isotretinoin as an effective and well-tolerated treatment option for erythrokeratoderma variabilis in a pediatric patient. Significant clinical improvement was achieved without adverse effects, supporting its potential use in children with refractory disease. Further studies are needed to better define the long-term safety of systemic retinoids in this population.

Abstract N°: ID-554

Topic: Genetics, inherited skin diseases

Early-Onset Gb3 Accumulation and Cell-Type-Specific Mitochondrial Dysfunction in Fabry Disease hiPSCs and Derived Cells

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Introduction

Fabry disease (FD) is an X-linked lysosomal storage disorder caused by deficient α-galactosidase A, resulting in globotriaosylceramide (Gb3) deposition. Dermatologically, angiokeratomas and neuropathic pain are hallmark features. However, the cellular mechanisms underlying Gb3 deposition and metabolic dysfunction remain incompletely defined.

Materials and Methods

Peripheral blood mononuclear cells from three male FD patients were reprogrammed into human induced pluripotent stem cells (hiPSCs) and subsequently differentiated into cardiomyocytes as a lineage-specific disease model using a 3D bioreactor-based differentiation system. Gb3, mitochondrial function, and oxidative stress were assessed by immunocytochemistry, Seahorse extracellular flux analysis, and reactive oxygen species (ROS) assays, respectively. In addition, global proteomic profiling was performed to identify disease-associated alterations in protein expression and to complement the functional metabolic analyses.

Results

FD hiPSCs exhibited Gb3 accumulation already at the undifferentiated stage, indicating that lysosomal storage pathology precedes lineage commitment. At this stage, FD hiPSCs showed increased metabolic activity, characterized by elevated mitochondrial respiration and increased oxidative stress, consistent with a compensatory mitochondrial hyperactive state. In contrast, cardiomyocytes differentiated from FD hiPSCs demonstrated impaired mitochondrial respiratory capacity despite persistent oxidative stress, indicating a transition toward energetic insufficiency upon lineage maturation. Proteomic profiling supported this functional shift, revealing differential regulation of proteins involved in mitochondrial oxidative phosphorylation, mitochondrial translation, and metabolic substrate utilization, consistent with early metabolic compensation followed by mitochondrial dysfunction in differentiated cells.

Conclusions

Our findings challenge the assumption that FD pathogenesis is limited to differentiated tissues and reveal key metabolic abnormalities already active in primitive cells. This early onset of cellular dysfunction raises questions about embryonic compensation and underscores the need for early therapeutic strategies targeting mitochondrial dysfunction and oxidative stress alongside substrate reduction. Such approaches may improve disease management and delay organ-specific manifestations.

Abstract N°: ID-645

Topic: Genetics, inherited skin diseases

scientific genetic research in patients with genodermatoses - ichthyosis

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Introduction

Research on the genetic aspects of ichthyosis has recently become highly relevant, due to the registration of cases of familial cases among the world's population.

Studying genetic markers in the clinical course of ichthyosis is a prognostic aspect in the early diagnosis of severe - syndromic forms of the disease.

The purpose of our research was to assess the identification of allelic variants and the association of genotype polymorphism of the GJB2 G/A (35delG) gene in patients with ichthyosis in the Uzbek population.

Materials and Methods

56 patients with ichthyosis aged 13 to 48 years were examined. Among the men, there were 34 patients and 22 women. All patients underwent clinical, molecular genetic, and statistical studies. All patients consulted with related specialists: a therapist, pediatrician, neurologist, ophthalmologist, endocrinologist, and others. The control group consisted of 40 healthy individuals of the corresponding age without any skin diseases.

Results

Comparative analysis of the frequency of distribution of alleles and genotypes of the GJB2 G/A (35delG) gene polymorphism among 118 DNA samples in 59 patients with ichthyosis revealed the presence of a normal G allele in 66.9% (79/118) of cases and a nonfunctional A allele in 33.1% (39/118) of cases, respectively. ($\chi 2=13.89$; $P=0.0002$; OR = 0.21; 95% CI 0.0888-0.5041). Whereas, in the control group of 37 healthy individuals, the frequency of the normal G allele of the GJB2 gene G/A (35delG) was 90.5% (67/74), and the mutant A allele of the GJB2 gene G/A (35delG) was 9.5% (7/74), respectively.

Analysis of the distribution of allelic variants of the GJB2 G/A (35delG) gene revealed a high frequency of the mutant A allele in the group of patients with ichthyosis, which exceeded the indicators of healthy individuals by 3.5 times. ($P<0.05$). Heterozygous G/A genotypes of the GJB2 gene were detected in 23 out of 59 patients, which constituted 38.9% and exceeded the indicators of healthy individuals by 4.8 times ($P <0.05$). Mutant A/A genotypes were detected 2.5 times more frequently compared to the control group and constituted 13.5% (8/59) of cases.

Conclusions

Analysis of the results of molecular genetic studies indicates that the A allele and heterozygous genotypes of the GJB2

G/A (35delG) polymorphism are significant molecular genetic markers of risk for the development of a severe form of ichthyosis - neuroichthyosis in the Uzbek population (P<0.05), which can be used for early prediction of dermatosis. ($\chi 2$=13.89; P=0.0002; OR = 0.21; 95% CI 0.0888-0.5041)

Abstract N°: ID-711

Topic: Genetics, inherited skin diseases

Congenital Focal Non-Epidermolytic Palmoplantar Keratoderma Due to a KRT16 Mutation in a Child: Differentiation from Pachyonychia Congenita and Considerations for Extracutaneous Screening

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Introduction

Inherited palmoplantar keratodermas comprise a heterogeneous group of genodermatoses caused by mutations affecting keratinocyte structural integrity. Focal non-epidermolytic palmoplantar keratoderma type 1 (FNEPPK1) is a rare subtype most commonly associated with heterozygous mutations in the *KRT16* gene.[1] While *KRT16* mutations are also implicated in pachyonychia congenita, these entities represent distinct phenotypes within a keratin disorder spectrum and can be differentiated based on clinical features and extracutaneous involvement.[2] Although FNEPPK1 is classically limited to palmoplantar skin, sporadic reports of esophageal involvement suggest a broader phenotypic range.

Materials and Methods

An 11-year-old boy presented with congenital hyperkeratotic lesions localized to the palms and soles. The lesions were focal in distribution and sharply demarcated (Figure 1,2). Plantar hyperkeratosis was most prominent over pressure-bearing areas, including the heels and metatarsal heads, consistent with mechanical stress–related accentuation.

Cutaneous examination revealed no additional skin lesions. Importantly, the nails were completely spared, with no evidence of nail dystrophy, thickening, discoloration, or subungual hyperkeratosis, and no oral or other mucosal abnormalities were detected. These findings were considered pivotal in differentiating FNEPPK1 from pachyonychia congenita, which is typically characterized by prominent nail involvement and mucosal changes. There was no family history of similar disease. Systemic examination was unremarkable.

Genetic testing was pursued to establish a precise molecular diagnosis, refine the clinical classification, guide systemic evaluation, and enable appropriate genetic counseling. Analysis revealed a heterozygous mutation in the *KRT16* gene, confirming the diagnosis of focal non-epidermolytic palmoplantar keratoderma (FNEPPK1).[1]

In light of previously reported associations between *KRT16* mutations and esophageal abnormalities, including leukokeratosis[3,4], the patient was referred to pediatric gastroenterology. Despite the absence of gastrointestinal symptoms, upper gastrointestinal endoscopy demonstrated pangastritis, distal esophagitis, and nodularity of the esophageal mucosa. Abdominal examination was normal, with no tenderness, guarding, or rebound.Proton pump inhibitor therapy was initiated.

Results

Topical compounded formulations containing 10% urea and 20% salicylic acid were prescribed for palmoplantar hyperkeratosis, resulting in marked clinical improvement. Long-term dermatologic and gastroenterologic follow-up was planned to monitor potential progression or emergence of extracutaneous involvement.

Conclusions

This case illustrates a well-defined phenotype of *KRT16*-associated FNEPPK1, characterized by focal palmoplantar hyperkeratosis accentuated at pressure points, complete sparing of the nails, and absence of mucosal involvement—features that are critical for differentiation from pachyonychia congenita.[5] Furthermore, it highlights the potential for clinically silent upper gastrointestinal abnormalities in pediatric patients. Given the limited number of reported cases and the lack of standardized screening recommendations, this case supports consideration of targeted extracutaneous evaluation and multidisciplinary follow-up in selected patients with *KRT16*-associated palmoplantar keratoderma.

Abstract N°: ID-748

Topic: Genetics, inherited skin diseases

Early-Onset Multiple Basal Cell Carcinomas in Xeroderma Pigmentosum Complementation Group E: A Case Report

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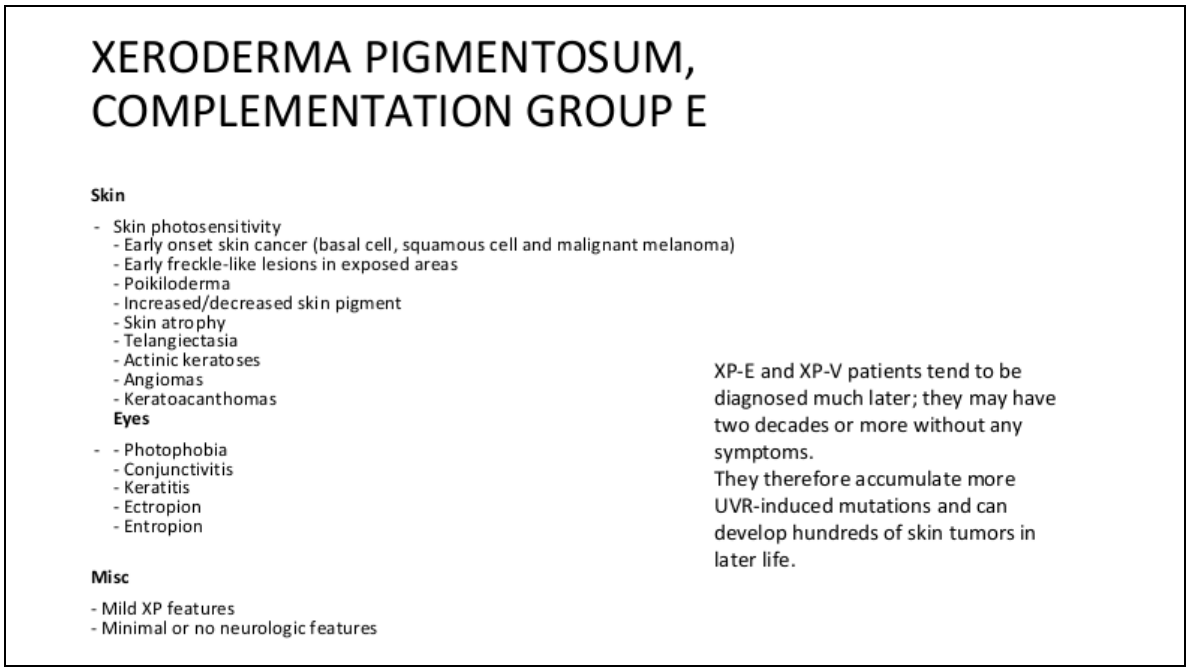
Introduction

Xeroderma pigmentosum (XP) is a rare autosomal recessive disorder caused by defects in nucleotide excision repair, leading to extreme ultraviolet (UV) sensitivity and a markedly increased risk of cutaneous malignancies at a young age. XP is genetically heterogeneous and classified into several complementation groups (XP-A to XP-G and XP-V). Xeroderma pigmentosum complementation group E (XP-E), associated with pathogenic variants or deletions in the *DDB2* gene, is considered a relatively mild subtype, often lacking neurologic involvement and therefore frequently diagnosed later in life. Despite this, cumulative UV exposure may result in multiple skin cancers. We report a young patient with early-onset multiple basal cell carcinomas (BCCs) associated with XP-E



Materials and Methods

An 18-year-old male patient was referred due to recurrent ulcerated facial lesions histopathologically diagnosed as basal cell carcinoma. Comprehensive dermatologic examination, histopathological evaluation, and molecular genetic testing were performed. Two incisional biopsies were obtained from suspicious facial lesions. Next-generation sequencing (NGS) was used to analyze XP-associated genes (*DDB2, ERCC2, ERCC3, ERCC4, ERCC5, POLH, XPA, XPC*). Copy number variation (CNV) analysis was additionally conducted to detect large genomic deletions. Clinical findings were correlated with histopathological and molecular results.

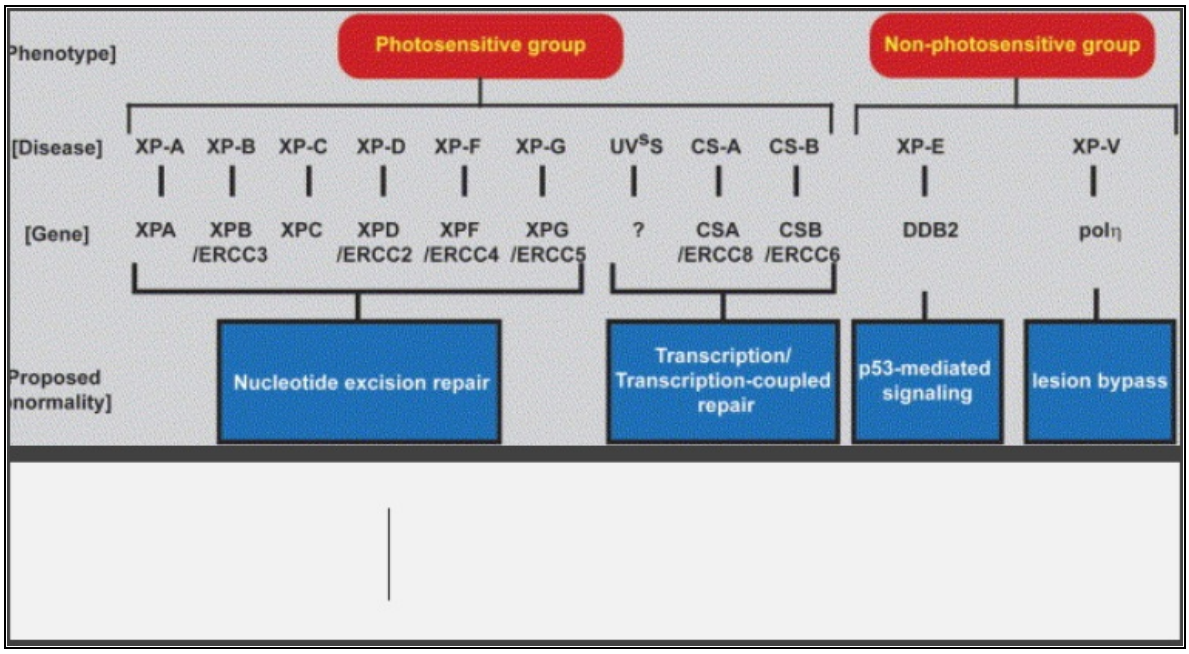
Results

The patient had Fitzpatrick skin type IV and was born to consanguineous parents, with no systemic comorbidities. He presented with bilateral infraorbital and lateral nasal ulcerated, crusted, and intermittently bleeding lesions that had appeared approximately one year prior. Facial examination revealed multiple lentigines on sun-exposed areas, while truncal skin examination was unremarkable.

Histopathological examination demonstrated basal cell carcinoma in both the right cheek and left lateral nasal lesions, accompanied by dense inflammatory infiltrates. The patient underwent wide local excision of the tumors.

NGS analysis did not identify pathogenic sequence variants in the analyzed XP-related genes. However, CNV analysis revealed a homozygous deletion involving exons 1–3 of the *DDB2* gene, consistent with xeroderma pigmentosum complementation group E. The molecular diagnosis correlated with the patient's relatively mild phenotype and absence of neurologic involvement.

A multidisciplinary management strategy was initiated, including strict photoprotection, regular dermatologic surveillance, oral vitamin D supplementation, systemic acitretin (25 mg/day), and field-directed topical imiquimod therapy.



Conclusions

This case illustrates that xeroderma pigmentosum complementation group E may present with early-onset multiple basal cell carcinomas despite a relatively mild clinical phenotype. XP-E should be considered in young patients with multiple or early-onset non-melanoma skin cancers, even in individuals with darker skin phototypes. Molecular genetic testing, including CNV analysis, plays a crucial role in establishing the diagnosis. Early recognition allows timely preventive measures and long-term surveillance, which are essential to reducing cumulative skin cancer burden and improving patient outcomes.

Abstract N°: ID-792

Topic: Genetics, inherited skin diseases

Management Challenges in Gorlin Syndrome: A Case Report and Therapeutic Review

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Introduction

Gorlin syndrome, also known as basal cell nevus syndrome, is a rare autosomal dominant disorder characterized by multiple basal cell carcinomas (BCCs), odontogenic keratocysts, and skeletal abnormalities. It results from mutations in the PTCH1 gene, leading to dysregulation of the Sonic Hedgehog (SHH) signaling pathway. The management of patients with Gorlin syndrome is complex due to the high tumor burden, risk of recurrence, and potential for systemic involvement. We report a representative case and discuss the evolving therapeutic landscape for managing multiple BCCs in this condition.

Materials and Methods

NA

Results

A 65-year-old male patient, born from a consanguineous marriage, was referred to the dermatology department for management of multiple cutaneous tumors. His medical history included 32 sessions of radiotherapy at age 36 for skin tumors and regular follow-up for surgically treated multiple cutaneous lesions. Clinical examination revealed numerous basal cell carcinomas, palmar and plantar pits, and odontogenic keratocysts, confirming the diagnosis of Gorlin syndrome. A subsequent CT scan of the face and brain confirmed the presence of the suspected jaw cysts and showed no cerebral abnormalities. No evident bone abnormalities or neurological deficits were noted. The patient was referred to explore alternative therapeutic options due to the high number of tumors and the limitations of repeated surgical excisions.

Conclusions

Our case illustrates the central therapeutic challenge in Gorlin syndrome: controlling a high, recurrent tumor burden while minimizing cumulative morbidity. While surgical excision remains a cornerstone for definitive treatment, its iterative use can lead to significant functional and aesthetic compromise, as seen in this patient's decades-long history. Alternative strategies must therefore be integrated. Photodynamic therapy is a valuable non-invasive option for superficial BCCs, offering excellent cosmesis. For more advanced or numerous lesions, targeted SHH pathway inhibitors like vismodegib and sonidegib represent a paradigm shift, yet their long-term use is limited by cost, side effects, and acquired resistance, making them more suitable for advanced rather than lifelong prophylactic management. Other modalities, such as topical imiquimod or itraconazole, play ancillary roles. Crucially, radiotherapy is generally contraindicated due to its tumorigenic potential, a principle underscored by this patient's history. In summary, no single therapy is ideal for Gorlin syndrome. Effective management necessitates a personalized, multidisciplinary approach that strategically combines surgical, topical, and systemic modalities, adapting to disease progression and patient tolerance. This case reinforces the need for continued research into more sustainable targeted therapies and optimized treatment protocols to improve long-term quality of life for affected individuals.

Abstract N°: ID-818

Topic: Genetics, inherited skin diseases

Porphyria Cutanea Tarda Secondary to Chronic Kidney Disease in a Non-Dialyzed Patient

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Introduction
Porphyria cutanea tarda (PCT) is the most common type of porphyria, caused by reduced activity of the hepatic enzyme uroporphyrinogen decarboxylase. It typically presents with vesiculobullous lesions and skin fragility in photoexposed areas. PCT may be hereditary or secondary to liver disease, alcohol intake, viral hepatitis, iron overload or renal impairment. We describe a case of acquired PCT in a non-dialyzed patient with advanced chronic kidney disease (CKD), highlighting the clinical features and therapeutic approach.

Materials and Methods
A retrospective analysis of clinical records, laboratory data and therapeutic course was conducted. The diagnosis was established based on clinical presentation and porphyrin quantification in urine. Relevant differential diagnoses and comorbidities were reviewed.

Results
A 62-year-old man with CKD stage 5 due to focal segmental glomerulosclerosis, not undergoing dialysis, presented with a two-month history of vesiculobullous lesions and erosions on the dorsum of the hands, with prior similar involvement of the lower lip. Physical examination revealed multiple tense bullae and erosions restricted to photoexposed areas. He also had extensive vitiligo with acrofacial predominance.

Laboratory evaluation showed elevated urinary uroporphyrins (174,2 µg/g creatinine) and total porphyrins (370 µg/g creatinine). Hepatitis C serology was negative, and the patient denied alcohol consumption. A diagnosis of acquired PCT secondary to CKD was made. The patient was started on hydroxychloroquine 200 mg/day and strict photoprotection, with topical agents used as needed. Progressive clinical improvement was observed.

Conclusions
This case underscores the importance of considering PCT in patients with advanced CKD presenting with photosensitive blistering dermatoses, even in the absence of dialysis. Recognition of this secondary form of PCT allows for timely management and reduction of cutaneous morbidity. Although both PCT and vitiligo may involve oxidative stress mechanisms, no established pathogenic link between the two conditions has been recognized in the current literature.

Abstract N°: ID-828

Topic: Genetics, inherited skin diseases

Intrafamilial variability of cutaneous manifestations in tuberous sclerosis complex: a case report

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Introduction

Tuberous sclerosis complex (TSC) is a rare genetic multisystem disorder characterized by marked variability in clinical expression, even among affected members of the same family. The disease may present at any age with a broad spectrum of phenotypic manifestations of varying severity. Cutaneous manifestations are among the most frequent features of TSC and often represent the initial clue to diagnosis; however, the heterogeneous presentation of the disease may lead to delayed or missed recognition.

Materials and Methods

We present a clinical case of familial tuberous sclerosis, which was diagnosed occasionally.

A mother and her two daughters, 18-year-old and 14-year-old, were consulted and examined by a dermatovenereologist.

Results

The younger daughter presented with hypopigmented macules on the trunk and extremities that had been present since birth but increased in number in one year. Based on clinical appearance, vitiligo was initially suspected. Subsequent dermatological evaluation of her older sister and mother revealed additional characteristic cutaneous findings. The older sister also exhibited hypopigmented macules on the lower extremities and a shagreen patch in the lumbar region. The mother presented with facial angiofibromas involving the nasal and cheek regions, as well as periungual fibromas of the fingers. After the repeated examination of the younger sister, a shagreen patch in the lumbar region was revealed. All three patients fulfilled two major diagnostic criteria for TSC of the 2021 International Tuberous Sclerosis Complex Consensus Group: a mother with facial angiofibromas and periungual fibromas and daughters with hypopigmented macules and a shagreen patch. Despite sharing the same familial background, the patients demonstrated age-dependent and intrafamilial variability in cutaneous manifestations. No family member was diagnosed with epilepsy. Following clinical diagnosis, all patients were referred for genetic evaluation to investigate possible TSC1 and TSC2 gene mutations.

Conclusions

This case highlights the marked intrafamilial variability of cutaneous manifestations in tuberous sclerosis complex and demonstrates how diagnosis may be delayed unless several affected family members are evaluated together. Increased awareness of age-dependent and heterogeneous dermatological presentations is essential for timely diagnosis and appropriate counseling of affected families.

Abstract N°: ID-875

Topic: Genetics, inherited skin diseases

Erythrokeratoderma Variabilis With Persistent Facial Involvement, An Affected Sibling And Secondary Dermatophyte Infection

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Introduction

Erythrokeratoderma variabilis (EKV) is a rare infantile-onset genodermatosis characterized by the coexistence of migratory erythematous plaques and fixed hyperkeratotic lesions. Persistent facial involvement and intrafamilial occurrence are uncommon and may lead to diagnostic delay and misinterpretation.

Materials and Methods

A 19-year-old male presenting with long-standing recurrent erythematous and hyperkeratotic skin lesions was evaluated clinically. Skin biopsy for histopathological examination and fungal studies including potassium hydroxide preparation and fungal culture were performed.

Results

The patient had widespread skin lesions since infancy, initially involving the lumbar area and later spreading to the extremities, neck and face. Fixed hyperkeratotic plaques persisted for years on the trunk and limbs, while erythematous patches migrated between different anatomical sites. Exacerbations were triggered by sweating and stress. Persistent erythematous and finely scaly involvement of the perinasal and perioral areas had been present since early childhood. Mucosal and palmoplantar involvement was absent.

The patient's 11-year-old sister had milder disease limited to migratory erythematous lesions on the trunk, indicating intrafamilial phenotypic variability.

Histopathological examination revealed orthokeratosis, irregular acanthosis and superficial perivascular lymphohistiocytic infiltrate with vascular proliferation, consistent with EKV. Periodic acid–Schiff staining was negative for fungal elements. Fungal culture from inguinal scaling demonstrated dermatophyte growth, confirming secondary dermatophyte infection.

The patient was treated with topical luliconazole for dermatophyte infection and systemic acitretin (25 mg/day) with topical calcipotriol/betamethasone for EKV, and was placed under regular clinical follow-up.

Conclusions

This case represents a rare EKV phenotype with persistent facial involvement and presence of an affected sibling.

Secondary dermatophyte infection may obscure the underlying genodermatosis and complicate diagnosis. Integrated clinical, histopathological and mycological assessment enables accurate diagnosis and appropriate combined antifungal and systemic therapy in EKV.

Abstract N°: ID-887

Topic: Genetics, inherited skin diseases

Extracutaneous manifestations in patients with inherited epidermolysis bullosa in the Russian EB Registry

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Introduction
Inherited epidermolysis bullosa (EB) is a group of genetic disorders characterized by skin fragility and spontaneous or trauma-induced blistering on the skin and mucous membranes. EB has a wide range of clinical manifestations, including extracutaneous involvement. Objective. To characterize extracutaneous manifestations in a cohort of Russian patients with inherited epidermolysis bullosa.

Materials and Methods
Data for patients in the Russian Federation were analyzed from the Russian epidermolysis bullosa Registry established in 2019. Data were collected from 2019 to 2024. Participants were children and adults with EB. All adult patients signed informed consent. Informed assent was obtained from children with EB.

Results
From 2019 to 2024 458 patients with EB were enrolled in Russian EB Registry. EB simplex (EBS), junctional EB, dystrophic EB were diagnosed in 230 (50,2%), 162 (35,4%) and 10 (2,2%) patients, respectively. In 56 (12,2%) patients EB wasn't subclassified. Data was analyzed only from patients with EB simplex and dystrophic EB. Among 230 patients with EB simplex, there were 167 (73%) children and 63 (27%) adults aged 18 and older, 125 (54%) males and 105 (46%) females. Among 162 patients with dystrophic EB, there were 104 (64%) children and 58 (36%) adults, 67 (41%) males and 95 (59%) females. EB was diagnosed clinically in 34 (27.0%) patients with dystrophic EB and 98 (42.6%) patients with EB simplex. Laboratory confirmation of the diagnosis was performed for 65% of patients with dystrophic EB and 25% of patients with EB simplex. Dystrophic EB was characterized by earlier onset: 93% of patients fell ill at birth or within the first month of life compared to 68% of patients with EB simplex ($p<0.05$). Patients with dystrophic EB exhibited more extensive skin involvement. Involvement of 20% or more of the body surface area was noted in 65% of patients with dystrophic EB and in 31% with EB simplex ($p<0.05$). Spontaneous blistering was more frequently reported by patients with dystrophic EB (71%) than with EB simplex (44%) ($p<0.05$). Dystrophic EB was more often accompanied by chronic skin ulcers (38% of patients) compared to simplex EB (7% of patients) ($p<0.05$), scarring alopecia – 17% and 3% respectively ($p<0.05$), and nail involvement – 83% and 36% respectively ($p<0.05$). Involvement of the oral mucosa was noted in 79 (61%) patients with dystrophic EB and in 28 (16%) patients with EB simplex ($p<0.05$), dental involvement – in 87 (69%) and 45 (26%) respectively ($p<0.05$). Secondary infection occurred more often in patients with dystrophic EB than with EB simplex (in 59% and 45% respectively, $p<0.05$). Pharyngeal and esophageal involvement was detected in 40% of patients with dystrophic EB and in 4% of patients with EB simplex ($p<0.05$), involvement of the stomach and/or small intestine – in 12% and 5% of patients respectively ($p<0.05$), involvement of the large intestine and/or rectum – in 29% and 6% of patients respectively ($p<0.05$). Pathology of the musculoskeletal system in dystrophic and EB simplex was noted in 37% and 9% of patients respectively ($p<0.05$), ocular involvement – in 28% and 8% of patients ($p<0.05$), ENT (ear, nose, throat) involvement – in 20% and 4% of patients ($p<0.05$), and involvement of the urinary tract – in 10% and 1% of

patients respectively ($p<0.05$).

Conclusions

In dystrophic EB, skin involvement is more severe than in EB simplex and is more often accompanied by extracutaneous involvement, which requires providing patients with medical care in relevant specialties. The association between the severity of skin involvement and the frequency of internal organ involvement with the EB subtype necessitates establishing the EB subtype using laboratory research methods for the dermatovenerologist to develop a comprehensive patient examination plan. The significant severity of skin involvement and internal organ involvement in dystrophic EB requires planning for greater volumes of medical care for these patients compared to EB simplex.

Abstract N°: ID-907

Topic: Genetics, inherited skin diseases

CLINICAL-GENETIC CHARACTERISTICS OF SKIN PHOTOAGING, OXIDATIVE STRESS AND CORRECTION METHODS

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Introduction

This study examines the pathogenesis of skin photoaging induced by ultraviolet radiation (UVR), specifically focusing on the role of oxidative stress and genetic polymorphisms (COL1A1, GSTT1, GSTM1). The severity of the condition was assessed using a proprietary visual scale developed during the study and d-ROMs tests. The results demonstrated that early identification of risk groups based on detoxification system genes (GSTT1, GSTM1) and the collagen gene (COL1A1), combined with the application of a combined pathogenetic therapy (GLISODin, Thulium laser, exosomes), possesses high clinical efficacy in improving skin quality and reducing the rehabilitation period.

Skin photoaging is a pressing issue in modern dermatocosmetology, with approximately 80% of visible facial aging signs attributed not to chronological age but to external factors, primarily insolation. At the center of the pathogenesis lies oxidative stress resulting from an increase in reactive oxygen species (ROS) and a deficiency in the endogenous antioxidant system. This process leads to collagen degradation and elastosis. In the context of Uzbekistan's sharply continental climate and high insolation, studying the molecular-genetic mechanisms of photoaging (including xenobiotic detoxification genes – GSTM1, GSTT1) and developing pathogenetically substantiated correction methods is of significant importance.

Materials and Methods

The study was conducted at the Republican Specialized Scientific-Practical Medical Center of Dermatovenereology and Cosmetology involving 103 women aged 18–65 years (main group) and 61 healthy donors (control group). The diagnostic complex included clinical assessment (Glogau scale and the author's proprietary scale), instrumental methods (Corneometry, Cutometry, Antera 3D), and biochemical tests (d-ROMs, PAT). Molecular-genetic analysis was performed using the "multiplex" PCR method to determine polymorphisms of the COL1A1 (rs1107946), GSTT1, and GSTM1 genes (n=53). Statistical processing was carried out using SPSS 26.0 software, with differences considered significant at $p<0.05$.

Results

Clinical-instrumental analyses revealed that 83.5% of patients exhibited impaired skin hydration (xerosis) and 70.9% presented with erythema (angiophotoaging). Molecular-genetic analysis established an accumulation of "null" (del) alleles, characterized by reduced functional activity of detoxification system genes (GSTT1 and GSTM1), in the main group. Specifically, the GSTT1 del allele was found to be 5 times more frequent in the main group compared to the control group (12.3% vs. 2.5%), proving to drastically increase the risk of disease development (OR=5.54). "Null" variants in the GSTM1 gene were also evaluated as a factor weakening the defense system against oxidative stress and increasing the risk of photodamage. Furthermore, it was confirmed that carriers of the COL1A1 A-allele have a 2.3 times higher risk of early wrinkle formation. Biochemical investigations revealed a strong correlation (r=0.81) between the level of oxidative stress (d-ROMs) and the clinical stages of photoaging. In clinical practice, the combined application of the GLISODin preparation with Thulium laser and exosomes demonstrated high efficacy. This approach shortens the rehabilitation period by 30–40%, reduces the risk of post-inflammatory hyperpigmentation, and reliably restores skin

elasticity properties.

Conclusions

Skin photoaging is a multifactorial process developing against a background of oxidative stress and genetic predisposition (GSTT1/GSTM1 del, COL1A1 A/A). The assessment of oxidative status using the developed 4-stage visual scale and the d-ROMs test possesses high prognostic value. A personalized treatment algorithm based on the patient's genetic profile (specifically GST system polymorphisms), combining systemic antioxidants and hardware methods, significantly improves clinical outcomes and minimizes the risk of complications.

Abstract N°: ID-930

Topic: Genetics, inherited skin diseases

Modulating Inflammation and Oxidative Stress in Epidermolysis Bullosa Skin Cell Models Using a Hydrogel-Delivered mTOR Inhibitor

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Introduction
Epidermolysis bullosa (EB) is a group of inherited skin disorders characterised by skin fragility, chronic inflammation, and impaired wound healing. Beyond keratinocyte dysfunction, activated dermal fibroblasts contribute to persistent inflammation and oxidative stress within wounds. Dysregulated mTOR signalling has been implicated in chronic inflammatory skin pathologies, highlighting mTOR inhibition as a potential disease-modifying strategy. Topical delivery of therapeutics in EB is challenging due to fragile skin, rapid wound exudation, and the need for sustained local action. Thermosensitive hydrogels, such as Poloxamer 407-based formulations, can provide a biocompatible, adhesive, and responsive platform that conforms to the wound surface, maintains drug stability, and enables sustained release directly at the site of injury. This study evaluates the therapeutic potential of MHY908, a novel mTOR inhibitor, delivered via a temperature-sensitive smart gel, in modulating inflammatory and oxidative responses in EB-relevant skin cell models.

Materials and Methods
Human keratinocytes and dermal fibroblasts were used to establish EB-like inflammatory models through stimulation with tumour necrosis factor-alpha (TNF-α, 0.1 ng/mL). The cytocompatibility of MHY908 was first evaluated using XTT assays to determine non-toxic concentration ranges (0–600 µM). MHY908 was subsequently formulated within a 20% (w/v) Poloxamer 407-based thermosensitive hydrogel at 0.025 %w/w, and characterised for adhesive properties, stability and *in vitro* release over 24 hours. Permeates from the release study was applied to both cell types, and inflammatory responses were quantified by measuring interleukin-6 (IL-6) secretion using ELISA. Intracellular oxidative stress was assessed using reactive oxygen species (ROS) assays.

Results
XTT analysis demonstrated that MHY908 was non-cytotoxic to both keratinocytes and dermal fibroblasts at concentrations up to 400 µM. Following formulation, the hydrogel exhibited favourable adhesive properties and maintained MHY908 stability for at least three months. Furthermore, the formulation provided sustained drug release, with approximately 65% of MHY908 released over 24 hours. TNF-α stimulation significantly increased interleukin-6 (IL-6) secretion in keratinocytes (97.43 ± 7.79 pg/mL) and fibroblasts (102.32 ± 9.21 pg/mL), confirming successful induction of EB-relevant inflammatory phenotypes ($p < 0.001$). Treatment with MHY908 (400 µM) significantly reduced IL-6 levels to 65.34 ± 5.41 pg/mL in keratinocytes and 82.42 ± 6.96 pg/mL in fibroblasts compared with TNF-α–treated controls.

Conclusions
MHY908 effectively attenuates inflammation and oxidative stress in both epidermal and dermal cell models relevant to EB. When delivered via a Poloxamer 407-based hydrogel, the formulation demonstrated sustained drug release and stability, supporting its potential as a promising localised therapeutic strategy for modulating the chronic inflammatory

wound environment in EB.

Abstract N°: ID-932

Topic: Genetics, inherited skin diseases

Ultrastructurally disordered leucocytes in Incontinentia pigmenti

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Introduction

The IKBKG (NEMO) signalling pathway is a multicomponent pathway that regulates the expression of hundreds of genes that are involved in various key cellular processes, including cell proliferation, cell survival, cell death, immunity and inflammation. Its mis-regulation is involved in many diseases such as Incontinentia pigmenti (IP), a rare X-linked genodermatosis in which skin changes are combined with anomalies of other organs.

Mutations of the IKBKG gene localised on the Xq28 chromosomal region are responsible for IP. Disorders of the IKBKG pathway are also involved in different haematological malignancies, which led us to ultrastructurally investigate blood cells in IP patients we had treated.

Materials and Methods

We investigated 6 members of one family, apart from the proband, 3 female relatives were affected: the proband's mother, the mother's sister and the proband's grandmother. The pedigree, genetic testing for IKBKG gene mutation, routine laboratory findings and ultrastructural analyses of leucocytes were done for the proband and relatives. All 4 patients were positive for IKBKG gene mutation, deletion of exons 4-10. All of them had typical clinical signs of IP according to Landy and Donnai's criteria confirmed by pathohistology.

For transmission electron microscopy investigation, leucocytes were fixed in glutaraldehyde, postfixed in osmium tetroxide and embedded in Araldite in a routine manner. The ultra-thin sections stained with uranyl acetate and lead citrate were analysed with transmission electron microscopes.

Results

In the IP affected subjects, we found pseudoplatelets budding from surface cytoplasm originating from granulocytes, monocytes and lymphocytes. It is known that in only two pathological conditions, leukaemias and acute infections, are small platelet-sized cytoplasmic fragments, not originating from megakaryocytes, observed in blood. The main explanation for this phenomenon is that leukaemic cells have the tendency to fragment and disrupt. However, further investigations in leukaemias have clearly indicated that pseudoplatelets originate from the cells of granulocyte line, monocytes and lymphoblasts by budding from their peripheral cytoplasm.

Besides pseudoplatelets, an unusual appearance of granulocyte and monocyte nuclei was observed. Nuclei of some monocytes were bizarrely lobulated, while nuclei of some granulocytes were radially segmented. In the nuclei of all types of leucocytes we observed electron-dense, solitary spherical granules surrounded by electron-lucent halo and perchromatin granules. This kind of nuclear aberration and the peculiar monocyte nuclei are similar to those seen in different types of leukaemias.

In one patient, giant perichromatin granules, very large in diameter, were observed. In addition to pseudoplatelets and nuclear anomalies, some of the neutrophil granulocytes were hypogranular. Perichromatin granules are composed mainly of mRNA and proteins, the increase in the number, and infrequently in size, may be an indicator of aberration in protein synthesis activity. It is possible that the presence of perichromatin granules in investigated patients also reflected a disturbance in RNA synthesis.

Conclusions

The finding of ultrastructurally disordered leucocytes with pseudoplatelets in 4 IP patients, compared to ultrastructural disorders of leucocytes in acute leukaemias and some acute infections, led us to hypothesize that a similar molecular mechanism may lay behind these disorders. The morphological appearance of pseudoplatelets in some way resembles apoptotic blebs. As IKBKG gene mutations are the cause of IP, and IKBKG gene mis-regulation is involved in different types of leukaemias, we hypothesized that pseudo-platelets may be the result of IKBKG gene mutation/mis-regulation of proapoptotic influence and its morphological form.

Abstract N°: ID-967

Topic: Genetics, inherited skin diseases

RARE ASSOCIATION OF AUTOIMMUNE POLYENDOCRINOPATHY-CANDIDIASIS-ECTODERMAL DYSTROPHY WITH LARGE GRANULAR LYMPHOCYTIC LEUKEMIA: THERAPEUTIC CHALLENGE FOR DERMATOLOGIST-VENEREOLOGIST

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Introduction

The autoimmune regulator (*AIRE)* gene encodes a transcription factor that is crucial for the negative selection of self-reactive T cells in the thymus. When *AIRE* genes are mutated, this process is disrupted, leading to the survival of autoreactive T-cells causing Autoimmune Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy (APECED), monogenic autosomal-recessive disease which belongs to inborn errors of immunity (prevalence 1:250.000). Patients with APECED suffer from chronic mucocutaneous candidiasis (CMC) without displaying susceptibility to any other pathogen. Permanent clonal expansion may drive hematologic malignancies, such as large granular lymphocytic leukemia (LGLL). The standard basis of therapy is hormone replacement, but patients who require immunosuppressive therapy have a significant risk of systemic candidiasis and others opportunistic infections.

We present a severe course of APCED complicated by LGLL requiring prolonged mycophenolate mofetil (MMF) therapy.

Materials and Methods

Direct sequencing of the *AIRE* gene in this patient revealed a homozygous R257X mutation resulting in a truncated, nonfunctional *AIRE*. In patient's parents we found the same heterozygous mutation. In the patient's serum, we detected several autoantibodies by indirect immunofluorescence and ELISA (antiadrenal, antiparietal, antinuclear, liver-profile antibodies).

Results

A 39-year-old woman had a history of enamel hypoplasia, and CMC from childhood. At the age of 15 years, she developed hypoparathyroidism and autoimmune hepatitis, which suggested possibility of APECED. At the age of 18 years, she was diagnosed with Addison's disease and pernicious anemia, while at 35 years, she developed a gastric neuroendocrine tumor which was surgically removed. At the age of 36 years, she was transfusion-dependent (hemoglobin 84 g/L, MCV 111 fL), despite parenteral B12 supplementation, accompanied by severe leukolymphocytosis (WBC 46.1×10^9/L, lymphocytes 39×10^9/L). Peripheral blood lymphocyte immunophenotyping (T-Ly CD3+ 99%, T-Ly CD4+ 2%, T-Ly CD8+ 97% , CD4/CD8 index 0,02, NK-Ly CD3-56+ 0.2%, B-Ly CD19+CD20+ 0.5%), bone marrow biopsy and investigation of T-cell receptor clonality showed T-cell large granular lymphocytic leukemia (LGLL). MMF (2x750 mg), indicated in LGLL, was introduced which led to significant laboratory improvement (WBC 11.9×10^9/L, Lymph 10×10^9/L, hemoglobin 104g/L, MCV 107 fL). At the age of 37 years, despite the improvement of hematological parameters with MFF therapy, CMC significantly worsened. The patient developed vulval condylomata acuminata and recurrent Herpes simplex virus labial infections. During the last 2 years of follow-up, removal of condylomata acuminata with liquid nitrogen and topical 5% imiquimod resulted in disappearance of the genital warts. The patient was advised to take Human Papillomavirus (HPV) vaccine. Systemic therapy (fluconazole 200 mg/day over 3 weeks, 2–3 courses per year) and chronic topical prophylaxis (nystatin suspension and amphotericin B lozenge) significantly improved the course of CMC.

Chronic prophylaxis with acyclovir (200 mg bid) reduced the HSV-1 recurrences. It is well-known that genital HPV infection is associated with cervical and anogenital cancers, while CMC can be complicated by oral squamous cell carcinoma.

Conclusions

Mutations in the AIRE gene impair normal immune tolerance mechanisms, enabling the persistence of autoreactive T-cells and autoantibodies, which contribute to multiple organ-specific autoimmune diseases and CMC. Our extremely rare case of APECD associated with LGLL demonstrates that administration of prolonged MMF for LGLL may be associated with worsening of CMC and relapses of HSV and HPV infections. Due to the high risk of malignancy, it is necessary to advise early vaccination against HPV and lifelong management of candidiasis and HSV. Careful monitoring is mandatory for early diagnosis of malignancies in APECED patients.

Abstract N°: ID-980

Topic: Genetics, inherited skin diseases

High-Risk Cutaneous Malignancy in Epidermodysplasia Verruciformis: A Rare Case

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Introduction

Epidermodysplasia verruciformis (EV) was first described in 1922 by Lewandowski and Lutz. It is a rare genodermatosis with autosomal recessive inheritance, characterized by increased susceptibility to cutaneous infections with specific types of human papillomavirus (HPV), related to a defect in cell-mediated immunity.
We report a case of EV associated with multiple epithelial carcinomas, detailing the clinical and evolutionary features of this condition.

Materials and Methods

A 33-year-old man, born to non-consanguineous parents and with no significant past medical history, had presented since the age of 12 years with flat wart-like lesions initially localized to the hands and feet, and later progressively extending to the knees.

During the past year, the course was marked by the rapid appearance and enlargement of multiple cutaneous tumors, prompting consultation. A diagnosis of epidermodysplasia verruciformis was then established.

Surgical excision of the largest lesion, located on the right frontal region, was performed with margin control. Histopathological examination revealed a moderately differentiated squamous cell carcinoma with multiple vascular emboli.

Dermoscopy of the facial lesions identified 14 suspicious lesions, including 9 highly suggestive of basal cell carcinoma, showing characteristic features: chrysalis structures, maple-leaf–like areas, concentric structures, ulcerations, as well as arborizing dotted vessels and globules.

In addition, the patient presented multiple achromic macules covered with pityriasiform scales, consistent with associated pityriasis versicolor.

Additional excision of the suspicious lesions was scheduled with histopathological analysis, combined with topical application of 5-fluorouracil and prescription of acitretin at a dose of 1 mg/kg/day for the verrucous lesions. A multidisciplinary discussion, including the oncology team, recommended adjuvant radiotherapy in view of the high risk of progression of the diagnosed squamous cell carcinoma.

Results

Lutz–Lewandowsky disease is a rare genetic disorder with a multifactorial origin, involving genetic, ultraviolet, and probably immunological factors. It is found worldwide, although it is rarely reported in Black patients.

Prognosis depends on the oncogenic potential of certain HPV types, which are responsible for cutaneous carcinomas in photo-exposed areas in 30–60% of cases.

Malignant transformation most often occurs after the age of 30, sometimes after 40, and represents a major turning point in disease progression.

Malignant lesions are observed almost exclusively in sun-exposed areas and may be associated with other cutaneous conditions or opportunistic infections, such as Fordyce angiokeratoma, tinea cruris, or pityriasis versicolor.

Tumor recurrences are frequent, even after surgery and radiotherapy, making long-term follow-up essential.

New therapeutic options (interferon, vitamin D analogues, retinoic acid–interferon combination therapy) offer promising perspectives.

Conclusions

Epidermodysplasia verruciformis is a rare genodermatosis, frequently associated with certain genetic abnormalities. We report a case of EV that progressed to malignant cutaneous transformation, leading to a significant change in prognosis.

Abstract N°: ID-985

Topic: Genetics, inherited skin diseases

Trichoscopic Characteristics of Hereditary Scalp Dysplasias: A Descriptive and Analytical Study

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Introduction
Hereditary scalp dysplasias are rare and heterogeneous disorders, often revealed during early childhood. Their diagnosis relies on the identification of abnormalities that may be difficult to characterize clinically. Trichoscopy is a non-invasive tool that allows detailed evaluation of the scalp. The aim of this study was to describe the trichoscopic features of hereditary scalp dysplasias and to assess their contribution to diagnostic and syndromic orientation.

Materials and Methods
A descriptive and analytical observational study was conducted including patients with suspected hereditary scalp dysplasia. Standardized trichoscopic examination was performed using a DermLite DL5 dermoscope with multizonal analysis. A trichoscopic severity score (DDSS) was applied to each patient. Statistical analysis was descriptive and exploratory, using non-parametric tests (Spearman correlation and Fisher's exact test), with statistical significance set at $p < 0.05$.

Results
Nine patients with a mean age of 5.4 ± 3.0 years and a sex ratio of 3.5 were included, all presenting with early-onset hair abnormalities. Clinical examination revealed decreased hair density in 77.8% of cases. Trichoscopy showed a predominance of single-hair follicular units (>60%) in 77.8% of patients and anisotrichosis in 100%. White dots and pigtail hairs were observed in patients with hypohidrotic ectodermal dysplasia and were absent in most other patients. At least one specific hair shaft abnormality was identified in all patients, with multiple abnormalities observed in 77.8% of cases. The most frequent abnormalities were trichorrhexis invaginata and trichorrhexis nodosa (77.8% each), with no cases of pili torti or monilethrix. The syndromic phenotype suggested Netherton syndrome in 77.8% of cases and hypohidrotic ectodermal dysplasia in 22.2%. The trichoscopic severity score (DDSS) was high (median 10/15) and showed a negative correlation with hair density and a positive correlation with the predominance of single-hair follicular units ($p < 0.05$). Absence of white dots was associated with absence of hypohidrosis ($p < 0.05$). Trichorrhexis invaginata was exclusively observed in patients with a Netherton syndrome phenotype ($p < 0.01$).

Our findings confirm the value of trichoscopy as a simple and non-invasive tool for the diagnostic orientation of hereditary scalp dysplasias. Quantitative follicular abnormalities and anisotrichosis reflect impaired follicular development, as previously described in the literature. Trichorrhexis invaginata, exclusively observed in patients with Netherton syndrome, appears to be a particularly suggestive diagnostic feature. Conversely, the presence of white dots in patients with hypohidrotic ectodermal dysplasia may reflect partially preserved sweat gland function. Finally, the association between a high DDSS and major follicular abnormalities suggests that trichoscopy may help assess disease severity and guide genetic evaluation.

Conclusions

The identification of characteristic trichoscopic patterns may enable improved phenotypic stratification and prioritization of genetic testing in hereditary scalp dysplasias.

Abstract N°: ID-1005

Topic: Genetics, inherited skin diseases

Response to secukinumab in a case of recalcitrant Darier disease

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Introduction
Darier disease (DD) is a rare autosomal dominant genodermatosis caused by mutations in the *ATP2A2* gene, resulting in impaired calcium homeostasis and abnormal keratinocyte adhesion. It is characterized by a chronic relapsing course with keratotic papules and plaques, predominantly affecting seborrheic areas, often complicated by secondary infection and inflammation. Disease management is challenging, as many patients are refractory to conventional therapies. Emerging evidence suggests a role of inflammatory pathways, including the IL-17 axis, in disease pathophysiology, supporting the potential use of biologic agents.

Materials and Methods
We report the case of a 56-year-old man with severe and recalcitrant DD who demonstrated a positive response to secukinumab after multiple unsuccessful therapies.

Results
The patient had a long-standing history of DD, characterized by widespread hyperkeratotic papules and plaques involving the face, cervical region, trunk, and suprapubic area, without oral or mucosal involvement. The disease course was marked by frequent exacerbations requiring multiple cycles of oral antibiotic therapy. Previous conventional treatments, including topical steroids and systemic retinoids (acitretin 25 mg daily), as well as surgical treatment of verrucous localized lesions, failed to achieve adequate control of the disease. Considering persistent severe disease and impaired quality of life, treatment with baricitinib 4 mg per day was initiated, without significant clinical improvement after 6 months. Treatment with secukinumab 300 mg monthly was subsequently started in association with acitretin 25 mg daily, leading to a marked and sustained clinical response, with a significant reduction in inflammatory lesions, fewer infectious exacerbations, and a marked improvement in quality of life. The response was sustained for a one-year follow-up, with a favourable safety profile and no relevant adverse events.

Conclusions
DD remains a therapeutic challenge, particularly in severe and refractory cases. This case highlights the potential efficacy of IL-17 inhibition with secukinumab as a therapeutic option for DD, supporting the hypothesis that inflammatory pathways contribute to disease activity. Although evidence remains limited, biologic therapies may represent a promising therapeutic option in selected patients. Further studies are needed to better define their role in the management of this genodermatosis.

Abstract N°: ID-1049

Topic: Genetics, inherited skin diseases

Cutaneous vascular malformations in familial cerebral cavernous malformations: a case report.

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Introduction

Cerebral cavernous malformations (CCM) are low-flow vascular lesions affecting 0.16-0.5% of the population. While approximately 80% of cases are sporadic, 20% are familial with autosomal dominant inheritance and incomplete penetrance.

Familial CCM (FCCM) is caused by loss-of-function mutations in three genes: CCM1/KRIT1 (53–65% of cases), CCM2/MGC4607 (around 20%), and CCM3/PDCD10 (10–16%). The presence of multiple cerebral cavernomas on neuroimaging is the key clinical indicator of familial disease, with roughly 85% of patients with multiple lesions harboring germline pathogenic variants. Cutaneous vascular malformations, although present in only about 9% of FCCM patients, represent an additional clinical marker that may support the diagnosis of familial disease. Three cutaneous phenotypes have been described in this setting: hyperkeratotic capillary-venous malformations, capillary malformations, and venous malformations.

Materials and Methods

We present a case illustrating the association between cutaneous vascular lesions and FCCM.

Results

A 69-year-old male with known multiple cerebral cavernomas under neurosurgical follow-up presented with violaceous papules on the left hemiface, right lateral neck, and upper chest that had developed approximately one year prior to consultation. The patient reported significant bleeding after a shaving injury. No family history of CCM was documented, and his children were asymptomatic and had not undergone neuroimaging. Physical examination revealed multiple soft, compressible, violaceous papules with a lacunar appearance on dermoscopy, distributed over the face, neck, and trunk. Doppler ultrasound was performed on the cutaneous lesions. It demonstrated a vascular signal only in the largest lesion on the right side of the neck, showing a millimetric central vessel with a low-velocity monophasic venous waveform on pulsed Doppler examination. These clinical and ultrasonographic findings were consistent with cutaneous venous malformations.

The coexistence of multiple cerebral cavernomas and cutaneous venous malformations strongly suggested familial CCM, and the patient was referred for germline genetic testing, which is currently pending. In FCCM, cutaneous vascular malformations are known to be strongly associated with CCM1/KRIT1 mutations, and a high proportion of patients with any cutaneous vascular malformation subtype carry pathogenic variants in this gene.

Conclusions

This case highlights the association between cutaneous vascular malformations and familial cerebral cavernous malformations. While the presence of multiple cerebral cavernomas remains the primary indicator for offering genetic

testing, cutaneous lesions represent an additional clinical marker that supports the diagnosis of familial disease and may facilitate the identification of at-risk individuals. Dermatologists should be aware of these cutaneous manifestations, as their recognition can contribute to timely referral, multidisciplinary management, and appropriate family screening. Given the lack of standardized protocols for monitoring these patients, follow-up should be individualized according to the neurological burden, genetic background, and cutaneous phenotype.

Abstract N°: ID-1063

Topic: Genetics, inherited skin diseases

Hair surface morphology in acral peeling skin syndrome: more than a skin-limited disorder?

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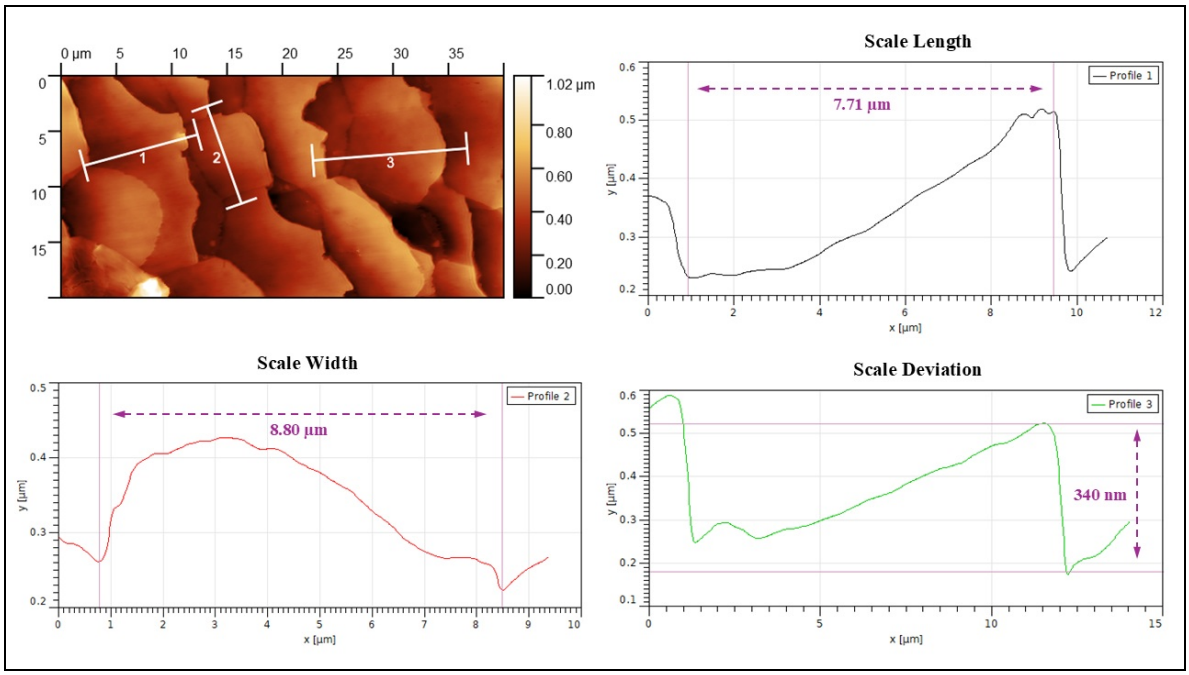
Introduction

Acral peeling skin syndrome (APSS) is a rare autosomal recessive genodermatosis characterized by superficial exfoliation and blistering of the skin, predominantly affecting the volar and dorsal aspects of the hands and feet. Clinical manifestations are commonly triggered by mechanical stress, humidity, and increased temperature, and the diagnosis may be challenging due to a nonspecific presentation, particularly in early childhood. Although APSS is generally considered a skin-limited disorder, isolated reports describe subtle hair-related abnormalities, including reduced hair density. In broader forms of peeling skin syndromes, easily removable hair has also been reported. Moreover, clinical observations suggest that the severity and expression of APSS may vary over time; however, data addressing potential age-related differences in APSS remain limited. The present study aims to contribute to a better understanding of hair characteristics in patients with APSS using non-invasive analytical methods, with particular emphasis on atomic force microscopy (AFM).

Materials and Methods

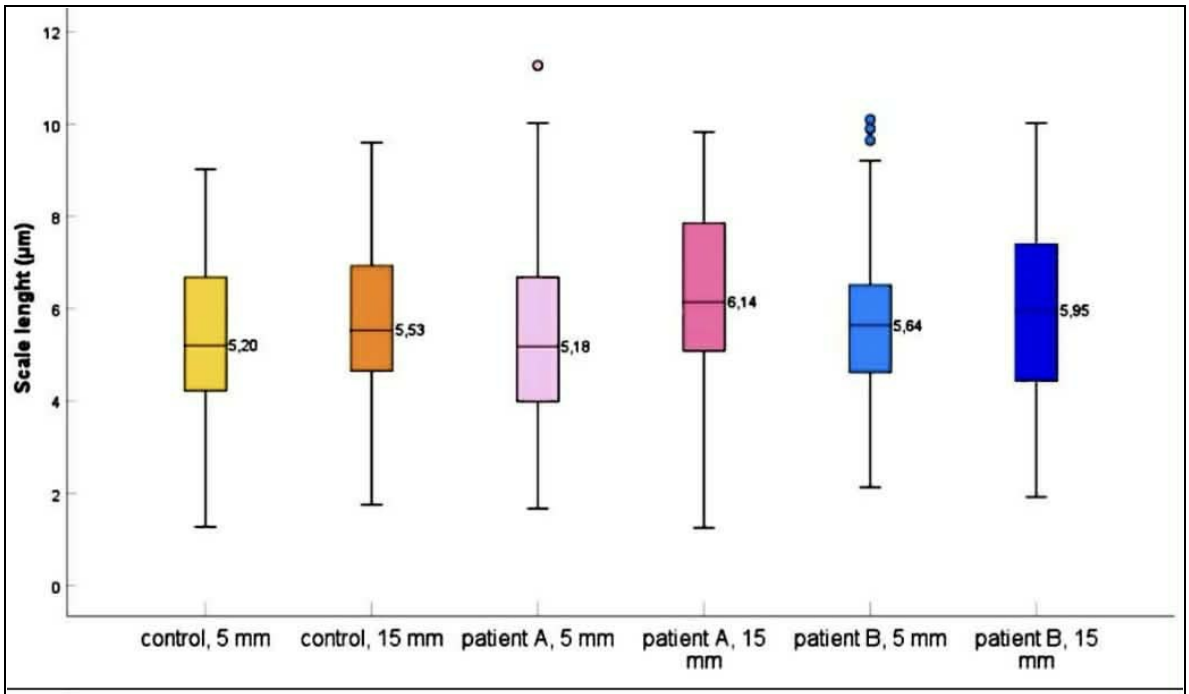
Hair surface morphology was analyzed by atomic force microscopy (AFM) in pediatric subjects of the same sex, including age-matched healthy controls and two patients with acral peeling skin syndrome, Patient A (6 years) and Patient B (2 years). For each subject, five hair shafts were analyzed; each hair was examined at two locations along the shaft (5 mm and 15 mm from the hair root), with five AFM images acquired at each location (ten images per hair in total). Cuticle scale length, width, and step height were measured using line profile analysis. Most measurements were conducted on scan areas of 40 × 20 µm; when this was not possible due to surface conditions, smaller scan sizes were applied. For presentation and comparative purposes, morphometric parameters obtained from healthy control hair samples were averaged and reported collectively as a single control group.

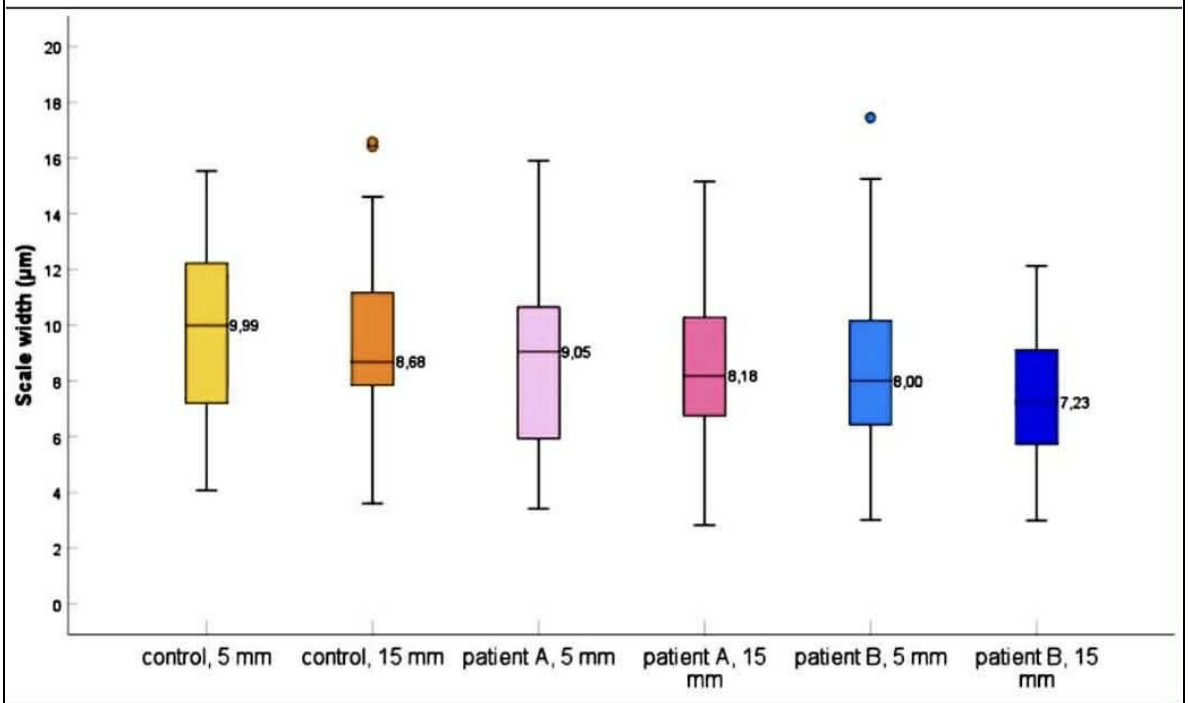


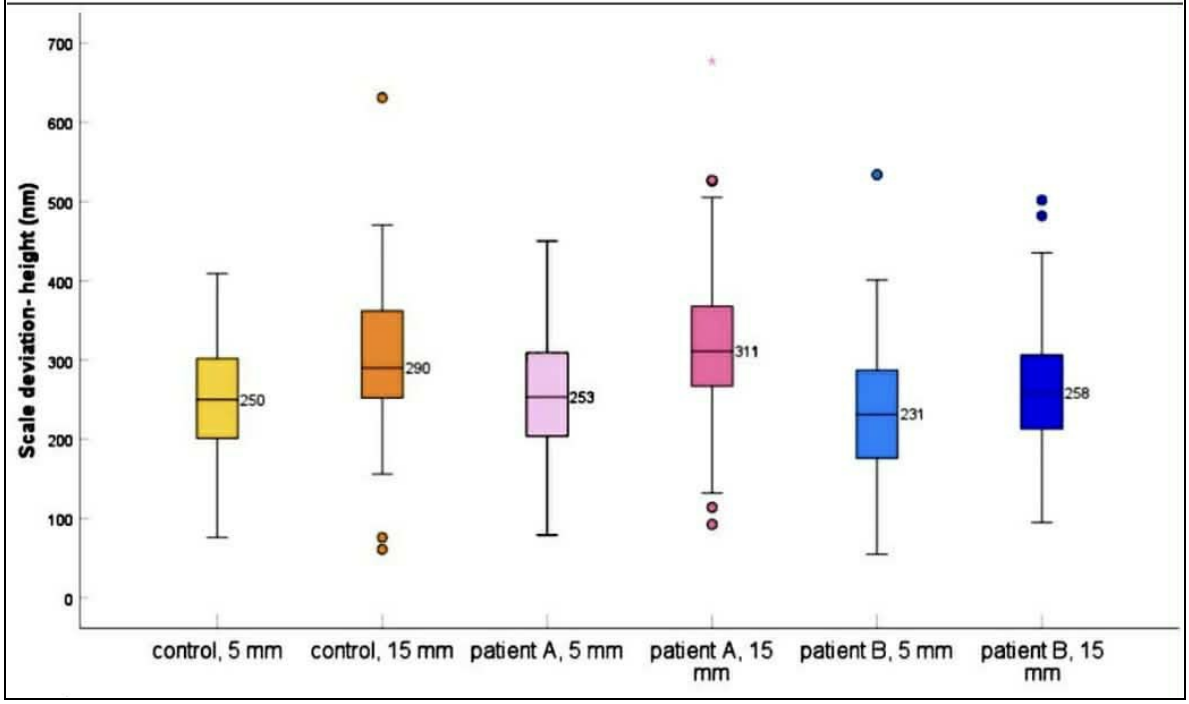
Parameters analyzed with AFM in terms of hair scale.

Results

Significant differences in scale step height and scale width were observed between controls and APSS patients, as well as between the two APSS patients themselves ($p < 0.01$). Consistent changes between measurements performed at 5 mm and 15 mm from the hair follicle ($p < 0.05$) reflected physiological structural variation along the hair shaft and confirmed the reliability of the AFM measurements.


Scale lenght (µm)
12
10
8
6
4
2
0
5,20
5,53
5,18
6,14
5,64
5,95
control, 5 mm
control, 15 mm
patient A, 5 mm
patient A, 15 mm
patient B, 5 mm
patient B, 15 mm


Scale width (µm)
20
18
16
14
12
10
8
6
4
2
0
9,99
8,68
9,05
8,18
8,00
7,23
control, 5 mm
control, 15 mm
patient A, 5 mm
patient A, 15 mm
patient B, 5 mm
patient B, 15 mm


Scale deviation- height (nm)
700
600
500
400
300
200
100
0
250
290
253
311
231
258
control, 5 mm
control, 15 mm
patient A, 5 mm
patient A, 15 mm
patient B, 5 mm
patient B, 15 mm

Box-and-whisker plots presenting all metric measurements (length, width, and scale step height) measured by AFM at 5 mm and 15 mm from the hair root in controls and APSS patients.

Conclusions

This study provides a comparative analysis of hair surface morphology in children diagnosed with acral peeling skin syndrome and in healthy controls using atomic force microscopy. The results demonstrate age-related differences in hair cuticle morphology among the APSS patients, with hair parameters observed in the older patient showing greater similarity to those of the control group. This observation is consistent with clinical reports suggesting that manifestations of acral peeling skin syndrome may become less pronounced with age. To our knowledge, this study represents one of the first AFM-based characterizations of hair morphology in patients with acral peeling skin syndrome. The findings contribute to a better understanding of potential structural hair alterations associated with this rare genodermatosis and provide a foundation for future studies investigating disease progression and age-related changes in APSS.

Abstract N°: ID-1123

Topic: Genetics, inherited skin diseases

Gentamicin as a read-through therapy in genodermatoses caused by premature termination codons: a systematic review

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Introduction

Genodermatoses caused by nonsense mutations leading to premature termination codons represent a group of rare disorders for which no causal therapies are currently available. Repurposing aminoglycosides as molecular read-through agents offers a unique opportunity to target the genetic cause of disease rather than its downstream manifestations. Beyond its antimicrobial properties, gentamicin has been shown to induce translational read-through of premature stop codons, potentially restoring partial expression of disease-related proteins. This off-label molecular mechanism has been explored across several rare inherited skin diseases. However, the available clinical evidence remains fragmented. We performed a systematic review to evaluate the molecular and clinical effects of gentamicin therapy in genodermatoses.

Materials and Methods

A systematic literature search was conducted across PubMed, Embase, the Cochrane Library, and ClinicalTrials.gov from database inception to December 2025. Publications reporting clinical use of gentamicin in genetically confirmed genodermatoses were considered eligible. Data were extracted on treatment characteristics, molecular outcomes, clinical response, and safety. The methodological quality of included studies was assessed using design-appropriate evaluation approaches. Owing to clinical and methodological heterogeneity, findings were synthesised narratively.

Results

Seventeen publications met inclusion criteria, reporting on patients with epidermolysis bullosa, Hailey–Hailey disease, hereditary hypotrichosis simplex, and Nagashima-type palmoplantar keratosis. Gentamicin was administered via topical, oral, intradermal, or systemic routes. Across diseases, gentamicin therapy was associated with partial restoration or increased expression of disease-related structural proteins, including type VII collagen and laminin-332. Clinically, most reports described reductions in blistering or erosions, improved wound healing, decreased mucosal involvement, and improvements in patient-reported outcomes. Safety findings were generally favourable, particularly for topical and oral formulations, although outcome reporting was heterogeneous and long-term follow-up was limited.

Conclusions

Gentamicin-induced read-through therapy represents a promising molecularly targeted approach for selected genodermatoses caused by nonsense mutations. While current evidence is based on heterogeneous and predominantly

low-level studies, consistent signals of molecular restoration and clinical benefit across multiple diseases support further prospective investigation of this repurposed therapeutic strategy.

Abstract N°: ID-1134

Topic: Genetics, inherited skin diseases

Plantar Hidradenoma Masquerading as Malignant Neurofibroma in NF1

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Introduction
Neurofibromatosis type 1 (NF1) is a complex genetic disease characterized mainly by cutaneous, neurologic, and skeletal manifestations, with an increased risk of benign and malignant peripheral nerve sheath tumors. In NF1 patients, new or rapidly evolving painful lesions, particularly on acral sites, raise concern for malignant transformation. However, not all suspicious lesions are neurogenic. We report a rare plantar hidradenoma clinically mimicking a malignant neurofibroma, highlighting the diagnostic challenge in NF1 patients.

Materials and Methods
A 67-year-old female diagnosed with NF1 at the age of 35 was referred for a painful plantar nodule that had rapidly enlarged over four weeks, causing gait impairment. All her daughters are affected by NF1; one of her granddaughters carries a heterozygous pathogenic NF1 splice-site variant (NC_000017.10:g.29670026G>C; NM_001042492.3:c.7063-1G>C).

On clinical examination, she had multiple café-au-lait macules, numerous cutaneous neurofibromas, bilateral axillary and right inguinal freckling, short stature, scoliosis, and Lisch nodules. The plantar lesion appeared ulcerated with hemorrhagic crusts and necrosis. Dermoscopy revealed a chaotic, asymmetric pattern with structureless dark blue–black and violaceous areas, whitish–yellow amorphous zones, and extensive ulceration, raising suspicion for malignancy. Cutaneous ultrasound showed a poorly defined, heterogeneous lesion involving the dermis and superficial subcutaneous tissue, with loss of normal skin stratification and absent vascularity on color Doppler. Given the context, a plexiform neurofibroma or malignant peripheral nerve sheath tumor was suspected. Surgical excision and histopathology were performed.

Results
Histopathology unexpectedly revealed a hidradenoma, an adnexal tumor exceptionally rare on the plantar surface. Complete excision followed by skin grafting resulted in an uneventful postoperative course and good functional recovery.

Conclusions
This case emphasizes that rapidly growing, painful plantar lesions in NF1 are not always neurogenic or malignant. Rare adnexal tumors such as hidradenoma can mimic malignant transformation both clinically and dermoscopically, particularly on acral surfaces. Awareness of these entities is essential to avoid diagnostic pitfalls. Histopathology remains

crucial for definitive diagnosis.

Abstract N°: ID-1212

Topic: Genetics, inherited skin diseases

Targeted IL-17A inhibition in Mendelian Disorders of Cornification: Clinical response to secukinumab in a patient with ALOX12B mutations

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Introduction

Mendelian Disorders of Cornification (MEDOC) are a heterogenous group of genodermatoses characterized by impaired keratinization and epidermal barrier dysfunction. Severity extends from mild scaling to life-threatening presentations at birth. Recent studies have demonstrated a “psoriasis-like” immune profile, characterized by an activation of Th17/IL-17 axis across various MEDOC genotypes. Targeted inhibition of Il-17 pathway has emerged as a potential therapeutic approach for selected patients.

Materials and Methods

We report a case of a 29-year-old female patient, followed at our dermatology department for generalized, congenital ichthyosis. She was born prematurely at 36 weeks of gestation, with a severe “harlequin-baby” presentation. She has been suffering since birth from a generalized fine scaling phenotype with severe erythema, mild palmoplantar keratoderma and ectropion. Conventional therapies, like keratolytics and systemic retinoids have been tried previously and failed. Since genetic testing has not been done at birth, Next Generation Sequencing (NGS) was performed.

Results

NGS identified two compound heterozygous substitutions c.1294C>T and c.1859C>A in ALOX12B gene (NM_001139.3) on chromosome 17. The first is a nonsense mutation, leading to the replacement of amino acid arginine by a premature termination codon (stop gain) at position 432 (p. Arg432*) of the ALOX12B protein. The second is a missense mutation, resulting on the substitution of the amino acid proline by glutamine at position 620 (p. Pro620Gln) of the same protein. Both mutations have been described in homozygosity and compound heterozygosity in individuals with Autosomal Recessive Congenital Ichthyosis 2 (OMIM 242100). Based on the previously described Th17-driven immune profile, the patient was started on secukinumab 300 mg at weeks 0,1,2,3,4 and then every 4 weeks. Within 4 weeks she demonstrated a remarkable clinical response, which has been maintained the following months.

Conclusions

Secukinumab may represent a therapeutic option for selected patients with MEDOC. Targeting IL-17A allows the modulation of inflammatory pathways that may contribute to disease expression. In our case, IL-17A inhibition was associated with clinical improvement following failure of conventional therapies. Further studies are required to define the role of biologics in the management of MEDOC. These observations support further evaluation of pathogenesis-based treatments in MEDOC and many other genodermatoses.

Abstract N°: ID-1217

Topic: Genetics, inherited skin diseases

Clinical and Pedigree-Based Identification of Autosomal Dominant Piebaldism in a Four-Generation Family

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Introduction

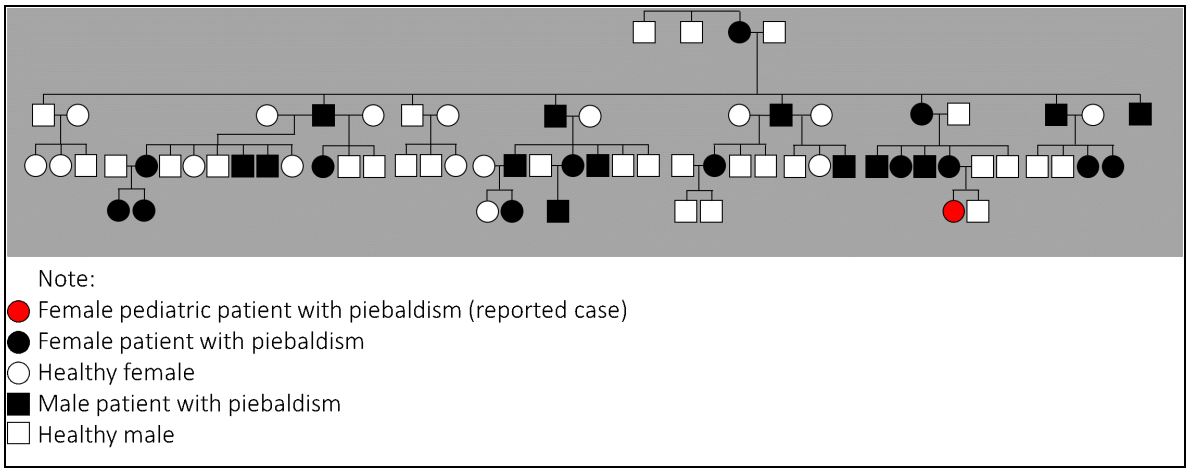
Piebaldism is a rare congenital pigmentary disorder caused by mutations in the *KIT* gene and inherited in an autosomal dominant pattern. It presents as well-demarcated depigmented macules with a characteristic distribution, frequently accompanied by a white forelock. Although clinically distinctive, diagnosis may be challenging in mild cases when characteristic features are concealed by cosmetic measures. In addition to cutaneous manifestations, piebaldism may affect psychological well-being and quality of life. This report emphasizes the value of clinical assessment and pedigree analysis in establishing the diagnosis of autosomal dominant piebaldism in the absence of molecular testing.

Materials and Methods

A 10-year-old girl presented with congenital, non-progressive depigmented patches involving the face, trunk, and extremities, along with circumscribed poikilosis in the frontal scalp region. A detailed family history was obtained, and a four-generation pedigree was constructed. Among 56 family members evaluated, 27 individuals exhibited similar pigmentary abnormalities of varying severity. Affected relatives spanned multiple generations and included the patient's mother, extended family members, and great-grandmother. Several individuals reported concealing typical features, such as white forelock and facial depigmentation, using hair dyes, cosmetics, or clothing.

Results

The proband showed classic features of piebaldism, including a prominent white forelock and well-defined depigmented macules with a predominantly central and ventral distribution. Pedigree analysis identified affected individuals in all four generations, involving both males and females. Of 56 family members, 27 (48.2%) were affected. The proportion of affected individuals by generation was 33.3% in the first, 75.0% in the second, 41.7% in the third, and 55.6% in the fourth generation. No mating between two affected individuals was identified, and unaffected offspring were observed among affected parents. Two family branches were entirely unaffected. These findings support autosomal dominant inheritance with affected individuals likely being heterozygous for the pathogenic allele, while homozygous mutations were considered unlikely. Phenotypic variability and cosmetic camouflage contributed to underrecognition in several family members.



Four-generation family pedigree demonstrating autosomal dominant inheritance of piebaldism

Conclusions

This case underscores the importance of meticulous clinical evaluation and pedigree analysis in diagnosing inherited pigmentary disorders, particularly in settings where molecular testing is unavailable. Piebaldism can be reliably identified through its characteristic phenotype and inheritance pattern. Thorough family history assessment is essential, as cosmetic concealment may obscure typical features and delay diagnosis. Patient education and genetic counseling are crucial to address psychosocial concerns and to inform families of the approximately 50% transmission risk to offspring when one parent is affected.

Abstract N°: ID-1224

Topic: Genetics, inherited skin diseases

Managing Selumetinib-Associated Skin Toxicities in a Neurofibromatosis Type 1 Patient with Inoperable Plexiform Neurofibromas

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Introduction
Plexiform neurofibromas (pNFs), benign tumors originating from Schwann cells, cause significant morbidity in neurofibromatosis type 1 (NF1) due to pain, disfigurement, and compression of vital structures. Selumetinib, a MEK1/2 inhibitor, has shown efficacy in reducing tumor volume in inoperable pNFs. However, dermatologic adverse effects (AEs) may impair quality of life and adherence, highlighting the need for effective management.

Materials and Methods
We report on a teenage NF1 patient with painful, inoperable pNFs treated with oral selumetinib (25 mg/m^2 twice daily). Eligibility criteria included significant morbidity, tumor size >3 cm, surgical inoperability, and performance status >70%. Baseline hematologic, hepatic, pulmonary, and cardiac assessments were performed. Cutaneous AEs were monitored every 3–6 months and graded using CTCAE v5.0. Tumor response and symptom improvement were recorded.

Results
Patients experience at least one cutaneous AE, most commonly xerosis, paronychia, and acneiform rash mostly in older patients with phototypes II–III. Our patient (skin phototype III) developed early acneiform rash and later phototoxicity/photosensitivity during sun exposure. Management included topical corticosteroids, emollients, and strict sun protection; topical clindamycin was irritative and poorly tolerated. No hair or nail changes were observed.

Conclusions
Selumetinib-related skin AEs may lead to treatment interruption in up to 20% of cases, with tumor rebound in 75% of those. Tailored dermatologic management is crucial to minimize AEs, prevent therapy discontinuation, and ensure sustained clinical benefit.

Abstract N°: ID-1277

Topic: Genetics, inherited skin diseases

Incontinentia Pigmenti: Report of two neonatal cases

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Introduction

Incontinentia pigmenti (IP) is a rare X-linked genodermatosis, predominantly affecting females. It is characterized by a typical cutaneous evolution through several stages following the lines of Blaschko and may be associated with neurological, ophthalmological, and dental abnormalities. We report two neonatal cases illustrating the clinical variability and evolutionary pattern of this condition.

Materials and Methods

Case 1

A 3-month-old infant, born after a well-followed pregnancy, with no family history of similar conditions, presented with cutaneous lesions starting at 10 days of life.

The initial eruption consisted of vesicular lesions distributed along the lines of Blaschko, which subsequently evolved into verrucous lesions.

Clinical examination revealed blaschkolinear hyperpigmentation predominantly affecting the back. No hair or nail abnormalities were noted. Neurological examination was unremarkable.

Case 2

A 15-day-old newborn, born after a well-followed pregnancy, without parental consanguinity, with a family history of similar symptoms in a cousin.

The disease began at birth with vesicular lesions localized to the left hand, followed by progressive extension to the rest of the body, in an afebrile context.

Physical examination showed:

- vesicles on an erythematous base following the lines of Blaschko on the upper and lower limbs;
- verrucous papules coalescing into plaques with a linear blaschkolinear distribution on the limbs;
- hyperpigmented lesions with a marbled appearance following the lines of Blaschko on the back and buttocks.

There was no alopecia, no onychodystrophy, and no neurological manifestations, including seizures or infantile spasms.

Results

Incontinentia pigmenti classically evolves through four cutaneous stages, which may be successive or overlapping: vesicular, verrucous, hyperpigmented, and hypopigmented. Both of our cases illustrate this typical evolution, with the coexistence of multiple stages in the same patient.

The presence of a positive family history in the second case supports the genetic origin of the disease. The absence of extracutaneous involvement in both patients highlights the phenotypic variability of IP and underlines the importance of long-term multidisciplinary follow-up.

Conclusions

Incontinentia pigmenti should be considered in any neonate presenting with vesicular or verrucous eruptions distributed along the lines of Blaschko. The diagnosis is primarily clinical and requires regular follow-up to detect potential extracutaneous involvement, even in the absence of initial signs.

Abstract N°: ID-1319

Topic: Genetics, inherited skin diseases

Intermediate-Dose Naltrexone for Refractory Hailey–Hailey Disease in an Elderly Patient with Multiple Comorbidities: A Case Report

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Introduction

Hailey–Hailey disease (HHD) is a rare autosomal dominant acantholytic dermatosis caused by ATP2C1 mutation, leading to impaired keratinocyte adhesion and recurrent erosions in intertriginous areas. Disease course is chronic and relapsing, often exacerbated by friction, infection, and emotional stress. Management is challenging, particularly in elderly patients with multiple comorbidities. Naltrexone has emerged as a potential therapeutic option in refractory cases. We report an elderly patient with familial HHD successfully treated with intermediate dose Naltrexone.

Materials and Methods

A 76-year-old female with underlying medical histories of Parkinson's disease, hypertension, arrhythmia, osteoporosis and adjustment disorder presented with recurrent painful scaly erosions over bilateral groin region for 3 years. Upon physical examination, she had painful and pruritic erythematous plaques and erosions on bilateral crural folds, accompanied with yellow crusting. First-degree family history was positive for similar complaints. She had been treated in the past with topical and oral antibiotics, antifungals and topical steroids but was refractory to all kinds of treatment. Systemic examination was unremarkable. KOH smear was negative. Excisional biopsy of the right groin region was performed. After inadequate response to previous treatment, oral intermediate-dose Naltrexone was initiated at 12.5 mg daily. Clinical response was assessed over two months.

Results

Histopathological analysis with hematoxylin and eosin (H&E) staining demonstrated parakeratosis, hyperkeratosis, and acanthosis with prominent suprabasal and intraepidermal acantholysis forming cleft-like spaces, compatible with the 'dilapidated brick wall' appearance . Elongated dermal papillae lined by basal keratinocytes projected into the acantholytic areas. Occasional dyskeratotic keratinocytes were noted. The upper dermis showed vascular proliferation with perivascular mononuclear infiltrates. Direct immunofluorescence revealed linear type IV collagen staining along the dermal–epidermal junction without blister formation. IgG, IgA, IgM, and C3 were negative. Findings were compatible with HHD. After two months of Naltrexone, marked reduction in erythema, erosion, and exudation was observed. Patient reported significant reduction of pain and pruritus with substantial improvement in quality of life. No adverse effects occurred.

Conclusions

This case demonstrates efficacy of intermediate dose Naltrexone in refractory familial HHD in a medically complex elderly patient. At the intermediate dose of 12.5 mg daily used in this case, Naltrexone provides both the immunomodulatory effects seen at low dose and potentially enhanced anti-inflammatory activity. The excellent safety profile and absence of drug interactions make Naltrexone particularly valuable in elderly patients with polypharmacy and multiple comorbidities. While most published HHS cases utilize low dose Naltrexone (1.5-4.5 mg daily), higher doses (25-50mg) have demonstrated efficacy in treating pruritus and other inflammatory dermatoses. This case adds to the growing evidence supporting intermediate-dose Naltrexone as a first-line option for refractory HHD, particularly in

vulnerable populations.

Abstract N°: ID-1351

Topic: Genetics, inherited skin diseases

Pediatric vascular ehlers–danlos syndrome: Two case reports with emphasis on cutaneous, dental, and histological Findings

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Introduction
Ehlers–Danlos syndromes (EDS) are inherited connective tissue disorders characterized by skin fragility, joint hypermobility, and abnormal wound healing. Diagnosis relies primarily on clinical and histological evaluation, while management remains essentially preventive. We report two cases of pediatric patients presenting clinical features suggestive of EDS.

Results

Patient 1

An 8-year-old boy presented with anetodermic and cicatricial lesions of the lower limbs, associated with marked skin hyperextensibility and ligamentous hyperlaxity. His medical history included right-sided cryptorchidism. Clinical examination revealed easy bruising and hematomas following minimal trauma, loose and highly extensible skin, papyraceous scars, a tendency toward wound dehiscence after suturing, and canaliform nail dystrophy of the right great toe. Chest radiography showed a boot-shaped heart, while dorsolumbar imaging revealed scoliosis. Electrocardiography demonstrated repolarization abnormalities, and Holter monitoring detected both ventricular and supraventricular extrasystoles. Ophthalmologic examination, performed to rule out lens subluxation, was normal. Skin biopsy showed an acanthotic orthokeratotic epidermis and a fibrous dermis containing numerous thin collagen fibers. Orcein staining revealed abundant elastic fibers with focal fragmentation.

Patient 2

A 14-year-old boy consulted for diffuse pain in the lower limbs that had been evolving for several months, associated with the progressive appearance of brownish macules and lesions on the legs. According to his parents, the patient had exhibited abnormal skin elasticity, skin fragility, and poor wound healing since early childhood, occurring after minimal trauma. Clinical examination revealed thin, soft, slightly extensible skin with atrophic “cigarette-paper” scars. Multiple brownish and violaceous macules were observed, predominantly over the anterior tibial region, suggestive of ochre dermatitis related to capillary fragility, along with numerous old ecchymoses on the lower limbs. No associated arthropathy was noted. Oral examination showed thin and fragile mucosa, delayed healing following extraction of a deciduous tooth, and dental crowding, suggestive of periodontal involvement of systemic origin related to a collagen disorder. This pronounced dental involvement constituted the distinctive feature of this case, in contrast to the absence of other visceral or osteoarticular manifestations.

Conclusions
Ehlers–Danlos syndrome is a rare connective tissue disorder primarily affecting the skin and joints. The vascular type is distinguished by a high risk of spontaneous vascular ruptures (iliac, splenic, or renal arteries) or visceral ruptures

(intestine, gravid uterus). The skin is typically thin, translucent, and fragile, with atrophic scars and frequent spontaneous bruising. Wound dehiscence may also occur following surgical procedures. These two pediatric cases illustrate the clinical variability of vascular EDS and emphasize the diagnostic value of cutaneous, dental, and histological findings, particularly when genetic testing is not readily available. Early recognition allows the implementation of appropriate preventive measures and follow-up

Abstract N°: ID-1353

Topic: Genetics, inherited skin diseases

WHEN THREE ACRAL KERATINIZATION DISORDERS MEET : A RARE CLINICAL TRIAD

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Introduction

Acral keratinization disorders constitute a heterogeneous group of rare dermatological entities characterized by abnormal epidermal differentiation and hyperkeratosis predominantly affecting the palms and soles. Marginal acral hyperkeratosis is a rare condition presenting with hyperkeratotic papules along the borders of the hands and feet, whereas punctate palmar keratoderma is characterized by multiple discrete keratotic lesions involving the palmar surface or creases. Aquagenic keratoderma, an uncommon acquired or hereditary disorder, manifests as transient whitish papules or plaques triggered by water exposure and is thought to be related to eccrine sweat duct dysfunction or alterations in the stratum corneum. The coexistence of these conditions is exceptional and suggests a shared pathophysiological background involving keratinization abnormalities.

Results

A 30-year-old Moroccan woman with no significant personal or familial medical history presented with a 10-year history of asymptomatic, non-pruritic hyperpigmented papular lesions involving the hands and feet. Four years after disease onset, whitish thickened plaques appeared on the feet, with marked accentuation after water exposure. Clinical examination revealed multiple monomorphic, closely clustered hyperpigmented micropapules, some flattened and others umbilicated, distributed bilaterally and symmetrically over the thenar eminences extending to the wrists and along the lateral borders of the feet. Small punctate keratotic lesions were observed on the distal palmar crease and the hypothenar area of the right hand. Whitish hyperkeratotic plaques were noted along the medial borders of both feet. Histopathological examination demonstrated acanthosis with marked hyperorthokeratosis. A topical treatment combining keratolytic agents and emollients was prescribed, leading to a partial but noticeable clinical improvement.

Conclusions

This observation highlights a rare coexistence of three distinct acral keratinization disorders. The overlapping clinical and histological features support the hypothesis of a shared underlying defect of keratinization and stratum corneum barrier function. Aquagenic plantar keratoderma in this setting may reflect eccrine sweat duct involvement or increased water permeability of an altered stratum corneum. Awareness of such associations is crucial to avoid diagnostic confusion with other palmoplantar dermatoses and may contribute to a better understanding and classification of acral keratodermas

Abstract N°: ID-1460

Topic: Genetics, inherited skin diseases

Tracing Blaschko's Blueprint: Early-Onset Linear Porokeratosis in Childhood with Clinicodermoscopic and Histopathological Correlation

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Introduction

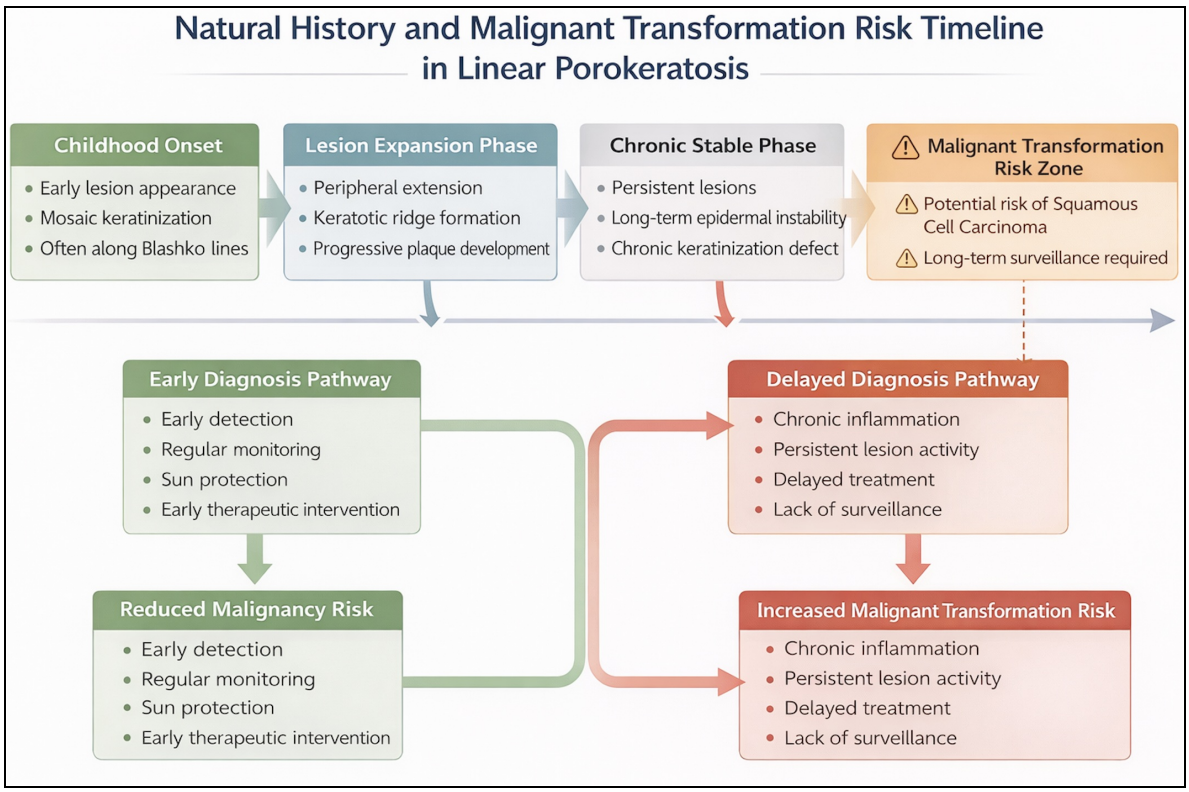
Linear porokeratosis is a rare disorder of keratinization caused by clonal proliferation of abnormal keratinocytes, typically presenting along Blaschko's lines during infancy or early childhood. Clinically, lesions appear as linear or annular plaques with sharply demarcated hyperkeratotic ridges and central atrophy. Histopathologically, the presence of a coronoid lamella is diagnostic. Among porokeratosis variants, linear porokeratosis is particularly significant due to its relatively higher risk of malignant transformation, especially into squamous cell carcinoma, compared with disseminated superficial actinic porokeratosis. Early recognition using clinicodermoscopic and histopathological correlation is therefore essential for timely therapeutic intervention and long-term oncologic surveillance.

Materials and Methods

Detailed clinical, dermoscopic, and histopathological evaluation was performed on a pediatric patient presenting with a linear keratinization disorder. Clinical morphology, lesion distribution, onset pattern, and systemic history were documented. Dermoscopy was performed to assess peripheral keratotic ridge morphology and central pigmentation patterns. A punch biopsy was obtained from the active lesion margin and processed with routine hematoxylin and eosin staining. Baseline lesion mapping and measurement were performed to facilitate longitudinal monitoring. Therapeutic planning was guided by disease extent, age of onset, and progression pattern.

Results

A five-year-old girl, with lesion onset first noticed at approximately nine months of age, presented with a progressively enlarging hyperpigmented patch over the left thigh. Over time, the lesion evolved into multiple coalescing plaques with raised keratotic margins arranged in a linear distribution consistent with a Blaschkoid pattern. The lesions remained largely asymptomatic, with gradual peripheral expansion and relative central flattening.Dermoscopy demonstrated a well-defined peripheral whitish hyperkeratotic rim with inner brownish pigmentation and focal vascular dots, correlating with known dermoscopic signatures of porokeratosis and supporting early non-invasive diagnostic suspicion.Histopathological examination confirmed the presence of a cornoid lamella, characterized by a thin column of parakeratosis overlying focal dyskeratotic keratinocytes with a reduced granular layer beneath, along with mild superficial perivascular lymphocytic infiltrate. These features established the diagnosis of linear porokeratosis.Given the very early age of onset, linear distribution, and literature-documented association of linear porokeratosis with relatively higher long-term malignant transformation risk compared to other variants, the patient was categorized as requiring structured long-term surveillance. At present follow-up, there was no clinical or histopathological evidence of dysplasia or malignant transformation.The patient was initiated on systemic therapy with close clinical monitoring. The family was counselled regarding chronic disease course, strict photoprotection, and the importance of long-term dermatological follow-up for early detection of potential malignant change.



Natural Disease Course and Early Diagnostic Pathway in Linear Porokeratosis

Conclusions

This case underscores the importance of integrated clinicodermoscopy and histopathology in accurately diagnosing early-onset linear porokeratosis. Pediatric presentation requires increased vigilance because of its progressive nature and documented higher malignant potential compared to other porokeratosis variants. Early diagnosis, appropriate systemic therapy, and structured long-term follow-up are critical in preventing disease progression and detecting early neoplastic transformation. This case highlights the value of multimodal diagnostic evaluation in improving prognostic stratification and guiding individualized long-term management strategies in rare keratinization disorders.

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Topic: Genetics, inherited skin diseases

Basal Cell Carcinomas Mimicking Acrochordons in Gorlin Syndrome: The Diagnostic Value of Dermoscopy

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Introduction

Gorlin syndrome, also known as nevoid basal cell carcinoma syndrome (NBCCS), is a rare genetic disorder with autosomal dominant inheritance, most commonly associated with mutations in the *PTCH1* gene, leading to constitutive activation of the Hedgehog signaling pathway. This alteration confers a predisposition to the early and multiple development of basal cell carcinomas (BCCs), often beginning in childhood or adolescence. In affected patients, BCCs may present with clinically misleading appearances, including acrochordon-like lesions mimicking benign skin tags. In this setting, dermoscopy plays a key role in identifying characteristic features suggestive of BCC and guiding prompt management

Materials and Methods

We report the case of a 15-year-old female patient with a history of multiple resected odontogenic cysts, who presented with several pedunculated pigmented cutaneous lesions located on the back and neck, initially interpreted as acrochordons. Clinical examination revealed hypertelorism, macrocephaly, dorsal kyphosis, and multiple palmar pits. Dermoscopic examination of the acrochordon-like lesions showed arborizing vessels, blue-gray globules, and ovoid nests, which are characteristic features of pigmented basal cell carcinoma. Surgical excision followed by histopathological analysis confirmed the diagnosis of BCC.
The diagnosis of Gorlin–Goltz syndrome was established based on the presence of several major criteria (multiple BCCs, odontogenic cysts, palmar pits) and minor criteria. In the absence of a family history, genetic testing was performed to investigate a de novo mutation, which revealed a pathogenic mutation in the *PTCH1* gene.

Results

In patients with Gorlin syndrome, basal cell carcinomas may exhibit atypical clinical presentations, including acrochordon-like morphology, making diagnosis challenging, particularly in young patients in whom BCCs are rarely suspected. Dermoscopy is an essential diagnostic tool, enabling the identification of specific morphological criteria such as arborizing vessels, blue-gray globules, and ovoid nests, even when the clinical appearance is misleading.
It is important to emphasize that Gorlin syndrome may arise not only through autosomal dominant familial transmission but also through de novo mutations, as observed in our patient. Recognition of associated clinical features, including craniofacial, osteoarticular, and cutaneous abnormalities, remains crucial in prompting genetic evaluation. Genetic confirmation allows for appropriate multidisciplinary management and targeted family screening.

Conclusions

Acrochordon-like basal cell carcinomas represent a significant diagnostic pitfall in patients with Gorlin syndrome. Dermoscopy enables early diagnosis despite deceptive clinical presentations and should be systematically performed when evaluating suspicious pedunculated lesions in young patients.