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Contents

Editorial

The latest issue of the *International Journal of Pediatric Dermatology* opens with a Letter to the Editor addressing the **Expert Panel on Pediatric Photoprotection**, convened by the World Health Academy of Dermatology and Pediatrics at Guglielmo Marconi University in Rome last March. The topic of photoprotection, particularly in pediatric populations, has garnered increasing attention in recent years - not only among researchers and dermatologists but also among pediatricians and the general public - due to emerging concerns regarding the potential health risks associated with sunscreens containing organic compounds. The short and long-term consequences of inadequate sun protection, including an elevated risk of skin cancer and melanoma, have long been recognized by both the scientific community and the public. Consequently, photoprotection-based prevention campaigns have gained traction since the 1980s. More recent concerns have focused on the safety profile of sunscreens, particularly those formulated with organic filters and those utilizing nanoparticle delivery systems, which may themselves pose health risks. Recent literature has consistently demonstrated that organic sunscreen agents are systemically absorbed and detectable in the bloodstream following topical application. Furthermore, these compounds have been implicated in endocrine disruption and carcinogenesis in animal models. Although extrapolation from animal studies to human health outcomes must be approached with caution, the precautionary principle suggests that alternative photoprotective strategies should be considered. The International Expert Panel provided authoritative recommendations on lifestyle modifications and sunscreen use tailored to pediatric populations, aimed at mitigating the adverse health effects of ultraviolet exposure. In alignment with the most current scientific evidence, the Panel identified non-nanoparticle zinc oxide formulations containing less than 25% active ingredient as the safest and most effective alternative to organic sunscreens.

This issue also features a case report by Maria Isabel Pastura (Buenos Aires), describing Dowling-Degos disease and exploring the differential diagnosis of **reticular pigmentary anomalies in pediatric patients**. Despite overlapping clinical presentations, these conditions differ significantly in terms of age of onset, anatomical distribution, progression, systemic associations, and distinctive histopathological and molecular characteristics.

Antonio Iannone and colleagues present the case of a 4-month-old Moroccan infant with pigmentary dermatitis involving the trunk and extremities. Clinical and dermoscopic findings supported the diagnosis of **Terra Firma Forme Dermatosis**.

Jessica Wright and Jeffrey Rein report a case of neonatal **human metapneumovirus infection accompanied by a diffuse rash and petechiae**. The authors propose that the presence of the Rumpel-Leede phenomenon (pressure-induced purpura) may obviate the need for further diagnostic investigations to exclude serious conditions such as vasculitis, thrombocytopenia, or meningococcemia in the context of febrile viral illness.

Finally, Theoharis C. Theoharides, a leading authority on mast cell biology, describes **five pediatric cases of cutaneous mastocytosis co-occurring with autism spectrum disorder**. He hypothesizes a non random association, suggesting that mast cell activation in cutaneous mastocytosis may

contribute to the pathogenesis of neurodevelopmental disorders. If validated, therapeutic strategies targeting mast cell activation could offer meaningful clinical benefits.

We hope you enjoy this issue.

Editor-in-Chief

Professor Fabio Arcangeli

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Letter to the Editor

International Panel Expert on "Photoprotection in pediatrica age". March, 01, 2025. Guglielmo Marconi University of Rome, Italy

F. Arcangeli[1], R. Karls[2], T. Lotti[1], G. Monfrecola[3], C. R. Payne[4], C. Romagnoli[5], G. Ruggiero[1], L. Sytnyk[6] and U. Wollina[7]

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KEYWORDS

Pediatric age,
Vitamin D,
Cutaneous melanoma,
Photoprotection

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Dear Editor,

Organized by the World Health Academy of Dermatology and Pediatrics, at the Guglielmo Marconi University in Rome, an international meeting of experts, including dermatologists and pediatricians, was held on March 1, 2025, to review and discuss photoprotection in pediatric age (Fig. 1, 2).

The meeting was highly successful, both in terms of participation and the relevance of the topics discussed, as well as the high scientific value of the presentations. Prof. Costantino Romagnoli outlined the main issues related to vitamin D, particularly its relationship with sun exposure. Prof. Giuseppe Monfrecola addressed photocarcinogenesis, emphasizing that in recent decades there has been an increase in both skin carcinomas and melanoma and that their prevention must start from the infancy. Prof. Fabio Arcangeli discussed the risk factors for cutaneous melanoma (Fig. 3), highlighting how sunburns during childhood significantly contribute to the development of melanoma in adulthood, and presented studies showing a reduction in melanoma cases among adolescents and young adults following photoprotection campaigns initiated in the 1980s.

Fig. 1. *Meeting program.*

Fig. 2. *Participants: Fabio Arcangeli, Raimonds Karls, Torello Lotti, Giuseppe Monfrecola, Christopher Rowland Payne, Costantino Romagnoli, Giuseppe Ruggiero, Liliana Sytnyk, Uwe Wollina.*

Risk Factors for Cutaneous Melanoma

Genetic

- A family history of melanoma ***RR 1,74**
- Atypical moles > 5 **RR 10,49** ****FAMMM and *****DNS**
- Many moles (N > 60) **RR 3,26**
- Giant Congenital Melanocytic Nevi 2 %
- *Xeroderma Pigmentosus*

Environmental

- *Skin that sunburns easily / Fair complexion* **RR 3,64**
- A history of sunburn (mainly in pediatric age) **RR 2,02**
- Sunbed exposure **RR 2,03**
- Weakened immune system (e.g. HIV)

there is clearly an interaction between genetics and environment

* RR Relative Risk when RS Standard Risk is 1

**FAAMM Familial Atypical Multiple Mole Melanoma nsyndrome

***DNS Dysplastic Nevus Syndrome

Fig. 3. *Risk Factors for Cutaneous Melanoma.*

Prof. Torello Lotti illustrated the most up-to-date phototherapy procedures for certain dermatological conditions (e.g., vitiligo, psoriasis, atopic dermatitis), stressing that, with the abandonment of PUVA therapy, modern phototherapy must meet criteria of relative safety and can only be proposed after the age of 16. Prof. Uwe Wollina elegantly recounted how sun exposure practices have evolved since the early decades of the last century and how the use of sunscreens has spread rapidly. However, paradoxically, sunscreen use alone has not reduced the incidence of skin cancers. Prof. Christopher Rowland Payne also spoke about sunscreens, citing examples of their improper use, such as insufficient application and neglecting areas near clothing. Both experts noted that many organic filters are now considered potentially harmful to human health due to their endocrine-disrupting properties, carcinogenesis stimulation, and potential harm to the environment.

Prof. Raimond Karls emphasized that protective clothing should always be prioritized during childhood. Regular clothing blocks 20% of UV rays (UPF 5), while special fabrics block 80% (UPF 50+). However, uncovered areas should still be protected with sunscreen. Prof. Liliana Sytnyk spoke about the importance of a diet rich in antioxidant foods to enhance natural photoprotection. Finally, Prof. Ruggiero presented the results of an Italian survey involving 107 family pediatricians (caring for 103,255 children aged 0 to 14 years) and 508 parents. The survey revealed a low level of awareness and the need to promote photoprotection education and awareness campaigns.

The Photoprotection Group of the Italian Federation of Pediatricians (FIMP), which promoted this survey, proposed a summary slogan named C.O.C.C.O. (Fig. 4), whose guidelines were approved by the international panel. The final conference document (Appendix 1) subsequently received extensive coverage in both national and international media.

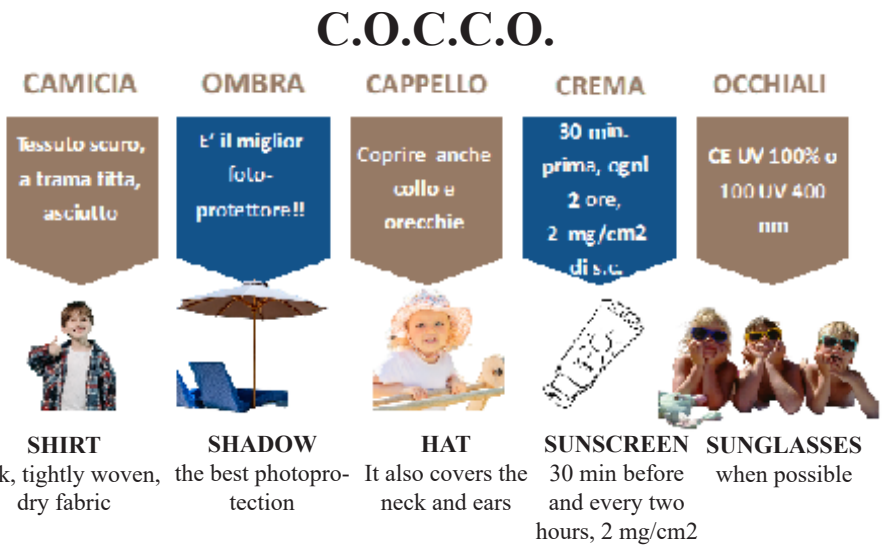

Fig.4. *C.O.C.C.O. guidelines.*

APPENDIX 1

Recommendations for Photoprotection in Pediatric Age

Vitamin D

• Sun exposure is essential for vitamin D production. Vitamin D deficiency is reported in 40-50% of the population aged 0 to 18 years in Italy and Europe. The skin produces 80% of vitamin D following sun exposure (dietary intake accounts for only 20%, of which only 60% is bioavailable). To ensure optimal vitamin D production, it is estimated that 15 minutes of sun exposure to the face and limbs, 2–3 times per week is sufficient.

The Dangers of the Sun

• Excessive and inappropriate sun exposure during childhood is a significant cause, in adulthood, not only of premature skin aging but also of the possible development of squamous cell carcinoma, basal cell carcinoma and cutaneous melanoma: the first one linked to cumulative sun damage, the others linked to repeated sunburns due to excessive acute photoexposures. Both DNA damage from UVB and UVA and immunesuppression UV-induced play a role in human photocarcinogenesis.

Prevention

To reduce the risk of skin cancer (both carcinoma and melanoma), the following measures are essential:
a) Identifying high-risk individuals, such as those with a RHP (Red Hair Phenotyphe) or patients taking immunessuppressive drugs.
b) Implementing effective photoprotection strategies to prevent sunburn and minimize lifelong ultraviolet ray exposure.
c) Following a diet rich in antioxidants (vitamins C, E, A, polyphenols, flavonoids, carotenoids), probiotics and elements such as zinc, selenium, copper.

Photoprotection in Pediatric Age

• Photoprotection in children is crucial and involves more than just applying sunscreen. It is a holistic practice that requires non-pharmacological measures and healthy lifestyle habits. The guidelines from the FIMP Photoprotection Group, known as COCCO (2), are endorsed.

• Infants under 6 months must not be exposed to direct sunlight.

• Children of all ages should avoid sun exposure whenever possible. Unlike adults, children have no desire for tanning and are not motivated to seek sun exposure intentionally.

When sun exposure is unavoidable (e.g. outdoor activities or at the beach) and if the UV index is equal to or higher than 3, the following precautions are recommended:

• Wear protective clothing, preferably in dark colors (darker colors provide better protection), dry fabrics (better than wet), and tightly woven materials

(denim, polyester, or cotton-polyester blends). Technical clothings with a high Ultraviolet Protection Factor (UPF) are ideal as they block approximately 80% of UV rays, unlike regular fabrics which only block 20% of UV radiation.

- Always wear a hat with a wide brim to protect the neck and ears (caps with visors leave these areas uncovered).
- Use sunglasses when possible (CE UV 100% or UV 400 nm) to protect the eyes from prolonged UV exposure.
- For exposed skin apply sunscreen, especially for fair-skinned children, using products with inorganic filters such as zinc oxide. Apply approximately 2 mg/cm² of skin (around 10-15 ml for a 5-year-old) 30 minutes before sun exposure, and reapply every two hours or after swimming.
- Opt for water-resistant, fragrance-free, and biodegradable products in eco-sustainable packaging when available.

Important points:

- Sunscreen should not create a false sense of security, leading to extended sun exposure.
- Avoid sun exposure between 11 am and 4 pm.

Sunscreens

Concerns over the toxicity of sunscreens have been raised by various pediatric associations (1). The use of inorganic filters is recommended during childhood (2) in order to avoid potential allergic reaction or even just hypothetical risks due to cutaneous absorption of organic filters (3). Additionally, these substances could harm the marine environment.

The World Health Organization, Centers for Disease Control, and American Academy of Dermatology continue to recommend sunscreen use for skin cancer prevention (4).

Sunscreens containing the physical filters ZnO and TiO 2 are considered GRASE (**G**enerally **R**ecognized **A**s **S**afe and **E**ffective) by the FDA (Food and Drug Administration) and pose minimal human or environmental safety concerns.

Recommendations:

- Do not use sunscreens under the age of six months
- Prioritize sunscreens with inorganic molecules (e.g., zinc oxide) that are broad-spectrum and stable, but avoid as a precaution formulations with nanoparticles or sprays.
- Combine sunscreens with natural antioxidants and immunostimulant ingredients.

It is recommended that Italian and European health authorities prudentially prohibit potentially harmful sunscreen ingredients and consider classifying sunscreens as drugs (as in the USA) rather than cosmetics, ensuring rigorous evaluation of their safety and efficacy.

Heliotherapy and Phototherapy

- Certain skin conditions (e.g., vitiligo, psoriasis, atopic dermatitis) may improve with sun exposure or artificial light. Heliotherapy should follow the guidelines mentioned earlier.
- Phototherapy, recommended only after the age of 16, may include UVB-NB (311 nm), excimer laser, and UVA-1 (355 nm) treatments. Photochemotherapy (PUVA) should only be considered if other treatments fail.

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Clinical Case

Reticular Pigmentary Anomalies in Pediatrics

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KEYWORDS

Dowling Degos disease, Gougerot-Carteaud, Acanthosis nigricans, Kitamura disease, Dohi disease, Naegeli-Franceschetti-Jadassohn Syndrome, Galli-Galli disease, Haber Syndrome

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ABSTRACT

Reticular pigmentary anomalies in childhood consists of different entities that clinically present with a common factor of a hyperpigmented reticular skin pattern. This is why they are particularly perplexing for the dermatologist in their daily practice. However, they differ from each other in terms of their age of onset, predominant location, preferred ethnicity, evolution, associated systemic involvement, distinctive histopathological and molecular characteristics, and their therapeutic response. A clinical case about a teenage male diagnosed with Dowling-Degos Disease, evaluated at the Pediatric Dermatology Service of Dr. Ricardo Gutiérrez Children's Hospital is reported as an example.

1. Introduction

Reticular pigmentary anomalies are a group of various described entities that present with characteristic reticular hyperpigmentation of the skin (1). Some of these may be associated with systemic involvement (2, 3). They are often perplexing for dermatologists in their practice, as the case studies are limited for most of them, making clinical differentiation difficult. These conditions exhibit an erratic response to available treatments (4-10). Almost all correspond to genodermatosis, although in the case of acanthosis nigricans, there can occasionally be a significant metabolic trigger in its pathophysiology (2, 3).

Due to their nature as chronic conditions, these have a significant social impact on pediatric patients as they predispose them to difficulties in accepting body image (especially during adolescence), rejection due to their aesthetic appearance, low self-esteem and a higher association with school bullying. In addition, occasionally these entities can be associated with limiting skin involvement, as in the case of those who have suppurative hidradenitis, or with implication of other organs, such as dental anomalies. This further justifies the need for detection to allow for the treatment of possible associated disorders.

The objective of this work is to review and compare the different etiologies, provide useful points for differentiation, and outline diagnostic and therapeutic approaches.

2. Clinical case

A 15-year-old male adolescent, previously healthy with no relevant family history, reports dermatosis of 2 years' duration. Physical examination reveals a reticular hyperpigmented plaque acquired in the anterior cervical region, with scattered macrocomedones, rough to the touch, with well-defined borders, measuring 5x10 cm (Fig. 1, 2). Possible differential diagnoses include: smooth muscle hamartoma, Becker's nevus, and reticular pigmentary anomaly. A biopsy of the cervical region reports: acanthosis, irregular elongation of crest networks, and mild basal hyperpigmentation; slight pigment drop and dilated hair follicles containing debris and keratin, surrounded by bundles of smooth muscle; moderate superficial perivascular linfohistiocytic inflammatory infiltrate, perianexial and comedocytic follicular dilation with mild basal hyperpigmentation. This is compatible with Dowling-Degos disease (Fig. 3). Topical treatment with Adapalene cream at 0.1% and Benzoyl Peroxide gel at 2.5% is initiated. After 4 months, it is supplemented with Dapsone gel at 7.5% with a very good response. Oral Azithromycin cycles at 500 mg per day are started, and photoprotection guidelines are recommended.

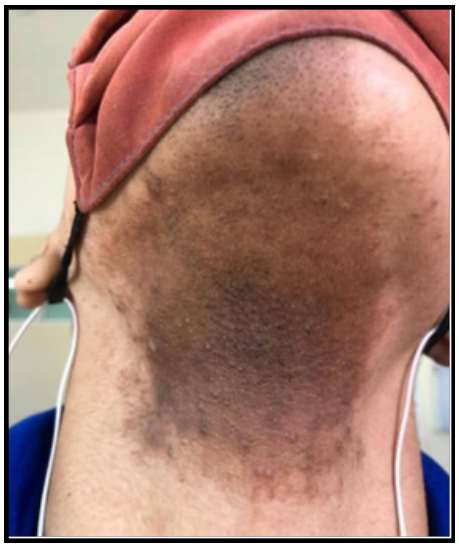

Fig. 1. *In the anterior cervical region: brownish rough plaque with macrocomedones inside.*

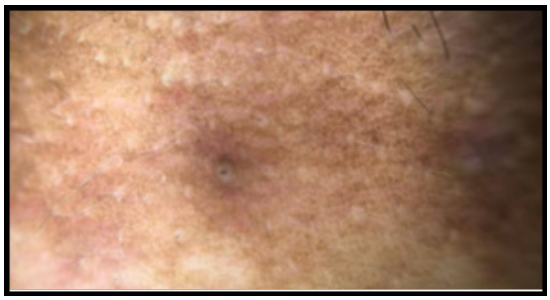

Fig. 2. *At higher magnification, a central macrocomedone is observed with peripheral brownish accentuation.*

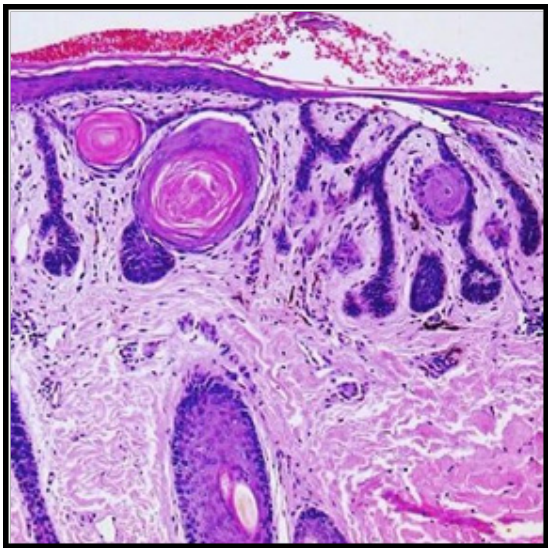

Fig. 3. *HyE at 100X: keratin-filled horn cyst (comedone); thinning of the suprapapillary epidermis; horn-like appearance due to interconnected crest networks; elongated crest networks; pigment loss.*

3. Discussion

A clinical approach to each entity is presented, along with tables of distinctive clinical features (Table I), molecular traits (Table II), histopathological characteristics (Table III), and therapeutic options (Table IV).

Table I. Summary of distinctive clinical features of each entity.

AN	Velvety hyperkeratotic plaques without pits. Onset at any age. Metabolic, syndromic, or hereditary association.
DD	Flexures, confluence. Onset in puberty.
K	Acral pits, early onset.
H	Verruciform papules on the trunk, facial erythema, pinpoint facial scars, early onset.
NFJ	Trunk and extremities, hypohidrosis, palmoplantar hyperkeratosis, and dental alterations.
D	Hypo/hyperpigmented macules on acral dorsal areas, acral atrophy, early onset.
GC	Trunk, scaly or velvety macules. Late onset. Possible hypopigmented lesions in high phototypes.
GG	Lentigines. Constant acantholysis in the basal layer. Late onset – adulthood.

Table II. Molecular features (1, 5, 11-13, 20, 23, 26, 28, 31).

DD	Mutations in KRT5, KRT14, POFUT1, and/or POGLUT1.
GC	Unknown.
K	Mutations in ADAM10.
D	Mutations in ADAR1 and/or ADAM10.
NFJ	Mutations in KRT1 and/or KRT14.
GG	Mutations in KRT5 and/or POGLUT1.
H	Unknown.
AN	Mutations in FGFR3 or INSR.

Table III. Comparative histopathological features (5, 7, 10, 11, 15, 16, 18-20, 26, 29).

DD	Epidermal digitiform proliferations and pilosebaceous follicle, elongation of crest networks, pigment incontinence, moderate hyperkeratosis.
GC	Compact hyperpigmentation, papillomatosis, thinning of the granular layer, epidermal atrophy.
K	Hyperpigmentation of basal keratinocytes, increased melanocytes, elongation of crest networks, epidermal atrophy.
D	Increased basal and epidermal melanin. Hypomelanosis in hypopigmented variants. No melanocytosis.
NFJ	Basal hyperpigmentation, moderate hyperkeratosis.
GG	Acantholysis. Dyskeratosis.
H	Hyperpigmentation of basal keratinocytes with slight elongation of crest networks. Dermal lymphocytic infiltrate.
AN	Dermo-epidermal hyperplasia, orthokeratosis, papillomatosis of the spinous layer, basal layer hyperpimentation without melanocytosis.

Dowling-Dego Disease (DD)

Is an autosomal dominant hereditary condition, infrequent, progressive, and symmetrical. It presents with round macules and papules that can be grayish, brownish, or blackish, asymptomatic, or mildly pruritic (11). They simulate comedones in the axillae, neck, and buttocks (5). Other manifestations include hypopigmentation, perioral pitting, and palmar and acral dorsal involvement (5). There is no internal systemic involvement (5, 11). A clinical-histological correlation is necessary for diagnosis.

It has been proposed that follicular occlusion is important in the pathogenesis of the disease, but it is not entirely clear. Mutations of the KRT5 gene, which codes for keratin 5 with loss of function, located on chromosome 12, have been described. This entity shows a fine linear Blaschko pattern, which reinforces the idea that the affected cells are keratinocyte precursors. It is important to mention the activity of the Notch signaling pathway, which determines cellular fate during embryogenesis, aiding the differentiation of the inter-

follicular epithelium, the hair follicle, and the homeostasis of melanocytes. This is relevant as mutations have been found in KRT14, POFUT1, and POGLUT1 (the latter two being part of the Notch pathway), affecting melanocytes and their melanosomes, which phenotypically express pigmentary defects (hyper- and hypopigmentation) (11-13).

Gougerot-Carteaud Confluent and Reticular Papillomatosis (GC)

Is a rare chronic condition that presents with exacerbations and remissions (4, 14, 15). It primarily affects women aged 10 to 35 years, with a preference for phototypes IV-V and VI (16). It consists of erythematous-brown papules or small warts forming confluent reticular pigmented plaques, located in the intermamary region, neck, and axillae, later affecting the abdomen, pubis, and face (4, 14-17).

Its etiopathogenesis is not yet defined. A genetic or acquired keratinization alteration has been described, which is the most widely accepted theory currently. Additionally, there could be an abnormal host response to fungal antigens from Malassezia furfur and/or bacterial antigens from Propionibacterium acnes, Staphylococcus epidermidis, and Actinomyces Dietzia (15, 16).

Kitamura Reticular Acropigmentation (K)

Is an autosomal dominant and very rare condition (6). It predominates in women in the first 20 years of life (18). It consists of atrophic depressed macules similar to freckles, arranged in a reticular pattern on the acral dorsal area and eventually on the face in the periorbital region (6, 18, 19). It may gradually affect other body areas (6, 18-20). Characteristic findings include palmo-plantar pits and fissures in the dermatoglyphics (18).

The mechanism involved is not yet known, although it appears to have similar pathophysiological bases to DD. There are case reports showing a mutation in the ADAM10 gene, which codes for a zinc metalloprotease (12).

Dohi Reticular Acropigmentation (D)

It presents with hyperpigmented and hypopigmented macules in a symmetrical reticular pattern on the dorsal surfaces of the hands and feet, primarily affecting young Japanese patients. It does not present with telangiectasias or atrophy. It is autosomal dominant, although there are reported cases of autosomal recessive and sporadic forms (7, 21, 22). It can extend proximally to the lateral neck and supraclavicular region and face (7, 22).

There are case reports of mutations in ADAR1 (adenosine deaminase, RNA-specific) on chromosome 1 and ADAM10, similar to what has been described for K (12).

Naegeli-Franceschetti-Jadassohn Syndrome (NFJ)

Is a rare autosomal dominant syndrome classified among ectodermal dysplasias (8, 23). It presents with partial or total absence of dermatoglyphics, palmoplantar keratoderma, hypohidrosis, reticular hyperpigmentation in skin folds, dental anomalies, and nail dystrophy (8, 23-25). The hyperpigmentation may completely disappear in adulthood.

The genes initially implicated code for keratin 1 and are located on chromosome 17q. Recently, the gene that codes for keratin 14 has also been described as a candidate (23).

Galli-Galli Disease (GG)

Is a rare autosomal dominant condition that typically presents between the second and seventh decades of life with confluent hyperkeratotic maculo-papules that later merge to form reticular patches and plaques on the neck, trunk, flexures, and extensions of the limbs. Isolated small macules may be observed in the same described areas (26). Like DD, it can be associated with suppurative hidradenitis (27).

It is associated with mutations in keratin 5, which may play a role in the function or transportation of melanosomes (12). Recently, it has also been linked to mutations in POGLUT1 (26).

Haber Syndrome (H)

Is a rare autosomal dominant condition characterized by photosensitive facial erythema similar to rosacea, manifesting in early adolescence, followed by the appearance of reticular hyperpigmentation on the trunk, proximal extremities, and axillae. Other signs include keratotic papules, comedonal lesions, and atrophic depressed scars. Multiple seborrheic keratoses appear during the first decade of life (10).

There have been few reports of this syndrome worldwide. It is not usually associated with mutations in keratin 5, but the spectrum of mutations expected for this entity is still unknown (10).

Acanthosis Nigricans (AN)

It consists of velvety brown plaques primarily in the skin folds of the neck, axillae, and groin (28), occurring in some hereditary, metabolic, and syndromic disorders (2, 3, 28-31). The prevalence is higher in individuals with darker skin (28).

Among its causal agents, we can mention:

• Mutations in the fibroblast growth factor receptor 3 (FGFR3): These have been identified as one of the genetic causes of hereditary acanthosis nigricans (AN), especially in early-onset extensive AN. It is known that mutations in this receptor cause various types of skeletal dysplasia that accompany AN, potentially leading to short stature in adulthood (28).

• Insulin resistance: Skin hyperpigmentation with AN is associated with insulin-like receptors in keratinocytes and dermal fibroblasts, and potentially with an estrogen-induced increase in glycosaminoglycan formation (29, 30). Additionally, AN has been found to be a composite marker of complex cardiometabolic risk, which can be a non-invasive, simple, and valuable clinical evaluation tool for public health screening to assess cardiometabolic risk in children (2, 3).

• Diet: Added sugar and servings of starchy foods have been associated with an increased risk of AN. This determines an association between diet and AN in young children (30).

• Mutations in the INSR gene: These lead to rare hereditary syndromes that cause insulin resistance, such as leprechaunism (Donohue syndrome), Rabson-Mendenhall syndrome, and type A insulin resistance (31).

4. Conclusion

Children with reticular pigmentary anomalies present similar skin manifestations, making it important to recognize the distinctive clinical features of each entity, their distribution, age of onset, and syndromic and metabolic associations. All of this will contribute to a clinical diagnosis that may eventually, according to the patient's needs, be accompanied by a histopathological study to support the suspected disease. Molecular studies are, in most of the developed entities, the way to arrive at a definitive diagnosis.

The proposed treatments in the literature are similar for all the pathologies mentioned in this work. However, there are some preferences (based on better therapeutic response) according to each disease. Nevertheless, no medication will offer a resolution of the case, as they all have a chronic and persistent evolution throughout life. Sun protection is of vital importance and should be promoted to prevent both worsening and exacerbation of the various mentioned conditions.

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DISCLOSURE

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Case Report

Terra Firma-Forme Dermatosis (TFFD)

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KEYWORDS

Terra firma-forme dermatosis, Duncan's disease, pigmentation disorder, hyperpigmented patches, dirty skin

ABSTRACT

The authors report the case of a 4-month-old child of Moroccan origins affected by pigmentary dermatitis extending to the body and limbs whose clinical and dermoscopic characteristics allowed a hypothetical diagnosis of Terra Firma Forme Dermatosis. Rubbing with 70 % isopropyl alcohol caused the lesions to disappear, confirming the diagnosis. This condition, whose origin is still not well understood, is decidedly rare in the first months of life.

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1. Introduction

Terra firma-forme dermatosis (TFFD), was first described in 1987 by Duncan as an acquired pigmentation disorder characterized by asymptomatic hyperpigmented patches or velvety plaques, which mimic the appearance of "dirty skin" (1). The anatomical sites most frequently affected are the trunk, extremities, neck and navel (2). TFFD affects both genders and all ages, although children and young adults have a higher risk to being affected. The etiopathogenesis is unknown. Delayed maturation of keratinocytes resulting in epidermal retention of keratin material and melanin was suggested (3). Diagnosis is clinical (appearance of the lesions), dermatoscopic (brown polygonal scales similar to plates arranged in a mosaic or cobblestone pattern) and confirmed with the rubbing test with 70% isopropyl alcohol.

2. Case Description

We describe the case of a 4-month-old boy of Moroccan origin, with hyperpigmented patches, brownish in color, rough to the touch, localized on the trunk and limbs, associated with cutaneous xerosis (Fig. 1). Cleansing with soap and water was ineffective. Dermatoscopic examination showed numerous polygonal brownish clods arranged in mosaic (Fig. 2). The disappeared of the lesions after rubbing with gauze soaked in 70% isopropyl alcohol (Fig. 3) confirmed the diagnosis of TFFD.

Considering the age of the child, skin xerosis and the wide spread of lesions, the home use of 10% urea cream was proposed with complete resolution. The age of the our child is unusual. The trhee youngest cases reported in the literature to date concern two girls aged 3 and 4 months and a boy aged 6 months (4-6).

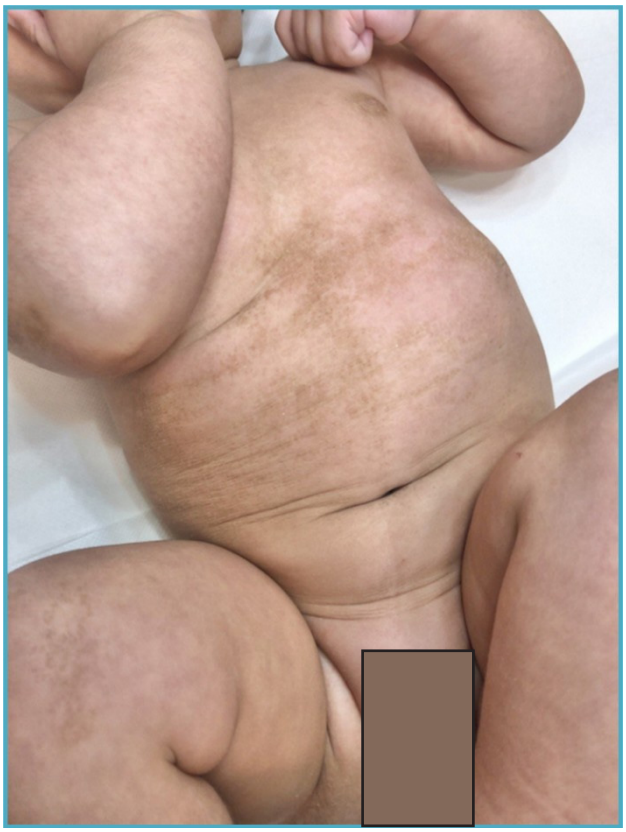

Fig. 1. *Hyperpigmented brownish patches localized on the trunk and limbs.*

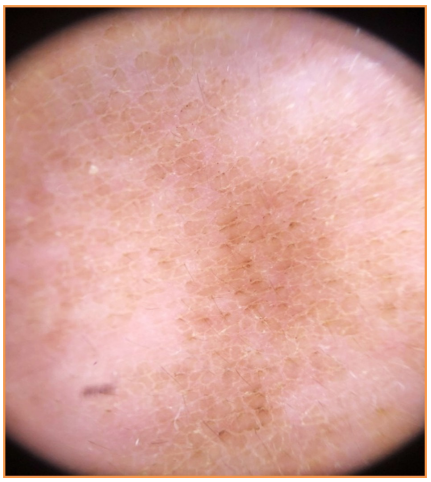

Fig. 2. *Dermatoscopic examination showed numerous polygonal brownish clods arranged in mosaic pattern.*

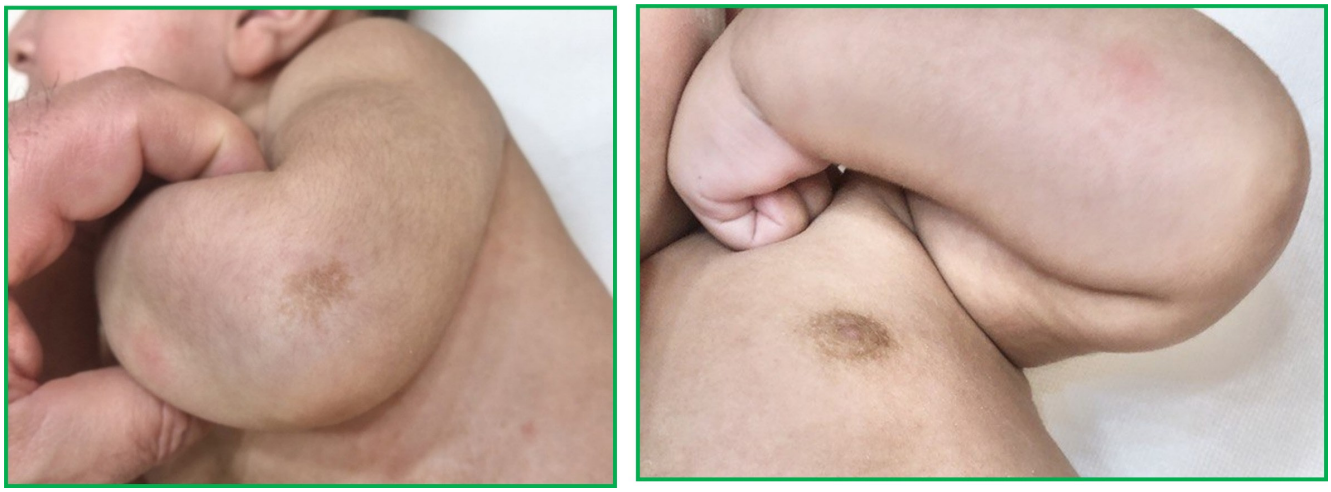

Fig. 3. *Before and after scrubbing with 70% isopropyl alcohol.*

3. Discussion

TFFD is a benign disease, very common but often underestimated. It is easy to recognize. Rubbing with 70% isopropyl alcohol is able to resolve pigmentation obtaining diagnostic and therapeutic results. It is thought that rubbing with alcohol may denature cellular proteins, breaking down hyperkeratotic lesions (7). The main differential diagnosis is dermatosis neglecta, which resolves after cleaning with soap and water.

4. Conclusion

Despite numerous reports, TFFD remains an underestimated pathology, especially in the first years of life. The case we presented is one of the few reported in literature. Although this condition appears to be completely benign, it is important to be able to recognize it and to this end it is sufficient the simple rubbing with alcohol, avoiding unnecessary diagnostic tests.

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Case report

Breaking Capillaries: an Unusual Rash in Human Metapneumovirus Infection

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KEYWORDS

Human metapneumovirus (hMPV), Rumpel-Leede phenomenon, petechiae, viral exanthem, capillary fragility, pediatric dermato-logy, differential diagnosis

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ABSTRACT

Human metapneumovirus (hMPV), an established cause of bronchiolitis in infants, has not been previously associated with significant cutaneous findings. We describe a case of an infant with hMPV infection who presented with a cephalocaudal rash and petechiae. Dermatologic evaluation revealed signs consistent with the Rumpel-Leede phenomenon. This case highlights the importance of recognizing pressure-induced purpura in the context of viral illness. Recognition of this benign pressure induced purpura will avoid unnecessary workup and isolation precautions.

1. Background

Human metapneumovirus (hMPV) is a leading cause of acute lower respiratory tract infections in young children, often presenting with symptoms similar to respiratory syncytial virus (RSV) (1). While its respiratory profile is well-documented, cutaneous manifestations are uncommon and poorly characterized in the literature. The Rumpel-Leede phenomenon, characterized by capillary rupture distal to venous compression, has been reported in scarlet fever, thrombocytopenia, diabetes mellitus, and occasionally during viral infections (2.) Scarlet fever, toxin-driven inflammation and mechanical compression may lower the capillary integrity threshold, facilitating rupture and petechiae in susceptible patients. Viral infections drive complex pathophysiology involving endothelial dysfunction, cytokine-mediated vascular leak, coagulation imbalance, and sometimes lasting microvascular changes. These mechanisms interact to cause manifestations ranging from petechiae and edema to thrombosis or hemorrhage. Awareness of this benign clinical sign is crucial to distinguish it from more ominous presentations such as vasculitis or meningococcemia (3.).

2. Case Presentation

Human metapneumovirus (hMPV) is a well-recognized etiology of bronchiolitis in infants but is not commonly associated with distinctive cutaneous manifestations. We report a case in which hMPV infection was complicated by a rash that mimicked exanthematous illnesses, leading to an extensive diagnostic evaluation. Careful morphologic analysis ultimately revealed findings consistent with the Rumpel-Leede phenomenon (2).

A previously healthy male infant presented with acute onset of cough, nasal congestion, and wheezing. Parents noted the development of a rash beginning in the postauricular region and spreading to the face, trunk, and upper extremities within hours. There was no conjunctivitis, Koplik spots, mucosal involvement, or fever exceeding 38 °C. His past medical history was notable only for mild eczema. Family history included recent group A Streptococcus pharyngitis in both parents. The patient's vital signs demonstrated tachypnea, tachycardia, and hypoxemia, requiring brief low-flow oxygen support.

On dermatologic examination, the child exhibited a diffuse, erythematous, fine-textured maculopapular eruption over the face and upper trunk. Superimposed petechial patches were observed on the upper extremities. Notably, following tourniquet application for intravenous placement, a sharply demarcated band of non-blanching petechiae developed distal to the compression site. Lesions were asymptomatic, spared the mucous membranes, and were confined to areas of increased venous pressure. Laboratory testing revealed a normal platelet count and coagulation profile. These findings were characteristic of the Rumpel-Leede phenomenon (tourniquet test positive), indicating capillary fragility rather than a systemic vasculitic or thrombocytopenic process (2).

Because the eruption's initial distribution suggested a cephalocaudal viral exanthem and occurred during an active measles outbreak, airborne isolation was instituted, and measles PCR and IgM testing were performed. Both were negative. A viral respiratory panel confirmed hMPV, and a rapid antigen test for Group A Streptococcus was positive. Although throat PCR was positive for Group A streptococcus, to our knowledge there is no reports in the medical literature to support a causative relationship between streptococcus pyogenes infection and the Rumpel-Leede phenomenon in absence of a strawberry tongue, scarletiform "sand paper" rash. The patient's rash remained stable, and petechiae resolved gradually without intervention. He was discharged home with amoxicillin and improved condition, with outpatient follow-up arranged.

3. Discussion

This is the first reported case of capillary fragility associated with hMPV infection. This patient's petechial eruption following tourniquet application, combined with a normal coagulation profile, supports a diagnosis of the Rumpel-Leede phenomenon (2). The Rumpel-Leede phenomenon is typically described in thrombocytopenic states, poorly controlled diabetes, or after mechanical stress, yet it can appear in otherwise healthy children during acute viral illnesses. Physicians should be aware of this presentation, particularly in pediatric patients, as its morphologic features—non-blanching petechiae in pressure-dependent distributions—distinguish it from morbilliform exanthems, toxin-mediated eruptions such as scarlet fever, and petechial rashes that suggest life-threatening infections (3, 4). Prompt recognition can prevent unnecessary hematologic investigations, empiric antibiotic therapy, and prolonged isolation precautions.

4. Conclusion

This is the first case to highlight the novel association between human metapneumovirus (hMPV) infection and the Rumpel-Leede phenomenon in an otherwise healthy infant. Recognition of this benign, pressure-induced purpura is essential in distinguishing it from more serious etiologies such as vasculitis, thrombocytopenia, or meningococcemia—particularly in the context of febrile viral illnesses. Awareness of this phenomenon can significantly impact a clinician's approach to care. Our findings expand the spectrum of cutaneous manifestations associated with hMPV and underscore the importance of careful dermatologic examination in the pediatric setting (Fig.1) (4, 5).

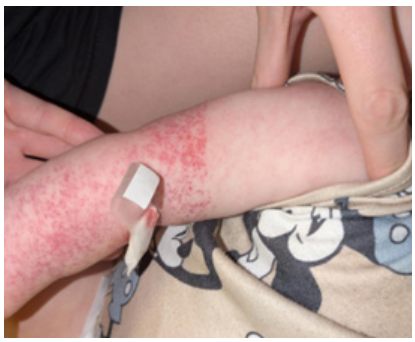

Fig. 1. *Confluent, non-blanching petechiae coalescing into a vio-laceous patch, distributed circumferentially on the distal upper ex-tremity. The rash is sharply demarcated at the proximal margin, with sparing of the skin proximal to the compression site.*

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Case Series

Five Cases of Pediatric Cutaneous Mastocytosis and Autism Spectrum Disorder

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KEYWORDS

autism, cutaneous mastocytosis, luteolin, mast cells, microglia, skin

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ABSTRACT

Here we report five cases of children with both Cutaneous Mastocytosis (CM), a pediatric condition of skin lesions containing mast cells, and autism spectrum disorder (ASD), a neurodevelopmental condition characterized by impaired communication and obsessive behaviors. This apparent comorbidity is intriguing given that the co-occurrence of these two conditions would be expected to be infrequent in the general population. The possible association between CM and ASD is supported by increasing evidence indicating a strong association between atopic dermatitis (AD), which involves mast cells, and ASD. Activated mast cells in CM and AD could contribute to their pathogenesis, hence inhibiting mast cell activation may have considerable benefit.

DISCLOSURE: ALL AUTHORS REPORT NO CONFLICTS OF INTEREST RELEVANT TO THIS ARTICLE.

1. Introduction

Cutaneous mastocytosis (CM) is a disorder manifesting in children during the first two years of life. (1) The exact prevalence is not known due to lack of sufficient epidemiological data, but it is estimated to be about 1:10,000 children (0.001%) (2). Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by impaired communication and obsessive behaviors affecting 1 in 31 (3.2%) children in the USA (3). There is no distinct pathogenesis or effective treatment for either CM or ASD (4, 5).

2. Methods

All children had been diagnosed with ASD by trained child psychiatrists using cutoff scores on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), as well as the validated scales of Autism Diagnostic Observation Schedule, Second Edition 1 (ADOS-2) and Diagnostic Interview-Revised (ADI-R). All children had mild to moderate ASD, as determined by using a composite score of 20-40 on the Childhood Autism Rating Scale (CARS), with the lowest score of 15 indicating normal behavior on all 15 scales, while the highest score of 60 indicates behavior is severely abnormal on all 15 scales). Fragile X, Tuberous Sclerosis, Rett and PTEN syndromes had been excluded on clinical evaluation and appropriate genetic analysis. Brain MRI and EEG were also normal. Improvement in ASD-related symptoms was rated using the Clinical Global Impression-Improvement (CGI-I) scale (1=very much improved; 2=much improved; 3=minimally improved; 4=no change from baseline; 5=minimally worse; 6=much worse; 7=very much worse). Children were referred to TCT for unusual skin lesions. Diagnosis of CM was made based on history of symptoms, clinical observation. and a positive of Darier's sign (itching and redness upon stroking of the affected lesion).

3. Results

Here we report five cases of children with CM and ASD (Table I). All patients were Caucasian (3-11 years old) and all but one were male. Diagnosis of CM was made). In all children, all basic blood values including liver and thyroid function tests were normal, and the serum level of the mast cell marker tryptase was <10 ng/ml.

Table I. *Demographics, CM characteristics and ASD-Symptom Improvement.*

Patient	Sex	Age (years*)	Site of Lesion	Type of Lesion	CGI-I
1	M	6	Arm	Solitary	2
2	F	11	Back	Solitary	2
3	M	3.5	Arm	Solitary	2
4	M	5.5	Back	Solitary	3
5	M	3	Leg	Diffuse	2

*Rounded up at the time of last encounter

There were four cases with solitary mastocytomas: One was present on the arm (Fig. 1a) and all others were on the torso (Fig. 1b-d); one case involved congenital diffuse CM (Fig. 1e).

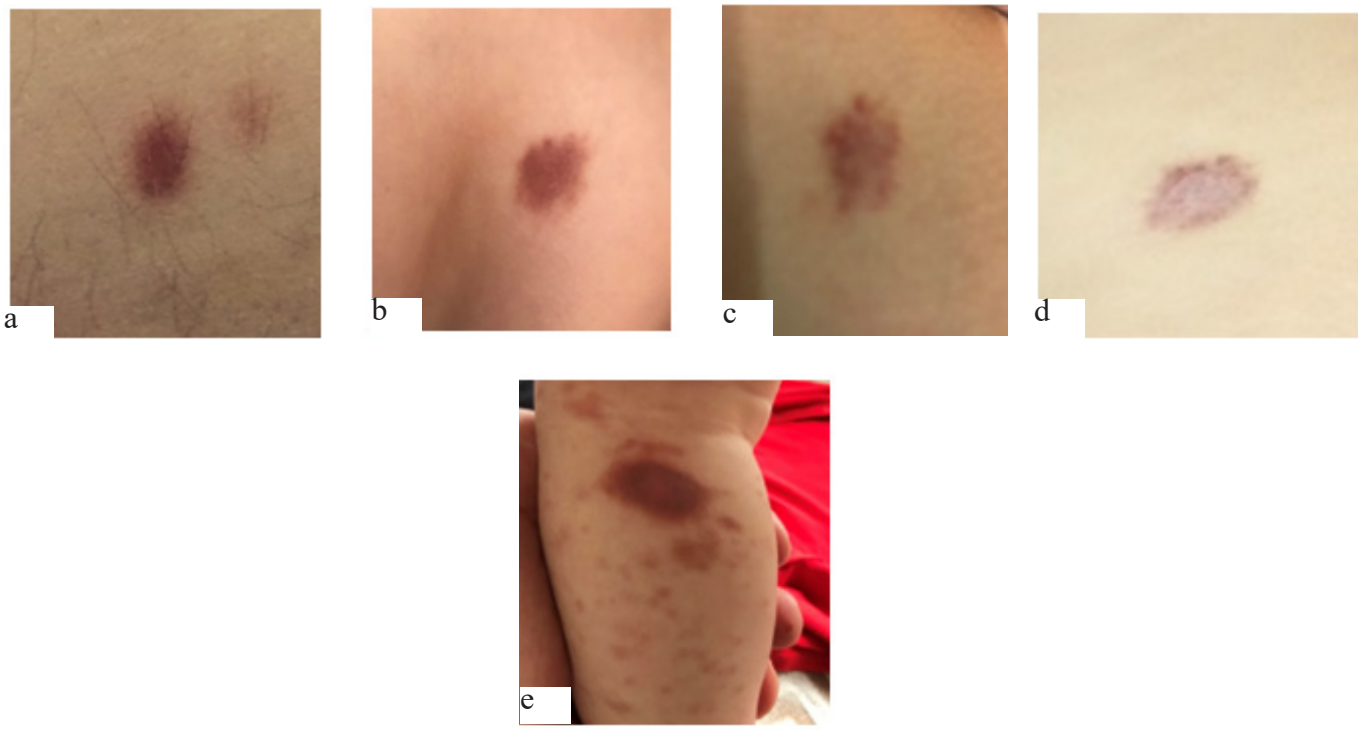

Fig. 1. *Photomicrographs of skin lesions:* ***a****. solitary mastocytoma lesion from the back of a 11-year-old Caucasian male;* ***b****. Photomicrograph of a solitary mastocytoma lesion from the arm of a 6-year-old Caucasian male;* ***c****. Photomicrograph of a solitary mastocytoma lesion from the abdomen of a 5.5-year-old Caucasian male;* ***d****. Photomicrograph of a solitary mastocytoma lesion from the abdomen of a 4-year-old Caucasian female;* ***e.*** *Photomicrograph of diffuse CM lesions from the leg of a 3-year-old Caucasian male.*

All children were administered a dietary supplement (NeuroProtek®, one softgel capsule twice per day for 6 months) containing the flavonoids luteolin, quercetin and rutin formulated in olive pomace oil (6). Additionally, a skin lotion containing the luteolin structural analogue tetramethoxyluteolin (7) (GentleDerm®) was applied on the lesional skin twice per day. All children continued with speech therapy sessions. Six months after initiation of thisintervention , parents reported that the skin lesions had "faded" and there was significant overall ASD symptom improvement using the CGI-I .

4. Discussion

We had previously reported that children born to mothers with systemic mastocytosis, which is characterized by a greater number of hyperactive mast cells (8), had a higher risk of being diagnosed with ASD than the general population (9).

The comorbidity of CM and ASD is intriguing especially since the prevalence of pediatric CM has been reported to be about 0.0001% and that of ASD is about 3.0% making the possibility of these two conditions co-occurring (3 in 1,000,000 or 0.0003%) extremely unlikely (Table II).

Table II. *Calculation of Chance of Comorbidity of CM and ASD.*

To determine the chance of comorbidity for two conditions, one multiplies the individual prevalence rates, assuming the conditions are independent. This means that one condition does not influence the likelihood of developing the other. To calculate the chance of comorbidity:

1. **Define the prevalence rates as probabilities:**
   - Condition A: 1 in 10,000, or $P(A)=1/10,000=0.0001$
   - Condition B: 3 in 100, or $P(B)=3/100=0.03$
2. **Multiply the probabilities.**
   - The probability of two independent events both occurring is
   - $P(A \text{ and } B)=P(A)\times P(B)$
   - $P(\text{Comorbidity})=0.0001\times 0.03=0.000003$
3. **Result**

The chance of comorbidity for these two conditions is 3 in 1,000,000, or 0.0003%.

Only one case of pediatric CM in a male child with motor and intellectual delay has been reported (10). Epidemiological studies have shown a statistically significant association between ASD and atopic dermatitis (AD) (11, 12), as well as other atopic diseases (13), all of which also involve activation of mast cells (14).

Mediators released from mast cells (15) could contribute to the pathogenesis of ASD by: (a) increasing the permeability of the blood-brain barrier (BBB) and allowing toxins to enter into the brain where they stimulate microglia leading to focal brain inflammation (14) and releasing metalloproteinases that could disrupt neuronal connectivity (16).

The flavonoids in the supplement and skin lotion used have been reported to inhibit human mast cells (17) and microglia (18). Moreover, the dietary supplement used had been reported to result in a significant decrease in serum levels of pro-inflammatory markers in children with ASD (19). A recent review stressed the possible significance of mast cells in the pathogenesis of ASD (20).

There are a number of limitations to be considered. The number of subjects was small and this case study was open-label; moreover, the improvement was subjective even though the scale used has been utilized in numerous investigators. The apparent improvement of symptoms noted may also be due to the natural course of the conditions. However, pediatric CM does not improve on its own until puberty and ASD-related symptoms do not typically resolve within 6 months regardless of speech therapy.

4. Conclusion

The apparent co-occurrence of CM and ASD is intriguing and could point to associations important for understanding pathophysiological interactions that may contribute to the development of both conditions in at least a subgroup of children. Any allergic manifestations and suspicious skin lesions in children with ASD should be investigated and addressed.

Abbreviations

ADOS-2 = Autism Diagnostic Observation Schedule, Second Edition
ADI-R = Diagnostic Interview-Revised
ASD = Autism Spectrum Disorder
BBB = blood-brain barrier
CARS-2 = Childhood Autism Rating Scale, Second Edition
CGI-I = Clinical Global Impression-Improvement
CM = cutaneous mastocytosis
DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition

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Disclosures
TCT is on the Medical Advisory Board of the Mastocytosis Society. He is also the Scientific
Director and shareholder in Algonot, LLC (Sarasota, FL).

Ethical considerations
This study conforms to the Declaration of Heksinski and the US Federal Policy for the Protection of Human Subjects. There is NO identifying patient information, and the author has permission to publish from the respective parents.

Community involvement
There was no community involvement other than the families of children with ASD reaching out to me because of the unusual skin lesions.

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