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Pederm Insights

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In this Issue

Pg No

Editor's Thoughts

Dear Colleagues,

The onset of the monsoon is a breeze to end the weeks of sweltering heat. While most of us are enjoying this monsoon, children are susceptible to a number of infections. This issue of "Pederm Insights" features a review of the literature on seasonal flu (influenza), which is frequently misdiagnosed as measles, atypical lesions in hand-foot-mouth disease (commonly referred to as tomato flu), and cutaneous manifestations of primary immunodeficiencies, with a focus on infections. There is also an interesting review of the infection risk in children treated with JAK inhibitors. An emphasis is placed on cutaneous infections in the journal review section. The guest editorial section by Dr. D. A. Satish highlights the journey of pediatric dermatology in the last four decades in India. Akin to other issues, we have a baffling photoquiz, an interesting case vignette, and drug therapy for superficial fungal infections.

Pediatric dermatology has achieved important milestones among residents in the past few years amidst glamorous cosmetic and procedural dermatology. However, in reality, this small branch stands at a crossroads today. The resident's column focusses on the start-up challenges faced by a certified pediatric dermatologist.

I thank all the editorial members for their support and contributions. I invite you all to the ***"Pediatric Dermatology Updates 2024"*** *conference to be held in Bengaluru on 28th and 29th September.*

Happy reading

Sahana M Srinivas

Editor-in chief

Guest Editorial

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Pediatric dermatology in the last four decades in India

There has been tremendous advancement in the speciality of dermatology in the last four decades. Several sub-specialities like dermatosurgery, aesthetic dermatology, dermatopathology and pediatric dermatology have emerged and grown substantially during this period.

The first international symposium on pediatric dermatology was held in Mexico City in 1972, and the International Society of Pediatric Dermatology was launched. The renowned Prof. Harper declared that pediatric dermatology was "officially born".

The torchbearers of pediatric dermatology in India were the late Prof. Rui Fernandez and Dr. Deepak Parikh. The foundations were laid in 1986, and the Indian Society of Pediatric Dermatology was born in 1995. Its first conference was held in November 1996.

A team of dedicated dermatologists in the country with a special interest in pediatric dermatology helped in conducting conferences, workshops and seminars; soon, the first issue of Indian Journal of Pediatric Dermatology was launched. All these focused activities helped kindle a keen interest in the subject amongst young dermatologists in the country.

There have been tremendous advancements in the understanding of etiopathogenesis, clinical features and management of several pediatric dermatoses in the last few decades. To name a few, recent advances in genodermatoses, infantile haemangiomas, atopic dermatitis, alopecia areata, etc. have been game-changers in our perspective of patient care.

The introduction of fellowships in pediatric dermatology by some universities has helped create a number of pediatric dermatologists in the country who are exclusively practicing the speciality. The special interest group (SIG) of IADVL is also helping to create widespread focus on our subject. The academic activities of the recently formed Pediatric Dermatology Foundation forum are creating keen interest amongst our community.

I pray and hope that there will be more research and publications on pediatric dermatoses in our country. I have no doubt that the future of pediatric dermatology is in the safe hands of young and bright dermatologists and the Pediatric Dermatology Foundation forum will help improve the quality of care to our patients. I invite you all to the "Pediatric Dermatology Updates 2024" conference to be held in Bengaluru on 28th and 29th September, 2024.

Contributors: Sahana M Srinivas, Jeta Buch, Divya Gupta, Sirisha Varala

Gökçe Ş, Dörtkardeşler BE, Aslan A. Normocomplementemic Urticarial Vasculitis Associated with A/H1N1 in a Child. Case Report. SN Compr Clin Med. 2020;2(12):2962-2964.

Urticarial vasculitis is characterized by pruritic and painful urticarial rashes associated with angioedema and purpura. The authors of this article report a child with urticarial vasculitis associated with Influenza A/H1N1. A four and half-year-old healthy girl, fully immunized presented with a 6-day history of fever, non-productive cough, nasal congestion and myalgia. Urticarial lesions were noted on the face and upper extremities after 3 days of onset of fever, accompanied by arthralgia, oedema and pain on hands and wrist. She was diagnosed as urticaria and managed with antihistamines. After 2 days the urticarial rashes turned into purpura with central clearing. The urticarial plaques persisted for more than 24 h along with pain and burning sensation and resolved with hyperpigmentation. There was no history of drug intake. Routine blood counts, renal function test, ESR, CRP, RA factors, serum immunoglobulin levels, chest X-ray, blood and urine cultures and serology (EBV, hepatitis A-B-C, HIV, CMV, parvovirus B 19) were normal. Nasopharyngeal swab specimen by multiplex PCR was positive for A/H1N1. She was started on oseltamivir 17 mg orally twice daily for 5 days, antihistamines and systemic steroids for 5 days. All the lesions resolved by 2 weeks without scarring.

Comments

The above report documented urticarial vasculitic rash secondary to Influenza A/H1N. In the current scenario, following the COVID-19 pandemic, there has been a surge in cases of measles (due to dent in vaccination) and measles-like rash (secondary to influenza/dengue) in children

Influenza also called as seasonal flu is a highly contagious, acute respiratory, self-limited infection caused by influenza virus most commonly seen in children. There are 4 types of influenza viruses, types A, B, C and D. Influenza A and B cause seasonal epidemics in humans. Currently circulating influenza subtypes in humans are A(H1N1) and A(H3N2) influenza viruses. Influenza B viral infection are more commonly associated with underlying comorbid conditions. Clinical features include abrupt onset of fever, chills, myalgia, rhinitis, croup, dry cough, pneumonia, bronchiolitis, gastrointestinal upsets and conjunctivitis. Skin manifestations are seen in 2 % cases in influenza A infection. Morphology includes macular/maculopapular rash (measles-like rash) or a vasculitic/purpuric eruption.

Measles presents with patterned morbilliform rash, that initially starts from the face and progressing to involve the trunk and extremities with involvement of palms and soles. On the contrary measles-like rash does not present with a patterned rash and does not involve palms and soles. Haemorrhagic and vasculitis like eruptions are uncommon in measles. It is important to differentiate between measles and influenza virus infections for prognostication.

{Submitted by: Sahana Srinivas)

Stripling S, Green LJ, Cartwright M, Enloe C, Wells N, Maeda-Chubachi T. Berdazimer gel for molluscum contagiosum: An integrated analysis of 3 randomized controlled trials. J Am Acad Dermatol. 2024; 90(2):299-308.

Molluscum contagiosum (MC) infection is usually self-limited and physicians commonly opt for a watch-and-wait strategy. Treatment is warranted because of its highly contagious nature and impact on quality of life. B-SIMPLE1 and B-SIMPLE2 were identical multicenter, randomized, double-blind, vehicle-controlled, parallel-group, phase III studies evaluating the efficacy and safety of berdazimer gel, 10.3%, conducted at 35 sites in the United States. B-SIMPLE4 was a multicenter, randomized, double-blind, vehicle-controlled, parallel-group, phase III study of the efficacy and safety of berdazimer gel, 10.3% completed at 55 sites in the United States. This integrated analysis of three large, randomized controlled trials (berdazimer sodium in molluscum patients with lesions [B-SIMPLE] 1, -2, and -4) evaluated the efficacy and safety of berdazimer gel, 10.3% versus vehicle applied as a thin layer once daily for 12 weeks in patients aged 6 months and older with 3 to 70 MC lesions. Efficacy, safety and tolerability assessment was done at weeks 0, 2, 4, 8 and 12. If all lesions cleared at a clinic visit, treatment was discontinued. However, patients continued with regularly scheduled visits through week 24. Treatment was reinitiated, if new lesions appeared or previously cleared lesions recurred after complete clearance. But no study treatments were provided after week 12. Of the 1598 patients enrolled (n = 917 berdazimer, n = 681: vehicle), berdazimer was superior to the vehicle at week 12 in complete clearance rates, 30.0% versus 19.8% (odds ratio, 1.75; 95% CI, 1.38-2.23, P < .001). Berdazimer also provided favorable outcome for partial clearance. Overall, berdazimer treatment was well tolerated. Application-site pain (18.7% vs 4.8% in berdazimer vs vehicle) and erythema (11.7% vs 1.3%), mostly mild to moderate, were the most common local skin reactions.

Comments

Berdazimer 10.3% gel exerts its antiviral effects on MC through protein nitrosylation and NF- kB modulation. It is recently US FDA approved topical medication for the treatment of molluscum contagiosum in patients aged one year and older. Berdazimer gel overcomes the challenge of targeted topical nitric oxide delivery and holds promise as an effective, safe, self- or caregiver- administered prescription medication treatment option for multiple MC.

(Submitted by: Jeta Buch)

Starkey SY, Mar K, Khaslavsky S, Seeburruth D, Khalid B, Virmani D, et al. Atypical cutaneous findings of hand-foot-mouth disease in children: A systematic review. Pediatr Dermatol. 2024;41:23-27.

Hand-foot-mouth disease (HFMD) is a common infectious disease in children. Lately, we are seeing atypical manifestations, often associated with coxsackie virus (CVA6). The authors of this study have conducted a systematic review on the clinical features and outcomes of pediatric HFMD with atypical cutaneous manifestations. After title and abstract screening of 1128 studies and full text review of 215 studies, 85 studies met inclusion criteria, representing 1359 cases of HFMD. The mean age of onset was 2.4 years (19 days-18 years), with a male predominance of 61 percent (387/635). The most common underlying dermatological condition was atopic dermatitis (93/109). Specific morphological data were reported in 833 cases. The most common morphological features included vesicles (53%, 440/833), papules (49%, 406/833), bullae (36%, 302/833), macules (20%, 165/833) and eczema herpeticum-like lesions (19%, 156/833). Other morphological patterns included purpuric/petechial (7%, 60/833) and Gianotti Crosti-like pattern (4%, 30/833). Common atypical sites included the hands and/or feet (61%, 637/1055), arms and/or legs (47%, 492/1055), face (45%, 472/1055), oral mucosa (31%, 328/1055) and trunk (27%, 282/1055). Other rare sites included genital area (15%, 163/1055) and generalized pattern (2%, 17/1055). CVA6 and non-typed enteroviruses (NTEV) were identified in 63% and 26% of cases respectively. The most common complications were nail changes (Beau's lines/onychomadesis; 21%) and desquamation (4%) which occurred at a mean duration of 2-3 weeks after symptoms. The limitation of this study was the heterogeneity of outcome reporting and the retrospective nature of the study.

Comments

In the past, CVA16 and EVA71 were the most frequently reported caused of HFMD prior to 2005. Classically, HFMD is morphologically characterized by oval to elliptical, greyish vesicles surrounded with a red halo distributed on palms, soles and oral mucosa. HFMD resolves spontaneously without complications. Over the past two decades, our understanding of the HFMD has greatly improved and it has received significant attention due to atypical manifestations. Currently, other EVs such as CVA6 and CVA10 are responsible for a significant proportion of HFMD cases and outbreaks. Numerous systematic reviews have summarized the atypical manifestations of HFMD. Atypical cutaneous presentations include papules, bullae, purpuric or petechial lesions, targetoid lesions, or lesions resembling eczema herpeticum, Gianotti-Crosti disease or Steven-Johnson syndrome. Recently in 2022, India was alerted about the occurrence of a febrile exanthem in Kerala called 'Tomato fever'. The most prominent feature is the eruption of red and painful blisters throughout the body that gradually enlarge to the size of a small tomato (**Sah R, et al An old virus with atypical presentation - Tomato flu? Lancet Reg Health Southeast Asia. 2022;7:100096**). This outbreak was not limited to only Kerala; it spread to neighboring states as well. There was a lot of debate regarding the cause of this outbreak, but finally it was attributed to a variant of HFMD. Knowledge about the atypical manifestations of HFMD is necessary for early recognition and diagnosis to prevent overt investigations and treatment.

(Submitted by: Sahana Srinivas)

Eichenfield LF, Siegfried E, Kwong P, McBride M, Rieger J, Glover D, et al. Pooled Results of Two Randomized Phase III Trials Evaluating VP-102, a Drug-Device Combination Product Containing Cantharidin 0.7% (w/v) for the Treatment of Molluscum Contagiosum. Am J Clin Dermatol. 2021;22(2):257-265.

Compounded cantharidin has been used for decades to treat molluscum contagiosum but lacks rigorous clinical evidence to support its safety and efficacy. VP-102 is a shelf-stable drug-device combination product. The device consists of an innovative applicator that contains an ether-free formulation of cantharidin within a sealed glass ampoule (0.7% weight/volume [w/v]). Participants aged ≥ 2 years were randomized 3:2 to topical administration of VP-102 or vehicle in two randomized, double-blind, vehicle-controlled phase III trials. In total, 310 participants received VP-102 and 218 received vehicle. Mean age was 7.5 years (range 2-60) for VP-102 and 6.8 years (Range 2-54) for vehicle. VP-102 was applied to all baseline and new lesions once every 21 days until clearance or for a maximum of four applications. Assessors blinded to treatment counted all lesions at each study visit and all adverse events (AEs) were documented. Complete clearance of all molluscum lesions at day 84 occurred in 50% of VP-102 participants and 15.6% of vehicle recipients ($p < 0.0001$). Mean molluscum lesion counts decreased 76% for VP-102 and 0.3% for vehicle at day 84 ($p < 0.0001$). The most common AEs in the VP-102 group were application site blistering, pruritus, pain, and erythema, which were generally mild or moderate in severity.

Comments

YCANTH (VP-102), now US FDA approved for the application of cantharidin (drug) to the molluscum contagiosum lesions via the special applicator (device) by a trained medical professional. It is hypothesized that cantharadin causes the activation or release of epidermal serine proteases that lead to tonofilament detachment, which in turn elicits intraepidermal blistering and inflammation that promotes shedding of infected keratinocytes and viral clearance. This therapy is associated with MC clearance and is well tolerated in the pediatric cohort when managed in-office by I.e by a trained medical professional to prevent improper use (ie. excessive application) and/or unintended ingestion by pediatric patients. However, this drug-device combination is still not available in India.

(Submitted by: Jeta Buch)

SClarke B, Yates M, Adas M, Bechman K, Galloway J. The safety of JAK-1 inhibitors. Rheumatology 2021;60:ii24–ii30.

The JAK family is crucial in the JAK-STAT pathway, which transduces signals from extracellular cytokines to the nucleus, affecting various immune responses. Selective inhibition can block cytokines implicated in inflammatory processes. Many pathways signal via JAK and the therapeutic treatment of immune-mediated inflammatory diseases benefits from the cytokine blockade effected by JAK inhibition. Long-term JAK pharmacovigilance studies are very much in their preliminary stages. Information on the safety comes from the randomized controlled trials, with no post-marketing pharmacovigilance study data available yet.

Risks of adverse events are broadly similar for JAK inhibitors as for other biological DMARD (bDMARDs) classes. However, there are important differences; for example, tofacitinib and baricitinib have an increased risk of herpes zoster reactivation, elevations in lipids, and decreases in haemoglobin and lymphocytes (including natural killer cells). Concerns have also emerged around a possible increased risk for venous thromboembolism (VTE) and arterial thromboembolism (ATE)

Infection Risk: All JAK inhibitors, including JAK1 selective agents, carry a risk of infections. Upper respiratory tract infections (including nasopharyngitis) are one of the most common non-serious infectious adverse events in the JAK1 trials.

Serious infection rates are low (two to four events per 100 person-years) and similar across JAK inhibitors and bDMARDs. Herpes zoster reactivation is notably associated with JAK inhibitors, with higher incidence in upadacitinib and filgotinib compared to placebo. Preventative measures, such as vaccination, are suggested. Real-world longitudinal data from analyses of tofacinib and baricitinib have reported higher incidence rates (4.4 and 3.2 per 100 patient-years, respectively) with substantially greater risk in older patients with co-prescription of glucocorticoids or methotrexate.

JAK inhibition is also associated with an increased susceptibility to both primary and reactivated HSV infections, however, these were reported less often than zoster in clinical trial data. There is a potentially dose-dependent increases in oral candidiasis, however most cases reported in the trials were non-serious.

The potential for reactivating latent tuberculosis (TB) with targeted therapies is well-known. Consequently, all JAK1 clinical trials have rigorously screened for TB before still enrolling participants. Active TB cases reported in JAK trials have been minimal. However, real-world clinical practice may not be as stringent in screening, making long-term studies and registries crucial for monitoring.

No cases of Pneumocystis jirovecii pneumonia were reported in the JAK clinical trials. However, one instance of cryptococcal pneumonia was noted in a patient on 15 mg daily upadacitinib in the SELECT-EARLY trial. Cryptococcal infections are rare but have also been observed in patients on tofacitinib and baricitinib, suggesting a possible mechanistic link. Fungal infections are a recognized risk with other tyrosine kinase inhibitors, highlighting the need for ongoing post-marketing surveillance to further understand this risk.

Comments

The article "Safety of JAK Inhibitors" reviews the safety profile of Janus kinase inhibitors used in treating immune-mediated inflammatory diseases (IMIDs). These drugs have fewer patient years of exposure data compared to other conventional immunosuppressants, making long-term safety conclusions premature. There is a slight increase in serious infections and other opportunistic infections like herpes zoster and flare up of latent tuberculosis, but these require further study. Long-term post-marketing studies are essential to establish the safety and differentiate between various JAK inhibitors.

(Submitted by: Divya Gupta)

Al-Herz W, Zainal M, Nanda A. A Prospective Survey of Skin Manifestations in Children With Inborn Errors of Immunity From a National Registry Over 17 Years. Front Immunol. 2021 30; 12:751469.

Cutaneous manifestations are an integral part of primary immunodeficiency disorders (PID). They can sometimes be the initial manifestation, giving a clue to the underlying disease. The current article is a prospective survey of children with PID from Kuwait National Primary Immunodeficiency Disorders Registry for a period of 17 years between 2004–2020. The authors aimed to determine the frequency and characteristics of skin manifestations in children with inborn errors of immunity and also looked at their relevance to specific molecular defects.

A total of 313 children with PID (162 males and 151 females) were studied. Molecular diagnosis was done in 71% of the patients. They categorised the patients according to the "International Union of Immunological Societies (IUIS) Primary Immunodeficiency Diseases Committee Report on Inborn Errors of Immunity" (2019). Majority of them belonged to the category of immunodeficiencies affecting cellular and humoral immunity (CIDs) (33.54%) followed by combined immunodeficiencies with associated syndromic features (Sy-CID) (23%) and others. One hundred twenty-six (40.3%) patients were found to have skin manifestations of which in 103 patients (33%), they were the presenting signs. Among the specific diseases, skin lesions were present in 100% of the patients with DOCK8 deficiency, hyper IgE syndrome and ataxia-telangiectasia.

Skin infections (40.5%) were the most common cutaneous manifestations, followed by eczematoid rashes and autoimmune skin associations. They were prevalent among patients with Sy-CID followed by CID. Bacterial skin infections were the most common, followed by viral and fungal infections. Amongst the bacterial infections, impetigo/folliculitis was commonly seen followed by abscesses, ecthyma gangrenosum, cellulitis and acute paronychia. Viral infections like warts and molluscum contagiosum were found to be more widespread and recurrent. In patients with hyper IgE syndrome, skin infections along with widespread eczematous rashes were a consistent finding. All patients with STAT3 deficiency and DNA Cross-Link Repair 1C (DCLREIC) deficiency and majority of patients with DOCK8 deficiency had abscess formation.

Other cutaneous manifestations like eczema and eczematoid rashes were more often seen in patients with CID, Sy-CID, hyper IgE, Wiskott–Aldrich syndrome and DOCK8 deficiency. Erythroderma and alopecia were consistent findings in children with Omenn syndrome. Autoimmune skin diseases were seen in 9.5% of cases and were more common in patients with complement deficiencies. An interesting finding in this study is that PID patients with skin manifestations had longer delay in diagnosis compared to patients without such manifestations. This has been attributed to lack of awareness among the treating physicians, pediatricians and dermatologists that such manifestations can be related to PIDs.

Comments

Although PIDs are rare, they are being more well defined, clinically and genetically in the recent times. The present study included a relatively large number of molecularly defined patients who were followed up prospectively over a long period of time and reiterated the fact that skin is an important organ involved in PIDs. Among the skin manifestations, recurrent and unusual infections with various bacterial, viral and fungal organisms are commonly seen in children with PID. It is very important for the dermatologists to be familiar with the varied cutaneous manifestations of PIDs and have a high index of clinical suspicion aiding in early diagnosis and proper management.

(Submitted by: Sirisha Varala)

Case Vignette

Red rash on the chin

Authors: Gautam Dethe, Pranit Farande, Ajit Barve

A 10-year-old boy, presented to the OPD with a red rash on the chin of four hours duration. On examination, an erythemato-purpuric patch was observed on the chin (Figure 1). Rest of the cutaneous and mucosal evaluation was unremarkable and the child was asymptomatic. General medical, family and drug history (including OTC drugs and alternative remedies) was noncontributory. There was no history of any similar episodes or easy bruisability in the past. The father noted that the child was playing with a newly bought plastic water bottle, that afternoon. On questioning the boy, he demonstrated the manner in which he was playing with the lid of the bottle.

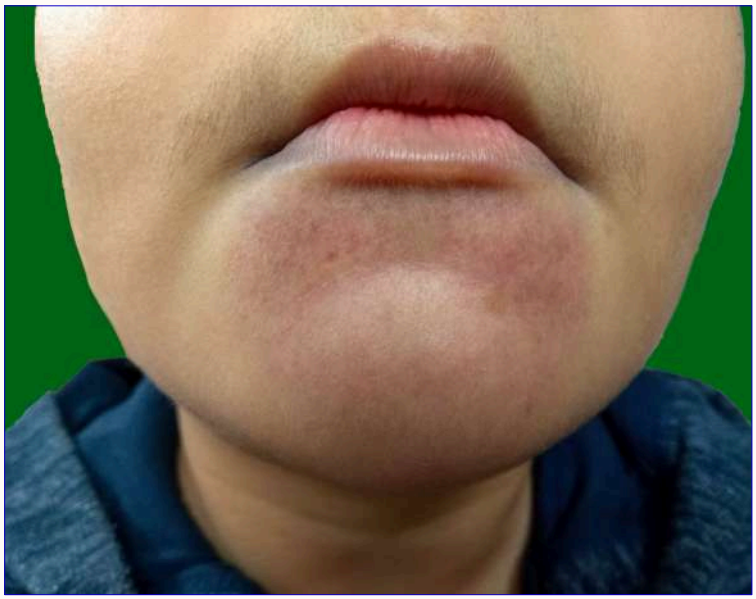

Fig 1

Diagnosis - Suction Purpura

Discussion

The erythemato-purpuric patch was due to the negative pressure created by the child sucking on the plastic lid. Suction purpura has been noted to occur from diverse causes. It can occur from various toys that may have rubber suckers on them, and at times, suction purpura has been reported even in parents, who may apply a child's rattle via rubber suckers to their forehead to entertain the child.[1,2] Suction purpura can occur in the context of alternative medicine practices like cupping.[1,3] Purpuric lesions on the back, due to mechanical force against a bathtub, or due to suction from cup shaped projections of a bath mat, have been reported.[4,5] Two cases of suction purpura on the chin have been reported where the children copied what they saw on social media. Such cases may be related to a "game" played by teenagers where the challenge is to put one's mouth over the opening of a bottle, cup or glass and suck in, until the air vacuum causes the lips to swell.[6] Multiple cases of suction purpura localized to the chin due to sucking air from a glass, have been reported, sometimes in the context of background psychological issues.[5,8] Kaliyadan described an irregular purplish purpuric pattern along the normal pseudonetwork pattern seen over the facial skin on dermatoscopy of a case of suction purpura on the face.[8]

The appearance of purpuric lesions in a child can be alarming. Thorough history, clinical examination and hematological investigations are necessary to pinpoint the cause of purpuric lesions. Unlike our case, the diagnosis of factitious purpura may not be apparent at first and extensive investigations may be needed to rule out other causes. Based on multiple reports in the literature and our case, we feel that an isolated purpuric patch on the chin should alert the physician to the possibility of suction purpura, among other causes.

References and further reading- (clickable links)

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Answer to PDF - Photoquiz 1

Author: Sirisha Varala

Clinical Data

A seven-year old boy presented with swelling of left leg of three months duration. It started initially as a small red raised lesion and progressed to involve the lower half of the left leg circumferentially. There was associated redness, pain and fever for 20 days following which the child was treated elsewhere with oral antibiotics and surgical debridement with no improvement. There was no history of prior trauma. Cutaneous examination revealed a single well defined hyperpigmented plaque, firm in consistency, present on the left leg involving the entire lower half circumferentially until the ankle joint (**figure 1**). Healed scar was present over the debridement site. There was no regional lymphadenopathy. Complete blood count, liver and renal function tests, Mantoux and chest X ray were normal. ESR was raised (20mm/h). An incisional biopsy was done and sent for histopathological examination with special stains (**figures 2, 3, 4**) and cultures (fungal and bacterial).

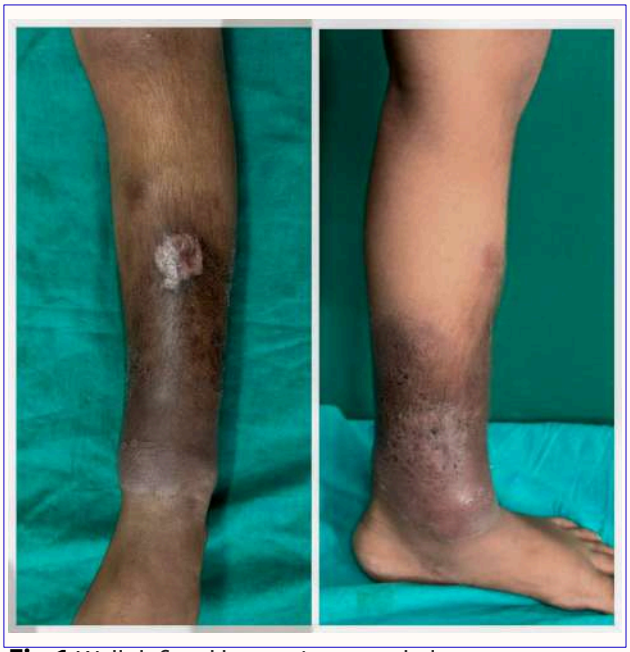

Fig 1 Well defined hyperpigmented plaque seen over lower half of left leg.

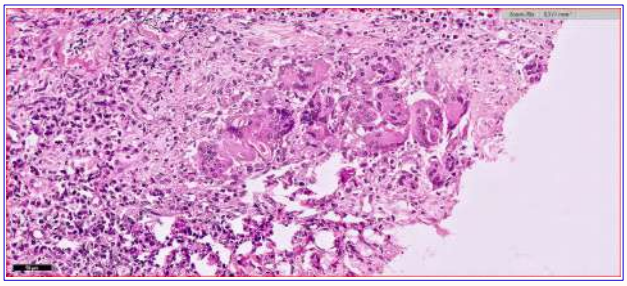

Fig 2 Foci of multiple histiocytes and giant cells in the lower dermis [H &E 40x]

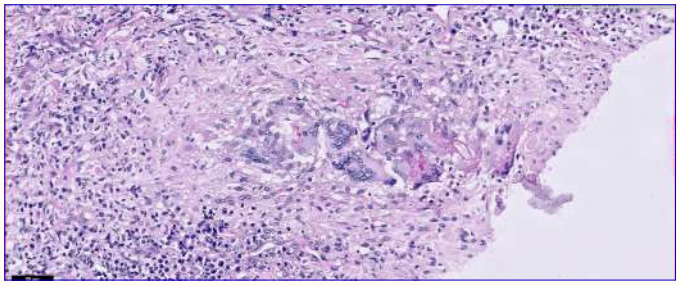

Fig 3 Positive PAS stain showing thin walled aseptate fungal hyphae

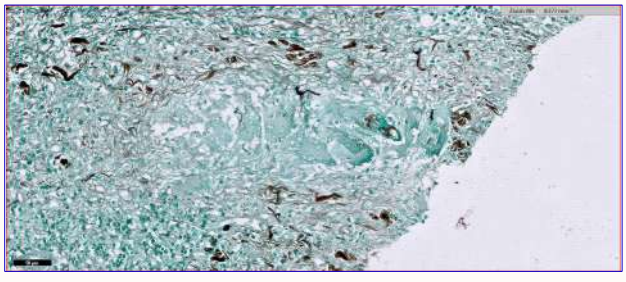

Fig 4 Positive GMS stain

Differential diagnosis considered were as follows

- Cellulitis
- Subcutaneous zygomycosis
- Lupus vulgaris
- Atypical mycobacterial infection
- Fibrosing panniculitis
- Soft tissue tumor

Investigations

- Skin biopsy for histopathological examination showed epidermis with mild orthokeratosis. Dermis showed sheets of neutrophils, lymphocytes, plasma cells and histiocytosis. Deeper dermis showed a focus of multinucleate giant cells with broad aseptate thin walled fungal hyphae.
- Special stains for Periodic acid-Schiff and Gomori methenamine silver stain was positive for fungal elements.
- KOH mount of tissue sample showed thin, branched, broad aseptate filamentous hyphae
- Culture was negative for fungal growth

Final diagnosis - Subcutaneous zygomycosis

Treatment

The child was streated with oral itraconazole at the dose of 4 mg/kg body weight with periodic LFT monitoring. The lesions started showing significant improvement post antifungal therapy.

Discussion

Zygomycosis is a subcutaneous fungal infection caused by organisms belonging to the phylum Zygomycota which includes two orders, Mucorales and Entomophthorales[1]. Entomophthoromycosis includes two distinct clinical forms, i.e., subcutaneous zygomycosis, caused by Basidiobolus ranarum and rhinofacial zygomycosis caused by Conidiobolus coronatus [2].

Subcutaneous zygomycosis, also called subcutaneous phycomycosis or basidiobolomycosis, is a chronic granulomatous infection of the skin and subcutaneous tissue in immunocompetent individuals, predominantly from tropical and subtropical countries with occasional reports from India [3]. The mode of infection is exactly not known; however minor trauma such as insect bites or thorn pricks can implant the spores. Children are most commonly affected.

Clinically it presents as a firm, well-circumscribed, woody, painless swelling with smooth, rounded edges where the fingers can be insinuated underneath and the swelling lifted off the underlying tissues, called the "insinuation sign". The overlying skin may be normal, erythematous, edematous, or hyperpigmented, but ulceration is rare [4]. The lesions usually involve the limbs or limb–girdle areas.

Diagnosis is by histopathology and fungal culture. Histopathology often shows dermal and sub-cuticular granulomatous mixed infiltrates with eosinophils, lymphocytes, plasma cells, giant cells, histiocytes and neutrophils with Splendore–Hoeppli like phenomena and fibrosis. Special stains such as PAS and Gomori–Grocott help in identifying the fungal elements. Culture on Sabouraud dextrose agar at 25°C–30°C shows creamy brown, furrowed, heaped up, and radially folded colonies. Lactophenol cotton blue wet mount shows large, broad vegetative hyphae, and thick-walled zygospores with beak-like appendages characteristic of Basidiobolus[5]. In 50% of the cases however, the fungal culture can be negative [6]

While regional lymph nodes are not commonly involved, deeper extension into muscle and viscera are possible complications. It mimics many other conditions like mycetoma, sporotrichosis, lupus vulgaris, soft tissue tumor, Burkitt's lymphoma, synovial sarcoma, and fibrosing panniculitis[1].

Common treatment options include potassium iodide (KI) [30 mg/kg/day as a single daily dose or divided into three doses] and itraconazole (100-200 mg/day) . The treatment duration is prolonged (6 months to 1 year). Other drugs like trimethoprim-sulfamethoxazole, amphotericin B, ketoconazole have also been used. The role of surgical resection is controversial and according to Prasad et al. surgery may hasten the spread of infection [4]

Subcutaneous zygomycosis in children is very commonly misdiagnosed and subjected to unnecessary surgical interventions. The characteristic firm to woody swelling with positive finger insinuation are the clinical clues in making the diagnosis.

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The correct answer to the PDF Photoquiz 1 is given by

Dr Yashashree Dungarwal, Senior Resident , Shri Vasantrao Naik Govt Medical College, Yavatmal, Maharashtra

PDF - Photoquiz 2

Authors: Preeti K Sheth, Resham Vasani

Clinical data

A three and half-year-old boy, born of a non-consanguineous marriage, presented with asymptomatic, raised, solid, skin coloured lesions on the trunk, progressively increasing in the past 1 year. He weighed 2.1 kg, had a short stature and stiffness of the joints. Family history was non-contributory.

General examination findings revealed a coarse facial phenotype with bushy eyebrows, depressed short bridge of the nose, widened nostrils and thickened lips (Figure 1). He had broad hands with short stubby fingers (Figure 2) and a protuberant abdomen. Cutaneous examination revealed small, firm, skin coloured papules like pebbles, arranged close together to form ridges in a reticular array. The papules (marked with blue arrow) were present bilaterally symmetrically between angles of scapulae, posterior axillary line and lateral side of the trunk. (Figure 3, 4). Bluish-black, ill-defined macules were spotted on the back (Figure 4). Mild hypertrichosis was seen over thigh and trunk.

A punch biopsy was done and sent for histopathological analysis with special stains (Figures 5 and 6).

Please answer the following questions:

1. What is your diagnosis?

2. The presence of one of the following is crucial to the diagnosis:
a) Mongolian spots
b) Hypertrichosis
c) Pebbly papules
d) Corneal clouding

3. The gold standard test leading to diagnosis is
a) Urine examination
b) Skin biopsy
c) Enzyme assay
d) Skeletal survey

4. Which special stain was used to confirm the diagnosis?
a) PAS stain
b) Aniline blue stain
c) Colloidal iron stain
d) Alcian blue stain

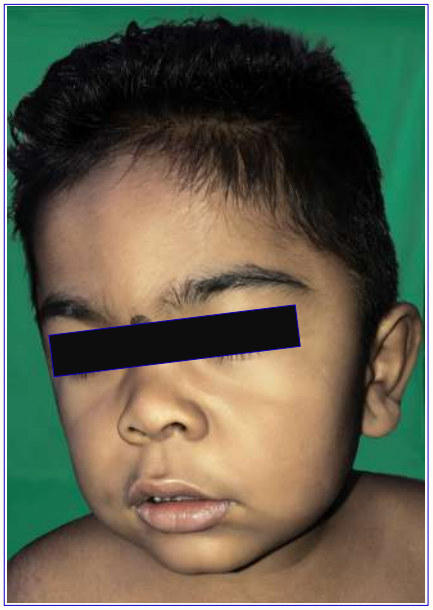

Fig 1

Fig 2

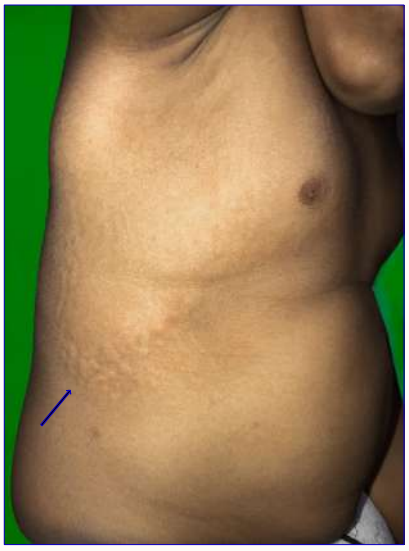

Fig 3

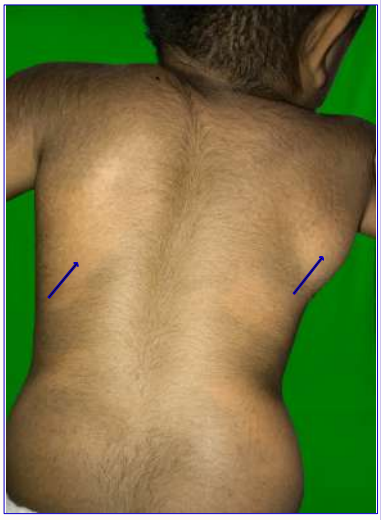

Fig 4

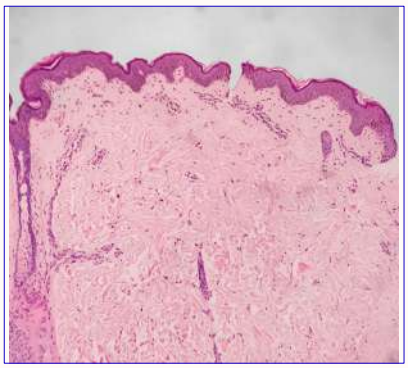

Fig 5

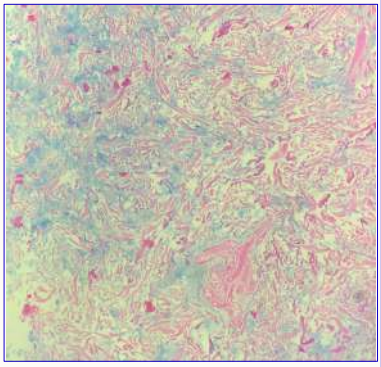

Fig 6

[Kindly mail your answers along with your affiliation to **peddermfoundation@gmail.com** before 10th September 2024. The winners of the PDF Photoquiz 2 will be announced in the next issue]

My experience as a Pediatric Dermatologist

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DDVL, FRGUHS (Pediatric dermatology)

Consultant Pediatric Dermatologist

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After passing my pediatric dermatology fellowship examination from the prestigious Indira Gandhi Institute of Child Health, Bengaluru, under the guidance of Dr Sahana M Srinivas, in 2019, I came out with overwhelming confidence in managing and counseling pediatric dermatology cases and joined the teaching institute, Mysore Medical College and Research Institute, Mysore, which was my postgraduate parent institute. My new journey began, my way of handling cases changed, the things I used to feel difficult even after completing 2 years of my post-graduation were eased. My teachers were really proud of my upgraded knowledge in managing pediatric cases and teaching our postgraduate students. Meanwhile, we conducted a CME program on pediatric dermatology where I had the opportunity to give a talk on 'Nutritional dermatosis in children' and join the panel discussion as a panelist. After a few months, the COVID era started, and I couldn't continue my work in medical college. Later, I went in search of job opportunities in private hospitals. Most of the prestigious hospitals rejected my resume as they already had a dermatologist and there was no room for an additional pediatric dermatologist.

Later in 2020, an exclusive mother-and-child hospital started in Mysore, which gave me the opportunity to start my career as a pediatric dermatologist. My career steps began there, and I had to prove the depth of my knowledge in the subject. Most of the dermatology cases were attended by pediatricians only until I saw an 8-month-old infant with nodular purpura with frequent ecchymosis, for which I suspected vitamin K deficiency bleeding and referred him to the hematology department, while other colleagues had missed this diagnosis. That was the first time my pediatrician colleagues started considering me for opinions. Cases that were referred to me by both pediatricians and dermatologists were steroid modified dermatoses, inappropriately treated and for counselling. The reason for not referring could be that parents did not want to pay for another consultation with a pediatric dermatologist or overzealous treatment from the pediatrician itself. Furthermore, Parents of one my pediatric patients told me that they were advised advised by a physician not to visit a pediatric dermatologist since they would likely start your child on methotrexate or other immunosuppressants.

The most common cause for referrals was pigmentary mosaicism, as attending doctors and parents were concerned about childhood vitiligo although, some children were already receiving pimecrolimus and topical steroids for the same condition. One of my cases,a child was initially diagnosed with pediatric vitiligo at two months of age, she was found to have pigmentary mosaicism. Later, at 5 months of age, child was diagnosed with global developmental delay. Hence, accurate diagnosis and counseling play a major role in pediatric dermatology practice. I used to see one or two pediatric dermatology cases per day on an OPD basis, and sometimes only three cases per week even after 4 years of my fellowship in pediatric dermatology, whereas my juniors and other colleagues practicing cosmetology made significantly more money. Now that it's been 5 years, I am practicing general dermatology in a government setting and exclusive pediatric dermatology in private hospitals. It takes time to establish oneself as a pediatric dermatologist in non-metropolitan areas due to a lack of awareness of this sub-specialty amongst the general population and even doctors of other specialties.

Drug therapy of superficial fungal infections - Prescribing information

Author: Ramkumar Ramamoorthy

Drug	Age group	Dosage	Duration
Ciclopirox olamine 0.77% cream	> 12 yrs	Twice daily As Nail lacquer (8%)	48 weeks
Ketoconazole Shampoo 2%	Safety in children not established	Once daily as an adjunctive therapy for Tinea capitis	
Selenium Sulphide Shampoo	Safety in children not established for 2.5%	Twice a week as an adjunctive therapy for tinea capitis	
Miconazole 2% cream	>2 yrs	Twice daily	
Clotrimazole 1% cream	>2 yrs	Twice daily	
Terbinafine 1% cream	>12 yrs	Twice daily	
Oxiconazole	>12 yrs	Once daily	
Eberconazole	>12 yrs	Twice daily	
Itraconazole	Safety not established in children. Optimum pediatric treatment schedules are not established.	For oral Solution -3 mg/kg taken on empty stomach Or 5mg /kg, beads from opened capsule can be placed in peanut butter and swallowed after taking food. Or Pulse therapy with 6-10 mg/ kg/day (One week/month for 3 months)	6 weeks
Terbinafine	>4 yrs	10-20 kg- 62.5 mg, 20 to 40 kg- 125 mg >40 kg - 250 mg	For tinea capitis 4 to 6 weeks or 2 weeks beyond clinical resolution
Griseofulvin	>2 yrs	Micronized 20 to 25 mg/kg, (suspension contains 125 mg/5 ml)	6 to 8 weeks – tinea capitis (drug of choice for Microsporum infections)
Fluconazole		6 mg/kg/week for 6 to 8 weeks- tinea capitis 12 weeks for onychomycosis - finger nails & 26 weeks – toe nails For candidiasis (children above 6 months of age) - 6 mg /kg on day 1 followed by 3mg/kg daily for 2 weeks	

Pityriasis versicolor

Topical- once daily application for 14 days (any of the above)

Selenium sulphide/ ketoconazole /zinc pyrithione shampoos to affected areas for 5 to 10 minutes and then washed off in the shower. Systemic treatment only in cases of recalcitrant or recurrent disease or if large areas are affected.

Monthly application of any of the above for 3 months may prevent recurrence

Systemic therapy- two weekly doses of fluconazole 400 mg or itraconazole 200 mg daily for 5 days

Tinea capitis

Fungal cultures may be negative in kerion. Scalp dermoscopy to visualize comma shaped hairs and corkscrew hairs may be a valuable aid.

Duration of treatment- 4 to 6 weeks for terbinafine (2 weeks after clinical resolution), 6 to 8 weeks for griseofulvin. Griseofulvin is abundantly excreted in sweat, however, terbinafine is not excreted in sweat and sebum production is not significant in prepubertal children. Terbinafine is directly incorporated in to hair follicles from systemic circulation. For these reasons, terbinafine is not a suitable choice for treating tinea capitis with ectothrix type of hair invasion.

Selenium sulphide shampoo (1 to 2-5%) or ketoconazole shampoo two to three times weekly to decrease the spread of infection.

Ectothrix infections are more contagious than endothrix infections. Children in whom treatment has been initiated should not share combs, hats, brushes, helmets or other items that come in contact with hair or play contact sports for 14 days to avoid transmission.

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For registration visit website: www.peddermfoundation.org