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A 7-Month-Old Who Has a Persistent Rash

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Presentation

A 7-month-old boy presents to the pediatric infectious diseases clinic with an unusual rash for the past 4 weeks. The rash appeared first on the back of his neck as a reddish-brown raised “spot” (Fig. 1). Over the past month, other reddish-brown macules and papules have appeared on his anterior trunk that later have developed a fine scale, followed in some places by erosions and black eschar formation. These lesions were neither vesicular nor pustular in appearance before eroding. The eschars eventually healed, leaving hypopigmented scars.

The infant has been asymptomatic otherwise and has gained weight during this time, maintaining his normal appetite and activity. There is no history of fever or discomfort. Initially, a pediatrician thought the infant had scabies and prescribed permethrin cream, but there was no improvement of the infant’s condition. The pediatrician then prescribed two courses of antibiotics (cephalexin and amoxicillin) for a presumed varicella infection complicated by bacterial superinfection. Again, there was no improvement. Because of the continued appearance of new lesions the infant was referred to a pediatric infectious diseases clinic.

The infant’s past medical history is unremarkable. He was delivered vaginally without complications at term and has been healthy otherwise until the rash appeared. There has been no animal exposure or travel. There is no history of a respiratory or gastrointestinal infection or administration of any medications before the onset of the rash. His immunizations are up to date, and he does not have any allergies. The family history is unremarkable.

Physical examination reveals a playful, smiling infant in no distress who has a heart rate of 112 beats/min, respiratory rate of 24 breaths/min, temperature of 36.4°C, and weight of 8.8 kg (75th percentile). Skin examination reveals reddish-brown papules and plaques measuring 0.5 to 1.5 cm in diameter (Fig. 2). The lesions

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appear to be in different stages of development; some are covered with a fine white scale, while others show erosion and black eschars. There is mild scarring and hypopigmentation where the earliest lesions had appeared. Most of the lesions are localized to the anterior trunk, especially in the periumbilical area and under the right axilla. No involvement of the palms, soles, or mucosal surfaces is appreciated. The posterior torso is spared. The rest of the examination is unremarkable.

A complete blood cell count shows a hemoglobin concentration of 12.4 g/dL, hematocrit of 35%, white blood cell count of 6,800/ mm³ (1% bands, 13% neutrophils, 74% lymphocytes, 6% monocytes, 4% eosinophils, and 2% basophils), and platelet count of 434,000/mm³. C-reactive protein concentration is ≤0.5 mg/dL.

Consultation with a pediatric dermatologist and a medical procedure confirm the clinical diagnosis.
Diagnosis: Pityriasis lichenoides et varioliformis acuta

A skin biopsy showed focal parakeratosis overlying a spongiotic epidermis, with occasional dyskeratotic keratinocytes and extravasated red blood cells in the epidermis and papillary dermis (Figs. 3 and 4). The reticular dermis contained a lymphocytic infiltrate that extended to the lower portion of the dermis and surrounding adnexal structures. These findings were compatible with pityriasis lichenoides et varioliformis acuta (PLEVA), an idiopathic acquired dermatosis characterized by evolving erythematous, scaly papules that develop vesiculation, ulceration, and necrosis.

Discussion

Etiology

PLEVA commonly is preceded by an upper respiratory or gastrointestinal tract infection. Epstein-Barr virus, Mycoplasma pneumoniae, Streptococcus pyogenes, Toxoplasma gondii, parvovirus B19, and adenovirus are among the infectious agents associated with the onset of this rash. Other potential triggers include antibiotics, antipyretics, and vaccines. These observations, plus biopsy findings of immune complexes composed of immunoglobulin M and complement component C3 in the dermoepidermal junction and blood vessels, support the hypothesis that PLEVA represents a hypersensitivity reaction to an infectious or noninfectious antigen. Recently, it has been suggested that in some cases the eruption represents a true cutaneous lymphoproliferative disorder due to the demonstration of monoclonal CD8+ lymphocytes infiltrating the skin.

Epidemiology

Once thought to be uncommon in children, recent reports suggest that the incidence of PLEVA may be underestimated in the pediatric population. The incidence of PLEVA peaks twice during childhood; the first peak occurs at 24 to 36 months of age and the second peak between 5 and 7 years of age. PLEVA rarely occurs before the second year after birth, although newborn cases have been described. No ethnic group seems to be affected predominantly over another. PLEVA has a mild male preponderance, with a male to female ratio close to 1.5:1. The incidence may be higher during the winter and fall.

Clinical Presentation

PLEVA usually presents acutely with crops of brown or reddish papules about 1 cm in diameter that have sur-
rounding erythema. New lesions appear rapidly, most frequently affecting the trunk, flexor surfaces, and proximal extremities. The soles, palms, and mucosal surfaces usually are spared. Facial and scalp involvement, although rare in adults, occur in 40% of children. Lesions usually change over time, and multiple stages of development coexist at any point. The lesions can acquire white scale; they evolve into vesicles, pustules, and then erosions and ulcers. The ulcer generally will develop a necrotic appearance and finally a black eschar before healing. Healing of the lesion usually results in a scar (“varioliform,” or “resembling smallpox”) and hypopigmentation or, less commonly, hyperpigmentation.

The presence of necrosis, vesiculation, and ulceration rather than the duration of symptoms distinguish PLEVA from pityriasis lichenoides chronica (PLC), the chronic form of pityriasis lichenoides. PLC is characterized by asymptomatic reddish-brown papules with white scale that usually do not erode, ulcerate, or necrose. Histologically, PLC is similar to PLEVA, but the observed changes are milder in PLC. It is common for patients to have lesions of PLEVA and PLC simultaneously. This coincidence suggests that both forms represent different ends of the spectrum of the same disease. Constitutional symptoms accompany PLEVA in two thirds of cases. Pruritus is the most common symptom, occurring in 50% of cases. Fever, arthralgias, and malaise occur less commonly.

Differential Diagnosis
The differential diagnosis of PLEVA includes scabies, varicella, erythema multiforme, secondary syphilis, Gianotti-Crosti syndrome, tularemia, erythema, papular urticaria, and vasculitis. In an immune competent host, varicella lesions appear within a 2-week period and usually develop rapidly, evolving from macule to papule to vesicle to crust in 2 to 3 days, whereas PLEVA lesions evolve more slowly. Scabies, secondary syphilis, and Gianotti-Crosti syndrome seldom show necrosis. Lymphomatoid papulosis, a form of cutaneous lymphoma, may be impossible to differentiate from PLEVA on clinical grounds; this distinction generally is made by skin biopsy, which usually shows the presence of CD30+ lymphocytes having the atypical features of LyP.

Classification
If PLEVA affects the trunk, head, and inguinal region, it is classified as central; if the eruption affects only the limbs, it is classified as peripheral. PLEVA is classified as diffuse if there is central and peripheral involvement. The diffuse form represents 60% to 74% of PLEVA cases, the central form 5% to 21%, and the peripheral form 18% to 20%.

Evaluation
There is often a delay in making the diagnosis of PLEVA due to its polymorphic appearance, indolent course, and broad differential diagnosis. Skin biopsy is the gold standard for diagnosis and always should be performed when PLEVA is suspected. Inflammatory markers such as C-reactive protein, erythrocyte sedimentation rate, and white blood cell count can be elevated as well as liver transaminases, but these findings are nonspecific.

Course
PLEVA is considered a self-limited disease. Ersoy-Evans et al (1) reported a median resolution time of 18 months (range 2 to 108 mo) for PLEVA and 20 months (range of 3 to 132 mo) for PLC. Relapses are common before complete resolution. Although initial reports suggested that the diffuse form had the fastest resolution rate and the peripheral form the slowest, this distinction has not been corroborated in more recent reports.

Complications
Febrile Ulceronecrotic Variant of Mucha-Habermann Disease
Febrile ulceronecrotic variant of Mucha-Habermann disease (FUMHD) is characterized by high fever and progression of the typical PLEVA lesions to larger (5 to 10 cm) and more painful ulcerative lesions with extensive necrosis as well as multorgan involvement, including liver, central nervous system, and coagulation abnormalities. This condition carries a fatality rate as high as 25%. Sepsis can complicate this presentation because of bacterial superinfection of the lesions. Mucosal involvement is more common in this condition. Skin biopsy is critical for making a timely diagnosis.

Malignancy
Although rare, cutaneous T-cell lymphoma can arise from PLEVA lesions. Some researchers have suggested that PLEVA is a premalignant condition representing the mildest end of a spectrum that includes PLEVA, PLC, lymphomatoid papulosis, and cutaneous T-cell lymphoma.

Associated Conditions
Juvenile idiopathic arthritis, immune thrombocytopenic purpura, nonskin lymphomas, and hemophagocytic syndrome have been associated with PLEVA.
Treatment
Evaluating the efficacy of therapies for PLEVA is difficult due to lack of randomized controlled trials and the relapsing and self-limited nature of the disease. Ultraviolet B phototherapy is the most effective treatment; however, long-term carcinogenic concerns in children preclude this treatment as first-line therapy.

Oral erythromycin at standard doses is the most prescribed medication for PLEVA and has demonstrated a 25% to 87% response rate in children. Tetracyclines also have been used in older children and adults. Clinical response may be obtained within 2 weeks, but it may take up to 2 months. If response is obtained, the antibiotic should be tapered to prevent flares; in most cases, the taper can be completed within 1 to 4 months after clinical response is obtained. There are reports of clinical success with azithromycin in erythromycin-refractory cases. It is unclear why antibiotics are effective in treating PLEVA, but it has been suggested that the immunomodulatory properties of the macrolides may play an important role in the improvement of lesions. Because PLEVA usually follows a benign course, some experts advocate observation without further intervention if antibiotics are unsuccessful.

Therapy with topical tacrolimus, systemic corticosteroids, and methotrexate has been successful in case reports. Symptomatic relief of pruritus with emollients, antihistamines, and topical corticosteroids is an important component of treatment; however, these medications have minimal, if any, effect on the skin lesions’ evolution.

In FUMHD, methotrexate can be life saving. Intravenous immunoglobulin, cyclosporine, and systemic corticosteroids also have been successful.

Patient Course
The patient was started on oral erythromycin three times a day and was scheduled for a 1-month follow-up visit with a dermatologist. Unfortunately, the patient did not show up to this appointment. Six months later he was evaluated in the emergency department for a viral gastroenteritis and was found to be free of skin lesions at that time.

Summary
- PLEVA should be considered in children who present with coexisting papules, ulcers, and eschars. These skin lesions heal, leaving a hypopigmented scar.
- Most children who have PLEVA are nontoxic in appearance and are healthy otherwise.
- If systemic symptoms are prominent, FUMHD should be considered.
- A skin biopsy is mandatory to confirm the diagnosis and exclude more serious conditions, such as malignancy or vasculitis.
- Erythromycin is the medication most commonly used as first-line therapy.
- Most PLEVA cases are self-limited, although some cases can have a relapsing course before resolving.

Reference

Suggested Reading
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