JAMA Dermatology Clinicopathological Challenge

A Solitary Scaly Plaque on the Lower Extremity of a Young Girl

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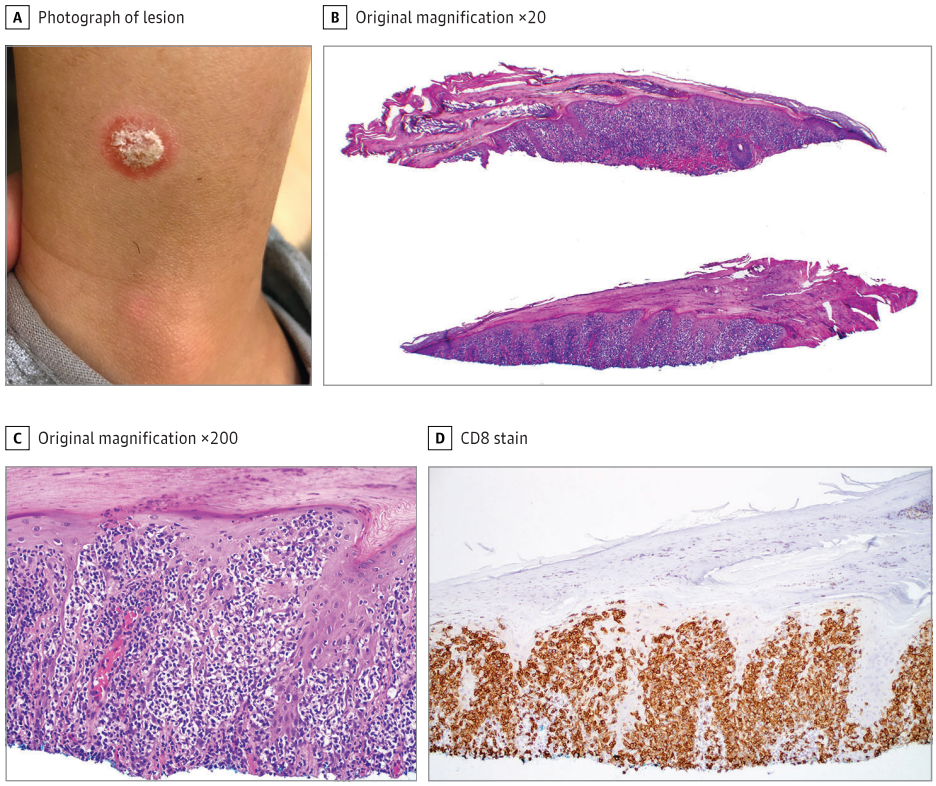

Figure. A, Image of a solitary plaque on the right lateral lower leg. B, Scanning view with hyperkeratosis, epidermal hyperplasia, and a lichenoid-like lymphoid infiltrate (hematoxylin-eosin). C, Biopsy results with marked epidermotropism of atypical lymphocytes (hematoxylin-eosin). D, Biopsy results with robust CD8 signal (magnification ×100).

A preschool-age girl presented for evaluation of an asymptomatic plaque on the right lower extremity that had been present for 1 year. Prior treatments included triamcinolone ointment and frankincense with no improvement. A potassium hydroxide preparation had negative results for fungal elements. Her medical history and family history were unremarkable. An examination found a 1-cm nummular plaque with centralized micaceous scale and a smooth erythematous border on the right lateral lower leg (**Figure**, A). A tangential-shave biopsy was performed to characterize the lesion. Histopathological testing revealed an epidermis featuring elongated rete ridges, keratinocyte enlargement, and a few Civatte bodies, with overlying parakeratotic crust and neutrophilic cell debris. Marked epidermotropism of atypical lymphocytes with irregular nuclear contours and halos, both singly and in small collections (Pautrier microabscesses) were also observed (Figure, B and C). Also, lymphocytes were present along the epidermal side of the dermoepidermal junction. Periodic acid–Schiff stained sections failed to show fungal or yeast elements. Immunohistochemical staining was markedly positive for CD3, CD5, and CD8 (Figure, D); CD4 reactivity was less robust and mainly restricted to dermal lymphocytes. Also, CD20 was present in 5% of dermal lymphocytes, and CD30 showed variable staining of 5% of lymphocytes.

WHAT IS YOUR DIAGNOSIS?

- **A.** Langerhans cell histiocytosis
- **B.** Lymphomatoid contact dermatitis
- **C.** Mycosis fungoides
- **D.** Pagetoid reticulosis

Diagnosis

D. Pagetoid reticulosis

Discussion

Based on clinical and pathologic findings, the patient was diagnosed with pagetoid reticulosis (PR), also known as *Woringer-Kolopp disease*. This is a rare, localized form of mycosis fungoides (MF).[1] It was first identified in 1939,[2] with approximately 50 well-documented cases reported in the literature since 1984.[1] This condition typically presents as an indolent, solitary, psoriasiform plaque located on the distal extremities.[3] It is often misdiagnosed as psoriasis, an eczematous process, or a bacterial or fungal infection.[4]

Although PR has been reported in both children and adults, it is exceedingly uncommon in the pediatric population.[1] The age range for reported cases[1,5] of pediatric PR is 2 to 13 years. In reported cases, 4 patients were male, and 3 patients were female (including the patient in this case). All patients presented with a solitary plaque on an extremity without signs of systemic involvement.

The histopathology of PR is characterized by a hyperplastic epidermis and epidermotropic infiltrate of atypical lymphocytes, presenting either singly or in groups.[3,4] Immunophenotypes that are $CD3^+$ and $CD8^+$, $CD3^+$ and $CD4^+$, and $CD4^-$ and $CD8^-$ have been described, with the last of these possibly representing γδ lymphoma. Variable expression of CD30 by the neoplastic population in the epidermis may also be present.[4] In contrast with cases in adults, most pediatric cases of PR have described a $CD3^+$ and $CD8^+$ immunophenotype.[1] The first case (to our knowledge) of a $CD8^-$ immunophenotype (with $CD8^+$ cells being confined to the dermis) in the pediatric population was recently reported.[5] In a review by Mourtzinos et al,[6] 53% of adults expressed a $CD8^+$ and $CD4^-$ immunophenotype, 36% expressed a $CD4^+$ and $CD8^-$ immunophenotype, and 11% expressed a $CD4^-$ and $CD8^-$ immunophenotype; 47% of adults expressed CD30 positivity.

Pagetoid reticulosis must be differentiated from other disorders with malignant features on histopathological testing, such as Langerhans cell histiocytosis, which exhibits characteristic ovoid cells with abundant eosinophilic cytoplasm and so-called coffee-bean nuclei infiltrating the papillary dermis. Immunohistochemistry staining for CD1a and CD207 is necessary to confirm the diagnosis.[7] Although Langerhans cell histiocytosis may appear in any age group, peak incidence occurs between 1 and 3 years of age. Cutaneous involvement is highly suggestive of multisystem disease and typically presents with skin-colored to erythematous papules and plaques that may eventually become scaly, crusted, or petechial.[8] Histopathological testing may be useful in differentiating PR from cutaneous pseudolymphomas, such as lymphomatoid contact dermatitis. Histology demonstrates a superficial, band-like T-cell infiltrate with epidermotropism. Spongiosis may be seen. Intraepidermal collections of mononuclear cells (pseudo-Pautrier microabscesses) may also be observed, which makes the distinction from PR more difficult. However, unlike PR, lymphomatoid contact dermatitis has a balanced ratio of $CD4^+$ to $CD8^+$ lymphocytes. It is most commonly encountered in adults and presents with erythematous and pruritic patches, papules, or plaques.[9] Lastly, PR should be distinguished from conventional MF, which most commonly presents on the trunk, buttocks, or other non–sun-exposed areas; PR is considered a localized variant of MF and tends to favor distal extremities. Typically, MF contains $CD4^+$ atypical lymphocytes infiltrating both the epidermis and dermis. In PR, the atypical lymphocytes (most commonly $CD8^+$) are restricted to the epidermis.[1,3,10] The typically unilesional, acral nature of PR also aids in differentiation.

Because PR is rare, there is no gold standard for treatment, and therapy should be tailored to the patient. Treatments including photodynamic therapy, surgery, radiotherapy, and high-potency topical steroids and have been used with success in pediatric patients. Complete remission was achieved in all reported cases in children.[1,5] Observation alone has not been used as a treatment in pediatric PR. Pagetoid reticulosis can affect patients of any age, and although it typically represents an indolent process, there is potential for recurrence and dissemination. Extracutaneous dissemination or death attributed to PR has never been reported. However, long-term follow-up is still recommended in all cases.[1,3] Reported follow-up times in pediatric PR have ranged from 8 months to 5 years.[1] This patient's parents opted for surgical excision. The site healed completely, with no evidence of recurrence at 6-week follow-up.

ARTICLE INFORMATION

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