Pagetoid reticulosis (Woringer-Kolopp disease) in a 2-year-old girl—Case report and review of the literature

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Key words: CD8; epidermotropism; pagetoid reticulosis; unilateral mycosis fungoides; Woringer-Kolopp.

INTRODUCTION

Localized pagetoid reticulosis, also known as *Woringer-Kolopp disease*, is a rare variant of mycosis fungoides (MF) characterized mostly by a solitary, persistent, scaly plaque, commonly involving the limbs of children or adults.[1] Its name derives from the microscopic findings of prominent intraepidermal (pagetoid) proliferation of neoplastic T cells.[1] We report the youngest PR patient, to our knowledge, in the literature and review all the pediatric cases of PR. We then compare the cases with those of the adult-onset variant.

Abbreviations used:

PR: pagetoid reticulosis
MF: mycosis fungoides
TCR: T-cell receptor

CLINICAL CASE

A 2-year-old girl, otherwise healthy, was seen for the presence of a slowly growing solitary asymptomatic verrucous plaque on the back of her left hand. Her parents first noticed the lesion 1 year before. On physical examination, a 4-cm, erythematous, infiltrated plaque covered by a thick whitish scale was present (Fig 1).

Histopathology found epidermal hyperplasia and a prominent infiltrate of atypical, small-to-medium size lymphocytes showing diffuse epidermotropism (Fig 2). Necrotic keratinocytes were also present.

Immunohistochemical studies showed diffuse reactivity for CD3, CD8 (Fig 3), and TIA-1; CD4 labelling was less intense and confined to the dermal lymphocytes. Occasional $CD30^+$ and $CD56^+$ lymphocytes were also found.

Histologic features and clinical presentation were consistent with the diagnosis of localized PR. T-cell receptor (TCR) gene rearrangement testing was positive for β and γ TCR. The patient received high-potency topical steroid treatment without improvement; a partial response was achieved instead with heliotherapy. Local superficial radiotherapy (20 Gy at 1.5 Gy fractions) achieved a complete response.

DISCUSSION

PR is classified as an indolent cutaneous T-cell lymphoma under the European Organization for Research and Treatment of Cancer system.[1] It was first described in 1939 in a 13-year-old boy.[2] Since 1984, about 50 cases, which have been immunohistologically well documented, have been reported. No gender predilection has been shown,[3] and although a wide age range has been reported, a large prevalence is documented in adults.[3] To the best of our knowledge, only 5 cases (including the current one) of pediatric PR have been described until now in the English-language literature. A summary of clinical features, histopathology with immunohistochemistry, and treatment of all cases is shown in Table I.

Age at diagnosis ranged from 2 to 13 years. Four patients were male and one female. All patients

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Funding sources: None.
Conflicts of interest: None disclosed.
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JAAD Case Reports 2019;5:104-7.
2352-5126

https://doi.org/10.1016/j.jdcr.2018.10.023

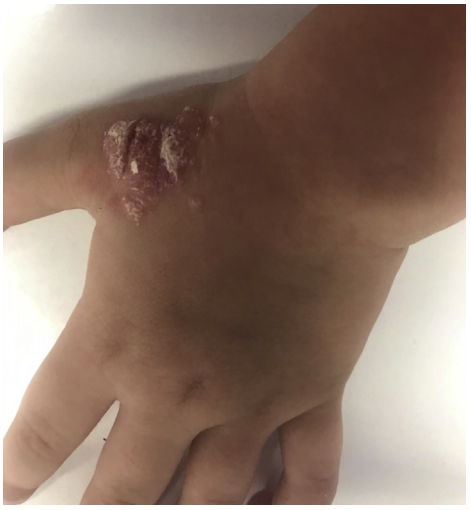

Fig 1. Slowly growing solitary asymptomatic verrucous plaque on the back of the hand of a 2-year-old girl.

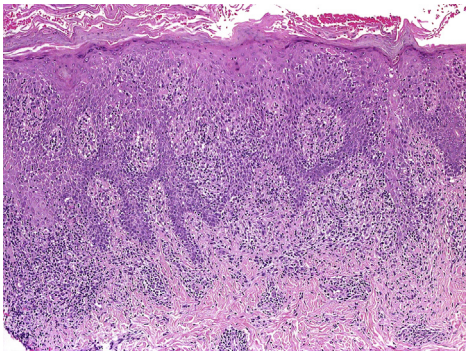

Fig 2. Photomicrograph of a skin biopsy specimen from the left hand at presentation shows epidermal hyperplasia and a prominent infiltrate of atypical, small-to-medium size lymphocytes, diffuse epidermotropism, and necrotic keratinocytes. (Hematoxylin-eosin stain.)

presented with a solitary lesion at the extremities. None of them had systemic involvement. Immunophenotype was similar in all patients, with a lymphocytic infiltrate expressing at least CD3 and CD8. In 2 cases, including ours, also $CD4^+$ lymphocytes were found but less represented and confined to the underlying dermis.[4] In 2 cases, T-cell receptor gene rearrangement analysis was performed and not detected (although it was positive in our case).[4,5] All patients underwent different treatments; complete remission occurred with photodynamic therapy sessions with topical 20% aminolevulinic acid, excisional biopsy, and radiotherapy. No relapse occurred in all reported cases from literature, with a follow-up that ranged from 8 months to 5 years. In our patient, radiotherapy was successful in clearing the lesion. Clinical presentation of pediatric cases of PR shows similar characteristics to that of the adult

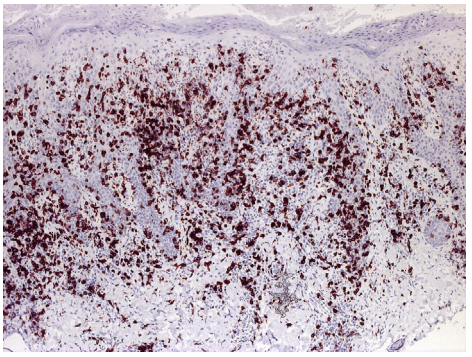

Fig 3. Immunohistochemical studies showed CD8 predominance of the epidermotropic lymphocytes.

counterpart with a unilesional psoriasiform or verrucous patch or plaque involving the distal extremities. Histologic examination evenly shows epidermal hyperplasia and parakeratosis with epidermotropic atypical lymphocytes. However, although immunophenotype in all the described children was $CD3^+$ and $CD8^+$,[4-6] the lymphocytic infiltrate in adults expressed $CD8^+/CD4^-$ (53%), $CD4^+/CD8^-$ (36%), $CD4^-/CD8^-$ (11%), and $CD30^+$ (47%).[7] The course of PR both in young and older patients was indolent without systemic implications. Localized PR should be distinguished from primary $CD8^+$ cytotoxic T-cell lymphoma, which, in contrast, is an aggressive disease, usually presenting with ulcerated lesions that follow a rapid course with poor prognosis. Patch stage of conventional mycosis fungoides could also be considered. Although PR is considered a variant of MF, clinically conventional MF tends to involve the trunk, buttocks, and proximal extremities, whereas the typical site of involvement in PR are the distal extremities. Histopathologically, the atypical lymphocytes, which show a prominent CD4 immunophenotype in MF, are present in the infiltrate both within the epidermis and dermis with less prominent epidermotropism. On the contrary, the epidermotropism of $CD8^+$ atypical lymphocytes is the most prominent and characteristic histologic feature in PR. In addition, eosinophils are absent in cases of PR. In contrast to conventional MF, neither extracutaneous dissemination nor disease-related deaths have ever been reported in PR.[1] In pediatric cases, annular lichenoid dermatitis of the youth could also be considered. However, annular lichenoid dermatitis of the youth has a predilection for the groin and flanks, and the lymphocytic infiltrate never shows a marked epidermotropic pattern, although its immunophenotype is usually $CD3^+/CD8^+$ like it occurs in PR.[8] Additional differential diagnoses include type D lymphomatoid papulosis, psoriasis, eczematous dermatitis, parapsoriasis, and dermatophytosis.

Table I. Literature review of all cases of pediatric PR

	Study	Age at diagnosis (y)/Sex	Body site	Lesion description	Immunophenotype	Primary treatment/response	Follow-up
1	Mendese et al[6]	10/M	Foot	Solitary, pink, ovoid, indurated plaque, 2.4 × 2 cm, with thick adherent yellowish scale	$CD3^+$, $CD8^+$	9 PDT sessions with topical 20% ALA in 13 mo (3 of them with i.l. ALA)/ complete response	NED at 2 y and 9 mo
2	Matsuzaki et al[5]	6/M	Thigh	Erythematous plaque, like a hypertrophic scar	$CD3^+$, $CD4^-$, $CD8^+$, $CD45RO^+$, $CD20^-$, $CD30^-$, $CD79a^-$ No TCR gene rearrangement	Excisional biopsy/complete response	NED at 5 y
3	Miedler et al[4]	5/M	Buttock	6 × 3 cm, coalescing, erythematous, scaly papules, forming a nonconfluent plaque	$CD3^+$, $CD4^+$ (predominant in the dermis), $CD8^+$ (predominant in the epidermis); No TCR gene rearrangement	Radiotherapy/complete response	NED at 8 mo
4	Woringer et al[2]	13/M	Forearm	Asymptomatic, large, oval, sharply circumscribed, 6- × 7-cm, plaque with polycyclic borders	-	Excisional biopsy	-
5	Current case	2/F	Hand	Asymptomatic, solitary verrucous erythematous, infiltrated, 4- × 4-cm, plaque, covered by a thick whitish scale	$CD3^+$, $CD8^+/CD4^+$ (less intense), TIA-1 TCR positive	Topical steroids/No response Heliotherapy/partial response Local superficial radiotherapy (20 Gy at 1.5 Gy fractions)/complete response	-

ALA, Aminolevulinic acid; *i.l.*, intralesional; *NED*, no evidence of disease; *PDT*, photodynamic therapy; *TCR*, T-cell receptor.

We report the youngest patient affected by PR, who is also the only female and the fifth pediatric case. Despite its rarity, PR should be included in the differential diagnosis of solitary slow-growing erythematous, verrucous plaque on distal extremities of children. Diagnosis should be made on clinical and histologic features, and immunohistochemistry represents the gold standard. Because of the rarity of this disease, there are no recommended treatment options, and clinicians should tailor therapy on patients' characteristics. First, we tried a 2-month course of topical clobetasol without success. Our second choice was phototherapy. Because of the summer season and sunny area, heliotherapy (the use of natural sunlight) was considered, as it is a popular form of treatment for psoriasis, atopic dermatitis, and patch stages cutaneous T-cell lymphoma in patients from European countries because of the favorable climate at these latitudes. We suggested the parents expose the patient for 26.3 minutes a day at 10:00 o'clock starting with 10 minutes and adding 30 seconds each day.[9] However, only a partial improvement was obtained after 2 months. Complete clearance was achieved using localized, superficial radiotherapy that has been suggested as one of the most effective treatment for pagetoid reticulosis with a recommended dose of 20 to 24 Gy.[10] Recurrence after therapy may occur but extracutaneous dissemination has never been reported.[1] The unilesional clinical presentation and the CD8 predominance of the epidermotropic lymphocytes seem to predict a benign course; however, long-term follow-up is advisable in any case.

REFERENCES

1. Cerroni L, Hodak E, Kempf W, et al., Variants of mycosis fungoides. In: Elder DE, et al.: WHO classification of skin tumours (4th ed). Lyon, 2018, p 231-233, ISBN 978-92-832-2440-2.
2. Woringer F, Kolopp P. Lésion érythémato-squameuse polycyclique de l'avant-bras évoluant depuis 6 ans chez un garçonnet de 13 ans: histologiquement infiltrat intra-épidermique d'apparence tumorale. *Ann Dermatol Syphil*. 1939;67:945-958.
3. Su O, Dizman D, Onsun N, et al. Treatment of localized pagetoid reticulosis with imiquimod: a case report and literature review. *J Eur Acad Dermatol Venereol*. 2016;30(2):324-326.
4. Miedler JD, Kristjansson AK, Gould J, Tamburro J, Gilliam AC. Pagetoid reticulosis in a 5-year-old boy. *J Am Acad Dermatol*. 2008;58(4):679-681.
5. Matsuzaki Y, Kimura K, Nakano H, Hanada K, Sawamura D. Localized pagetoid reticulosis (Woringer-Kolopp disease) in early childhood. *J Am Acad Dermatol*. 2009;61(1):120-123.
6. Mendese GW, Beckford A, Krejci N, Mahalingam M, Goldberg L, Gilchrest BA. Pagetoid reticulosis in a prepubescent boy successfully treated with photodynamic therapy. *Clin Exp Dermatol*. 2012;37(7):759-761.
7. Mourtzinos N, Puri PK, Wang G, Liu ML. CD4/CD8 double negative pagetoid reticulosis: a case report and literature review. *J Cutan Pathol*. 2010;37:491-496.
8. Di Mercurio M, Gisondi P, Colato C, Schena D, Girolomoni G. Annular Lichenoid dermatitis of youth: Report of six new cases with review of the literature. *Dermatology*. 2015;231(3):195-200.
9. Moosa Y, Esterhuyse DJ. Heliotherapy: a South African perspective. *S Afr Med J*. 2010;100(11):728-733.
10. Lee J, Esterhuyse DJ. Clinicopathologic features and treatment outcomes in Woringer-Kolopp disease. *J Am Acad Dermatol*. 2008;59:706-712.