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PAGETOID RETICULOSIS IN A 5 YEAR OLD BOY

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Abstract

We present a rare case of pagetoid reticulosis arising in a five year old white boy. He had a history of a large chronic erythematous, scaly patch on his left buttock that had shown intermittent partial response to a topical anti-fungal medication. A punch biopsy revealed dramatic epidermal hyperplasia, with parakeratosis and prominent exocytosis of single and clustered mononuclear cells (Pautrier's microabscesses) into the epidermis. Some of these exhibited hyperchromatic nuclei with irregular contours. They stained prominently for CD3, CD4 and CD8, with a predominance of CD8 + cells. T cell receptor gene rearrangement by PCR was negative for a clonal process on a second biopsy that was sub diagnostic on routine sections.

Pagetoid reticulosis is an indolent, unilesional variant of mycosis fungoides, in which the atypical T cells may express a CD4-/CD8+ phenotype. This is in contrast to primary cutaneous epidermotropic CD8+ cytotoxic T-cell lymphoma, which is often very aggressive with a poor outcome. Pagetoid reticulosis is exceedingly rare in children and adolescents. Two features predict a benign course in this 5 year old child: the unilesional clinical presentation and the CD8 predominance of the epidermal lymphocytes.

Introduction

Background

Pagetoid reticulosis was first described in 1939 by Woringer and Kolopp^{1,7} at the Clinique Dermatologique in Strasbourg, France. They reported a 13-year-old boy with a 6 year history of an asymptomatic, large, oval, sharply circumscribed 6 – 7 cm plaque with polycyclic borders that involved the left forearm. Physical exam and laboratory work-up were otherwise unremarkable. The clinical differential diagnosis included cutaneous tuberculosis and lupus erythematosus. Histologic examination of a biopsy of the lesion demonstrated many, large intraepidermal cells of uncertain etiology. These cells had clear cytoplasm and nuclei with dark chromatin and irregular borders. After consultation with Civatte, director of the Musée

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d'Histologie de Saint-Louis in Paris, and Pautrier, Woringer's teacher at the Clinique Dermatologique in Strasbourg, Woringer's differential diagnosis included nevus with exuberant cells, extra-mammary Paget's disease, and mycosis fungoides. Interestingly, Pautrier felt mycosis fungoides was unlikely based on the clinically indolent nature of the lesion over the patient's 6 year course^{1,7}.

Classification of pagetoid reticulosis

The current WHO-EORTC classification defines pagetoid reticulosis as "a variant of mycosis fungoides characterized by the presence of localized patches or plaques with an intraepidermal proliferation of neoplastic T cells"². Immunophenotype of the neoplastic T cells is variable (CD4+/CD8-, CD4-/CD8+, or CD4-/CD8-). Demonstration of clonality is not a required criteria². Clinical features overlap with early patch stage mycosis fungoides, and histologic and immunophenotype can be indistinguishable from aggressive epidermotropic CTCL. As a result, pagetoid reticulosis is best viewed as a diagnosis requiring clinicopathological correlation, with clinical findings of utmost importance in guiding diagnosis and thereby prognosis and treatment.

Case Report

A 5-year-old white boy presented with a 2-year history of a persistent scaly patch on his left buttock. He was otherwise healthy and his past medical history was unremarkable. The lesion had shown intermittent partial response to topical anti-fungal medication.

A full skin examination was notable for 6x3 cm lesion on the left buttock, consisting of coalescing, erythematous, scaly papules forming a non-confluent plaque (Fig 1). No subtle disseminated lesions were present. Clinical differential diagnosis included eczematous dermatitis and granuloma annulare.

Punch biopsy showed dramatic epidermal hyperplasia with parakeratin and prominent exocytosis of single and clustered mononuclear cells (Pautrier's microabscesses) into the epidermis (Fig 2a, b). Some of these exhibited hyperchromatic nuclei with irregular contours. They stained prominently for CD3, CD4 and CD8, with a predominance of CD8+ cells in the epidermis (Fig 2c, d) compared with CD4+ cells, which were predominantly dermal (Fig e, f). T cell receptor gene rearrangement by PCR was negative for a clonal process on a second biopsy that was sub-diagnostic non-diagnostic histologically.

This unilesional process with CD8 predominance by immunohistochemistry is consistent with pagetoid reticulosis. This patient received radiotherapy, 36 Gy at 1.5 Gy fractions with complete resolution and no recurrent lesions after 8 month follow up. Localized electron beam therapy, when correctly performed, is highly effective and without systemic or significant long term local toxicity.

DISCUSSION

Pagetoid reticulosis is a rare variant of mycosis fungoides that typically presents as chronic, large, localized, erythematous patches or plaques involving the distal extremities. There is a reported male predominance (2:1)³, and a wide age range at onset (range of 2 to 79 yo, 20% <18 yo, 15% <10 yo, and mean 40 yo)^{1,3,4,5,6}. There are only two other reported cases of pagetoid reticulosis arising in children under the age of five years old. One of the two cases had similar histological and immunohistochemical findings. The other case was part of a larger series in which case specific details were not provided.

Histologic examination of pagetoid reticulosis demonstrates epidermal hyperplasia and parakeratosis with striking infiltration of the epidermis by atypical mononuclear cells both singly and in clusters (Pautrier's microabscesses). Nuclei of the atypical cells are hyperchromatic with irregular nuclear contours. The papillary dermis may show a mixed infiltrate of lymphocytes or histiocytes, but should not reportedly contain neoplastic T cells².

Immunophenotype of the neoplastic T cells is variable, with CD4+/CD8-, CD4-/CD8+, and CD4-/CD8- cases described. CD30 is also often expressed². Of note, clonality of the atypical T cells has not been consistently demonstrated, and is not mentioned as criteria for diagnosis in the WHO-EORTC classification. However, the majority of recently published accounts of pagetoid reticulosis conclude that it is a clonal T-cell disorder^{3,4,5,7}.

CD4-/CD8+ cases such as this one must be distinguished from primary CD8+ cytotoxic T cell lymphoma, which, in contrast is aggressive, lacks a patch/plaque stage, often presents with ulcerated lesions and follows a rapid clinical course with poor outcome. CD4+/CD8- cases must be distinguished from the patch stage of classic mycosis fungoides (MF). Clinically, MF tends to involve the trunk, buttocks, and proximal extremities, in contrast to pagetoid reticulosis, which tends to involve the distal extremities. Histologically, the atypical lymphocytes in MF are present both within the dermis and epidermis, with less prominent epidermotropism. Conversely, atypical lymphocytes are not present within the dermis in pagetoid reticulosis and the epidermotropism is often the most prominent histologic feature. In addition, eosinophils are often present within the dermal infiltrate in cases of MF, and absent in cases of pagetoid reticulosis⁴. Pityriasis lichenoides should also be included in the differential diagnosis of lesions with prominent exocytosis of lymphocytes but nuclear irregularities and pleomorphism are not present. Clinical course is also different with recurrent crops of small scaly lesions that heal over weeks.

Recommended treatment options for pagetoid reticulosis include radiotherapy and surgical excision. Although local recurrence after therapy occurs in selected cases, extracutaneous dissemination or disease-related deaths have never been reported².

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REFERENCES

1. Woringer F, Kolopp P. Lesion erythémato-squameuse polycyclique de l'avant-bras évoluant depuis 6 ans chez un garçonnet de 14 ans: histologiquement infiltrat intra-épidermique d'apparence tumorale. *Ann Dermatol Syphil* 1939;67:945-958.
2. Willemze R, et al. WHO-EORTC classification for cutaneous lymphomas. *Blood* 2005;105:3768-3785. [PubMed: 15692063]
3. Mandojana RM, Helwig EB. Localized epidermotropic reticulosis (Woringer-Kolopp disease). *J Am Acad Dermatol* 1983;8(6):813-829. [PubMed: 6602816]
4. Haghighi B, et al. Pagetoid Reticulosis (Woringer-Kolopp Disease): An immunophenotypic, molecular, and clinicopathologic study. *Mod Pathol* 2000;95:318-323.
5. Burns MK, Chan LS, Cooper KD. Woringer-Kolopp disease (localized pagetoid reticulosis) or unilesional mycosis fungoides? An analysis of eight cases with benign disease. *Arch Dermatol* 1995;131(3):325-329. [PubMed: 7887663]
6. Crowson AN, Magro CM. Woringer-Kolopp disease. A lymphomatoid hypersensitivity reaction. *Am J Dermatopathol* 1994;16(5):542-548. [PubMed: 7802169]
7. Cribier B. History: Frederic Woringer (1903-1964) and Woringer-Kolopp Disease. *Am J Dermatopathol* 2005;27:534-545. [PubMed: 16314708]

Fig. 1. Coalescing, erythematous, scaly papules forming a non-confluent plaque on the left buttock of a 5 year old boy.

Fig. 2.
Punch biopsy of the left buttock lesion: **a, b**, H & E stain showing dramatic epidermal hyperplasia with parakeratin and prominent exocytosis of single and clustered mononuclear cells (Pautrier's microabscesses) into the epidermis (**a**, 10x, **b**, 40x); **c, d**, CD8 immunostain demonstrating predominantly CD8+ staining of the atypical lymphocytes within the epidermis (**c**, 10x, **d**, 40x); **e, f**, CD4 immunostain demonstrating dermal infiltrate of CD4+ lymphocytes without involvement of the epidermis (**e**, 10x, **f**, 40x).