A 68-year-old male presented to our dermatology clinic complaining of an approximate 4-year history of a rash on his right foot. A few weeks prior to the presentation, he developed superimposed ulceration, which prompted him to seek medical attention. He was first seen in the emergency room where he was treated with IV antibiotics and analgesics. After no significant improvement, he was referred to the dermatology clinic for further management. On physical examination, erythematous-scaly plaques were observed on the medial and lateral aspects of the right foot, extending to the plantar surface. In addition, a 4.5 cm erosion was observed on the plantar aspect of the right foot [Figure 1]. Two 3 mm punch biopsies were performed at the edge of the ulcer. One was sent for histopathologic analysis and the other for tissue culture.

**Histopathologic Findings**

A dense and monotonous infiltrate of small-to-medium-sized lymphocytes were observed throughout the papillary dermis and extending to the base of the punch biopsy specimen [Figure 2]. Multiple aggregations of the lymphocytes were also observed within a pale and macerated epidermis. A TCR-gene rearrangement assay revealed a monoclonal population of T-cells. On immunohistochemical evaluation, the atypical lymphocytes stained for CD2, CD5, CD8, and CD30 [Figure 3]. The lymphocytes failed to stain with CD3, CD4, CD7, TIA-1, Granzyme B, Beta-F1, CD56, and AIK-1. An in-situ hybridization study was negative for Epstein-Barr virus (EBV). The Ki67 index was approximately 50–60%. No organisms grew on the tissue culture.

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What is Your Diagnosis?

Answer

Pagetoid Reticulosis.

Discussion

Pagetoid reticulosis (PR), first described by Woringer and Klopp in 1939, is an uncommon cutaneous T-cell lymphoma, that classically presents as a solitary, psoriasiform plaque on acral sites.\(^1\) The clinical differential diagnosis may include psoriasis on volar skin, chronic eczematous dermatitis, or even non-melanoma skin cancer (e.g., Bowen’s disease). Distinguishing histopathologic features include epidermal hyperplasia and marked epidermotropism of atypical lymphocytes throughout the epidermis.\(^1,2\) As these clinical and microscopic features are similar to what is observed in mycosis fungoides, some sources consider PR as a solitary variant of that disease. Moreover, the natural history of PR is generally indolent with little propensity for dissemination or systemic involvement.

Due to its ability to mimic other conditions, a skin biopsy and clinicopathologic correlation is critical for establishing the correct diagnosis. Histologically, PR exhibits a hyperplastic epidermis with atypical “pagetoid cells,” either singly or in nests. Immunophenotypic findings for the atypical epidermal cells are somewhat variable but always demonstrate a T-cell phenotype. Typically, the cells are CD2+, CD3+, and CD5+. Expression of CD4 and CD8 can fluctuate, with CD8+, CD4+ and CD4/CD8 double negative variants having all been reported (in decreasing order of frequency).\(^1,3\) CD7 expression is often lost, and CD30 reactivity can be variable.\(^1\) Treatments for PR may include topical nitrogen mustard, high potency topical steroids, localized radiation therapy, and surgical excision. The optimal choice of therapy is often dependent on the size of the lesion and other individual case-dependent parameters.\(^4\)

The longstanding, solitary nature, and acral localization of our patient’s lesion, combined with the microscopic features demonstrating a highly epidermotropic CD8+ lymphoid infiltrate without overt signs of cytotoxicity were felt most compatible with a diagnosis of PR. Unusual features, in this case, were the development of superficial ulceration and lack of beta-F1 staining, which led to the consideration of other more aggressive cutaneous lymphomas in the differential diagnosis. Early-evolving “primary cutaneous aggressive CD8+ epidermotropic T-cell lymphoma” was considered, but this entity is usually Granzyme+, beta-F1+, and CD30−.\(^5\) Furthermore, “primary cutaneous gamma-delta T-cell lymphoma” was also considered, but the indolent clinical presentation combined with the lack of Granzyme B and CD56 expression argued against this entity.\(^5\) Furthermore, a lack of beta-F1 staining does not always imply an aggressive gamma-delta T-cell lymphoma phenotype, as it has been found on occasion in indolent T-cell lymphomas such as mycosis fungoides and PR.\(^3,4\) Last, type “D” lymphomatoid papulosis may also demonstrate similar histology as seen in this case. However, that entity typically presents as relapsing and remitting papulo-nodules in multiple locations such as the trunk and extremities, which did not fit with the clinical presentation in this case.

The ulceration, in this case, was felt to be most likely representing chronic maceration and secondary impetiginization of the lesion rather than direct cytotoxicity from the lymphoma. Although not classically associated with ulceration, PR has previously been observed to display this clinical feature.\(^4\) A thorough analysis of the other clinical and histopathological features, in this case, was critical in avoiding the diagnosis of more aggressive lymphoma. Our patient underwent further work up to exclude systemic involvement, which included a CBC with differential, LDH, and PET-CT scan. All of these studies were found to be within normal limits. The patient underwent localized radiation therapy (24 Gy in 12 fractions) which completely cleared his lesions. He had remained in clinical remission for 2 years.

Learning Points

- PR presents as a localized psoriasiform plaque on acral skin and can masquerade as psoriasis and chronic eczematous dermatitis
- The histopathology of PR is characterized by a dense CD8+ lymphocytic infiltrate with marked epidermotropism
- Other cutaneous T-cell lymphomas on the histopathologic differential diagnosis for PR include primary cutaneous aggressive CD8+ epidermotropic T-cell lymphoma, CD8+ mycosis fungoides, and primary cutaneous gamma-delta T-cell lymphoma

Figure 3: CD8 immunostain (×40)
Localized electron beam radiation therapy is a highly effective treatment option for PR.

**Declaration of patient consent**
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**
There are no conflicts of interest.

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