



# Epidermotropic marginal zone lymphoma: An uncommon cutaneous B-cell lymphoma responsive to rituximab

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## INTRODUCTION

Epidermotropism refers to a state of abnormal colonization of the epidermis by leukocytes, which often reflects a clonal T-cell or monocyte dyscrasia. Epidermotropism is a distinctive pattern of passive migration into epithelial structures that is not otherwise attributable to the normal function of innate and adaptive immunity. Epidermotropism has been associated with mycosis fungoides (MF), Sézary syndrome, Woringer-Kolopp disease, and Langerhans cell histiocytosis.<sup>1</sup> Epidermotropism is thought to be attributable to the local intraepidermal environmental milieu, which serves as an attractant to neoplastic immune cells (eg, CCR4 and CCR10 on malignant T cells interacting with CCL17 and CCL27 on keratinocytes in the setting of MF).<sup>2</sup> Although rare, cutaneous B-cell lymphoma can also display an epidermotropic pattern.<sup>3</sup>

We encountered a gentleman with a generalized papulosquamous eruption, which was discovered to be epidermotropic marginal zone lymphoma (MZL), a type of B-cell lymphoma that frequently involves the skin, spleen, and bone marrow, who was successfully treated with rituximab. This case represents the eighth report of epidermotropic MZL and supports that rituximab may represent a rational first-line therapy for managing this rare condition, particularly in the setting of generalized cutaneous or visceral disease.

## CASE REPORT

A previously healthy 69-year-old man presented for the evaluation of an unexplained generalized

### Abbreviations used:

MF: mycosis fungoides  
 MZL: marginal zone lymphoma

cutaneous eruption. Six months before presentation, asymptomatic lesions developed on his chest and abdomen that subsequently disseminated to his back, buttocks, and proximal extremities. Despite the progression of his eruption, the patient felt well—he did not experience weight loss, fevers, night sweats, or other constitutional symptoms.

On physical examination, indurated, red-to-brown papules and plaques were present on the patient's chest, abdomen, back, and buttocks (Fig 1). His eruption had a predilection for flexural sites, and some lesions displayed striking linear configurations following skin cleavage lines. Given the papulosquamous morphology and the distribution of his eruption, the clinical impression was pityriasis rosea or a pityriasis rosea–like drug reaction. Two lesional biopsies were obtained to establish the diagnosis.

Histopathologic examination from each biopsy was similar and demonstrated a dense superficial lymphocytic infiltrate that expanded and effaced the papillary and superficial reticular dermis. Significant epidermotropism was seen (Fig 2, A). The lymphocytes had a noncerebriform small, round morphology, and there were few admixed lymphoplasmacytoid cells. The dermal and epidermotropic infiltrate stained positively for

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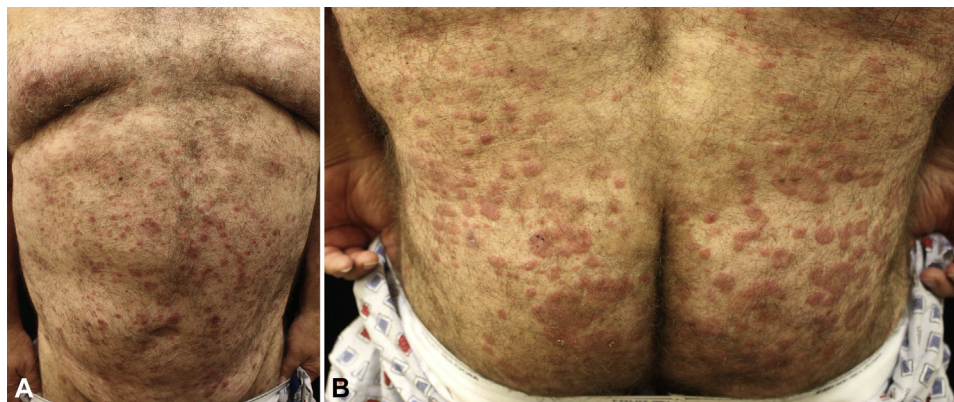
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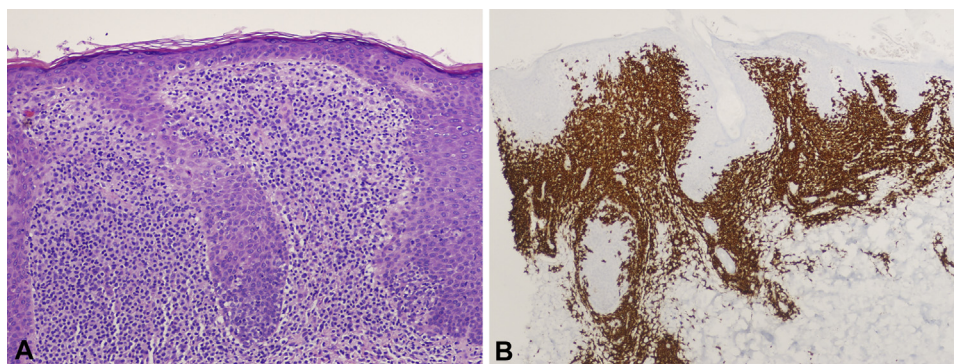
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**Fig 1. A,** Epidermotropic marginal zone lymphoma. Indurated, red-to-brown papules and plaques on the patient's chest, abdomen, and back. **B,** Numerous edematous, red-to-brown plaques were present on his buttocks.



**Fig 2. Epidermotropic marginal zone lymphoma. A,** Atypical lymphocytic infiltrates localized to the papillary dermis, along with multiple areas of exocytosis of lymphocytes into the epidermis (epidermotropism), were seen. **B,** The neoplastic cells stained positively for CD20. (**A,** Hematoxylin-eosin stain; original magnifications:  $\times 20$ ; **B,** CD20 immunohistochemical stain; original magnification:  $\times 4$ .)

CD20 and PAX5 (Fig 2, B), whereas the T-cell marker CD3 showed sparse staining, with a normal CD4/CD8 ratio. Follicle center markers including BCL6 and CD10 were negative. The histopathologic and immunopathologic features were characteristic of epidermotropic MZL.

After a diagnosis of epidermotropic MZL was made, the patient underwent evaluation for systemic disease. A bone marrow biopsy showed a low-grade B-cell lymphoproliferative disorder, similar to that of the skin. A positron emission tomography scan found lymphomatous splenic infiltration.

The patient underwent treatment with 4 weekly infusions of rituximab, 375 mg/m<sup>2</sup>, and within 3 months he experienced marked regression of his cutaneous disease. Repeat radiographic imaging found an interval decrease in the size of his spleen, signifying an objective response. Since achieving near total clinical remission, the patient remains under the close observation of medical oncology services.

## DISCUSSION

Epidermotropic MZL is an exceedingly rare B-cell lymphoma that frequently affects the skin. This disorder has been exclusively described in older men with a mean age of 64 years. Interestingly, epidermotropic MZL often presents as a papulosquamous eruption that mimics pityriasis rosea, albeit with a more protracted course (eg, months to years).<sup>3</sup>

In most cases, the histopathologic features of epidermotropic MZL are characterized by an inflammatory infiltrate of small, round lymphocytes that are largely confined to the papillary dermis, along with striking epidermotropism. The immunophenotypic profile of epidermotropic MZL displays immunohistochemical positivity for the B-cell markers CD20, CD79a, and PAX but does not stain for follicle center markers, such as BCL6 and CD10, or T-cell markers, such as CD3.<sup>3</sup> Importantly, by histopathology alone, the diagnosis of epidermotropic MZL may be difficult to establish,

as it frequently exhibits a low-power architecture that can be easily mistaken for T-cell lymphoproliferative disorders such as MF, based on the superficial bandlike array of inflammatory infiltrate and significant epidermotropism.<sup>3</sup> In these settings, immunohistochemical staining for B-cell markers represents an indispensable diagnostic test.

Although the pathogenesis underlying the epidermotropism observed in this subtype of MZL is poorly understood, the aberrant expression of CXCR3 may play a role, as the innate ligand for CXCR3 is interferon- $\gamma$ -induced protein 10, which is expressed by keratinocytes and stromal cells of the spleen and bone marrow.<sup>4-6</sup> Not surprisingly, in addition to cutaneous involvement, patients with epidermotropic MZL have a risk of splenic and bone marrow involvement.<sup>7,8</sup>

Because of its rarity, literature describing the management of epidermotropic MZL is based largely on case reports and small series. Without treatment, the disease has a relatively indolent course, with survival outcomes similar to that of early-stage MF. Based on his tumor's expression of CD20, our patient received 4 weekly infusions of rituximab, which resulted in a prompt, near-complete clinical response. Clinical improvement of epidermotropic MZL after treatment with rituximab has been previously reported,<sup>8</sup> and the observed benefit may relate to its ability to deplete B cells expressing the CD20 antigen. Considering its selectivity for B cells, in cases of generalized cutaneous or visceral disease, rituximab may represent a rational initial approach for managing epidermotropic MZL, although additional studies using larger cohorts of patients are needed to validate this recommendation.

Epidermotropic MZL represents a distinctive nosologic B-cell lymphoma that should be considered a diagnostic possibility in older men who present with an unexplained papulosquamous eruption resembling pityriasis rosea. The neoplastic

cells show tropism for the skin, spleen, and bone marrow, likely reflecting the critical dependence of these cells for a preferred microenvironment. It may be that the sustained growth and proliferation by specific cytokines and receptor ligand interactions expressed exclusively within certain organs may also account for its indolent clinical course.<sup>6</sup> Based on our experience and that of others,<sup>8</sup> rituximab may represent a rational choice for treating generalized epidermotropic MZL.

#### REFERENCES

1. Piepkorn M, Tigelaar RE. The intracutaneous growth of murine lymphomas: epidermal invasion is characteristic of multiple tumor phenotypes. *J Invest Dermatol.* 1984;83(4):281-285.
2. Wong HK, Mishra A, Hake T, Porcu P. Evolving insights in the pathogenesis and therapy of cutaneous T-cell lymphoma (mycosis fungoides and Sezary syndrome). *Br J Haematol.* 2011;155(2):150-166.
3. Magro CM, Momtahan S, Lee BA, Swanson DL, Pavlovic MD. Epidermotropic B-cell lymphoma: a unique subset of CXCR3-positive marginal zone lymphoma. *Am J Dermatopathol.* 2016;38(2):105-112.
4. Tensen CP, Flier J, Van Der Raaij-Helmer EM, et al. Human IP-9: A keratinocyte-derived high affinity CXC-chemokine ligand for the IP-10/Mig receptor (CXCR3). *J Invest Dermatol.* 1999;112(5):716-722.
5. Suefuji H, Ohshima K, Karube K, et al. CXCR3-positive B cells found at elevated frequency in the peripheral blood of patients with MALT lymphoma are attracted by MIG and belong to the lymphoma clone. *Int J Cancer.* 2005;114(6):896-901.
6. Ohshima K, Suefuji H, Karube K, et al. Expression of chemokine receptor CXCR3 and its ligand, mig, in gastric and thyroid marginal zone lymphomas. Possible migration and autocrine mechanism. *Leuk Lymphoma.* 2003;44(2):329-336.
7. Baykal C, Erdem S, Kılıç S, Nalçacı M, Büyükbabani N. Epidermotropic skin involvement of splenic marginal zone B-cell lymphoma: a diagnostic challenge. *J Cutan Pathol.* 2017;44(3):312-314.
8. Gómez-de la Fuente E, Villalón LB, Calzado-Villarreal L, Pinedo-Moraleda F, López-Estebananz JL. [Splenic marginal zone B-cell lymphoma with epidermotropic skin involvement]. *Actas Dermosifiliogr.* 2012;103(5):427-431.