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Cutaneous B-cell pseudolymphoma treated with imiquimod

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To the Editor,

Cutaneous pseudolymphoma is a type of lymphocytic infiltrate with histopathological and/or clinical features resembling those of lymphoma (1). Cutaneous pseudolymphoma can be classified as B-cell (Spiegler–Fendt), T-cell (Jessner–Kanof) or mixed type. Some authors consider Jessner–Kanof T-cell pseudolymphoma a variant of cutaneous lupus erythematosus (CLE) tumidus (2). Pseudolymphoma type B may represent the cutaneous manifestation of the second stage of Lyme disease (3). We describe a patient with cutaneous B-cell pseudolymphoma (CBPL) that responded well to imiquimod therapy.

A 70-year-old man presented with a 6-month history of itchy infiltrating plaque between the second and third toe of the left foot (Fig. 1a). He denied a history of insect bites or exposure to any medication. His medical history was unremarkable. Laboratory tests were within normal limits, including a negative result for *Borrelia* antibodies. Histopathological examination revealed dermal lymphoid infiltration, deeply burdened by squeezing artifacts, forming lymphoid follicles and rich in eosinophils. The overlying epidermis displayed mild orthohyperkeratosis, psoriasiform hyperplasia, and spongiosis (Figs. 2a, 2b). Immunohistochemical examination revealed that the lymphoid follicles consisted of CD20-positive B cells, with retained $CD21^{+}$ follicular dendritic cell meshwork and $Bcl\text{-}6^{+}$ reactive germinal centers, with polarized proliferative activity, as demonstrated by Ki-67 (Figs. 2c–f). Clinical, histopathological, and immunohistochemical findings confirmed the diagnosis of CBPL. Topical steroids, intralesional triamcinolone, and topical tacrolimus were employed without success. The patient declined cryotherapy and surgical intervention. Imiquimod 5% cream applied three times per week resulted in complete resolution of the lesion after 3 months (Fig. 1b). No recurrence was observed after 1 year of follow-up.

Most CBPL cases are idiopathic, but they may develop as a response to contact dermatitis, arthropod reactions, tattoo dyes, vaccinations, drugs, or bacterial infections. Reported culprits include cytotoxins, anticonvulsants, antipsychotics, antihypertensives, antibiotics, and immunological therapies (4). Despite the absence of a history of insect or arthropod bites and negative Borrelia antibodies, the presence of eosinophil-rich lymphocytic infiltrates in the pathological results increased the likelihood of B-cell pseudolymphoma following arthropod or insect bites in our patient.

There is a lack of standardized treatment for CBPL, but generally accepted options include observation, antibiotics, topical, intralesional, and systemic corticosteroids, cryosurgery, photochemotherapy, local radiation therapy, and surgical excision (5). In our patient, imiquimod was administered with occlusion for enhanced penetration, three times a week for 3 months. Although Baumgartner-Nielsen and Lorenzen (6) reported the regression of pseudolymphoma lesions with imiquimod using a regimen of 5 days per week for 6 weeks, we decided to change the schedule of the treatment to 3 days per week over a period of 3 months to minimize the risk of irritation. The lesion disappeared at the end of the 3 months, and no relapse was observed during the follow-up period.

Imiquimod is an immunomodulator that activates toll-like receptor 7, thereby increasing the levels of proinflammatory T-helper 1 cytokines, which activate cytotoxic T lymphocytes and natural killer cells (7). It stimulates the recruitment of dendritic cells and the production of interleukin-1, interleukin-6, tumor necrosis factor, and interferon-alpha. Imiquimod has been successfully used for the management of cutaneous B-cell lymphomas refractory to conventional treatments (8). We believe that the regression of the pseudolymphoma lesion in our patient is due to the intensity of the inflammatory reaction induced by imiquimod.

This case highlights the potential utility of topical imiquimod for the management of recalcitrant CBPL. Further studies are warranted to elucidate its role in treatment, mechanism of action in such patients, and the optimal dosing regimens.

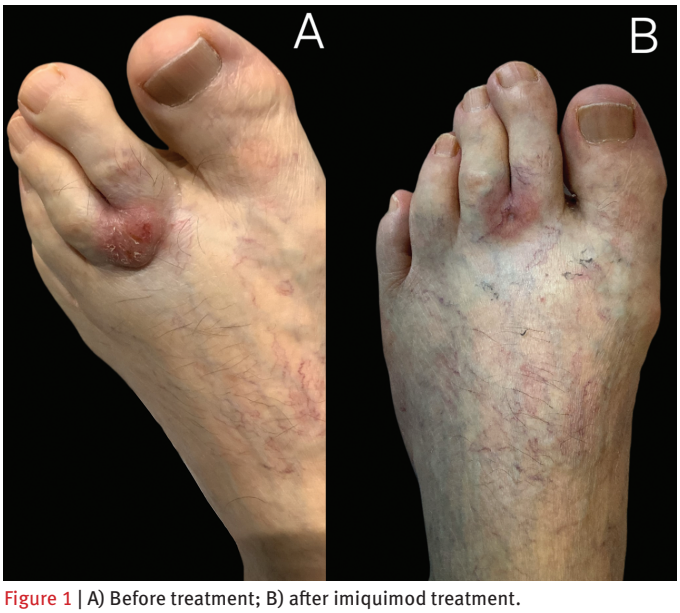

Figure 1 | A) Before treatment; B) after imiquimod treatment.

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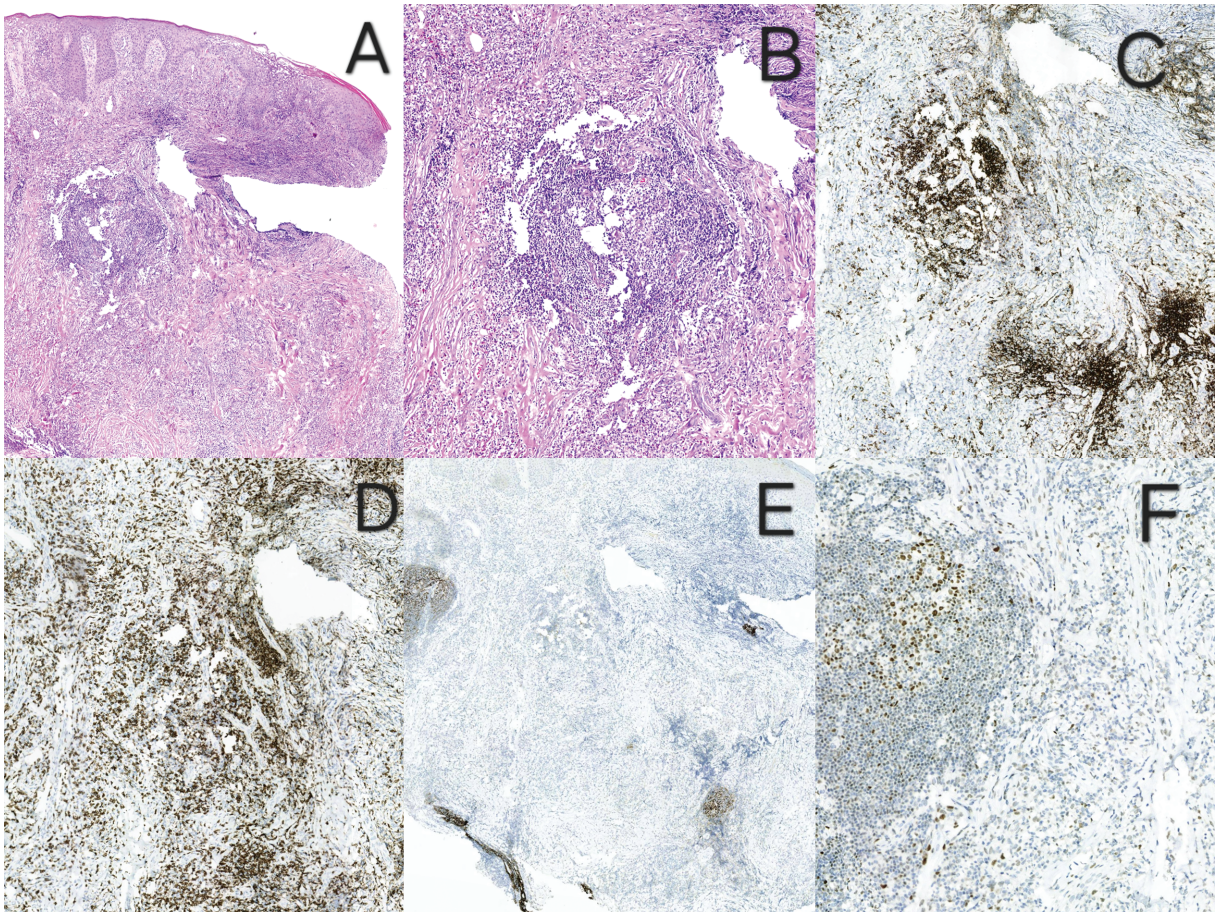

Figure 2 | A,B) A dense infiltration rich in eosinophils surrounding blood vessels throughout the entire dermis (hematoxylin&eosin; ×20, ×100); C) most of the cells in lymphoid infiltration stained with CD20, the B-cell marker (×40); D) T lymphoid cells between the B lymphoid cells, highlighted by CD3 (×40); E) CD21 staining reveals a dendritic network within lymphoid follicles (×20); F) Ki-67 showed high proliferative activity in reactive lymph nodes (×40).

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