

A case of lupus erythematosus profundus unresponsive to hydroxychloroquine but successfully treated with belimumab

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Sir,

A 42-year-old female was diagnosed with systemic lupus erythematosus (SLE) based on the findings of malar rash, chilblain lupus in the digits, Raynaud phenomenon, joint pain in the extremities, positive serum anti-nuclear antibody (1:320, homogeneous and speckled), anti-Sm antibody, and hypocomplementemia, at the age of 16 years. She was under follow-up with oral prednisolone (10 mg/day) at our hospital. She presented to our department, complaining of tenderness of the scalp, which began one year previously during the course of prednisolone tapering. Physical examination revealed painful, indurated plaques and subcutaneous nodules in the postauricular and occipital regions with hair loss (Fig. 1). A biopsy revealed lobular panniculitis with focal dermal infiltration of inflammatory cells (Fig. 2a). Higher magnification revealed fat cell degeneration, lipogranuloma with foam cells, lymphohistiocytic and neutrophil infiltration in the subcutis, hyaline fat degeneration, and fibrosis of the subcutaneous tissues (Fig. 2b). Direct immunofluorescence examination showed linear deposition of IgM in the epidermal basement membrane (Fig. 2c). Immunohistochemistry revealed that mononuclear cells were positive for CD3, CD4, CD8, CD20, CD27, and CD79a (Figs. 3a – 3d). The addition of dapsone (75 mg/day), methotrexate, and hydroxychloroquine (HCQ) (200 mg/400 mg on alternate days) resulted in little effect. In the second biopsy, which was taken twelve months after the initial biopsy, CD3-positive cells were markedly reduced in the dermis but still observed in the subcutaneous tissues, whereas CD20-positive cells were unchanged in the

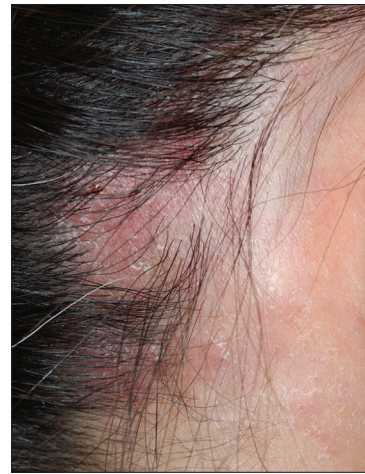


Figure 1: Tender subcutaneous nodules with superficial scaly erythema on the right postauricular area.

dermis (Figs. 3e and 3f). Belimumab (200 mg) was then subcutaneously administered every week, and six months later, the induration and pain disappeared, and her alopecia recovered.

B-cells have been implicated in the pathogenesis of SLE due to production of autoantibodies and cytokines [1,2]. B-cells are reported to infiltrate the lesional skin of discoid LE [3,4], and high expression of B-cell activating factor (BAFF) is observed in cutaneous LE (CLE), including LE profundus (LEP). Interferon- α (IFN- α) is a key cytokine in the pathogenesis of SLE, and has multiple effects, one of which is the upregulation of BAFF [5]. Recent studies have shown that patients with chronic CLE share B-cell abnormalities and expansion of effector B-cell subsets, suggesting that chronic CLE may benefit from B-cell

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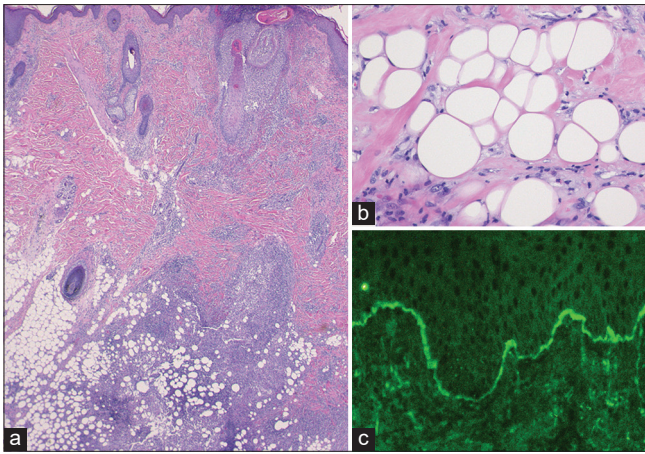


Figure 2: a) Histopathological features showing lobular panniculitis with focal dermal infiltration of mononuclear cells. b) Higher magnification showing fat cell degeneration and sclerotic stroma. c) DIF showing IgM deposition in the basement membrane.

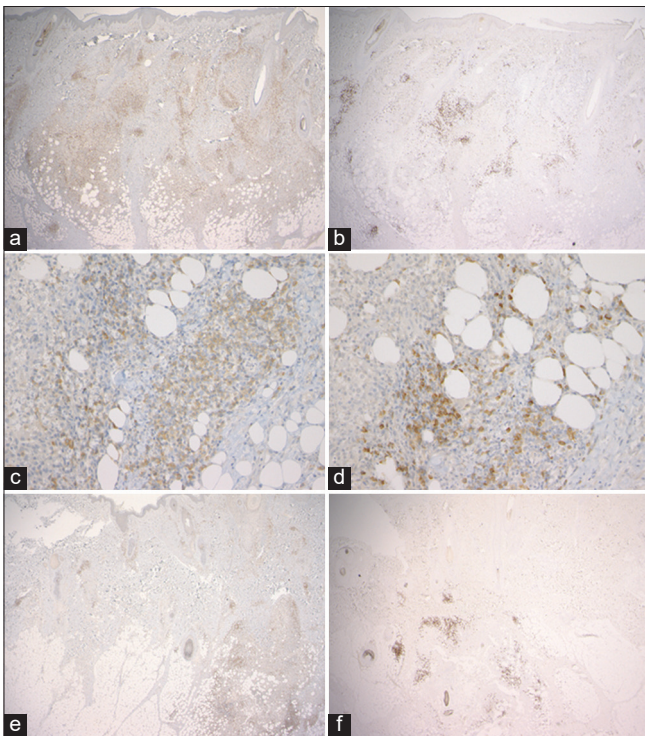


Figure 3: Immunohistochemistry showing positive expression of a) CD3, b) CD20, c) CD27, d) and CD79a. Expression of e) CD3 and f) CD20 in the scalp lesion of the second biopsy (original magnification: b×20, c×400, d×200, e×20, f×20, g×200, h×200, i×20, j×20).

targeting therapies [6]. In the present case, CD20-, CD27 (memory B-cells)-, and CD79a-positive B-cells were observed in the subcutis, suggesting the role of B-cells in LEP.

Belimumab is a human monoclonal antibody that specifically binds to soluble B-lymphocyte stimulator

(BLyS), and has been used for SLE. Belimumab showed significant improvements in maculopapular eruption, alopecia, and DLE in patients with SLE [7]; however, reports on the clinical response of CLE to belimumab are scarce at present. LEP is sometimes resistant to various therapies, and the response rate of LEP to HCQ is lower among CLE subtypes. Our patient with SLE suffered from tenderness and alopecia, which were unresponsive to previous therapies but successfully treated with belimumab. Our case may suggest that B-cells play an important role in the pathogenesis of LEP, and belimumab is a promising new therapy for refractory LEP.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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