

A rare association of bullous pemphigoid with mycosis fungoides and Sézary syndrome



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INTRODUCTION

Bullous pemphigoid is a chronic autoimmune mucocutaneous subepidermal blistering disease associated with various autoimmune and neurologic conditions as well as certain medications. Although found not to be associated with overall malignancy, it may be associated with hematologic malignancies.¹ Specifically, bullous pemphigoid has rarely been observed with cutaneous T-cell lymphoma or mycosis fungoides.²⁻⁴ Three reports describe the association of bullous pemphigoid with cutaneous T-cell lymphoma and mycosis fungoides, in which blistering lesions of bullous pemphigoid manifested after ultraviolet phototherapy was initiated.²⁻⁴ To date, no cases of bullous pemphigoid with previously untreated mycosis fungoides with Sézary syndrome have been reported; here we describe the first such case to our knowledge.

CASE REPORT

A 66-year-old man from the Caribbean islands who had a history of hypertension controlled with nifedipine and mycosis fungoides stage IVa (T4NXM0B2) presented to our dermatology clinic with erythroderma (involving >80% of his body surface area), pruritus, and tense blistering. He described intermittent episodes of erythema and scaling that began approximately a year before the diagnosis of mycosis fungoides, which was rendered a few months before he presented to us. At presentation, he had not yet initiated therapy, and this was the first time he endorsed blistering since his diagnosis of mycosis fungoides. The examination result was notable for desquamating erythroderma

involving more than 80% of the body surface area; multiple tense blisters filled with clear fluid on the right thigh and the right side of the face, scalp, and abdomen, without oral involvement; hemorrhagic crusting of the trunk and extremities; and intense pruritus (Fig 1). His only medication on presentation was nifedipine for hypertension, which he had been receiving for 1 year.

Skin biopsies showed pauci-inflammatory subepidermal split with basket-weave stratum corneum, occasional dyskeratinocytes in the epidermis, mild to moderate superficial perivascular and interstitial lymphocytic infiltrate, and scattered melanophages within the dermis (Figs 2 and 3). Immunohistochemistry further revealed a mixture of T cells (CD3⁺, CD4⁺, and CD8⁺) and B cells (CD20⁺) with a normal ratio, and retained CD7, consistent with a reactive process. Periodic acid-Schiff special stain result was negative for fungal organisms. Direct immunofluorescence with salt-split thickness assay found C3 deposition in both the roof and the floor, fibrinogen deposition on the floor, and lack of IgG, IgA, and immunoglobulin M, consistent with the diagnosis of bullous pemphigoid. Laboratory results indicated presence of BP180 antibody, a significantly elevated lactate dehydrogenase level (818 U/L), elevated white blood cell count (27,000 μ l), elevated CD4 count (10,073 cells/mcl), CD4:CD8 ratio greater than 20 (80), and Sézary cell count of 38%. Results for blood cultures, hepatitis panel, HIV, human T-lymphotropic virus type I, and BP230 antibody were negative. Peripheral blood flow cytometry revealed abnormal T-cell population; CD3⁺, CD4⁺, CD2⁺, and CD5⁺; T-cell receptor γ

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Fig 1. Bullous pemphigoid in a patient with mycosis fungoides and Sézary syndrome. **A**, Clinical photographs of the right side of the abdomen, depicting scaly erythroderma with extensive bullous involvement, as well as areas of patchy hypopigmentation. **B**, Clinical photographs of the right leg, depicting scaly erythroderma with extensive bullous involvement, as well as areas of patchy hypopigmentation.

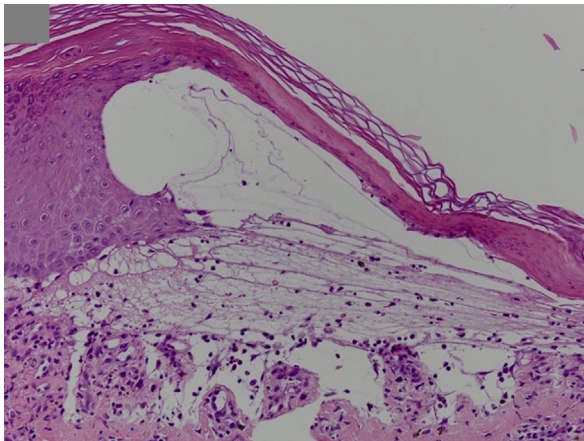


Fig 2. Bullous pemphigoid in a patient with mycosis fungoides and Sézary syndrome, showing a skin punch biopsy of the right side of the abdomen. A pauci-inflammatory subepidermal split with eosinophils within a bulla, basket-weave stratum corneum, occasional dyskeratinocytes in the epidermis, mild to moderate superficial perivascular and interstitial lymphocytic infiltrate, and scattered melanophages within the dermis. (Hematoxylin-eosin stain; original magnification: $\times 10$.)

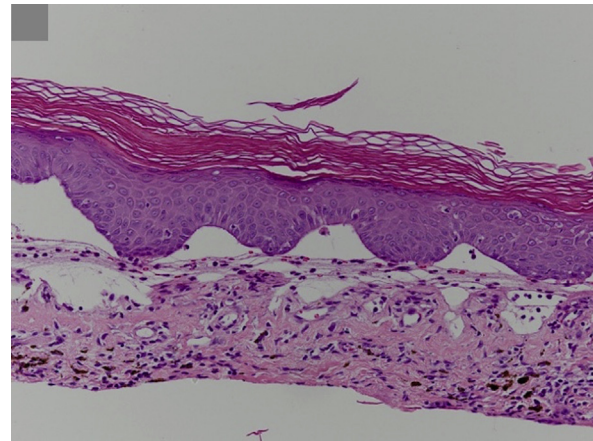


Fig 3. Bullous pemphigoid in a patient with mycosis fungoides and Sézary syndrome, showing a skin punch biopsy of the right leg. A pauci-inflammatory subepidermal split with eosinophils within a bulla, basket-weave stratum corneum, occasional dyskeratinocytes in the epidermis, mild to moderate superficial perivascular and interstitial lymphocytic infiltrate, and scattered melanophages within the dermis. (Hematoxylin-eosin stain; original magnification: $\times 10$.)

clonal gene rearrangement; and aberrant loss of CD7 expression, as well as CD56⁻. Flow cytometry from bone marrow biopsy found an abnormal T-cell population, comprising 30% of all cells analyzed,

with CD2⁺, CD3⁺, CD4⁺, CD5⁺, CD30⁺, CD8⁻, and aberrant loss of CD7. In the setting of negative results for human T-lymphotropic virus type I, these findings were consistent with Sézary syndrome.

Computed tomography of the chest, abdomen, and pelvis revealed diffuse enlarged lymphadenopathy, including the axillary, iliac, and inguinal regions.

The patient received a diagnosis of bullous pemphigoid and Sézary syndrome. Treatment was started with topical (triamcinolone 0.1% ointment to the body and hydrocortisone 2.5% ointment to the face twice daily) systemic high-potency corticosteroids (intravenous methylprednisolone 40 mg 3 times per day, tapered to 20 mg), oral methotrexate 20 mg weekly, and extracorporeal electrophoresis. He was discharged after a 10-day hospital stay, undergoing a 1-month prednisone taper starting at 20 mg and a weekly 20-mg dose of methotrexate. Two weeks after discharge, he was free of any bullae and his erythroderma and desquamation had improved significantly. He continued receiving extracorporeal electrophoresis, with consideration given to initiate brentuximab vedotin, given CD30⁺ lymphoma cells.

DISCUSSION

Although pemphigoid-associated malignancy is becoming increasingly recognized, only a few reports have noted concomitant bullous pemphigoid with cutaneous T-cell lymphoma, the majority of which are associated with ultraviolet phototherapy,²⁻⁴ and only 1 case with peripheral blood involvement, although that patient had been previously treated with psoralen ultraviolet A before disease progression and development of bullous pemphigoid.⁴ Korekawa et al⁵ reported the first case of bullous pemphigoid associated with mycosis fungoides. To our knowledge, our patient represents the first case of untreated mycosis fungoides with Sézary syndrome associated with bullous pemphigoid. However, the patient was also receiving the antihypertensive medication nifedipine, which had been started within the last year. It is unclear whether the medication was initiated

before the development of cutaneous blisters, although the likelihood that nifedipine contributed to the development of bullous pemphigoid is low. Although nifedipine has been implicated in inducing pemphigus,⁶⁻⁸ only 2 known cases of nifedipine-associated bullous pemphigoid have been identified.^{9,10} Considering that there may be an association between bullous pemphigoid and hematologic malignancies,¹ we conclude that bullous pemphigoid may be associated with Sézary syndrome and hereby report what is to our knowledge the first such case.

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