Epidermolysis Bullosa Acquisita in Association With Mantle Cell Lymphoma

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PRACTICE **POINTS**

- Epidermolysis bullosa acquisita (EBA) is an uncommon blistering disorder and few cases have been associated with malignancy.
- Diagnosis of EBA is challenging and requires exclusion of other blistering diseases.

To the Editor:

A 46-year-old man presented with multiple tense bullae and denuded patches on the palms (Figure 1A) and soles (Figure 1B). The blisters first appeared 2 months prior to presentation, shortly after he was diagnosed with stage IVB mantle cell lymphoma, and waxed and waned in intensity since then. He denied antecedent trauma or friction and reported that all sites were painful. He had no family or personal history of blistering disorders.

The mantle cell lymphoma initially was treated with 4 cycles of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) chemotherapy more than 2.5 years prior to the current presentation, which resulted in partial remission, followed by R-ICE (rituximab, ifosfamide, carboplatin, etoposide) therapy as well as autologous stem cell transplantation; complete remission was achieved. His recovery was complicated by a necrotic small bowel leading to resection. Eighteen months following the second course of chemotherapy, a mass was noted on the neck; biopsy performed by an outside dermatologist revealed mantle cell lymphoma.

Punch biopsy revealed a subepidermal bulla. Six weeks later, biopsy of a newly developed hand lesion performed at our office revealed a subepidermal cleft with minimal dermal infiltrate (Figure 2). Direct immunofluorescence was negative for immunoglobulin and complement deposition.

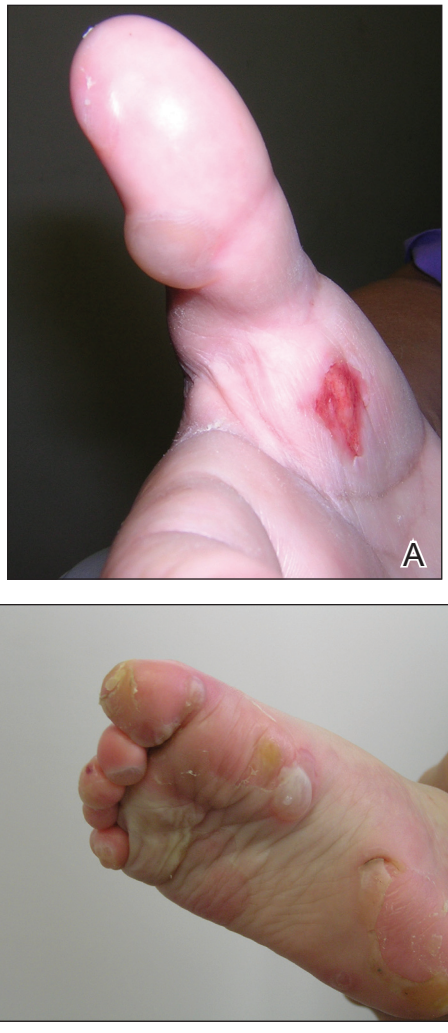

FIGURE 1. Epidermolysis bullosa acquisita bullae on the finger with an erosion of the palm (A) and multiple bullae on the sole (B).

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The authors report no conflict of interest.

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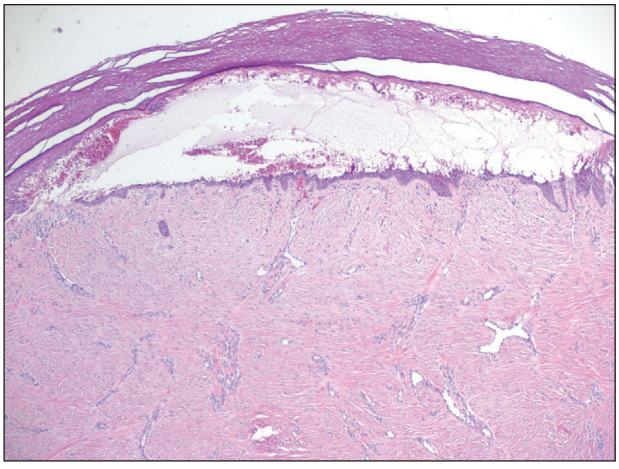

FIGURE 2. A subepidermal cleft with reepithelization of the base and minimal inflammation (H&E, original magnification ×100).

Porphyrin elevation was not detected with a 24-hour urine assay. New lesions were drained and injected with triamcinolone, which appeared to hasten healing.

Mantle cell lymphoma is a distinct lymphoproliferative disorder of B cells that represents less than 7% of non-Hodgkin lymphoma cases.[1] The tumor cells originate in the mantle zone of the lymph nodes. Most patients present with advanced disease involving lymph nodes and other organs. The disease is characterized by male predominance and an aggressive course with a median overall survival of less than 5 years.[1]

Epidermolysis bullosa acquisita is a rare blistering disease that usually develops in adulthood. It is a subepidermal disorder characterized by the appearance of fragile tense bullae. Epidermolysis bullosa acquisita can be divided into 2 subtypes: inflammatory and mechanobullous (classic EBA).[2] Inflammatory EBA presents similarly to bullous pemphigoid and other subepithelial autoimmune blistering diseases. Vesiculobullous lesions predominate on the trunk and extremities and often are accompanied by intense pruritus. The less common mechanobullous noninflammatory subtype, illustrated in our case, presents in trauma-prone areas with skin fragility and tense noninflamed vesicles and bullae that rupture leaving erosions. Associated findings may include milia and scarring. Lesions appear in areas exposed to friction and trauma such as the hands, feet, elbows, knees, and lower back. The differential diagnosis includes dystrophic epidermolysis bullosa, porphyria cutanea tarda, and pseudoporphyria. Dystrophic epidermolysis bullosa is ruled out by family history and disease onset at birth. The lesions of porphyria cutanea tarda and pseudoporphyria occur on sun-exposed areas; porphyrin levels are elevated in the former. Direct immunofluorescence of a perilesional EBA site usually reveals IgG deposition.[3] Negative direct immunofluorescence in our case could have resulted from technical error, sample location, or response to systemic immunosuppressive treatment.[4]

Epidermolysis bullosa acquisita is caused by autoantibodies against type VII collagen.[2,3] After the autoantibodies bind, a complement cascade reaction is activated, leading to deposition of C3a and C5a, which recruit leukocytes and mast cells. The anchoring fibrils in the basement membrane zones of the skin and mucosa are disrupted.[5,6] Injection of anti–type VII collagen antibodies into mice induces a blistering disease resembling EBA.[7] In a study of 14 patients with EBA, disease severity was correlated to levels of anticollagen autoantibodies measured by enzyme-linked immunosorbent assay.[8]

Epidermolysis bullosa acquisita has been linked to Crohn disease and approximately 30% of EBA cases occur in patients with this disease.[9,10] Two case reports document an association with multiple myeloma.[11,12] Treatment often proves challenging and unsatisfactory; valid controlled clinical trials are impossible given the paucity of cases. Successful therapeutic outcomes have been reported with oral prednisone,[13] colchicine,[14] cyclosporine,[15] dapsone,[16] and rituximab.[17] Our patient received 2 separate courses of rituximab as part of chemotherapy for mantle cell lymphoma without measurable improvement. He was lost to follow-up after recurrence of the lymphoma and we learned from his wife that he had died.

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