

Tense Bullae With Widespread Erosions

What's the diagnosis?



A 50-year-old black man presented with a new-onset widespread pruritic bullous eruption 7 months after being diagnosed with human immunodeficiency virus. The CD4 lymphocyte count was 421 cells/mm³ and viral load was 7818 copies/mL. Results of a viral culture were negative for herpes simplex virus. Dermatologic examination revealed numerous intact tense bullae as well as scattered erosions on the trunk and extremities. Postinflammatory hyperpigmentation was prominent, with some areas of hypopigmentation and depigmentation.

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The Diagnosis: Linear IgA Bullous Dermatitis

A biopsy specimen from an intact vesicle was obtained. Histologic findings showed a basket weave stratum corneum suggestive of an acute process. There was subepidermal separation with an inflammatory infiltrate of neutrophils (Figure 1). Direct immunofluorescence yielded a pattern of IgA deposition along the dermoepidermal junction (Figure 2). A diagnosis of linear IgA bullous dermatosis (LABD) was made. The patient was started on 100 mg daily of dapsone. The dose was subsequently increased to 175 mg twice daily, resulting in complete clearance. He became dermatologically disease free after 10 months and the dapsone was successfully tapered.

Linear IgA bullous dermatosis is an autoimmune subepidermal blistering disease with linear IgA deposits found along the basement membrane of the skin. There are 3 major categories of LABD: drug induced, systemic disorder related, and idiopathic.¹ Patients with LABD present with a pruritic vesicobullous eruption that tends to favor the trunk, proximal extremities, and acral regions of the body. Mucous membrane lesions are present in less than 50% of patients.² Linear IgA bullous dermatosis may resemble bullous pemphigoid, erythema multiforme, dermatitis herpetiformis, or toxic epidermal necrolysis. The gold standard for diagnosis is immunofluorescence staining that shows linear IgA deposition along the skin's basement membrane.¹ Prognosis for LABD is variable; there is risk for persistence and scarring.² The drug-induced form of LABD is associated with clearance with the removal of the inciting agent.¹

There are several autoimmune disorders that have been described in association with human immunodeficiency virus (HIV).³ Autoimmune bullous dermatoses, while described, are very uncommon in the setting of HIV infection. Previously reported cases include bullous pemphigoid, epidermolysis bullosa acquisita, pemphigus herpetiformis, pemphigus vegetans, pemphigus vulgaris, and cicatricial pemphigoid.⁴⁻¹² The presentation of LABD in an HIV-positive patient is extremely rare.

There are 3 proposed mechanisms by which HIV and autoimmune bullous dermatoses coexist: unregulated B-cell activation, loss of T-suppressor cell regulation, and molecular mimicry. In patients with HIV, infected macrophages increase production of IL-1 and IL-6, causing nonspecific stimulation of B cells. Further production of tumor necrosis factor and other lymphotoxins may kill CD8⁺ T-suppressor cells, which further reduces B-cell regulation and

production of nonspecific antibodies. Unregulated B-cell activation could lead to proliferation of antself-specific B cells and autoantibodies. Additionally, various autoantibodies may arise due to mimicry between HIV antigens and human proteins. Some of the antibodies produced may be cytotoxic antilymphocyte antibodies that further disrupt B-cell regulation.^{13,14}

Zandman-Goddard and Shoenfeld¹⁴ proposed a staging system of autoimmune disease and HIV with respect to CD4 count and viral load. Stage I is clinical latency of HIV, with a high CD4 count

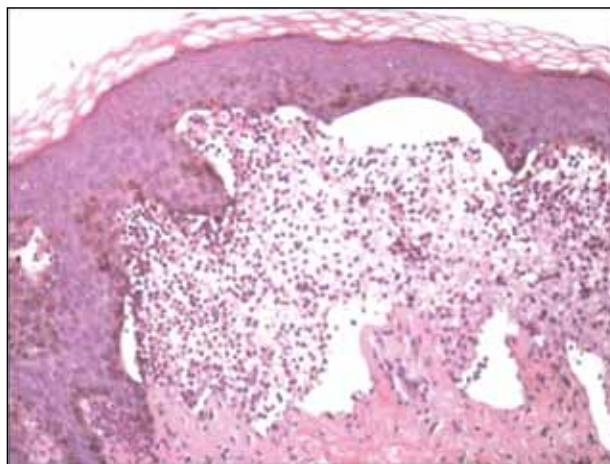


Figure 1. Subepidermal separation with an inflammatory infiltrate composed of neutrophils (H&E, original magnification $\times 20$).

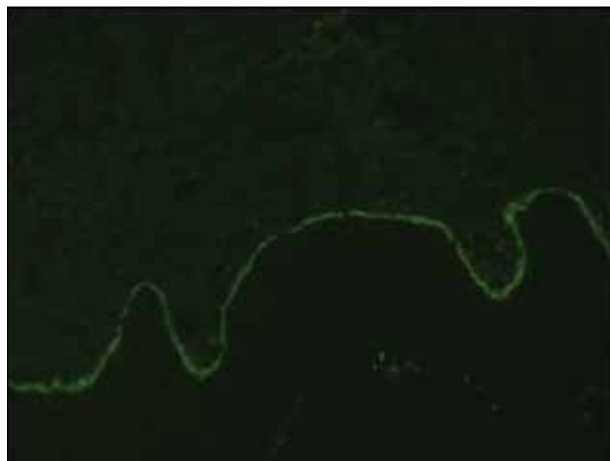


Figure 2. Direct immunofluorescence with linear deposition of IgA along the basement membrane zone (original magnification $\times 20$).

(>500 cells/mm³) and high viral load, which correlates with an acute infection of HIV and an intact immune system. Autoimmune disease can be seen in this stage. Stage II is cellular response, a quiescent period without overt manifestations of AIDS. The CD4 count is declining (200–499 cells/mm³), indicating immunosuppression, and the viral count is high. Autoimmune disease can occur and typically includes immune complex-mediated disease and vasculitis. Stage III is immune deficiency. The CD4 count is low (<200 cells/mm³), viral load is high, and AIDS develops. Autoimmune disease is not seen during this stage. Stage IV is the period of immune restoration following the advent of highly active antiretroviral therapy. There is a high CD4 count (>500 cells/mm³) and low viral load. There is a resurgence of autoimmune disease in this stage. Autoimmune disease can occur with an immune system capable of B- and T-cell interactions and a normal CD4 count. Autoimmunity is possible in stages I, II, and IV.¹⁴ Our patient developed bullous disease in stage II.

Although uncommon, autoimmune disease is possible in the setting of immune deficiency. The presence of autoimmune disease in a patient with HIV can only be seen during certain stages of infection. Knowledge of the possible scenarios of autoimmune disease can assist the clinician with monitoring status of the HIV infection or immune reconstitution.

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