Linear IgA Bullous Dermatosis Associated With Vancomycin and Disseminated Varicella-Zoster Infection

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Linear IgA bullous dermatosis (LABD) is characterized by linear deposits of IgA at the basement membrane zone. Most cases are idiopathic, but medications, infections, autoimmune disorders, and malignancies have been documented as potential inducers. We report a case where both vancomycin and varicella-zoster infection were present as triggers.

Linear IgA bullous dermatosis (LABD) is a blistering disease characterized by linear deposits of IgA in the basement membrane zone.[1,2] Although most cases are idiopathic, there have been documented reports associating LABD with malignancies, autoimmune diseases, medications, and infections.[3-13] We describe a patient on vancomycin therapy who developed LABD and a disseminated varicella-zoster infection. Vancomycin therapy and varicella-zoster infection have been described as potential inducers of LABD. However, our case is unusual because both varicella and vancomycin use were present concomitantly.

Case Report

A 92-year-old African American man with a history of dementia, hypertension, and chronic anemia was admitted to our medical center for an enterococcal urinary tract infection. He was on several medications, including antibiotics, aztreonam, hydrochlorothiazide, and levofloxacin for one week followed by vancomycin. During the third week of hospitalization, a blistering eruption was observed on his forearms, which progressed over the next 24 to 48 hours.

Physical examination revealed multiple, discrete, 2- to 6-mm tense vesicles on an erythematous base over the arms, axillae, abdomen, groin, and penile shaft. A closer inspection revealed that some of the vesicles were umbilicated (Figure 1). Coalescing urticarial erythematous plaques also were present on the upper back and shoulders. The face, mucous membranes, palms, and soles were not involved. Because of the presence of both umbilicated and nonumbilicated vesicles and the observation of urticarial plaques in a patient on vancomycin, diagnoses of both varicella-zoster infection and drug-induced LABD were suspected.

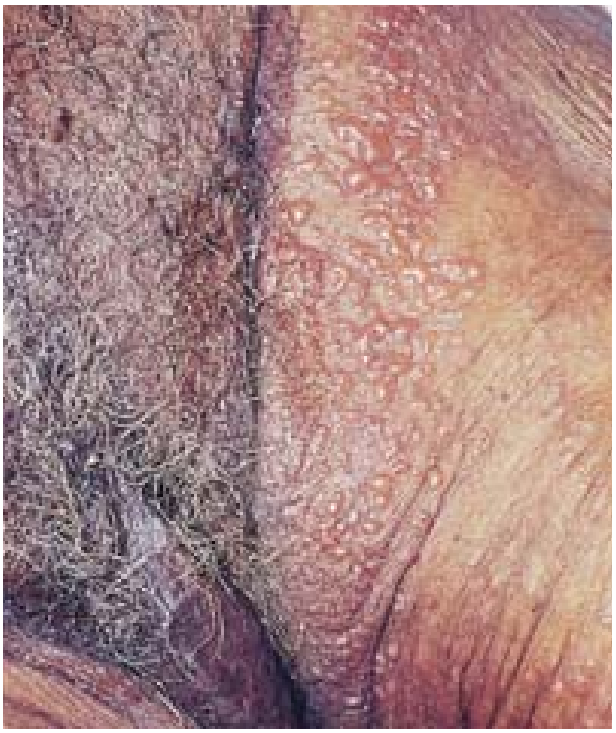

Figure 1. Multiple vesicles involving the groin, some umbilicated.

A complete blood count revealed a white blood cell count of $9.7\times10^3/cm^3$, with 5.8% eosinophils, a

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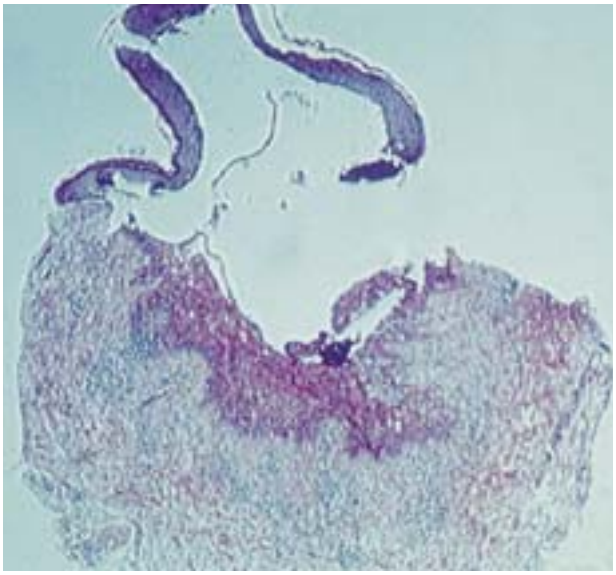

Figure 2. Subepidermal bulla with underlying mixed inflammatory infiltrate (H&E, original magnification ×4).

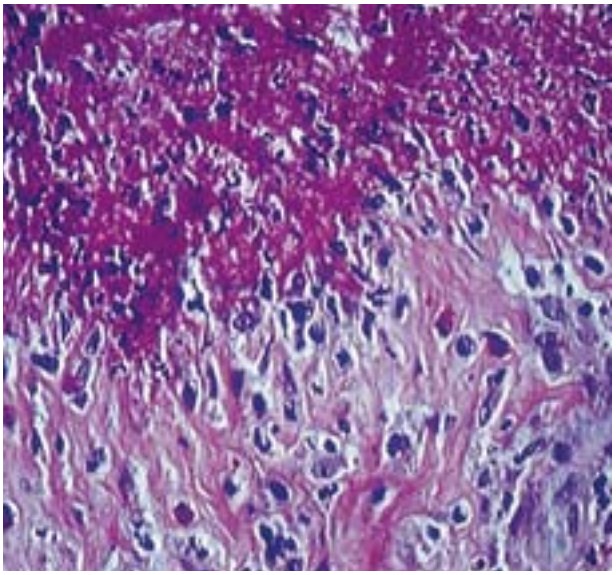

Figure 3. Close-up shows numerous neutrophils and some eosinophils (H&E, original magnification ×40).

hemoglobin level of 11.8 g/dL, and a hematocrit level of 35.4%. The serum chemistry evaluation was within normal limits except for a serum urea nitrogen level of 51 mg/dL and a creatinine level of 2.2 mg/dL.

A skin biopsy taken from an intact nonumbilicated blister showed a subepidermal vesicle, with mainly neutrophils and eosinophils inside the vesicle and in the underlying dermis (Figures 2 and 3). There was no evidence of viral infection in this specimen. Direct immunofluorescence of intact perilesional skin revealed linear deposits of IgA in the basement membrane zone (Figure 4). A culture of the base of an umbilicated blister was positive for varicella-zoster virus.

Vancomycin was discontinued on the day the eruption was discovered. Aztreonam and levofloxacin had been stopped 2 weeks earlier. Only hydrochlorothiazide was maintained. It was not known if our patient had prior exposure to vancomycin. No active therapy was administered, other than intravenous acyclovir for 10 days, and the eruption cleared within 3 weeks of cessation of vancomycin. However, the patient died several weeks later secondary to urosepsis.

Comment

Although LABD has unique immunopathology, the variable clinical presentation and histologic findings may resemble dermatitis herpetiformis and bullous pemphigoid.[2,14]

Vancomycin therapy is the most common cause of drug-induced LABD.[6] Other drugs implicated include amiodarone, captopril, cefamandole, diclofenac, lithium, and phenytoin.[7-10] Clinically, drug-induced LABD differs from the idiopathic type by an absence of mucosal involvement, spontaneous remission upon removal of the offending agent, and disappearance of immune deposits from the basement membrane zone after clinical resolution.[7] Our patient typically lacked mucosal disease, and the lesions resolved within 3 weeks of discontinuation of vancomycin without any active therapy. Aztreonam and levofloxacin were unlikely culprits because these drugs were discontinued 48 hours after initiation. Hydrochlorothiazide also was eliminated as a potential cause because the eruption cleared without its discontinuation.

Several cases have been published reporting an association between LABD and varicella-zoster infection.[11,12] Thune et al[11] reported the case of a 5-year-old boy with linear IgA dermatosis that developed several weeks after varicella-zoster infection. Blickenstaff et al[12] described an older adult man with disseminated varicella-zoster infection who was found to have linear IgA deposition when a lesion was biopsied. Similarly in our patient, histologic and immunopathologic findings were characteristic of LABD, while viral cultures were positive for varicella-zoster. LABD has been associated with other infections, including chronic active hepatitis, upper respiratory tract, tetanus, and gynecologic infections.[5,13] These cases, as well as the case presented, strongly suggest a connection between LABD and certain infections. Additionally, specific medications and infections can induce immunologic reactions that lead to the development of LABD in predisposed individuals.

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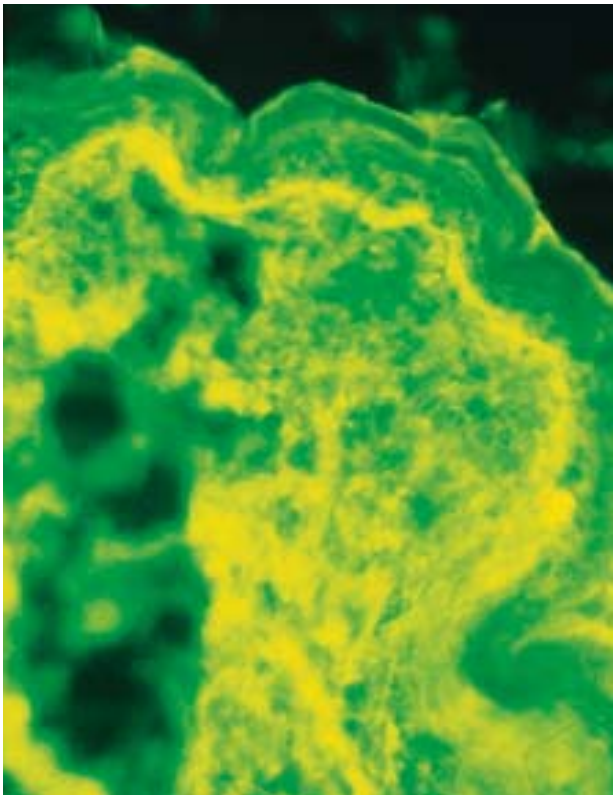

Figure 4. Direct immunofluorescence reveals linear deposits of IgA (original magnification ×10).

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It is important when faced with an acute vesicular eruption to realize that more than one factor may be involved. The diagnosis of a combination of varicella-zoster infection and drug-induced LABD should be considered so that both early antiviral therapy and prompt discontinuation of medication can be instituted.

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