

Vancomycin-Induced Linear IgA Bullous Dermatitis: Morphology Is a Key to Diagnosis

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Vancomycin-induced linear IgA bullous dermatitis (LABD) previously has been described; however, past reports have suggested that the clinical presentation is nonspecific. We present a case of vancomycin-induced LABD with a suggestive clinical presentation; specifically, groups of annularly arranged vesicles. We propose that this clinical presentation strongly suggests drug-induced LABD and should raise a clinician's suspicion of vancomycin as the offending agent. This awareness may guide the antibiotic management of the patient while the clinician awaits histopathologic correlation.

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Case Report

A 46-year-old man with no relevant medical history was admitted for aspiration pneumonia secondary to an alcohol withdrawal seizure. The patient's sputum grew numerous organisms including methicillin-resistant *Staphylococcus aureus*. During the course of hospitalization, the patient was treated with numerous antibiotics including vancomycin. Twelve days into the course of vancomycin, the patient developed a diffuse erythematous vesicular rash, and the dermatology service was consulted. On examination, the patient had a diffuse macular and papular erythematous rash with tense vesicles and bullae, as well as oral bullae and erosions. It was noted that the vesicles were annularly

arranged in a "string of pearls" on a mildly erythematous base (Figure 1). Furthermore, several of the bullae were sausage shaped, suggestive of the coalescence of annularly arranged vesicles. The patient reported the eruption to be extremely pruritic. Given the morphology of the lesions, the consulting team highly suspected a diagnosis of vancomycin-induced linear IgA bullous dermatitis (LABD). Based on this clinical suspicion, vancomycin was discontinued while all other antibiotics were continued. A biopsy for standard histopathology and immunofluorescence were performed. Results of the biopsy, which were available after 48 hours, confirmed the diagnosis of vancomycin-induced LABD (Figures 2 and 3), by which time the eruption was already improving. The patient made a full recovery.

Comment

The first case of vancomycin-induced LABD was reported by Baden et al¹ in 1988 and was specifically noted to have a "nondiagnostic appearance" despite its somewhat unique "cluster of jewels" annular arrangement of bullae. Annularly arranged tense bullae have been reported in other cases of vancomycin-induced LABD² and in other drug-induced linear IgA disease.^{3,4} There have been numerous other reports in the literature of linear IgA disease secondary to vancomycin and to other drugs including lithium carbonate,³ amiodarone,⁴ captopril,⁵ diclofenac,⁶ and phenytoin.⁷ When this reaction pattern is seen in a clinical setting that suggests a drug eruption, vancomycin continues to be the most common cause of all reported cases.

The clinical presentation of vancomycin-induced LABD previously has been described as highly variable and nondiagnostic.^{8,9} Various presentations reported in the literature include tense bullae with straw-colored fluid contents on a variably erythematous base, targetoid lesions,⁵ mucous membrane involvement, and pruritus as common

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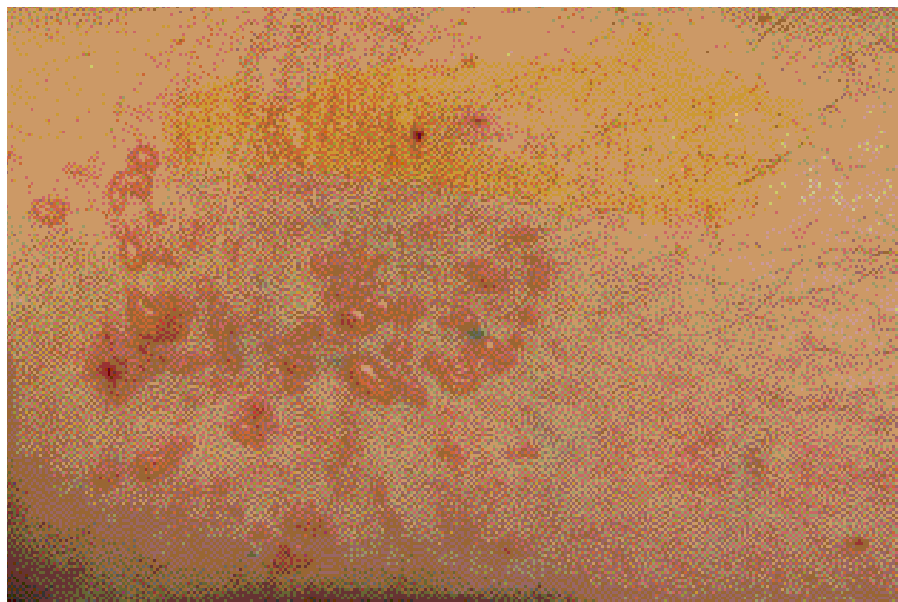


Figure 1. Annularly arranged vesicles on the patient's arm forming a "string of pearls."

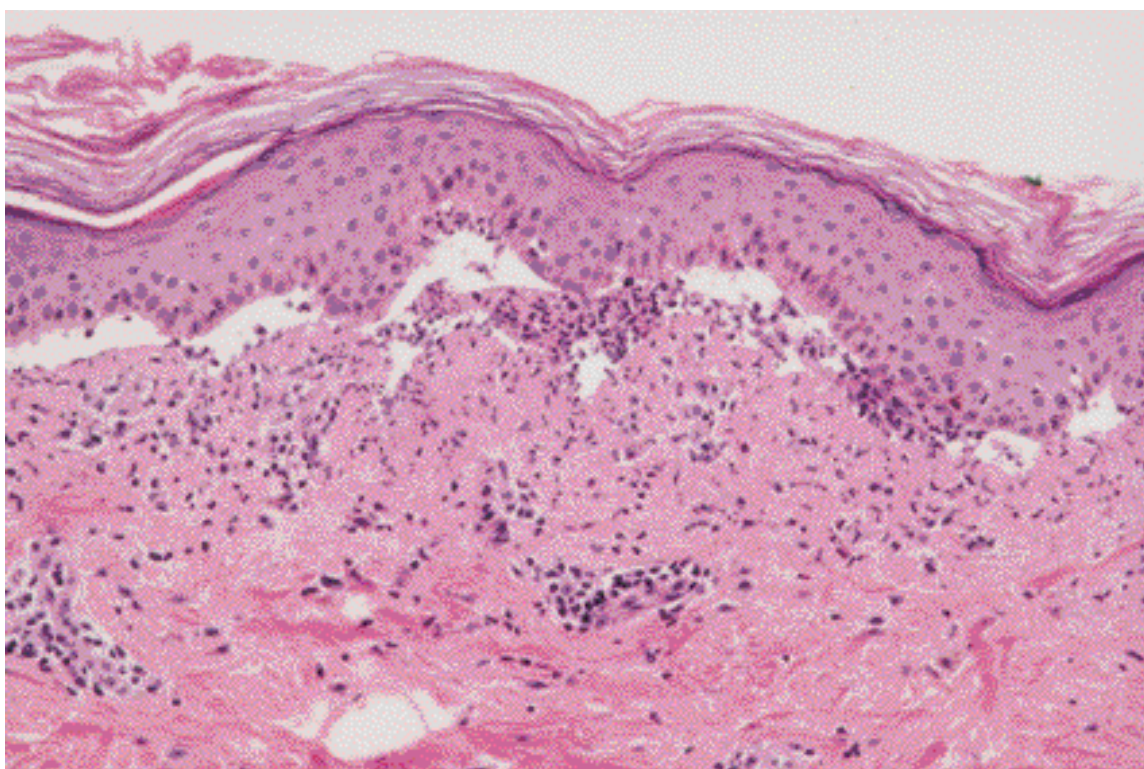


Figure 2. Subepidermal clefting with abundant neutrophils at the dermal-epidermal junction (H&E, original magnification $\times 40$).

symptoms. Lesions tend to appear anywhere from 24 hours to 15 days after the first dose of the offending agent.¹⁰ The clinical differential typically includes bullous pemphigoid, erythema multiforme major,¹¹ dermatitis herpetiformis, and chronic bullous disease of childhood.

We argue here that the acute onset of annularly arranged bullae resembling dermatitis herpetiformis or chronic bullous disease of childhood in a patient taking multiple antibiotics is highly suggestive of linear IgA disease. In cases such as this, vancomycin should be highly suspected as the cause,

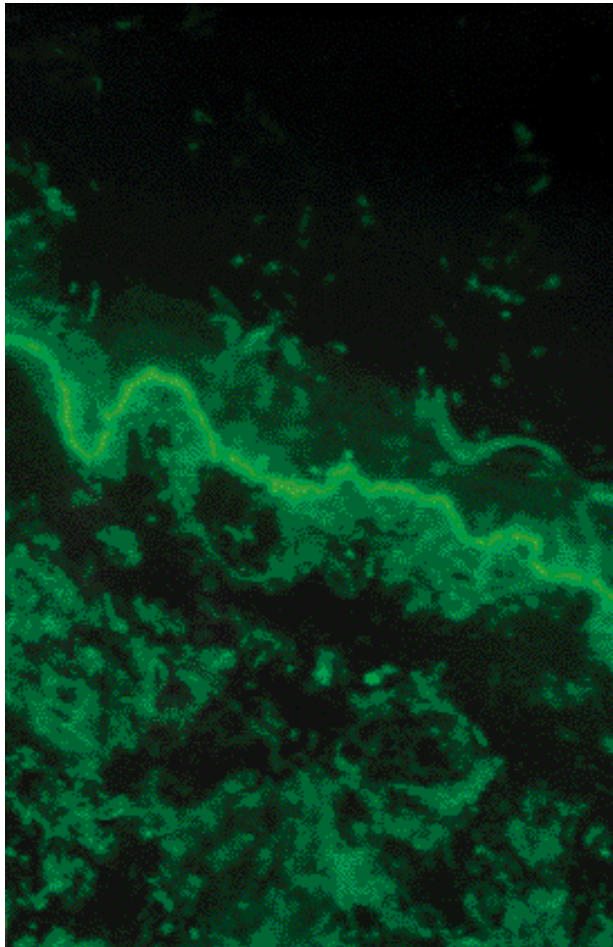


Figure 3. Linear IgA along the basement membrane (immunofluorescence, original magnification $\times 40$).

though vancomycin commonly is not implicated in other cutaneous hypersensitivity drug reactions.¹² Pending the results of a skin biopsy, suspicion of vancomycin over other agents could benefit severely ill or septic patients in need of broad-spectrum antibiotics.

A definitive diagnosis of linear IgA disease is made by the performance of a biopsy. The classic histopathology specimens of vancomycin-induced LABD show an aggregation of neutrophils at the dermal-epidermal junction with subepidermal cleft formation. Results of immunofluorescence show linear IgA along the basement membrane zone. Recent investigations have revealed specific antigens in vancomycin-induced LABD including IgA antibodies to LAD285 and both IgA and IgG antibodies to BP180.¹³ When these histologic findings are present in a patient with a clinical presentation suggestive of LABD, the diagnosis is made definitively. In cases such as this, vancomycin and other known causes of LABD should be suspected.

Conclusion

Past reports of vancomycin-induced LABD have suggested that the clinical presentation is variable and not necessarily similar to dermatitis herpetiformis or chronic bullous disease of childhood. Although atypical cases do occur, vancomycin-induced LABD can be strongly suspected when a patient presents with annularly arranged tense vesicles or bullae in a clinical setting suggestive of a drug eruption in a patient taking vancomycin. Pending the results of a biopsy, a clinical suspicion of vancomycin-induced LABD can guide the preliminary decision regarding which medication(s) must be discontinued.

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