

Linear IgA bullous dermatosis protracted by vancomycin-loaded bone cement



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INTRODUCTION

Linear IgA bullous dermatosis (LABD) is a sub-epidermal, vesiculobullous eruption that can be drug induced, often by vancomycin.¹ We describe a rare case of an 80-year-old woman with vancomycin-induced LABD whose disease continued to progress despite drug cessation, likely attributable to continued drug elution from vancomycin-loaded bone cement from a recent shoulder arthroplasty revision.

CASE REPORT

An 80-year-old woman, with a medical history significant for moderate chronic kidney disease (stage IIIa), hypertension, atrial fibrillation, and numerous orthopedic procedures, underwent a left total shoulder arthroplasty revision in the setting of a *Staphylococcus epidermidis* joint infection. The procedure entailed prosthesis explantation, placement of a vancomycin-loaded cement joint spacer, and intravenous vancomycin and rifampin antibiotic therapy. Two weeks after the procedure, she presented to our clinic with an abrupt onset of pruritic, burning, painful skin lesions accompanied byodynophagia, vulvar pain, and increased lacrimation. She denied experiencing intolerance to these antibiotics with prior use, recent exposure to other medications or allergens, or previous skin diseases. Physical examination found scattered tense vesiculobullae with negative Nikolsky and Asboe-Hansen signs, erosions and erythematous patches favoring the right arm (Fig 1, A) and left shoulder, and oral erosions. Because of concern for a drug hypersensitivity contributing to the patient's symptoms, all intravenous antibiotics were discontinued, and biopsy specimens were obtained from the right arm for pathologic examination.

Abbreviation used:

LABD: linear IgA bullous dermatosis

Laboratory evaluations found a negative varicella zoster virus direct fluorescent antibody stain, and a basic metabolic panel was significant for stable moderate chronic kidney disease, unchanged from baseline before vancomycin initiation. Sections from a punch biopsy of the right arm showed a dense, subepidermal infiltrate composed almost exclusively of neutrophils (Fig 1, B), and portions showed early subepidermal vesicle formation (Fig 1, C). Direct immunofluorescence displayed linear IgA deposition in the basement membrane zone, and a diagnosis of LABD was made.

Five days after the discontinuation of intravenous vancomycin, despite 4 days of systemic corticosteroid therapy (60 mg [0.6 mg/kg] prednisone daily), our patient's vesicular eruption continued to evolve. She reported intense pruritus and burning pain causing distressing insomnia. A repeat physical examination found widespread progression of disease with additional lesions on her shoulders and arms, which demonstrated the crown of jewels or string of pearls sign (Fig 1, D) classically associated with LABD. Scattered superficial erosions were appreciated on the palatine, buccal, and vulvar mucosa. Although expected to be undetectable given the time since drug cessation, serum vancomycin levels were obtained and remained elevated at 5.7 $\mu\text{g/mL}$, suggesting continued release from the joint spacer, as the drug should have cleared in roughly 2 days based on renally corrected drug elimination calculations. Treatment was escalated to 80 mg prednisone daily (0.8 mg/kg) with triamcinolone 0.1% ointment

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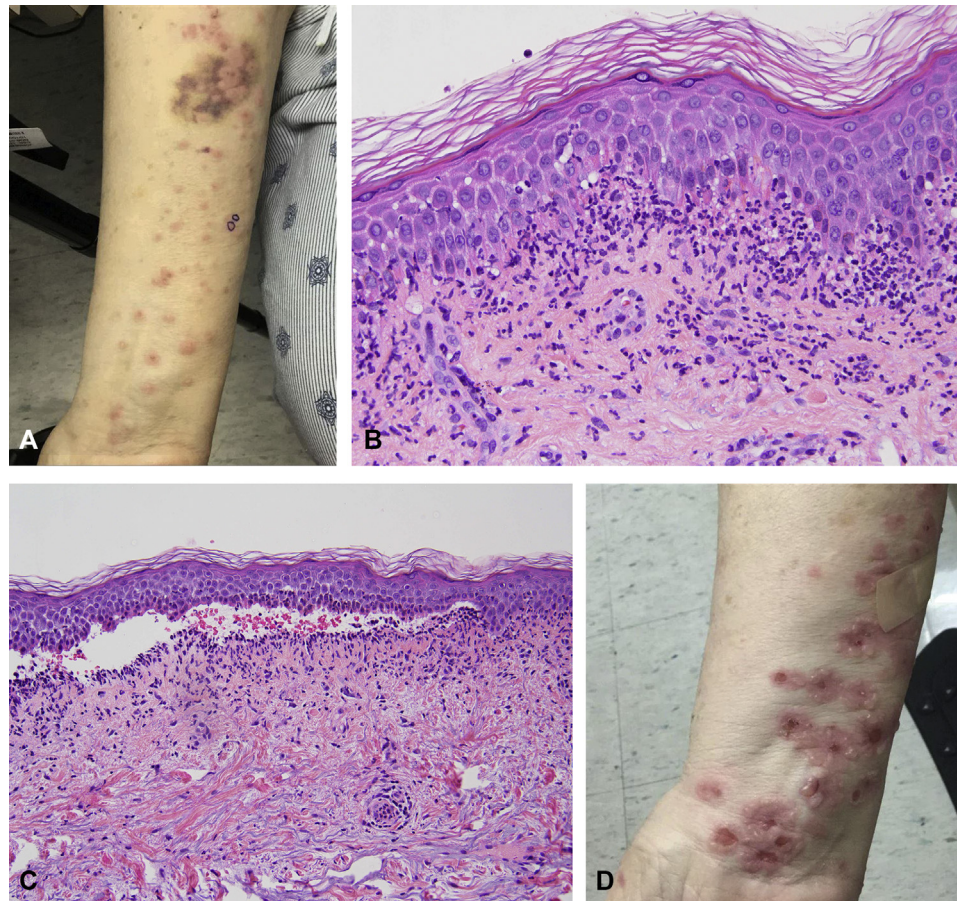


Fig 1. LABD protracted by vancomycin-loaded bone cement. **A**, Initial clinical presentation with vesicular eruption on right arm. **B**, Histopathology shows a dense subepidermal infiltrate composed almost exclusively of neutrophils. **C**, Histopathology shows early blister formation. **D**, Five days after initial presentation, with clinical progression and classic crown of jewels or string of pearls on right arm. (**B** and **C**, Hematoxylin-eosin stain; original magnifications: **B**, $\times 10$; **C**, $\times 4$.)

applied twice daily and hydroxyzine, 25 mg once daily, as needed for symptom management.

Vesicle formation ceased 10 days after intravenous vancomycin discontinuation, and systemic steroids were tapered. Two weeks after presentation, erosions were healing appropriately, and vancomycin levels were less than $3.5 \mu\text{g/mL}$. Serum vancomycin levels were undetectable at 6 weeks, and disease has since remained quiescent with cessation of steroids.

DISCUSSION

LABD is relatively rare, with an estimated incidence of 0.6 per 100,000 adults. It typically affects adults over the age of 60 with a slight female predilection. Classically, LABD presents as annular erythema with a ring of tense vesicles or bullae distributed symmetrically on the trunk and extremities; however, the morphology can vary from expanding annular plaques to tense bullae

mimicking bullous pemphigoid, and even morbilliform and epidermal necrolysis-like eruptions as rarely reported in cases of vancomycin-associated LABD.² Mucous membranes are affected in 40% of patients.³

An association between LABD and drug exposure, most commonly vancomycin, is well documented.^{1,3} Acting as a hapten, it is thought that vancomycin stimulates an immune response with exaggerated IgA production in susceptible individuals, resulting in a cutaneous eruption, on average, 8.2 days after drug initiation.³ Direct immunofluorescence of perilesional skin, the gold standard for diagnosing LABD, shows characteristic deposition of IgA in a linear distribution along the basement membrane zone with neutrophilic inflammation.¹⁻³ Drug cessation is the mainstay of treatment, with new lesion formation typically resolving 1 to 3 days after discontinuation. For recalcitrant disease, as

seen with our patient, systemic corticosteroids or dapsone may be indicated.³

One of the most commonly reported complications of reverse total shoulder replacement is infection.⁴ Treatment of a periprosthetic joint infection involves a 2-stage revision, whereby the joint is explanted and a cement spacer loaded with high-dose antibiotics, typically aminoglycosides and/or vancomycin, is incorporated until subsequent reimplantation.⁵ Through elution of antibiotics into the joint fluid, these cement spacers ensure high local antibiotic concentrations in the joint space and result in significantly reduced infection rates.⁴ Unfortunately, however, systemic absorption of these antibiotics is common. A prospective study found absorption from vancomycin-loaded cement spacers to peak within hours of placement and remain detectable (range, 1.8-14.38 $\mu\text{g/mL}$) for up to 8 weeks after placement, even in patients who did not receive simultaneous intravenous vancomycin therapy.⁵

Systemic toxicity from vancomycin-loaded cement spacers is rarely reported in the literature, with acute kidney injury being the most common adverse effect, followed by rare hepatic failure and bone marrow depression.⁶ There are few reports of vancomycin-loaded cement spacers being associated with adverse dermatologic events, including an unspecified rash and a diffuse desquamating rash after implantation of vancomycin-loaded cement.^{7,8} Other reports describe adverse dermatologic effects after exposure to vancomycin via systemic and vancomycin-loaded cement spacers simultaneously, including 2 cases of hypersensitivity syndrome/drug reaction with eosinophilia and systemic symptoms,⁹ as well as a nonspecified drug eruption after arthroplasty revision.¹⁰ To our knowledge, no associations between vancomycin-loaded bone cement and LABD have been reported in the literature.

We report an unusual case of a patient with vancomycin-induced LABD whose symptoms unexpectedly evolved despite intravenous vancomycin cessation. Continued systemic absorption of vancomycin from antibiotic-loaded bone cement, along with decreased renal clearance secondary to

moderate CKD may have contributed to the protracted course of our patient's disease. Careful consideration should be made when identifying a source for LABD and when considering the complications of antibiotic-impregnated cement spacers.

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