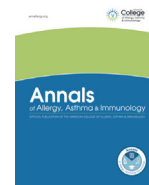




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Letter

Linear IgA bullous dermatosis: a rare manifestation of vancomycin hypersensitivity

Vancomycin is one of the most widely used antibiotics and, because of its prevalent use, several common side effects have been well described, such as “red man” syndrome, agranulocytosis, and ototoxicity. In addition, it has been associated with hypersensitivity reactions including immunoglobulin E-mediated anaphylaxis, linear immunoglobulin A (IgA) bullous dermatosis (LABD), drug reaction with eosinophilia and systemic symptoms syndrome, acute interstitial nephritis, and Stevens-Johnson syndrome and toxic epidermal necrolysis.¹ Although a few case reports have documented vancomycin as the most frequent inciting factor for LABD,^{1–4} formal studies validating the causal relation and eliminating reporting bias are lacking because it remains a relatively uncommon phenomenon.

An 88-year-old man with a medical history of hypertension, diabetes, and coronary and peripheral arterial disease underwent amputation of his second left toe and subsequently developed post-operative fever. He was empirically treated with vancomycin and piperacillin plus tazobactam. He was transitioned to meropenem because of microbiological sensitivities and eventually was discharged home on oral levofloxacin. Two weeks later, he presented with fever, hypotension, altered sensorium, and a diffuse rash. The rash consisted of multiple urticarial well-delineated plaques with superimposed clear, fluid-filled, flaccid bullae with a characteristic “crown of jewels” distribution (figurate grouping of vesicles along the urticarial plaque margin). No mucosal involvement was noted, which ruled out erythema multiforme major and Stevens-Johnson syndrome. At admission, he was resuscitated with fluids. Blood and urine cultures were obtained to rule out an infectious etiology. Because the fever resolved and cultures remained negative, an infectious cause was deemed unlikely. Clinical appearance of rash was characteristic of LABD, which is associated with vancomycin use. He was empirically treated with topical triamcinolone and 40 mg/d of oral prednisone, which was tapered over 2 weeks. The diagnosis was confirmed by skin biopsies demonstrating strong linear deposition of IgA along the basement membrane at direct immunofluorescence (Fig 1). Clinically, the patient responded well with no new lesions and resolution of existing lesions.

Linear IgA bullous dermatosis is a rare blistering skin disorder that is characterized by deposition of IgA antibodies along the basement membrane. It can be idiopathic or drug induced, with mucosal involvement seen in the 2 forms but more frequent in idiopathic presentations.^{4,5} Vancomycin has been recognized as a common inciting factor.^{1,2,4,5} LABD also is recognized as the most frequently reported vancomycin-related hypersensitivity reaction.³ However, a recent case report did implicate piperacillin and tazobactam in a similar case of drug-induced LABD.⁶ Our patient did receive these 2 drugs. Although

we cannot be certain of the offending agent, vancomycin is statistically more likely to have been the cause. In a few cases, drug-induced lymphocyte stimulation testing has been performed, which could provide supporting information for identifying the offending agent.⁷ However, the accuracy of such testing and its cost-benefit assessment remains unclear. Penicillins, cephalosporins, sulfonamides, and rifampin are some other common antibiotics that have been linked to LABD.⁸ Other nonantibiotic drugs associated with LABD include diclofenac, furosemide, captopril, and lithium.⁵

The symptoms of LABD begin within 1 month of exposure to the inciting agent and can persist for several weeks after drug cessation. The severity of the reaction does not appear to correlate with serum vancomycin levels.¹ New lesions can continue to erupt for up to 2 weeks after drug cessation. The clinical presentation is often similar to that of dermatitis herpetiformis of gluten-sensitive enteropathy and other bullous disorders such as pemphigus vulgaris, paraneoplastic pemphigus, bullous pemphigoid, erythema multiforme, and Stevens-Johnson syndrome and toxic epidermal necrolysis.¹ It is characterized by diffuse urticarial plaques with heterogeneous papules, vesicles, or bullae,² primarily involving the trunk and extremities, often having mucosal involvement.¹

Early diagnosis is the key to appropriate management and understanding of the prognosis.² The diagnosis is confirmed by a perilesional skin biopsy demonstrating linear IgA deposition along the basement membrane at direct immunofluorescence and

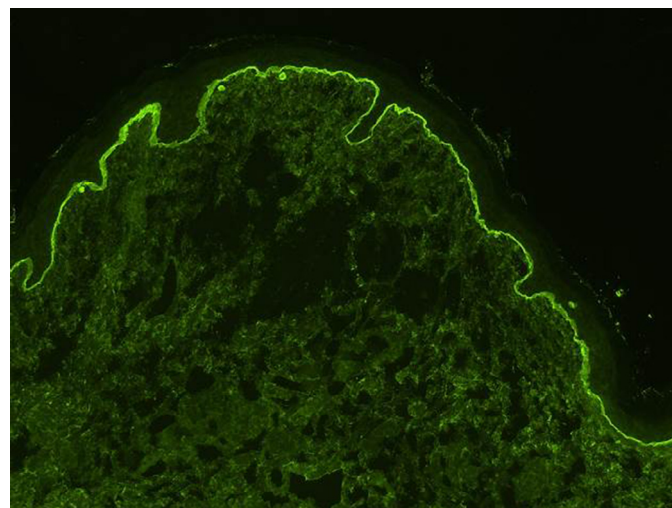


Figure 1. Direct immunofluorescence of perilesional biopsy showing linear deposition of immunoglobulin A along the basement membrane.

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subepidermal clefting with eosinophilic infiltrate at histology. Studies to identify dermal antigens have found IgA antibodies to LAD285 and dual IgA and IgG responses to BP180.¹

Drug-induced LABD usually resolves spontaneously with cessation of the drug, but severe cases might require prednisone and/or dapsone with a quick taper over 4 to 6 weeks.¹ Prolonged systemic therapy is rarely needed. Cutaneous lesions heal over several weeks without scarring, but mucosal lesions can be complicated by stricture formation and scarring. When patients are rechallenged with vancomycin after such an episode, they might have a more severe recurrence with shorter latency and a longer course.² Because vancomycin is widely used, it is important to recognize this as a potential hypersensitivity reaction, which can be life threatening without early identification.

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