

Images in Allergy

Linear Immunoglobulin A Bullous Disease (LABD) Triggered by Amoxicillin Clavulanic Acid in a Child

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Linear IgA bullous dermatosis (LABD) is a rare autoimmune blistering disorder characterized by subepidermal blisters with linear IgA deposition along the dermal-epidermal junction. Some cases are drug induced.

A 2.5-year-old girl was admitted to the emergency department of our children's hospital with a bullous, itchy rash that appeared

6 days after antibiotic therapy with amoxicillin/clavulanic acid (Amx/Ca) for fever, cough, and rhinitis. Tense bullae rapidly spread to >50% of her body surface, with a typical clinical appearance: groups of new small blisters arising at the periphery of older bullae, looking like a "crown of jewels" (Figure 1, A). The results of laboratory tests performed on admission were



FIGURE 1. A, Acute phase of LABD. B, Relapse phase of LABD. C, Flare-up of LABD after patch tests. LABD, Linear IgA bullous dermatosis.

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normal including a complete blood count with differential, routine chemistries, serum IgA, and glucose-6-phosphate dehydrogenase level. Testing for celiac disease was negative. Polymerase chain reaction (PCR) was negative for *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Epstein-Barr virus* (EBV), nasopharyngeal swab for EBV PCR was negative, and EBV and Coxsackie virus serologies were negative.

The histological examination revealed a subepidermal blistering disorder, and direct immunofluorescence revealed the presence of IgA along the basement membrane of the epidermis in a linear pattern, consistent with a diagnosis of LABD.

The patient was initially treated with intravenous corticosteroids (methylprednisolone 1 mg/kg/day) for 7 days, followed by a combination of oral dapsone (daily dose 1 mg/kg) and oral prednisone (2 mg/kg/day). Oral corticosteroid therapy was progressively tapered over 2 months. Dapsone therapy was continued for 14 months. No relapses were observed after 2 months (Figure 1, B) with complete recovery at 6 months.

The Naranjo scale was used to assess Amx/Ca causality, and a score of 7 ("probable adverse drug reaction") was calculated.

Three months after recovering from the disease she was sent for an allergy evaluation. Patch tests (PTs) with Amx/Ca at 20% in petrolatum and lymphocyte transformation tests (LTTs) were performed.¹

The PT was removed after 48 h and was negative; however, 12 hours after its application, the patient developed a flare of a bullous eruption in the same sites of the initial reaction (Figure 1, C).

After 11 days of stimulation with Amx or Amx/Ca, specific T lymphocytes showed significant proliferation (Figure E1, available in this article's Online Repository at www.jaci-inpractice.org).

Drug-induced LABD in the pediatric population has been reported to be caused mainly by antibiotics.²

This is the first pediatric case in which the presence of T specific lymphocytes toward Amx/Ca has been proven *in vitro* via LTT. Moreover, the application of PT with the culprit drug resulted in a flare-up of the bullous lesions. This could be explained by a possible reactivation of sensitized T lymphocytes after skin contact with the eliciting drug in sites distant from the PT. Although the utility of PT and LTT in the workup of LABD has not been defined, this case suggests that these tests may be useful.

REFERENCES

1. Pichler WJ, Tilch J. The lymphocyte transformation test in the diagnosis of drug hypersensitivity. *Allergy* 2004;59:809-20.
2. Ho JC, Ng PL, Tan SH, Giam YC. Childhood linear IgA bullous disease triggered by amoxicillin-clavulanic acid. *Pediatr Dermatol* 2007;24:E40-3.

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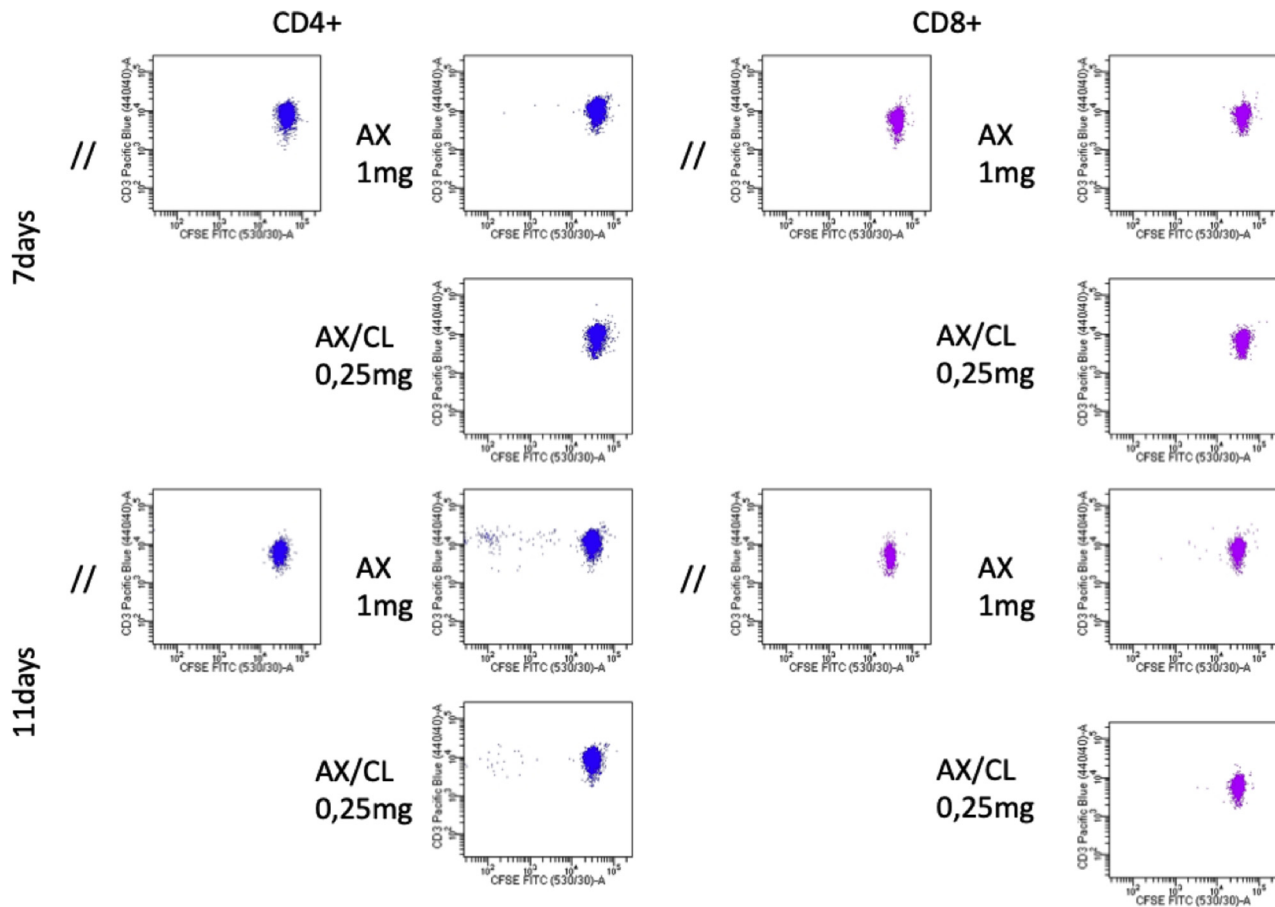


FIGURE E1. *In vitro* β -lactam-specific proliferative response (LTT). Cytofluorimetric analysis of CD4+ and CD8+ proliferating lymphocytes was performed after 7 and 11 days of incubation of CFSE3-marked PBMCs with 2 different concentrations of Amx or Amx/Ca. *Amx/Ca*, Amoxicillin/clavulanic acid; PBMC, peripheral blood mononuclear cell.