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## **Linear IgA bullous dermatosis induced by atezolizumab: a case report**

Seba Almutairi,<sup>1</sup> Dana Alessa<sup>1,2</sup>

<sup>1</sup>Division of Dermatology, King Abdulaziz Medical City, Ministry of National Guard Health Affairs, Riyadh; <sup>2</sup>College of Medicine, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia

**Correspondence:** Seba Almutairi, Division of Dermatology, King Abdulaziz Medical City, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia.

E-mail: almutairiseba@hotmail.com

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## **Abstract**

Linear IgA Bullous Dermatitis (LABD) is a rare immune-mediated vesiculobullous disease that was reported to be induced by infections or medications. Atezolizumab is a monoclonal antibody targeting programmed cell death ligand-1 (PD-L1), it has been used to treat multiple cancers. Here, we report a case of drug induced LABD following the administration of Atezolizumab.

## **Introduction**

Linear IgA Bullous Dermatitis (LABD) is a rare immunobullous disease, that affects 0.2-2.3 cases per one million yearly.<sup>1</sup> It presents with an abrupt onset of urticarial plaques, vesicles and bullae, mostly on the face, scalp, and limbs. On histopathology, LABD shows a subepidermal blister with dermal neutrophilic infiltration seen by Hematoxylin and Eosin (H&E), and a linear deposition of IgA at the basement membrane zone seen by Direct Immunofluorescence (DIF). Although LABD is typically idiopathic, it may occasionally be provoked by infections or medications. In adults, drug-induced LABD accounts for 37.5% of cases, with vancomycin being the most frequently reported drug.<sup>2</sup>

Atezolizumab is a monoclonal antibody that inhibits programmed cell death ligand-1 (PD-L1). It is used as an anti-cancer treatment and exerts its effect by activating anti-tumor immune responses. PD-L1 inhibitors have been linked to several drug-induced dermatoses.<sup>3</sup> Atezolizumab has been recently reported to cause LABD in one patient.<sup>4</sup> Here, we report the second case of drug induced LABD following the administration of Atezolizumab.

## **Case report**

This was a 79-year-old man known to have Diabetes Mellitus and hepatocellular carcinoma (HCC). He presented to the emergency department with a 1-week history of a painful generalized rash. His symptoms started 2 weeks after getting a single dose of 1200mg Atezolizumab and 750mg Bevacizumab to treat his HCC. His medication history included Nivolumab and Lenvatinib, which were stopped 4 months earlier. On physical examination, he had multiple tender erythematous plaques, bullae and erosions in generalized distribution including the palms and soles. (Figure 1A) The body surface area was ~10%, and Nikolsky sign was positive. The mucous membranes were also involved, with multiple erosions over the buccal mucosa, soft palate, and nasal mucosa. (Figure 1B). The differential diagnoses included Stevens-Johnson Syndrome (SJS), Bullous Pemphigoid, Pemphigus Vulgaris, Paraneoplastic Pemphigus, Generalized Bullous Fixed Drug Eruption, and LABD. Two 4-mm skin punch biopsies were taken for H&E and DIF. There was subepidermal blister with a linear neutrophilic band. (Figure 2) DIF showed linear basal deposition of IgA, without IgG,

IgM and C3. These findings were consistent with the diagnosis of LABD. After evaluating the patient medications and a review of the literature, it was decided that Atezolizumab was the most likely culprit drug. The patient was admitted for supportive management, and Atezolizumab was discontinued. The patient was started on Dexamethasone 4mg IV twice daily. The patient condition rapidly improved, and he was discharged on Prednisone 25mg daily on day 4. On 1-week follow-up, the patient had no active lesions, and there were no signs of recurrence. Two weeks later, the patient passed away due to cardio-pulmonary arrest secondary to locally advanced and metastatic HCC.

## Discussion

LABD is a rare immune-mediated subepidermal vesiculobullous disease. The pathogenesis is thought to be due to circulating IgA antibodies directed against multiple basement membrane antigen including Bullous Pemphigoid Antigen 2 (BPAg2), type VII Collagen, and Laminin-332.<sup>1</sup> LABD is usually idiopathic but may be rarely related to infections or medications. It has been linked to several drug classes such as antibiotics and non-steroidal anti-inflammatory agents.<sup>2</sup> The most common reported drug is vancomycin accounting for 56% of all reported cases.<sup>2</sup>

The exact pathogenesis of drug induced LABD is not clear. T cells and cytokines were demonstrated to play a role in the pathogenesis. In one study of patients with drug-induced LABD, there was a significant increase in the levels of CD8+ cytotoxic T cells.<sup>5</sup> Atezolizumab is a monoclonal antibody that selectively inhibits PD-L1, which leads to the inhibition of T-cell apoptosis.<sup>6</sup> This may lead to increased levels of CD8+ T cells, which may explain the development of LABD in this case. However, for LABD, there has only been one reported case.<sup>4</sup>

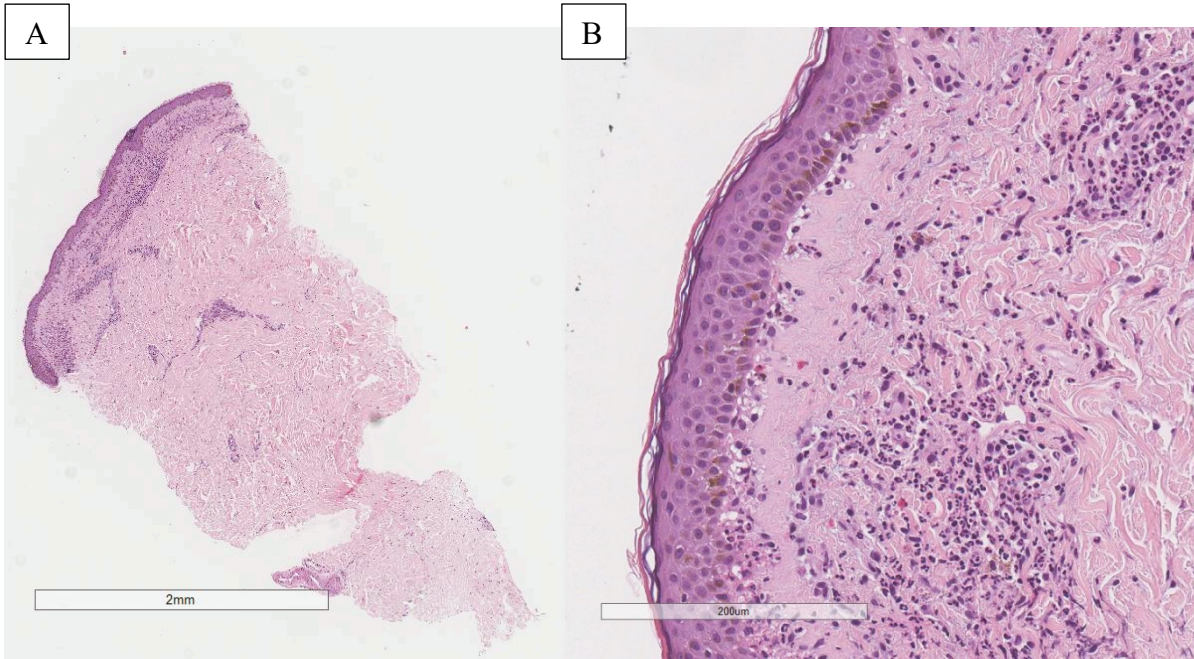
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**Figure 1. A) Multiple erythematous eroded plaques with hemorrhagic crusts over the (A) trunk; B) buccal mucosa.**



**Figure 2. A) Low magnification of the skin punch biopsy with a moderate linear subepidermal mixed inflammatory infiltrate (hematoxylin and eosin, x4); B) Higher magnification of the skin punch biopsy which shows an early basal blister formation with vacuolar alteration in addition to the moderate linear subepidermal and perivascular neutrophils with scattered eosinophils (hematoxylin and eosin, x40).**