CASE REPORT

Toxic Epidermal Necrolysis/ Stevens-Johnson Syndrome-like Linear IgA Bullous Dermatosis as a Manifestation of Pembrolizumab

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SUMMARY

Linear IgA bullous dermatosis, also known as linear IgA dermatosis, is a rare subepithelial vesiculobullous disease characterized by linear IgA deposition at the basement membrane zone. Clinically, it presents as tense vesicles or bullae, with histopathology demonstrating subepidermal blistering and a predominantly neutrophilic infiltrate. A linear pattern of IgA deposition at the basement membrane zone via direct immunofluorescence is a hallmark finding for diagnosis. However, this rare autoimmune dermatosis can manifest heterogeneously and non-classically, making histopathological studies critical for accurate diagnosis and subsequent treatment.

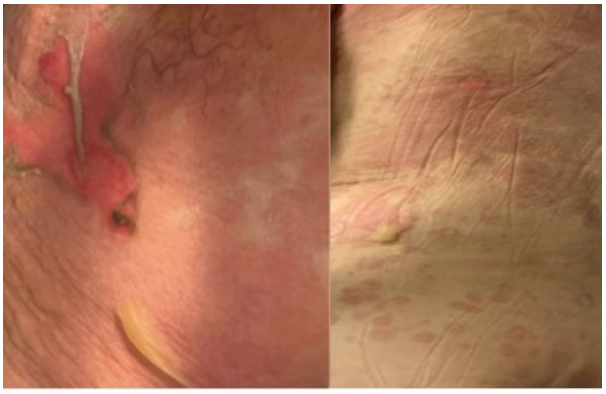
In this report, we discuss a rare case of a patient presenting with linear IgA bullous dermatosis exhibiting clinical features similar to Stevens-Johnson Syndrome (SJS)/Toxic Epidermal Necrolysis (TEN), induced by pembrolizumab.

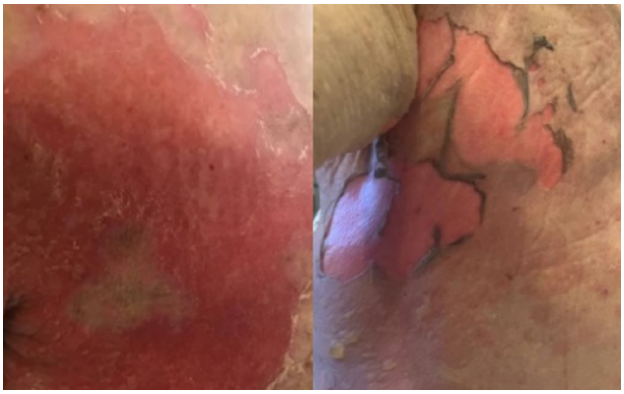
INTRODUCTION

Linear IgA bullous dermatosis was first described by Bowen in 1901; however, it was not recognized as a distinct entity from dermatitis herpetiformis until 1979. Linear IgA bullous dermatosis is a rare autoimmune vesiculobullous disease with very low incidence. It can be idiopathic or drug-induced. The drug-induced form is more common in adults and tends to be more severe than the idiopathic variant, though it rarely mimics toxic epidermal necrolysis (TEN). Drug-induced linear IgA bullous dermatosis typically occurs within the first 1 to 15 days following the administration of the causative drug and resolves within two weeks of its discontinuation. While vancomycin is the drug most commonly associated with this condition, other medications have also been implicated. Toxic epidermal necrolysis (TEN) and Stevens-Johnson Syndrome (SJS) are severe and potentially life-threatening drug-induced reactions affecting the skin and mucous membranes.

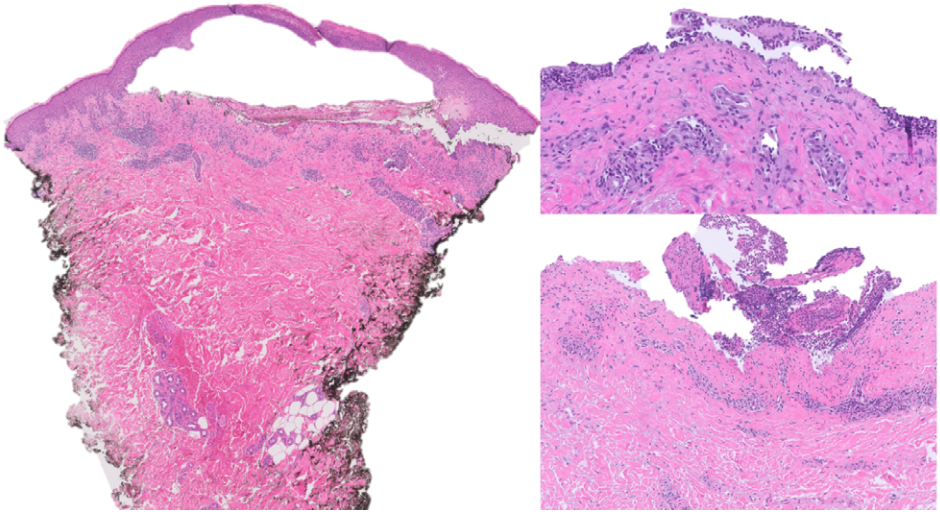
CLINICAL CASE

A 65-year-old male with a history of stage IV squamous cell lung cancer, currently undergoing chemotherapy and recently treated with pembrolizumab, was ad-





Figures 1 and 2: Macules fused to form large, flaccid bullae. These vesicles were fragile and highly pruritic.



Figures 3 and 4: Subepidermal blister with neutrophils and eosinophils. Note the absence of interface epidermal changes.

mitted to the emergency department with fatigue, hypotension, and a diffuse pruritic rash consisting of large macules and blisters on the torso, back, and extremities (Figures 1 and 2). No fever was observed. The skin lesions predominantly consisted of macules that coalesced into large flaccid bullae. These vesicles were fragile and filled with yellowish purulent fluid, and the skin was painful to touch. No mucosal involvement was noted.

The patient received two cycles of pembrolizumab one week prior to developing this extensive dark-colored blistering skin eruption. Due to its association with the medication, the initial clinical diagnosis included toxic epidermal necrolysis/Stevens-Johnson syndrome (TEN/SJS) and bullous pemphigoid. Two skin biopsies were performed—one for hematoxylin and eosin (H&E) staining and another for direct immunofluorescence (DIF). The H&E-stained biopsy revealed a subepidermal blister with neutrophils and eosinophils (Figures 3 and 4). DIF demonstrated a strong linear deposition of IgA along the basement membrane zone without evidence of IgG or IgM deposits (Figure 5). Serology for bullous pemphigoid was negative. The final diagnosis was toxic epidermal necrolysis/Stevens-Johnson syndrome-like linear IgA bullous dermatosis (LABD). The inflammatory erythema resolved after three days of treatment with high-dose corticosteroids.

DISCUSSION

Linear IgA bullous dermatosis (LABD) is a rare autoimmune blistering disease that can be associated with underlying conditions such as inflammatory

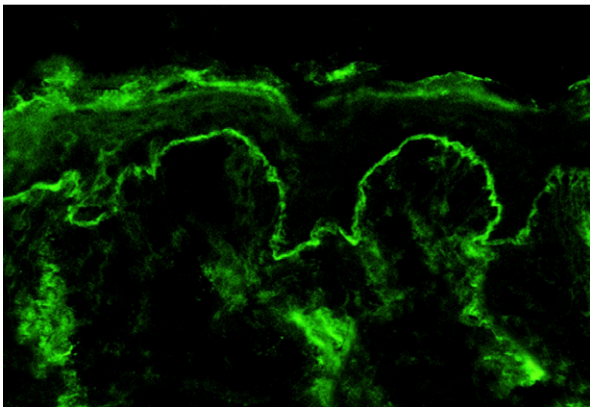


Figure 5: Direct immunofluorescence shows a strong linear deposition of IgA.

bowel disease, malignancies, and rheumatoid arthritis[1] LABD can be idiopathic or drug-induced[2,3] Several drugs have been implicated in LABD, with vancomycin and phenytoin being the most common. Cases of LABD mimicking other blistering diseases, such as bullous pemphigoid, pemphigus vulgaris, dermatitis herpetiformis, impetigo, and non-blistering diseases, have been reported. However, it is rare for LABD to present as toxic epidermal necrolysis/Stevens-Johnson syndrome (SJS/TEN)-like, as in the case presented in this report.[4,6]

Given the evolution of the disseminated rash in this patient (including generalized erythematous scaling skin lesions) and its association with pembrolizumab administration, along with the positive direct immunofluorescence (IFD) showing linear IgA deposits, we propose that the eruption was indeed a linear IgA bullous dermatosis (LABD) with a TEN/SJS-like presentation. Pembrolizumab is an anti-PD-1 antibody that suppresses negative immune regulation caused by PD-1 receptor signaling, leading to the reversal of T cell suppression and antitumor responses. Pembrolizumab has been associated with immune-related adverse events, with skin and the gastrointestinal tract being the most affected.

A wide range of cutaneous eruptions has been reported, including lichenoid reactions, eczematous dermatitis, psoriasis, sarcoidosis, and TEN/SJS-like reactions, in addition to bullous pemphigoid. The treatment for LABD presenting as TEN/SJS does not differ from conventional LABD, although the severity of skin lesions requires more attention. The withdrawal of the suspected drug, when present, is the first and sometimes the only step; however, systemic corticosteroids may be necessary in some cases. The prognosis will also depend on the patient's comorbidities.

In summary, we present a rare case of LABD with characteristics similar to and overlapping with those observed in SJS/TEN. As shown in this report, LABD can present with a heterogeneous clinical presentation that, among its numerous skin manifestations, can rarely mimic TEN/SJS?[7,12] It is important to include LABD in the differential diagnosis of vesiculobullous skin eruptions, with routine histological examination and IFD being highly recommended for accurate diagnosis.

CONCLUSION

As immune checkpoint inhibitors are increasingly used, dermatologists should be familiar with and carefully assess the cutaneous adverse effects, paying special attention to the range of blistering skin reactions secondary to these drugs. In this report, we present a case of LABD associated with pembrolizumab. This case emphasizes the importance of clinicopathological correlation, with particular emphasis on IFD results. This dermatosis can present in a quite heterogeneous and unconventional manner, so a high index of suspicion should be maintained to reach an accurate iagnosis, especially if there is a prior history of pembrolizumab use.

CONFLICTS OF INTEREST

None reported.

FUNDING SOURCES

None.

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