Case Report

Unilateral Localized Bullous Pemphigoid Associated with Chronic Venous Stasis: A Case Report

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ABSTRACT

Localized Bullous Pemphigoid (LBP) is a rare form of Bullous Pemphigoid (BP), it is usually related to trauma and can appear on any wound or surgery site. Chronic venous stasis has not been described as a predisposing factor. We present the case of an 80-year-old Hispanic man with a previous history of chronic venous stasis and surgical intervention in both legs, who presented with a unilateral form of LBP, initial treatment with clobetasol topical ointment, and compression therapy resulted in complete remission. The present case shows a unique presentation of LBP but also highlights the importance of chronic venous stasis as a triggering factor.

INTRODUCTION

Bullous Pemphigoid (BP) is a chronic autoimmune disease caused by autoantibodies targeting the hemidesmosomal proteins BP180 and BP230 [1]. BP may also manifest locally, following exposure to triggers [2]. Localized Bullous Pemphigoid (LBP) is a rare subtype that can appear on any wound or surgery site after radiotherapy, PUVA therapy or dynamic phototherapy and in patients with chronic edema of the lower limbs [3,4]. To our knowledge, there are few case reports of LBP in the setting of venous stasis and it is hypothesized that pre-existing epidermal inflammation in the setting of venous stasis could represent the triggering factor [5]. We describe a case of a male patient with unilateral bullous pemphigoid in the lower leg who had a history of chronic venous stasis.

CASE REPORT

An 80-year-old Hispanic man with a 6-month history of itchy tense blisters on his left lower limb. He had a previous history of chronic venous stasis on both legs. Surgical intervention for venous stasis on both legs was performed previously, but there was no improvement on his left lower limb. Examination revealed numerous tense bullae with circular erosions, hematic crust and perilesional erythema limited to the left lower leg and limb (Figure 1).

Punch biopsies were taken from an intact bulla and perilesional skin. Histologic examination found a subepidermal blister with perivascular and interstitial eosinophilic infiltration. The basal membrane was visible in the blister's roof using type IV collagen immunohistochemistry. Direct immunofluorescence was negative. (Figure 2).

Although the direct immunofluorescence was negative, these findings were suggestive of unilateral localized bullous pemphigoid. Initial treatment with clobetasol propionate topical ointment twice daily and compression therapy resulted in clinical improvement

with complete remission of the lesions after one month of treatment. (Figure 3).

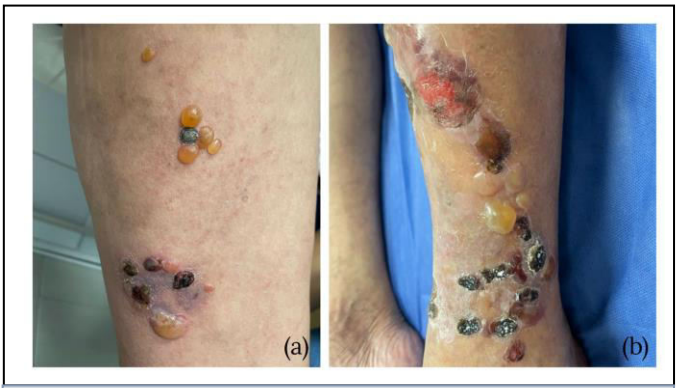

Figure 1: Tense blisters. (a): left thigh, (b) left lower limb.

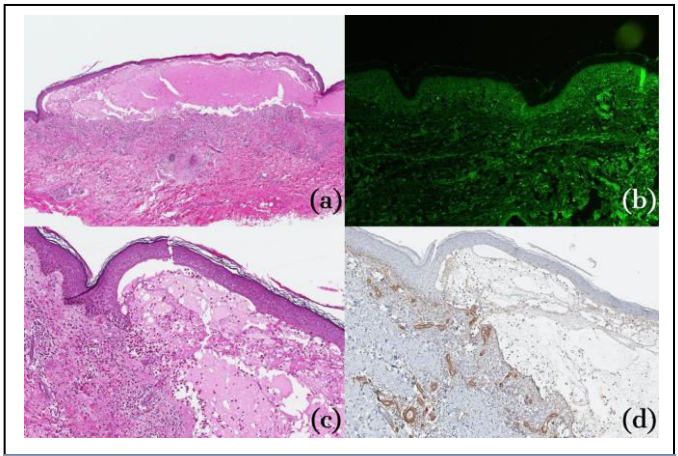

Figure 2: (a) H&E 4x Subcutaneous blister with eosinophilic infiltrate. (b) Negative direct immunofluorescence for IgG. (c) H&E 20x Subcutaneous blister with eosinophilic infiltrate. (d) Positive type IV collagen in the roof of the blister.

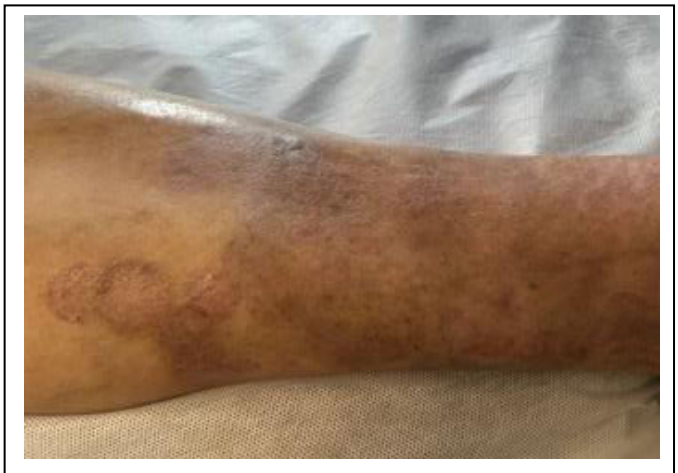

Figure 3: Post inflammatory hyperpigmentation, left lower limb.

DISCUSSION

LBP refers to the occurrence of site-restricted clinical BP lesions in patients with no history of BP for a minimal duration of 3 months [6]. It usually occurs in male patients older than 70 years as blistering eruptions, tense pruritic bullae and vesiculobullous dermatitis [7,8]. BP is one of the most prevalent forms of bullous disease, with an annual incidence of 2.4 to 21.7 new cases per million [9,10]. However, it is uncommon in its localized form with a prevalence of 2.5% of all cases of BP [6].

The pathogenesis of BP is caused by circulating autoantibodies that bind to BP230 and BP180 [7], causing complement activation, inflammatory cell recruitment, and the release of proteolytic enzymes 10. When LBP is caused by trauma, it can appear anywhere on the body; otherwise, it is most common in the lower limbs [4]. Radiotherapy has been described as the most common presumed trigger factor, followed by thermal or chemical burns, surgical procedures, UV exposure, colostomy, urostomy and drugs including neuroleptics and diuretics [11,6]. To our knowledge, the association between venous stasis and LBP has been reported in just one previous case [5]. When LBP is related to trauma, some authors mention the creation of neo-antigens by the trauma, while others believe that the anti-BP180 and anti-BP230 antibodies were already present and were recruited by the trauma [12]. It has been hypothesized that the immunologic changes associated with venous stasis could represent the triggering factor for the generation of localized disease [5]. Extravasation of blood and plasma, which includes mediators of innate and adaptive immune responses to circulating tissues [13], disrupts the immune system causing damage and predisposing to autoantigen presentation, autoreactive T lymphocyte production, and autoantibody-producing B cells [5,14].

Clinical-pathological correlation, as well as serological tests to detect circulating antibodies, are used to make the diagnosis [15]. Although the clinical and histologic findings were consistent with LBP, all immunoreactants were found to be negative on direct immunofluorescence in our case, so this finding was considered a false negative. It has previously been recommended that BP sampling from the lower extremities should be avoided because of the high rate of false negatives [15]. The Weigand study found that in a retrospective series,

33% of PA patients had false negatives. Following that, Perry D et al conducted another retrospective study with 79 patients and only 4 false negatives, indicating that the lower extremities should not be avoided as biopsy sites in BP [16]. Even though the course of this disease is usually benign there is a risk of progressing to a generalized form in around 36.8% of cases if BP180 antibodies are present [17].

CONCLUSION

In conclusion, we present a unique case of unilateral LBP associated with venous stasis and previous history of surgical intervention in both legs, highlighting the hypothesis of immunologic changes associated with venous stasis as a triggering factor for LBP. This case and similar cases previously reported, should increase awareness of this condition, and LBP (especially if arising in sites of trauma) should be considered as a differential diagnosis.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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