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Urticarial Bullous Pemphigoid: A New Case Report

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Abstract

Background: Bullous pemphigoid (BP) is the most common autoimmune bullous disease and it primarily affects the elderly population. It typically presents with tense bullae and severe pruritus. Non-bullous pemphigoid is a subtype of BP characterized by lacking the typical bullae formation with different presentations including erythematous, eczematous, urticarial, polycyclic, targetoid, nodular, lichenoid, vesicular and erythrodermic. **Aim:** to document a new case presentation of urticarial BP who was treated for several years as chronic urticarial and chronic eczema. **Case Report:** A 56-year-old male patient presented with a history of recurrent severely pruritic urticarial wheals for 4 years duration involving the lower abdomen, lower back, upper and lower extremities associated with excoriations, keratosis, and post-inflammatory hyperpigmentations on resolved sites, diagnosed as urticarial BP on histopathology & direct immunofluorescence study (DIF) and was improved on systemic doxycycline therapy. **Conclusion:** BP can be presented with atypical manifestation. Urticarial BP is a rare variant of non-bullous pemphigoid that should be taken into consideration in the differential diagnosis of an atypical urticarial wheal not responding to conventional therapy.

Keywords

Bullous Pemphigoid, Non-Bullous Pemphigoid, Urticarial Bullous Pemphigoid, Direct Immunofluorescence, Doxycycline

1. Introduction

BP is a rare autoimmune blistering disease, with an annual incidence ranging from 6 to 13 new cases per 1 million populations per year [1] [2] [3] [4]. BP typically affects elderly people (65 - 75 years of age) and males are slightly more af-

fected than females [2] [5].

Classically, BP is clinically characterized by large (1 - 3 cm), tense, serous, or hemorrhagic bullae, which appear on erythematous, urticarial, or eczematous lesions or normal skin. Blisters evolve into eroded and crusted areas and then heal with no scarring. Sometimes post inflammatory changes in pigmentation or milia might be visible [6]. The bullae generally appear in clusters and quickly become widespread.

The sites of predilection include the lower abdomen, proximal extremities (especially the inner thighs), and flexor surfaces of the forearms, groin, and axillae. The face and the neck are usually not affected. The involvement of the oral cavity is rare, limited to 10% - 30% of patients [2]. The onset of classical BP is often characterized by a non-bullous phase of variable duration; from weeks to several months and in a few cases, it may be the only manifestation of BP. Some authors report that such conditions in up to 20% of the patients [1] [2]. Lesions are itchy erythematous or eczematous patches and urticarial plaques [7]. A correct diagnosis during this phase might be difficult, since the early lesions are non-specific and might resemble a broad spectrum of conditions, such as chronic prurigo, eczema, urticaria, and toxic drug reactions. Therefore, in elderly patients with a long-lasting highly pruritic eczema-like or urticarial erythema, after excluding more common etiologies, BP should be taken into consideration in the differential diagnosis [8] [9].

Histological findings are not pathognomonic but highly suggestive of BP. In early phases, subepidermal clefts, eosinophilic spongiosis, and/or an infiltrate of eosinophils in the upper dermis lining the dermal-epidermal junction are detectable [10]. While the histologic changes in established lesions are characterized by subepidermal bullae, by the absence of acantholysis, and by a superficial dermal infiltrate mainly with eosinophils and few neutrophils or lymph-monocytes; although, neutrophil-predominant cases may also exist [1].

DIF is the strongest criterion for diagnosis since it is found positive in nearly 100% of patients [7]; Kershenovich *et al.* refer to it as an obligatory criterion [11]. DIF of perilesional skin shows a continuous linear deposition of IgG (70% - 90% of patients), C3 (90% - 100% of patients), or both, along the basement membrane zone (BMZ).

Indirect immunofluorescence (IIF) studies can demonstrate in 60% - 80% of patients the presence of circulating IgG autoantibodies that typically bind to the epidermal side of salt-split normal human skin [2]. Systemic corticosteroid therapy is the mainstay of therapy for bullous pemphigoid. Large doses should be used initially [12]. Dapsone or sulfapyridine is effective in some patients [13]. Immunosuppressive may be employed as an adjunct to corticosteroid therapy [12].

In the present case report, we are describing a 56-year-old male patient who presented with a history of recurrent severely pruritic annular urticarial wheals for 4 years duration involving the lower abdomen, lower back, upper and lower extremities associated with excoriations, keratosis, and post-inflammatory hyper-

pigmentations on resolved sites, diagnosed as urticarial BP on histopathology & DIF and was improved on systemic doxycycline therapy. The written consent form was taken from the patient about the publication of his condition.

2. Case Report

A 56-year-old male patient presented to our dermatology clinic with a history of 4 years duration of recurrent severely pruritic skin rashes involving the abdomen, lower back, and both upper and lower extremities. Some rashes last more than 24 hours and on resolving reveal pigmentations and relapse again. For several years he was diagnosed as a case of chronic urticarial and chronic eczema and received multiple modalities of treatments including topical steroids, systemic antihistamines, and biological therapy Omalizumab injection. The patient partially responded to a short course of systemic prednisolone tablet 20 mg but relapsed after discontinuation. Past medical and drug history were negative. On examination, the patient presented with widespread erythematous urticated annular wheals involving the lower abdomen, lower back, and upper and lower extremities associated with excoriations, keratosis due to long-standing scratching, and post-inflammatory hyperpigmentations on the sites of resolved lesions [Figures 1-3].

On a blood test assessment, the level of eosinophils and IgE were both elevated [Table 1]. A skin biopsy was taken, and urticarial vasculitis was included in the differential diagnosis. The histopathological findings were non-specific and showed compact orthokeratosis, acanthosis, minimal spongiosis with eosinophils, and moderately severe superficial perivascular lymphocytic infiltrate with many eosinophils [Figure 4]. DIF study revealed positive linear basement membrane deposition of C3, faint IgG, and negative IgM consistent with a diagnosis of urticarial BP [Figure 5, Figure 6].

Treatment started with an oral doxycycline capsule of 100 mg daily for one month in combination with high potency topical Clobetasole Ointment 0.05%. After one month of followed-up, a dramatic response to therapy was observed

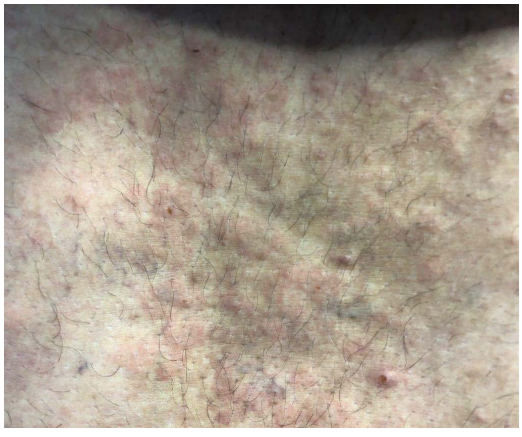


Figure 1. Urticarial BP in a 56-year-old male patient showed multiple erythematous urticarial wheals involving the lower back.

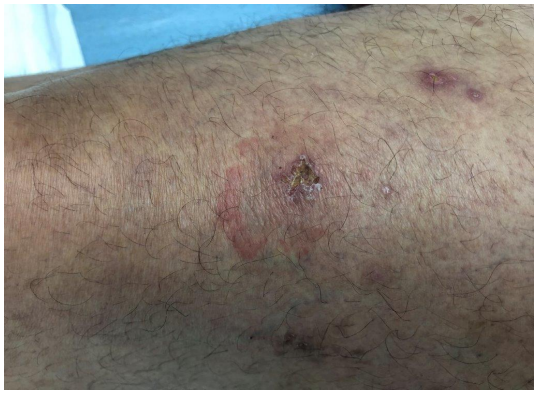
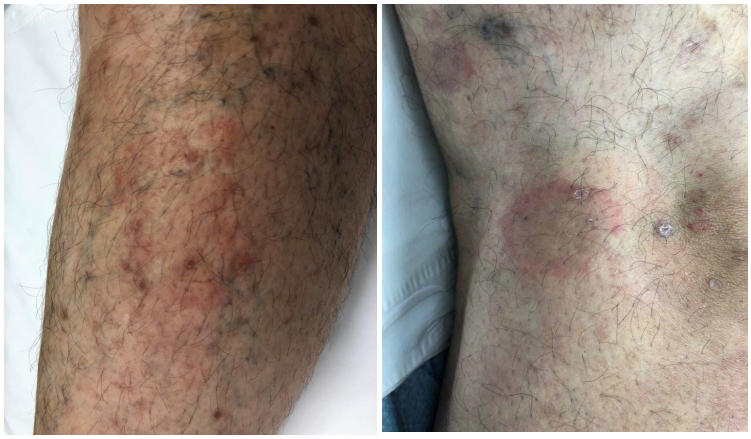
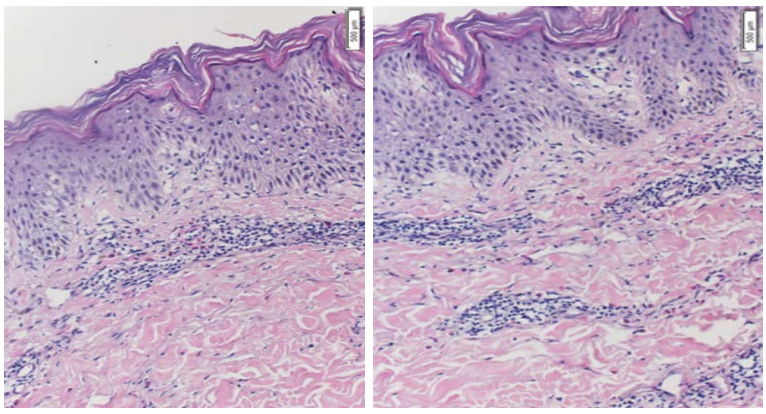


Figure 2. Urticarial BP in a 56-year-old male patient showed erythematous annular ring-shaped wheals on the right anterior thigh. Note the multiple crustations due to sever pruritus.



(A) (B)

Figure 3. Urticarial BP in a 56-year-old male patient showed erythematous annular ring-shaped urticarial wheals; (A) Left anterior leg; (B) Left knee. Note multiple keratosis on the knee joint due to chronic pruritus.

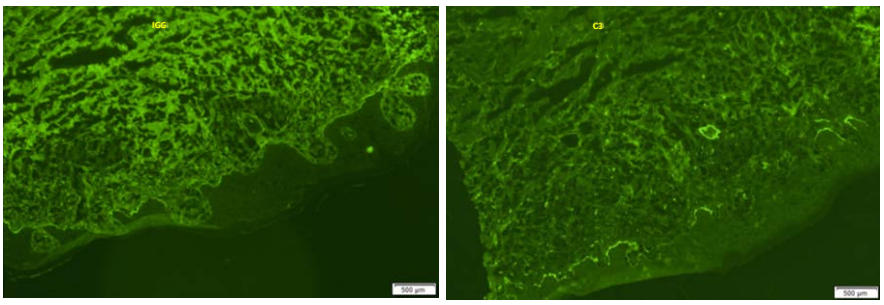


(A) (B)

Figure 4. Hematoxylin and Eosin (H & E) stained section showed compact orthokeratosis, the epidermis is acanthotic with minimal spongiosis and eosinophils. There is a moderately severe superficial perivascular infiltrate of lymphocytes with many eosinophils. Original magnification × 10 (A), (B).

Table 1. Serum eosinophils count and IgE levels.

	Patient's blood sample	Normal range
Eosinophils count	7.3%	<6%
IgE levels	1758 IU/ml	<380 IU/ml



(A) (B)

Figure 5. DIF showed a positive linear basement membrane deposition for C3 and faint IgG in a 56-year-old male patient with a history of urticarial BP. (A) IgG; (B) C3.

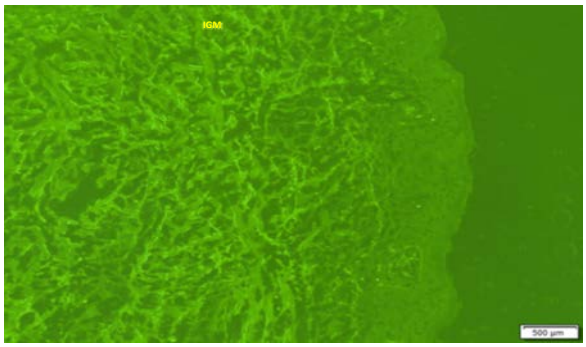


Figure 6. DIF showed a negative linear basement membrane for IgM in a 56-year-old male patient with a history of urticarial BP.

where complete resolved pruritus and urticarial wheals left post-inflammatory hyperpigmentations on some resolved sites. Therapy was continued for another one month then stopped. 2 month followed-up later, there were no signs of relapse [Figures 7-9].

3. Discussion

The classical BP is characterized by the presence of tense pruritic bullous eruption. In contrast to non-bullous BP which is characterized by the absence of typical bullae formation and the atypical manifestation of erythematous and/or urticarial pruritic wheal which might continue for months or years without bullous formation as reported in the literature [14] [15] [16].

As with many dermatoses like chronic eczema and chronic urticaria, the skin biopsy could be non-specific for diagnosis of BP unless high suspicion is taken especially if not respond to conventional therapy and with DIF study can prove the diagnosis.

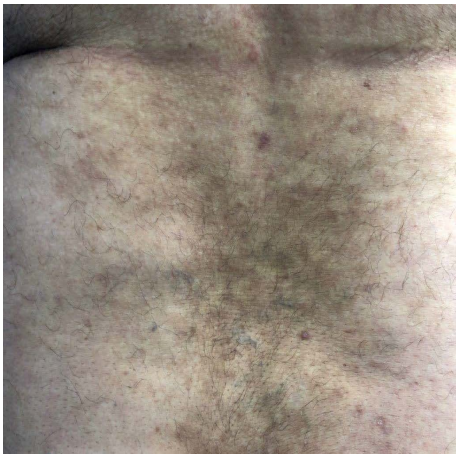


Figure 7. Urticarial BP in a 56-year-old male patient 2 months after treatment with doxycycline showed complete resolved wheals leaving post-inflammatory hyperpigmentations over the lower back.

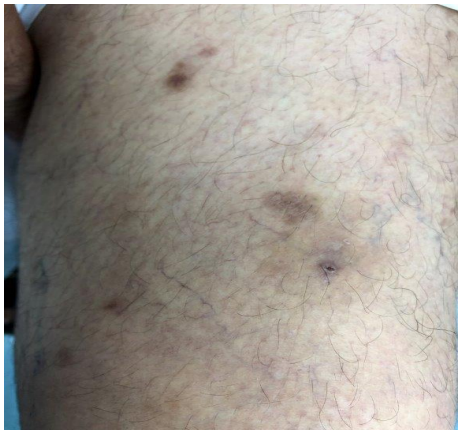
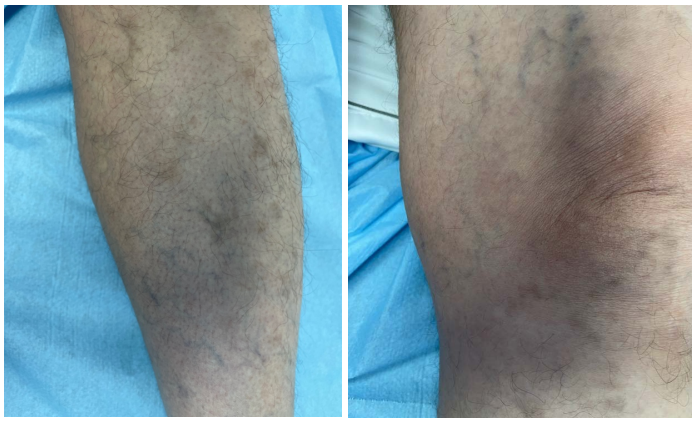


Figure 8. Urticarial BP in a 56-year-old male patient 2 months after treatment with doxycycline capsule showed complete resolved wheals leaving post-inflammatory hyperpigmentations over the right anterior thigh.



(A) (B)

Figure 9. Urticarial BP in a 56-year-old male patient 2 months after treatment with doxycycline showed complete resolved wheals leaving slight post-inflammatory hyperpigmentation.

In our case study, we are describing a 56 year-old-age male patient with a long history of recurrent severely pruritic, urticarial skin eruptions for 4 years duration associated with peripheral blood eosinophilia and high IgE level. The histopathologic features were compatible with many conditions such as eczema, urticarial vasculitis, drug eruption, and superficial arthropod bite reaction. The DIF study confirms the diagnosis of BP showing linear IgG and C3 binding at the basement membrane zone.

Urticarial vasculitis presented with recurrent episodes of urticarial lesions; persistent greater than 24 hours; residual hyperpigmentation following resolution; histology showing leukocytoclastic vasculitis. [17]

Regarding therapy, urticarial BP responded very well to the Doxycycline capsule and the improvement was dramatic within the first 4 weeks where signs and symptoms of pruritus and urticarial wheals resolved completely without relapse after 2 months of followed-up when stopped therapy this indicates that doxycycline is the drug of choice in the treatment of urticarial BP.

The long duration of symptoms until a correct diagnosis was made (4 years) indicates that knowledge of the different appearances of BP is crucial especially when the clinical presentation is doubtful and in the absence of blistering in non-bullous pemphigoid which makes the diagnosis hard for clinicians leading to misdiagnosis and treatment delay. Hence, it is important to highlight the urticarial variant of BP and to raise awareness among physicians so they have a high index of suspicion for non-bullous pemphigoid and a low threshold for investigating it, this will subsequently allow early recognition and treatment for those patients.

4. Conclusion

In conclusion, BP can be presented with atypical manifestations. Urticarial BP is a rare variant of non-bullous pemphigoid that should be taken into consideration in the differential diagnosis of atypical urticarial wheals not responding to systemic antihistamines or biological therapy.

Disclosure

This study is an independent study and not funded by any of the drug companies.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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