

BULLOUS PEMPHIGOID - A CASE REPORT

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ABSTRACT

Bullous pemphigoid is a blistering eruption characterized by large, tense bullae on the flexor surfaces, trunk, and intertriginous regions. Bullae may arise on an inflammatory urticarial base or on previously normal skin. It is classified as a type II hypersensitivity reaction, with the formation of anti-hemi-desmosome antibodies. Occurs primarily in the elderly. Childhood bullous pemphigoid may affect infants, may be localized to vulva in girls.

KEYWORDS: Bullous pemphigoid, blisters, autoimmune, vesicles, bullae, elderly, adults, rare, auto-antibodies, sup-epidermal.

INTRODUCTION

Bullous pemphigoid (BP) is a rare, autoimmune, chronic skin disorder characterized by blistering, urticarial lesions (hives) and itching. Less commonly these blisters can involve the mucous membranes including the eyes, oral mucosa, esophagus and genital mucosa. It typically presents in older adults as a generalized intensely itchy blistering skin condition. We will discuss a case of bullous pemphigoid in this case report which is a rare entity.

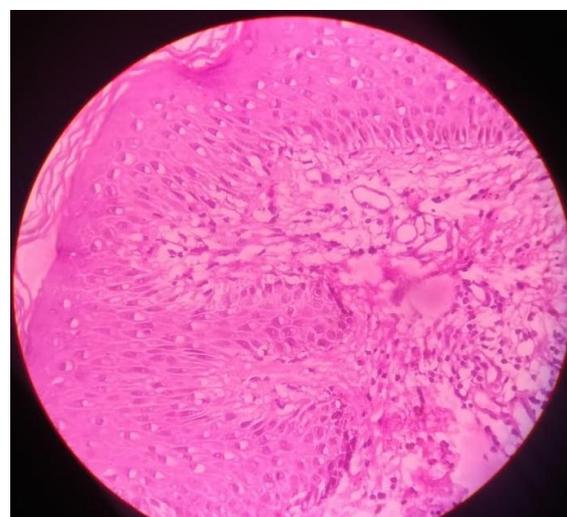
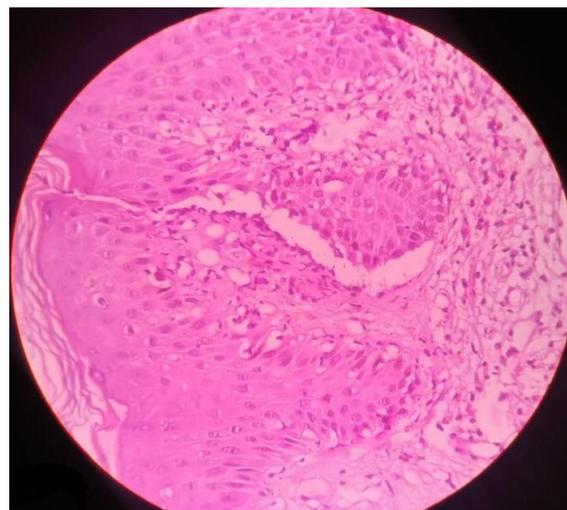
CASE REPORT

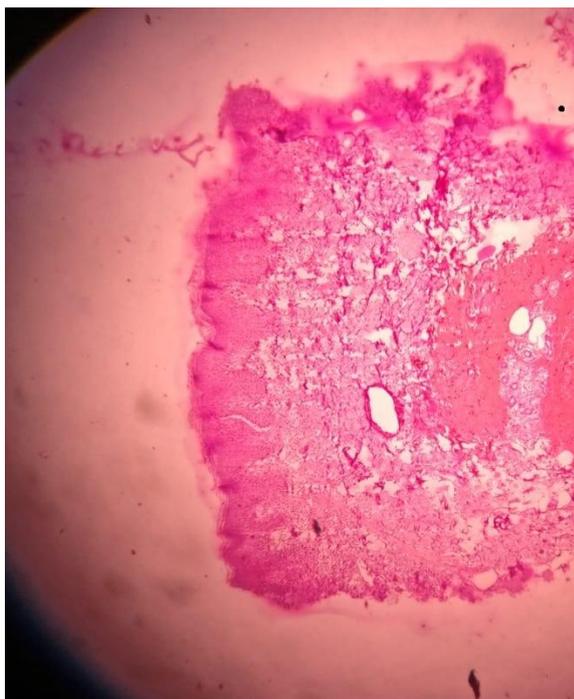
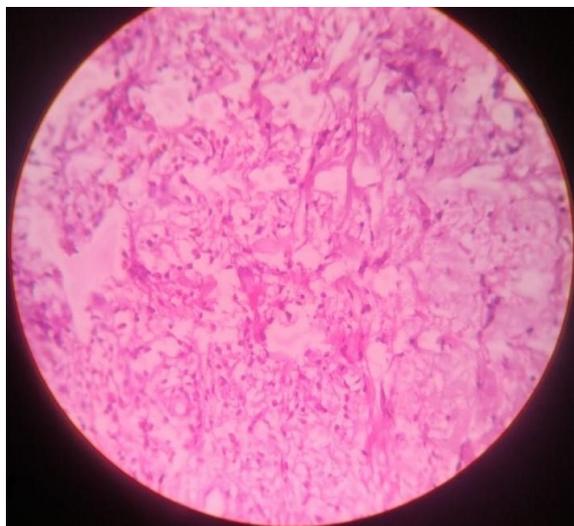
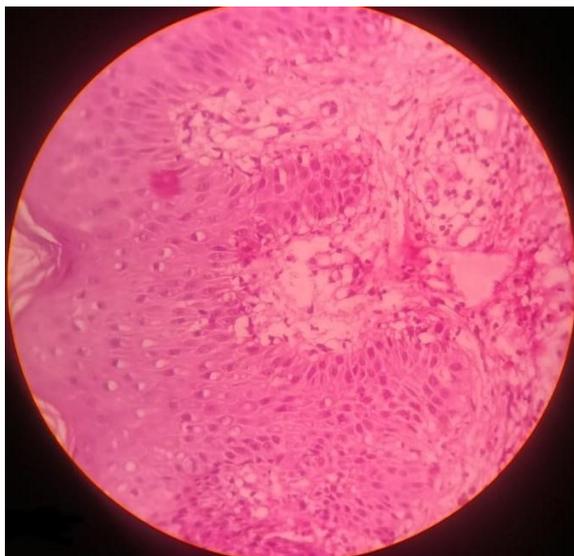
51 yrs old female came to the OPD with a history of multiple fluid filled lesions present all over the body associated with itching and burning sensation since 10 days. 4mm punch biopsy was taken from the blisters present on the right hand and sent for histopathological examination.

Pathology

Gross Description: Received a single greyish-white punch biopsy specimen measuring 1cc in volume which was all embedded.

Microscopic features: Section showed epidermis with sub-epidermal vesicles, basal cell vacuoles degeneration and papillary dermis. Capillaries surrounded by lymphocytes and eosinophils are seen in papillary dermis and superficial dermis.





DISCUSSION

Bullous Pemphigoid is a common sub-epidermal, blistering, autoimmune disease of skin due to IgG antibodies to the hemidesmosomal antigens - Bullous pemphigoid antigen 1 and 2. Patients present with tense bullae, which do not rupture easily, on an erythematous base. Sub-epidermal blister with eosinophils and superficial dermal edema are essential features. Direct immunofluorescence (DIF) shows linear IgG (usually IgG4) and complement deposits at the basement membrane zone with n-serrated pattern.

Epidemiology

- Incidence of 10-5 new cases per million people per year but depends on age of population since incidence significantly increases after age 70 years.
- Accounts for 80% of subepidermal autoimmune bullous diseases.

Etiology

- Autoantibodies generated against BP1 antigen (230 kD, hemidesmosome desmoplakin 1 and 2) and BP2 antigen (180 kD **type XVII collagen**), both hemidesmosome and lamina lucida).
- Emerging side effect associated with the use of checkpoint inhibitors like Pembrolizumab and Nivolumab A.
- Can be induced by other medications like Efalizumab and Etanercept

Pathophysiology

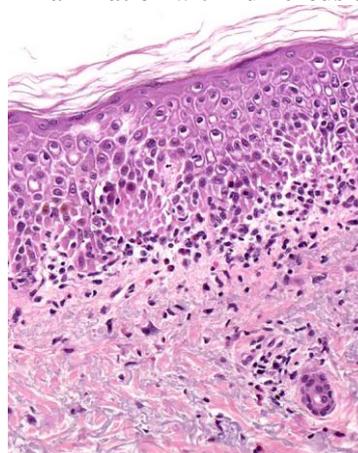
The bullae are formed by an immune reaction, initiated by the formation of IgG autoantibodies targeting Dystonin, also called Bullous Pemphigoid Antigen 1 and/or type XVII collagen, also called Bullous Pemphigoid Antigen 2 which is a component of hemidesmosomes. A different form of dystonin is associated with neuropathy Following antibody targeting, a cascade of immunomodulators results in a variable surge of immune cells, including neutrophils, lymphocytes and eosinophils coming to the affected area. Unclear events subsequently result in a separation along the dermoepidermal junction and eventually stretch bullae.

Clinical features

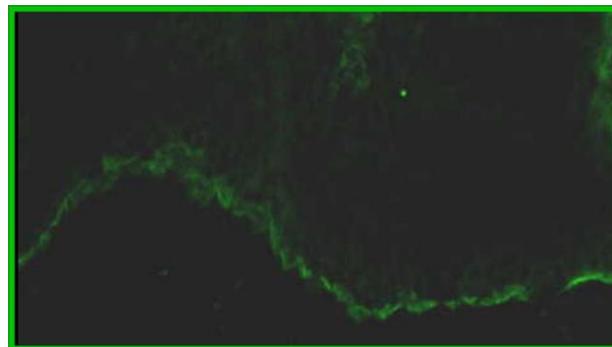
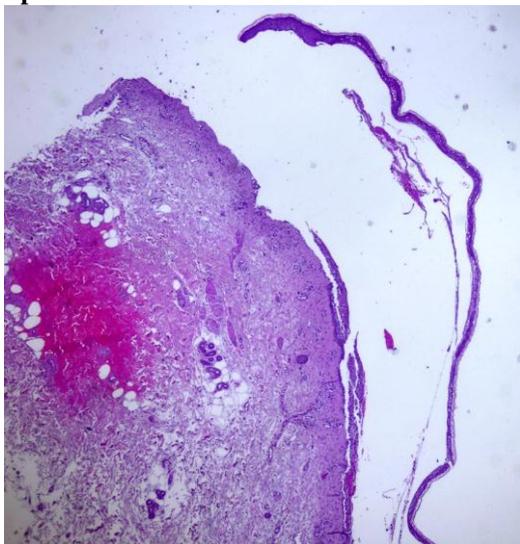
- Multiple tense bullae of different sizes on flexor surfaces, trunk, intertriginous regions and mucosa
- Bullae don't rupture easily and heal without scarring
- Can develop on normal or erythematous skin
- Oral lesions present in 10% - 40%
- May flare up after years without symptoms.

Clinical images**Histopathology**

- The initial abnormality consists of sub-epidermal edema. The subsequent separation of the epidermis from the papillary dermis results in the formation of a sub-epidermal bullae.
- Eosinophils, lymphocytes, and neutrophils comprise most of the inflammatory cells in and around the bullae.
- Unilocular, sub-epidermal, non-acantholytic blisters with festooning (suspended in a loop between two points) of dermal papillae, infiltrate including eosinophils located in blister cavity and in the dermis.
- Mild interface changes can be seen in early or prodromal lesions
- In established lesion, the changes are mostly inflammatory cell rich, may become neutrophil-rich.
- Eosinophilic microabscesses and rarely neutrophilic microabscess are seen.
- Eosinophilic spongiosis may be seen in clinically erythematous skin bordering the lesion.
- Eosinophilic "flame figures" can be rarely seen.

Superficial inflammation with numerous eosinophils**Adjuncts to Microscopic Diagnosis**

Linear deposits of IgG and C3 are found along the basement membrane zone in both bullous pemphigoid and cicatricial pemphigoid on direct immunofluorescence examination.

Sub-epidermal bullae**CONCLUSION**

Diagnosis consist of at least 2 positive results out of 3 criteria (2-out-of-3 rule):

- (1) pruritus and/or predominant cutaneous blisters, (2) linear IgG and/or C3c deposits (in an n- serrated pattern) by direct immunofluorescence microscopy (DIF) on a skin biopsy specimen, (3) positive epidermal side staining

by indirect immunofluorescence microscopy on human salt-split skin (IIF SSS) on a serum sample. Routine H&E staining or ELISA tests do not add value to initial diagnosis.

Treatments include class I topical steroids (clobetasol, halobetasol, etc.) which in some studies have proven to be equally effective. However, in difficult-to-manage or widespread cases, systemic prednisone and powerful steroid free immunosuppressant medications, such as methotrexate, azathioprine or mycophenolate mofetil, may be appropriate. The anti-CD20 monoclonal antibody rituximab has been found to be effective in treating some otherwise refractory cases of pemphigoid.

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