Bullous pemphigoid: Case report and review of literature

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Πομφολυγώδες πεμφιγοειδές: Αναφορά περίπτωσης και ανασκόπηση της βιβλιογραφίας

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Case report
Αναφορά περίπτωσης

SUMMARY: Bullous pemphigoid (BP) is an autoimmune bullous disease characterized by subepithelial blistering mostly affecting elderly but may be seen in all ages. A 52-year-old female patient came with a chief complaint of itching, redness and ulcer in the hands and oral cavity for the past 2 weeks. The examination revealed ulcerated lesions in palate and buccal mucosa. Erythematous lesions were also seen in upper limb. Incisional biopsy was done and histological examination revealed bullous pemphigoid. The patient was immediately started with systemic and topical steroids and was continued for 3 weeks. The extra-oral lesions were healed and intraoral ulcerations subsided after 3 weeks.

KEY WORDS: Autoimmune bullous disease, ulcerated lesions, steroids.

ΠΕΡΙΛΗΨΗ: Το πομφολυγώδες πεμφιγοειδές (BP) είναι μια αυτοάνοση φυσαλιδώδης νόσος που χαρακτηρίζεται από την παρουσία μεγάλων τεταμένων πομφολύγων επί εδάφους ερυθηματώδους εξανθήματος κυρίως σε ηλικιωμένους ασθενείς αλλά μπορεί να παρατηρηθεί σε όλες τις ηλικίες. Μια 52χρονη γυναίκα ασθενής ήρθε με ένα κύριο παράπονο κνησμού, ερυθρότητας και έλκους στα χέρια και στη στοματική κοιλότητα τις τελευταίες 2 εβδομάδες. Η εξέταση αποκάλυψε ελκωτικές βλάβες στην υπερώα και στο στοματικό βλεννογόνο. Ερυθηματώδεις αλλοιώσεις παρατηρήθηκαν επίσης στο άνω άκρο. Έγινε βιοψία και η ιστολογική εξέταση αποκάλυψε πομφολυγώδες πεμφιγοειδές. Η ασθενής ξεκίνησε αμέσως συστηματική και τοπική αγωγή με στεροειδή που συνεχίστηκε για 3 εβδομάδες. Οι εξω - στοματικές αλλοιώσεις υφέθηκαν και τα ενδοστοματικά έλκη υποχώρησαν μετά από 3 εβδομάδες.

ΛΕΞΕΙΣ ΚΛΕΙΔΙΑ: Πομφολυγώδες πεμφιγοειδές, Αυτοάνοση φυσαλιδώδης νόσος, ελκωτικές αλλοιώσεις, στεροειδή.

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INTRODUCTION

Bullous pemphigoid (BP) is an autoimmune bullous disease characterized by subepithelial blistering common in elder patients but can also be seen in all ages. The incidence of the disease is 3 per 100,000 persons in a year.[1] Large blisters on skin and oral erosions are the most common characteristics associated with BP and these blisters appear on normal or inflamed skin.[2] Most patients with BP have circulating autoantibodies directed against one of two hemidesmosomal proteins (BP180 and BP230). The risk factors of BP include old age, neurologic diseases and some particular drugs, including furosemide and spironolactone, NSAIDs, amoxicillin, PD1/PD-L1 inhibitors, gliptins, and TNF-alpha inhibitors.[3] Drug induced bullous pemphigoid occurs up to 3 months after medication initiation and is usually noted during a younger to older subset of patients. The diagnosis is mainly based on the clinical features and the histhopathological features.[4] Using direct and indirect immunofluorescence the circulating and in situ autoantibodies directed against hemidesomsomal proteins can be visualized. Using ELISA, immunoprecipitation and immunoblotting Serum anti-BP180 and anti-BP230 autoantibodies are quantified.

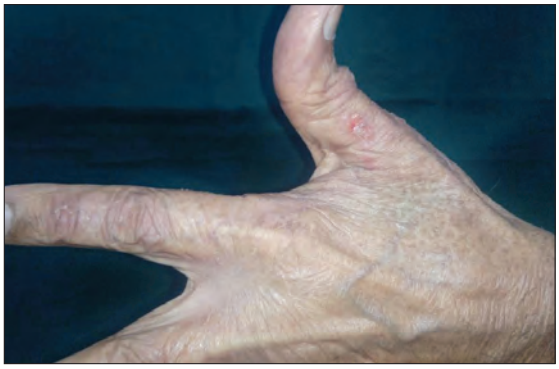

Fig. 1: Pruritic crusted erythematous papules on the skin.

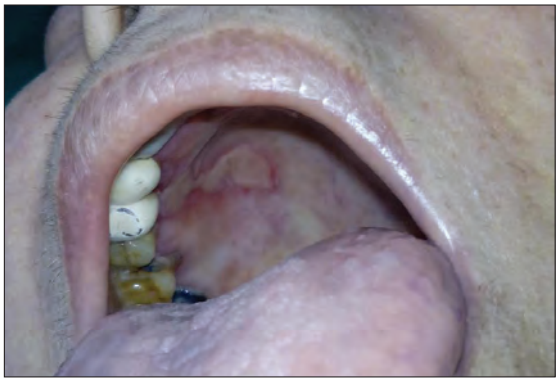

Fig. 2: Severe involvement of the palate with desquamation and ulceration.

Table 1
Outline of Bullous pemphigoid

Etiology	Clinical diagnosis	Lab diagnosis	Differential diagnosis	Current treatment types
The Bullous pemphigoid can occur due to • The autoantibodies directed against proteins arranged at the dermal-epidermal junction • It can also occur when taking systemic medications. The lesions start to appear up to three months after taking systemic medications. • The systemic medications which cause BP induced eruptions are furosemide and spironolactone, NSAIDs, amoxicillin, PD-1/PD-L1 inhibitors, gliptins, and TNF-alpha inhibitors.	• BP is characterized by highly pruritic urticaria-like or erythematous lesions on which tense blisters may develop over a period of time. The patients usually develop vesicles which may progress to large blisters with clear fluid and blood. • The lesions are present on the trunk and the flexor surface of the extremities and are less common in head and neck region. • The Nikolsky sign is negative. But positive nikolsky sign is also seen in some cases and hence in those cases BP should not be ruled out.	When BP is suspected two biopsies should be taken one for histopathologic examinations and other for direct immunofluorescence study (DIF). • The histopathology examination shows subepidermal clefting and an inflammatory infiltrate mainly consisting of eosinophils. • The characteristic DIF picture in BP is a linear deposition of IgG and or C3 along the basal membrane. Other immunoglobulins, including IgA, IgM and IgE, may also be present. • Another histologic feature described as characteristic of BP is an n-serrated pattern of IgG deposition.	1. Dermatitis herpetiform 2. Epidermolysis bullosa 3. Linear IgA dermatosis 4. Mucous membrane pemphigoid 5. Erythema multiforme	Mild and moderate -Topical clobetasol Severe disease - Combined with systemic treatment, (a) prednisolone (b) an immunomodulant, e.g., dapsone or doxycycline, or (c) prednisolone plus an immunomodulant.

CASE REPORT

A 52-year-old female patient came with a chief complaint of itching, redness and ulcer in the hands and oral cavity for the past 2 weeks. These ulcers were seen initially in the palate (Figure-1) and buccal mucosa. Later the patient noticed small blisters in the upper limb which crusted in a week (Figure-2). The patient's medical history revealed that the patient was a type II diabetic and also hypertensive for the past 2 years and was under medication for the same. The patient was taking Glimepiride (2mg) + Metformin (100mg) (Glycomet gp2 forte) and Vildagliptin (V Small). The patient's dental history revealed patient underwent endodontic treatment 5 years back.

Investigation - Liver and renal function tests and complete blood count, HbA1c was ordered and no abnormality was detected. The hemoglobin A1c level was less than 7 percent. Nikolsky sign was absent. Incisional biopsy was taken and was sent to histhopathological examination. Histhopathological examination revealed parakeratinized stratified squamous epithelium with subepithelial split. Basal cells were intact with surface epithelium. Areas of subepithelial inflammatory cell infiltrate were seen particularly lymphocytes. In the connective tissue region bundles of collagen fibers and extravasated red blood cells are seen. A diagnosis of bullous pemphigoid was made. Direct immunofluorescence was done for the confirmation. The patient was prescribed Tab prednisolone 20mg twice daily for 1 week and the dose was tapered to 10mg for 2 weeks, Tab betamethasone 0.5 mg for swish and spit once daily, ointment Clonate-F cream to be applied twice daily on the affected area on the skin. Systematic steroids were stopped after 3 weeks. The extra-oral lesions were healed and intraoral ulcerations subsided after 3 weeks. The patient was followed up for 3 months and no recurrence of the lesions were seen.

DISCUSSION

Bullous pemphigoid (BP) is the most common autoimmune subepidermal blistering disease which most commonly seen in elder population but can also be seen in all ages which has got no gender predilection. It all starts with an itching which can last for months to years and it is usually seen in the lower extremities. Tense blisters develop on normal or inflamed skin in chest, proximal extremities and/or abdomen.[6] The blister wall is usually thick, cannot be broken that easily. Physical examination shows a negative Nikosky's sign. The precipitating factors include ultraviolet (UV) light, either UVB or psoralen with ultraviolet A (PUVA), radiation therapy and also due to certain drugs such as urosemide and spironolactone, NSAIDs, amoxicillin, PD1/PD-L1 inhibitors, gliptins, and TNF-alpha inhibitors.[7] The summary of bullous pemphigoid is shown in Table 1.

Oral bullae rupture rapidly and forms erosions mainly in buccal mucosal surface, palate, gingiva, tongue and lower lip. Generally, the oral lesions of bullous pemphigoid are slow growing and less painful than pemphigus vulgaris. Differential diagnosis of bullous pemphigoid includes erosive form of lichen planus, Pemphigus vulgaris and other subepithelial bullous lesions. The erosive and ulcerative forms of lichen planus frequently exhibit white Wickham striae at the periphery along with ulcerations and erosions.[8] PV usually has more extensive erosion of mucosa and skin involvement.[9] The characteristic Direct immunofluorescence picture in BP is a linear deposition of IgG and or C3 along the Basement membrane. Other immunoglobulins, including IgA, IgM and IgE, may also be present. Another histologic feature described as characteristic of BP is an n-serrated pattern of IgG deposition. A predominance of IgG deposit intensity would suggest another diagnosis, such as epidermolysis bullosa acquisita. A small percentage of patients with BP have C3 deposits only 12

The topical steroids clobetasol and betamethasone can be used for localized oral lesions. The patients need systemic steroids and immunosuppressive drugs such as azathioprine, mycophenolate and rituximab only in the extensive course of disease. Antibiotics such as tetracycline, doxycycline, minocycline can be given in the case of moderate course of the disease.[10] BP is a chronic disease and hence the patients should be followed till the lesions are completely healed. Patients should be looked for any drug side effects and also to make sure their symptoms are controlled. Once the disease is stable an attempt to stop the treatment at 2 to 5 intervals should be done.[11]

CONCLUSION

Based on the clinical examination, histologic and immunofluorescence features, a diagnosis of bullous pemphigoid is made. Corticosteroids (both topical and systemic) are used predominantly among the various immunomodulatory drugs preferred. Routine follow-up is necessary in order to prevent the exacerbations and remissions.

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