Drug associated bullous pemphigoid in oral cavity

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Abstract

Bullous pemphigoid is an autoimmune skin disease characterized by large tense blisters with solitary oral manifestation a rarity. We report a case of 48-year-old male with chief complain of wound on the left side of mouth with history of hydrochlorothiazide use. On intraoral examination, desquamation was present in palatal gingiva which was tender on palpation. Biopsy of the lesion on histopathology reported oral pemphigoid. On immunofluorescence test linear deposits of C3 and immunoglobulin G was found. This showed that importance of complete history with histopathology and immunofluorescence test is must for early diagnosis and treatment is essential for prevent further dermatological progression.

Keywords: Bullous pemphigoid, hydrochlorothiazide, immunofluorescence

Introduction

Bullous pemphigoid (BP) is a subepidermal immunobullous disease most prevalent in elderly patients. It is an autoimmune disease where autoantibodies are directed against antigen or glycoproteins specifically BP180 or BP230 located on hemidesmosomes at lamina lucida of basement membrane causing sub-basilar split. Skin disease is characterized by large tense blisters with oral manifestation in about 10–20% of the cases. The pemphigoid lesion occurring in the mucosa of oral cavity is the mucous membrane pemphigoid while oral cavity is spared in case of BP. Independent oral manifestation of BP is rare. However, here we present a case of oral BP lesion.

Case Report

A 48-year-old male, Mr. Kumar from Bihar, India presented to our department with chief complaint of wound in the mouth since 6 months. It was chronic in onset, constant in progression, non-painful with no history of bleeding or discharge. There was previous history of on and off blisters in the lip. Patient was taking amlodipine 5 mg once daily since 2 year and hydrochlorothiazide 2.5 mg once daily since 1 month.

On intraoral examination, erosion of irregular shape and size of about 3.5 cm in length and 1 cm in breadth at greatest dimension were present in the palatal gingiva from 25 extending 0.5 mm beyond 28, with erythema of the surrounding tissue and involving marginal, interdental papilla, and attached gingiva [Figure 1]. On palpation the lesion was tender and non-indurated, Nikolsky Sign and Bulla spreading sign was negative. Gel. QUADRAGEL® local application thrice a day was prescribed for 1 week long with appointment for biopsy. On laboratory investigation, erythrocyte sedimentation rate was elevated (35 mm/h). Incisional biopsy was done with COE-PAK®. Histopathological reported parakeratinized stratified squamous epithelium with sub-basilar split suggesting oral pemphigoid lesion. On direct immunofluorescence linear immune deposits of immunoglobulin G (IgG) and C3 along the dermoepidermal junction was seen [Figure 2].

Discussion

BP is a chronic mucocutaneous disease which can manifest from the oral cavity and spread to the skin and other mucous membranes. It can be life-threatening immunopathologic dermatologic disease. In general, BP occurs in elderly patient from sixth to seventh decades.[1] Our patient was just 48 years old. In our case, age factor is suggestive of deviation from classical BP.

From the drug history, it was identified that patient recently started using hydrochlorothiazide since 1 month as his blood pressure medication. Drug-associated BP (DABP) is a term used to describe instances of BP demonstrating clinical, histological, or immunopathological features identical or similar to those
of the idiopathic form of the disease. DABP may be associated with the systemic ingestion or topical application of particular drugs. In our case, age factor is suggestive of deviation from classical BP. Over 90 agents have been implicated as a cause of DABP, including diuretics, ACE inhibitors, and antibiotics. Among them, diuretics are the frequent cause of DABP which can be the possible cause BP arises when autoantibodies are generated against two hemidesmosomal proteins, BP230 and BP180. This leads to the activation of the complement cascade, inflammatory cell migration, and formation of subepithelial bullae. Immunological mechanism suggested in a case of BP induced by the non-thiol drug was induction of autoantibodies by directly binding to the 180-kilodalton BP antigen (BPAG2) in the BMZ resulting in an alteration of its antigenic properties.

Direct immunofluorescence is found to be the gold standard test. Direct immunofluorescence shows the presence of IgG and C3 deposits along the basement membrane zone. Histopathological report reveal sub-basilar split which is the same result as in our case. Our case resembles most of the observed difference between DABP and idiopathic BP as given by Verheyden et al.

Thus, the conclusive diagnosis of DABP was arrived on the basis of history, clinical presentation, and immunological findings.

Recommended dosage for oral prednisolone is 0.3–1.25 mg/kg body weight/day, controls disease within 1–2 weeks, followed by which the dose is tapered. In our case, initial use of topical triamcinolone was found ineffective which can be due to causative drug still in systemic circulation. Along with change of drug regimen for controlling patient’s blood pressure, tapered steroid regimen of oral prednisolone starting with 60 mg once daily was started for 1 week and after which it was gradually tapered in course of 5 weeks. Complete resolution was observed at the end of 6 weeks [Figure 3].

Conclusion

DABP although rare in occurrence, poses severe life-threatening changes if undiagnosed at early stage. Oral manifestation of DABP, if present, is difficult to diagnose as similar lesion can be seen in other vesiculobullous disorders like mucous membrane pemphigoid. Complete history with histopathology and immunofluorescences test is must for diagnosing BP and differentiating it from DABP and preventing further progression of disease.

References

1. Glick M. Burket’s Oral Medicine. 12th ed. Connecticut: PMPH; 2015.
2. Verheyden MJ, Bilgic A, Murrell DF. A systematic review of
drug-associated bullous pemphigoid. Acta Derm Venereol 2020;100:adv00224.
3. Schmidt E, Zillikens D. Immunoabsorption in dermatology. Arch Dermatol Res 2010;302:241-53.
4. Kim RH, Brinster NK. Practical direct immunofluorescence. Am J Dermatopathol 2020;42:75-85.