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Case Study

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PEMPHIGUS VULGARIS: CASE WITH DIAGNOSTIC DILEMMA

[1*]Dr. Debarati Deb, [2]Dr. Rupam Sinha, [3]Dr. Subhadeep Maity, [4]Dr. Harshvardhan Jha, [5]Dr. Mainak Datta, [6]Dr. Sthita Datta

[1,5,6]Post Graduate Trainee, [2]Professor and HOD, [3]Assistant Professor, [4]Assistant Professor
Department of Oral Medicine and Radiology, Haldia Institute of Dental Sciences and Research, Haldia, West Bengal.

***Corresponding Author: Dr. Debarati Deb**

Post Graduate Trainee, Department of Oral Medicine and Radiology, Haldia Institute of Dental Sciences and Research, Haldia, West Bengal.

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ABSTRACT

Pemphigus Vulgaris is an autoimmune disease which can cause blistering of the skin and mucous membrane; they are fragile and break away leaving extremely painful erosions. The mechanism behind this is the binding of immunoglobulin G(IgG) autoantibodies to desmoglein(DSG) 1 & 3. Histological feature shows intraepithelial cleft and Tzanck cells. In these case reports; we discussed two cases of pemphigus vulgaris in oral cavity with their clinical manifestations. We have also reported the effect of treatments after two consecutive recalls where the patient got satisfactory relief from their previous signs and symptoms.

KEYWORDS: Autoimmune, desmoglein, pemphigus, corticosteroid.

INTRODUCTION

Pemphigus is a chronic autoimmune disease characterized by blistering in the epithelium affecting mucocutaneous surfaces. The term is derived from the Greek word 'pemphix' in 1971 by Wichman, which means bubble or blister. In pemphigus; IgG autoantibodies are higher against desmoglein (DSG) 1 & 3 which binds the stratified squamous epithelial cells together. It can be classified into: pemphigus vulgaris, pemphigus vegetans, pemphigus erythematosus, pemphigus foliaceus, paraneoplastic pemphigus, Fogo selvage, Herpetiform pemphigus and IgA pemphigus. Among them, pemphigus vulgaris is the most common which is subclassified into: mucosal-dominant, mucocutaneous and cutaneous types. In Paraneoplastic pemphigus, autoantibodies are directed against both DSG 1 and DSG 3 and in Fogo selvage, IgG autoantibodies are directed against DSG 1.[1] Incidence of pemphigus vulgaris is rare (0.1-0.5 cases /1000000 per year and has a slight predilection to women. primarily seen in adults during the 5th or 6th decade of life.[2] We describe two cases of oral pemphigus vulgaris and their management followed by a review of the current literature.

CASE REPORT

A 38 years old male patient (Case-1) and a 60 years old female patient (Case-2) reported to the department of Oral medicine and radiology; with the chief complaints of continuous burning sensation in the whole mouth since 15 days. The past medical and dental history of Case-1 were non-contributory but in case-2, the patient had Diabetes and Rheumatoid arthritis for which she was taking medications.

On extraoral examination in Case-2, diffused ulcerated areas were seen with ruptured blisters and crusted surface, superadded by whitish fungal infections on the hands, elbows and legs[Figure-1A,B,C]. On intraoral inspection, Case 1 showed diffuse ulcerated areas on buccal mucosa with involvement of palatal region. The ulcers were erythematous in buccal mucosa and palate [Figure-2 A,B,C]. In case -2, diffuse multiple ulcerated areas with ruptured blisters were seen on right and left buccal mucosa with involvement of lower labial mucosa and hard palatal region. The ulcers were erythematous with whitish superadded fungal infections. [Figure-3 A,B] On palpation, the ulcerated areas were tender, with diffuse margin and bleeding under provocation in both the cases.

Based on the above mentioned clinical features in both the cases; provisional diagnosis of Pemphigus Vulgaris was given with differential diagnosis as Bullous Pemphigoid, and Erythema Multiforme.

Complete haemogram were advised along with Immunoglobulin Assay. The haematological reports was normal and IgE level was increased in both cases. However, in case-2 the blood sugar level was high.

Incisional biopsy specimens were taken from buccal mucosa in both the cases and were sent for histopathological analysis.H/P report revealed superficial parakeratinized squamous epithelium with moderate acantholysis and suprabasilar split along with the stromal tissues which show profuse extravasated RBC and large, rounded keratinocytes with a hypertrophic nucleus and a

perinuclear halo suggestive of Tzanck cells.[Figure- 4 A,B]. Under the direct immunofluorescence assay, intercellular deposition of immunoglobulin G showing characteristic "fish‑net appearance". [Figure-5]

Based upon all the clinical and histopathological features, Pemphigus vulgaris was given as the final diagnosis in both cases.

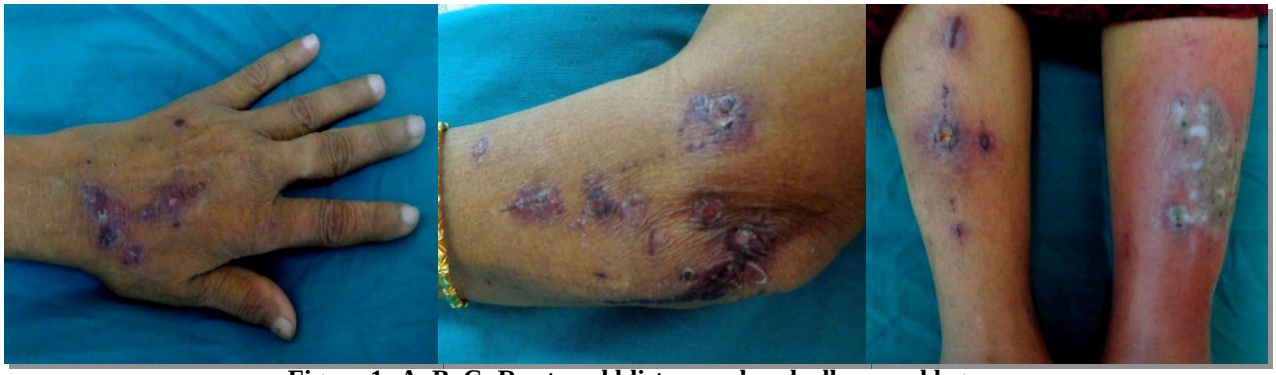

Figure 1: A, B, C: Ruptured blisters on hand, elbow and legs.

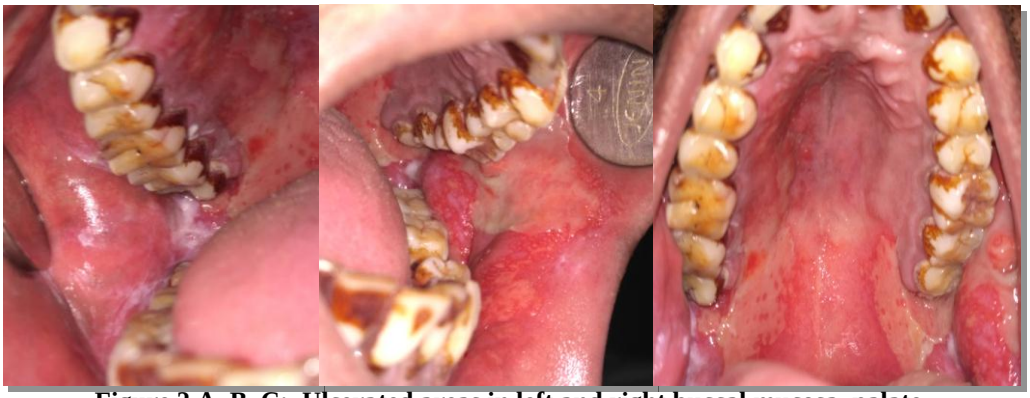

Figure 2 A, B, C: Ulcerated areas in left and right buccal mucosa, palate.

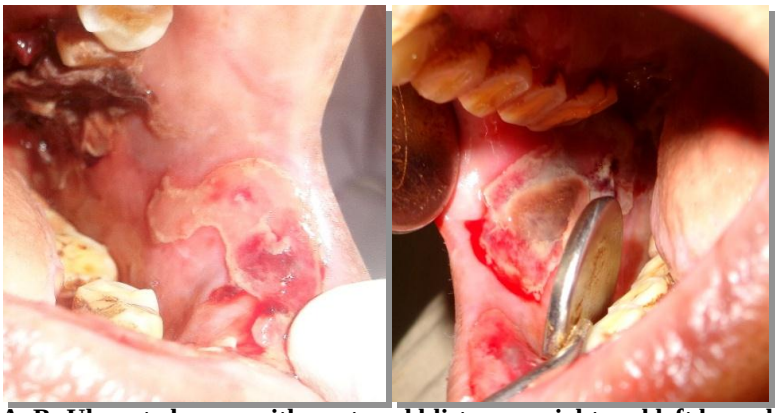

Figure 3 A, B: Ulcerated areas with ruptured blisters on right and left buccal mucosa.

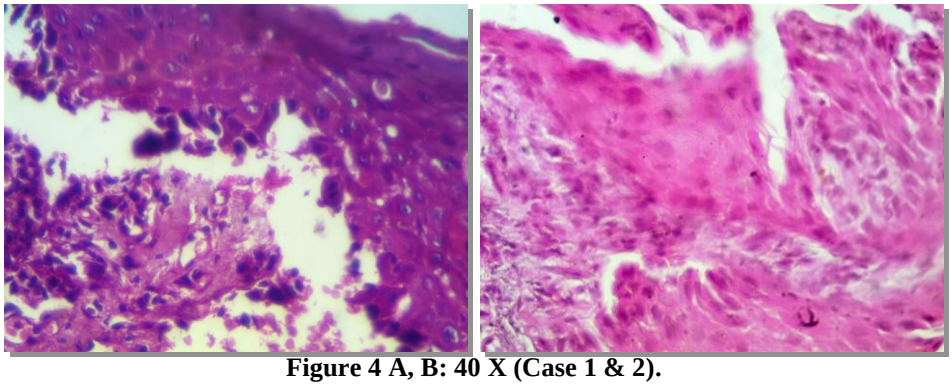

Figure 4 A, B: 40 X (Case 1 & 2).

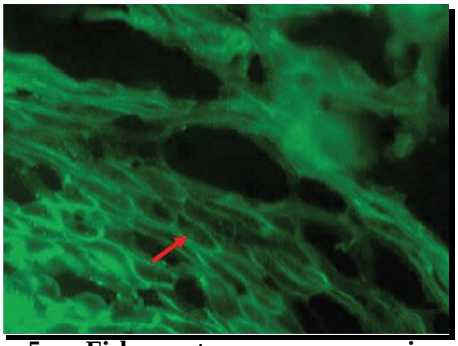

Figure 5: Fish net appearance in direct immunofluorescence.

Treatment plan was given as followes

In case -1, Systemic prednisolone -20mg thrice daily (1mg/kg/day) was advised for 15 days followed by tapering dose for another 1 month. In case-2 , as the patient had diabetes, we could not advised her any systemic corticosteroids, instead we have given systemic antifungal Iatraconazole(200mg)once daily for 7 days and Prednisolone (20mg) mixed with 20 ml water for swish and spit twice daily for 1 month. For the extraoral ulcerations we gave her ointment of Beclomethasone (0.025%) and Neomycin (0.5%) and Clotrimazole (1%) mixed in equal proportion to be applied thrice daily for 1 month. Ointment of Triamcinolone acetonide (0.1%) was advised to be applied in the affected intraorl areas after meals for a period of 1 months. Ointment of antiseptic, analgesic, anaesthetic gel to be applied intraorally thrice daily in the affected areas for a period of 1 month and Vitamin supplement once daily for 30 days were also advised in both cases. Follow up were done in 15,30 and 60 days intervals which showed a good prognosis of the disease in both the cases. [Figure 6 & Figure 7]

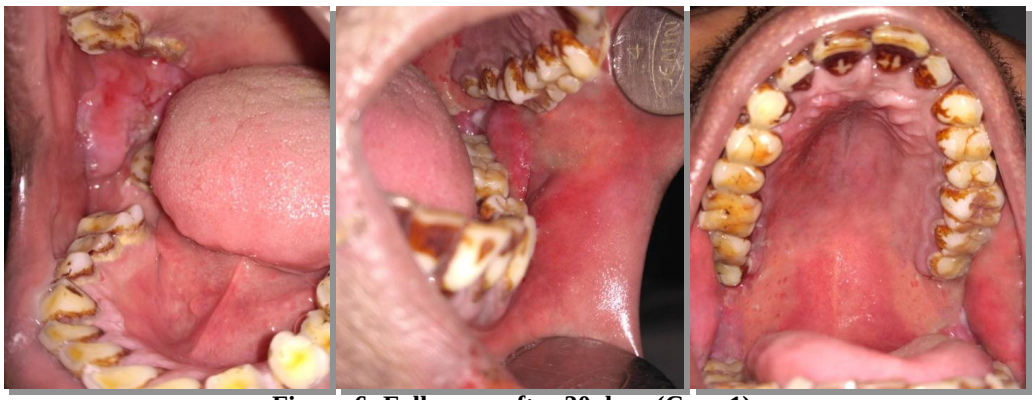

Figure 6: Follow up after 30 days (Case-1).

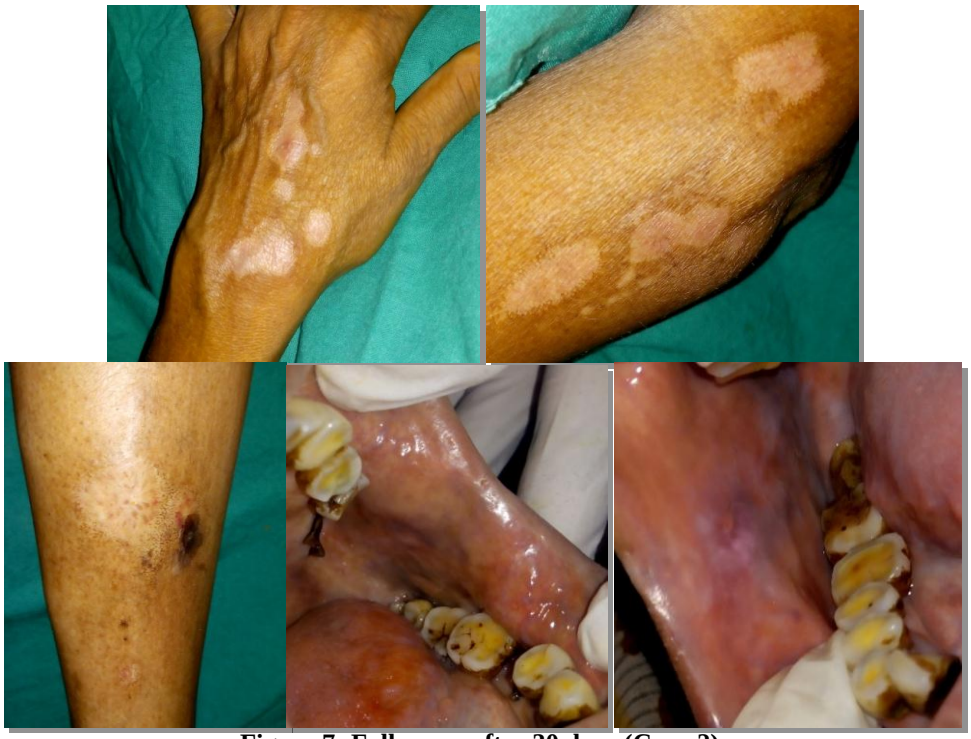

Figure 7: Follow up after 30 days (Case-2).

DISCUSSION

Pemphigus is characterized by mucocutaneous intraepithelial blisters formation and erosions, mediated by circulating IgG autoantibodies raised against desmogleins 1 and 3, causing acantholysis.[3] These desmoglein proteins help in maintaining the intercellular adhesion within stratified squamous epithelium. Acantholysis is the basic pathophysiology behind pemphigus which is of two types; primary and secondary depending upon damage to the desmosomes. Pemphigus shows primary acantholysis.[4] Several HLA alleles have been identified as risk factors in pemphigus such as; HLA-DRB1*0402, HLA-DRB1*1401, HLA-DRB1*1404 and HLA-DQB1*0503.[5] It is also linked to the secretion of key inflammatory molecules (TNF, IL-1α and IL-6) by keratinocytes after autoantibody binding.[6] Other environmental factors are some drugs (penicillamine, captopril) which causes acantholysis, herpes simplex virus, some dietary habits and physiological and psychological stress.[7] In our cases the patients had painful oral ulcers casuing burning sensation and difficulty in chewing food. The first sign appears on oral cavity before skin and other mucosal sites. Skin lesions present as flaccid fluid filled blisters which break to form large denuded areas. Pemphigus can be misdiagnosed clinically as pemphigoid or other vesiculobullous lesions. Therefore; the biopsy and histopathology remains the gold standard for diagnosis. In general terms the histopathological specimen of pemphigus shows suprabasillar splits and Tzank cells. In recent times, immunofluorescence assay has become the new diagnostic tool for this disorder. In direct immunofluoresences, IgG antibodies and complement C3 protein deposit on cell surface in a fishnet pattern. Highly specific and sensitive ELISA can also detect the autoantibodies in pemphigus.

The treatment is always corticosteroids in both systemic and local forms in tapering doses such as Predisolone in systemic form and Triamcinolone acetonide (0.1%) in local form. The tapering of prednisolone is done by 25% every 2 weeks intervals and when the dose reaches <20 mg tapering should be slower. In those cases a reduction of 5 mg with 4 weeks intervals should be given.

Methylprednisolone(IV) in short-term high-dose could be given in refractory cases.[8] The other group of drugs which are used are Immunomodulators such as Mycophenolate mofetil and Azathioprine.[9] The latest drug is Rituximab (monoclonal antibody) which has shown very promising result by targeting CD20+ B cells.[10] Intravenous immunoglobulin present in human plasma, contains ≥95% IgG antibodies and only trace amounts of IgA or IgM can also be given in case of prmphigus.[11] In severe or refractory cases of pemphigus plasmapheresis can be effective . It means plasma exchange with albumin or fresh frozen plasma, or extracorporeal immunoadsorption with protein A, which binds with IgG.[12]

CONCLUSION

We dentists should be familiar with clinical presentation of Pemphigus vulgaris. If not treated quickly, it has a high morbidity rate (5%–10%). That is why an effective treatment procedure needs to be planned out to get a better prognosis with the purpose of minimal discomfort and decrease the morbidity rate of the patients.

Declaration of patient consent

The authors certify to obtain all the appropriate consent forms from the patients for their images and other clinical information to be reported in the journal.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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