TPM Vol. 32, No. S5, 2025
ISSN: 1972-6325
https://www.tpmap.org/

Open Access

DIAGNOSTIC PITFALLS IN A CASE OF ORAL PEMPHIGUS VULGARIS: CASE PRESENTATION WITH REVIEW AND UPDATE OF RECENT TREATMENT STRATEGIES

DR. SEETHALAKSHMI CHIRANJEEVI M.D.S
READER, DEPARTMENT OF ORAL MEDICINE AND RADIOLOGY, SREE BALAJI DENTAL COLLEGE, PALLIKARANAI, CHENNAI – 600100

DR. MARIA PRISCILLA WINCY M.D.S
SENIOR LECTURER, DEPARTMENT OF ORAL MEDICINE AND RADIOLOGY. SREE BALAJI DENTAL COLLEGE, PALLIKARANAI, CHENNAI – 600100

DR. ARAVINDHA BABU M.D. S
PROFESSOR & HEAD, DEPARTMENT OF ORAL PATHOLOGY, SREE BALAJI DENTAL COLLEGE, PALLIKARANAI, CHENNAI – 600100

AISHVARYA RUKMANI
SAVEETHA MEDICAL COLLEGE, SAVEETHA INSTITUTE OF MEDICAL AND TECHNICAL SCIENCES

ABSTRACT
Pemphigus is an autoimmune bullous disease clinically characterized by blistering and erosions of the skin and/or mucous membranes. Early lesions are manifested in the oral region in almost 50%-60% of the patients, which often hinders the diagnosis. Early diagnosis and treatment can significantly improve the course and prognosis of the disease. The present case report is on "Oral Pemphigus Vulgaris" which was diagnosed early and showed good clinical improvement. Since early lesions are manifested orally, dental professionals must have adequate knowledge and be familiar with clinical manifestation of pemphigus vulgaris to ensure early diagnosis and treatment, since this in turn determines the prognosis and course of the disease.

INTRODUCTION

"Diagnosis is not the end, but the beginning of practice". A right diagnosis leads to appropriate treatment, improved success outcomes, reduction of unnecessary medical expenses and psychological well-being. In a clinical scenario, there are times when a dentist may face a dilemma during the diagnosis. The present case report is on one such case on "Oral Pemphigus Vulgaris". Pemphigus Vulgaris belongs to the pemphigus group of autoimmune disorder. [1] It is potentially life-threatening and characterized by bulla and ulcers in the mucocutaneous region. Early lesions are manifested in the oral region in almost 50%-60% of the patients, and followed by the skin. Hence the oral lesions are often considered as the "first sign". [2,3] This often hinders the diagnosis. However, early diagnosis and treatment determine the course and prognosis of the disease.

CASE REPORT

A 38 year old female patient resident of Chennai, Tamil Nadu, reported with the chief complaint of pain and soreness in the mouth and difficulty in chewing solid food and liquids for the past one year. History revealed that the pain and soreness had progressively increased in severity in the past two months. At the time of presentation, the patient had noticed ulcers of the mouth which bled on brushing. Patient had visited another dentist and was prescribed lignocaine gel for topical application. However, the patient reports that there was no improvement in the pain or ulcer healing. The patient did not report skin lesions or involvement of other mucosal sites. Patient was known diabetic and under medication for the past two years (Tab. Metformin 500 mg, twice daily). A review of family history was

noncontributory. Patient gave no history of smoking, alcohol consumption or any deleterious habits. Patient also gave a history of difficulty in brushing for the past six months.

On general examination, the patient was moderately built. Intra-oral examination revealed ulcerative lesions present on bilateral buccal mucosa along the line of occlusion extending from retro commissural areas to the retromolar trigone posteriorly (Figure 1). Lesions extended superiorly from the line of occlusion and were irregular in shape covered by pseudomembrane with erythematous surrounding. On manipulation, bleeding was present. Similar lesions with irregular borders associated with flaacid bullae were present in the upper buccal vestibule in relation to molar region. Nikolysky's sign showed a positive reaction. Generalized teeth attrition, grossly decayed 46 and gingival inflammation with bleeding on probing were present.

The clinical presentation of chronic multiple oral ulcers, flaccid bullae and positive Nikolysky sign in this case led to provisional diagnosis of vesiculo-bullous lesion affecting the oral cavity. Pemphigus vulgaris, mucous membrane pemphigoid, bullous lichen planus, and para neoplastic pemphigus were considered for differential diagnosis.

Incisional biopsy was performed from perilesional site of the ulcer in relation to the right buccal mucosa. Histopathological examination revealed traces of basal cells and few suprabasilar cells of stratified squamous epithelium with underlying connective tissue stroma. The epithelium shows basal layer arranged in the row of tombstone appearance with prominent acantholysis and acantholytic cells are evident. The stroma is moderately collagenized with diffuse chronic inflammatory celI infiltrate. Numerous endothelial lined blood vessels engorged with RBCs are seen. Deeper connective tissue shows normal appearing muscle fibers and adipocytes. Based on the histopathological findings, a final diagnosis of pemphigus vulgaris was made

(Figure 2). However, confirmatory diagnosis was done with Direct Immunofluorescence (DIF). DIF showed prominent intercellular deposition of antibodies directed against IgG and C3(Figure 3)

A definitive diagnosis of PV was made based on clinical, histopathological and DIF findings. Initially, the patient was prescribed prednisolone tablets 20 mg, which were to be taken twice daily along with multi-vitamin. Topical application of Kenacort (triamcinolone gel, 0.1%) was recommended to be used twice daily on the oral sores. A gradual reduction of the areas of ulcerations on the buccal mucosa was seen. On the first follow-up, the patient had 50% reduction in symptoms with partial healing of lesions, erythema and inflammation in relation to ulcers had reduced. The oral hygiene of the patient was monitored and scaling and root planing was done once the condition improved. After 2 months, (Figure 4) the dose was tapered to 10 mg, twice daily. Over the past 6 months, prednisolone was gradually tapered down as there was complete regression of the lesions.

DISCUSSION

Pemphigus is a group of potentially life-threatening, autoimmune, blistering diseases of the skin and mucous membranes. It is characterized by acantholysis (loss of keratinocyte to keratonicyte adhesion), which is induced by circulatory autoantibodies to intercellular adhesion molecules.[4-6] In pemphigus vulgaris, it is the binding of IgG autoantibodies to desmoglein 3, a transmembrane glycoprotein adhesion molecule present on desmosome, leading to seperation of cells. The oral mucosa is the initial site of involvement in 70%-90% of the cases before involvement of the skin and other mucosal sites. It appears as a thin walled bullae arising on otherwise normal skin or mucosa. [4,5]

The characteristic sign of pemphigus vulgaris is positive Nikolysky sign, i.e application of pressure to apparently normal areas resulting in the formation of a new lesion. A characteristic sign of this disease is obtained by the application of pressure to intact bullae. The bullae enlarges by extension to an apparently normal surface in pemphigus vulgaris lesions. [7]

Biopsy and direct immunofluorescence are necessary investigations to rule out other blistering diseases. Biopsies are best done on intact vesicles and bullae less than 24 hours old. Characteristic suprabasilar acantholysis with Supra basilar split can be appreciated in pemphigus vulgaris which can distinguish this condition from subepithelial blistering diseases such as mucous membrane pemphigoid, bullous lichen planus and chronic ulcerative stomatitis. pemphigus vulgaris, Indirect immunofluorescence shows characteristic deposition of IgG and other C3 antibodies that bind to the cell surface of perilesional skin or mucosa are noted. It helps in distinguishing pemphigus from pemphigoid and other chronic oral lesions. [3-7]

The treatment of pemphigus vulgaris can be challenging. Various treatment options have been investigated for Pemphigus Vulgaris, however, it is generally managed with local and systemic corticosteroid therapy due to its low cost and easy availability. Topical application of steroids can be done in the form of paste, an ointment or a mouthwash administered.

Systemic corticosteroid therapy is preferred in extensive oral lesions or involvement of other mucosa and skin. Systemic treatment of corticosteroids is administered in 2 phases: a loading phase, to control the disease, and a maintenance phase, which is further divided into consolidation and treatment tapering. [2] Current guidelines recommend loading treatment with prednisone at doses of 0.5-1.5 mg/kg/day until disease control is achieved, which is approximately two weeks or more. Then either the dose is increased to 2 mg/kg/day if disease control is not achieved or tapered by as much as 25% per week unless relapse occurs. [9] According to British Guidelines for Treatment of PV, a maintenance therapy of 10 mg/day prednisolone is recommended [12] However, prolonged administration of high doses of systemic corticosteroids can cause adverse effects such as hypertension, osteoporosis, atherosclerosis, peptic ulcer disease, aseptic necrosis, diabetes mellitus/glucose intolerance, susceptibility to infections, and septicemia.[10]

Drugs that provide potential corticosteroid-sparing effect such as dapsone, gold, and systemic antibacterials can be in combination with other immunosuppressant agents such as azathioprine, methotrexate, and cyclophosphamide. [13-15] Dapsone, an anti-inflammatory agent given at a dose ranged of 50 and 300 mg/day (mean 150 mg/day) produce clinical response in the first week of treatment. [16,17] However, dapsone is associated with serious adverse effects like hemolytic anemia in patients with a G-6-PD deficiency, sulfone syndrome, methemoglobinemia, agranulocytosis, and neuropathies. [11]

Methotrexate, an immunosuppressant agent, can be instituted as a corticosteroid-sparing agent in patients who had been treated with doses of prednisone. A study performed on 53 patients showed that methotrexate in a lower dose of 5 mg/week orally, caused more rapid and effective improvement. Also, tapering off of systemic corticosteroids was more rapid in patients who started early treatment than those patients who received methotrexate much later in the course of their disease. [18]

Other immunosuppressant drugs such as Mycophenolate Mofetil, Azathioprine, Chlorambucil have been used along with systemic steroids. Newer therapies like Rituximab (Anti-CD20 Chimeric Monoclonal Antibody Therapy), Dexamethasone-Cyclophosphamide Pulse Therapy, immunoablative therapy with high-dose cyclophosphamide without stem-cell rescue, Plasmapheresis, Extracorporeal Photochemotherapy (photopheresis), and Intravenous Immunoglobulin Therapy have been documented, however, there are inadequate evidence supporting the success in clinical outcomes. [11,20] These alternative treatment modalities are tried in non responsive or severe cases of pemphigus vulgaris.

CONCLUSION

Pemphigus Vulgaris, a autoimmune disease manifests it's early lesions in oral cavity, hence, dental professionals must have adequate knowledge and be familiar with clinical manifestation of pemphigus vulgaris to ensure early diagnosis and treatment, since this in turn determines the prognosis and course of the disease. Systemic steroids are the mainstay of treatment of pemphigus. Also, there are no protocols for optimal dose of steroids and considering the potential adverse effects of steroids, trials must be performed on multiple adjuvant treatment modalities which could be a life saver.

REFERENCES

1. Subadra K, S S, Warrier S A. Oral Pemphigus Vulgaris. Cureus. 2021 Sep 15;13(9):e18005. doi: 10.7759/cureus.18005. PMID: 34671517; PMCID: PMC8521543.
2. Arpita R, Monica A, Venkatesh N, Atul S, Varun M. Oral Pemphigus Vulgaris: Case Report. Ethiop J Health Sci. 2015 Oct;25(4):367-72. PMID: 26949302; PMCID: PMC4762976.
3. Kuriachan D, Suresh R, Janardhanan M, Savithri V. Oral lesions: the clue to diagnosis of pemphigus vulgaris. Case reports in dentistry. 2015;2015(1):593940.
4. Dagistan S, Goregen M, Miloglu O, Cakur B. Oral pemphigus vulgaris: A case report with review of the literature J Oral Sci. 2008;50:359–62
5. Kumar SJ, Anand SN, Gunasekaran N, Krishnan R. Oral pemphigus vulgaris: A case report with direct immunofluorescence study. Journal of Oral and Maxillofacial Pathology. 2016 Sep 1;20(3):549.
6. Shamim T, Varghese VZ, Shameena PM, Suddha S. Pemphigus Vulgaris in oral cavity. Clinical analysesof 71 cases. Med Oral Pathol Buccal. 2008;13:2622–2626
7. Urbano FL. Nikolsky's Sign in Autoimmune Skin Disorders. Hospital Physician. 2001:23–24.

8. Yeh SW, Sami N, Ahmed RA. Treatment of pemphigus vulgaris: current and emerging options. American journal of clinical dermatology. 2005 Oct;6:327-42.
9. Eming R, Sticherling M, Hofmann SC, et al. S2k guidelines for the treatment of pemphigus vulgaris/foliaceus and bullous pemphigoid. J Dtsch Dermatol Ges. 13:833-44, 2015. * Guidelines on the management of PV, outlining regimens for induction, consolidation, and tapering of systemic medications
10. Truhan AP, Ahmed AR. Corticosteroids: a review with emphasis on complications of prolonged systemic therapy. Ann Allergy 1989; 62: 375-91
11. Yanovsky RL, McLeod M, Ahmed AR. Treatment of pemphigus vulgaris: Part 1–current therapies. Expert review of clinical immunology. 2019 Oct 3;15(10):1047-60.
12. Pedrosa MC, Rohrer RM, Kaplan MM. Alternate-day prednisone in the maintenance immunosuppressive therapy after orthotopic liver transplantation. Clin Transplant. 9:3225, 1995.
13. Bystryn JC, Steinman NM. The adjuvant therapy of pemphigus: an update. Arch Dermatol 1996; 132: 203-12
14. Bystryn JC. Therapy of pemphigus. Semin Dermatol 1988; 7: 186-94
15. McDonald CJ. Cytotoxic agents for use in dermatology. I. J Am Acad Dermatol 1985; 12: 753-75
16. DeMento FJ, Grover RW. Acantholytic herpetiform dermatitis. Arch Dermatol 1973; 107: 883-7
17. Piamphongsant T. Pemphigus controlled by dapsone. Br J Dermatol 1976; 94: 681-6
18. Mashkilleyson N, Mashkilleyson AL. Mucous membrane manifestations of pemphigus vulgaris: a 25-year survey of 185 patients treated with corticosteroids or with combination of corticosteroids with methotrexate or heparin. Acta Derm Venereol 1988; 68: 413-21
19. Atzmony L, Hodak E, Gdalevich M, Rosenbaum O, Mimouni D. Treatment of pemphigus vulgaris and pemphigus foliaceus: a systematic review and meta-analysis. American journal of clinical dermatology. 2014 Dec;15:503-15.
20. Ahmed AR, Spigelman Z, Cavacini LA, Posner MR. Treatment of pemphigus vulgaris with rituximab and intravenous immune globulin. New England Journal of Medicine. 2006 Oct 26;355(17):1772-9.

Figure 1:

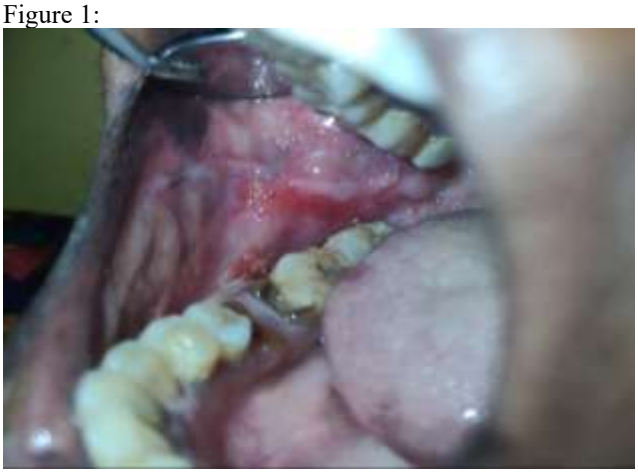

Figure 2:

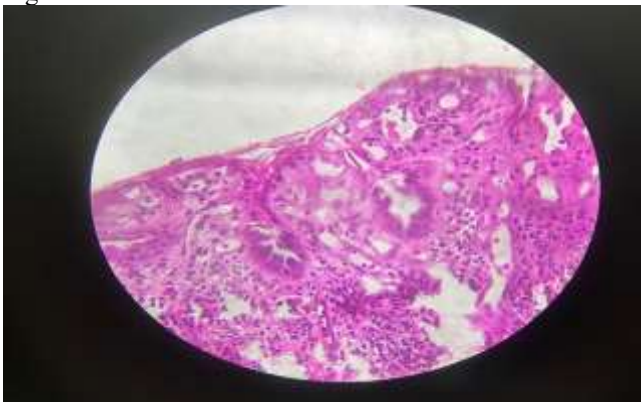

Figure 3:

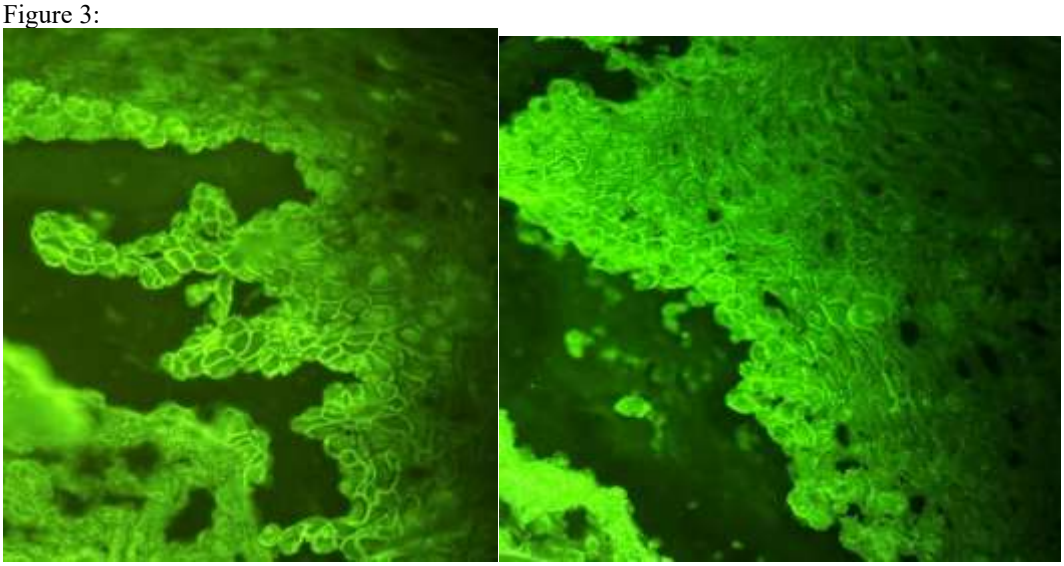

Figure 4:

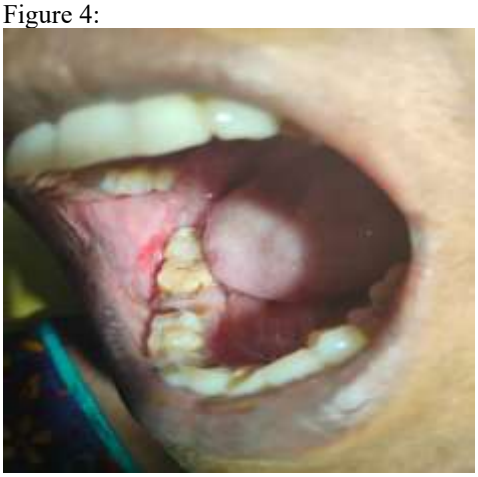

Figure 2:

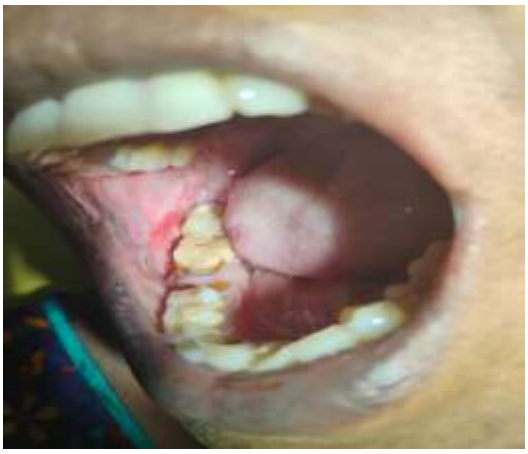

Figure 3