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Chronic Multiple Ulcers in Oral Cavity- A Case Report of Oral Pemphigus

Dr. M K Navya[1*], Dr. Sujatha G.P[2], Dr. Sangeeth Siddabassappa[3], Dr. Ashok L[4]
[1]Postgraduate student, Department of Oral Medicine & Radiology, Bapuji Dental College & Hospital, Davangere, Karnataka, India
[2]Professor, Department of Oral Medicine & Radiology, Bapuji Dental College & Hospital, Davangere, Karnataka, India
[3]Reader, Department of Oral Medicine & Radiology, Bapuji Dental College & Hospital, Davangere, Karnataka, India
[4]Professor & Head, Department of Oral Medicine & Radiology, Bapuji Dental College & Hospital Davangere, Karnataka, India

Case Report

***Corresponding author**
Dr. M K Navya

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Abstract: Pemphigus is a group of mucocutaneous blistering disease which can be seen involving only the oral cavity also. The cutaneous lesions are preceded by oral lesions in many cases reported in the literature. This condition is very painful and it affects the quality of life of the patient. Early diagnosis of the disease will improve its prognosis and quality of life of patients as severe conditions are life threatening. Here were are reporting a similar case of Pemphigus Vulgaris.

Keywords: Chronic multiple ulcers, Pemphigus, Steroids.

INTRODUCTION

Pemphigus is a group of autoimmune blistering disease which compromises the quality of the life of person affected severely. This disease causes painful ulcerations or blisters. Pemphigus vulgaris (PV) is the most frequently observed member of this group characterized by the formation of intraepithelial blisters. It is a rare disease which affects about 0.1-0.5 cases/100,000 individuals per year and is most commonly seen in the fifth or sixth decade of life [1]. This disease has a female predominance and some races especially Ashkenazi Jews and Mediterranean and South Asian origin are more commonly affected, may be related to HLA- II genes [2].

CASE REPORT

A 36 year old female patient came with the complaint of painful ulcers in lips and oral cavity since 3 months. History of painful ulcers present since 3 months. Ulcers were insidious in onset, initially involving only the lips later involving the whole oral cavity.

Ulcers were initially small in size and gradually increased in size to involve entire lips & oral mucosa. Associated with pain since 3 months. Pain was sudden in onset, continuous, severe in intensity and aching type. Burning sensation was also present since 8 days. Sudden in onset, intermittent, localized and aggravated on having food and relives on having water. Vas for pain and burning sensation was 9. Patient had consulted many physicians in Jagalur previously in last 3 months and were given topical anesthetics and antifungal agents but the pain did not subside and later patient got admitted in dermatology ward in CG hospital Davangere 1 week prior to reporting to us. She was given chlorhexidine mouth wash, candid gum paint and 10 mg prednisolone 3 times daily for 5 days. But pain and ulcer did not subside and patient was then referred to us. Patient had weakness due to inability to eat food and also difficulty in speech and swallowing. On extra oral examination, Solitary submandibular lymph nodes were palpable bilaterally, soft, mobile and tender. Mouth opening was12mm. Solitary healed bulla was evident on the left arm which was blackish in color, about 1cm in size, roughly round with dry surface and normal surrounding area. Diffuse ulcers with crust formation was evident on upper and lower lip in the vermillion border. Extending over the entire lip, base of ulcers was erythematous in some area and yellow slough in some areas, borders were irregular and diffuse, surface had crustation and surrounding mucosa appeared dry. On palpation, the lesion on left arm was soft, non-scrapable, surface was rough, non-tender and the lesion on lips were tender, soft in consistency with bleeding and peeling of mucosa. On intra oral examination, Multiple diffuse ulcers were evident involving the entire upper & lower labial mucosa, right & left buccal mucosa with erythematous base and whitish pseudomembrane, margins were irregular and diffuse. Generalized erythema was evident on the gingiva with inflamed marginal and interdental papillae. Whitish patch was evident on the dorsal aspect of the tongue, about 4.5 × 2.5 cm in size, irregular and diffuse margins with erythematous surrounding area.(FIG 1)

On palpation, all inspectory findings were confirmed. The ulcers were soft and tender. The pseudomembrane was scrapable leaving erythematous base below. Gingiva was also soft in consistency and peeling of the epithelium was evident and was also tender. The lesion on the tongue was scrapable leaving erythematous base and tender. Based on history and clinical examination a provisional diagnosis of chronic multiple ulcers involving oral mucosa & Candidiasis on dorsum of tongue was given. Differential diagnosis of pemphigus and pemphigoid was considered. Complete haemogram revealed a raised ESR of 40mm/hr.

Considering pemphigus vulgaris as the diagnosis based on history and clinical examination, Patient was admitted and given intravenous infusion of methylprednisolone 40mg/10ml OD for 2 days and Candid gum paint was given to be applied on tongue 3 times daily.

After 2 days, remission of erythema surrounding the ulcers were evident and healing of ulcers were evident, Crust formation over the lips was seen and Pain and burning sensation had reduced. VAS – 7, Patient was able to speak and have solid food.

A solitary swelling was evident on left retro-commissural area, about 1 cm in diameter, pink in color, with whitish periphery and erythematous surrounding area. On palpation, soft to firm in consistency, pedunculated and non-tender suggestive of traumatic fibroma. Debridement of the lesion was carried out using normal saline and patient was advised Tab. Prednisolone-10 mg (2-2-2) ×3days, Cap. Pan D 1-0-0×3 days & Benzydamine hydrochloride-0.15% (Coolora gargle) 4-5 times daily (Fig-2). The dosage of prednisolone was tapered and patient was recalled after 1 week. Complete healing of ulcers in oral cavity was evident, ulcers on vermillion border of lips showed crust formation and evidence of healing but mild bleeding was evident on manipulation of the lower lip (Fig-3). VAS reduced to 4 for pain and burning sensation. Quality of life of the patient had improved. The dosage of steroid given was tapered to Tab. Prednisolone 10 mg (1-1-1) ×1 week, (1-0-1) ×1 week, (0-0-1) ×1 week, Cap. Pan D (1-0-0) ×3 weeks & Benzydamine hydrochloride-0.15% (Coolora gargle) 4-5 times daily. Patient was evaluated after 1 month (Fig-4) and patient was followed up for 3 months. Based on the therapy, therapeutic final diagnosis given was Pemphigus Vulgaris involving lips and oral mucosa, Candidiasis on dorsum of tongue and Traumatic fibroma on left retro-commissural area.

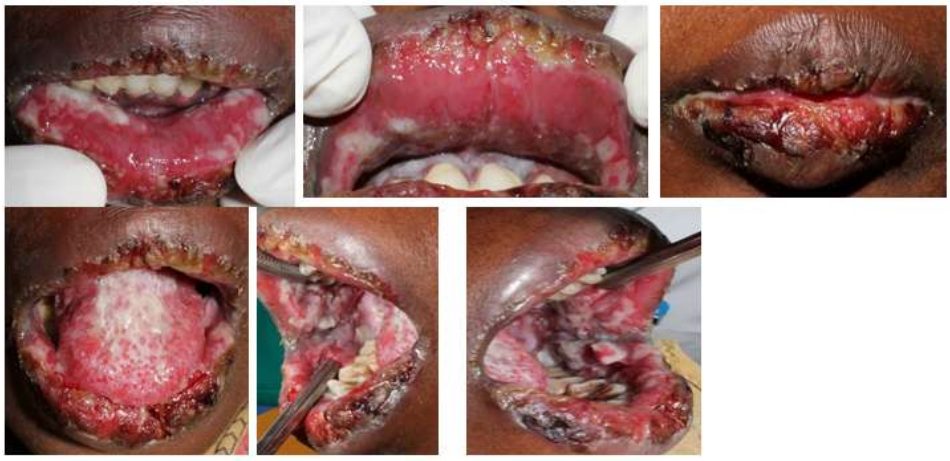

Fig-1: Multiple ulcers were evident on lips and oral mucosa with formation of pseudomembrane over it.

Fig-2: Appearance of lesion 2 days post therapy and debridement. Solitary swelling is evident on the retro-commissural area on left buccal mucosa.

Fig-3: Healing of ulcers and crust formation over the ulcers on lips were evident after 1 week follow up

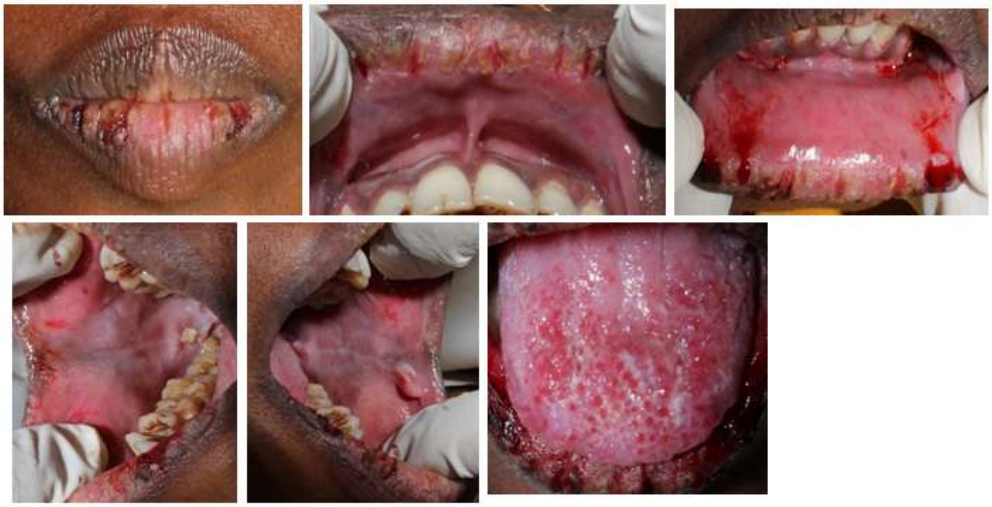

Fig-4: Complete healing of the ulcers on the lips and oral cavity was evident post 1 month therapy.

DISCUSSION

Pemphigus is a group of autoimmune blistering disease which compromises the quality of the life of person affected severely. This disease causes painful ulcerations or blisters. Pemphigus vulgaris (PV) is the most frequently observed member of this group characterized by the formation of intraepithelial blisters. It is a rare disease which affects about 0.1-0.5 cases/100,000 individuals per year and is most commonly seen in the fifth or sixth decade of life [1]. This disease has a female predominance and some races especially Ashkenazi Jews and Mediterranean and South Asian origin are more commonly affected, may be related to HLA- II genes [2].

Etiology

Other than genetic predisposition Pemphigus is believed to have autoimmune mechanism where in circulating auto-antibodies of IgG type are detected. Drugs like Sulfhydryl Radical eg. Pencillamine, Captopril & Active Amide Group eg. Phenol drugs, Rifampicin, Diclofenac are seen to be associated with Pemphigus. Role of viruses was suggested by Ruocco et al in 1996. He detected association of Herpes simplex virus & HHV-8 with Pemphigus considering it as one of etiologic factor. Association with other Disorders like Rheumatoid Arthritis, Lupus Erythematosus, Myasthenia Gravis & Pernicious Anemia have also been seen. Smoking, pregnancy and high exposure to pesticides and diet having garlic, onion have also caused Pemphigus [3].

Pathogenesis

Certain hypothesis is associated with pathogenesis of Pemphigus. They are [4]:

- The Desmoglein compensation hypothesis - In 1999, Amagai and Stanley proposed the desmoglein (Dsg) compensation theory based on the distribution of Dsg1and Dsg3 in the skin and mucosa. The clinical typing of pemphigus (PV and PF) and the main clinical symptoms of PV (mucosaldominant and epidermal–mucosal types) are determined on the basis of both the differential antigenic distribution and generation of autoantibodies [5].
- Multiple hit hypothesis- According to this hypothesis multiple hits by both Dsg and non-Dsg autoantibodies are required to cause acantholysis in pemphigus. The proposed auto-antigens are adhesion molecules such as- Dsg1, Dsg2, Dsg3, desmocollins, plakoglobin, collagen XVII/BP180 and the receptor molecules such as- α3 AChR, α9 AChR, pemphaxin and other annexins [6].

- Antibody induced apoptosis theory- This theory hypothesized that apoptosis may possibly be responsible for the underlying mechanisms of acantholysis. The mechanisms of apoptosis in PV may be based on the PV IgG-triggered activation of signalling pathways, such as the epidermal growth factor receptor activation-dependent intracellular signalling (extracellular signal-regulated kinase) pathway and the apoptosis (FasR) pathway [7].
- Basal cell shrinkage theory and apoptolysis theory- Claude *et al*., proposed a new hypothesis of pemphigus pathogenesis in 2006, which suggests that after the pathogenic PV autoantibody binds to the keratinocyte receptor, a series of signal transduction pathways trigger the rupture of the cytoskeleton, resulting in the collapse and shrinkage of the keratinocytes. This hypothesis explains why PV acantholysis mainly occurs at the basal layer, even though the keratinocytes in the superior basal layer remain connected [4].

Clinical features

Oral mucosal involvement is considered to be initial manifestation in majority of PV patients. In a retrospective review of 71 cases seen over 7 years, 53.52% patients had their disease onset in the oral mucosa, while 23.94% had onset on skin and oral mucosa simultaneously. The buccal mucosa and the hard palate were the commonest site of involvement, followed by lips, tongue, floor of the mouth, and gingiva in decreasing order of frequency. The cases presented with either erosions or ulcers [8].

Cutaneous features are classical lesion of thin walled Bulla arising in otherwise normal skin or mucosa. Lesion extends peripherally to leave large denuded skin. Nikolsky's sign and Asboe – Hansen sign are positive in this disease. Acute or chronic paronychia, subungual hematomas and nail dystrophies can also be seen. Scaly and crusted erosions can be seen which on peeling will show erythematous base. Early lesion will be well demarcated & localized but later will extend to the periphery. Face, scalp & upper trunk will also be involved in cutaneous pemphigus [9].

Differential diagnosis

PV should be differentiated from other blistering diseases like pemphigoid, bullous lichen planus, erythema multiforme, herpes zoster infection, herpangina when oral cavity is involved. Based on the chronicity, location, clinical appearance of lesion PV can be clinically differentiated from other blistering diseases [2].

Investigations

Biopsy should be done to carry out histopathology which will show suprabasal blister formation & acantholysis and immunofluorescence study detects IgG against Dsg 1 and Dsg 3, also ELISA can be carried out to distinguish anti-DSG1 antibodies from anti-DSG3 antibodies in serum, to distinguish PV from PF and for determining disease activity and prognosis [10].

Treatment

For Topical therapy**,** Benzydamine hydrochloride 0.15%**,** Chlorhexidine gluconate 0.2%**,** 1: 4 hydrogen peroxide solutions. Betamethasone sodium phosphate 0.5 mg tablet - 10 mL - four times daily**,** **t**opical cyclosporin (100 mg /mL) and Gentian violet can be used which has both antifungal and antiseptic activity [11].

According to guidelines of European Dermatology Forum and European Academy of Dermatology & Venereology recommend initial prednisolone dose at 0.5 mg–1.5 mg/kg/d. If control is not reached within 2 weeks we need to increase dose up to 2 mg/kg. Slow standardized tapering of corticosteroid is commenced over about a 4-month period should be done called as the Werth taper. When Prednisolone above 100 mg/day is required then pulse treatment oral or intravenous (IV) should be considered. IV Betamethasone with oral prednisolone has shorter time to remission and less adverse effects. Pulse regimen used is 100 mg/d of IV dexamethasone for 3 days every 2–3 weeks. Pulse therapy with IV dexamethasone is reliable in refractory PV [12, 13].

Prolonged use of steroids (>4months) can lead to hypertension, DM, osteoporosis, In such scenario steroid sparing agents are used like Mycophenolate mofetil, Azathioprine, Cyclophosphamide, Cyclosporin, IVIG & Infliximab as adjuvant therapy [14].

CONCLUSION

Pemphigus is a life threatening autoimmune chronic blistering disease that involves in the squamous epithelia and mucous membrane of skin. Pemphigus shows effect on quality of life of patients as ulcers are very painful and bleed making it difficult to eat and drink. Corticosteroids remain the mainstay of treatment for pemphigus. Dexamethasone-cyclophosphamide pulse therapy has revolutionized the management of pemphigus in India and abroad for nearly 3 decades now. Corticosteroid-based treatment, along with adjuvants, has significantly brought down the high mortality rates that had been observed in precorticosteroid era. Present day research is largely based on elucidating the pathogenesis beyond the anti-desmoglein antibodies, and newer diagnostic and treatment approaches.

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