ORIGINAL RESEARCH PAPER

Volume-7 | Issue-7 | July-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

"ORAL LESIONS OF MUCOUS MEMBRANE PEMPHIGOID A CAUTIONARY SIGNAL FOR SKIN MANIFESTATIONS, LATER PEMPHIGUS VULGARIS"

Dental Science

Anilkumar L Bhoweer Ex-Professor, Oral Medicine & Radiology, Consultant Oral Diagnostician & Maxillofacial Radiologist & Dental Surgeon, Mumbai, Maharashtra, India;

Sudarshan G Ranpise* Professor and Head, Department of Oral Medicine & Radiology, Bharati Vidyapeeth Dental College, CBD, Navi Mumbai, Maharashtra, India.*Corresponding Author

ABSTRACT

Pemphigus is chronic autoimmune disease characterised by formation of vesicles and bulla. It is commonly seen involving skin and mucosa. Oral mucosa is more common than any other mucosa. Conjunctiva also can be seen affecting eyes. There are four varieties of pemphigus, that is, P. Vulgaris, P. Vegetans, P. Foliaceous and P. Erythematous.

Pemphigus basically is an autoimmune disease and antibodies are present in the intercellular substance of prickle cell layer, causing loss of cell adhesion causing Acantholysis and separation of epithelium from basement membrane, leading to bulla formation and presence of Tzank cells is diagnostic of Pemphigus and requires early attention & treatment to avoid further risk to life.

Two patients with initial oral bullous lesion ulcers are reported, with treatment. The patients were comfortable with steroid oral cream & tapering systemic doses and follow-up. Both of them later had skin lesions which were referred to Physicians & treated by skin specialists for treatment with history of oral pemphigoid lesions and were happy with relief.

KEYWORDS

Bullous lesions, non-healing ulcers, autoimmune disease, early management, suprabasillae Bulla, Tzank cells, Nicholsky's sign.

Introduction

Pemphigus is a group of potentially fatal disease which can affect skin and oral mucous membrane[2,1] and conjunctivitis in the eyes. Most commonly, oral lesions occur as early feature with blistering and ulcerations in many cases. The occurrence is usually after the fourth and fifth decade and both elderly men and women can be affected but it is almost double in females.[2] When blisters occur in the mouth, they rupture easily, causing painful ulcerations in the oral cavity. Commonly, buccal mucosa, palate, lips and soft palate & gums are involved.[3] It is very essential for the Dental Surgeons to identify and diagnose these blisters and ulcers in the mouth, as they don't respond to common medicines and are extremely painful. Biopsy procedure is necessary to confirm the diagnosis and for final confirmation of immunoglobulins.[4,5] Early diagnosis and proper treatment to be given is required for the relief of the patient and its potentiality should be thought to affect skin. Later, we are presenting two cases of pemphigoid oral lesions, developing skin lesions after their mouth lesions were cured completely. Then they were referred to Physician and the Skin Specialist with history of oral pemphigus lesions. It is important for proper treatment & care of the patient as it could be treated with early manifestation of skin, as it is known to be fatal if not handled early and properly.[6]

Case reports

Case 1

A female patient, age 73 years, was referred with complaint of ulcers in the mouth. She had history of hypertension, no diabetes or other illness, allergy to sulfa drugs and disquamative gingivitis. The ulcers were on both cheeks; the left cheek mucosa ulcer was quite big in size (Fig. 1), almost involving the entire left cheek. There were ulcerated blisters with inflamed, reddish area on the right cheek near the muccobuccal fold and reddish, ulcerative mucosa up to the angle of the mouth and whitish loose surface mucosa intermittently. The eyes were not involved.

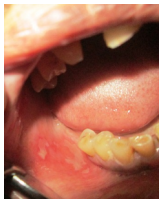


Fig.1: Ulcerated blisters, reddish area on right cheek

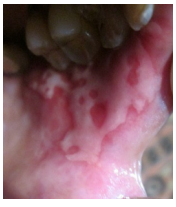


Fig.2: Raw reddish ulcerated area on Left cheek (ruptured bulla)

It appears on left side a large bulla ruptured, leaving raw reddish ulcerated area (Fig. 2) with a lot of pain and discomfort and not responding to the local mouthwashes and gum paints which were prescribed by the Dentist who referred her for Diagnosis and management. She had history of allergy to medicines, especially sulpha drugs, had hypertension & menopause, but no history of Diabetes.

Differential diagnosis of oral ulcerative lesion due to Oral Lichenplanus was also considered. Since large bullous non-healing lesion, it was clinically labelled as Bullous pemphigus with typically hanging mucosa surface on the ulcer (bullous). Biopsy was advised first to microscopically confirm the diagnosis and with immunoflurosis study later, if required.

The patient was consented for the procedure after discussions. Incisional Biopsy of the left cheek lesion was done and the patient was started with the medicines immediately, as the Biopsy report takes 3 to 4 days.

She was given Betamethasone 0.5mg dispersible tabs to rinse the mouth after dissolution of tablet in water and in the mouth for some time, swishing around in the mouth, and then to swallow. 1-1-1x 3 days and Levamasol tablet, as adjunct medicine daily, 1 tab. x3 days. Local steroid oral cream was also given to apply, oral local anaesthetic & antiseptic cream to apply thrice daily to the lesion with specially made soft cheek tray (Fig. 3) for quick response, as the medicine does not get washed away with saliva. Instructions were given how to place the soft cheek tray with medicine (Fig. 4). She was also advised Betadine mouthwash twice a day to prevent suprainfection. She was advised semisolid liquid diet with milk, fruits, juice, water and ice application from the outside at facial area of cheeks.

Fig.3: Soft cheek tray with medicine

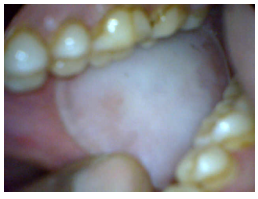
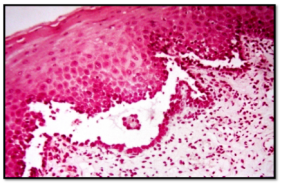
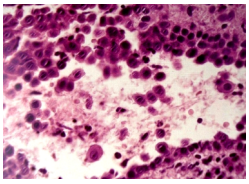


Fig.4: Soft cheek tray with medicine placed in cheek

The patient was explained the steroid treatment with tapering doses and necessary observation follow-up as required and to cooperate.

The Histopathology report after 4 days revealed as "perakeratotic stratified squamous epithelium is evident. Epithelium is separated from the underlying connective tissue core. Epithelial separation is noted at the level of basement membrane. Fibrous and adipose tissue stroma with mild inflammatory cell reaction is evident. Bulla

formation, acantholysis was positive and the presence of Tzank cells." Impression – Pemphigoid (Figs.5, 6)

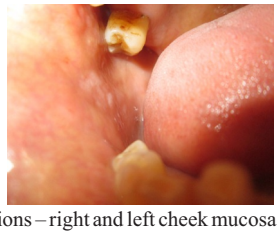



Figs.5, 6: Histopathology report images

Follow-up after 3-4 days revealed good healing changes, responding to medicines and good relief from pain and discomfort. Medicine to continue, as advised.

Then, after 4 days, follow-up revealed that the ulcers were reduced in size & less painful and the patient could eat soft food and was much more comfortable. Patient was then advised to take Betamethasone 0.5mg dispersible tabs twice daily x4 days and Levamasol tab. 1 daily x4days; then 1 tab. daily x4 days and then 1 tab. alternate day x 1 week as advised & Tab. Levamasol and continue with local application twice daily till the next follow-up. She was also given multivitamins and B-complex medicines and advised to follow rigidly the tapered dose and maintain follow-ups as advised & to observe after every four days. Ulcers were healing well, were reduced in size and less inflamed. Epithelium was forming over the original ulcerated area.

As it is possible to have fungal (Candid) superinfection following steroid therapy, white patches did form on this patient also in oral cavity, scrappable enough. Then it was necessary to give antifungal oral gel to apply on the areas in the mouth and also gargle with betadine mouthwash. The fungal suprainfection was controlled fast with the treatment (Fig. 7, 8). She was advised to have blood sugar and CBC blood investigation. The blood sugar was normal & CBS blood was Ok.

Figs.7, 8: Post-Treatment healed lesions – right and left cheek mucosa

The patient was very happy after 4 weeks of treatment and symptomless. The steroid treatment was stopped after maintenance dose for four days, as no lesion now & the patient was happy & able to eat food comfortably, with swallowing also improved. The patient was then advised to see the Physician and instructed to observe for any recurrence, as even rarely skin manifestation occurs which may require treatment by a skin specialist. Oral check-up was advised every one month after that.

This patient came after 3 months after curing mouth lesions, to show ulcerative lesion on the sole of the leg and foot (Fig.9, 10). She was advised blood sugar investigation to rule out Diabetes and also CBC report. She was then referred to Physician and was told to immediately refer to a Skin specialist for early care of the lesion with prior history of oral lesion pemphigus.

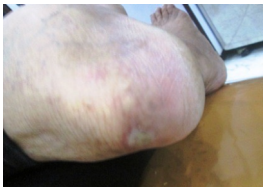
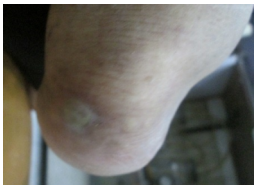



Fig.9, 10: Foot/leg ulcerated lesions

Case 2

Female patient of 75yrs. with ulcers in left cheek for many days, redness of alveolar gums & could not use dentures. There was no response to treatment by local doctors' & dentists' medicine and then was referred for diagnosis & management.

The patient was edentulous, wearing full denture, but alveolar gum irritation and redness was positive with Disquamative Gingivitis. The dentures were intolerable and hence could not use them and eat. She had swallowing difficulty also. Nail cracks (Fig.11) and anaemia was also suggestive.

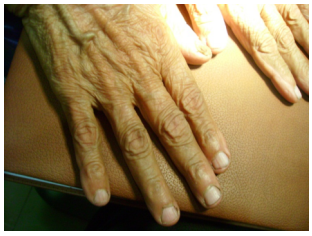


Fig.11: Nail cracks

Left cheek ulcerated area (Fig.12) and ruptured bulla on the gingiva positive; disquamative gingivitis evident (Figs.13, 14). Nicholsky's sign of the soft bulla appears nearby. No skin lesion. She was treated at many places for mouth ulcers, but got no relief with the given treatment and with the swallowing difficulty and for oral ulcer problem was referred for diagnosis & management.

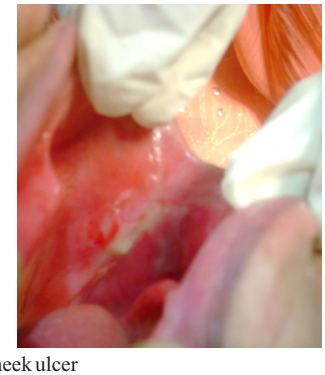


Fig.12: Left cheek ulcer

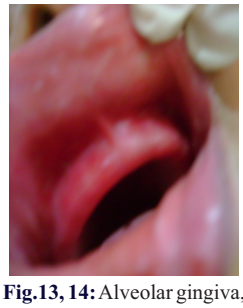
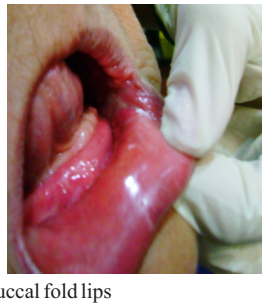



Fig.13, 14: Alveolar gingiva, muccobuccal fold lips

Biopsy of the ulcerative lesion revealed typical bullous lesion above the basement membrane and ulcerative mucosa at places with Histopathological diagnosis confirming pemphigoid lesion (Fig. 15.)

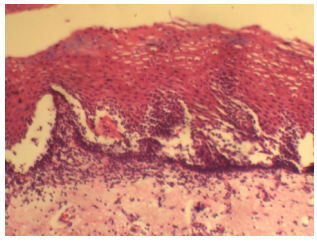


Fig.15: Histopathology report image

She was treated with local steroid cream for 15 minutes with soft tissue cheek tray (Fig.16) & advised to use upper & lower dentures with cream in alveolar region, palatal surface, with instructions not to gargle, eat or drink for 20 minutes after that, and also advised Betadine mouthwash twice daily, in the morning & before going to sleep. She was advised to use her own dentures & put the local steroid cream given to her. This helps the patient as the cream does not get washed away with the saliva. She was also given tapering dose of

Betamethasone 0.5mg. dispersible tab for 3 weeks, to swish around in the mouth & then swallow. She was also given Levamesol tab. additionally, as an adjunct medicine. Later, the maintenance dose tapered, with 1 tab. daily for one week; then 1 tab. alternate day for one week and half tab.alternate day for one week, etc. with reduced dose of Levamesol tab. She was also advised local cream of local anaesthetic and antiseptic with soft tray daily, as advised. Afterwards, regular follow-up was done and the patient was very cooperative and happy.

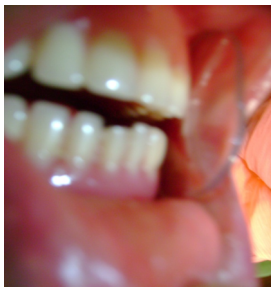
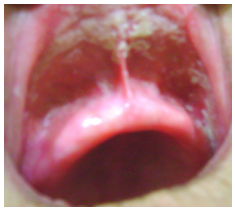
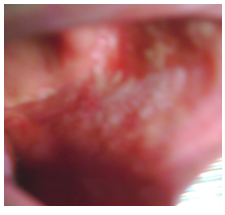


Fig.16: Wearing dentures, with soft cheek tray with local cream

Candid infection developed (Figs.17, 18) and was treated with Candid oral gel application as advised. The improvement was very good & she was happy & could eat with her dentures. Candid oral gel was also given to prevent and control Candidiasis suprainfection. Later, even antifungal treatment was stopped.





Figs.17, 18: Candid infection

The lesions healed very well (Figs. 19, 20, 21) and the patient could swallow food without any difficulty in about one month and three weeks. She was observed later. She was advised to use the denture later with adhesive paste for few more days, until the lesion on the alveolar mucosa and gingival area totally healed well.

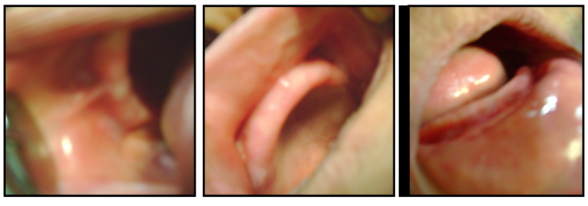


Fig.19, 20, 21: Post-treatment, cheeks & alveolar region

The patient was later referred back to her Physician for maintenance of general health and health check-up, blood sugar, CBC blood, vitamin supplements, etc. as required. Also, regular check-up was advised to see if any skin lesions follow after a few days and weeks and was informed that if skin lesion appears, early treatment will be required by a skin specialist. She was advised regular oral check up every month.

After 3 months, the patient had lesion on the arm (Fig.22) and she was referred to a Physician to refer to a skin specialist immediately for the needful treatment with prior history of oral lesion of pemphigus cured.

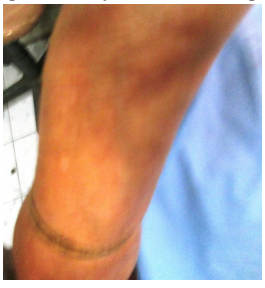


Fig.22: Arm lesion

Discussion

Pemphigus is having four types - Pemphigus Vulgaris, Pemphigus Vegetans, Pemphigus Foliaceous and Pemphigus Erthematosus. Pemphigus is an autoimmune disease. Pemphigus is a group of life-threatening autoimmune mucotuneous disease . Pemphigus Vulgaris was fatal until the introduction of steroid therapy and early diagnosis was more important to start the proper treatment. In most of the cases, oral mucosa is the sole initial site. The oral cavity blisters with rupture and formation of non-healing ulcers not responding to general medicines & later involvement of other sites of the skin is very common. Therefore, the role of the Dental Surgeon plays an important part in early detection, diagnosis and initiation of early treatment to save the patient's life. Sometimes, the oral cavity is alone the site, with blister formation and ulceration. Later on, other sites of the body, such as the skin surface, get involved.

In our first case, the patient had big blisters (bullous formation) in the mouth on the left cheek and other small ulcers. It was a female patient, age 73 years, who reported with large bullous lesion in the left cheek, rupturing with quite big ulceration and not responding to many common drugs. Pemphigus commonly occurs in women, almost double in number than males , and usually in elderly persons above 40 to 50 years.

Our patients were both females, with one 73yrs. old but having teeth and the other 75 years old who was edentulous, wearing full dentures and with involvement of the gingiva, cheeks & other parts of the oral cavity and also involving throat posteriorly, with difficulty in swallowing. She was unable to wear dentures. For Differential Diagnosis, ulcerative Lichenplanus was also considered and to be confirmed by Biopsy.

The Biopsy procedure, which is important in Diagnosis, can reveal sub-epithelial suprabasillar bulla formation & the presence Tzank cells and Acanthylosis . Blowing of air over the neighbouring region also has bulla (bleb formation) (Nicholsky's sign) and, most of the time, Biopsy confirms the diagnosis . However, if required, an Immunofluorescence study may be required to see the immunoglobin and complement to confirm Ig.

Both the patients were given Betnesol 0.5mg. dispersible tabs (steroid) to swish in the mouth after dissolution in water and after swishing to swallow. This to repeat at least 3 times daily & then to observe. Both patients were non-diabetic. Both were given local steroid cream to be applied with soft cheek trays & dentures. After 3 to 4 days observation, improvement was revealed in the lesions. The patients were advised to continue the treatment every week and follow-up with tapering dose. The Biopsy report confirmed our diagnosis, with suprabasillar bulla and the presence of Tzank cells, etc. Later, as improvement occurred, the dose was reduced to 2 tabs. per day for one week & later on to taper further. Both patients were also given local steroid & antiseptic & local cream to apply with special soft tray which gave quicker relief, comfort and healing.

We noticed quicker improvement in the lesion with local cream applied on the soft tray to place on the cheek over the lesion for 20 minutes, with no food or drink after the application of the medicine for further 20 minutes. This method helps in quicker healing of the lesion, since the local cream does not get washed away with saliva & it remains in contact with the lesion for a sufficient period of time.

Thus, very good & quickest improvement was seen and ulcers healed well in a short time with quite good results. Our second patient could use dentures and eat and had no difficulty in swallowing. The tapering and maintenance dose was planned & follow up was also advised.

These patients were referred to the Physician with a note for follow-up and any skin lesions and then to refer to a skin specialist.

Both our patients came to show skin lesions (the first patient came after 3 months) with big ulcers on the soles of the feet. The foot lesions were referred to a skin specialist with history report of the lesions in the oral cavity & pemphigoid. The second patient developed hand skin lesions on the hand almost after 3 months when she came for follow-up. She was also asked to see a skin specialist for further treatment with history of oral pemphigoid lesions and follow-ups were also advised.

Both patients were alright later.

Conclusion

The role of Oral Diagnostician in early diagnosis & proper management of the pemphigus lesion in the oral cavity is stressed, as it is an early signal for possible occurrence of generalized skin lesions (Pemphigus Vulgaris) which could be life-threatening.

References

1. M. Black, M.D. Mignona and C. Scully, "Number II. Pemphigus vulgaris", Oral Diseases, Vol.11,no.3, 119-130, 2005.
2. A. Iamaroon and others, "Characterization of oral pemphigus vulgaris in Thai Patients", Journal of Oral Science, vol.48, no.1, pp.43-6,2006.
3. M.D. Mignogna, L. Lo Muzio and E. Bucci, "Clinical features of gingival pemphigus pemphigus vulgaris", Journal of Clinical Periodontology, vol.28, no.5, pp.489-493, 2001.
4. F. Femiano, "Pemphigus vulgaris; recent advances in our understanding of its pathogenesis", Minerva Stomatologica, vol.56, no.4, pp.215-223, 2007.
5. C. Scully and S.J. Challacombe, "Pemphigus vulgaris: update on etiopathogenesis, oral manifestations and management", Critical Reviews in Oral Biology and Medicine, vol.13, no.5, pp.397-408, 2002.
6. J.C. Bystryn and J.L. Rudolph, "Pemphigus", The Lancet, vol.366, no.9479, pp.61-73, 2005.
7. Diana Kuriachan et al, "Oral Lesions: The Clue to Diagnosis of Pemphigus Vulgaris", Case Reports in Dentistry, Volume 2015, Article ID593940.