

# Advantage of Topical Corticosteroid over Systemic Adjuvant Therapy in Mucocutaneous Pemphigus Vulgaris : A Case Report

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## Abstract

Pemphigus is a potentially life threatening autoimmune disease that causes blisters and erosions of the skin and the mucous membrane. Even though systemic steroid therapy is the main stay among the treatment protocol, due to its adverse effects, adjuvant chemotherapeutic agents like Azathioprine are preferred for long term management. Azathioprine has proven curative benefits for dermal lesions but it has potential side effects of persistent oral ulceration. Here we describe a case of mucocutaneous Pemphigus Vulgaris which was under long term Azathioprine therapy, presented with persistent oral ulcers. We could effectively manage the case with topical corticosteroids after stopping Azathioprine. Even though adjuvant therapy has proven benefits in managing Pemphigus vulgaris, the clinicians should be cautious about its adverse effect.

**Keywords:** Pemphigus, chronic oral ulcers, steroids, Azathioprine.

## INTRODUCTION

Pemphigus is a chronic inflammatory autoimmune bullous disease. There are 0.5 to 3.2 cases reported each year per 100,000 populations, with the highest incidence in the 5th and 6th decade of life, with male to female ratio of 1:2. The major variants of Pemphigus are Pemphigus Vulgaris, Pemphigus Vegetans, Pemphigus foliaceus, Pemphigus erythematosus, Paraneoplastic pemphigus (PNP). Pemphigus Vulgaris is the most common form of Pemphigus, accounting for over 80% of cases. In the majority of patients, it affects the oral mucosa and is sometimes difficult to diagnose when only mucosal involvement is present.

Lesions may occur anywhere on the oral mucosa, but the buccal mucosa is the most commonly affected site followed by involvement of the palatal, lingual and labial mucosa. Gingiva is the least commonly affected site and desquamative gingivitis is the commonest manifestation of the disease when gingiva is involved. In many patients, oral lesions are followed by the development of skin lesions. If oral pemphigus vulgaris can be recognized in its early stages, treatment may be initiated to prevent the progression of the disease to skin involvement. Diagnostic delays of greater than 6 months are common in patients with oral pemphigus vulgaris. The oral cavity may be the only site of involvement for a year or so, and this may lead to delayed diagnosis and inappropriate treatment of a potentially fatal disorder. Here we describe a case with oral manifestation of muco-cutaneous pemphigus, effectively managed with topical corticosteroid after stopping long term adjuvant monotherapy.

## CASE REPORT

A 64 year old male patient reported to our department of Oral Medicine and radiology with chief complaint of pain and ulcers of mouth since 1 month. Medical history revealed that patient was diagnosed of Pemphigus Vulgaris and was under long term

Azathioprine therapy since 1 year. Skin lesions was not active for past 7 months but there was exacerbation of oral ulceration in between and the present episode started 1 month back with blister formation following a cheek bite. Gradually blisters ruptured and severe redness with slough noted over entire mouth. Then he had severe burning sensation and became intolerant to hot and spicy food.

Patient was under medication for hypertension. On extra oral examination, right and left forehead region dry eroded crustations were seen. No pus discharge or bleeding was noted. On hands dry scales and crusted areas scattered all over the palmar area, phalanges and interdigital areas which extends to extensor and dorsal surfaces. Similar lesions were noted on dorsal surfaces of lower extremities which extends upwards.

Intra orally an intact bulla of size 1.5x1 cm present in the lower labial mucosa in lower labial mucosa in relation to 43,44 region. Multiple clusters of superficial eroded area with necrotic slough with an inflamed erythematous base all over left buccal mucosa which extends from left commissure to pterygomandibular raphe and soft palate region were noted. Similar lesions were noted on right buccal mucosa and ventral surfaces of tongue. Nikolskys sign elicited positive. Provisional diagnosis was given oral manifestation of Pemphigus Vulgaris. Routine blood examination revealed neutropenia. Histopathological examination confirmed the clinical diagnosis.(fig 1)

Since the long-term azathioprine therapy has persistent neutropenic oral ulceration as potential side effect, we decided to stop the medication and started off with topical corticosteroid-Prednisolone 10mg swish and spit off three times daily considering the medical status of the patient. After 1 week follow up there was drastic reduction in symptoms and clinical appearance. Topical steroids were tapered and stopped after 2 months and no relapse, either dermal or intraoral was noted during the follow up periods of 6 months.

## DISCUSSION

Pemphigus is a group of potentially life threatening autoimmune mucocutaneous disease characterised histologically by epithelial blistering and immunologically by IgG autoantibody directed against keratinocyte cell surface. It is derived from a Greek word "Pemphix" which means bubbles or blister. Here auto antibodies are directed against adhesive proteins Dsg1 and 3 which results in loss of cell-cell contact followed by acantholysis and intraepithelial vesiculations. Most common predisposing factors includes environmental factors like drugs, viral infections, contact allergens, diet etc.

More than 80% of mucoocutaneous pemphigus vulgaris shows oral lesions and in around 60% cases these lesions appears first. Buccal mucosa is most common site intraorally. Lesions are mostly characterized by thin walled bullae varying sizes from few millimeters to several centimeters on skin or mucosal surfaces. Bullae rapidly breaks and continues to extend peripherally. Application of pressure to an intact bulla results in its extension to apparently normal surface which is called Ash- boe Hansen sign. By giving lateral tangential pressure to apparently normal area results in formation of new lesion which is named as Nikolsky's sign. Both signs were positive in our case.

Diagnosis can be done by history taking, clinical examination eliciting nikolskys sign initially. Biopsy from perilesional tissues shows intraepithelial split and acantholysis. Tzanck smear also shows acantholytic cells. Indirect and direct immunofluorecence can be used for diagnostic purpose which will show deposits of IgG and compliment around acantholytic cells.

Systemic corticosteroids remain the gold standard treatment for pemphigus vulgaris. However prolonged therapy (>4months) with systemic steroids can be attributed to severe adverse effects like diabetes, hypertension, weight gain etc., so adjuvant agents like azathioprine and mycophenolate mofetil are often considered for steroid-sparing treat-

ment. Azathioprine is the most common prescribed immunosuppressant. But azathioprine has been implicated as a cause of neutropenic ulcerations in the oral cavity, commonly buccal mucosa. However the monotherapy of pemphigus with adjuvant agent is also associated with a risk of relapse when compared to steroid therapy.

In our case patient was on Azathioprine monotherapy for past 1year and there was complete remission of dermal lesions. But exacerbation was noted in the form of recurent oral ulcerations for past 1 month. Eventhough the histopathology was suggestive of Pemphigus Vulgaris (fig2), the coexistent neutropenia favors for an Azathioprine induced oral ulcerations. We could successfully manage the case with topical steroids after stopping Azathioprine and complete remission was seen after 1 month and no recurrence on 6 month follow up.

## CONCLUSION

Even though adjuvant monotherapy is prescribed for steroid sparing effect, its irrational use cannot be justified. The clinician must be aware about the possible drug related adverse effects and treatment strategies must be planned accordingly. The patient should be periodically followed up with necessary laboratory investigations so that any developing complications can be reverted at the earliest.



Fig 1: Intra oral vesicle and mucosal erosions

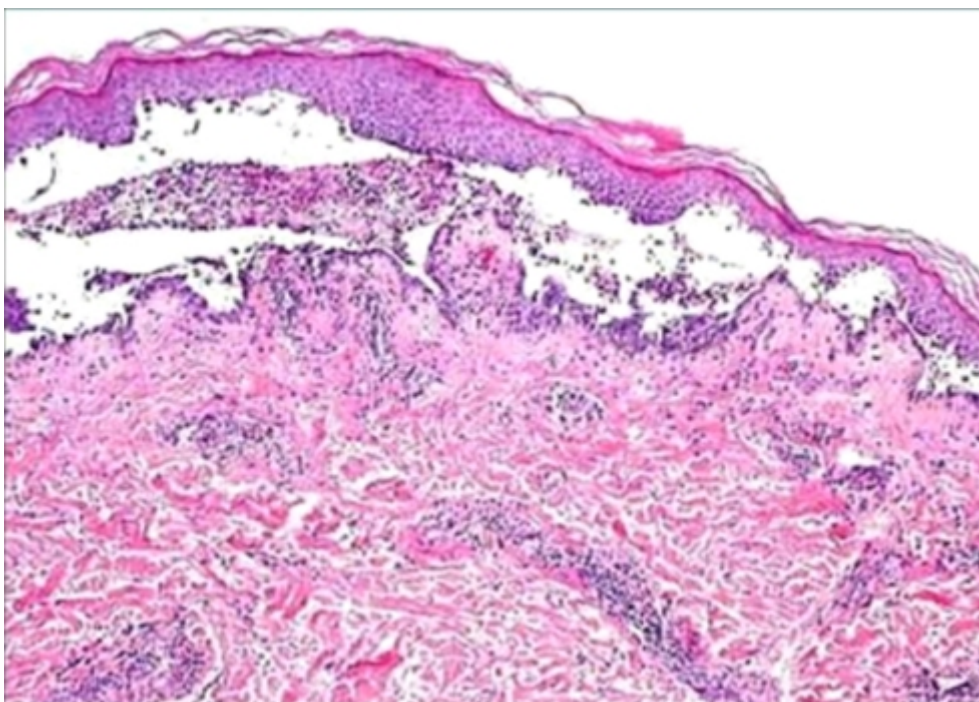


Fig 2: Histopathology showing intra epithelial split



## REFERENCES

1. Shamim T, Varghese VZ, Shameena PM, Suddha S. Pemphigus Vulgaris in oral cavity. Clinical analyses of 71 cases. Med Oral Pathol Buccal 2008; 13:2622-6.
2. C. Scully, O Paes De Almeida, SR Porter and JJH Crilkes. Pemphigus Vulgaris, manifestations and long term management of patient with oral lesions. British Journal of Dermatology 1999;140 (1):84-89.
3. S Kauvsi, M Danesh pazhooh, F. Farahani R, Abedini, V Lajevardi and C Chams davatchi. Outcome of Pemphigus Vulgaris. Journal of the European Academy of Dermatology and Venereology. 2008;22 (5) :580-584.
4. Michael H, Carrian S. Pathogenesis, Clinical Manifestation and diagnosis of Pemphigus.  
url:<http://www.uptodate.com/store> July 7, 2013.
5. Shirakata Y, Amagai M, Hanakawa Y, Nishikawa T, Hashimoto K (1998). Lack of mucosal involvement in pemphigus foliaceus may be due to low expression of desmoglein 1. J Invest Dermatol 110: 76-78
6. Ahmed AR, Graham J, Jordon RE, Provost TT (1980). Pemphigus: current concepts. Ann Intern Med 92: 396-405.
7. Scully C, Challacombe SJ (2002). Pemphigus vulgaris: update on etiopathogenesis, oral manifestations, and management. Crit Rev Oral Biol Med 13: 397-408.
8. Cheng SW, Kobayashi M, Kinoshita-Kuroda K, Tanikawa A, Amagai M, Nishikawa T (2002). Monitoring disease activity in pemphigus with enzyme-linked immunosorbent assay using recombinant desmogleins 1 and 3. Br J Dermatol 147: 261-265.
9. Gregoriou, Stamatis et al. "Management of Pemphigus Vulgaris: Challenges and Solutions." Clinical, Cosmetic and Investigational Dermatology 8 (2015): 521-527. PMC. Web. 27 Feb. 2017.
10. The role of adjuvant therapy in pemphigus: A systematic review and meta-analysis. Atzmony L, Hodak E, Leshem YA, Rosenbaum O, Gdalevich M, Anhalt GJ, Mimouni DJ Am Acad Dermatol. 2015 Aug; 73(2):264-71