Oral Mini Pulse Therapy: Report of A Case and Review of the Literature

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Summary
Oral lichen planus (OLP) is a chronic mucocutaneous disease with an unknown aetiology, affecting 0.5-2% of the population and with a predilection for females in fourth to fifth decade of life. Most oral lichen planus lesions are asymptomatic but the atrophic and erosive forms of OLP can cause symptoms ranging from spontaneous soreness to severe pain interfering with eating, speech and swallowing. Various drugs have been used for the treatment of OLP including corticosteroids and other immunomodulators. However, no therapy is considered as the single most effective and without side effects in the management of this enigmatic disease. This paper presents a case of successful management of extensive, symptomatic atrophic OLP with a novel treatment protocol: oral mini pulse therapy with betamethasone. In spite of using long-term systemic corticosteroids, side effects were minimal and clinically uneventful. Further controlled trials with this therapy may provide a definitive mode of treatment for severe OLP cases.

Key Words: Oral Lichen Planus, Betamethasone, Oral Mini Pulse

Introduction

Lichen planus is a chronic inflammatory disease involving skin and mucosa. It is one of the most common diseases that manifests itself in the oral cavity [1] and characteristically involves the buccal mucosa, tongue, and gingiva, floor of the mouth, lips, and palate [2]. The exact cause of oral lichen planus (OLP) is unknown, but it represents a cell-mediated immune response with infiltrating cell population composed of both T4 and T8 lymphocytes [3].

Carrozzo and Gandolfo (1999) have described various treatments for oral lichen planus (*Table 1*) [4]. Among the different therapies described for OLP, topical and systemic corticosteroids remain the mainstay of a management protocol. Topical corticosteroids are used as the first-line drugs, particularly for mild lesions, whereas systemic steroids are reserved for multiple, widespread and unresponsive lesions. Although corticosteroids are the most useful among various drugs in the management of OLP, they are not without significant side effects such as secondary infections, thromboembolic phenomena, gastrointestinal complications, osteoporosis, diabetes, psychological disorders, cardiovascular disorders and myopathy, hence there has been a considerable effort to find alternative methods of treatment [5].

In the recent years, pulse therapy (PT) has been widely used in the treatment of various immunological related disorders. This was first described by Pasricha and Ramji (1984) [6]. It is defined as discontinuous or intermittent intravenous infusion of very high doses (megadoses) of drugs over a short time [7]. The theoretical aims of pulsing are to achieve more rapid and effective disease control compared with conventional oral dosing, thus allowing a reduction in long-term maintenance corticosteroid doses and their side effects [8]. However, the patients on corticosteroid PT have to be continuously monitored in a hospital set-up because high doses of drugs are given intravenously. This may be particularly unnecessary in patients with only oral lesions without skin involvement. To address this problem, some 20 years ago a new therapeutic regimen called oral mini pulse therapy (OMP), taking advantage of pulsing and allowing for oral administration with lesser dosages, was devised [9]. It ensures better compliance and

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***Table 1**. Empirical treatments for oral lichen planus (modified from Carrozzo and Gandolfo, 1999 [4])*

Corticosteroids	
Topical	**Systemic**
Betamethasone phosphate	Prednisone
Betamethasone valerate	Methyl-prednisolone
Clobetasol propionate	
Fluocinolone acetonide	
Fluocinonide	
Fluticasone propionate	
Hydrocortisone hemisuccinate	
Triamcinolone acetonide	
Retinoids	
Topical	**Systemic**
Fenretinide	Acitretin
Isotretinoin	Etretinate
Tazarotene	Isotretinoin
Tretinoin	Temarotene
	Tretinoin
Immunosuppressive agents	
Azathioprine	
Cyclosporin	
Others	
Amphotericin A	Levamisole
Basiliximab	Magnetism
Diethyldithiocarbamate	Mesalazine
Dapsone	Phenytoin
Doxycycline	Photopheresis
Enoxaparin	Psychotherapy
Glycyrrhizin	PUVA
Griseofulvin	Reflexotherapy
Hydroxychloroquine sulphate	Surgery
Interferon	Tacrolimus
	Thalidomide

decreases the risk of short- and long-term side effects associated with corticosteroid therapy [10]. The OMP regimen was primarily designed for treating patients having fast spreading/extensive vitiligo to achieve the same therapeutic results as PT with minimum side effects [11]. It has also been tried for treatment of lichen planus and alopecia totalis [12]. In this article, a case of symptomatic atrophic oral lichen planus successfully treated with oral mini pulse therapy is described, together with a review of literature of this novel therapy.

Case Report

A well-built and well-nourished 58-year-old male patient visited the Department of Oral Medicine and Radiology, Dr Syamala Reddy Dental College, Hospital and Research Centre, Bangalore, India, with the chief complaint of having experienced a burning sensation in his mouth for one year, which was aggravated when taking hot and spicy food. The patient had previously been treated at a different hospital with laser therapy and topical triamcinalone acetonide 0.1% for one month but without much relief. His past medical, family and personal history were not contributory to the chief complaint. A general physical examination revealed no abnormality and vital signs were within the normal limits. On intra-oral examination, a diffuse erythematous lesion involving the maxillary and mandibular facial and buccal gingiva was noted (*Figure 1*). The palate also presented with an extensive erythematous lesion surrounded by a thin

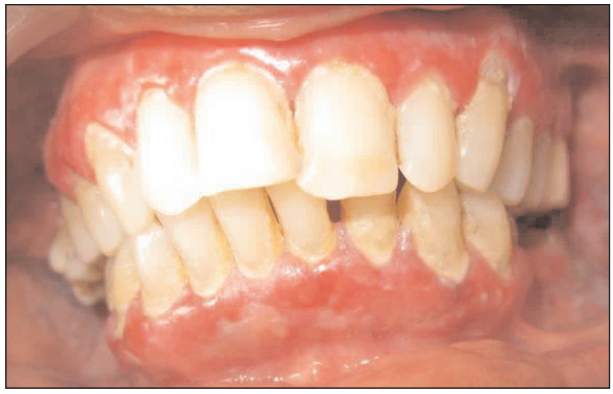

***Figure 1.** Erythematous lesion involving the maxillary and mandibular facial and buccal gingiva*

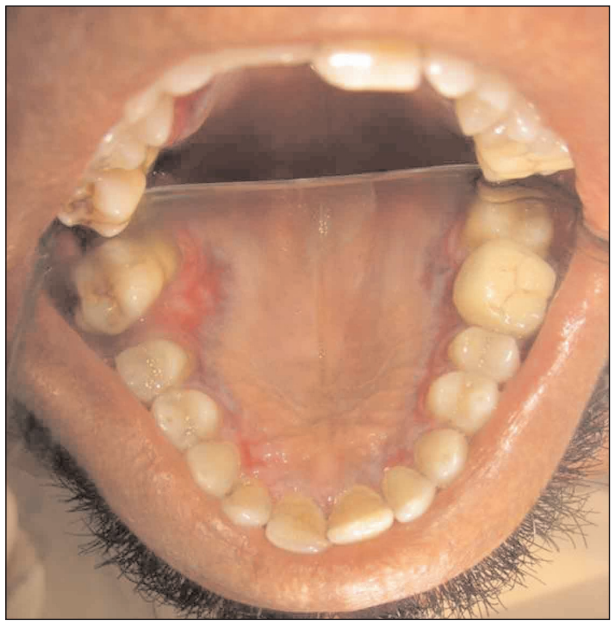

***Figure 2.** Palatal mucosa presented with an extensive erythematous lesion surrounded by a thin white linear striae.*

white linear striae. Buccal mucosa and lateral borders of the tongue presented with diffuse white striae arranged in a reticular fashion *(Figures 2* and *3a-c*). Based on the clinical findings, a provisional diagnosis of atrophic oral lichen planus was given. The patient's haematological investigations, renal and liver function tests were within the normal limit. Following written informed consent, an incisional biopsy was performed at two sites, one on the right buccal mucosa and the second on the palatal mucosa near the right maxillary tuberosity region. The specimen from the buccal mucosa was split into two sections, one was transferred to normal saline for direct immunofluorescence study

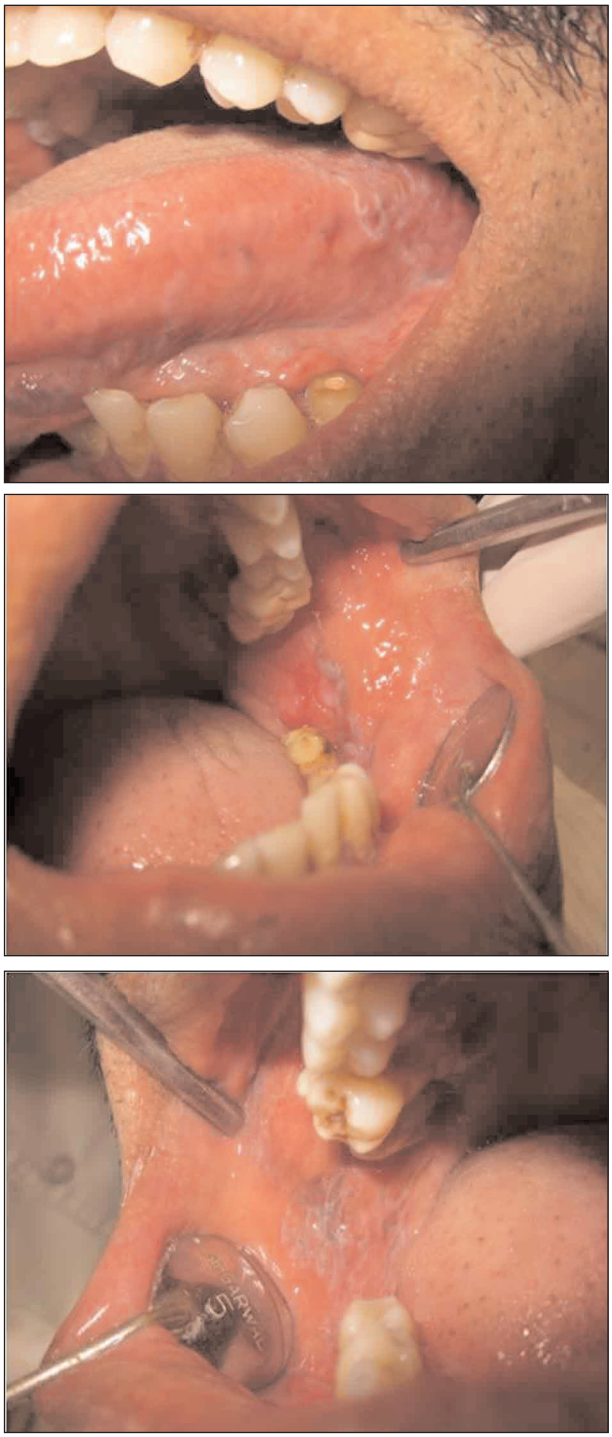

Figure 3 (a-c). *Buccal mucosa and lateral borders of the tongue presented with diffuse white striae arranged in a reticular fashion*

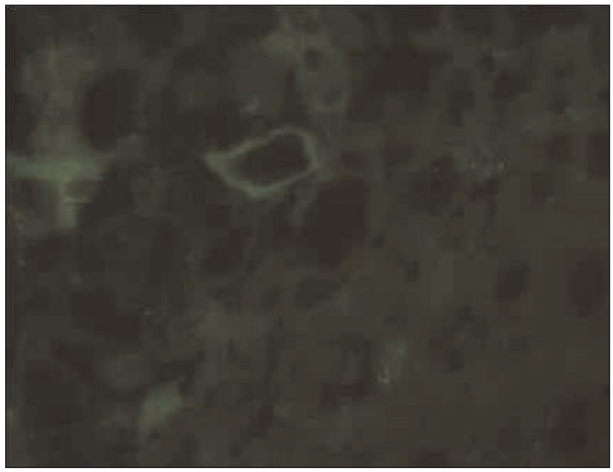

Figure 4. *Direct immunofluorescence demonstrated IgM and C3 at the basement membrane zone*

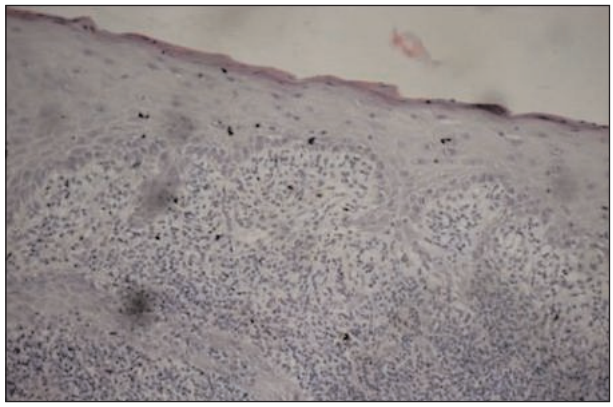

Figure 5. *H&E stained specimen showing oral lichen planus with mild dysplasia on the palatal mucosa.*

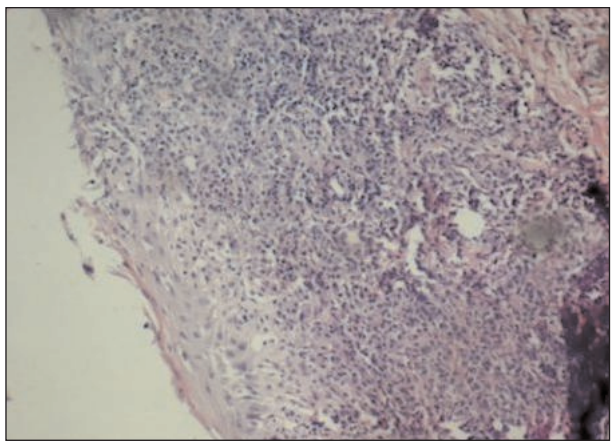

Figure 6. *H&E stained specimen showing oral lichen planus on the buccal mucosa.*

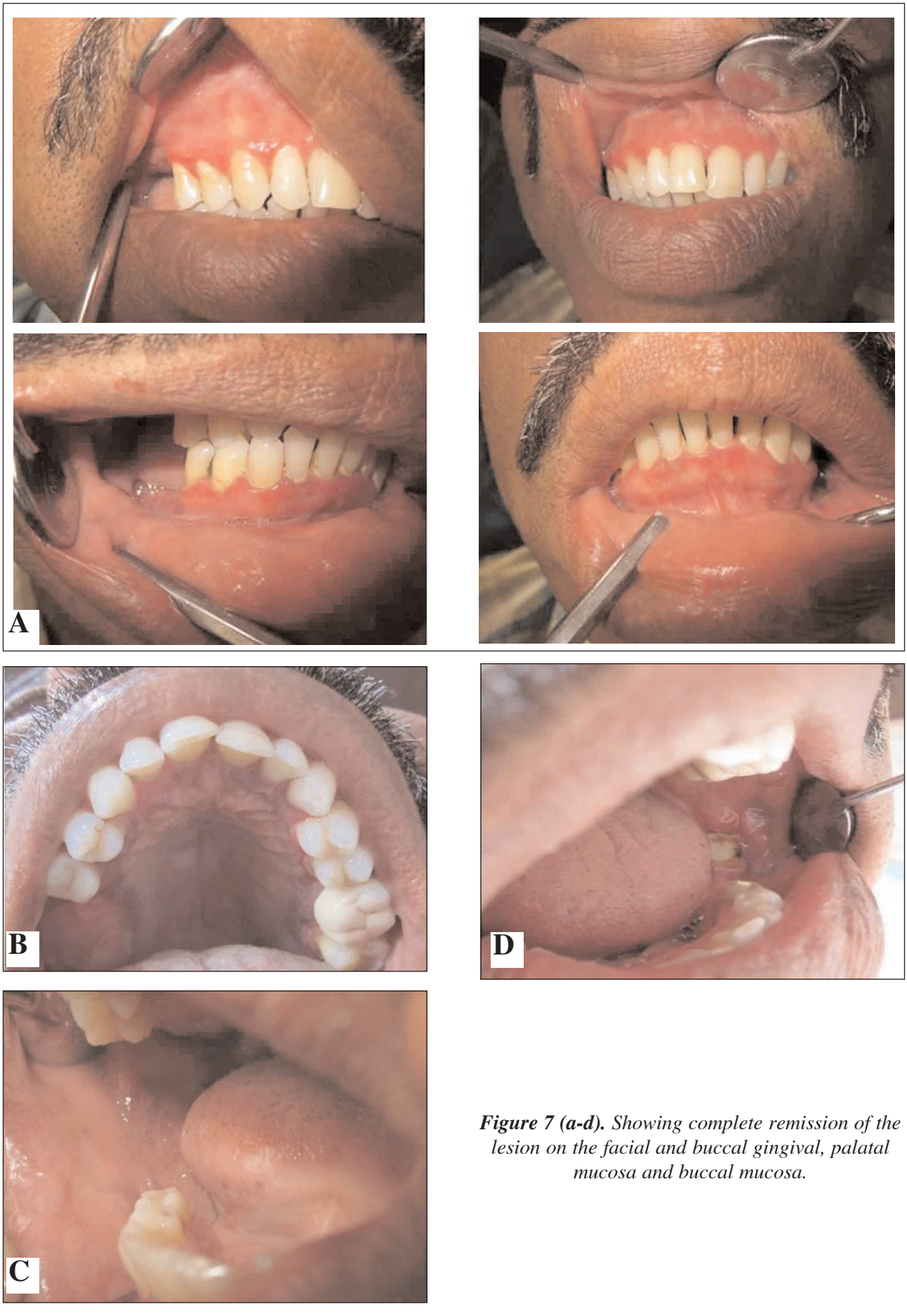

Figure 7 (a-d). *Showing complete remission of the lesion on the facial and buccal gingival, palatal mucosa and buccal mucosa.*

and the other was transferred into formalin for histopathological examination. Direct immunofluorescence demonstrated immunoglobulin M and complement component C3 at the basement membrane zone (*Figure 4*), consistent with the diagnosis, and histopathology revealed features of oral lichen planus, with mild dysplasia on the palatal mucosa analysis (*Figure 5*) and without dysplasia on the buccal mucosa (*Figure 6*).

The patient was educated and motivated regarding proper plaque control and rinsing twice daily with benzydimine hydrochloride mouth rinse. He was started on 5 mg betamethasone (10 tablets of 0.5 mg betamethasone) as a single dose in the morning after breakfast for two consecutive days followed by five days off, every week for a period of three weeks. Weekly assessments revealed gradual and consistent reduction in the burning sensation. Following this, his dose of betamethasone was tapered by 0.5 mg every week. At the sixth week, the patient developed a new ulcerative lesion on the left buccal mucosa. Hence, from the sixth to the ninth week the patient was maintained on a dose of 3.5 mg betamethasone. During this period the ulcerative lesion disappeared and the erythema present on the other areas healed, with the pigmentation and burning sensation completely reduced. From the tenth week the dose was further tapered down by 0.5 mg every week. At the fifteenth week the patient was taking 0.5 mg and this dose was maintained for three weeks. The therapy was stopped after complete remission of the lesions was achieved (*Figure 7a-d*). A summary of the treatment schedule followed is presented as a flow chart (*Figure 8*). The patient was monitored at regular intervals for weight gain, alteration in blood pressure, and also subjected to haematological investigations, renal and liver function tests. At the fifth week of therapy, a decrease in the white blood cell count (WBC) and haemoglobin level and an increase in the erythrocyte sedimentation rate (ESR) were noted, which improved markedly after tapering the dose. For the last four months, the patient has been under continuous follow up and has not reported with any new lesions.

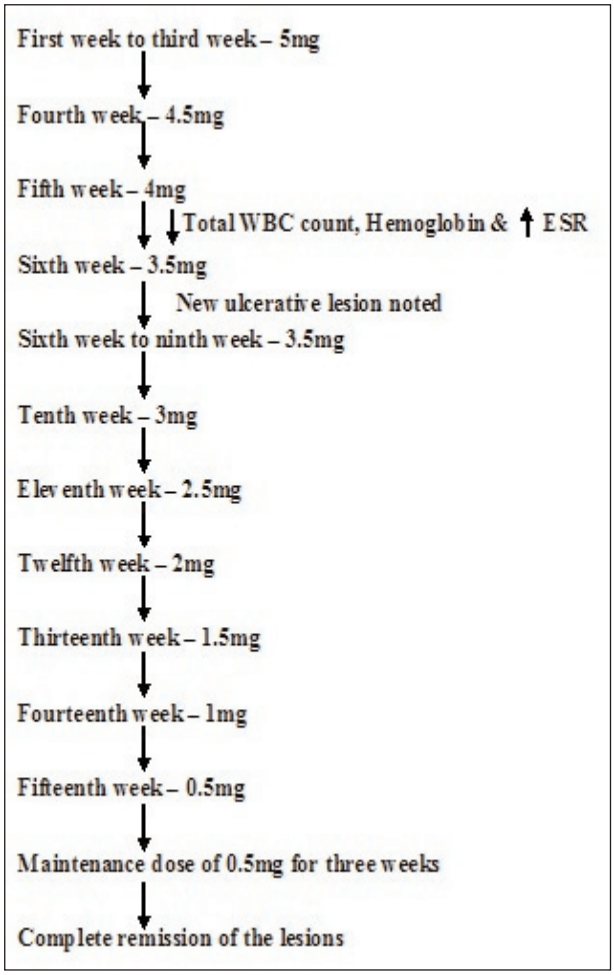

Figure 8. *Flow chart.*

Discussion

As stated in the introduction, oral lichen planus is a chronic mucocutaneous disease with an unknown aetiology [13]. The disease affects 0.5-2% of population with a predilection for females and the mean age of onset in the fourth to fifth decade of life [14]. It has a chronic remitting and relapsing course with little tendency for spontaneous remission thereby making management of OLP a challenge for clinicians.

Corticosteroids are considered the most effective agents in the treatment of OLP, with topical agents being preferred over systemic drugs except during acute exacerbations [15]. Topical corticosteroids when applied for a short duration are safe, but prolonged use can produce side effects such as secondary candidiasis and, rarely, atrophy of the oral mucosa [16]. Furthermore, the risk of adrenal suppression as a result of systemic absorption from oral mucosa is not insignificant [17]. It is also uncomfortable for the patient to apply medication frequently. Systemic corticosteroids, on the contrary, are of great value during the acute exacerbation of symptoms and are often used in combination with topical corticosteroids. However, adverse effects of systemic corticosteroids are common, particularly when used for a long time. In the form of oral mini pulse therapy, corticosteroids have shown efficacy with few and acceptable side effects, in diseases such as vitiligo and alopecia areata [18]. OMP was used for the administration

of 5 mg betamethasone orally once daily for two consecutive days in a week for a period of three weeks to three months. A literature review revealed a few case reports and series where OMP has been used effectively and safely to treat lichen planus.

Joshi *et al.* (1999) [19] treated a patient suffering from generalised and bullous lichen planus with oral mini pulse therapy consisting of 5 mg betamethasone given orally as a single daily dose on two consecutive days every week. In addition, betamethasone dipropionate 0.01% gel twice a day for topical application on the oral and genital lesions was also advised. Within two weeks fresh lesions had stopped appearing completely and older lesions started subsiding rapidly. The bullae subsided without any scarring. OMP was tapered in a step-wise manner, reducing it by 0.5 mg every week, and was completely stopped within the next ten weeks. There were no side effects of the therapy. The lesions did not relapse during the 12-month follow-up period.

Mittal *et al.* (2000) [10] conducted a study in ten patients, six males and four females between 7-60 years of age, who had experienced lichen planus for a period of one month to two years. The patients were treated with betamethasone 5 mg orally on two consecutive days in a week for three months. There was an excellent (75-100%) response in six (60%) patients and a good (50-75%) response in four (40%) patients. None of the patients experienced significant side effects from the therapy and there were no treatment failures. The authors concluded that betamethasone on two consecutive days in a week as oral mini pulse therapy may be a safe, effective and a better therapeutic alternative for the treatment of lichen planus.

Al-Mutairi *et al.* (2005) [20] treated acute generalised lichen planus with weekly betamethasone 5 mg oral mini pulse therapy. Systemic treatment with oral corticosteroids in the form of ten tablets of betamethasone 0.5 mg in a single dose was given after breakfast on two consecutive days every week. Complete arrest of progression, control of itching, and flattening of lesions was achieved within three weeks, allowing tapering of the dose of corticosteroid by 0.5 mg every two weeks over the next ten weeks. No side effects of corticosteroid therapy were noted during the follow up.

A study was conducted by Malhotra *et al.* (2008) [18], in which 49 patients with moderate to severe oral lichen planus were randomly allocated to receive either OMP comprising 5 mg of betamethasone orally on two consecutive days per week (group A) or triamcinolone acetonide (0.1%) paste application thrice daily (group B) for three months followed by stepwise tapering during the next three months. Treatment response was assessed by the change in the score, which was based on the number of sites involved and the areas affected. Changes in the symptoms and side effects were also recorded. Patients were followed up after treatment for three months to look for relapse. A good to excellent response was seen in 17 of 25 (68.0%) patients in group A as compared with 16 of 24 (66.0%) in group B at 6 months. A symptom-free state was achieved in 13 of 25 (52%) patients in group A and 12 of 24 (50%) in group B. Relapse occurred in nine of 23 (39.1%) patients in group A after 13.78 ± 6.96 weeks as compared with five of 23 (21.7%) in group B after 19.20 ± 1.79 weeks. The investigators concluded that betamethasone administered via an OMP improves the clinical outcome in patients with moderate to severe oral lichen planus and though the treatment was equally effective as topical triamcinolone acetonide, the response is earlier, especially in erosive diseases. Thus, OMP may be a useful and convenient alternative either as a monotherapy or to achieve rapid symptomatic relief during periods of exacerbations.

Rashid *et al.* (2008) [21] studied 40 patients with lichen planus, of whom 20 patients in group A received 5 mg betamethasone mini pulse therapy for two consecutive days in a week for six weeks along with loratadine and 20 patients in group B received a loratadine tablet daily for the same period. It was clearly observable that the number of lichen planus lesions were drastically decreasing in group A and only slightly increasing in group B during the follow-ups. They concluded that betamethasone oral mini pulse therapy was found to be more effective than loratadine in the treatment of lichen planus.

In the case presented here, in spite of a long course of corticosteroids, major side effects were easily avoided without compromising the clinical outcome of the therapy. The main advantage of OMP is its easy administration without hospital admission, unlike pulse therapy. But the drawback of OMP is that its success depends on patient compliance. In our case, a clear dosage schedule was given to the patient, so that the patient took the medication on the particular day without any confusion. Previous studies have used betamethasone in OMP and the same regimen was followed in our patient. However, other corticosteroids—such as methylprednisolone and dexamethasone—should also be tried as part of OMP. In some dermatological lesions, these have achieved better results when compared to betamethasone and hence future studies should compare the efficacy of different corticosteroids OMP in the management of OLP. Also,

a combination of OMP with steroid-sparing drugs might be beneficial and remains to be evaluated in terms of success and avoidance of relapse.

Conclusion

This case provides further evidence that oral corticosteroid pulse therapy is an effective treatment modality to arrest extensive erosive oral lichen planus lesions. The advantages of OMP are its convenient dosage schedule, efficacy, insignificant side effects and no sustained suppression of the endogenous cortisol production. Hence this therapy can be employed as a routine treatment modality for oral lichen planus as it offers a non-invasive option that yields significant improvements in the symptoms as well as objective signs of the condition.

Acknowledgement

The authors would like to thank the patient who gave permission to include his photographs and details of his treatment.

Funding

No external funding was used for the current work.

Contributions of each author

- PK performed the clinical investigations and treatment of the patient, and carried out the literature review and manuscript preparation.
- SB provided guidance throughout the treatment and follow-up of the patient.
- JVR contributed to the literature review and preparation of the manuscript.
- MP and MT contributed to the literature review.
- SG provided support in the preparation of photographs and writing of the paper.

Statement of conflict of interest

The authors declare no conflict of interest.

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