

Treatment of oral lichen planus with photodynamic therapy mediated methylene blue: A case report

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ABSTRACT

Oral lichen planus (OLP) is a common chronic disease of uncertain origin. Many patients with OLP are refractory to all available therapies. The photodynamic therapy (PDT) was used as a possible alternative method in the treatment of lichen planus. Two patients with five oral lichen planus lesions were treated using topical PDT mediated by methylene blue (MB-PDT). The patients were followed up on sessions 3, 7, 15 days and 1 to 9 months after PDT. Clinical improvement was achieved in four lesions. Two lesions showed complete remission, and another two lesions had about 50% clinically improvement 3-9 months after a single session of PDT. No response detected in one lesion. MB-PDT blue seems to be an effective alternative treatment for control of OLP. In our opinion, this preliminary result warrant further studies in order to show the efficacy of MB-PDT in control of OLP for a longer period of time.

Key words: *Oral lichen planus, photodynamic therapy, methylene blue*

INTRODUCTION

Lichen planus (LP) is a relatively common, chronic dermatologic disease that often affects the oral mucosa (1). OLP is reported to occur in 0.5-2.2% of the population, with a peak incidence in the 30-60 years age range and with a female predominance of 2:1. Unlike oral lesion, skin lesions are usually self limited, lasting only one year or less.

The etiology of LP involves a cell-mediated immunologically induced degeneration of the basal cell layer of epithelium (1). Two basic types of lesion occur: totally white (keratotic) and white (keratotic) with red (atrophic, erosive, bullous) (2). The occurrence of squamous cell carcinoma in most series ranges from 0.4 to 2% per a 5-year observation period (3). Treatment options of OLP are numerous, including topical

and systemic agents (4). Because LP is an immunologically mediated condition, corticosteroids are recommended. Topical corticosteroids remain the mainstay of therapy. However, therapeutic results are often disappointing. Photodynamic therapy (PDT) is an effective therapy for premalignant and malignant cutaneous lesions (5). It has also been reported as effective in treating psoriasis. We are reporting the results of oral lichen planus with Methylene blue mediated PDT in two cases.

CASE REPORTS

The Patients were referred to the clinic of Iranian center for medical laser (ICML), ACECR, to undergo PDT. Methylene

blue (MB) was used as photosensitizer. It was prepared 0.05 gr per 100 cc. Ten minutes prior to laser irradiation, patients gargled MB for 5 minutes. A diode laser (Lumina®, Russia; 632 nm, CW) was used as light source. The lesions and 1 cm of their surrounding marginal zone were illuminated with a spot size of 2.5-3 cm². Large lesions were illuminated with multiple spots. A fluence of 100 J/cm² was used. The patients were followed up on sessions 3, 7, 15 days and 1 to 9 months after PDT. At the follow up sessions; lesions were examined to detect any residual lesion. Lesions were exactly measured and digital photographs were taken before PDT and at follow up session. Response rates were assessed clinically by amount of reduction in surface area of lesions.

Patient 1

A 52-year-old woman was referred to Oral Medicine Department of Tehran University by a specialist. Her medical history was positive for hypertension and taking propranolol and fluxitin.

Her complaint was burning sense. Clinical examination revealed an atrophic area with white striae in her right mandibular and left maxillary gingiva vestibule (Figure 1). Before treatment we use vital staining with toluidine blue for rule out of malignancy, then patient signed a written consent statement after receiving a full verbal explanation of treatment, including the potential benefits and risks of treatment. One week after a single session of PDT the lesions completely disappeared and results of treatment were stable for 9 consecutively months of following.

Patient 2

A 60-year-old man with a 12-year history of OLP had previously been treated with topical steroids. He had three keratotic lesions in left and right buccal mucosa and tongue. patient signed a written informed consent statement after receiving a full verbal explanation of treatment, including the potential benefits and risks of treatment (Figure 2).

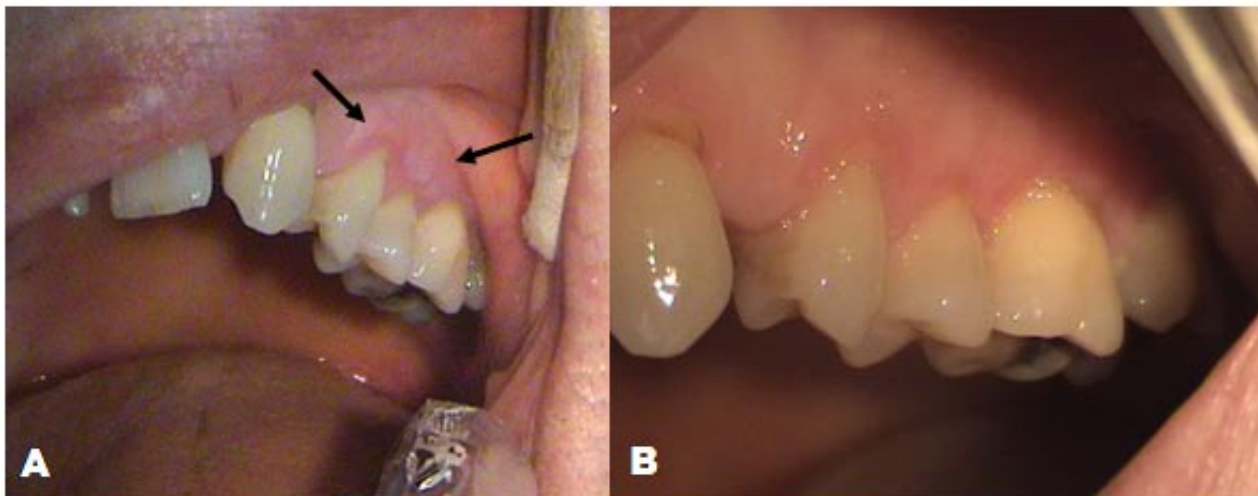


Fig. 1. Atrophic and keratotic lichen planus lesion on the left upper gingival before photodynamic therapy (PDT) (A). Complete response after 9 months follow-up (B).



Fig. 2. Keratotic lichen planus lesion on the left buccal mucosa before photodynamic therapy (PDT) (A). Partial response after 2 months follow-up (B).

He was treated as the same method as mentioned above. A week after treatment reduction size in right buccal lesion was about 40% and in left lesion 20%. Tongue lesion shows no sign of response, results of treatment were stable for 2 months of following.

DISCUSSION

Oral lichen planus (OLP) is a chronic inflammatory disease characterized by relapses and remissions. It is a cell-mediated immune condition of unknown etiology, in which T lymphocytes accumulate beneath the epithelium of the oral mucosa and increase the rate of differentiation of the stratified squamous epithelium, resulting in hyperkeratosis and erythema with or without ulceration (1).

There is currently no cure for OLP. Treatment is aimed primarily at reducing the length and severity of symptomatic outbreaks. Topical steroids are the first choice agent for the treatment of symptomatic, active OLP (4). Other topical agents that have been used in cases resistant to topical steroids include retinoids, azathioprine, cyclosporine, tacrolimus, and mycophenolate mofetil. Oral and topical PUVA therapy with low-dose UVA is effective in treating OLP of the various forms, but it seems to have too many side-effects, mainly nausea and the potential for carcinogenicity (6). Topical application of psoralen is promising, but still experimental.

The treatment of dysplastic LP may require additional approaches directed at dysplastic/genetic changes that make use of current management for oral dysplasia, in addition to the anti-inflammatory management reviewed earlier (7). Current approaches to the management of oral dysplastic lesions include excision (laser or surgical), topical therapies including vitamin A and vitamin A analogues, topical chemotherapy (such as bleomycin), and systemic treatment with vitamin A analogues and other miscellaneous agents (7). The treatment of symptomatic OLP, especially the erosive variant, represents a perplexing therapeutic challenge. Despite numerous existing remedies, there are many treatment failures.

One such promising modality is photodynamic therapy (PDT). PDT is a technique that uses a photosensitizing compound, activated at a specific wavelength of laser light, to destroy the targeted cell via strong oxidizers, which cause cellular damage, membrane lysis, and protein inactivation (8). PDT has been used with relative success in the field of oncology, notably in head and neck tumors (9).

The exact mechanism of action of PDT is unclear. It would appear to act on hyperproliferating cells, such as are present in malignancies and psoriasis, with selective uptake of photosensitizers into these cells (10). It has been suggested that PDT may have immunomodulatory effects and may induce apoptosis in the hyperproliferating inflammatory cells which are present in psoriasis and lichen planus. This may reverse the hyperproliferation and inflammation of lichen planus.

Nearly a century ago the antibacterial characteristics of the

phenothiazine dye Methylene blue (MB) were described and attributed to its photodynamic 6 properties. MB itself has been used in medical practice for more than 100 years and is recognized as having very low tissue toxicity. Clinical uses of MB include the treatment of ifosfamide encephalopathy, methemoglobinemia, urolithiasis, and cyanide poisoning (11). In addition, 0.5% MB is commonly used to stain the esophagus of patients with a history of Barrett's esophagus and the bronchial lesions/pulmonary nodules of potential lung cancer patients (12). MB can be administered to human beings orally or intravenously in high doses without any toxic effects (13). Unlike other photosensitizers; MB can be administered topically and orally and it may be a preferred choice for superficial lesions in skin and oral cavity. The fact that MB has a strong absorption at wavelengths longer than 620 nm, where light penetration into tissue is optimal, has led to the using of MB as a promising candidate for PDT. Previous studies showed ALA-mediated PDT that in addition to being a somewhat painful therapy, the drug when topically applied does not penetrate deeply (14).

In this study, five lesions had been treated with MB-mediated PDT. Two lesions completely resolved (Complete response). A partial response (more than 50% improvement) was observed in two other lesions. There was no recurrence in improved lesions after 9 months follow-up. No improvement was observed in lesion on the tongue.

We could find one report of the use of PDT for hypertrophic lichen planus of the penis (15). Kirby and et al. used ALA-mediated PDT twice for treating of the lesion. The lesion had completely resolved after 4 weeks. At 6-month follow-up there was no recurrence.

We believe this therapy may be effective in the treatment of oral lichen planus as well as neoplastic conditions. Further studies are needed to confirm the efficacy of PDT in the treatment of oral lichen planus.

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