CLINICAL CASES

Ewa Krawiecka1, B–D, Elżbieta Szponar1, A, E, Barbara Dorocka-Bobkowska2, E, F

Severe Oral Lichen Planus Responsive to Topical Cyclosporine A – Case Report

Ciężka postać liszaja płaskiego wrażliwego na miejscowe leczenie cyklosporyną A – opis przypadku

1 Department of Oral Mucosa Diseases, Poznań University of Medical Sciences, Poznań, Poland
2 Department of Prosthetic Dentistry, Poznań University of Medical Sciences, Poznań, Poland

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of article

Abstract

Oral lichen planus (OLP) is a chronic, inflammatory, mucocutaneous disease of an autoimmune origin. The disorder may be painful and debilitating and complete resolution is rarely observed. Although there are controversies in the management of symptomatic OLP, topical steroids are considered to be the first line of treatment. Topical cyclosporine (CS) therapy has shown conflicting results in many studies. This paper presents the case of a 70-year-old female patient with a history of hypertension, hypothyroidism and erosive OLP presented with a chief complaint of severe pain and burning sensation on the palate. The patient used acrylic removable partial dentures. OLP was resistant to standard treatment with topical steroids, but responded well to topical CS. Topical administration of the CS solution (“swish-and-spit” method) resulted in marked improvement in the degree of erythema, pain and discomfort. The follow-up showed longer remissions and milder lesions than prior to the therapy and no adverse systemic reactions (Dent. Med. Probl. 2015, 52, 2, 241–245).

Key words: oral cavity, lichen planus, cyclosporine, steroids.

Słowa kluczowe: jama ustna, liszaj płaski, cyklosporyna, steroidy.

Oral lichen planus (OLP) is a common, chronic, inflammatory mucocutaneous disease. The prevalence ranges from 0.5 to 2% of the general population, with a predominance among females over 40 years of age [1]. The exact cause of the disease remains unclear. It has been suggested that immune disorder plays a significant role in the pathogenesis of OLP, specifically related to an abnormal T-cell mediated response to antigens of basal epithelial keratinocytes [2–4]. Predisposing factors include diabetes, hypertension, hypothyroidism, infection of the hepatitis C virus and psychological stress [2, 5, 6]. Lichenoid lesions, resembling OLP, may occur as a reaction to several drugs or metallic materials, or may be found in other autoimmune diseases, such as lupus erythematosus (LE) or chronic ulcerative stomatitis (CUS) [7–9]. There are several clinical forms of OLP, with reticular and erosive being most common, followed by plaque-like and atrophic presentations [1, 2]. The disorder might be painful and debilitating, especially with erosive OLP. This form is presented as shallow erosions and erythematous areas, surrounded by white, lace-like lesions. The eruptions are usually bilateral and symmetrical [1, 2]. Although the most common site for the lesions is the buccal mucosa, the tongue, gingiva, lips, and in some cases, the pal-

This paper was presented on the 12th Biennial Congress of the European Association of Oral Medicine, 12–14 September, 2014, Antalya, Turkey.
ate may be affected. One of the symptoms of OLP may be desquamative gingivitis [8]. OLP demonstrates a recalcitrant course with remissions and exacerbations. Complete resolution is rarely observed. Treatment of the non-reticular forms of OLP is difficult and it is concentrated mainly on relieving the pain and prolonging the remission periods. Although there are controversies in the management of symptomatic OLP, topical steroids are considered to be the first line treatment [1, 7]. Topical cyclosporine therapy has shown conflicting results in many studies.

In this paper we present a case of severe erosive OLP, resistant to steroids, but responsive to topical cyclosporine A.

**Case Report**

A female patient aged 70 was admitted to the Department of the Oral Mucosa Diseases at Poznan University of Medical Sciences with painless, white lesions on the oral mucosa detected during a routine dental visit. She was a non-smoker, she did not report any unusual dietary habits and had used acrylic removable partial dental dentures for 8 years. The medical history of the patient included hypertension, hypothyroidism and erosive OLP presented with a chief complaint of severe pain and burning sensation on the palate. The afflictions resulted in a disturbance of her food intake and the use of partial dentures. An exacerbation of the OLP was reported in the past few months, with persistent erosions and only short remission periods. According to the medical records, OLP had been diagnosed 6 years earlier and was confirmed histopathologically. The patient was administered several therapies with topical steroids (hydrocortisone, dexamethasone). Previous treatment of the oral mucosa lesions also included topical anti-fungal agents (nystatin, miconazole).

Examination disclosed bilateral, white, non-removable, lace-like lesions on buccal mucosa and shallow erosions involving the hard palate and maxillary gingiva (Fig. 1). Desquamative gingivitis was also observed in the maxilla. The patient also presented denture-induced erythema on the palate (Fig. 2). The partial removable dentures were found to be unstable and were a possible source of trauma to the oral mucosa. No skin involvement was detected. Dexamethasone was prescribed to be applied on the erosions, 3 times a day for 3 weeks. The follow-up visit showed no healing process in erosions. Moreover, the course of the disease was complicated by a secondary candidiasis. The patient was also referred to the Department of Prosthetic Dentistry and scheduled for new removable partial dentures.

Mucosa specimens from the right buccal area and the hard palate were collected for histopathological evaluation. The epithelial findings included acanthosis (“saw tooth appearance”) and minor hyperkeratosis. Chronic inflammation was noted, with infiltrate consisting primarily of T-lymphocytes, in apposition to the basal cell layer. Liquefaction degeneration within the lower epithelial layers and the minor dysplasia were detected. The diagnosis of OLP was confirmed. Figure 3 presents the histopathological picture of the collected material.

Since the patient did not respond to the treatment and the erosions persisted, she was direct-
ed to the Department of Dermatology. During the hospitalization, indirect immunofluorescence (IF) of the mucosal biopsy showed the presence of anti-nuclear antibodies (IgG, IgG4), reactive with lower layers of the epithelium. Diagnosis of chronic ulcerative stomatitis (CUS) was suggested. However, direct immunofluorescence (DIF) did not reveal the presence of the antibodies.

The patient was prescribed chloroquine, administered orally (250 mg per day), and topical hydrocortisone. The implemented treatment did not result in improvement of the clinical picture of OLP and, according to the patient, caused severe gastro-intestinal disorders.

Since the patient was unresponsive to the previous, standard treatment, cyclosporine A (CS) was prescribed in consultation with a dermatologist, used as a mouthwash (“swish-and-spit” method) twice a day for four weeks. The therapy produced a significant improvement in the OLP. The degree of erythema, pain and discomfort were substantially diminished.

However, after ceasing administration of the drug, exacerbation recurred. Once-daily administration of the drug was then continued for about a year to prevent the relapses. The follow-up visits showed longer remissions (a few weeks to a few months) and milder lesions than prior to the therapy and no adverse systemic reactions. Anti-fungal topical treatment with fluconazole was applied every 3 months to avoid the secondary candidiasis. Routine whole blood tests produced results which remained within the normal limits.

Discussion

Management of OLP is difficult and the results may not be satisfactory. Asymptomatic reticular forms do not require any treatment, whereas in erosive and atrophic OLP the goal is to achieve longer remission periods and to lower the severity of pain and discomfort [10, 11]. Topical steroids are most widely accepted in the therapy of OLP due to their effectiveness, availability and low cost [12, 13]. Therapeutic options include betamethasone, clobetasol, fluorocinolone, hydrocortisone, triamcinolone and dexamethasone, applied as gels, ointments, rinses or injections directly into the lesion. Topical administration has few side-effects, with secondary candidiasis being the most common. However, this therapy is the mainstay in treating mild to moderately symptomatic OLP [1]. In patients with severe, multifocal symptomatic lesions a systemic course of steroids might be used. Clinicians must therefore be aware of the numerous side effects of systemic steroid therapy, and that not all patients are responsive to steroids or may not use them. It is also contraindicated in patients with herpetic infections, glaucoma, pregnancy, HIV infection, tuberculosis, diabetes mellitus or hypertension [1]. With regard to the contraindications, there have been several alternative approaches suggested. These include the use of retinoids, tacrolimus or pimecrolimus, chloroquine, azathioprine or cyclosporine [7].

In our patient, the lesions on the mucosa on the hard palate may also be related to the use of unstable acrylic removable partial dentures. The lesions may be regarded as a form of denture stomatitis, plaque-related oral disease, which is a common disease in acrylic denture wearers [14, 15]. It has been assumed that instability of the dentures and unbalanced occlusion gives rise to mechanical irritation from the denture plate. Additionally, the isolated oral mucosa tissues under a maxillary denture form their own microenvironment, which disturbs the normal microbiological balance [14, 15]. Moreover, the surface roughness of the heat-polymerized acrylic resin of the denture and hydrophobic interactions are regarded as the main factors that affect the adhesion of Candida and subsequent biofilm formation on acrylic surfaces [16].

Cyclosporine is an immunosuppressant that inhibits calcineurin, the enzyme responsible for the gene transcription of interleukine-2 (IL-2). Its ability to suppress T-cell cytokines might potentially diminish the improper immunological response in OLP [3, 8]. CS has successfully been used in treating a variety of autoimmune disorders [9]. However, CS therapy in OLP has been controversial. In the
patient described here, a standard treatment regimen failed to be effective, while CS was used successfully. Similar cases showing impressive results in resistant OLP have been reported [8, 17]. Demitsu et al. [17] described a steroid-resistant lichen plano- nus of the lower lip that responded well to topical CS applied by finger. A double-blind analysis comparing topical CS to a placebo was carried out by Eisen et al. [10] on sixteen patients. Marked improvement in erythema, erosion, reticulation and pain was observed only in the CS recipients, with no systemic side effects reported and with longer remissions in most of the patients. No adverse reactions were observed in our patient as well. Three randomized, controlled trials to compare topical CS with steroids in erosive OLP were conducted [3, 12, 18]. The only double-blind analysis reported included 40 patients divided into groups receiving CS or topical clobetasol. In this study, the steroid appeared to be more effective in clinical improvement, but comparable to CS in its effects on symptoms. However, CS gave more stable results after discontinuing the therapy and showed lower incidence of side-effects [18]. Both remaining trials suggest that topical CS is no more effective than steroids (triamcinolone) or provided no beneficial effects in symptomatic OLP [3, 12]. Other less encouraging study results have been reported. Itin et al. [19] treated 7 patients with hydrophilic CS applied topically, of whom only one demonstrated total clearing of the lesions. Levell et al. [20] administered topical CS (mouthwash, 100 mg/mL) to 7 patients, with no distinct improvement after 4 weeks of the therapy. Most of the trials were conducted on small samples, and used different formulas, dosage and pattern of application of the drug, which may affected the therapeutic outcomes. Some meta-}

analysis studies have been conducted on the topic of treating OLP. The authors noted that there was no strong evidence in favor of any therapy for OLP. It has been suggested that there is a need to standardize the methodology of future OLP intervention trials [11, 21].

The mechanism of topically administered CS in OLP remains unclear. It has been suggested that the positive effects are likely due to systemic absorption [19, 22]. On the other hand, CS blood concentration was rarely detected in the studies where a blood analysis was performed after administration [3, 18]. High absorption potential of the oral mucosa was shown since the CS levels detected in oral mucosa specimens after topical administration of the drug were comparable to those found in psoriatic lesions after systemic use [10]. Hence, CS appears to act directly in situ through the suppression of activated T-cells [14].

There have been some disadvantages reported with the topical use of CS. They include a bad taste and burning sensation, gastrointestinal discomfort, dizziness and swelling lips [3, 7, 23, 24]. Systemic administration of CS may cause severe side effects, such as hypertension, nephrotoxicity and gingival overgrowth [7, 25]. The high cost of the therapy might limit its use, especially when prolonged treatment is considered [7, 24]. Moreover, the pharmacological formulas available are designed for systemic use. The CS solutions may be applied topically by finger, or via a “swish-and-spit” method, but such administration might not be precise. However, the case we report provides evidence that topical use might have a positive effect on severe OLP and should be considered as an alternative treatment in resistant forms of the disease.

References
Oral Lichen Planus – Case Report


Address for correspondence:

Barbara Dorocka-Bobkowska
Department of Prosthetic Dentistry
Poznań University of Medical Sciences
Bukowska 70
60-812 Poznań
Poland
Tel.: +48 61 8547 202
E-mail: b.dorocka@gmail.com

Conflict of interest: None declared

Received: 9.10.2014
Revised: 11.11.2014
Accepted: 22.12.2014