CASE REPORT

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Candidiasis in Oral Lichen Planus: Complication of Topical Corticosteroid Overuse

Oral Liken Planusta Kandidiazis: Aşırı Topikal Kortikosteroid Kullanımına Bağlı Komplikasyon

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ABSTRACT

Objectives: Topical steroids represent the mainstay of management for symptomatic oral lichen planus (OLP), owing to their effectiveness in alleviating pain and inflammation. However, their use may result in adverse effects, such as secondary oral candidiasis (OC), influenced by factors such as potency, duration and frequency of use, and site of application. This study presents a case of OC following topical steroid therapy for OLP, emphasizing the importance of patient compliance in treatment.

Case report: A 78-year-old woman diagnosed with cutaneous lichen planus four months prior was referred to our clinic for evaluation of new oral lesions. Erosive OLP lesions on the buccal and labial mucosa and tongue were noted upon intraoral examination. The patient was prescribed mometasone furoate 0.05% spray to be used twice daily. As a result of the patient using the medication at a higher dose and frequency than recommended, pseudomembranous OC was observed on the buccal mucosa and soft palate at the follow-up appointment two weeks later. The patient was prescribed an oral suspension of nystatin (100,000 IU) for gargling four times a day, and complete resolution of the OC was achieved within a period of 14 days. Subsequently, the OLP lesions reverted to a reticular form with appropriate use of the topical steroid. The patient remains under regular follow-up at our clinic.

Conclusion: Secondary OC may obscure and/or aggravate the clinical features and symptoms of OLP, potentially hindering effective management. Close monitoring of pharmacological therapy and timely intervention for secondary OC are crucial for achieving optimal treatment outcomes.

Keywords: *Adverse effect, Corticosteroid, Oral candidiasis, Oral lichen planus.*

ÖZET

Amaç: Topikal kortikosteroidler, ağrı ve enflamasyonu hafifletme konusundaki etkinlikleri nedeniyle semptomatik oral liken planusun (OLP) temel tedavi seçeneğidir. Ancak ilaçların etkinlik gücü, kullanım süresi, sıklığı ve uygulanma bölgesi gibi faktörlere bağlı olarak sekonder oral kandidiazis (OK) gibi yan etkilere yol açabilirler. Bu çalışmada, OLP tedavisinde topikal steroid kullanımına bağlı olarak gelişen bir OK olgusu sunulmakta ve hasta uyumunun tedavi sürecindeki önemi vurgulanmaktadır.

Olgu sunumu: Dört ay önce kutanöz liken planus tanısı konmuş olan 78 yaşındaki kadın hasta, yeni ortaya çıkan oral lezyonların değerlendirilmesi amacıyla kliniğimize sevk edilmiştir. İntraoral muayenede bukkal ve labial mukozada, ayrıca dilde eroziv OLP lezyonları tespit edilmiştir. Hastaya, günde iki kez kullanılmak üzere mometazon furoat %0,05 sprey reçete edilmiştir. İlacın önerilenden daha yüksek dozda ve daha sık kullanılması sonucunda, iki hafta sonraki kontrol randevusunda bukkal mukozada ve yumuşak damakta psödomembranöz OK geliştiği gözlenmiştir. Hastaya günde dört kez gargara yapması için nystatin oral süspansiyon (100.000 IU) reçete edilmiş ve 14 gün içinde OK tamamen ortadan kalkmıştır. Sonraki süreçte, topikal steroidlerin uygun kullanımıyla OLP lezyonları retiküler forma gerilemiştir. Hasta, kliniğimizde düzenli takip edilmektedir.

Sonuç: Sekonder OK, OLP'nin klinik belirtilerini ve semptomlarını gizleyerek ve/veya şiddetlendirerek tedavi sürecini olumsuz etkileyebilir. Bu nedenle, farmakoterapinin dikkatle izlenmesi ve sekonder OK gelişmesi durumunda erken müdahale edilmesi, optimal tedavi sonuçlarının elde edilmesinde kritik öneme sahiptir.

Anahtar kelimeler: *Yan etki, Kortikosteroid, Oral kandidiazis, Oral liken planus.*

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Introduction

Lichen planus (LP) is a common T-cell-mediated chronic inflammatory mucocutaneous condition of unknown aetiology that affects the skin, scalp, nails, and the mucous membranes of the oral cavity, oesophagus, and genitals. Oral mucosal lesions may manifest independently or in association with cutaneous lesions.[1-4] Oral lichen planus (OLP) is predominantly observed among middle-aged women over the age of 40, with a reported female-to-male ratio of approximately 3–4:1. The worldwide prevalence of OLP varies between 0.5% and 2.2%.[1,4-6]

OLP manifests clinically with a wide spectrum of intraoral findings, including reticular, papular, atrophic, erosive/ulcerative, plaque-like, and bullous forms, or a combination of two or more of these.[2-5] A common feature of all clinical variants of OLP is the presence of white lines, known as "Wickham's striae." The reticular variant, which appears as asymptomatic reticular white striations, is the most prevalent clinical form of OLP. The atrophic, erosive/ulcerative, and bullous variants are typically symptomatic, presenting as erythematous-ulcerated areas surrounded by white striae at the periphery.[4] OLP lesions characteristically exhibit bilateral and symmetrical distribution, with the most frequently affected sites being the buccal mucosa, tongue, and gingiva.[1,4-8] Patients with OLP commonly report complaints ranging from a sensation of roughness to burning, pain or discomfort in the affected areas. These symptoms are aggravated by thermal, chemical, or mechanical irritation of the affected tissue during activities such as consumption of hot, spicy, and acidic foods, use of oral hygiene products, brushing, flossing, or periodontal procedures such as scaling and root planing and may have a detrimental effect on the patients' life quality and limit their ability to maintain proper oral hygiene.[1,8,9]

Given the uncertain aetiology of OLP, current treatment strategies primarily aim to provide symptomatic relief.[9] The chronic clinical course of OLP, with fluctuations in disease activity characterised by recurrent episodes of exacerbation and remission, varies significantly both between patients and within individual patients over time, posing a management challenge for clinicians.[4,8,10] A number of treatment options are available for OLP, including topical and systemic corticosteroids, topical and systemic retinoids, azathioprine, calcineurin inhibitors (e.g. cyclosporine, pimecrolimus, tacrolimus), dapsone, griseofulvin, hydroquinone, laser therapy, mycophenolate, phototherapy, and thalidomide.[11] The selection of the most appropriate treatment plan is dependent on many factors, including the general health status of the patient, the presence of underlying psychological factors that may trigger the condition, the location and extent of oral lesions, the severity of symptoms, the degree of patient compliance with the treatment plan, potential drug interactions, and the cost-effectiveness of the selected treatment modalities.[12]

Topical corticosteroids are considered the most effective and reliable treatment option to alleviate the signs and symptoms of OLP, owing to their capacity to modulate the local immune response and are recommended as the first-line therapy for long-term symptomatic management of OLP.[2,3,9] However, a significant challenge in the management of OLP with corticosteroids is the risk of developing secondary oral candidiasis (OC), which is a frequent consequence of long-term corticosteroid therapy. The risk is dependent on numerous factors, such as the potency of the corticosteroid, the duration and frequency of use, and the site of application, and requires antimycotic therapy.[1,13-17]

In this study, a case who developed OC during topical steroid treatment for OLP is presented and the importance of patient compliance in treatment is emphasised.

Case Report

A 78-year-old woman, diagnosed with cutaneous LP four months earlier, was referred by her dermatologist to the dental outpatient clinic of the Faculty of Dentistry, Marmara University, Oral and Maxillofacial Radiology Department, for dental consultation due to oral lesions that had appeared two weeks prior. The patient had a medical history of hypertension, arrhythmia, angina pectoris, nephritis, and asthma and

was taking valsartan and hydrochlorothiazide (80 mg/12.5 mg), apixaban (5 mg), sotalol hydrochloride (80 mg), trimetazidine dihydrochloride (20 mg), allopurinol (300 mg), and spironolactone (25 mg). She had no smoking history and no known allergies. Informed consent for the case presentation was obtained from the patient.

Extraoral examination revealed the presence of polygonal, flat-topped papular lesions with symmetrical distribution on the hands and feet. The skin was observed to be dry and scaly. The patient reported using topical corticosteroids for the treatment of these lesions, which had been previously confirmed to be LP by histopathological examination, as per the instructions provided by her dermatologist.

A thorough intraoral examination revealed painful erosive-ulcerative lesions accompanied by radiating white striae on bilateral buccal mucosa, labial mucosa, and tongue (Figure 1A-C). Following an evaluation of the patient's clinical history and the observation of the lesions, a diagnosis of "erosive-ulcerative OLP" was established. The patient was informed about general precautions to be taken in the management of OLP, including the importance of stress management, maintaining meticulous oral hygiene, and avoiding thermal, chemical, or physical trauma to the oral mucosa. She was prescribed mometasone furoate 0.05% spray, to be applied 1 puff twice daily (50 micrograms per puff) for two weeks.

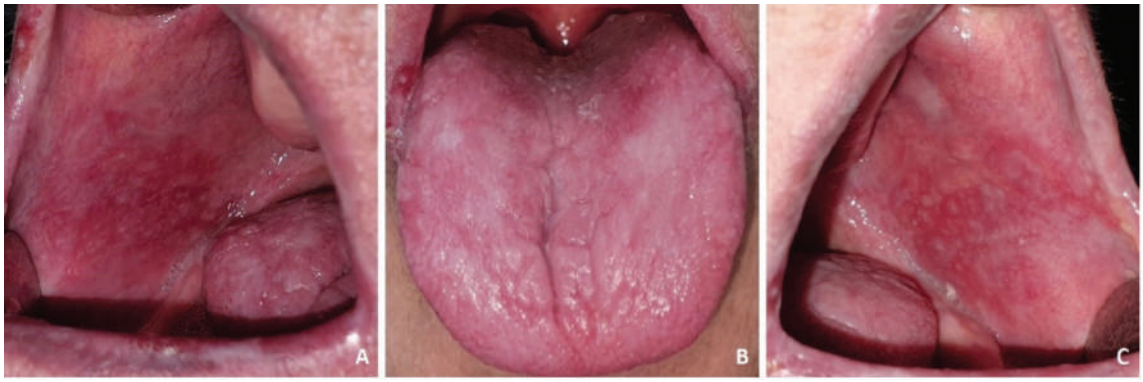

Figure 1A-C. Erosive-ulcerative oral lichen planus lesions with radiating white striae on (A&C) bilateral buccal mucosa and (B) tongue.

At the subsequent follow-up appointment, two weeks later, pseudomembranous OC was observed on the buccal mucosa and soft palate (Figure 2A-C). Further questioning revealed that the patient had been using the mometasone furoate 0.05% spray, which had been highly effective in relieving her symptoms. However, she had been applying the spray at a higher dose and frequency than prescribed – specifically, using 2 puffs four times per day (400 micrograms), instead of the recommended 1 puff twice daily (100 micrograms). The patient was instructed to gargle with an oral suspension of nystatin (100,000 IU) four times daily, which resulted in the complete resolution of OC within 14 days (Figure 3A-C).

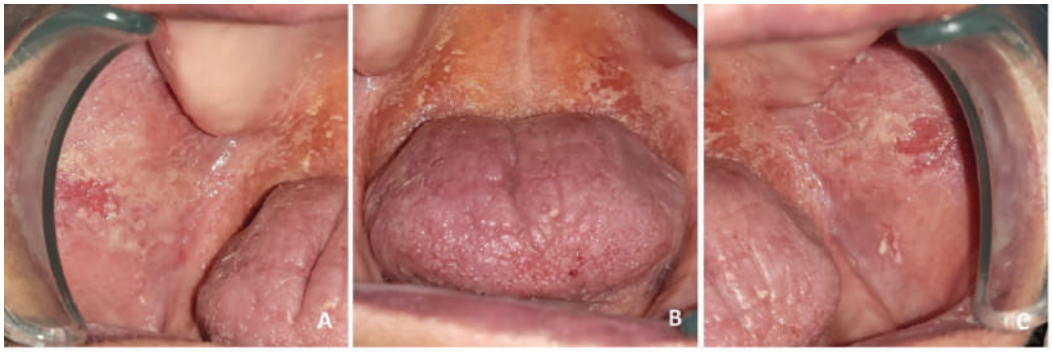

Figure 2A-C. Pseudomembranous oral candidiasis on (A&C) bilateral buccal mucosa and (B) soft palate due to overuse of mometasone furoate 0.05% spray at the follow-up visit two weeks later.

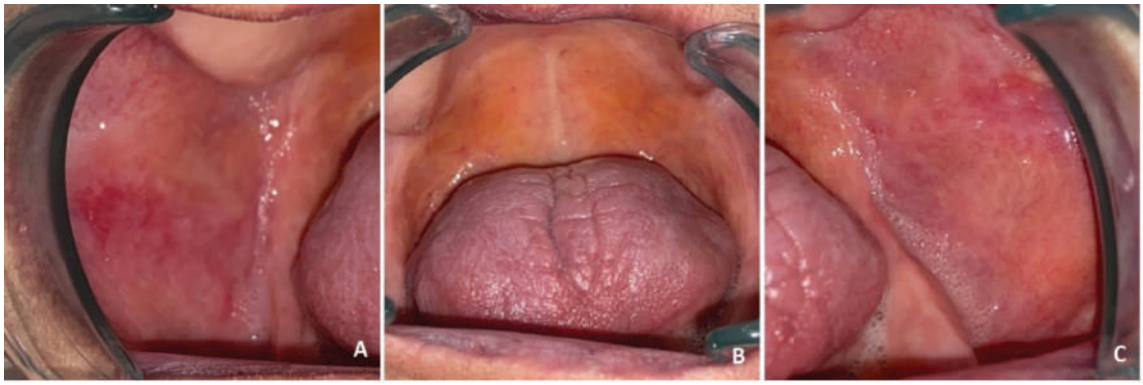

Figure 3A-C. Complete resolution of oral candidiasis on (A&C) bilateral buccal mucosa and (B) soft palate within 14 days with nystatin oral suspension (100,000 IU) use four times daily.

Following the appropriate use of the prescribed topical steroid, the erosive-ulcerative OLP lesions underwent a complete transformation into reticular form after a period of six weeks, resulting in a substantial reduction in the symptoms and signs of oral lesions, as well as a significant improvement in the patient's quality of life (Figure 4A&B). The patient continues to attend regular follow-ups at our clinic, monthly for the first three months, followed by every six months to monitor the course of the disease, control oral hygiene, and evaluate treatment compliance.

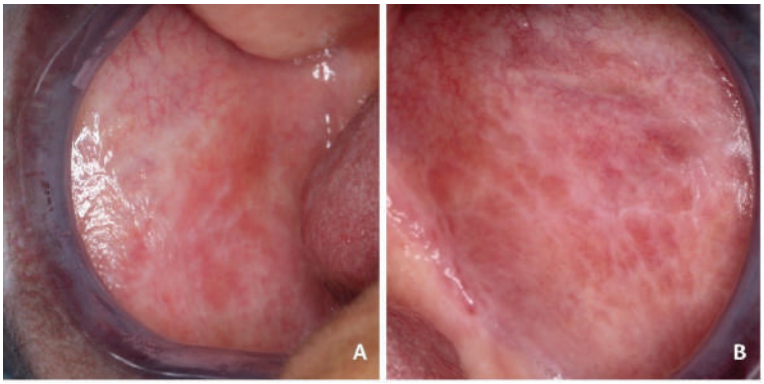

Figure 4A&B. Following the appropriate use of the prescribed topical steroid, the erosive-ulcerative oral lichen planus lesions underwent a complete transformation into the reticular form after six weeks.

Discussion

Although asymptomatic OLP does not require treatment, it is recommended that irritation caused by sharp tooth cusps, fractured restorations, and unopposed teeth should be eliminated and monitored. Oral hygiene control has been shown to be beneficial in OLP management.[18] Most patients with erosive OLP are symptomatic and approximately 90.9% have involvement of multiple oral sites. The erosive form is characterized by a longer duration, involvement of a greater number of sites (oral, oesophageal, and genital), and a higher prevalence in elderly patients compared to the reticular or atrophic forms, as observed in the present case.[19]

Topical corticosteroid treatment, whether as a standalone modality or in conjunction with systemic steroids, is recommended as the primary therapeutic approach for symptomatic OLP cases due to minimal side effect profile and cost-effectiveness in long-term management.[1,18] Many studies have demonstrated the efficacy of adhesive base, aqueous solution, spray, mouthwash, microemulsion, soluble tablet, and intralesional injection forms of various topical corticosteroids including fluocinonide, betamethasone, mometasone furoate, clobetasol propionate, triamcinolone acetonide, fluocinolone acetonide, fluticasone propionate, prednisolone, and dexamethasone.[7,10] Since it is

important that the mucosal surface remains in contact with the steroids for a period of minutes, formulations including mouthwashes or adhesive pastes are widely recommended.[2]

A review of the literature indicates that mometasone furoate is a viable treatment option for erosive-ulcerative OLP, with statistically significant reductions in pain and erythema/ulceration surface area, and no serious side effects reported.[20] Considering its efficacy and proven safety in the management of erosive-ulcerative OLP symptoms, mometasone furoate - routinely used in the management of symptomatic OLP cases in our clinic - was selected as the most appropriate treatment for the patient presented.

The most frequently observed adverse effect associated with topical corticosteroid therapy is OC, caused by the overgrowth of candida in the oral flora.[10] It has been demonstrated that a variety of yeast species, especially *Candida albicans*, can be isolated from the oral cavity of individuals who do not present any clinical symptoms of OC.[4] However, it is believed that systemic and local factors that decrease the resistance of the individual facilitate the transition of yeasts from a commensal to a parasitic state. Systemic factors predisposing to OC include nutritional deficiencies, endocrine disorders, steroid/antibiotic/immunosuppressive/cytostatic treatment, smoking, malignancies, and immunopathies. Local factors include mechanical trauma, epithelial changes resulting from other oral mucosal diseases, denture use, low salivary flow rate and pH.[4,13-16,21,22]

Some of these factors have been identified in patients suffering from OLP. It has long been recognized that epithelial cell defects are present in OLP lesions. Moreover, a significant body of studies has demonstrated that the LP reaction is the consequence of a cell-mediated immunological response to antigenic alterations in the basal cell layer.[21] In addition to allergic reactions, xerostomia, and sensitivity to mechanical irritants, a relatively high incidence of endocrine disorders, such as diabetes mellitus, has been observed in patients diagnosed with OLP.[14,21] The presence of hyperkeratosis, a histopathological feature of OLP, creates favourable conditions for candida adhesion, colonisation, and infection.[21,23] Similarly, clinically observed erythema or superficial erosion in OLP lesions may be indicative of the disease itself or of superimposed candidiasis. Both conditions have the potential to cause mucosal soreness and pain.[23] Previous studies have reported that disruption of mucosal integrity and changes in composition of the oral microenvironment promote and facilitate candida species colonization and subsequent invasion in erosive OLP patients.[4,24] Long-term corticosteroid treatment in OLP patients may also facilitate the growth of candida and the transition from commensalism to parasitism, impair host resistance and immune responses to candida species, and induce OC by modulating inflammatory processes and cell-mediated immunity.[4,13-16] Secondary OC is more common in patients with OLP undergoing topical steroid therapy, with documented incidences ranging from 11.4% to 76.7%.[4,8,10,14,17,21,25] In particular, the atrophic, erosive-ulcerative, and bullous OLP variants are erythematous, symptomatic, and frequently associated with OC.[4,17,24,25] The reticular form, on the other hand, typically manifests asymptomatically and is not associated with candidal infection. Therefore, the majority of studies on OC in OLP patients have focused on the erosive type of OLP, as in our case.

The development of secondary OC may complicate the management of atrophic and erosive-ulcerative OLP forms in particular, as it often obscures and/or exacerbates clinical signs and symptoms, causes burning, soreness, discomfort, and pain, and requires antifungal treatment.[4,8,14,21,24-26] Nystatin, fluconazole, miconazole, ketoconazole, and amphotericin B are the most commonly prescribed antifungal agents for the therapeutic management of OC. Alternative therapeutic agents such as chlorhexidine have also been shown to have both antibacterial and antimycotic properties.[15,23] Despite the uncertain relationship between candida colonization and OLP, it has been frequently observed that antimycotic treatment of erosive lesions with secondary OC results in clinical improvement and symptom relief, with OLP lesions transforming to reticular

form.[4,21,26] Nystatin suspension, which is routinely prescribed for the treatment of OC cases in our clinic, was used in the treatment of OC in the presented patient and it was observed that OC disappeared completely and OLP lesions transformed into a reticular form after antifungal treatment. One of the most controversial issues is whether antifungal agents should be used as a standard protocol for secondary OC prophylaxis when treating OLP with corticosteroids.[18] Clinical experience and training in the management of such cases depend on the implementation of a carefully selected protocol, which may vary from one clinician to another. It is important to emphasise that failure to consider the possibility of a candidal infection may lead to ineffective treatment of OLP. It is strongly advised that patients diagnosed with OLP should be monitored closely in terms of fungal infections for the initial 2 months. In the erosive-ulcerative OLP subtype, where topical steroids are frequently administered, the risk of candida superinfection is significantly higher, and these potential prognostic indicators may assist clinicians in identifying such OLP patients as being at risk of candida superinfection.[17]

Furthermore, the possibility of malignant transformation of OLP due to hyphal invasion by candida species has also been suggested, and this has been attributed to the production of carcinogenic candida metabolites, including nitrosamine and acetaldehyde.[27,28] The use of antifungal agents in selected OLP cases may reduce the capacity of *Candida albicans* to synthesise carcinogenic compounds such as N-nitrosobenzylmethylamine.[26] OLP lesions with known risk factors for oral malignancy, including tobacco use, alcohol consumption, or candidal superinfection, require careful follow-up due to the increased possibility of malignant transformation.[29]

Conclusion

In conclusion, topical corticosteroids represent a highly effective and safe treatment option for symptomatic OLP and are therefore recommended as the first-line therapy. Due to its chronic nature, complete clinical remission remains difficult to achieve in most OLP cases, even with appropriate treatment. No single management approach is universally applicable and the optimal strategy varies between patients. The choice of the potency, formulation and dosage of the topical steroid to be used, which affects the response to treatment, depends on professional judgement. It is important to tailor the frequency of topical steroid application, duration of treatment, and concomitant antifungal use for each patient, taking into account the patient's overall health status, severity of OLP lesions and compliance with the treatment plan. Appropriate management of OLP will have a significant impact on reducing pain and therefore enhancing the quality of life for a significant number of patients.

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Conflicts of interest

The authors declare that they have no conflict of interest.

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Author contributions

Idea/Concept: B.G Design: B.G Control/ Supervision: B.G, S.Y, B.A Literature Review: BG, ŞEY, SY, BA Data Collection and/ or Processing: B.G, Ş.E.Y Analysis and/or Interpretation: B.G, Ş.E.Y Writing the Article: B.G, Ş.E.Y, S.Y, BA. Critical Review: B.G, Ş.E.Y, S.Y, B.A

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