



Oral leukoplakia: Failure of topical imiquimod 5%

Oral lökoplaki: Topikal imiquimod %5'in başarısızlığı

Özlem Özbağcıvan, Turna İlknur, Sevgi Akarsu, Banu Lebe*, Emel Fetil

Dokuz Eylül University Faculty of Medicine, Department of Dermatology; *Department of Pathology İzmir, Turkey

Keywords: Imiquimod, leukoplakia, failure, topical therapy

Anahtar Kelimeler: İmikimod, lökoplaki, başarısız, topikal tedavi

To The Editor,

The most common precancerous lesion of the oral mucosa is leukoplakia, which is defined as a white oral lesion that is not related to another disease process. Timely workup and effective management of leukoplakia is essential to prevent the development of squamous cell carcinoma. Recently, some studies have reported successful therapy with imiquimod 5% cream, which holds promise for a new and effective topical treatment option¹⁴. Herein, we describe a patient with oral leukoplakia that failed to respond to a 16-week trial of topical imiquimod 5%.

A 65-year-old woman presented with an 8-month history of white plaque on the left side of the tongue (Figure 1a), causing a burning sensation. She had no history of typical risk factors. A lesional biopsy confirmed the diagnosis of oral dysplastic leukoplakia (Figure 1b), and tested negative for human papillomavirus infection. We recommended surgical interventions, but the patient requested treatment with topical options. After a sterile gas was used to dry the mucosa, imiquimod cream 5% was applied to the lesion for 20 minimum every other day. The duration was increased up to a total time of two hours for three times a week. After 16

weeks, however, no improvement was seen (Figure 1c) and the control biopsy revealed the persistent dysplasia (Figure 1d). She then agreed to surgical interventions, and after four cycles of cryotherapy with a two-week interval, she was clinically (Figure 1e) and histopathologically clear (Figure 1f). The clinical relevance of oral leukoplakia is primarily related to its association with oral cavity squamous cell carcinoma. The initial management is the elimination of the causative factors, especially the use of tobacco. When no possible cause is found, or when the lesion does not disappear, it is essential to consider the effective therapeutic options. Surgical interventions include total excision, laser therapy, and cryotherapy but the available evidence on medical therapy is very limited⁵.

Imiquimod 5% cream is a novel immune modulator with localized therapeutic effects at the drug application site capable of enhancing local production of immune-stimulating cytokines, providing antiviral and antitumoral activity. It has been approved for the treatment of genital warts, actinic keratosis and superficial basal cell carcinoma if surgery or other treatment options are inappropriate. However, imiquimod use is currently increasing, especially for off-

Address for Correspondence/Yazışma Adresi: Özlem Özbağcıvan MD, Dokuz Eylül University Faculty of Medicine, Department of Dermatology, İzmir, Turkey
Phone: +90 505 295 25 66 E-mail: ozlem.ozbagcivan@deu.edu.tr **Received/Geliş Tarihi:** 07.05.2019 **Accepted/Kabul Tarihi:** 16.10.2019
ORCID: orcid.org/0000-0001-7190-3969



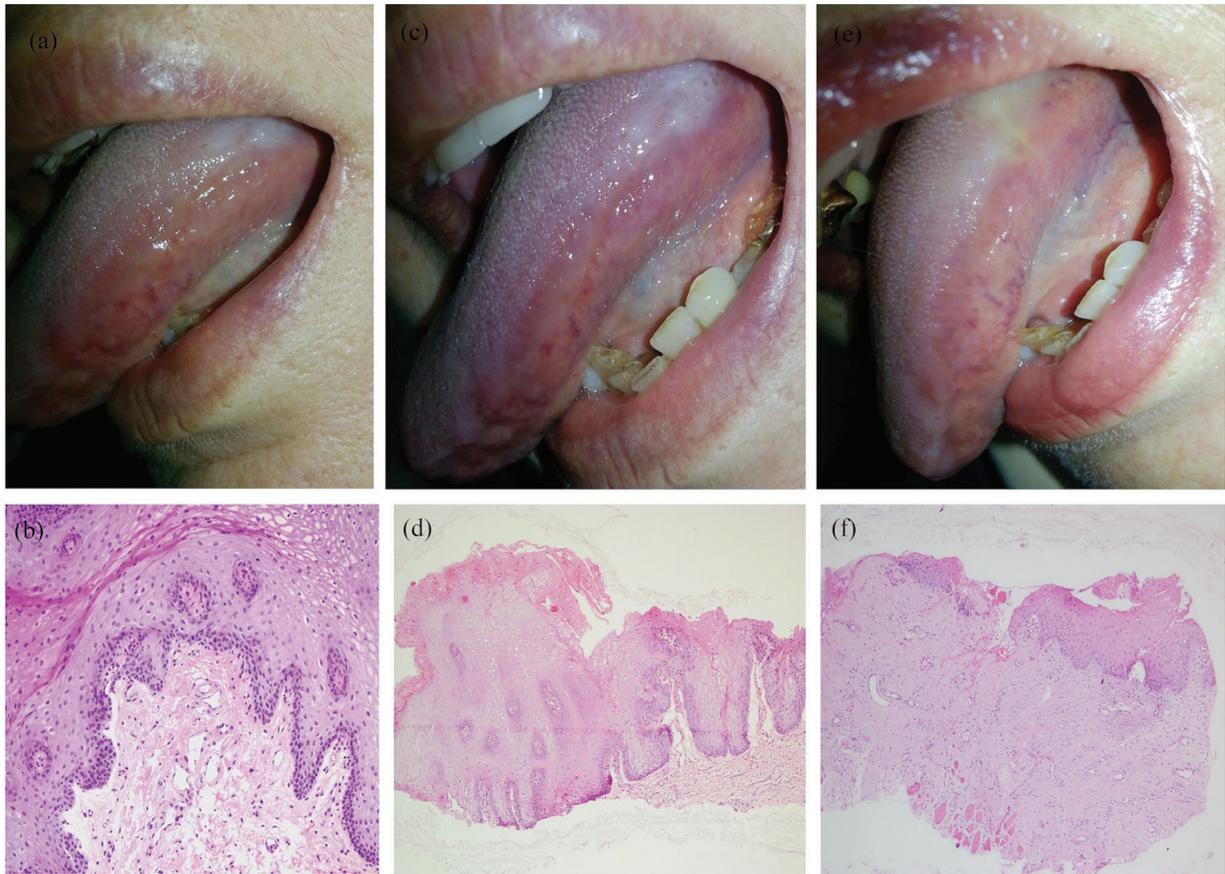


Figure 1. a) Leukoplakia on the left side of the tongue, b) irregular hyperplasia in the epithelium and dysplastic changes in the basal and suprabasal layers hematoxylin & eosin (H&E, x20), c) failure of imiquimod 5% after 16 weeks of therapy d) persistent dysplasia after imiquimod 5% treatment (H&E, x20), e) healing with a slight cicatricial area after cryotherapy, f) regenerative changes and chronic granulation tissue in the lamina propria after cryotherapy (H&E, x20)

label conditions. Although creams are typically not used intraorally because they can be easily washed away with continuous saliva turnover, efficient penetration of imiquimod in the oral mucosa has been emphasized in previous reports¹. Given the side effect profile or difficulty of application of a cream in oral mucosa for a long period of time, the patient's adherence to the recommendations may be a concern with the failure of therapy. However, our patient was properly educated, and she was fully compliant with the therapy.

Although there are at least four recent reports of successful treatment of oral leukoplakia with imiquimod 5%, our case failed to respond. This case emphasizes that when using imiquimod for off-label uses, physicians must monitor the patients for treatment failure, and clinical and histological follow-up should be provided. Informed consent was obtained.

Ethics

Informed Consent: Informed consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ö.Ö., T.İ., S.A., B.L., E.F., Concept: Ö.Ö., Design: Ö.Ö., Data Collection or Processing: Ö.Ö., B.L., Analysis or Interpretation: Ö.Ö., T.İ., S.A., B.L., E.F., Literature Search: Ö.Ö., Writing: Ö.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. Allam JP, Erdsach T, Wenghoefer M, Bieber T, Appel TR, Novak N: Successful treatment of extensive human papilloma virus-associated oral leukoplakia with imiquimod. *Br J Dermatol* 2008;158:644-6.
2. de C Monteiro JS, de Oliveira SC, Reis Júnior JA, et al: Effects of imiquimod and low-intensity laser ($\lambda 660$ nm) in chemically induced oral carcinomas in hamster buccal pouch mucosa. *Lasers Med Sci* 2013;28:1017-24.
3. Gkoulioni V, Eleftheriadou A, Yiதாகis I, et al: The efficacy of imiquimod on dysplastic lesions of the oral mucosa: An experimental model. *Anticancer Res* 2010;30:2891-6.
4. Martinez-Lopez A, Blasco-Morente G, Perez-Lopez I, et al. Successful treatment of proliferative verrucous leukoplakia with 5% topical imiquimod. *Dermatol Ther* 2017;30.
5. Lodi G, Franchini R, Warnakulasuriya S, et al: Interventions for treating oral leukoplakia to prevent oral cancer. *Cochrane Database Syst Rev* 2016;7:CD001829.