Aydın Dental Journal

Journal homepage: http://dergipark.ulakbim.gov.tr/adj

PROLIFERATIVE VERRUCOUS LEUKOPLAKIA: FIVE YEARS FOLLOW-UP

Behçet EROL[1], Sercan KÜÇÜKKURT[1], Tuğçe BİÇER AYTUGAR[2], Nihan AKSAKALLI[4]*

ABSTRACT

Background: Proliferative verrucous leukoplakia (PVL) is the rarest and stubborn subtype of oral leukoplakia (OL). The origin of PVL is still unknown and because the possible risk factors of OL are not in complete accordance with PVL, diagnosing the disease is very hard. PVL also needs special attention because of the high progression rate of squamous cell carcinoma and verrucous carcinoma.

Case Report: A 54 year old female patient was admitted to our department with the complaint of painless white lesions in anterior region of the floor of the mouth. In the light of the clinical and radiological findings, with the initial OL diagnosis, lesion was excised using electrocautery as a whole under local anesthesia and sent for histopathological examination. Final diagnosis was "Proliferative Verrucous Hyperplasia". After 60 months of follow-up, there was no recurrence.

Conclusion and Clinical Relevance: Since PVL has high progression rate for malign lesions and high relapse rates, it is important to detect the disease at early stages, and long term follow-up after surgical excision is needed.

Keywords: *leukoplakia, proliferative verrucous leukoplakia, potentially malignant disorders, oral cancer, verrucous hyperplasia*

ÖZET

Giriş: Proliferatif verrüköz lökoplaki (PVL), oral lökoplakinin (OL) en nadir görülen ve inatçı tipidir. PVL'nin kökeni halen tam olarak anlaşılamamıştır. PVL ile OL'nin muhtemel risk faktörlerinin birbirine uyum göstermemesi de hastalığın teşhisini zorlaştıran bir faktördür. Ayrıca PVL, yüksek oranda squamous cell karsinoma ve verrüköz karsinoma'ya dönüşüm gösterme oranı nedeniyle de dikkat edilmesi gereken bir hastalıktır.

Olgu Sunumu: 54 yaşındaki bir kadın hasta, kliniğimize ağız tabanında yerleşim gösteren ve 5-6 yıldır iyileşme göstermeyen ağrısız beyaz lezyon şikayetiyle başvurmuştur. Klinik ve radyolojik tanıların eşliğinde, oral lökoplaki ön tanısı ile lezyon elektrokoter yardımıyla eksize edilmiş ve histopatolojik incelemeye gönderilmiştir. Histopatolojik tanı proliferatif verrüköz lökoplaki olarak konulmuştur. Yapılan 60. ay takibinde nüks gözlenmemiştir.

Sonuç ve Klinik Önem: PVL'nin yüksek oranda malign lezyonlara dönüşüm gösterebilmesi ve yüksek nüks oranı nedeniyle, hastalığın erken tanısı ve tedavi sonrası dönemde uzun dönem takiplerinin yapılması önem arz etmektedir.

Anahtar Kelimeler: *lökoplaki, proliferative verrüköz lökoplaki, premalign lezyonlar, oral kanserler, verrüköz hiperplazi*

[1] *Istanbul Aydın University, Faculty of Dentistry, Department of Oral and Maxillofacial Surgery, Istanbul, Turkey*
[2] *İzmir Katip Çelebi University, Faculty of Dentistry, Department of Oral and Maxillofacial Surgery, Izmir, Turkey*
[3] *Istanbul University, Institute of Oncology, Department of Tumor Pathology and Oncologic Cytology, Istanbul, Turkey*

INTRODUCTION

Oral leukoplakia (OL) is a common premalign disease of oral mucosa. It may be defined as a white patch or plaque that cannot rubbed-off, which may be associated with any other disease clinically or histopathologically.[1] OL is macroscopically evaluated under two main classes; Homogeneous and non-homogeneous. Proliferative verrucous leukoplakia (PVL) is a subtype of the non-homogeneous type.[2]
PVL is slightly newer than the other types of OL, and it was defined by Hansen et al.[3] in 1985. Origin of PVL is still unknown and because the possible risk factors of OL are not in complete accordance with PVL, it is very hard to diagnose. PVL is also the rarest and stubborn type of OL[4].

PVL needs special attention because of its high rate of progression to squamous cell carcinoma and verrucous carcinoma.[4] Clinically, it is characterized with the slow growth tendency on cheek mucosa and gingiva, and observed as papillary verrucoid hyperkeratotic plate. Distinct from other subtypes of OL, it is not highly associated with smoking. Incidence of PVL is more frequent in females over the age of 60 years.[5]

CASE REPORT

A 54 year old female patient was admitted to our department with the complaint of painless white lesions in anterior region of the floor of the mouth, which had not recovered for 5-6 years. The patient had no systemic disease, and smoked a pack of cigarette per day for 10 years.

In the clinical examination; lobule, hard, immobile, hyper keratinized and paving-stone like white lesions that started from the right of the lingual frenulum but especially localized on the left side and reach towards the 2nd molar teeth through the lingual sulcus and embodied the floor of the mouth mucosa, lingual gingiva and alveolar crest, were determined. (Fig. 1) There was no lymphadenopathy. In the orthopantomography examination, there was no finding that led to an intraosseous pathology. (Fig. 2)

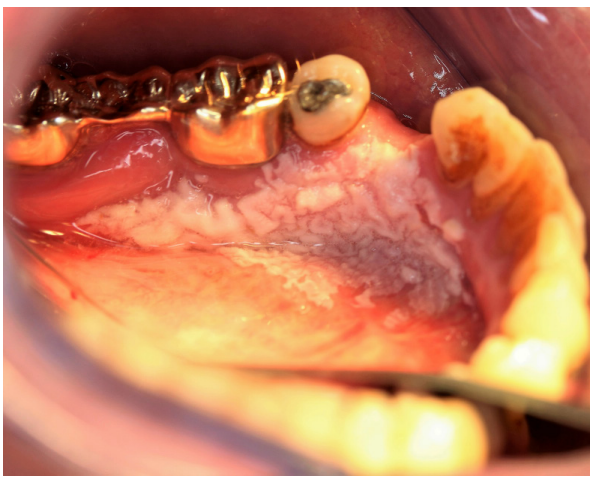


Figure 1. Pre-operative intraoral image

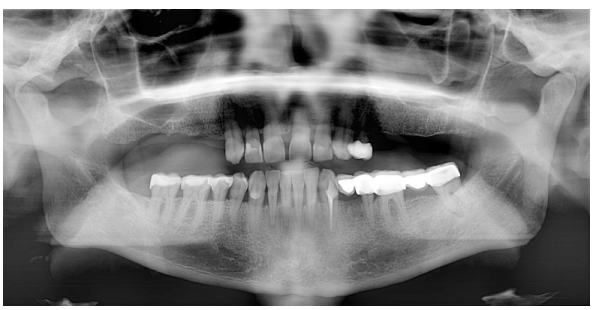


Figure 2. Pre-operative orthopantomography image

In the light of the current clinical and radiological findings, with the initial OL diagnosis, lesion was excised using electrocautery as a whole under local anesthesia and sent for histopathological examination. Remaining oral mucosa was

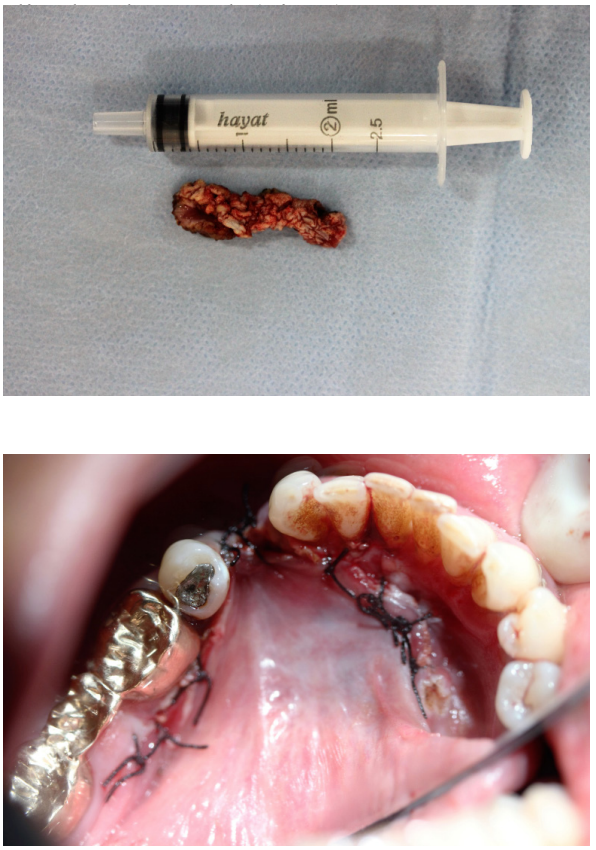


Figure 3. Post-operative image and Excised lesion

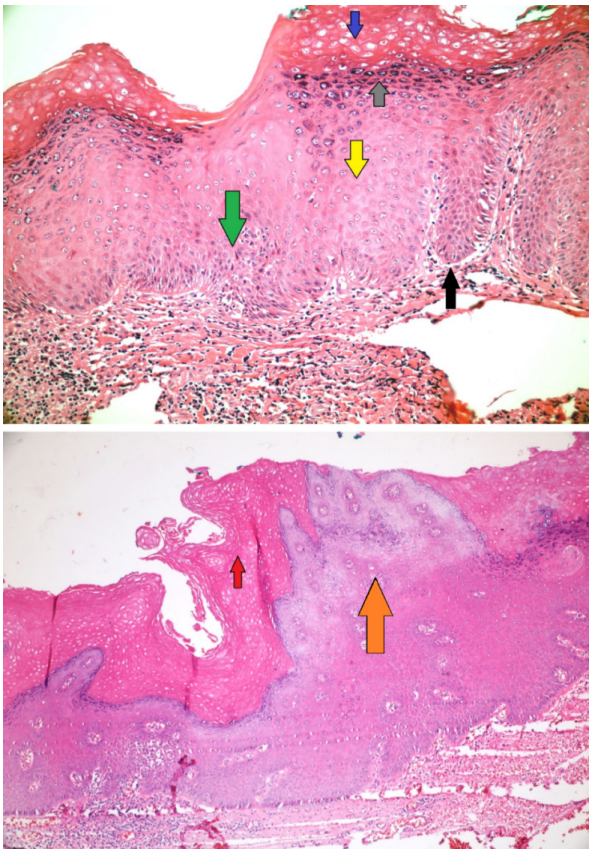
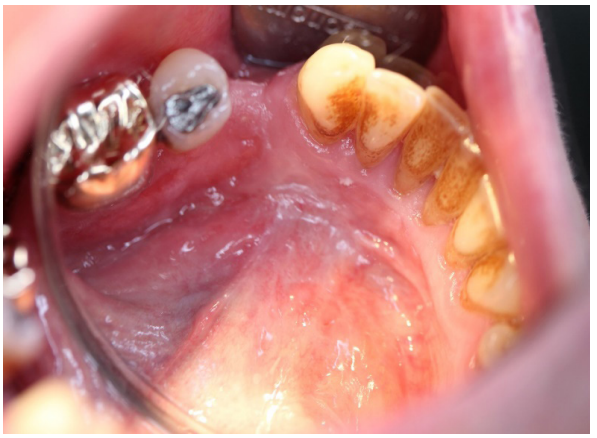
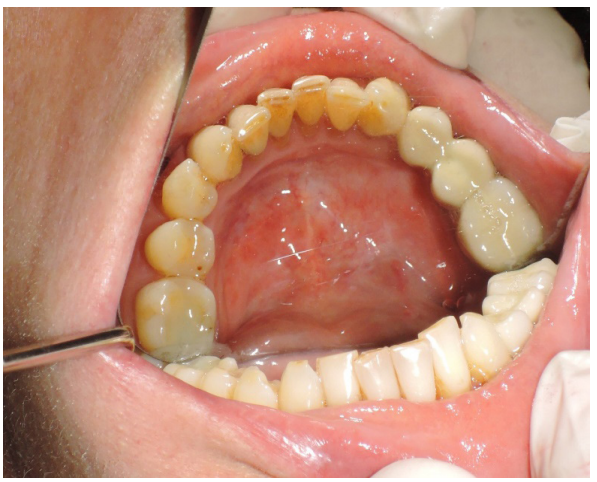


Figure 4. Histopathological images (Green arrow: Increase of nucleus-cytoplasm ratio, large mononuclear cells, hyperchromatic nuclei and increase in mitosis, Blue arrow: Keratin, Yellow arrow: Acanthosis, Grey arrow: Hypergranulosis, Black arrow: Papillomatosis, Orange arrow: Verrucous morphology, Red arrow: Keratin) (H&E x200)

In the histopathological examination; it was reported that there was no abnormal mitosis in the 3.5 x 1.2 x 0.7 cm sized soft tissue specimen; there was no carcinoma in situ from the bottom to the top; intermediate cellular and intermediate structural dysplasia were detected, and final diagnosis was "Proliferative Verrucous Hyperplasia". (Fig. 4)

Postoperative period was uneventful and the patient was taken into follow-ups once every three months for the first year and once every six months in the following years. After 60 months, there was no recurrence. Follow-ups of the patient still continue. (Fig. 5 and 6)





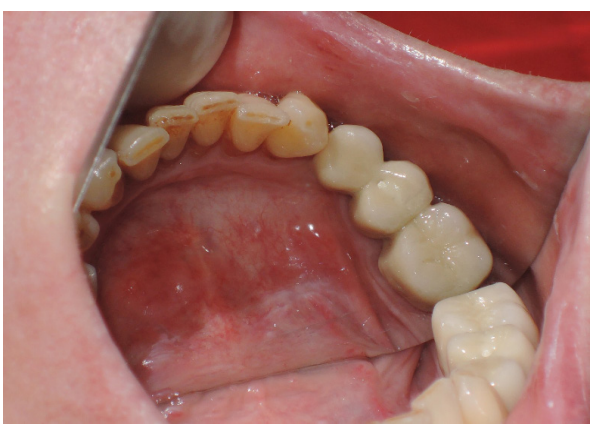


Figure 5. Follow-up images (12, 36 and 60 months)

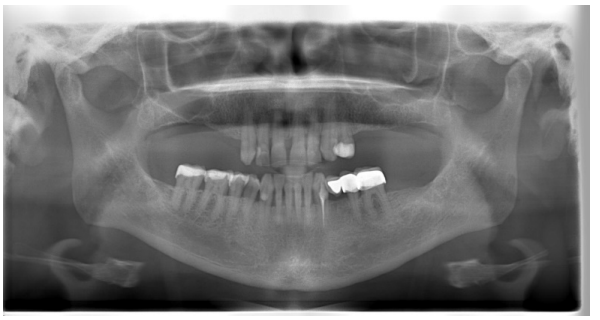


Figure 6. Follow-up Orthopantomography (60 months)

DISCUSSION

In order to diagnose PVL, Cerero et al.[6] suggested five major and four minor criteria and stated that at least three major criteria, or with a combination of two major and two minor criteria must exist. The major criteria are; 1. Leukoplakia to include at least two different areas in the oral region like gingiva, alveolar crest and palate, 2. To be located in a verrucous field, 3. Lesion to spread and grow in the development phase of the disease, 4. Occurrence of a relapse in the treated area, 5. Display of simple epithelial hyperkeratosis, verrucous hyperplasia, verrucous carcinoma or squamous cell carcinoma in the histopathologic examination. The minor criteria are; 1.To consist of at least 3 cm field where all affected area is included, 2. Patient to be female, 3. Patient to be a non-smoker, 4. Disease to exist for at least five years. Our case is consistent with the four major criteria (1, 2, 3 and 5) and three minor criteria (1, 2, and 4).

PVL is a progressive developmental disease and usually develops in 4 clinical phases. 1. Focal early period. 2. Showing regional enlargement. 3. Verrucoid/warty development. 4. Cancer development.[5] It is thought that our case was in phase three while it was

interfered with. Batsakis et al.[7] suggested that histopathological appearance of PVL needs to be examined in 4 phases. According to this classification: 1. Clinical flat leukoplakia that does not include any atypical cell. 2. Verrucous hyperplasia 3. Verrucous carcinoma, and 4. Squamous carcinoma. In the histopathological examination of our case, there were findings consistent with phase two.

Differential diagnosis for OL includes other white lesions of the oral cavity such as oral candidiasis, liken planus, linea alba, leukoedema and friction keratosis.[5]

In a systemic review, Abadie et al.[4] stated the average age as 63.9 for 329 PVL patients. 220 patients were women (66.9%), where only 96 of them (34.78%) reported tobacco usage. Gingiva takes the first place as the lesion area, buccal mucosa is reported as the second. While general relapse rate is reported as 157 (71.2%) of PVL and/or carcinoma in the treated patients, invasive carcinoma development was observed in 177 (63.9%) patients. In another systemic review, Pentenero et al.[8] reported that 322 (%71.5) of the 450 patient was female and the average age was 63.2. Average rate of smoking was determined as 35.3%. Recurrence rate was reported as 77.6%. Silverman and Gorsky[9] reported the same malign transformation rate in smokers and non-smokers. Similarly, Gandolfo et al.[10] reported no connection between malign transformation of OL and tobacco usage.

It is known that PVL has higher risks than other types. Malign transformation time interval of PVL has been reported between 4.7 - 11.6 years with a mean of 6 years.[6] Some areas, like floor of the mouth and ventral surface of tongue has higher dysplasia and carcinoma transformation rates as 45%.[11] Histopathologic examinations can provide more accurate results about determining the premalign lesion transformation than clinical observations. In our case, intermediate dysplasia was determined as a result of the histopathological examination.

For surgical excision of PVL, scalpel and electrocautery can be used. In our case, surgical excision with electrocautery was preferred as it provides relatively bloodless surgical area. Abadie et al.[4] reported the relapse rates after surgical excision on 222 patients as 71.2%. Radiotherapy, laser therapy, chemotherapy, photodynamic therapy, topical agents, cryotherapy, multiple biopsy and retinoids can be considered as other treatment options. It has been reported that non-surgical treatment options of PVL does not provide the desired success on their own or in combination. The most effective approach was to determine the cancer at early stages by executing regular checks and executing invasive wide localization when possible.[5]

Since PVL has high progression rate for malign lesions and high relapse rates, it is important to determine the disease at early stages and long term follow-up after treatment is needed.

REFERENCES

[1] Lodi G, Sardella A, Bez C, Demarosi F, Carrassi A. Interventions for treating oral leukoplakia. The Cochrane database of systematic reviews. 2006(4):CD001829.

[2] Kumar A, Cascarini L, McCaul JA, Kerawala CJ, Coombes D, Godden D, et al. How should we manage oral leukoplakia? The British journal of oral & maxillofacial surgery. 2013;51(5):377-83.

[3] Hansen LS, Olson JA, Silverman S, Jr. Proliferative verrucous leukoplakia. A long-term study of thirty patients. Oral surgery, oral medicine, and oral pathology. 1985;60(3):285-98.

[4] Abadie WM, Partington EJ, Fowler CB, Schmalbach CE. Optimal Management of Proliferative Verrucous Leukoplakia: A Systematic Review of the Literature. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery. 2015;153(4):504-11.

[5] Gillenwater AM, Vigneswaran N, Fatani H, Saintigny P, El-Naggar AK. Proliferative verrucous leukoplakia: recognition and differentiation from conventional leukoplakia and mimics. Head & neck. 2014;36(11):1662-8.

[6] Cerero-Lapiedra R, Balade-Martinez D, Moreno-Lopez LA, Esparza-Gomez G, Bagan JV. Proliferative verrucous leukoplakia: a proposal for diagnostic criteria. Medicina oral, patologia oral y cirugia bucal. 2010;15(6):e839-45.

[7] Batsakis JG, Suarez P, el-Naggar AK. Proliferative verrucous leukoplakia and its related lesions. Oral oncology. 1999;35(4):354-9.

[8] Pentenero M, Meleti M, Vescovi P, Gandolfo S. Oral proliferative verrucous leucoplakia: are there particular features for such an ambiguous entity? A systematic review. The British journal of dermatology. 2014;170(5):1039-47.

[9] Silverman S, Jr., Gorsky M. Epidemiologic and demographic update in oral cancer: California and national data--1973 to 1985. Journal of the American Dental Association. 1990;120(5):495-9.

[10] Gandolfo S, Castellani R, Pentenero M. Proliferative verrucous leukoplakia: a potentially malignant disorder involving periodontal sites. Journal of periodontology. 2009;80(2):274-81.

[11] Silverman S, Jr., Gorsky M, Lozada F. Oral leukoplakia and malignant transformation. A follow-up study of 257 patients. Cancer. 1984;53(3):563-8.