

Proliferative Verrucous Leukoplakia with Dysplastic Changes

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ABSTRACT:

Proliferative verrucous leukoplakia is one of the rare premalignant white lesions with highest conversion rate to malignancy. It grows gradually and irreversibly with multifocal presentation, exophytic and verrucous appearance. This lesion has been reported resistant to all therapeutic approaches including both non-surgical and surgical. Predisposing factors include female gender in the 6th decade of life. Proliferative verrucous leukoplakia has the highest tendency to neoplastic transformation and progression to oral squamous cell carcinoma and oral verrucous carcinoma in majority of the cases. The case of proliferative verrucous lesion clinically appearing benign presented here but on histopathology proven dysplasia in a patient with the history of smoking which he stopped six years back.

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INTRODUCTION:

Proliferative Verrucous Leukoplakia (PVL) was categorized by the World Health Organization as “aggressive and distinct form of Oral Potentially Malignant Disorder (OPMD)” in the year 2005, with unknown etiology. OPMD are a group of conditions that are defined as “clinical presentations that carry a risk of cancer development in the oral cavity, whether in a clinically definable precursor lesion or in a clinically normal mucosa”. PVL grows gradually, persistently, and irreversibly, and it is mainly characterized by multifocal presentation, exophytic and verrucous appearance¹. It is resistant to surgical and non-surgical approaches alike with highest recurrence and neoplastic conversion rate. It transforms to oral Squamous Cell Carcinoma (SCC) and oral Verrucous Carcinoma (VC)¹⁻³. It has the highest malignant transformation rate among the other white lesions

that is 47.7%⁴. While the chances to progress into oral squamous cell carcinoma is 70-100%⁵. Its diagnosis is based on the association of clinical and histopathological aspects.

In this case report, clinical case of Proliferative Verrucous Leukoplakia-PVL, which has been transformed to oral Verrucous Carcinoma were discussed. The literature revealed that it is included in the Oral Potentially Malignant Disorders, considering the neoplastic transformation of Proliferative Verrucous Leukoplakia to Verrucous Carcinoma. Moreover, it was suggested the National Institute for Health and Care Excellence (NICE) to make modifications in its head and neck cancer guidelines. It is recommended that Pakistan Association of Oral and Maxillofacial Surgeons (PAOMS) to make specific guidelines for the diagnosis of OPMD especially PVL.

CASE REPORT:

A 49-years married male patient presented to the oral medicine/diagnosis department of Sindh Institute of Oral Health Sciences, Karachi Pakistan, with the complaint of dental pain. During the clinical examination, a white lesion on the left buccal cheek mucosa was accidentally found. Lesion had thick, nodular, exophytic, verrucous surface 2 to 3 cm in size extending from oral commissure to the posterior part of the buccal mucosa. The lesion was slowly progressing over 6 years span with no sudden change during the past years [Figure 1]. Upon probing of any complain related to the lesion, the patient disclosed that he sometimes burning sensation was felt on the same side of the buccal mucosa. No other complaint of pus or blood discharge related to the lesion. The patient also gave history of similar lesion on right side of the buccal mucosa, which was surgically removed 7 years back, the lesion was biopsy proven leukoplakia. There was no cervical lymphadenopathy. Other findings included poor oral hygiene with heavy extrinsic staining of tobacco.

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The patient had a history of smoking for 20 years with the consumption of 4 to 5 cigarettes per day and chewing tobacco in the past which he discontinued in 2008. He complained of insomnia with no known co-morbid and has been taking diazepam drug orally to treat insomnia.

Biopsy of the lesion under local anesthesia was performed and sent for histopathological analysis as these lesions has highest rate of conversion to neoplasia. Figure 2 shows the macroscopic features of biopsy comprised of single pale white, irregular, partially mucosa covered piece of tissue measuring 1x1x0.9cm and mucosa measuring 1x1 cm. Microscopic examination of the lesion revealed multiple fragments of squamous mucosa shows papillomatosis, hyperkeratosis with focal elongation of rete-ridges. At places dysplastic changes are seen. Cells show mild dysplasia, dyskeratotic squamous cells are present [Figure 3]. Special stains for fungus (PAS+/-D) highlights fungal hyphae and

spores. The immunohistochemical stain CK5/6 highlights intact mucosal lining. A final diagnosis of Oral Verrucous Carcinoma was established [Figure 4]. The patient is then referred to affiliated hospital for surgical excision in the department of Oral and maxillofacial surgery.

DISCUSSION:

Proliferative Verrucous leukoplakia is a rare pathological lesion. It is common in females of 60 years or more in age with no alcohol or smoking habit ⁶. The lesion commonly affects gingiva, buccal mucosa and alveolar ridge while tongue is rarely involved⁷. This case differs not only in gender as well as age predilection for the lesion. The lesion showed dysplastic changes over the period of 6 years with no clinically evident features of malignancy. These changes include no sudden increase in size, no presence of ulceration/red lesion and no lymph node enlargement. In the absence of habit, dysplastic conversion of the lesion is an alarming sign. Hence, long term follow-up of these lesions is very important. Diagnosis is on basis of the modified Carrard criteria⁷. Table 1 compares the reported cases of proliferative verrucous leukoplakia in the past decade. It shows the variation of the lesion not only in demographics but also in location and histopathological characteristics. Because the stages of progression of different sites in multifocal lesions are not always the same, patients should be continuously watched, with regular and repeating biopsies taken whenever there are changes in color, appearance, or size, as well as when new lesions appear. Patients with a whitish innocuous look and recurrence occurrences should be checked every six months as well. PVL can advance to VC or OSCC over time despite repeated treatment interventions, implying that PVL is linked to diffuse submicroscopic alterations in the oral mucosa, also known as "field cancerization" ⁷.

Literature review also supports that it is an aggressive premalignant lesion. various studies have reported that initial diagnosis varied from dysplasia to carcinoma in-situ to Squamous Cell Carcinoma ^{1,5-6}. Recurrence rate is very high

Figure 1 Clinical picture of the lesion



Figure 2 Macroscopic features of biopsy

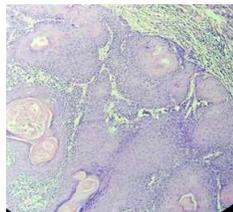


Figure 3 Histopathological picture showing dysplastic changes



Figure 4 Fungal hyphae in the lesion.

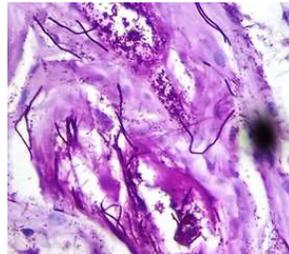


Table 1 Summary of Case reports published on Verrucous Leukoplakia

Year of Publication	Demographics	Location	Histopathological feature
2011 ⁶	52 yrs Female	Right buccal mucosa + Palate	Verrucous leukoplakia with mild to moderate dysplasia
2017 ⁸	30 yrs Male	Left Lingual Margin	Verrucous hyperplasia with mild to moderate dysplasia
2019 ⁹	36 yrs Female	Gingiva	Early stage of PVL
2020 ¹	75 yrs Female	Multiple proliferative lesions	Hyperkeratosis and mild epithelial changes
2020 ¹⁰	65 yrs Male	Right Buccal Mucosa	Mucosal stratified epithelium showing corrugated overgrowths with squamous epithelium which is hyperkeratotic and acanthotic.

in these lesions irrespective of the treatment option utilized alone or in combination. Most used option is surgery and laser ablation⁷. Recurrence can be at the same site or some other region in the oral cavity. Extensive resection is only suggested in cases with histopathological proven oral squamous cell carcinoma with bone invasion⁷. It was aimed to support the evidence that proliferative verrucous leukoplakia is an aggressive white lesion and should be treated as such, as well as it should be put in the list of alarming lesions as described in NICE guidelines 2015 on “Suspected cancer: Recognition and referral” as below¹¹:

1. “A lump on the lip or in the oral cavity consistent with oral cancer.”
2. “A red or red and white patch in the oral cavity consistent with Erythroplakia or erythro-leukoplakia.”

It was recommended to highlight this pathology in local association of PAOMS to put forward evidence-based guidelines on early recognition of these lesions and referral by general dentist to minimize the risk of malignant transformation and mortality. Longitudinal studies are suggested to find out the factors that affect its conversion to Oral squamous cell carcinoma and the prevalence of these lesions among the white lesions in our population.

CONCLUSION:

Proliferative verrucous lesions have a high conversion rate to malignancy as well as high recurrence rate. Early diagnosis and 6 monthly follow up of benign lesions could decrease the morbidity associated with them.

Authors Contribution:

Sanaa Ahmed: Idea, Data curation, writing of final manuscript
Muhammad Nasir: Data Curation, writing of initial draft
Sibghat Ullah Khan: writing of Initial Draft
Maria Naz Shaheen: Data curation and Visualization
Uzma Bukhari: Writing of histopathological part of the case presentation and its interpretation

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