Journal of Interdisciplinary Histopathology
www.scopmed.org
DOI:10.5455/jihp.20161019105523

Case Report

Proliferative verrucous leukoplakia: A case report with emphasis on diagnosis and treatment

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Received: May 05, 2016
Accepted: October 02, 2016
Published: October 27, 2016

ABSTRACT

Proliferative verrucous leukoplakia (PVL) is characterized by development of multiple keratotic plaques with roughened surface projections. Since its introduction in 1985 by Hansen *et al.,* PVL of the oral mucosa still remains an enigma and is difficult to define as a sub-entity of leukoplakia. Although the lesion typically begins as simple, flat hyperkeratosis indistinguishable from ordinary leukoplakic lesion, PVL exhibits persistent growth and eventually becomes exophytic and verrucous in nature. As the lesion progresses, they may go through a stage indistinguishable from verrucous carcinoma but may later develop dysplastic changes or transform into full-fledged squamous cell carcinoma usually within 8 years of initial PVL diagnosis. PVL is unusual among the leukoplakia variants in having a strong female predilection and minimal association with tobacco usage. Presenting here, a case of PVL transforming into verrucous carcinoma with areas of suspected malignancy in a 53-year-old male with habit of chewing tobacco quid and beedi smoking 4-6 times a day since 20 years, with a chief complaint of pain and burning sensation of the oral cavity and multiple oral lesions for 1 month. This paper will elaborate typical behavior pattern of the lesion and will discuss this rare entity in light of current information.

KEY WORDS: Leukoplakia, oral cancer, proliferative verrucous leukoplakia, squamous cell carcinoma, verrucous carcinoma

INTRODUCTION

Hansen *et al.* (1985) described proliferative verrucous leukoplakia (PVL) as a distinct entity of leukoplakia, presenting as verrucous, or exophytic lesion with progressive histological changes in sequential biopsies such as hyperkeratosis, different grades of dysplasia, verrucous carcinoma, and squamous cell carcinoma (SCC) [1]. In 2005, the WHO defined PVL as a rare subtype of oral leukoplakia with unknown etiology, affecting more commonly women (men: women proportion of 1:4) in the 60's, with a high risk of malignant transformation and diagnosis based on the association of clinical and histopathological features [2]. We are presenting here an interesting case of PVL in a male patient with a habit of chewing tobacco quid.

CASE REPORT

A 53-year-old male patient reported to the department with a chief complaint of pain and burning sensation in the left back cheek region for 1 month. The patient was asymptomatic 1 month back. Initially, the lesion was painless white patch which got ulcerated and was then associated with pain on eating hot and spicy food. The patient had a habit of chewing tobacco quid and beedi smoking 4-6 times a day for 30 years. Extraoral examination did not reveal any noticeable findings. On palpation, left submandibular lymph nodes were found to be enlarged and fixed. Intraoral examination revealed multiple white patches on the oral mucosa involving right buccal mucosa [Figure 1a], left labial mucosa [Figure 1b], left side of the palate [Figure 1c], and left alveolous [Figure 1d]. The lesion for which the patient reported was ulcerative and verruca papillary and was extending from left mandibular canine to pterygo-mandibular area involving alveolus. The surrounding mucosa was pigmented. The surface was rough with a warty appearance with palpable multiple projections giving leathery feel on touch. Lesion on right buccal mucosa was present for the last 3 years, extending anteroposteriorly from right first mandibular premolar to right pterygo-mandibular raphae and

there was no change in the texture and size of the lesion over the years. On investigations, OPG revealed ill-defined irregular moth-eaten radiolucency extending from left canine region anteriorly to pterygomandibular raphae posteriorly [Figure 2]. The provisional diagnosis of carcinoma of left alveolus and PVL was established. Incisional biopsy of lesion related to patient's chief complaint (left labial mucosa and alveolus) was performed. Histopathology revealed hyperorthokeratotic epithelium with surface irregularity and exophytic verrucous or church spire-like keratin cuffing with prominent granular cell layer. There was evidence of bulbous rete ridges with elephant foot like pushing margin [Figure 3] Dysplastic changes, epithelial pearl, indistinct basement membrane, and few atypical mitotic figures were noted in epithelium [Figure 4] Connective tissue was dense fibrocellular with juxta-epithelial intense chronic inflammatory cell infiltration. Considering all the clinical and histopathologic features, we confirmed the diagnosis as PVL progressing to verrucous carcinoma with questionable invasion. Incisional biopsies from multiple sites were not performed as the case was referred to Sidhivinayak cancer hospital Miraj for further treatment and management.

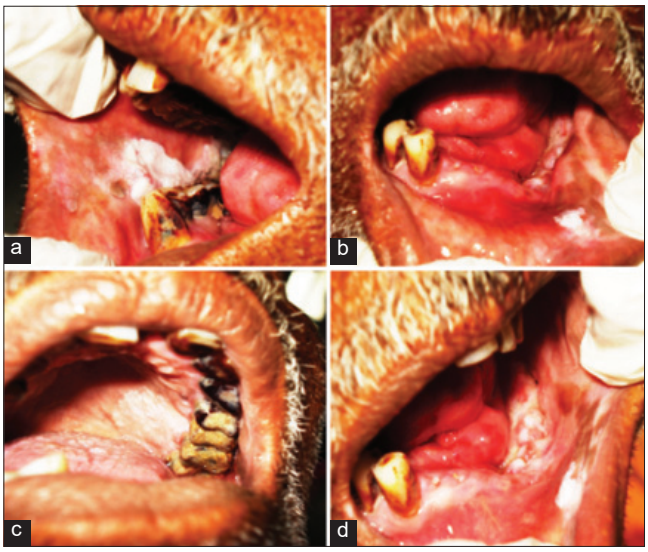

Figure 1: (a) Verrucous leukoplakia on right buccal mucosa, (b) Leukoplakia on left labial mucosa, (c) Leukoplakia on left side of the palate, (d) Ulcerative and verruca papillary lesion on left alveolus

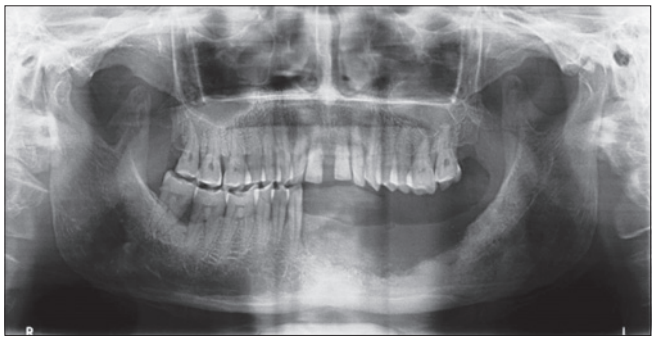

Figure 2: Ill-defined irregular moth eaten radiolucency extending from left canine region anteriorly to pterygomandibular raphe posteriorly

DISCUSSION

PVL was first defined in 1985 (Hensen) as a disease of unknown etiology, not always associated with known risk factors of oral cancer and exhibits a strong tendency to develop areas of carcinoma.[1] With the introduction of the term PVLthe previously used term "oral florid papillomatosis"has disappeared from the literature. PVL is a disease of elderly females as given in original report by Hensen [1] with mean age of occurrence being 62 years in their patients and male to female ratio of 1:4. Human Papillomavirus appears to have a significant role in the etiology of PVL as reported by Eversole [3]. The alcohol and tobacco use has not been directly related to PVL etiology, although studies report that at least 30% of the PVL patients are smokers [2]. However, the case we are presenting here is a 53 years old male patient with the habit of chewing tobacco quid. One of the hallmarks of PVL is its variable and progressive clinical presentation. PVL may

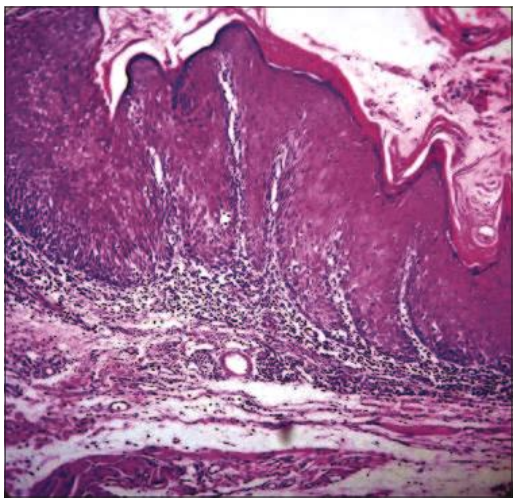

Figure 3: Hyper orthokeratotic epithelium and exophytic verrucous or church spire like keratin cuffing with prominent granular cell layer with bulbous rete ridges with elephant foot like pushing margin

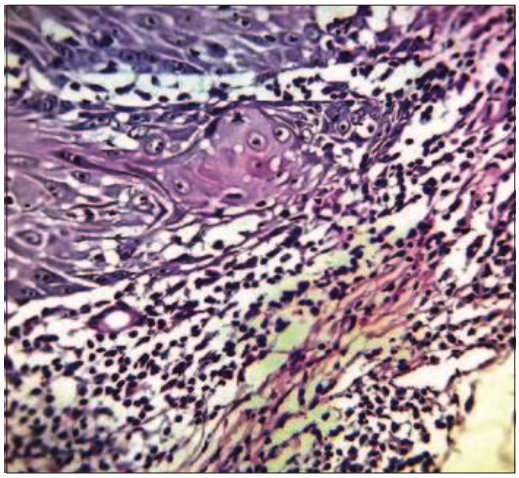

Figure 4: Dysplastic changes, epithelial pearl, indistinct basement membrane and few atypical mitotic figures in epithelium

appear on any soft tissue surface of the oral cavity and may present as a single distinct lesion or, less often, as scattered multifocal growths involving several oral sites. A case of PVL with cutaneous involvement has also been reported [4]. The most affected oral sites described in the literature are alveolar ridges, buccal mucosa and tongue, followed by labial mucosa and hard or soft palate [5-7]. Our findings are similar to that described in the literature expect for the involvement of tongue and soft palate. The natural history of PVL begins as a benign unifocal, homogenous leukoplakia that is persistent and slow growing. At this stage diagnosis of PVL is difficult because of its innocuous character but over a period, this benign lesion soon acquires a verrucous or papillary surface, sometimes showing areas of erythematous change, becomes multifocal or widespread and at mean times become malignant [8]. Our case had similar findings.

Many case series reported so far describe histopathology of PVL as a characteristic exophytic verruciform pattern with bulbous rete ridges and acanthosis, but dysplasia seems to be a late feature. The absence of dysplasia in early lesions may lead to less aggressive form of treatment.

DIAGNOSTIC CRITERIA FOR PVL GIVEN BY DIFFERENT AUTHORS

In generally, diagnosis is made according to Hansen's [1] first definition of PVL in 1985.

Ghazali *et al*.[8] established the following criteria and that all their proposed criteria should be met without exclusion.

1. The lesion starts as homogenous leukoplakia without evidence of dysplasia at the first visit.
2. With time, some areas of leukoplakia become verrucous.
3. The disease progresses to the development of multiple isolated or confluent lesions at the same or different site.
4. With time, the disease progresses through the different histopathological stages reported by Hansen *et al*.[1] (1985).
5. The appearance of new lesions after treatment.
6. A follow-up period of no <1 year.

After analyzing the results of 7 case series, Cerero-Lapiedra *et al*.[9] have proposed 5 major and 4 minor criteria as well as various combinations among them, to allow for a definitive diagnosis of PVL.

Major Criteria

a. A leukoplakia lesion with more than two different oral sites, which is most frequently found in the gingiva, alveolar processes and palate.
b. The existence of a verrucous area.
c. That the lesions have spread or engrossed during the development of the disease.
d. That there has been a recurrence in a previously treated area.
e. Histopathologically, there can be from simple epithelial hyperkeratosis to verrucous hyperplasia, verrucous carcinoma or oral SCC, whether *in situ* or infiltrating.

Minor Criteria

a. An oral leukoplakia lesion that occupies at least 3 cm when adding all the affected areas.
b. That the patient be female.
c. That the patient (male or female) be a non-smoker.
d. A disease evolution higher than 5 years.

They suggested one or two following combinations of the criteria should meet to make the diagnosis of PVL, that is:

1. Three major criteria (being E among them) or
2. Two major criteria (being E among them) + two minor criteria.

Our case was fulfilling 4 major and one minor criterion and fitted well in the diagnosis of PVL.

Malignant transformation rate of PVL can be >70%, reaching up to 100% in some cases. 74.62% of the published cases reports give a mean malignant transformation rate of 6.08 years. Therefore, the early diagnosis of PVL can be beneficial in the prognosis of these patients [1,9,10]. Distant metastasis and regional node involvement may be a late feature in this condition [11]. In our case, the left regional lymph node was involved similar to the reported findings.

The treatment procedures employed for PVL are surgery, carbon dioxide laser therapy, and photodynamic therapy [12]. Photodynamic therapy would appear to offer the best prognosis as it will be able to cover the treatment of multiple sites with minimal morbidity. It is important to analyze any verruciform leukoplakic lesion carefully to have the earliest possible diagnosis. PVL is a persistent and progressive oral lesion that requires very close follow-up along with early and aggressive treatment to increase the chances of a favorable outcome.

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Source of Support: Nil, Conflict of Interest: None declared.