Case Report:

HPV induced Proliferative verrucous Leukoplakia: Case Report

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Abstract:

Proliferative verrucous leukoplakia (PVL) is a recently delineated entity that is defined as a diffuse, white and smooth or papillary or wart like area of the oral mucosa caused by varying degrees of epithelial hyperplasia.\(^1\) The synonymous term is oral florid papillomatosis. Ismail mullah a 32yr old man reported to Ymt Dental College and Hospital with a chief complaint of a white growth protruding out of the mouth since 1 yr. Patient also reported of esthetic concern and reduced mouth opening due to the growth. The patient first noticed a small white growth 1 year back in the lower left region of the mouth. The patient ignored the growth since it was small and painless. PVL has different features in these populations. Treatment recommendation includes multiple techniques such as CO2 laser surgery, surgery with radiotherapy, cryotherapy, retinoid, systemic vitamin A, bleomycin and photodynamic therapy.\(^{12}\) Whether PVL progresses especially rapidly in Asian or Indian populations requires further investigation. The health of these patients, especially their immune status, warrants examination for its contribution to the aetiology of PVL.

Introduction:

Proliferative verrucous leukoplakia (PVL) is a recently delineated entity that is defined as a diffuse, white and smooth or papillary or wart like area of the oral mucosa caused by varying degrees of epithelial hyperplasia.\(^1\) The synonymous term is oral florid papillomatosis. In 1985, Hansen et al coined the term “proliferative verrucous leukoplakia” (PVL). PVL is known for its aggressive pathology, given its multifocal involvement, tendency to recur after removal, and high rate of malignant transformation, which can be higher than 70%, reaching 100% in some cases.\(^2\) Its malignant transformation rate varies from 0.1% to 17.5%.\(^3,4,5\) PVL is of uncertain etiology but may be associated with human papillomavirus (HPV) infection. They suggest that HPV-16 infection may play an important role in these lesions, although some have failed in patients with PVLG to detect HPV-DNA by PCR. Lesions of PVL tend to be slow-growing, persistent and irreversible which in time, becomes exophytic and wart like, display verrucal projections and areas of erythematous change within white patches, and have the appearance of verrucous and nodular leukoplakia.\(^2\) Ultimately, many progress to invasive cancer, and 30% or more of patients with PVL die of this disease.\(^6\)

Case Report:

Ismail mullah a 32yr old man reported to Ymt Dental College and Hospital with a chief complaint of a white growth protruding out of the mouth since 1 yr. Patient also reported of esthetic concern and reduced mouth opening due to the growth. The patient first noticed a small white growth 1 year back in the lower left region of the mouth. The patient ignored the growth since it was small and painless. The growth rapidly increased in size thereafter. Hence patient consulted a local physician for the same, six months back. The physician advised him to undergo a biopsy for the growth. The biopsy revealed it to be a benign HPV
induced lesion. Patient was then advised with a homeopathic medication which he continued for 3 months, after which there was initial reduction in the size of the growth. He discontinued the medicine 3 months back and the growth has increased rapidly since then to the present size. Past dental and family history were non contributory. General examination revealed that the patient was well oriented with time space and person.

Extra-oral examination revealed that the face was symmetrical. No obvious swelling or deformity was seen. The lips were incompetent due to growth on the lips and the mouth opening was reduced. On palpation of the temporomandibular joint, there was no clicking, deviation or tenderness present. Lymph nodes were non palpable.

Intra orally, a whitish exophytic proliferative growth was seen in the left labio-buccal mucosa extending from the commissural area to mesial of 36 involving the occlusal line and crossing it in a linear fashion and extending superiorly in the area of maxillary premolar, to involve the attached gingiva and the labial surfaces of the maxillary teeth extending from distal of 23 to the mesial of 27. The surface of the growth was hyperkerototic, exuberant and exophytic with multiple nodular projections with fissures in between. The periphery of the growth had white keratotic areas. The hyperkeratotic growth had rough surface giving a warty appearance with palpable multiple papillary projections of hyperkeratotic tissue giving leathery feel. The growth was friable, non scrapable and non tender.

Based on the above clinical findings, a provisional diagnosis of proliferative verrucous leukoplakia was given. There was no involvement of the bone in the radiograph. An incisional biopsy was done and the specimen was sent for histopathological and for HPV analyses.
The histopathology of the specimen revealed stratified squamous epithelium with hyperkeratosis, parakeratosis and acanthosis with verrucoid hyperplasia. Focal koilocytotic change and lymphoid infiltrate at the dermoepidermal junctions was noted. Mild atypia of basal keratinocytes and occasional keratotic pearl was seen. There was no unequivocal evidence of invasive malignancy. The overall picture was suggestive of verrucoid lesion with mild atypia consistent with HPV induced wart.

PCR was done for HPV detection which revealed presence of HPV DNA and the genotype revealed HPV 16 in the sample. Based on the above findings, a final diagnosis of HPV induced proliferative verrucous leukoplakia was given. The patient was advised wide excision of the growth with laser as a treatment modality and a follow up after 6 months.

DISCUSSION

PVL is a progressive condition which develops initially as a white plaque of hyperkeratosis that eventually becomes a multifocal disease with confluent, exophytic and proliferative features. This is in accordance with the findings in our case report. The lesions are slow-growing yet persistent, as well as irreversible and resistant to all forms of treatment with a high recurrence rate. PVL as described by Hansen develops through a histopathological continuum stages from - normal oral mucosa (0), homogeneous leukoplakia (2), verrucous hyperplasia (4), verrucous carcinoma (6), papillary squamous cell carcinoma (8), and poorly differentiated carcinoma (10), in which the odd scores refer to a status intermediate between those referred to a status intermediate encompassing 10 between those referred to by the adjacent even scores. Recently Bagan et al 2010 also proposed a set of diagnostic criteria to allow for the early identification of PVL cases. The proposal includes
five major criteria and four minor criteria as the following:

Major criteria (MC):
1) A leukoplakia lesion with more than two different oral sites, which is more frequently found in the gingival and alveolar processes and palate.
2) The existence of a verrucous area
3) The lesions spread or become engrossed during development of the disease.
4) Recurrence in a previously treated area.
5) Histopathologically, there can be simple epithelial hyperkeratosis to verrucous hyperplasia, verrucous carcinoma or oral squamous cell carcinoma.

Minor criteria (mc):
1) An oral leukoplakia lesion that occupies at least 3cm when adding all the affected areas.
2) The patient is female
3) The patient (male or female) is a nonsmoker
4) A disease evolution more than 5 years.

Our case fulfilled all the major criterias and two minor criterias. The most common locations are the gingiva or alveolar ridge (often extending into the vestibule), tongue, and buccal mucosa-sites that traditionally have not been considered high-risk areas for the development of oral squamous cell carcinoma, with the exception of the tongue. Immunohistochemical studies by Gopalakrishnan R et al. 9 found mutated and wild-type p53 over expression in HPV and oral SCC. Flow cytometric analysis was given by Kahn MA13, Lowe et al.10 observed the positive association between histopathological severity and nuclear morphometrical alteration in cases of PVL. PVL being an clinical diagnosis, exact nature of the lesion can only be judged by its histopathological evaluation. The disease reported here developed rapidly within one year of the patient’s initial clinic visit. Therefore, we speculate that when PVL progresses to moderate dysplasia or malignancy, it is supposed to develop rapidly and not remain so chronic as its early stage. Furthermore, previous studies have primarily focused on Caucasian subjects, reflecting the growth status and properties of PVL only among these ethnic groups, so there is little knowledge of PVL in Asian or specifically Indian populations11. Therefore, it must be determined whether PVL has different features in these populations. Treatment recommendation includes multiple techniques such as CO2 laser surgery, surgery with radiotherapy, cryotherapy, retinoid, systemic vitamin A, bleomycin and photodynamic therapy.12 Whether PVL progresses especially rapidly in Asian or Indian populations requires further investigation. The health of these patients, especially their immune status, warrants examination for its contribution to the aetiology of PVL.

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