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Case Report

Dentistry Section

Verrucous Hyperplasia Masquerading as a Verrucous Carcinoma: A Diagnostic Challenge

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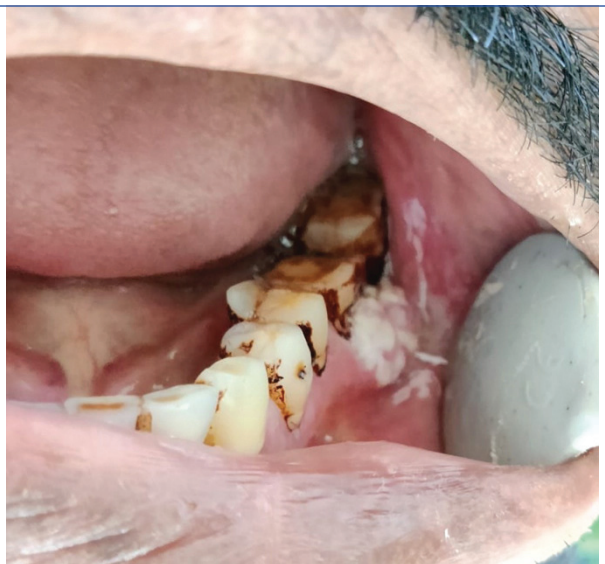
ABSTRACT

Verrucous Hyperplasia (VH) is a rare exophytic oral mucosal lesion that can progress to Verrucous Carcinoma (VC) and it has increased probability of converting into Squamous Cell Carcinoma (SCC). These lesions present diagnostic difficulties to the clinician. In diagnosing this, histopathology remains the gold standard. In VH cases, these entities can be distinguished by the lack of invasive growth; as a result, when performing a biopsy of the lesion's epithelium, it is critical to include a margin with adequate depth. Therefore, it is pivotal that biopsies of verrucous lesions include a lesional margin with adequate depth. The present case report discusses about the VH, of a 53-year-old male patient presented with a complaint of non healing growth in the left lower back tooth region. During clinical examination, well-defined oval soft growth with cauliflower like projections on the surface was present and measured 2×1 cm with well-defined borders. Treatment plan includes surgical excision. The lesion was sent for histopathological examination and the final diagnosis was made. The patient was reviewed for three months, no recurrence of the lesion was observed during the follow-up period.

Keywords: Biopsy, Exophytic, Non healing, Papillary projections

CASE REPORT

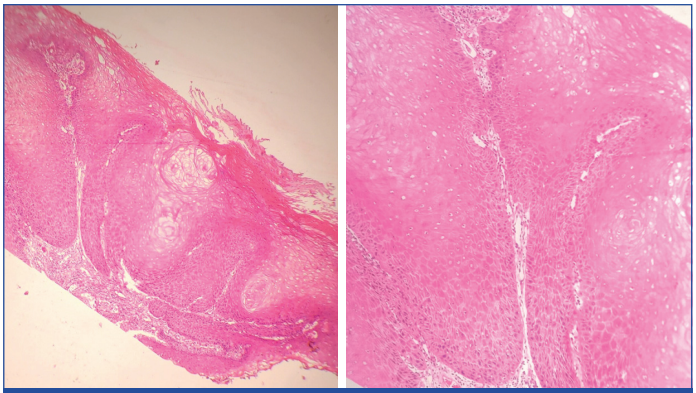
A 53-year-old male patient presented with a non healing growth in the left lower back tooth region for past 6 months. Initially, the lesion was small in size, and gradually it attained the present size. History revealed that he used to chew paan 12 times a day for the past 33 years and had quit the habit since one year. On clinical examination, a well-defined oval soft growth with cauliflower like projections on the surface was present and measured 2×1 cm with well-defined borders in left lower buccal vestibule [Table/Fig-1]. On palpation, the growth was non tender, non scrapable, non indurated and no bleeding was present on touch. All inspectory findings were confirmed. Based on the clinical findings, the case was provisionally diagnosed as VC. The differential diagnosis was proliferative verrucous leukoplakia, VH.



[Table/Fig-1]: Clinical image of Verrucous Hyperplasia (VH) in the left buccal vestibule in relation to 36.

Routine blood parameters were checked and all were under normal limits. Under local anaesthesia, the growth was removed by wide surgical excision and sent for histopathological examination.

Microscopic examination revealed parakeratinised stratified squamous epithelium covering connective tissue stroma. The surface epithelium showed hyperkeratosis with finger like papillary projections in the corneal layer [Table/Fig-2]. The epithelium also exhibited acanthosis, spongiosis and basilar hyperplasia with bulbous to elongated retepegs [Table/Fig-3]. The underlying connective tissue showed loose to dense collagen fibres with inflammatory cells predominantly lymphocytes. Based on the microscopic features, a final histopathological diagnosis of VH was made.



[Table/Fig-2]: Parakeratinised stratified squamous epithelium covering connective tissue stroma. The surface epithelium showed hyperkeratosis with finger like papillary projections in the corneal layer (H&E, 10x).
[Table/Fig-3]: Epithelium exhibited acanthosis, spongiosis and basilar hyperplasia with bulbous to elongated retepegs (H&E, 40x). (Images from left to right)

The patient was subsequently followed-up periodically over the next three months with no signs of recurrence.

DISCUSSION

Verruco papillary lesions of the oral cavity are a diverse set of lesions, with Oral Verrucous Hyperplasia (OVH) establishing itself as a difficult entity to choose from a spectrum of benign, potentially malignant, and malignant lesions. OVH is a precursor of OVC, which subsequently progresses to SCC at a later stage and which can be clinically and histopathologically challenging during diagnosis [1]. Verrucous lesions appear as a cauliflower-like, slow-growing growth that can be solitary, numerous, or diffuse, affecting large areas of

the oral mucosal surface and having a sessile or pedunculated base. It usually appears either pink or white depending on the degree of keratinisation. The lesions are classified as "papillary" implying nipple-like surface projections and "verrucous" implying a roughened surface, commonly a wart or wart like [2].

Chang KC et al., studied a pathological features of betel quid-related oral epithelial lesions in Taiwan, where he concluded that betel quid-related group displayed a higher incidence of VH [3]. According to Hazarey VK et al., the most common habit related with VH growth is the placing of tobacco-betel-lime quid (a mixture of slaked lime, chewing tobacco, and betel leaf pieces) in the buccal vestibule [4]. The current case also associated with paan chewing habit in relation to buccal vestibule.

The following clinical criteria are essential for diagnosing VH of the oral cavity [5]:

a) Clinically, it presents in two forms:
   i An exophytic, fleshy verrucopapillary outgrowth with a white and/or pink surface colour;
   ii A white, plaque-like exophytic verrucous lesion that may mimic verrucous leukoplakia. In both instances the clinical term 'Exophytic Verrucous Hyperplasia (EVH)' should be used.

b) EVH may occur in any anatomical site in the oral cavity and would be more than 1 cm in size.

c) Unlike Proliferative Verrucous Leucoplakia (PVL), EVH is a discrete and solitary lesion.

d) EVH may co-exist with oral submucous fibrosis.

e) The clinical presentation of EVH could misdiagnosed as a SCC or VC. Absence of induration is a cardinal feature of EVH. The present case satisfied an above criteria as exophytic, verrucopapillary outgrowth with a white surface. So, it can be misdiagnosed as a VC.

OVH and OVC may not be able to be distinguished from one another histologically. Recognising the exophytic growth pattern of OVH from the combined exophytic and endophytic growth pattern associated with a VC is the most accurate way to distinguish these entities on routine Haematoxylin and Eosin (H&E) stain tissue sections. In contrast to OVH, they are only evident at the same level as the adjacent epithelium whereas in VC, the projections of neoplastic epithelium are seen deep to the adjacent uninvolved epithelium [6]. Epithelial dysplasia and cytological atypia have frequently been identified as significant related features (66%) in VH [7]. Our case is also concordance with a similar histological feature.

According to Paral K et al., a decrease in stromal smooth muscle actin and an increase in CD34+ dendritic cells favour a VH diagnosis [8]. Mallick S et al., found that all cases of Oral Squamous Cell Carcinoma (OSCCA), 86% of VC, and 39% of VH were aneuploid in a ploidy analysis research [9]. According to Klieb H and Raphael S, an immune-reactivity of tumour cells to ki67, p53, and also stromal cell expression of Matrix Metalloproteinase (MMP)-1 promotes a diagnosis of VC [10]. In contrary, Sharma P et al., compared the expression of the p53 (tumour suppressor gene) in VH and VC and discovered that the rates of expression were identical. Sharma P et al., observed that p53, Mouse Double Minute (MDM)-2, p21, and Heat Shock Protein (HSP)-70 expression could not distinguish between VH and VC. These results appear to back up the theory that VH is a morphologic variety of VC [11]. Sharp differences in loss of heterozygosity have been noticed between reactive hyperplasia and VH/VC, suggesting that microsatellite analysis could be a helpful diagnostic technique for distinguishing between reactive hyperplasia and VH/VC [12].

Tamboon E et al., conducted a study on association of Human Papilloma Virus (HPV) and Epstein Barr Virus (EBV) in OVC and OVH. He discovered that all 35 OVC and OVH samples (100%) tested negative for both HPV and EBV infections [13]. Although a study in Thailand found that one (25%) of a total of four OVC cases had HPV-16/18 co-infection [14].

The accurate diagnosis made by the clinician and the pathologist which is accomplished by having awareness and knowledge of the lesion's clinical and histological presentation is the key to the successful treatment of VH. Due to the overlapping clinical features, VH and VC can be treated using methods that are similar. Surgical excision, chemotherapy, radiotherapy, cryotherapy, or a combination of these has all been used in the treatment of VH. Excision surgery is the most common and dependable form of treatment [15]. Hwang MJ et al., stated that topical 5-aminolevulinic acid-mediated photodynamic therapy and cryogun (Brymill Corp.) cryotherapy are both efficient treatment options for VH and leukoplakic lesions [16].

Patients with OVH had 5 year disease-free and cancer-free survival rates of roughly 40% and 70%, respectively. Heavy betel nut chewing advanced oral submucous fibrosis, non buccal lesions, and non tongue lesions were risk factors for malignant transformation; dysplasia had no effect on the results. The poor prognosis of OVH was linked to the gene amplification of CTTN, FOLR3, ORAOV1, PPFIA1, and RNF121 [17].

CONCLUSION(S)

Verrucous lesions appear as cauliflower-like, slow-growing masses that can be single, multiple, or diffuse, affecting massive areas of the skin or mucosal surface. For the diagnosis of such lesions, a thorough history and clinical examination are a must requirement. To avoid misdiagnosis and discrepancy, clinicopathologic correlation is always recommended. In the present case, as it mimicked VC, serial histopathological sections were essential to procure the appropriate final diagnosis.

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