

## Case Report

**Verrucous Hyperplasia, Proliferative Verrucous Leukoplakia And Verrucous Carcinoma –A Diagnostic Dilemma - Case Report.**

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## ABSTRACT

The definition of leukoplakia is unusual in that it makes the diagnosis dependent not so much on definable appearances as on the exclusion of other entities that appear as oral white plaques. Leukoplakia or tobacco pouch keratosis may be seen on adjacent mucosal surfaces, and verrucous carcinoma is a lesion that may develop from the high risk precancer, proliferative verrucous leukoplakia (PVL). Verrucous carcinoma represents 1 % to 10% of all oral squamous cell carcinomas, depending on the local popularity of tobacco use. Many verrucous carcinomas arise from the oral mucosa in people who chronically use chewing tobacco or snuff, typically in the area where the tobacco is habitually placed. Both PVL and verrucous carcinoma may have been reported in the past by the name Oral florid papillomatosis.

**KEY WORDS:** Proliferative, Verrucous, Leukoplakia, Verrucous carcinoma, Verrucous Hyperplasia, Tobacco

## INTRODUCTION

Oral leukoplakia (leuko = white; plakia = patch) is defined by the World Health Organization (WHO) as "a white patch or plaque that cannot be characterized clinically or

pathologically as any other disease." The term is strictly a clinical one and does not imply a specific histopathologic tissue alteration.<sup>[1]</sup> The definition of leukoplakia is unusual in that it makes the diagnosis dependent not so much on definable appearances as on the exclusion of other entities that appear as oral white plaques. Such lesions as lichen planus, morsicatio (chronic cheek nibbling), frictional keratosis, tobacco pouch keratosis, nicotine stomatitis, leukoedema, and white sponge nevus must be ruled out before a clinical diagnosis of leukoplakia can be made.<sup>1,2</sup> Verrucous carcinoma represents 1 % to 10% of all oral squamous cell carcinomas, depending on the local popularity of spit tobacco use. The only epidemiologic assessment of this tumor in a western culture reported an average annual incidence rate of one oral lesion per 1 million population each year.<sup>[1,2]</sup>

## CASE REPORT

A 35 year old male patient visited to department of oral medicine and radiology with a chief complaint of white patch like growth on his left side of cheek inside the mouth since 2 years. History of present illness dates back to 2 years. The growth gradually increased in size over the past 2 years and has

attained the present size. Patient is asymptomatic otherwise. There was no history of any pain, discharge, bleeding from the growth. Patient became conscious about the growth 1 ½ years back, and had visit S.N Medical College, Agra, where incisional biopsy procedure was being carried out. Patient claimed that the hospital authorities have given a normal impression about the biopsy reports; hence he was prescribed some medications which patient discontinued after a month. Patient has lost the previous report details. The purpose of the present visit is also out of conscious. He claimed that after the last procedure, the growth has slightly increased in size. He has a habit of chewing tobacco 2-4 pouches / day since 7 years. On Extra oral examination, involving head, face and neck regions when inspected, was normal. On palpation in the left sub-mandibular region revealed a tender, slightly enlarged lymph node, which was movable without any fixity to surrounding structures.

On Intra oral Examination (*Fig-1*), a unilateral and solitary exophytic lesion seen on left buccal mucosa extending upto left angle of the mouth, posteriorly 2.1 cm from angle of the mouth on the buccal mucosa. Superiorly extending opposite the cervical regions of 23,24,25 and inferiorly upto cervical regions of 33,34,35 about 1.4 cm. Lesion is brown with irregular borders having a sessile base and a pale colour more with a whitish tinge. No discharge or surface ulceration was seen on the surface. Surrounding mucosa was apparently normal. On palpation, all inspector findings were confirmed

related to position, discharge and surface ulcerations. On slight stretching of the left cheek, there was a presence of y-shaped groove in the anterior aspect of the lesion. Y-shaped groove was 2mm deep. Open ends of Y were 3 mm apart and they run posteriorly upto the posterior border of the lesion (*Fig-2*). There was no local rise of temperature. Lesion was non-tender, slightly movable, attached to underlying buccal mucosa epithelium. Lesion had a rough surface, fibrosed type of texture. Margins of the lesion were clearly defined and the lesion was hard in consistency. Other evident findings were white homogenous patch on right buccal mucosa and smoker's palate which can be attributed to patient's positive history regarding deleterious habits (*Fig-3*).

A differential diagnosis of Squamous Papilloma, Condyloma acuminatum, Condyloma latum, Verruca vulgaris, Focal epithelial hyperplasia, Verrucous carcinoma, Hypertrophic Candidiasis and plaque type Lichen Planus, was given. Punch biopsy and Incisional biopsy was done. The H and E stained sections shows epithelium of stratified squamous in nature and shows proliferation in the form of broad and blunt rete pegs which are proliferating in one single plane. The epithelium shows acanthosis and in few areas show parakeratinization. One area shows parakeratin plugging. Underlying stroma shows Juxta epithelium dense infiltrate interspersed in thick collagenous stroma. (*Fig-4, 5*) Few blood vessels are also seen. Features were suggestive of "*Verrucous Hyperplasia*".



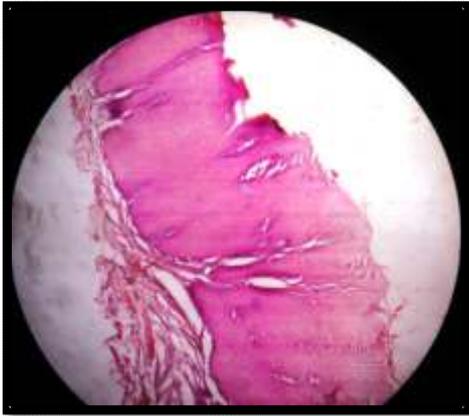
**Fig: 1** Intraoral View showing lesion on left buccal mucosa



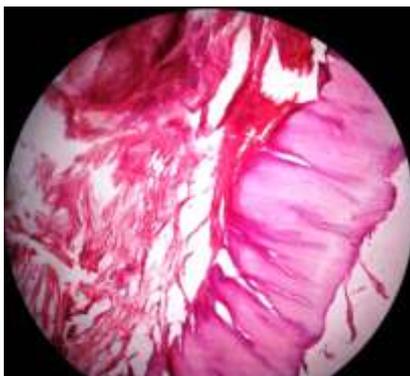
**Fig: 2** Palpation of the lesion shows a Y shaped groove in the centre of the lesion



**Fig: 3** Right buccal mucosa showing leukoplakic patch



**Fig: 4** Histopathological section showing proliferation in the form of broad and blunt rete pegs which are proliferating



**Fig: 5** Histopathological section showing epithelium having acanthosis, para-keratinization & parakeratin plugging

#### DISCUSSION

**Proliferative verrucous leukoplakia (PVL)** is characterized by the development of multiple keratotic plaques with roughened surface projections.<sup>[1-5]</sup> After its introduction in 1985 by Hansen et al, proliferative verrucous leukoplakia (PVL) of the oral mucosa still remains an enigmatic and difficult to define subentity of leukoplakia.<sup>[3]</sup> With the introduction of the term PVL. The previously used term "oral florid papillomatosis" has disappeared from the literature.<sup>[3]</sup> Although the lesions typically begin as simple, flat hyperkeratosis that are indistinguishable from ordinary leukoplakic lesions, PVL exhibits persistent growth, eventually becoming exophytic and verrucous in nature.<sup>[1,2,3]</sup>

As the lesions progress, they may go through a stage indistinguishable from verrucous carcinoma, but they later usually develop dysplastic changes and transform into full-fledged squamous cell carcinoma (usually within 8 years of initial PVL diagnosis).<sup>[1,3]</sup> PVL is unusual among the leukoplakia variants in having a strong female predilection (1:4 male-to-female ratio) and minimal association with tobacco use.<sup>[1,2]</sup>

**Verrucous Carcinoma (Snuff Dipper's Cancer; Ackerman's Tumor)** is a variant of oral squamous cell carcinoma characterized by a predominantly exophytic overgrowth of well differentiated keratinizing epithelium having minimal atypia and with locally destructive pushing

margins at its interface with underlying connective tissue.<sup>[1,4,5]</sup>

Verrucous carcinoma(VC) first described in 1948 by Lauren V. Ackerman is a distinct variant of differentiated SCC with low grade malignancy, slow growth and no or only low metastatic potential.<sup>[6]</sup> The tumor may also be found on different sites including skin, paranasal sinus, bladder and anorectal region, male and female genitalia, sole of the foot, and ear.<sup>[6]</sup> It is often associated with long-term use of smokeless tobacco although examples occur among nonusers. Betel nut chewing, poor dental hygiene and Human Papilloma Virus (HPV) infection have been implicated in the development of oral VC. The likelihood of detecting HPV in VC was found to be 29.5% and 46.5% in oral SCC.<sup>[1,6,7]</sup> The similar clinical and histologic appearance of VC affecting the upper aerodigestive tract, genitalia (condyloma acuminatum), and extremity skin (carcinoma cuniculatum) raises the possibility of a common cause.<sup>[8-11s]</sup>

Verrucous carcinoma is found predominantly in men older than 55 years of age. In areas where women are frequent users of spit tobacco, however, elderly females may predominate. The most common sites of oral mucosal involvement include the mandibular vestibule, the buccal mucosa, and the hard palate.<sup>[1,3,5,6]</sup> Oral verrucous carcinoma has a characteristic gross appearance. These lesions are almost always large, exophytic, soft, fungating, slow growing neoplasms with a pebbly mamillated surface.<sup>[6,7]</sup> The lesion appears as a diffuse, well demarcated, painless, thick plaque with papillary or verruciform surface projections resembling a cauliflower.<sup>[8]</sup>

Shear and Pindborg described a condition termed verrucous hyperplasia in 1980. Both lesions closely resemble each other clinically and pathologically. Verrucous hyperplasia has been considered an antecedent stage or early form of verrucous carcinoma and is believed to have the same biological potential. Verrucous hyperplasia and verrucous carcinoma are indistinguishable clinically.<sup>[8]</sup>

. Both PVL and verrucous carcinoma may have been reported in the past by the name Oral florid papillomatosis.<sup>[1,8]</sup> The

clinical association with leukoplakia is significant, and the evidence indicates that untreated leukoplakia may develop into a verrucous hyperplasia and/or a verrucous carcinoma in time. The diagnosis of verrucous hyperplasia and verrucous carcinoma is primarily based on histological criteria, being distinguished from each other by an exophytic and endophytic growth pattern respectively.<sup>[3,8,9,10]</sup> More recently, studies have further confirmed the association between Human papilloma virus(HPV) and VC by detecting HPV– DNA types 6, 11, 16, and 18 by polymerase chain reaction (PCR), restriction fragment analysis, and DNA slotblot Hybridization.<sup>[6,7]</sup> The importance of the diagnosis of PVL lies in the awareness of both the clinician and pathologist that apparently innocent looking oral verrucous lesions, irrespective of their colour and irrespective of the presence of dysplasia may in time progress into verrucous carcinoma or squamous cell carcinoma.<sup>[3,8]</sup> Multiple deep biopsies are recommended to avoid the problem of under-diagnosis. Because metastasis is an extremely rare event in verrucous carcinoma, the treatment of choice is surgical excision without radical neck dissection.<sup>[9,10]</sup> Chemotherapy using bleomycin may reduce the size of verrucous carcinoma, but it is not considered a definitive, stand-alone treatment.<sup>[1,3,5,9]</sup>

Recently successful treatment of an extensive VC with intra-arterial infusion of methotrexate or topical 5- aminolevulinic acid-mediated photodynamic therapy was reported.<sup>[6,11]</sup> The five years disease-free survival with surgical therapy was found to be 77.6% which correlates well with control rates reported in the literature.<sup>[7,10]</sup>

## CONCLUSION

Proliferative verrucous hyperplasia, verrucous leukoplakia and verrucous carcinoma appear similar clinically, or may coexist, and their disease progression towards malignancy varies, as verrucous hyperplasia may transform into either verrucous carcinoma or squamous-cell carcinoma. Many a times it is difficult for the oral diagnostician to differentiate clinically, hence a thorough clinical knowledge and in-depth

microscopic evaluation is required both clinicians and pathologists to diagnose this dilemma.

#### REFERENCES

1. Neville, Damm, Allen, Bouquot, Oral and maxillofacial pathology; 3<sup>rd</sup> edn, Saunders. pp 388- 397, 422- 423.
2. Martin S. Greenberg, Michael Glick, Burket's Oral Medicine Diagnosis and Treatment; 11th edn. BC Decker pp.88-89.
3. Editorial, Oral proliferative verrucous leukoplakia revisited; Oral Oncology. 2008; 44: 719– 721.
4. RA Cawson, EW Odell, S Porter, Cawsons Essential of Oral pathology and Oral medicine, 8th edn. Churchill Livingstone, pp 265 and 289.
5. Shafer, Hine, Levy: Shafer's text book of Oral Pathology, 6<sup>th</sup> Edition. Elsevier pp116-118.
6. Depprich RA, Handschel JG, Fritzeimer CU, Engers R, Norbert R. Kubler Hybrid; Verrucous carcinoma of the oral cavity: A challenge for the clinician and the pathologist Oral Oncology EXTRA, 2006; 42: 85–90.
7. Walvekar RR, Chaukar DA, Deshpande MS, Pai PS, Chaturvedi P, Kakade A, Kane SV, D'Cruz AK. Verrucous carcinoma of the oral cavity: A clinical and pathological study of 101 cases. Oral Oncology, 2009; 45:47– 51.
8. Alper Alkan, Emel Bulut, Omer Gunhan, Bora Ozden Oral Verrucous Carcinoma: A Study of 12 Cases; European Journal of Dentistry 2010; 4: 202-207.
9. Wood NK, Goaz PW, White lesion of the Oral Mucosa, Differential Diagnosis of Oral and Maxillofacial lesions, Fifth Edn, Elsevier publication, 113-115.
10. Addante RR, McKenna SJ. Verrucous Carcinoma. Oral Maxillofacial Surg Clin N Am, 2006; 18: 513–519.
11. Yu CH, Chen HM, Hung HY, Cheng SJ, Tsai T, Chiang CP. Photodynamic therapy outcome for oral verrucous hyperplasia depends on the clinical appearance, size, color, epithelial dysplasia, and surface keratin, thickness of the lesion, Oral Oncology 2008; 44: 595– 600.

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