

## 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 spit 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, 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 60 year old patient visited to department of oral medicine and radiology, SVSIDS Mahabubnagar Andhra Pradesh, with a chief complaint of white patches on her left side of cheek inside the mouth since 1 year. Patient was asymptomatic before one year, and then she observed a small area of white patches on her left side of the cheek region within the mouth which was slightly burning on chewing of spicy foods. Gradually the whitish area increased in its size. She has a habit of chewing tobacco since 27 years.

On *Extra oral* examination (**Fig.1**) involving head, face and neck regions when inspected, was normal. On palpation in the left submandibular region revealed a tender, slightly enlarged lymph node, which was movable without any fixity to surrounding structures.

On *Intra oral Examination* (**Fig.2**), there was a mouth opening of 40 mm, with generalized-dental fluorosis, and poor periodontal status. An irregular shaped solitary nodular, white hyperkerototic lesion of approximately 4x5 cm. was visible on the left side of the lower buccal vestibule of the mouth. It was extending anteriorly from the distal margin of the lower

left canine, posteriorly extending up to the third molar region. Medially the lesion was engraving the gingiva of the molar and the premolar regions and laterally it was extending around 1.5 cm. from the lower occlusal plane.

The surface of the lesion was hyperkeratotic, exuberant and exophytic with multiple nodular projections with fissures in between. The surrounding mucosa was normal in structure and color. On palpation, inspectory findings like site, shape, and extent were confirmed. The hyper keratotic lesion had rough surface giving a warty appearance with palpable multiple projections of hyperkeratotic tissue giving leathery feel on touch. The periphery of the lesion viz. distally and antero-superiorly, there were homogenous white keratotic areas suggestive of mixed type of homogenous as well as granular type. The lesion on palpation was not tender. The lesion was non scrapable. It was provisionally diagnosed as verrucous type of leukoplakia.

A differential diagnosis of Verrucous carcinoma, Hypertrophic Candidiasis and plaque type Lichen Planus, was given. Punch biopsy and Incisional biopsy was made. The H and E stained sections shows hyperkeratotic stratified squamous epithelium overlying a fibrous connective tissue at one end and the other end shows broad pushing retepegs with parakeratin plugging filling the craters. Abundant keratinisation is evident within the epithelium. Few islands of lesional epithelial cells are seen within the connective tissue. Overall histopathologic features are suggestive of Verrucous carcinoma with questionable infiltration (Fig.3).

## Discussion

**Proliferative verrucous leukoplakia (PVL)**, is characterized by the development of multiple keratotic plaques with roughened surface projections<sup>1,2,3,5</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>.

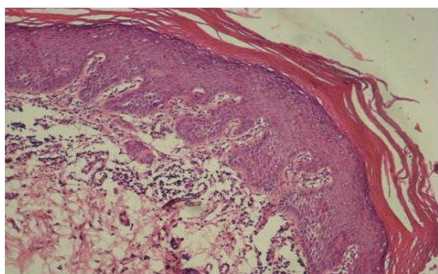
Verrucous carcinoma (VC) first described in 1948 by Lauren V. Ackerman is a distinct variant of differentiated SCC with low grade malignancy, slow growth and no or only low metastatic potential<sup>6</sup>. The tumor may also be found on different sites including skin, paranasal sinus, bladder and anorectal region, male and female genitalia, sole of the foot, and ear<sup>6</sup>. It is often associated with long-term use of smokeless



Fig 1. Extra oral view of the patient



Fig .2. Intra oral view showing rough,wartyand plebby surface



**Fig.3. Histopathological section showing broad 'pushing retepegs' with abundance of keratin on surface.**

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>8,10</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<sup>8</sup>. 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>3,8-10</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 slot-blot 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 underdiagnosis<sup>9</sup>. 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<sup>9</sup> 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 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.

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