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Oral squamous papilloma: A case report and review of literature

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Abstract
Oral squamous papilloma (OSP) is a benign proliferation of the stratified squamous epithelium, resulting in a papillary or verrucous exophytic growth. It is the common lesion of the oral mucosa with a predilection for the mucosa of the hard and soft palate. These lesions are neither transmissible nor threatening. It is related to Human Papilloma virus (HPV) types 16,18,6 and 11 (HPV 16, HPV 18 HPV 6 and HPV 11) which contain double stranded DNA, even though the controversy regarding its pathogenesis still exists. It is important to diagnose it correctly as it may mimic malignant lesions. We present a case of oral squamous papilloma along with a review of literature.

Keywords: oral squamous papilloma, human papilloma virus, koilocytes

Introduction
Oral squamous papilloma is a benign proliferation of the stratified squamous epithelium, which results in a papillary or verrucous exophytic mass induced by Human papilloma virus [1-3]. These are common lesions of the oral mucosa with the predilection for the mucosa of the hard and soft palate including the uvula and the vermillion of the lips. These lesions are neither transmissible nor threatening. Oral and oropharyngeal squamous papillomas occur mainly between 30 and 50 years of age. They represent about 8% of oral tumors in children [4]. A papilloma (plural: papillomas or papillomata) is defined as a small solid benign tumor of the epithelium with a clear-cut border that projects above the surrounding tissue [5]. Many considered its pathogenesis as being from the human papilloma virus (HPV). Till the date, about 150 different types of HPV have been identified [6], but recent literature suggests the presence of HPV may be merely an incidental finding unrelated to the development of a squamous papilloma (Marx and Diane, 2003). Most HPV's that infect mucous membranes belong to the group of alpha-papilloma viruses, are considered high risk (16 and 18) and represent approximately 70% of conditions of higher degree of malignant transformation while those of low risk (HPV types 6 and types 11) are the most common types associated with benign lesions [7].

Case Report
A 39-year old male patient reported to the department of Oral Medicine and Radiology with a chief complaint of pain in upper left back region of jaw since last 2 months. Intraoral examination revealed a diffuse, white, papillary growth on the left maxillary alveolar ridge, just behind the maxillary third molar of size 1X1cm approximately. On palpation, the growth was sessile, slightly tender, soft in consistency and arose from the underlying soft tissue (Fig.1). Patient's history revealed the occurrence of similar lesion about 6 months ago on the left buccal mucosa which was diagnosed as squamous hyperplasia. The present lesion has shifted more posteriorly than the previous lesion and it is now on the maxillary alveolar ridge. Patient had a habit of chewing tobacco and gutkha 2 to 3 times daily for around 10 years, presently he left the habit since last 6 months.

Past medical and family history was non-contributory. Based on the history, clinical features and the nature of the growth, a provisional diagnosis of Squamous papilloma was given along with differential diagnosis of verruca vulgaris, condyloma acuminatum, Verruciform Xanthoma and squamous cell carcinoma (SCC). Routine blood investigations were done, which showed no significant change in any value. The lesion then completely excised (Fig 2) and send to the department of Oral Pathology and Microbiology for the confirmation of diagnosis (Fig 3). On microscopic examination, the hematoxylin and eosin (H & E) (Fig.4) stained section showed exophytic parakeratinized stratified squamous epithelium with finger- like projections. Koilocytes were also seen in the superficial and middle epithelial cell layers. Underlying connective tissue stroma was in the form of thin cores (Fig.5) extending into finger-like projections suggestive of squamous papilloma.

The patient was observed over a period of 3 and 6 months respectively and no recurrence or new growth was noted elsewhere (Fig.6).

Fig 1: Pre-operative view

Fig 2: Post-operative view

Fig 3: Excised biopsy specimen

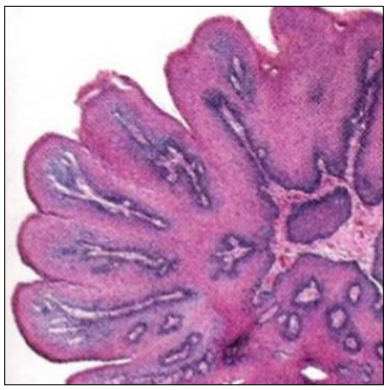

Fig 4: Histopathological View (10X)

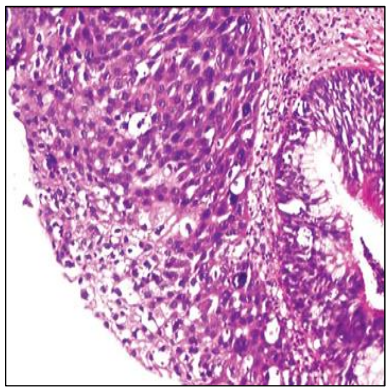

Fig 5: Histopathological view (40X)

Fig 6: Follow up after 6 months

Discussion

Oral squamous papilloma is the fourth most common oral mucosal mass and is found in four out of every 1,000 lesions [8]. It is a generic term that is used to include papillary or verrucous growths composed of benign epithelium and minor amounts of supporting connective tissue.

Accounting for 3 – 4% of all biopsied oral soft tissue lesions this entity was first reported as a gingival wart by Tomes in 1848. It is a localized, benign HPV–induced epithelial hyperplasia. It is caused by Human Papilloma virus types 16 and 18 (HPV 16 and 18) and types 6 and 11 (HPV 6 & HPV 11). The infection starts when the virus penetrates the new host through microinjuries. The development of this incubation phase into active expression depends on three factors: cell permeability, virus type and host immune status [4]. Infection by HPV acts as an initiator and additional somatic mutations are essential, where the occurrence of these alterations is facilitated by smoking, other co-existent infections, dietary deficiencies and hormonal changes, all considered to be co-factors in the pathogenesis [9]. The pathogenesis is that, the double stranded viral DNA integrates with the host DNA leading to the development of papilloma [10].

There is no clearly defined mode of transmission and mostly occurs spontaneously [11]. Theories have proposed multiple pathways including perinatal transmission (during the passage through an infected birth canal and in utero, as a transplacental or ascending infection), autoinfection from oro-genital contact by hand and sexual transmission by oro-genital contact [12]. However, some studies could not demonstrate a correlation between the practice of oral sex and HPV infection, suggesting that there could be other non-sexual transmission mechanisms. The primary means of HPV transmission to children is the ingestion of viral particles of infected cells from the birth canal.

Oral squamous papilloma may be found on the vermilion portion of the lips and any intra oral mucosal site, with a predilection for the hard and soft palate and uvula[1]. The latter three sites account for approximately one third of all lesions. In present case, the lesion was seen on the maxillary alveolar ridge, just behind maxillary third molar. The lesion generally measures less than 1 cm and appears as pink-to-white depending on the keratinization, exophytic granular or cauliflower-like surface alterations. The lesion is generally asymptomatic, but our case was symptomatic. It may be pedunculated or sessile in configuration. Squamous papillomas are traditionally divided into two types : isolated-solitary and multiple-recurring. Present case was isolated-solitary but it was recurred. The isolated-solitary is usually found in an adult's oral cavity, while the multiple-recurring is mostly found in a child's laryngo tracheobronchial complex. The isolated-solitary lesions are exophytic, pedunculated growths that resemble a cauliflower in appearance. They are usually white, but can occasionally be pink. Human Immuno virus (HIV) positive patient have multiple oral lesions. Malignant transformation of a papilloma is more common in the multiple-recurring type. Dos Reis *et al*. reported a case in which squamous papilloma lesions occurred concurrently in the oral cavity and genital area [13]. It occurs with equal frequency in both men and women[3]. It can occur at any age and also seen in children and adolescents, usually 30-50 years of age.

Differential Diagnosis

1. Verruciform Xanthoma: This lesion has a distinct predilection for the gingiva and the alveolar ridge. Histopathologically, it demonstrates papillary, acanthotic surface epithelium covered by a thickened layer of parakeratin. Connective tissue papillae are composed almost exclusively of xanthoma cells- large macrophages

with foamy cytoplasm.
2. Inflammatory papillary hyperplasia: This lesion appears under ill-fitting denture. Histopathologically, it shows fibrous and epithelial hyperplasia resulting in papillary surface projections. Heavy chronic inflammation is also present.
3. Condyloma accuminatum: This lesion would be larger than the papilloma, would have a broader base, and would appear pink-to-red as a result of less keratinization. Histopathologically, it shows acanthotic stratified squamous epithelium forming a blunted projection.
4. Focal epithelial hyperplasia (Heck disease): Multiple squamous papillomas are seen. Histopathologically, it shows prominent acanthosis of the epithelium with broad and elongated rete ridges.
5. Fibro-epithelial polyp: Flattened pink mass that is attached to the palate by a narrow stalk. It is easily lifted with a probe, which demonstrates its pedunculated nature [3]. Histopathologically, it shows hyperparakeratotic epithelium with irregular hyperplasia of the rete ridges.
6. Fibroma: It is painless, broad-based swelling that is paler in color than the surrounding tissue. The surface may occasionally be ulcerated, particularly in larger lesions. It is typically found in frequently traumatized areas, such as the buccal mucosa. Histopathologically, it shows nodular mass of fibrous connective tissue covered by stratified squamous epithelium.
7. Verruca vulgaris: It most often arises in children. The skin of the hands is the mostly affected. Oral mucosal lesions usually found on the vermilion border, labial mucosa, or anterior tongue. Histopathologically, it is characterized by a proliferation of hyperkeratotic stratified squamous epithelium arranged in finger-like, pointed projections with connective tissue cores. Chronic inflammatory cells often infiltrate the supporting connective tissue.

Histopathologically, it is characterized by a proliferation of keratinized stratified squamous epithelium arranged in finger-like projections with fibrovascular connective tissue cores. The connective tissue may show chronic inflammatory infiltrate. The keratin layer is thickened in lesions with a white clinical appearance, and the epithelium typically exhibits a normal maturation pattern. Some papillomas may demonstrate basilar hyperplasia and mitotic activity, which can be mistaken for mild epithelial dysplasia. Koilocytes (virus-altered epithelial cells with crenated, pyknotic [small and dark] nuclei surrounded by clear halos) sometimes are evident high in the spinous cell layer.

Laboratory diagnosis

Detection of the virus by conventional biopsy is very difficult as only changes caused by the virus can be observed. Electron microscopic analysis shows viral particles. The other methods of detection are in- situ hybridization, immunohistochemistry (IHC) and polymerase chain reaction (PCR) techniques.

Immunohistochemistry

P53 (TP53 or tumor protein), PCNA (proliferating cell nuclear antigen), CD44 (cell-surface glycoprotein involved in cell-cell interactions, cell adhesion and migration) and Bcl-2 (B-cell lymphoma 2) are overexpressed in case of malignant transformation and in papillomas with epithelial dysplasias [14].

Treatment

The preferred treatment is surgical excision. Either routine excision or laser ablation can be used. Other treatment modalities include electrocautery, cryosurgery, and intralesional injections of inter-feron. Recurrence is not common, except in patients infected with human immunodeficiency virus.

Conclusion

A case of oral squamous papilloma in a 39-year old male patient reported along with a discussion on etiology, clinical features, histopathological appearances, differential diagnosis and immunohistochemistry. An early clinical diagnosis as well as histopathological examination of these lesions is important because of their association with oral dysplasias and carcinomas.

More recently, gene therapy and vaccines targeted against HPV are currently under trial whereby HPV vaccines should eventually reduce the impact of these viruses on human health. At present two vaccines have been developed :cervarix and Gardasil provide protection against HPV types 6,11,16,18 and both existing vaccines are able to create a robust humoral immune response which is much more effective than the levels of antibodies that can be acquired after a general infection.

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