

# Squamous papilloma in the oral cavity: case presentation and review of the literature

## Abstract

Oral Squamous Papilloma is the most common benign tumor that can be found in the oral cavity, the main etiologic factor is Human Papilloma Virus (HPV), the route of transmission of this virus is through direct contact, despite being a lesion with benign characteristics, it has been observed in recent years that HPV infection is directly associated with the presence of Squamous Cell Carcinoma in the oral cavity, becoming a factor of importance that must be addressed by the different health services worldwide. We present the case of a 63-year-old male patient who attended the Dental Clinic of the Faculty of Dentistry of the Pontificia Universidad Javeriana Bogotá - Colombia. Through the intraoral examination, a papillary lesion on the soft palate was found. An excisional biopsy was performed and the diagnosis is confirmed by histopathological examination.

**Keywords:** papilloma, HPV, oral cavity, diagnosis

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## Introduction

Squamous papilloma is the most common benign epithelial tumor of the oral mucosa, it is identified as an exophytic proliferation giving rise to papillary lesions with finger-like projections.<sup>1</sup> It constitutes 2.5% of the lesions of the entire oral cavity, larynx, bronchial tree, esophagus, bladder, anus and genital tract.<sup>2</sup> The main etiologic factor of these lesions is the Human Papillomavirus (HPV), which comprises different types within the Papillomaviridae family, they do not contain any envelope, their diameter is 55nm, and their capsule is icosahedral (72 capsomere protein).<sup>3</sup> Most HPVs that infect mucous membranes belong to the group of alpha-papillomaviruses, are considered high risk (16 and 18) represent approximately 70% of conditions of higher degree of malignant transformation while those of low risk (6 and 11) are the most common types associated with benign lesions.<sup>3</sup> In the United States, during the years 2009 to 2010, a cross-sectional study was conducted in the civil population of the patients and it was reported that the prevalence rate of oral HPV infection in men and women between 14 and 69 years of age was 6.9% and of HPV 16 was identified in 1%. A higher rate of HPV was identified in men than in women, and between 30 and 34 years and between 60 and 64 years.<sup>4</sup> According to the site of infection, HPVs that infect the oral cavity are considered mucocutaneous. The literature associates HPV with the appearance of anogenital warts, cancer of the oropharynx, dysplasia and cervical cancer, at least 40 types of HPV can infect the skin, genitals and mucous membranes.<sup>4</sup> Its transmission is diverse: it can occur in the perinatal period and later in life, by sexual contact and autoinoculation, although some authors also suggest a possible transmission by saliva, oral sex has been established as the main method of transmission of HPV in mouth.<sup>5</sup> The lesions are limited specifically to the squamous epithelium of the mucous membranes,

after the infection of the basal layer and a variable incubation time, the replication and assembly of virions occurs in conjunction with the squamous cell differentiation. When the infections are in low layers, the number of viral copies per cell is also too low to transmit the disease, in subclinical infections, viral replication of DNA and transcription are active, the observable lesions contain the active virus, these are usually exophytic, flat, papillomatous or verruciform, endophytic or less observable.<sup>6</sup> In the case of lesions located in the uvula or in places close to it, patients usually have difficulty swallowing food, therefore surgical excision should be performed as soon as possible.<sup>7</sup> The aim of this article is to review the literature and present the case of a squamous papilloma of the soft palate.

## Case presentation

A 63-year-old male patient resident of the city of Bogotá, who attends the dental clinics of the Faculty of Dentistry of the Pontificia Universidad Javeriana, was referred to the oral pathology clinic. The patient with a history of Diabetes Mellitus type II diagnosed about 1 year ago controlled with Metformin 800mg twice a day, smoked 20 cigarettes a day for about 40 years. At the time of clinical examination a vegetative lesion with a pedunculated base of approximately 8mm in diameter, whitish in color was observed at the soft palate level lateral to the base of the uvula, the patient does not know the time of evolution.

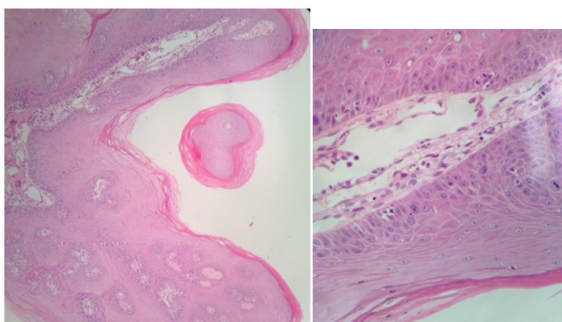
According to the clinical examination and the data obtained during the anamnesis, the following presumptive diagnosis was obtained: squamous papilloma. As a treatment, the following procedure is performed: excisional biopsy of a vegetative lesion of the soft palate. After asepsis and antisepsis, the anesthetic (lidocaine 2% with epinephrine 1: 80000) is applied at the perilesional level, the

incision is made with electrocautery around the lesion and the sample is obtained. Subsequently, the sample of the lesion is placed in 10% formalin, labeled and sent for histopathological study.



### Histopathological examination report

Proliferation of stratified keratinized squamous epithelium, arranged in finger-like projections with fibrovascular connective tissue cores, the superficial layer of keratin is denser in lesions with a more white clinical appearance. The koilocytes are clear epithelial cells with small pyknotic nuclei.



Postoperative control after 8 days.



### Discussion

The squamous papilloma located in the oral cavity is a frequent, asymptomatic lesion, which is usually detected through the clinical examination by the dentist. Depending on the degree of keratinization, the color of the surface of the lesion varies between red, pink or white, the most common places are the palate and the tongue, the age of presentation ranges from 20 to 50 years, with the lesions being mostly unique. Devi et al.,<sup>1</sup> mention that in a sample of 464 squamous papillomas of the oral cavity, 34.3% of these lesions were located in the palatal complex (hard palate, soft or uvula), the majority being benign and asymptomatic.<sup>7</sup> Benign squamous papilloma is associated with low risk types of HPV 6 and 11,<sup>8</sup> affecting patients of all ages, but more often diagnosed from the second to fourth decade of life,<sup>8</sup> which suggests that the appearance of these lesions is more frequent in people with active sexual life. However, some studies have not been able to demonstrate a correlation between the practice of oral sex and HPV infection, suggesting also that they operate non-sexual transmission mechanisms. Significant levels of HPV infection have been observed in the mouth of children aged 1 year and younger than 19 years of age, therefore studies support the vertical transmission of HPV to the oral cavity of the mother to the baby, in addition to other modes of transmission that include autoinoculation, although the lack of concordance between the HPV genotype in the oral and anal sites indicates that this is a rare modality.<sup>8</sup> The viral life cycle begins when the virus enters through microabrasion to the basal layer, joining the surface receptors of the basal layer (Integrin 6, Heparan Sulfate and CD69); the virions may or may not be incorporated into the nucleus of the cells, however the viral proteins E1, E2, E6, E7 are expressed at low levels; after cell division, the infected cells migrate to the suprabasal zone and begin to differentiate by activating a transcriptional cascade coordinated with the viral genome.<sup>5</sup> HPVs are characterized by a special tropism for squamous epithelial cells and keratinocytes. The synthesis of viral DNA and the expression of viral genes (especially for those that encode capsid proteins) are related to the level of differentiation of keratinocytes. The normal viral replication cycle is a highly regulated process, depending both on some viral proteins encoded by the viral genome and the degree of differentiation of the infected cell; the infection usually begins in the basal and para-basal cells of the squamous epithelium. Changes in keratinocytes from the basal layer to the surface of the epithelium provide a suitable micro-environment for productive cellular replication.<sup>6</sup>

Histologically, HPV infection can be observed as an acanthotic, dyskeratotic lesion with keratinocyte multinucleation and koilocytosis. These histological features occur when infection becomes productive,

viral genes are sequentially expressed from early genes to late genes, followed by squamous epithelial differentiation, from basal and parabasal cells, where the early portions of the genome are more active and proceed to the upper layers of the epithelium (intermediate and superficial), together with the formation of the complete virion (i.e., the infected viral particle). The classic viral cytopathic effects that may appear: koilocytosis in particular, is considered as the obvious expression of a viral cytopathic effect. The koilocytic cell shows a thicker cytoplasm at the level of the inner wall of the membrane and morphologically crashed atypical cell nucleus. Histologically, HPV infection can be observed as an acanthotic, dyskeratotic lesion with keratinocyte multinucleation and koilocytosis.<sup>6</sup>

The most common differential diagnosis suggested was that of a condyloma. This lesion can be mistakenly considered a papilloma because the macroscopic aspect can also show a surface similar to a cauliflower. These entities can be differentiated macroscopically, microscopically and immunologically. The number of elements, the size of the lesion, the stem, the location and the color can help distinguish them. Other similar entities include verruca vulgaris, verruciform xanthoma, verrucous carcinoma, among others.<sup>2</sup> The treatment of choice of squamous papilloma is surgical excision, there are various forms of surgical treatment, one of which is cryosurgery, which is defined as the surgical technique based on the destruction of affected or unwanted cells and tissues, through the action of the cooling elements at subzero temperature, this treatment has advantages because there is no bleeding, minimum need for anesthesia, the postoperative period is faster and less traumatic.<sup>9</sup> The form of replication of HPV is different depending on the type of lesions; in benign lesions, the HPV genome is found in an extrachromosomal episomal (plasmid) form, whereas in malignant lesions, viral DNA is integrated into the host genome.<sup>10</sup> Regarding the association of HPV with the development of cancer in the oral cavity, it is manifested: the integration of the viral genome in the host cell is a very rare event, affecting the host chromosomes in fragile sites, after the transformation to carcinogens the neoplastic process progresses rapidly. The integration of HPV in the host genome induces the increase of the expression of E6 and E7 proteins, since the integration results, produces the interruption of the E2 gene of HPV, which is a negative regulator of the transcription of proteins E6 and E7. High-risk HPV E6 and E7 oncoproteins can independently induce genomic instability in normal human cells.<sup>11</sup> As expressed above, the incidence rates of base of tongue cancer and tonsil has increased gradually, according to data from the National Cancer Institute, Epidemiology in the United States, from 1973 to 2001 it was documented that base of tongue cancer and palatine tonsils increased between 2 to 4% annually, these two locations being the most frequent.<sup>12</sup>

HPV seems to have tropism by Waldeyer's lymphoepithelial ring, in lingual and palatine tonsils, in these areas there are deep intussusceptions (tonsillar crypts), in which, the immature cells are more easily exposed to HPV, so the lesions are more frequent in these areas. More recent studies obtained data in North America on the incidence of cancer of the oral cavity and oropharynx, with lower percentages of HPV-16 in carcinomas of the oral cavity (0-4%), while higher percentages were observed in cancers of the oropharynx (63-82). %, these findings suggest that HPV-16 is more likely to be detected in the oropharyngeal territory than in the oral cavity.<sup>13</sup> Within the preventive plan, at present there are two vaccines that protect against HPV 16 and 18, which cause 70% of cases of carcinoma of the uterine cervix. Vaccines may confer some cross-protection against

other less common types of HPV that are also the cause of this cancer. One of the vaccines also protects against types 6 and 11, which cause anogenital warts.

The bivalent vaccine called (Cervarix) offers protection against HPV types 16 and 18, the accepted indications for the bivalent vaccine are only cervical cancer and its precursors.

The quadrivalent vaccine (Gardasil) includes protection against HPV 6 and 11 because genital warts are benign mucosal lesions of the mucosa caused by the human papillomavirus (HPV), most commonly types 6 and 11. These lesions are part of one of the most common viral sexually transmitted infections and are very common in people with more than 10 sexual partners throughout their life or in sexual partners, where at least one had genital warts, the use is limited to cancers of the vulva, the vagina and the anus and their precursors.<sup>14</sup> Regarding the oral cavity, until 2015, only 9 cases have been reported in which the quadrivalent vaccine was applied in patients with oral lesions associated with HPV, with encouraging results in short-term patients, however in patients with immune alterations, the effectiveness of the vaccine on present lesions decreases considerably.<sup>15</sup> Despite this, in the preventive field, in the few studies that are being carried out to date, a reduction in the prevalence of oral HPV 16 - 18 lesions is observed among vaccinated women, however, are still questioned because the indication of the vaccine is based on the epidemiology of HPV in the cervix, so it is necessary to carry out studies that provide definitive evidence for the use of the vaccine as a method preventive in the development of oral cancer.<sup>14</sup>

## Conclusion

The squamous papilloma is a common benign lesion among patients attending the dental practice, however according to recent studies, HPV is closely associated with the development of oral squamous cell carcinoma, therefore the dentist is under an obligation to examine the oral cavity of patients looking for lesions that may indicate neoplastic process caused by HPV, since in the early stages, the response to treatment confers a favorable prognosis and inform patients about the risk factors for developing this disease and its preventive methods.

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## Conflict of interest

The author declares that there is no conflict of interest.

## References

1. Frigerio M, Martinelli-Kläy CP, Lombardi T. Clinical, histopathological and immunohistochemical study of oral squamous papillomas. *Acta Odontologica Scandinavica*. 2015;73(7):508-515.
2. Gleason AG, Poncem DMSG, Gaspar DV. Diagnosis and treatment of solitary tongue papilloma. Case report and literature review. *Revista Odontológica Mexicana*. 2016;20(1):e39-e43.
3. Pringle GA. The role of human papillomavirus in oral disease. *Dental clinics of North America*. 2014;58(2):385-399.
4. Rajendra AS, Ogle OE, Williams D, et al. Epidemiology of Oral and Maxillofacial Infections. *Dental clinics of North America*. 2017;61(2):217-233.



5. Rautava J, Syrjänen S. Human papillomavirus infections in the oral mucosa. *The Journal of the American Dental Association*. 2011;142(8):905–914.
6. Campisi G, Panzarella V, Giuliani M, et al. Human papillomavirus: Its identikit and controversial role in oral oncogenesis, premalignant and malignant lesions (Review). *Int J Oncol*. 2007;30(4):813–823.
7. Devi RS, Rajsekhar B, Srinivas GV, et al. Unusual length of pedicle: Pedunculated squamous papilloma of uvula causing unusual dysphagia of long duration in a child of 10 years. *Case reports in dentistry*. 2014.
8. Kennedy RA. HPV for the oral surgeon. *Oral Surgery*. 2016;9(1):4–9.
9. Estrada Pereira GA, Márquez Filiu M, González Heredia E, et al. Crioterapia en pacientes con papiloma escamoso bucal. *Medisan*. 2014;18(6):762–768.
10. Lizano Soberón M, Carrillo-García A, Contreras Paredes A. Infección por virus del papiloma humano: epidemiología, historia natural y carcinogénesis. *Cancerología*. 2009;4:205–16.
11. Díaz MG, Vargas LAM, Torres AM, et al. La infección por virus del papiloma humano afecta el pronóstico del cáncer orofaríngeo escamocelular. Revisión de la literatura/Human Papillomavirus Infection Affects Squamous Oropharyngeal Cancer Prognosis. Literature Review. *Universitas Odontologica*. 2015;33(71):69–77.
12. Cleveland JL, Junger ML, Saraiya M, et al. The connection between human papillomavirus and oropharyngeal squamous cell carcinomas in the United States: implications for dentistry. *J Am Dent Assoc*. 2011;142(8):915–924.
13. Kreimer AR. Prospects for prevention of HPV-driven oropharynx cancer. *Oral Oncol*. 2014;50(6):555–559.
14. Castillo A. HPV infection and carcinogenesis in the upper aero-digestive tract. *Colombia Médica*. 2011;42(2):233–242.
15. Cyrus N, Blechman AB, Leboeuf M, et al. Effect of quadrivalent human papillomavirus vaccination on oral squamous cell papillomas. *JAMA dermatol*. 2015;151(12):1359–1363.