Pacific Journal of Medical and Health Sciences
ISSN: 2456-7450 | Vol.9, No. 1, 2024, pp - 66-71

PJMHS
PACIFIC JOURNAL OF MEDICAL AND HEALTH SCIENCES

Review

Human Papilloma Virus Related Lesions of Oral Cavity

Swamini Mishra[1], Tushar Phulambrikar[2], Pooja Mahay[3], Tanvi Dosi[3], Neha Hissariya[4], Gauri Vijayvergiya[4], Urvashi Yadav[1]and Priyanka[1]

[1]Postgraduate Student, [2]Professor and Head, [3]Professor, [4]Senior Lecturer

Department of Oral Medicine and Radiology, Sri Aurobindo College Of Dentistry, Indore, MP, Bharat

***Corresponding Author Email:** swaminimishra07@gmail.com

ABSTRACT

Human Papilloma Virus is most commonly sexually transmitted viral infection in the world. Papilloma virus is one of the oldest virus and causative agents of a group of oral lesions. Currently the incidence of HPV related oral lesions are steadily rising globally. This review gives an insight into the structure, transmission, and morphological characteristics of HPV and oral lesion related to HPV.

KEYWORDS: Human papilloma virus, HPV oral cavity, Oral condyloma, Oral lesions

HUMAN PAPILLOMA VIRUS

Human Papilloma viruses (HPVs) are a large and diverse group of epitheliotropic double-stranded DNA viruses. There are up to 225 types of HPVs divided into 5 groups (α, ß, γ, μ, and ν)[1]. Persistent HPV infection is one of the important sexual transmitted diseases (STDs) associated with more than 5% of all cancers in the world. In other words, globally more than half of all malignancies related to infection are caused by HPV[2]. HPV infection is associated with several proliferative, wart like lesions of the skin and mucosa.

Papilloma viruses are small, non-enveloped, epitheliotropic, double-stranded DNA viruses that infect mucosal and cutaneous epithelia in a wide variety of higher vertebrates in a species-specific manner and induce cellular proliferation. More than 100 types of human Papilloma viruses (HPVs) have been identified and approximately half of them infect the genital tract. Many types of HPV have been found in cervical cancers, while others are found rarely or not at all in large series of cancers, which gives rise to the nomenclature of 'high-' and 'low-risk' HPVs. These other types are associated with other anogenital and oropharyngeal cancers.

The genomes of all HPV types contain approximately eight ORFs that are all transcribed from a single DNA strand. The open reading frames (ORF) can be divided into three functional parts: the early (E) region that encodes proteins

(E1–E7) necessary for viral replication; the late (L) region that encodes the structural proteins (L1–L2) that are required for virion assembly; and a largely non-coding part that is referred to as the long control region (LCR), which contains *cis* elements that are necessary for the replication and transcription of viral DNA [Figure 1][3].

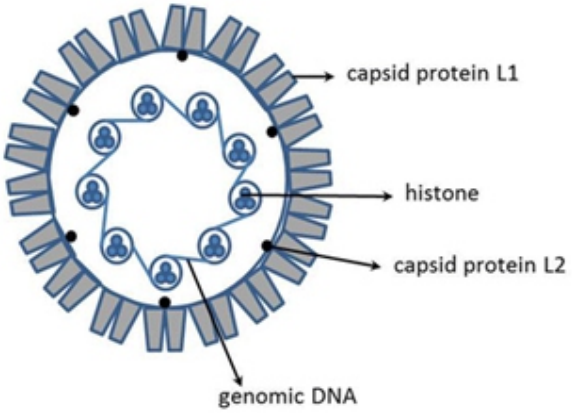

Figure 1: Structure of Human Papilloma Virus

Papilloma viruses are highly epitheliotropic; specifically, they establish productive infections only within stratified epithelia of the skin, the anogenital tract and the oral cavity[4].

The life cycle is thought to be initiated by the infection of basal epithelial cells, presumably at sites of injury. Although several potential receptors have been reported, it is unclear which of them is of physiological importance. Basal cells comprise the proliferating cellular component of stratified epithelia, in which the viral genome is established when a low copy number, nuclear plasmid and early genes are expressed preferentially although at low levels.

The viruses enter the epithelium through micro lesions and infect the basal epithelial cells where they maintain a copy number of 50–100 genomes per cell. Upon cell division, one daughter cell will remain part of the basal epithelium, while the other daughter cell will migrate up to the next level and start to differentiate. At this stage the viral DNA will segregate with the two daughter cells and replicate to maintain the 50–100 copies per cell. Virus can show productive and latent infection phase. In productive cycle the HPV have to reach cells from the basal layer of epithelium and allows keratinocytes to proliferate and express the replication of DNA, providing an environment for initial viral genome replication.

Viral latency is characterized by cessation production of new virus particles, without eradication of virus from the body. It is a complication of HPV infection in which HPV DNA can remain latent within the cells even though others have entered the productive cycle.

The transmission of HPV can occur through various ways across various mucosal sites which include sexual transmission (orogenital sex, deep kissing, and prolonged tongue to tongue contact), autoinoculation, perinatal transmission and indirect transmission through contact with hands. It can be extra genital to extra genital, extra genital to genital, genital to genital or genital to extra genital.

ORAL LESIONS

Verruca Vulgaris (VV)

VV, or the common wart, is the main presentation of cutaneous HPV infection and accounts for 70% of warts. An estimated 10% of children and young adults are affected, with peak incidence occurring in teenagers ages 12–16. VV may be found anywhere on the skin, but is most common on the periungal region of the hands. While common on the skin, VV is relatively uncommon intraorally.

Clinically, the mucosal lesions appear similarly to their cutaneous counterparts. The labial mucosa and palate are the most common intraoral sites. The lesions are pink to white, sessile, usually less than one centimeter, and display exophytic fronds [Figure 2]. Seldom, a few VV may occur simultaneously or in clusters, representing multiple sites of infection, but solitary lesions are typical[8] caused by HPV 2 and 4. Treatment depends on location, type, and size which include cryotherapy, electrocautrization, curettage, laser ablation keratolytic agents.

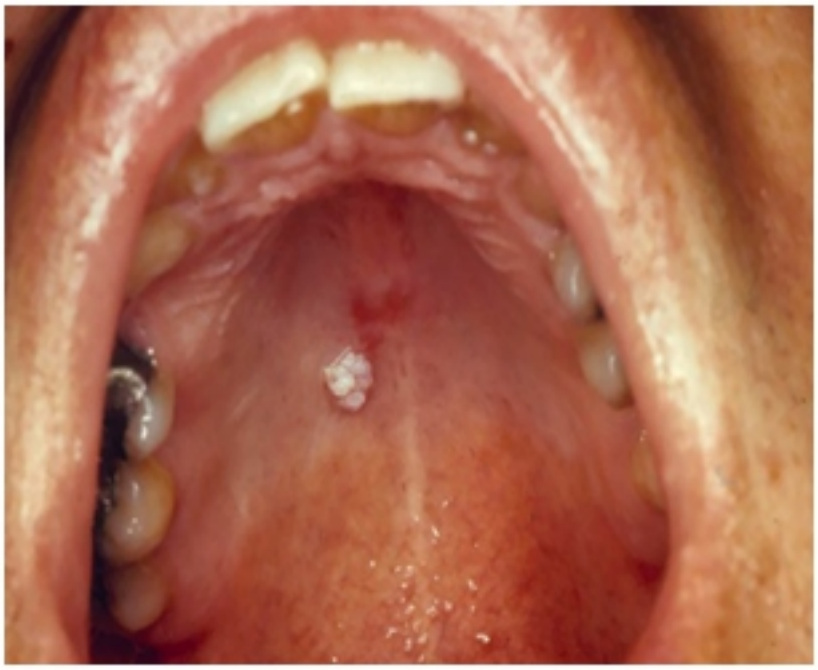

Figure 2: Lesion of Verruca Vulgaris
(Image Courtesy: Dr. Duane Schafer)

Squamous Papilloma (SP)

SP is a common lesion and the most frequent benign oral epithelial entity in both children and adults. In a large study of consecutive oral examinations of Army inductees, SP was the second most commonly encountered pathologic entity overall. Adults experience the highest incidence, with increases between the third and seventh decades. The palate and tongue are most commonly affected, but any site may be involved.

Clinically, SP is characterized by exophytic projections described as "finger-like", "Cauliflower" or "warty" are also common surface descriptors [Figure 3]. SPs are usually pedunculated, with color ranging from white to pink/red. The lesions are rarely larger than 5 millimeters in greatest dimension and usually solitary[9,10], caused by HPV 6 and 11. Treatment includes complete surgical excision of the base of lesion, along with a small area of surrounding tissue to prevent its recurrence.

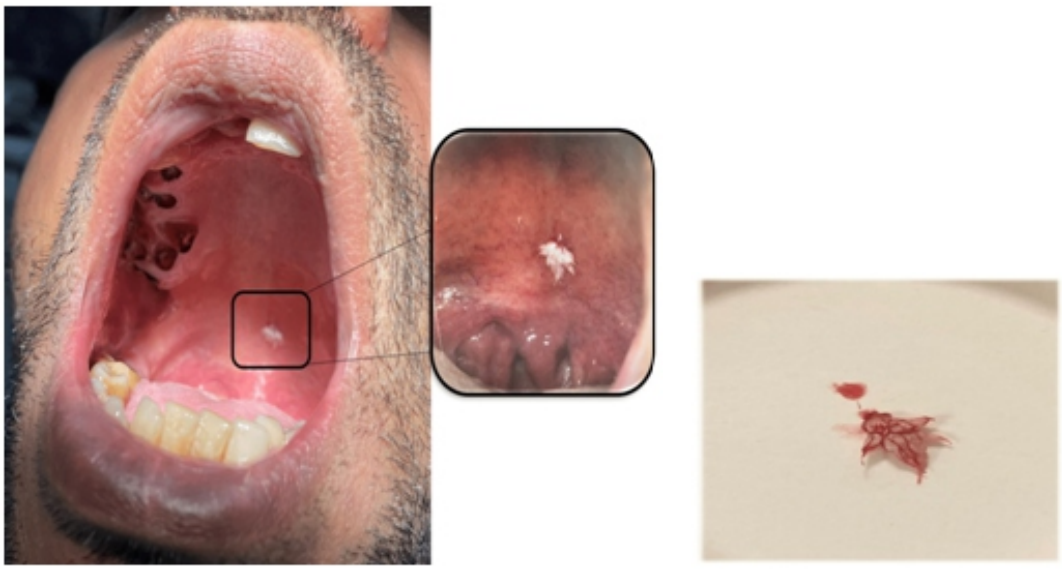

Figure 3: Squamous Papilloma

Condyloma Acuminatum

Condyloma accuminatum is a sexually transmitted HPV-related squamo-proliferative lesion occurring predominantly in an anogenital location. Oral lesions are transmitted through orogenital sexual contact.

Condyloma accuminata are larger than squamous cell papillomas and present as multiple broad based, cauliflower-like lesions with blunt processes frequently larger than 1cm [Figure 4]. The most common intraoral sites of involvement include the labial mucosa, lingual frenum and soft palate.

HPV subtypes 6 or 11 are aetiologically implicated, although high-risk subtypes may also be involved. Oral condyloma accuminata can be treated with cryotherapy or surgical excision[7].

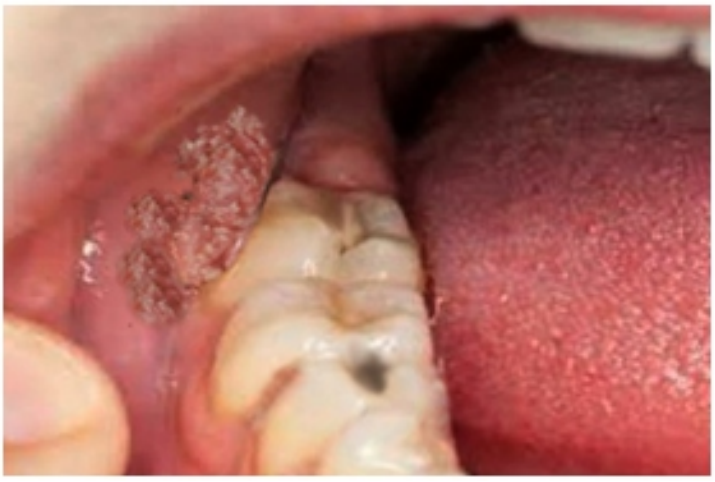

Figure 4: Oral Condyloma
(Image Courtesy: S Bhimji)

Multifocal Epithelial Hyperplasia (Heck's Disease)

Focal epithelial hyperplasia (FEH), or Heck's disease, is a rare disease of the oral mucosa; it is mostly found in children or young adults who are immune-suppressed and who live in regions with low socioeconomic status. It is characterized by asymptomatic papules on the oral mucosa, gingiva, tongue, and lips.

Multifocal Epithelial Hyperplasia presents as multiple mucosal coloured nodules measuring 2-10mm in size with a characteristic cobblestone appearance [Figure 5][5]. The lesions are predominantly present on the lips and gingivae, but can be identified at all oral mucosal sites. HPV types 13 and 32 are the usual causative agents in MEH. Lesions are clinically recognisable and resolve spontaneously within a few-months, obviating the need for treatment. Surgical or medical therapy is only indicated for large lesions which have caused functional and/or severe aesthetic complications[7,11].

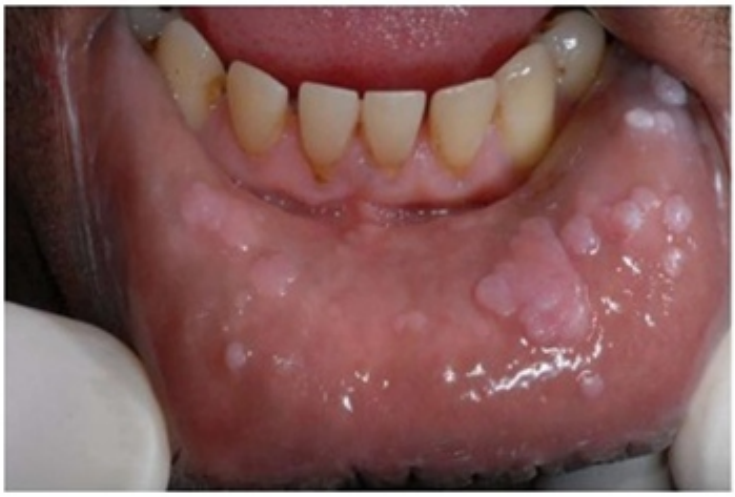

Figure 5: Multifocal Epithelial Hyperplasia

Oropharyngeal Carcinoma (OPCs)

The oropharynx consists of the palatine tonsils, base of tongue and soft palate. Most HPV-associated OPCs develop in the palatine tonsillar area. The tumours are characterised by early cervical lymph node metastases, which are frequently cystic in nature and may be the only clinical feature at the time of presentation. HPV-associated OPCs have a characteristic non-keratinising histological appearance.

HPV infection leads to transformation of oral epithelium by altering the tumor suppressor pathway and targeting the p53 and pRb genes leading to carcinogenetic changes.

Clinically, HPV-associated tumors can appear as a strawberry-like exophytic lesion, frequently at the base of the tongue or in the tonsil area. Most show poorly differentiated pathologic findings and cystic changes in the metastatic neck lymph nodes. As described, the transformation of normal oral mucosa in OSCC could be related to precancerous lesions, such as oral leukoplakia (OL), oral erythroplakia (OE), oral lichen planus (OLP), nicotine stomatitis, tobacco pouch keratosis, and oral submucous fibrosis. The role of HPV in malignant transformation of precancerous lesions has not been confirmed.

PREVENTION AND TREATMENT

The management of HPV infection depends on the type and severity of the infection. For the precancerous stage of HVP infections, include strategies as excision, ablation and immunotherapy. The gold standard is various excisional procedures of the transformation zone where the extent of excision depends on the lesion size.

In case of oropharyngeal squamous cell carcinoma, cisplatin – based chemotherapy has been the primary therapeutic approach. Radiotherapy or surgical intervention is the choice of treatment during the primary early stage.

HPV Vaccines

There are two types of vaccines against HPV: prophylactic and therapeutic HPV vaccines.

The commercial prophylactic HPV vaccines use HPV VLP to generate neutralizing antibodies against HPV major capsid protein L1.

Therapeutic HPV vaccines can eliminate preexisting lesions and infections by generating cellular immunity against HPV infected cells. HPV E6 and E7 oncoproteins are ideal targets for therapeutic intervention. Both proteins are constitutively expressed in all levels of the epithelium of HPV infected cells and play a crucial role in the induction and maintenance of HPV associated cancer[14].

CONCLUSION

Human Papilloma Virus is common and highly contagious virus showing various health hazards. There are over two hundred types of HPV and infections by many strains can resolve on their own. But it is also the initiating factor behind various epithelial lesions and cancers like cervical/ anogenital/ oral/ laryngeal/ lungs. Early detection and treatment can significantly improvise the outcomes of the diseases, vaccination and screening tests are the useful tools for the same. By understanding and spreading the awareness related to potential risk and complication of the infection we can protect the impact of HPV worldwide.

CONFLICTS OF INTEREST: None

FINANCIAL SUPPORT: None

REFERENCES

1. Soheili M, Keyvani H, Soheili M, Nasseri S. Human papilloma virus: A review study of epidemiology, carcinogenesis, diagnostic methods, and treatment of all HPV-related cancers. Med J Islam Repub Iran. 2021 May 22; 35:65. doi: 10.47176/mjiri.35.65.
2. Haley CT, Mui UN, Vangipuram R, Rady PL, Tyring SK. Human oncoviruses: Mucocutaneous manifestations, pathogenesis, therapeutics, and prevention: Papillomaviruses and Merkel cell polyomavirus. *J Am Acad Dermatol.* 2019; 81(1):1–21.
3. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Human Papillomaviruses. Lyon (FR): International Agency for Research on Cancer; 2007. (IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, No. 90.) 1, Human Papillomavirus (HPV) Infection.
4. Howley, P.M. & Lowy, D.R. (2001) Papillomaviruses and their replication. In: Knipe, D.N. & Howley, P.M., eds, *Field's Virology*, Philadelphia, PA, Lippincott, Williams & Wilkins, pp. 2197–2229 .
5. Ethel-Michele de Villiers, Claude Fauquet, Thomas R Broker, Hans-Ulrich Bernard, Harald zur Hausen, Classification of papillomaviruses, Virology, Volume 324, Issue 1, 2004, Pages 17-27.
6. Prabhu SR, Wilson DF. Human papillomavirus and oral disease - emerging evidence: a review. Aust Dent J 2013;58:2-10; quiz 125.
7. VAN HEERDEN, WFP; RAUBENHEIMER, EJ and BUNN, BK. Human papillomavirus infection of the oral cavity: what the dentist should know. *S. Afr. dent. j.* [online]. 2017, vol.72, n.2 [cited 2024-03-24], pp.52-55.

8. Plasencia JM. Cutaneous warts: diagnosis and treatment. *Prim Care.* 2000; 27(2):423–434.

9. Betz SJ. HPV-Related Papillary Lesions of the Oral Mucosa: A Review. Head Neck Pathol. 2019 Mar; 13(1):80-90. doi: 10.1007/s12105-019-01003-7.

10. Darwish G. Squamous Papilloma of the Soft Palate: A Case Report. Cureus. 2023 Apr 11; 15(4):e37423. doi: 10.7759/cureus.37423.

11. Galanakis A, Palaia G, Tenore G, Vecchio AD, Romeo U. Focal epithelial hyperplasia in a human immunodeficiency virus patient treated with laser surgery. World J Clin Cases. 2014 Jul 16; 2(7):293-6. doi: 10.12998/wjcc.v2.i7.293.

12. Chaturvedi AK, Engels EA, Anderson WF, Gillison ML. Incidence trends for human papillomavirus-related and-unrelated oral squamous cell carcinomas in the United States. Journal of clinical oncology. 2008 Feb 1; 26(4):612-9.

13. Kim SM. Human papilloma virus in oral cancer. J Korean Assoc Oral Maxillofac Surg. 2016 Dec; 42(6):327-336. doi: 10.5125/jkaoms.2016.42.6.327. Epub 2016 Dec 27.

14. Wierzbicka M, Józefiak A, Jackowska J, Szydłowski J, Goździcka-Józefiak A. HPV vaccination in head and neck HPV-related pathologies. Otolaryngologia Polska. 2014 Jul 1; 68(4):157-73.