

HPV INFECTIONS ASSOCIATED WITH ORAL MUCOSA

Dr. Garima Srivastava*, Dr Yadvandra Yadav, Dr. Shilpi Singh, Dr. Mohit Wadhawan, Dr. Md. Shadab
Kalim, and Dr Abhishek Sourabh

India.

*Correspondence for Author: Dr. Garima Srivastava
India.

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ABSTRACT

Human papillomavirus (HPV), small non enveloped DNA tumor virus , of papillomavirus family , causes genital warts, common warts, plantar warts and flat warts. Its frequency is about 9-13%. Oral mucosa may play significant role in HPV transmission and its persistent infection in the oral mucosa increase the risk of developing carcinoma. Regular and scrupulous examination of it is most important tool in detecting HPV-associated changes in the oral mucosae . HPV16 being the most prevalent genotype other being HPV 2, 4, 6, 11, 13, 18 and 32. HPV positivity occurs in vermilion border, hard palate, labial mucosa and labial commissures .According to biologic behavior there are various lesions associated with it .Benign lesions being squamous papilloma , verruca vulgaris ,condyloma acuminatum , focal epithelial hyperplasia and premalignant or malignant lesions are leukoplakia, squamous cell carcinoma , lichen planus, verrucus carcinoma. HPV infection is constrained to the basal cells of stratified squamous epithelium, of the oral mucosa the only tissue in which it replicates. The accessible HPV vaccines cover the HPV genotypes found most commonly in the oral mucosa, but their defensive effect against oral cancer remains to be elucidated.

KEYWORDS: HPV infection, oral mucosa, carcinoma, HPV vaccines.**INTRODUCTION**

HPV are small icosahedral particles that infect the dermal or epithelial layer of the skin. The World Health Organization estimates that between 9-13% (~630million) of the world population has an HPV infection. "as discussed by Patel.^[1]" Of the 120 or so recognized types of the virus, a few grounds are diversity of benign wart-like lesions of the skin and genital and oral mucosae, at the same time as others are aetiologically associated with cervical and anogenital cancers. "as discussed by Prabhu.^[2]" The benign oral lesions are linked with HPV 2, 4, 6, 11, 13, and 32 (squamous papilloma , verruca vulgaris ,condyloma acuminatum , focal epithelial hyperplasia) and premalignant malignant or malignant lesions are linked with HPV 16 and 18 (leukoplakia, squamous cell carcinoma, lichen planus , verrucus carcinoma) "as discussed by Garlick.^[3]" In this paper biological aspects of HPVs and their role in the development of a range of oral mucosal lesions are briefly reviewed for the point of updating oral health professionals and raising the alertness of budding associations being established flanked by HPVs and some oral diseases counting oral cancer.

STRUCTURE

Human Papillomaviruses, small non-enveloped DNA tumor viruses with a virion size of 52-55 nm in diameter "as discussed by Hiller.^[4]" The important structural

proteins of HPV include Overall Caspid ,Major Caspid Protein L1, Minor Caspid Protein L1 "as discussed by Patel^[1]" The structure of HPV, chiefly the two late capsid proteins (L1 and L2) are certainly a large amount chief proteins in conditions of figuring out habits to prevent infection of HPV. The pentameric and subsequent capsomeric structure of the L1 protein is considerable in developing vaccines against the HPV.

LIFE CYCLE of HPV and CARCINOGENESIS

There are series of event in the life cycle of HPV as it enters the body and finally causes carcinogenesis. The first event is the actual infection by a causing HPV strain, which occurs through small basal skin layer lacerations or minor abrasions in the oral mucosa . As soon as it enters the host body, the virus sheds it's protein coat (Overall Caspid ,Major Caspid Protein L1, Minor Caspid Protein L1) and the double stranded DNA infects cellular nuclei. The oncogenic genes E6 and E7 are the first gene to be expressed sooner after infection. The role of E6 and E7 gene is to inhibit normal cellular apoptosis and also to inhibit cell growth regulation in order. These are pre-cancerous changes in the host cells as it will eventually lead to cancer. Purposely, E6 binds to a normal cellular protein, p53, which is involved in regulating cellular growth. In fact, p53 signals cells to undergo apoptosis when DNA damage occurs and is also highly significant in the repression of replication during DNA damage. E6 also

functions to activate telomerase which create telomeres on DNA strands so as to accommodate continuous replication. E7 simultaneously binds to another cellular protein, retinoblastoma protein (Rb). It is the function of Rb to suppress tumors and the E7 interaction inactivates Rb thereby allowing unchecked cellular growth (tumors). As the cells infected with HPV DNA replicate rapidly and continuously, the cells start traveling upwards towards more superficial layers of mucosa, carrying viral DNA with them. The next 4 genes to be activated of the HPV genome are E1, E2, E4 and E5. E1 and E2 work in coordination to replicate the viral genome where E1 is a helicase and E2 is a transcription factor. As cells replicate, newly created cells underneath are pushed outward. Then finally two structural genes are expressed, L1 and L2. The fully enclosed icosahedral virus then reaches the outer layer of the skin. "as discussed by Walmsay.^[5]" Of the 120 recognized types, nearly 45 types of HPV have been found to be associated with Carcinoma. "as discussed by Burd^[6]"

ORAL TRANSMISSION OF HPV

The normal oral mucosa may serve as a pool for new HPV infections and/or as a source of recurring HPV associated lesions. The prevalence of HPV in normal oral mucosa is about 0.6% to 81% "as discussed by Ragin^[7]". Multiple pathways for HPV transmission to the oral cavity are known to exist. These include sexual transmission, autoinfection and rarely through perinatal transmission of the neonate by passage of an infected birth canal of the mother. Oral sex is a well recognized mode of its transmission. Oral HPV attainment was found to be more positively associated with number of oral sex and open mouth kissing partners than with the number of vaginal sex partners. "as discussed by Souza^[8]". However, there is no such evidence to suggest that the virus is transmitted from person to person through saliva.

HPV and ORAL LESIONS

Human papillomavirus presence in the oral mucosa is closely related with a variety of papillomatous disorders. A brief review of all these disorders are as follows.

HPV association with squamous cell papilloma

HPV were first reported in squamous papillomas in 1967. "as discussed by Frithiof.^[9]" Oral squamous papillomas are known to be caused by HPV 6 and 11. "as discussed by Eversole.^[10]" They are wart-like lesions showing various projections which tend to be pedunculated. The papillary projections are generally pointed and finger-like or rounded and cauliflower-like in appearance. If excessive keratinization is present, the lesion appears white and less keratinized lesions are often raspberry-like and pinkish in colour. They are usually single and less than 1 cm in size as seen in oral mucosa.

HPV association with oral condyloma accuminatum

Condyloma accuminatum, also known as venereal wart, is a sexually transmitted disease. HPV types 6, 11 and 16 are found in oral condyloma lesions. "as discussed by Manganaro^[11]" Condyloma accuminatum is principally seen on the skin and mucosal surfaces of the anogenital tract. "as discussed by Sehgal^[12]" Oral condyloma accuminatum lesions are seen to be caused by oral sex or from autoinoculation of the virus in adults. "as discussed by Choukas^[13]" Commonly it is seen in tongue, gingiva, soft palate and lips. Lesions may be multiple and confluent and generally larger than squamous papillomas. "as discussed by Laipis^[14]" They present as a broad, sessile, pink or white mass with blunt projections producing a cauliflower-like or mulberry-like appearance.

HPV associated with focal epithelial hyperplasia (Heck's disease)

Focal epithelial hyperplasia (FEH), generally known as Heck's disease, The aetiological agent of FEH was first identified in 1983 and was nominated as HPV 13. "as discussed by Pfister^[15]" HPV 32 was also identified with the disease in 1987 "as discussed by Beaudenon^[16]" FEH commonly occurs in children. FEH lesions are multiple asymptomatic lesions of normal mucosal colour as they are well demarcated round to ovoid, flat lesions measuring 1–10 mm in diameter. Lesions are sessile, clustered, with cobblestone appearance. Frequent sites of occurrence are lower labial mucosa, buccal mucosa, labial commissures, upper labial mucosa, tongue, gingivae, alveolar mucosa and palatal mucosa. "as discussed by Jeramillo^[17]"

HPV associated with verruca vulgaris

Verruca vulgaris is a skin wart, with uncommon oral involvement. Oral sites include the labial mucosa of the lower lip and the vermilion border of lips. Lesions are painless and appear as sessile, papillomatous, exophytic hyperkeratotic lesions. It is caused by HPV 2 and 4. "as discussed by LR Eversole^[18]"

HPV associated with oral leukoplakia

Leukoplakia essentially means a white patch. It is a well demarcated white/grey keratotic patch which may appear flat, smooth, fissured, granular or nodular in appearance. HPV type 16 and 18 have been identified in leukoplakia lesions.

HPV associated with proliferative verrucous leukoplakia

Proliferative verrucous leukoplakia is a different form of oral leukoplakia. "as discussed by Hansen^[19]" Gingiva and alveolar ridges are its favoured sites. It is a slow growing hyperkeratotic lesion that tends to spread and become multifocal, and develops as a wart-like lesion over time. "as discussed by Hansen.^[19]"

HPV associated with oral lichen planus

Lichen planus is a chronic mucocutaneous disorder which is immunologically mediated. Often it involves oral mucosa with white hyperkeratotic or red erosive lesion patterns. Among various factors, viral aetiology of Lichen planus has been proposed in recent years. The presence of HPV DNA in 15.4% in lichen planus is seen “as discussed by Ostwald^[20]”

HPV associated with oral squamous cell carcinoma

Oral squamous cell carcinoma (OSCC) is a disease of the oral cavity in which the gene that controls the cell growth and apoptosis are mutated, leading the cell to invade into deeper tissue and metastasize. Tumor progression in epithelium has been classified as normal, hyperplastic (non dysplastic), dysplastic carcinoma in situ and invasive carcinoma. A recent study has found that the risk of developing OSCC in relation to HPV-16 . Head and neck cancers increased with increasing numbers of oral sex partners in relation with HPV infection . “as discussed by Herrero^[21]”

HPV associated with oral verrucous carcinoma

Oral verrucous carcinoma , also known as Ackerman’s tumour, is a common variant of oral squamous cell carcinoma. HPV DNA types 6, 11, 16 and 18 have been shown to be linked with it. Clinically it is an exophytic, soft, fungating, painless, slow growing and locally aggressive lesion . “as discussed by Lubbe^[22]”

EARLY DETECTION AND VACCINATION

HPV vaccines that are now on the market were developed to prevent cervical cancer. These vaccines prevent an initial infection with HPV types that can cause oropharyngeal cancers.

These vaccines prevent infection with HPV types 16, 18, 6 and 11, and are primarily designed for the prevention of cervical cancer and genital warts.

CONCLUSION

It is evident that the relevance of HPV and oral lesions are expanding , of particular importance the relationship between some cases of oral cancer and HPV-16. From the dental practitioners’ point of view, where appropriate, patient education with regard to oral transmission of HPV and its possible role in the causation of a series of oral lesions including oral cancer should be built-in for protective strategy.

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