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Human papilloma virus

İnsan papilloma virüsü

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Abstract
Human papillomavirus (HPV) is a double-helix DNA virus in the papillomaviridae family. HPV has an affinity for epithelial tissue and causes benign and malignant changes to the stratified epithelium of the epidermis and mucous membranes. HPV is an etiological factor in many benign and malignant lesions of the head, neck, urogenital organs, skin, and mucous membranes. The role of HPV in the pathogenicity of squamous cell carcinoma in the head and neck area was first recognised in 1983 after findings showed histopathologic similarities between oral cancer and HPV infection. Because HPV has been implicated as the etiological factor for oral squamous cell carcinoma, HPV infection can be regarded as a subgroup of cancers affecting the oropharyngeal region. Due to these characteristics, HPV infection has been of particular interest in the field of maxillofacial surgery and dentistry. Screening, oral findings, early diagnosis, and proper treatment are of paramount importance in many HPV-related infections.
Keywords: Human Papillomavirus; HPV; Oral Cancer.

Öz
İnsan Papilloma Virüsü (HPV) papillomaviridae ailesinden çift sarmal yapıya sahip bir DNA virüsüdür. HPV epidermisin ve mukoz membranın çok katlı yassı epitelinde benign ve malign değişikliklere neden olur. HPV baş, boyun, ürogenital organlar, deri ve mukoz membranlarda görülen birçok benign ve malign lezyonların etyolojik faktörleri arasında gösterilmektedir. HPV'nin baş boyun bölgesinde gözlenen skuamöz hücreli karsinomanın patogenezinde rol aldığı ilk olarak 1983 yılında oral kanser ve HPV enfeksiyonu arasındaki benzerlik gösterildikten sonra anlaşıldı. Oral skuamöz hücreli karsinomada etiyolojik faktör olduğu için HPV enfeksiyonu orofarengeal bölge ile ilişkili kanserlerin bir alt grubu olarak ele alınabilir. Bu özellikleri nedeniyle Maksillofasiyal Cerrahinin ve Diş Hekimliğinin yakın ilgi alanına girmiştir. Birçok HPV ile ilişkili enfeksiyonda özellikle tarama, oral bulgular, erken teşhis ve tedavi büyük öneme sahiptir.
Anahtar Kelimeler: İnsan Papilloma Virüsü; HPV; Oral Kanser.

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Human papillomavirus (HPV) is a double-helix DNA virus in the papillomaviridae family. There are 12 species in the papillomaviridae family, including the alpha, beta, gamma, mu, and nu genera, and seven more genera constituting the animal papillomaviruses (1). Currently, 30 to 40 oncogenic HPV types are known, which are divided into three clinical categories: HPVs with low risk of cancer [6, 11, 40, 42, 43, 44, 54, 55, and 62], potentially high-risk HPVs [26, 53 and 66] and high-risk HPVs [16,18, 31, 33, 35, 39, 45, 51, 56, 58, 59, 68, 73, and 82] (2,3). While more than 12 HPV types are found in the oral cavity, the most frequently seen include types 2, 4, 6, 11, 13, 16, 18, 30, and 32.

Benign oral lesions are related to types 2, 4, 6, 11, 13, and 32, whereas malignant oral lesions are related to types 16 and 18 (4). Among all HPV types, the roles of HPV-16 and -18 in cervical and nasopharyngeal cancers were the first described, and are among the most important causes of tongue cancers, especially in young individuals (5). Gillison and colleagues found HPV-16 in 10% of patients with oral cancer and HPV-18 in 1% (6). Hermann and colleagues reported the co-infection of HPV-18 and Epstein–Barr Virus (EBV) in a 20-year-old patient diagnosed with tongue cancer (7). Cruz and colleagues observed HPV-16 and EBV infections in 30% of oral squamous cell carcinoma (OSCC) cases (8,9). HPV-16 exists in 84–93% of OSCC cases related to HPV (aside from tongue cancers), indicating its importance in OSCC (10-14).

Physiopathology

HPV has an affinity for epithelial tissue and causes benign and malignant changes to the stratified epithelium of the epidermis and mucous membranes. There are three types of HPV infections in the oral cavity: clinical, subclinical and latent infections. Clinical infections are defined by lesions in the mucous membranes that present as macroscopic changes. Subclinical infections are characterised by the absence of macroscopic changes and subjective symptoms; the existence of HPV infection in this phase can be verified with colposcopic, cytologic, histologic, and molecular analyses (15). Latent infection is the most frequent form of the disease. In latent infections, clinical symptoms have disappeared, making it difficult to reach histological or cytological diagnoses (15,16). The role of HPV in the pathogenicity of squamous cell carcinoma in the head and neck area was first recognised in 1983 after findings showed histopathologic similarities between oral cancer and HPV infection (17). This hypothesis was accepted by the International Agency for Research on Cancer in 2009 upon obtaining powerful evidence, and HPV-16 was defined as a causative agent of OSCC (18).

Mode of Transmission and Detection of HPV

HPV is most commonly known for its relationship to cervical cancer, and several studies have shown that HPV is transmitted sexually. However, there are many unknown factors regarding the mode of HPV transmission to the oropharynx, with 30–40% prevalence among oropharyngeal carcinoma cases (19,20,21). As high-risk HPV can cause malignant transformations in epithelial cells, HPV was identified as a risk factor, together with tobacco and alcohol use, of the development of OSCC in the oropharynx (19,22).

Numerous methods have been developed to detect the existence of HPV nucleic acids, including polymerase chain reaction (PCR), in situ hybridization and immunohistochemical p16 scans (23,24). HPV detection techniques can be classified as: 1. selective amplification of the targeted nucleic acid, 2. labelled amplification of HPV nucleic acids and 3. nucleic acid hybridization tests.

Relation of HPV to Other Infections

HPV does not always cause infections in the oral mucosa on its own; sometimes it causes co-infections alongside other viruses. For example, increased lesions related to HPV have been observed in patients infected with HIV, and such lesions on the face and in the oral cavity are typical in AIDS patients. Many clinical diseases are related to HPV, including oral papillomas, verruca vulgaris, filiformis and planus, focal epithelial hyperplasia and condyloma accuminata, Bowenoidpapulosis, epidermodysplasia verruciformis, and cervical and anogenital squamous intraepithelial neoplasms. Increases in oral lesions related to HPV have been noted, including papilloma, condyloma and focal epithelial hyperplasia. These infections are related to decreases in CD4+ levels and suppression of the defence system in general following antiretroviral therapy. Papillomas with or without stems are frequently located in the palate, mucosa of the cheeks and angles of the lips in the form of giant papillomas similar to the anogenital condyloma with a pinkish-white appearance. Verrucous lesions related to HPV tend to recur and spread, and are rather resistant to treatment (25-32).

In 1966, Scott reported that white spongiform nevi could be related to herpes simplex virus; however, no such studies on this disease were carried out using viral antigens or nucleic acids (33). Cox and colleagues identified HPV-16 DNA in oral white spongiform nevus lesions for the first time in 1992 (34). HPV replication has been found to develop in relation to the differentiation of epithelial cells, as white spongiform nevus is mainly a disease related to keratinocyte differentiation (35,36).

Protection

Screening, early diagnosis and treatment are important, particularly for infections related to HPV. Notably, many patients with oral cancers have diets poor in fresh fruits, vegetables and vegetable oils, and rich in protein, such as fish. A healthy and balanced diet is thought to be a protective factor against cancer.

Treatment plans for individuals diagnosed with HPV must take into account many factors, including the level of spread of the lesion, the patient's age and desire to have children. Based on these factors, the most appropriate treatment modality can be selected, including electro-cauterization, cryotherapy, laser vaporization or conization, hot or cold conization, and hysterectomy (37,38).

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HPV is the major causative agent of cervical cancer. Cervical cancer can be differentiated from other cancer types as a "preventable" cancer. Therefore, screening, early diagnosis and early treatment are important when diagnosing and treating infections related to HPV. The spread of HPV into the oral mucosa outside the urogenital area, causing infectious lesions in the head and neck area, is a major concern. It is important to increase the level of public awareness on vaccination studies and systematically follow and educate HPV-positive patients about the diverse treatment methods available.

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