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Human Papilloma Virus (HPV) impact in the development of head and neck Cancer

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Abstract

This review article focuses on the impact of the human papilloma virus on the development of head and neck cancer and also its effect on immune response. Human papillomavirus (HPV) is one of DNA oncogenic viruses transmitted sexually, non-sexual, and vertically infecting basal epithelial cells, causing several types of cancers worldwide like cervical cancer in low-income countries and head and neck cancer in high-income countries like oropharyngeal cancer particularly among the younger age group. This cancer expands beyond the oropharynx, like the throat, tonsils, and tongue base. Thus, a vaccine could be used to decrease the number of cancers.

Keywords: Cancers, HPV, Head, Neck, Vaccine.

HPV and Head and Neck Cancer are A Growing Concern

Head and neck cancer (HNC) ranked the seventh most common tumor worldwide, and oropharyngeal squamous cell carcinoma (OPSCC) represents about half of these malignancies (1). HPV constitutes 71% and 51.8% of all oropharyngeal squamous cell carcinoma in the USA and UK (2). Globally, the percentage of oropharyngeal carcinoma caused by HPV was 33%, and the prevalence varies depending on the geographical region, ranging from 0% in southern India to 85% in Lebanon (3).

Head and neck cancer has been assessed to be responsible for about 4.1% of all cancer cases and 3.7% of cancer-related deaths worldwide (4). In the early stages, head and neck cancers are often asymptomatic but may sooner or later present as pain-caused by lesions like white or red area, known as leucoplakia and erythroplakia, respectively. Other symptoms at later stages of head and neck cancer may lead to bleeding, loose teeth, trouble wearing dentures, dysphagia, dysarthria, odynophagia, and the development of a

head and neck mass (5). In different developed and developing countries, cancers of the head and neck diversity have been revealed to be correlated with exposure to many traditional risk factors such as tobacco consumption like chewing or smoking (6); drinking of alcohol (7) consumption of nitrosamine-rich canned foods (8); infection with virus-like human papillomavirus (HPV) (9); environmental factors and growing prevalence of lifestyle like exposure to ultraviolet, and lack of fruit and no starchy vegetables lead to dietary deficiency (10), However, a paradigm and standard shift has occurred in current years with the emergence of human papillomavirus (HPV) as a significant and growing concern virus contributes to the development of head and neck cancers.

The Role of HPV in developing Head and Neck Cancer

The most common cause of head and neck cancer, in addition to smoking and alcohol, is human papillomavirus (HPV) infection, which represents the main cause (11). HPV is more common in the general population, mainly in males than females, and most of them eradicate this virus due to active immune response or remain asymptomatic (12). HPV, mainly 16 and 18, have been increasingly implicated in the aetiology of oropharyngeal squamous cell carcinoma, which is a type of head and neck cancer that includes the back of the throat, the base of the tongue, tonsils, and soft palate. Strains 16, 18, or 31 can integrate themselves within human nuclear DNA by the rolling circle method, which is a mode of reproduction leading to cell transformation due to the presence of E6 and E7 viral oncogenes that play an important role in carcinogenesis. The HPV genome either present in pure episomal form (E1, E2, E4, E5, E6, E7) or a mixture of integrated episomal genome (E6, E7) (13). E6 binds protein p53 protein indorsing its degradation (In healthy state, P53 arrests cells from progressing to the G1 phase of the cell cycle and initiates apoptosis), but E7 binds the retinoblastoma (Rb) protein and cyclin-dependent kinase inhibitor leading to its inactivation ending in unregulated cell division, genomic instability, and loss of apoptosis. HPV infects the basal epithelial cells where replication occurs that need E1 and E2 proteins and transcriptional repressor of the proteins E6 and E7, and E2 regulates the expression of these genes (14). Moreover, the antigenic landscape in head and neck cancer caused by HPV is due to a mutation in many tumour suppressor genes that are targeted by the immune system of the host (15,16).

The Immune Response to HPV

In order to establish infection, the human papillomavirus should evade the host immune response and manipulate it to begin persistent infection and initiate carcinogenesis and tumor progression (17). This interaction between the virus and immune system is very complex starting from the first line of defense mechanism is macrophage and other antigen-presenting cells that present the viral peptide and viral oncoproteins E6 and E7 to naïve T cells, resulting in activation and differentiation of these cells into Tc ending in cell lysis through granzymes perforin pathway (18). Some viral oncoproteins can downregulate significant histocompatibility antigen (MHC) class I and class II molecules on the cell surface and inhibit tumor antigen presentation via these molecules (19). This virus also causes dysregulation of cytokines secretion (IFN-gamma) and cytokines transcription factors (STAT) proteins, which is the key to the virus persistence (20). Other immune cells will contribute to eradicating this virus, like NK cells and antibodies-

secreting cells directed against viral oncoproteins E6 and E7 (21). Tumor infiltrating lymphocytes (TIL) are important in determining the prognosis of this disease (22). This immune response was regulated through T reg cells and expression of inhibitory receptors PD-1 on T cells that bind PD-L1 on tumor cells or antigen-presenting cells (PD-1/PD-L1 axis) and transcription factor TCF-1 (23). Thus, the oncogene proteins E6 and E7 were used as targets for vaccine therapies (24). The humoral immunity is also stimulated through the production of antibodies, mainly IgG and less IgA and IgM, that are directed against HPV E6, E7, and other E proteins that are detected in the plasma of many patients using them as biomarkers in detecting disease, recurrence, and prognosis (25)The formation of memory B cells, long-lived plasma cells, and antibodies forming cells in the peripheral blood results from humoral immune system stimulation, which mediates prolonged protection against this virus (26,27)HPV is associated with many types of cancer, like breast (28), ovary (27), prostate (29) , esophagus(30) , and lichen planus disease (31). It is also associated with head and neck cancer, and one of the distinguishing features in HPV causing head and neck cancer is the presence of intratumorally B lymphocytes, either scattered unstructured form or aggregate forming lymphoid follicles with germinal centers expressing BCL6, AICDA, and TCL1A genes in association with TFH CD4+ T cells (32,33). Thus, a good understanding of the tumor-specific immune response leads to better development of many therapeutic methods and syntheses of vaccines that target the viral-specific antigens. HPV has evolved numerous plans to evade the immune response, like inhibition through E6 and E7, modulating the function of innate immune cells, the function of many immune cells, establishing a latent state, and undergoing genetic changes to evade immune recognition (34).

Implications for Prevention and Treatment

The persistence of HPV infection in the region of the head and cancer leads to chronic inflammation and dysregulation of the immune system, creating a promising situation for cancer development. This implies prevention and treatment strategies for HPV, like vaccination, which primarily targets the young age group, preventing head and neck cancer development. Early detection can be achieved via regular oral examinations and the development of specific screening tests. Health education on HPV vaccination in school-aged subjects may effectively increase HPV vaccination coverage in many countries (35). Thus, concomitant vaccination (HPV16/18) and screening appear to be an accurate option for the control and elimination of cancer quickly (36). Additionally, the cytology of screening tests showed changes with the vaccination strategy (37) .

Conclusion

HPV has emerged as a significant risk factor for head and neck cancer, especially squamous cell carcinoma of the oropharyngeal region. Therefore, understanding the HPV roles in the growth of head and neck cancer is considered an essential step for establishing the prevention program via earlier detection and treatment strategies.

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None

Ethics statement

The authors declare that the author approved that this research follows the journal's Attach Ethic Approval guidelines as appeared on the journal's author guidelines page.

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