THE ROLE OF HUMAN PAPILLOMAVIRUS IN HEAD AND NECK CANCER

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BACKGROUND

A great number of people die from cancer of the oral cavity and pharynx every year. Alcohol and tobacco are disposing factors for developing this type of cancer, but human papillomavirus (HPV) also is now known to be associated with head and neck cancer, especially SCC of the oropharynx. There are indications that the prevalence of HPV-induced head and neck cancer is increasing, while the prevalence of tobacco- and alcohol-induced cancer is declining. This entity is most commonly diagnosed in non-smoking middle-aged white males. The majority of the patients present with asymptomatic, persistent neck masses despite antibiotic therapy. An awareness of this condition and a high degree of suspicion is necessary for timely diagnosis.

METHODS- MATERIALS

A systematic review of the literature was conducted using the NIH Pubmed search engine, and all the recent studies regarding the role of the HPV in the head n neck cancer were included.

RESULTS

HPV infection is the most common sexually transmitted disease in the world. HPV may be transmitted by any type of sexual activity. In the United States alone, it is estimated that 20 million people are currently infected, and 6.2 million acquire a new infection each year. Smoking further increases the risk of HPV infection. The specific association of HPV 16 and oropharyngeal cancer was reported as early as 1998, in a study from City of Hope in which 60% to 70% of oropharyngeal cancer cases were HPV-associated. Currently, HPV 16 accounts for 90% of high-risk oral HPV infections. Until recently, however, the role of HPV in the pathogenesis of HNSCC has been controversial, mainly because the detection rates of HPV DNA have been highly variable, ranging from 0% to 100%.

The wide variation in HPV detection rates can be explained by several factors, such as samples, i.e. whether frozen; formalin fixed or paraffin embedded scrapings or oral rinses, sensitivity of the HPV testing method, as well as the coverage of HPV genotypes in the test panel. Currently, there is no consensus on the most appropriate method to detect HPV in HNSCC. The HPV testing methods are mostly based on detecting HPV DNA in cancer tissues either with in situ hybridization or PCR or both.

HPV infection has been associated with more favourable disease outcome, although the reason for this is not clear. Further studies are needed to dissect the HPV-positive HNSCC in more detail.

In diagnosis, additional methods of HPV DNA testing are needed, such as p16, p53 epidermal growth factor receptor immunostaining or real-time PCR for HPV oncoproteins E6 and E7, to delineate which subgroup of HPV-associated HNSCC has the most favourable outcome after chemo- or radiotherapy. In addition, the identification of activated pathways will aid in developing new treatment modes for these cancers. More information is also needed on why HPV copy numbers are higher and HPV integration is rarer in tonsillar cancer than in other HPV-related HNSCCs. Also more natural history studies on symptomatic HPV infections in the head and neck region are urgently needed to identify those infections that have an increased risk of progression towards malignancy.

CONCLUSIONS

HPV-positive HNSCC appears to be different from HPV-negative HNSCC both in its molecular and clinical features. The research field focusing on HPV in HNSCC is expanding rapidly and we hope that a consensus regarding preferred methods for defining 'true HPV positive' will be reached. In future, it may be possible to select more advanced and individual treatment strategies based on the molecular and aetiological differences in HNSCC, especially with regard to HPV. Further molecular research into HPV-positive cancers will expand our understanding of head and neck cancer biology and may provide the basis for developing new treatment strategies. We anticipate that the role of vaccines and new specifically targeted drugs for HPV will eventually be revealed.

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