HPV in Head and Neck Cancers

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The human papillomavirus (HPV) is a recently identified risk factor for the development of head and neck squamous cell carcinomas (HNSCCs), in addition to the traditional risk factors of tobacco and alcohol use. HPV-related cancers can occur throughout the upper aerodigestive tract, but are more often localized to the tonsillar and base of tongue regions (i.e., oropharynx), accounting for 70 per cent of all oropharyngeal tumours.[1] Since the mid-1980s, the incidence of HPV-positive oropharyngeal cancers has increased by 225 per cent in the United States.[1] European and Canadian data reveal the same trend of increasing incidence, confirming that this disease is a global epidemic.[2,3] Given that a unique HPV-related disease exists begs the question, how are these cancers distinct from HPV-negative disease?

Risk factors

Oral HPV infection is a necessary antecedent to the development of HPV-related HNSCC. These infections are present in approximately 6.5 per cent of the general American population, with the 'high risk' oncogenic type, HPV 16, present in one per cent of those infections.[4] HPV-positive HNSCC is also associated with lifetime number of vaginal- and oral-sex partners, young age at first intercourse, history of genital warts, and marijuana use.[5]

Clinical characteristics

HPV-positive disease tends to occur in younger, healthier individuals with less tobacco and alcohol exposure than HPV-negative disease.[6] At the time of diagnosis, HPV-related cancers tend to be of advanced stage, accompanied by regional node-positive disease.[3] Because of the propensity for nodal involvement, treatment for HPV-related oropharyngeal cancer commonly includes radiotherapy with concurrent cisplatin-based chemotherapy.

Prognosis

HPV-positive disease is associated with better overall survival and local disease control compared to HPV-negative disease.[6,7] Three-year survival is greater than 85 per cent in HPV-related disease, and patients have approximately half the risk of death from cancer compared to those with HPV-negative disease.[1,6] However, even in HPV-related cancers, smoking remains a negative prognostic factor associated with inferior outcomes.[6] Although treatment with chemoradiotherapy achieves excellent disease control, patients often suffer acute and long-term toxicities such as mucositis, dry mouth, swallowing impairment, and feeding-tube dependence.

Future directions

In light of the treatment-related toxicities, attempts toward treatment deescalation are necessary to minimize treatment burden and improve quality of life. Current studies examining the use of EGFR-inhibitors in place of cisplatin[8] and transoral robotic surgery instead of radiotherapy[9] will undoubtedly shape the treatment of HPV-related HNSCC in the future. HPV vaccines also hold great promise to impact public health, but the effectiveness of vaccines designed to prevent cervical HPV infections, relative to the prevention of oral HPV infections, is unknown.

Summary

HPV-related HNSCC is a significant, distinct clinical problem. Alongside strides to deintensify cancer treatment, primary preventative measures will be critical components in the battle against HPV-related cancers. Raising public awareness about safeguarding against sexually-transmitted diseases, and examining the impact of HPV vaccines on the prevalence of HPV-related HNSCCs, are crucial steps in stemming the progression of this disease epidemic.

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