

Cancer Virus: The Story of Human Papillomavirus

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Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer globally; however, the incidence is much higher in the developing countries, including Pakistan, India, and Sri Lanka.¹ Despite a decreasing incidence of HNSCC in general, attributed to a decrease in the prevalence of smoking,² the incidence of oropharyngeal squamous cell carcinoma is rising.^{3,4}

Human papillomavirus (HPV) has for some time been suggested to be involved in the carcinogenesis of oropharyngeal cancer. The HPV is a small, circular double-stranded DNA virus that was first identified in 1949.⁵ Up till now, over 100 different HPV types have been identified. The HPV subtypes are divided into high-risk and low-risk HPV based on their malignant potential. Approximately, 15 high-risk subtypes are known but only HPV subtypes 16, 18, 31, 33, and 35 have been identified playing a role in the development of oropharyngeal head and neck cancer. The HPV 16 is the most common type detected in oropharyngeal cancer accounting for 90 to 95% of the HPV-positive tumors.⁶ The International Agency for Research on Cancer (IARC) now recognizes HPV as a risk factor for oropharyngeal cancer, and accumulating molecular and epidemiological data now show that high-risk types of HPV are responsible for a subset of oropharyngeal cancer.⁷

Majority of the HPV-positive oropharyngeal cancers lack association with the traditional risk factors, such as tobacco and alcohol.⁸ Alike HPV-associated cervical cancers, HPV-positive oropharyngeal cancers are also sexually transmitted. It is assumed that HPV infection precedes the development of HPV-positive head and neck cancers, and the presence of high-risk HPV infection on the oral mucosa and seropositivity increases the risk of development of head and neck cancers.⁹ Therefore, risk

factors for oral HPV infection are likely to be risk factors for HPV-positive head and neck cancers.

The incidence of oropharyngeal cancer rates varies widely internationally with significant differences even within population. In the last decade, a drastic rise in the incidence of oropharyngeal cancer in several western countries has been observed,¹⁰ with rates higher in males than in females with a ratio from 2:1 to 5:1. At the same time, the prevalence of HPV in those tumors has increased in a similar way indicating that HPV, in fact, is responsible for this increase. Human papillomavirus has been found in 45 to 95% of the oropharyngeal tumors and the prevalence of HPV 16 has been quite homogenous around the world in contrast to the cervical cancer, where the prevalence of different types of HPV varies around the world.

Human papillomavirus-positive oropharyngeal cancers also constitute a distinct subgroup clinically. These tumors are usually poorly differentiated and nonkeratinized and have a basaloid appearance in contrast to the HPV-negative tumors that are more moderately differentiated and keratinized. The HPV-positive tumors also demonstrate significantly lower levels of chromosomal mutations and patients with HPV-positive oropharyngeal cancers in general, especially tonsillar cancers, tend to be younger at the time of diagnosis. Most patients have no prior history of tobacco and/or high alcohol consumption and have generally a better performance status compared to the HPV-negative patients. Overall, the prognosis is better in HPV-positive oropharyngeal cancer patients compared to patients with HPV-negative tumors independent of nodal status, age, stage, tumor differentiation, or gender.¹¹

The HPV-positive oropharyngeal cancers are recognized as a distinct subset of HNSCC with a favorable outcome. The natural history and the tumor development biology of HPV infection in head and neck tumors are not yet fully understood. Therefore, further well-designed clinical trials are needed to better understand the disease process to optimize the treatment for each individual patient in the future.

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