Oropharynx: Epidemiology and Treatment Outcome

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Oropharyngeal (OP) carcinoma comprises over half of all head and neck cancers in the United States. While the incidence of squamous cell carcinoma (SCC) in the other head and neck sites has been steadily declining in association with smoking cessation, the incidence of SCC in the OP is rising, especially in younger patients and has been linked to the exposure of the human papillomavirus (HPV).

The treatment of OP carcinoma is complex because of the intricate anatomy of the involved organs, their rich lymphatic networks, and their critical function in the activities of daily living. Such treatment therefore requires a multidisciplinary approach.

This chapter focuses on the epidemiology of OP squamous cell carcinoma, specifically looking at the emerging role of HPV virus in their development.

It also describes the different treatment options for these tumors with a focus on those for organ preservation.

Finally, it highlights recent advances in treatment using molecularly targeted therapies and modern radiation delivery using intensity-modulated approach with the goal to minimize treatment-related toxicity in these highly curable patients.
2.1 Introduction

Oropharynx squamous cell carcinoma (OPSCC) has emerged as one of the most common malignancies in the head and neck (HN) sites. Around 123,000 new cases of oropharyngeal (OP) cancers are estimated to occur annually worldwide, resulting in 79,000 annual deaths (Parkin et al. 2001). In the United States, the incidence of OP cancers in 2008 is estimated to be 35,310 new cases, from which 7,590 deaths will occur (Jemal et al. 2008). The oropharynx, which comprises of the soft palate, uvula, tonsillar fossa and pillars, glossotonsillar sulci, lateral and posterior pharyngeal wall, vallecula, and base of tongue, harbors a rich lymphatic network. Therefore, tumors arising from this region are likely to have early nodal involvement and ~60% of these patients present with stage III–IV tumors at diagnosis (Greene et al. 2002).

The treatment of OP cancers has evolved over time. Although either surgery or radiation therapy (RT) remains the main treatment modality for early-stage OP cancers, concurrent chemoradiation therapy (CRT) has largely replaced RT alone for locally advanced neoplasms. Recent advances in RT techniques and molecular technologies have ushered in a new age of novel therapy for OP cancers, which holds promise for a better outcome with potentially less normal tissue toxicity. In this chapter, we will focus on the new developments in epidemiology and treatment approaches for OPSCC.

2.2 Epidemiology

The most common histology for OP tumors is squamous cell carcinoma (SCC). Established risk factors for these tumors include tobacco exposure (either directly or indirectly), alcohol consumption, genetic and environmental factors such as diet, poor oral hygiene, and RT exposure (Rosenquist 2005). A synergism between smoking and alcohol abuse has been described and could increase the relative risk of these cancers as much as 30-fold (Castellsague et al. 2004). Marijuana consumption has also been linked to the development of OPSCC (Zhang et al. 1999).

While the overall incidence of other HNSCC has been declining since the early 1980s because of smoking cessation, the incidence of OPSCC has either been stable or rising, especially in younger populations (Ernster et al. 2007; Sturgis and Cinciripini 2007) This is due to the increasing number of OPSCC associated with human papillomavirus (HPV). Reports indicated that up to 50–60% of OPSCC might harbor HPV DNA, depending on the detection method used (Gillison et al. 2000; Gillison and Shah 2001; Mork et al. 2001; Dai et al. 2004). HPV is most commonly found in tonsillar and base of tongue tumors, with HPV16 being found in the vast majority (>90%) (Gillison et al. 2000; Dahlgren et al. 2003). Evidence for the causal relationship between the presence of HPV and HNSCC incidence comes from prospective studies, indicating increased risk for developing HNSCC in patients who are seropositive for anti-HPV antibodies. In a large, nested case-control study from a Scandinavian cohort of almost 900,000 individuals, HPV-16 seropositivity was observed on the average of 9.4 years prior to the onset of disease and was associated with a 14-fold increased risk of OPSCC (Mork et al. 2001). Recent case-control studies suggest that HPV(+) and (−) tumors have distinct risk factor profile. While HPV(−) tumors had the traditional association with tobacco and alcohol use and poor oral hygiene, HPV(+) HNSCC was independently associated with marijuana exposure and several measures of sexual behavior (such as increasing numbers of lifetime vaginal or oral sex partners, casual sex participation, no barrier use during vaginal or oral sex, and history of a sexually transmitted disease) but not with tobacco or alcohol consumption (DSouza et al. 2007; Gillison et al. 2008).

Some studies have suggested that HPV-related OPSCC not only represents a molecularly distinct disease but is also associated with a better prognosis (Gillison et al. 2000; Fakhry et al. 2008; Weinberger et al. 2006; Licitra et al. 2006). Figure 2.1 shows the disease-specific survival (DSS) curves for HPV(+) and (−) patients treated at our institution. A recent meta-analysis confirmed that HPV(+) OPSCC patients had a 28% lower risk of death than their negative counterparts (Ragin and Taioli 2007). The reason for this difference in prognosis is unclear but could be related to the distinct molecular and epidemiologic profiles of these tumors. HPV(+) tumors are more likely to be undifferentiated, have basaloid histology, and more frequent nodal metastasis (Fakhry and Gillison 2006). At the molecular level, they