HEAD AND NECK CANCER: AN OVERVIEW*

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ABSTRACT

Head and neck cancer (HNCA) is a group of cancers that includes the oral cavity, tongue, mouth, pharynx, and larynx. HNCA results in approximately 10,000 deaths annually. It is the eighth most common cancer in men and is becoming increasingly more common in women. The 2 chief risk factors for HNCA are tobacco smoking and alcohol consumption; smoking cessation can return the risk of HNCA in smokers to a level near that of never-smokers in approximately 10 years. The main sign of HNCA is a painless neck mass. More than 90% of HNCAs are squamous cell cancers, and most HNCA is local or regional upon presentation.

Surgery and radiotherapy are the main treatments for HNCA and can cure local disease in approximately 80% of cases. Because regional or distant disease is less curable and more likely to result in severe disfigurement or dysfunction, early diagnosis of HNCA is crucial.

Biologic targets in HNCA include epidermal growth factor receptor (EGFR) and vascular endothelial growth factor (VEGF). Substantial research has established that EGFR and VEGF are overexpressed in HNCA. In addition, EGFR and VEGF levels also function as prognostic indicators and indicators of potential response to radiotherapy. Future directions in HNCA research include the study of the correlation between gene-expression patterns and incidence, progression, and response to treatment. (Adv Stud Pharm. 2006;3[1]:8-11)

Head and neck cancer (HNCA) is a group of cancers that includes the oral cavity, tongue, mouth, pharynx, and larynx, or some combination thereof. Nearly 40,000 new cases of HNCA occur annually (Figure 1).1 Approximately 25% of patients with HNCA die each year, which results in approximately 10,000 deaths annually.1 HNCA is the eighth most common cancer in men and is slightly less common in women, in whom it does not represent one of the top 10 most common forms of cancer.1 Although HNCA is less common in women than in men, its incidence in women has been increasing as a result of an increase in the use of tobacco and alcohol in women.1

STAGING AND RISK FACTORS

Staging of HNCA is extremely complex. Such staging involves the use of different staging systems for each of more than 10 different areas of the oral cavity and different methods of classifying tumors, malignant lymph nodes, and metastatic disease for each staging system. However, despite the dissimilarity in their staging, the various HNCAs have many common characteristics. For instance, the strongest risk factors

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for all forms of HNCA are tobacco smoking and alcohol consumption. Thus, advising patients to stop or to avoid smoking is a key means of combating HNCA. By quitting smoking, smokers can reduce the risk that they will be diagnosed with HNCA by 50% after 3 to 5 years of smoking cessation, and this risk begins to approach that of never-smokers after approximately 10 years of smoking cessation. Although consumption of alcohol of any kind has been clearly associated with the development of various dysplasias of the oral-mucosal tract, in contrast to tobacco smoking, no correlation has been established between cessation of alcohol consumption and a decreased risk of HNCA.

**SIGNS AND SYMPTOMS**

The main sign of HNCA is a painless neck mass, which may enlarge to the size of a softball or small football before the patient seeks medical attention. Other signs and symptoms of HNCA include odynophagia, dysphagia, hoarseness lasting weeks or months, hemoptysis, trismus, and a nonhealing oral ulcer, which can be relatively small and yet still represent a clinically significant sign of HNCA.

**HISTOLOGY AND COMMON PRECURSORS**

Because the main type of tissue in the lining of the aerodigestive tract consists of squamous cells, more than 90% of HNCAs are squamous cell cancers. In addition, certain premalignant lesions are commonly associated with HNCA. These include leukoplakia and erythroplakia; both are frequently associated with various degrees of dysplasia that can be identified microscopically in a biopsy specimen.

**STAGE DISTRIBUTION, PATTERN OF SPREAD, AND RECURRENCE**

Most HNCAs are local or regional cancers; distant, metastatic HNCA occurs fairly rarely (Figure 2). The typical pattern of HNCA spread is into the locoregional lymph nodes along the jawline, then deeper into the secondary lymph node layers; distant metastases are limited. The prevalence of later-stage HNCAs involving regional disease or distant metastases is greater in African Americans than in whites (Figure 2). This difference in stage and death rate between whites and African Americans has not yet been attributed to genetic differences between tumor types but instead may be a result of the timing of the initial medical evaluation of HNCA symptoms.

Diagnosis of HNCA places the patient at elevated risk for diagnosis of a second HNCA, which typically recurs locally at the site of the initial tumor. Another common pattern of recurrence is contralateral to the side on which the primary tumor occurred.

![Figure 1. Epidemiology of Head and Neck Cancer in the United States](image1)

![Figure 2. Stage Distribution of Head and Neck Cancer in the United States](image2)
**TREATMENT**

Surgery and radiotherapy are the main treatments for HNCA, although specific treatment depends on the stage and site of the disease. In approximately 80% of cases, local disease can be cured by surgery or radiation (Figure 3). In contrast, regional disease is likely to be cured with these methods in approximately 50% of cases, and distant, metastatic disease is likely to be cured in approximately 30% of cases. Thus, early diagnosis of HNCA is crucial for maximizing the chances that treatment will be curative. Moreover, regional or distant disease is more likely to result in severe disfigurement or dysfunction. As a result, initial tumor debulking through chemotherapy before surgery or radiotherapy is often used to improve the cosmetic and functional results of therapy in patients with advanced disease. Therefore, early diagnosis of HNCA also is crucial for minimizing the complications of treatment. Despite a recognition of the importance of early diagnosis, the 5-year survival rate after treatment of HNCA has only improved by a few percentage points since 1976 in the population as a whole and has not improved at all in African Americans (Figure 4).

**POTENTIAL BIOLOGIC TARGETS**

Although platinum-containing chemotherapeutic agents have been found to be somewhat more effective than other agents in treating HNCA, no specific chemotherapeutic agents have been found to target HNCA. To enable oncologists to develop agents that are better able to target molecules that are overexpressed in HNCA, research on the role of the epidermal growth factor receptor (EGFR) was initiated more than 25 years ago. This research established that EGFR is almost universally overexpressed in squamous cell cancers, including HNCA, and that the degree of EGFR expression correlates with the degree of dysplasia. For example, as a squamous cell progresses from being a normal cell to becoming a malignant cell, and as the malignant cell becomes more malignant, a corresponding increase in the number of EGFRs occurs. More recently (approximately 10 years ago), several studies have supported the correlation between increased expression of vascular endothelial growth factor (VEGF) and HNCA. In addition to correlating with the degree of malignancy of HNCA, EGFR and VEGF levels also serve as prognostic indicators and indicators of the potential response to radiation therapy of HNCA. Thus, modulation of the expression of EGFR and VEGF can be expected to render HNCA more radiosensitive. Since the time of this presentation, the US Food and Drug Administration has subsequently approved cefuximab for 2 indications in HNCA. The first use is in combination with radiation for patients with unresectable squamous cell HNCA. The second use is for patients with metastatic HNCA that have already failed traditional chemotherapy.
CONCLUSIONS

The incidence of HNCA is strongly related to tobacco smoking and alcohol use, and promoting smoking cessation is an important means of decreasing HNCA incidence. Local HNCA can be treated with surgery or radiation, although patients may be left with substantial deformities and dysfunction that can result in the need for tube or parenteral feeding. Because of the biologic importance of EGFR and VEGF in HNCA, using chemotherapeutic or biologic agents to target EGFR and VEGF is a rational strategy for increasing 5-year survival rates in HNCA, which have improved little since 1976. The study of the correlation between gene-expression patterns and incidence, progression, or response to treatment in HNCA represents a key future direction in HNCA research.

REFERENCES