

Other Solid Tumors

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INTRODUCTION

Head and neck cancer, melanoma, sarcoma, and carcinoma of unknown primary site are distinct malignancies each with its own epidemiology, histopathology, treatment, and prognosis. Head and neck cancer and melanoma are relatively common, but sarcomas and unknown primary carcinoma are rare. Recent advances in understanding of the molecular biology of cancer and the interaction between the immune system and malignancy have improved therapeutic options for patients with these diseases.

HEAD AND NECK CANCER

Definition and Epidemiology

Head and neck cancers are squamous cell carcinomas that arise from the mucosal lining of the oral cavity, oropharynx, nasopharynx, hypopharynx, and larynx (Fig. 60-1). Other malignancies arising from structures within the head and neck, such as salivary gland tumors or thyroid cancers, differ in regard to biology, presentation, natural history, pathology, and response to therapy.

Head and neck cancer accounts for 3.2% of new cancer diagnoses in the United States. In 2013, there were expected to be 53,640 patients diagnosed with this disease and 11,520 deaths. Chronic exposure to tobacco smoke and alcohol have been considered the strongest risk factors for developing this disease, but in recent decades human papilloma virus (HPV) has been responsible for a dramatic increase in the incidence of oropharyngeal squamous cell carcinoma. Patients with HPV-associated oropharyngeal cancer are typically younger than patients with HPV-negative disease and often have minimal history of tobacco or alcohol use. Rather, these patients share a history of high-risk sexual behaviors, including earlier age at first intercourse and a large number of partners. Nasopharyngeal squamous cell carcinoma is relatively uncommon in the United States and is distinct from other head and neck cancers, given its association with Epstein-Barr virus (EBV) infection.

Pathology

Approximately 95% of all cancers arising from the squamous epithelium of the upper aerodigestive tract are squamous cell carcinomas. Mucosal melanomas, adenocarcinomas, and neuroendocrine tumors are also encountered. Squamous cell carcinomas are subdivided into well differentiated, moderately well differentiated, and poorly differentiated types based on their degree of resemblance to normal squamous epithelium. Poorly differentiated disease is more aggressive and has a worse prognosis. Nasopharyngeal carcinomas are also classified as either

keratinizing or nonkeratinizing, the latter strongly associated with EBV infection.

The increasingly common HPV-associated oropharyngeal cancer differs in molecular profile from alcohol- and smoking-related squamous cell carcinoma. For example, head and neck cancer related to alcohol and tobacco smoke is frequently associated with mutations in the tumor suppressor gene *TP53* and decreased expression of the cell cycle regulatory protein p16-INK4a. Conversely, HPV-associated oropharyngeal cancer displays wild-type *TP53* with increased expression of p16-INK4a. Immunohistochemistry results demonstrating p16-INK4a establishes a diagnosis of HPV-related disease.

Clinical Presentation

The presentation of patients with head and neck cancer depends on the location of the primary tumor and the extent of local disease. Disease dissemination to distant sites is uncommon at the time of diagnosis, so patients rarely have signs or symptoms of metastatic disease at presentation. Tumors of the nasopharynx often block the Eustachian tube or cause epistaxis. Oral cavity tumors may manifest with a painful, ulcerated lesion. HPV-associated oropharynx cancer usually manifests with cervical lymphadenopathy; the primary tumors are often small and asymptomatic. Cancer of the hypopharynx manifests with dysphagia and that of the larynx with hoarseness.

Metastases develop late in the course of this disease, commonly in lung or bone. Patients may also develop hypercalcemia as a paraneoplastic syndrome related to ectopic production of parathyroid hormone-related protein.

Diagnosis and Differential Diagnosis

The diagnosis of squamous cell carcinoma requires biopsy. Staging is accomplished by a combination of imaging and careful inspection of the upper aerodigestive tract. Second primary cancers are common in patients with a history of heavy alcohol and tobacco abuse. CT, MRI, and positron emission tomography (PET) can detect nodal involvement not appreciated on physical examination as well as distant metastases. Patients with squamous cell carcinoma who have cervical lymphadenopathy and no apparent primary site at presentation require random biopsies of the base of the tongue and surrounding tissues, in combination with an ipsilateral tonsillectomy, to identify the occult primary site.

Treatment and Prognosis

The prognosis of head and neck cancer depends on tumor stage. The American Joint Committee on Cancer (AJCC) TNM staging