

Cases in Head and Neck Cancer

A Multidisciplinary Approach

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Preface

In general, head and neck cancer (HNC) accounts for approximately 3% of new cases of cancer in the United States with a male-to-female ratio for HNC estimated as 4:1. The incidence of patient cases with HNC resulting from the use of tobacco products is dropping due to increased societal awareness and antitobacco education. However, the overall incidence of oropharyngeal HNC is increasing as a consequence of the human papillomavirus (HPV).

Assessment and treatment of HNC requires multidisciplinary and integrative care. HNC carries a considerable burden to patients and families, including costs associated with diagnosis, treatment, hospitalization, and medications. Aside from costs that are directly attributable to HNC, there is a considerable load imposed from secondary conditions such as disordered mechanisms of airway protection (cough and swallow). These conditions are nearly ubiquitous among HNC patients at the time of diagnosis and initial treatment, and persist in over half of patients with HNC 5 or more years following diagnosis. Taken alone or together, these conditions increase the likelihood of lung infection and death. A separate financial burden in the form of physician visits, hospitalization for lung infection, medications (particularly antibiotics) to treat the lung infection, and alternative modes of nutritional support (such as tube feeds) for patients with HNC may occur. Yet, by no means is the suffering from HNC and its sequelae merely financial. Cancer, in all its forms, can exert devastating psychosocial and psycho-emotional effects on both patients and caregivers. For patients with HNC, disorders of airway protection transform eating and drinking, activities which are typically as pleasurable as they are necessary, into potential sources of embarrassment or rejection. This can lead to depression and isolation, both of which are factors that negatively impact quality of life (QoL). Health care profession-

als who treat patients with HNC have an obligation to continually improve the quality and effectiveness of our care. We are also obliged to explore and develop additional, effective, treatment options for our patients that can potentially lessen the financial and interpersonal burdens imposed by this disease.

There are limited resources that provide a comprehensive description of complex HNC cases. Therefore, this book was written by experts in otolaryngology, medical oncology, radiation oncology, speech pathology, nursing, radiology, and dietetics in order to provide a comprehensive presentation of the complexity of the patient with HNC. Health literacy, humanistic care approaches, and information pertaining to diagnostic and clinical concerns are presented to help successfully manage patients with HNC. The cases cover contemporary practice issues surrounding HPV, robotic or minimally invasive surgery, combined modality treatments, reflux management, and the critical role of the speech pathologist are threaded throughout the entire management process. Additionally, issues of survivorship and caregiver burden are included. Finally, unique intervention protocols are highlighted for airway protection along the continuum of prevention, pre-radiation, and post-radiation.

The multimedia component of this book is extraordinary, including complete cases with accompanying images (PET, MRI, CT), surgical video, treatment approaches, and so on. Our intended audience is for graduate education in speech pathology, medical school education, resident education, continuing education for practicing speech-language pathologists, nurse case managers, dieticians, and any person involved on a head and neck cancer team. The models of team practice demonstrate the commitment to the ideal treatment of HNC with the ultimate goal of preserving health and patient quality of life.

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Florida Hospital Cancer Institute is recognized as one of America's Best Hospitals in Cancer Treatment and is accredited as a Comprehensive Cancer Care Center. The authors' affiliation with the Florida Hospital Cancer Institute, the premier nature of their care teams, and their whole person-centered approach motivated the creation of *Cases in Head and Neck Cancer: A Multidisciplinary Approach*. Ultimately, we hope our book will guide future clinicians to care for the patient with head and neck cancer in the most intelligent and respectful manner.

We are grateful to all of our authors for their wisdom and time spent creating a volume of work that documents their contemporary methods of assessment and treatment of patients with head and neck cancer. With their expert contributions, we are one step closer to helping educate the professional community on the distinct nature and needs of patients with head and neck cancer.



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*To patients and their families surviving with Head and Neck Cancer
and to future clinicians who will have the privilege of treating and caring for these individuals.*



PART I

Demographics and Definitions



I

Head and Neck Cancer Demographics and Team Management

Bari Hoffman Ruddy, Jeffrey J. Lebman, Nikhil Rao, Christine Sapienza, and Henry Ho

INTRODUCTION

This introductory chapter reviews cancers of the head and neck (HNC) with particular focus on the most common variety of HNC, squamous cell carcinoma (HNSCC). Specifically, this chapter reviews

- the incidence and prevalence of HNCs;
- the locations and varieties of HNCs;
- the primary causes and symptoms of HNSCC;
- the variety of HNSCC types and the disease staging process;
- treatment options for HNC, including
 - surgery,
 - radiation,
 - chemotherapy, and
 - combined modality;
- the makeup of the multidisciplinary clinical and research team involved in the assessment and treatment of patients with HNC; and
- future directions for HNC treatment.

HEAD AND NECK CANCER STATISTICS

Cancer is a class of diseases characterized as the uncontrolled growth of abnormal or malignant cells

(National Cancer Institute, 2015). Cancer cells can arise anywhere in the human body, dividing beyond normal limits. Cancer cells may accumulate and form tumors, invade adjacent tissue or structures, and/or spread to other locations in the body via blood or the lymphatic system, a process referred to as *metastasis*.

In 2015, the American Cancer Society estimated that there would be 59,340 new cases of HNC and that an estimated 12,290 people will die of this disease. Overall, HNC accounts for approximately 3% of new cases of cancer in the United States. The male-to-female ratio for HNC is estimated as 4:1 (Jemal, Siegel, Xu, & Ward, 2010).

HNC SITES

HNC can affect the skin, mucous membranes, glandular structures, neurovascular elements, and supportive soft tissues and bones in the head and neck. Leukoplakia, a white patch or plaque, is often the visible presentation of a precancerous lesion or early stage carcinoma, requiring biopsy in order to determine its characteristics. HNCs frequently emerge within the

- oral cavity: lips, floor of mouth, oral tongue, buccal mucosa, gingival, retromolar trigone**, and hard palate;

- oropharynx: tonsil, soft palate, base of tongue, and lateral/posterior pharyngeal wall;
- nasopharynx;
- hypopharynx: pyriform sinus;
- larynx: glottic, supraglottic, and subglottic;
- nasal cavity and paranasal sinuses;
- salivary glands: parotid, submandibular, sublingual, and minor salivary glands;
- ear: external ear, middle ear, and temporal bone;
- neck: thyroid gland and lymph nodes; and
- regional soft tissues and supporting bones.

**The retromolar trigone is a small mucosal area behind the last molar of the lower jaw. Cancer identified in this location often rapidly spreads to adjacent oral structures.

Head and Neck Cancer Types

Squamous cell carcinoma is the most common. Other less common HNC types include the following (Mendenhall, Riggs, & Cassisi, 2005):

- Sarcoma arises from connective tissue.
- Adenocarcinoma develops in the glandular lining of an organ.
- Mucoepidermoid carcinoma develops in the salivary glands. Aggressiveness is largely dependent on histologic grade. The high grade (poorly differentiated) is associated with more aggressive behavior, and the lower grade is often associated with a more benign natural history.
- Adenoid cystic carcinoma occurs in major or minor salivary glands. It may recur many years after treatment and has a tendency to follow nerves.
- Acinic cell carcinoma occurs in the salivary glands of the head and neck.
- Lymphoma begins in cells of the immune system. There are many subtypes, and the tumor behavior varies significantly depending on the precise classification. Broadly, lymphomas are divided into Hodgkin's and non-Hodgkin's categories.

- Melanoma arises from the melanocytic system of the skin or other organs.

HEAD AND NECK SQUAMOUS CELL CANCERS

Head and neck squamous cell cancer (HNSCC) originates within the mucus membranes of the nasal cavity, sinuses, lips, oral cavity, salivary glands, tongue, soft palate, pharynx, and larynx and is the fifth deadliest cancer worldwide (Chaukar et al., 2009; Lee, Wang, Mu-Hsin, Chang, & Chu, 2013; Ma et al., 2013; Melo Filho et al., 2013) with survival rates ranging from 30% for cancers of the oral cavity and pharynx to 50% for laryngeal cancers. Five-year survival rates from 2001 to 2007 indicated a 60.8% survival rate for laryngeal cancer, oral cavity and pharynx (Chaukar et al., 2009; Lee et al., 2013; LoTempio et al., 2005; http://surveillance.cancer.gov/publications/factsheets/SEER_Cancer_Survivor_Fact_Sheet.pdf). Approximately 95% of cancers of the oral cavity and the oropharynx are squamous cell carcinomas (Hsu et al., 2008; Snow, Wackym, & Ballenger, 2009; Spitz, 1994). A portion of squamous cell cancers test positive for the human papillomavirus (HPV-16). Squamous cell histologic grading includes keratinizing versus nonkeratinizing, and well-differentiated to poorly differentiated cellular characteristics. Variants of squamous cell cancer types can include undifferentiated carcinoma, lymphoepithelioma, spindle cell carcinoma, and verrucous carcinoma.

PRIMARY CAUSES OF HNSCC

The primary risk factors linked to the development of HNSCC are inhaled cigarette or marijuana smoke, pipe and cigar smoke, as well as chewing tobacco. The greatest risk occurs when anatomical areas and their susceptible epithelium are directly exposed to these toxins. The risk level is dependent on daily consumption, type, toxicity, and manner of tobacco use (Casper & Colton, 1998; Sapienza & Ruddy, 2012).

A synergistic effect exists when tobacco use is combined with consumption of alcohol, creating a higher risk of cancer development compared to if each was consumed independently. Although tobacco use and alcohol have consistently been implicated as a causative factor for HNC, it can develop in their absence; although it is significantly less common (Spitz, 1994). Additionally, although laryngopharyngeal reflux (LPR) has been largely implicated in esophageal disease, a recently identified relationship between severe LPR and HNC disease exists (Lipan, Reidenberg, & Laitman, 2006). Recent research shows that a portion of head and neck squamous cell cancers test positive for the human papillomavirus (HPV). There are numerous types of HPV; the type most frequently associated with oropharyngeal cancer is HPV-16. HPV-18 has also been associated with this cancer (Kreimer, Clifford, Boyle, & Franceschi, 2005). Studies have also found that oral HPV infections can be acquired through sexual contact (D'Souza et al., 2007). The incidence of these HPV-positive squamous cell carcinomas has increased in recent decades, especially in younger individuals. HPV-positive tumors have been associated with better survival rates than HPV-negative tumors (Ang et al., 2010). Please see Chapter 5 for contemporary and detailed information regarding HPV-positive tumors in the oropharynx.

GENERAL CANCER STAGING

American Joint Committee on Cancer Staging (AJCC) Guidelines

The TNM staging system developed by the American Joint Committee on Cancer (AJCC) Staging (<http://www.cancerstaging.org>) correlates with survival outcomes and is organized as follows:

T: Tumor (extent of primary tumor)

N: Nodal disease (lymphatic spread; regional metastasis)

M: Metastasis (distant; spread outside head and neck region)

- Primary tumor (T)
 - TX: Primary tumor cannot be assessed
 - T0: No evidence of primary tumor
 - Tis: Carcinoma in situ
- Stage 0
 - Tis, N0, M0
- Stage I
 - T1, N0, M0
- Stage II
 - T2, N0, M0
- Stage III
 - T3, N0, M0
 - T1, N1, M0
 - T2, N1, M0
 - T3, N1, M0
- Stage IVA
 - T4a, N0, M0
 - T4a, N1, M0
 - T1, N2, M0
 - T2, N2, M0
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 - T4a, N2, M0
- Stage IVB
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- Stage IVC
 - Any T, any N, M1

Tumor staging takes into account the size of a tumor, how deep it has penetrated, whether it has invaded adjacent organs, if it has metastasized to lymph nodes, and whether it has spread to distant organs. Management is typically prescribed and/or changed based on the stage at initial diagnosis or recurrence, and remains a powerful predictor of survival. The staging system is clinical, based on the best possible estimate of disease extent recorded before treatment. The assessment of the primary tumor is based on inspection and palpation, when possible, and by visual endoscopic/stroboscopic examination. In order to accurately stage the cancer, the tumor must be confirmed histologically by biopsy. Radiographic studies such as CT, MRI, or PET scans help delineate the degree of local extent, as well as potential regional lymphatic and distant metastatic spread (Mendenhall, Riggs, & Cassisi, 2005).

PRIMARY TUMOR STAGING

Staging Supraglottic (Above the Vocal Folds) Cancer

- T1: Tumor limited to one subsite of supraglottis with normal vocal fold mobility
- T2: Tumor invades mucosa of more than one adjacent subsite¹ of supraglottis or glottis or region outside the supraglottis (e.g., mucosa of base of tongue, vallecula, or medial wall of piriform sinus) without fixation of the larynx
- T3: Tumor limited to larynx with vocal fold fixation and/or invades any of the following: postcricoid area, pre-epiglottic tissues, paraglottic space, and/or minor thyroid cartilage erosion (e.g., inner cortex)
- T4a: Tumor invades through the thyroid cartilage, and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of the neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus)
- T4b: Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

¹Determination varies for different parts of the head and neck.

Subsites Include the Following

- False vocal folds
- Arytenoids
- Suprahyoid epiglottis
- Infrahyoid epiglottis
- Aryepiglottic folds (laryngeal aspect)

Note: Supraglottis involves many individual subsites. Patients with supraglottic cancers typically present with symptoms of sore throat, painful and effortful swallowing, referred ear pain, change in voice quality, or neck mass. Early vocal fold cancers are associated with chronic and progressive hoarseness. Cancers arising in the subglottic area commonly

involve the vocal fold(s) once they become symptomatic, and thus, symptoms usually relate to a contiguous spread (Castellanos, Spector, & Kaiser, 1996).

Staging Glottic (at the Level of the Vocal Folds) Cancer

Glottic presentation may vary by volume of tumor, anatomic region involved, and the presence or absence of normal vocal fold mobility:

- T0: No evidence of primary tumor
- Tis: Carcinoma in situ: confined to tissues lining the larynx
- T1: Tumor limited to the vocal fold(s), which may involve anterior or posterior commissure, with normal mobility
- T1a: Tumor limited to one vocal fold
- T1b: Tumor involves both vocal folds
- T2: Tumor extends to supraglottis and/or subglottis and/or with impaired vocal fold mobility
- T3: Tumor limited to the larynx with vocal fold fixation and/or invades paraglottic space, and/or minor thyroid cartilage erosion (e.g., inner cortex)
- T4a: Tumor invades through the thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck, including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus)
- T4b: Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

Staging of Subglottic (Below the Vocal Folds) Cancer

- T1: Tumor limited to the subglottis
- T2: Tumor extends to vocal fold(s) with normal or impaired mobility
- T3: Tumor limited to larynx with vocal fold fixation
- T4a: Tumor invades cricoid or thyroid cartilage and/or invades tissues beyond

the larynx (e.g., trachea, soft tissues of neck, including deep extrinsic muscles of the tongue, strap muscles, thyroid, or esophagus)

- T4b: Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

Staging of Oropharyngeal Cancer

- T1: Tumor is 2 cm (about three-quarter inch) across or smaller
- T2: Tumor is larger than 2 cm across but smaller than 4 cm (about 1 ½ inch)
- T3: Tumor is larger than 4 cm across. For cancers of the oropharynx, T3 also includes tumors that are growing into the epiglottis.
- T4a: Tumor is growing into nearby structures. This is known as *moderately advanced local disease*.
 - For oral cavity cancers: the tumor is growing into nearby structures, such as the bones of the jaw or face, deep muscle of the tongue, skin of the face, or the maxillary sinus.
 - For lip cancers: the tumor is growing into nearby bone, the inferior alveolar nerve (the nerve to the jawbone), the floor of the mouth, or the skin of the chin or nose.
 - For oropharyngeal cancers: the tumor is growing into the larynx (voice box), the tongue muscle, or bones such as the medial pterygoid, the hard palate, or the jaw.
- T4b: The tumor has grown through nearby structures and into deeper areas or tissues. This is known as *very advanced local disease*. Any of the following may be true:
 - The tumor is growing into other bones, such as the pterygoid plates and/or the skull base (for any oral cavity or oropharyngeal cancer).
 - The tumor surrounds the internal carotid artery (for any oral cavity or oropharyngeal cancer).

- For lip and oral cavity cancers: the tumor is growing into an area called the *masticator space*.
- For oropharyngeal cancers: the tumor is growing into a muscle called the *lateral pterygoid muscle*.
- For oropharyngeal cancers: the tumor is growing into the nasopharynx (the area of the throat that is behind the nose).

Staging of Nasopharyngeal Cancer

- T1: Tumor confined to the nasopharynx, or tumor extends to oropharynx and/or nasal cavity without parapharyngeal extension (e.g., without posterolateral infiltration of tumor)
 - T2: Tumor with parapharyngeal extension (posterolateral infiltration of tumor)
 - T3: Tumor involves bony structures of skull base and/or paranasal sinuses
 - T4: Tumor with intracranial extension and/or involvement of cranial nerves, hypopharynx, or orbit, or with extension to the infratemporal fossa/masticator space

CANCER SPREAD

Cancer spread or *metastasis* refers to the migration of cancer cells from the site of initial presentation, to other areas of the body not previously involved. Cancer spread can be characterized as local, lymphatic, or hematogenous. Initial spread is usually regional, involving tissues adjacent to the tumor cells. Most primary tumors arise as surface lesions and spread by local invasion laterally as well as deeply, following a pathway of least resistance between fascial planes. Muscle tissue frequently becomes invaded by laryngeal and tongue cancers. Bone and cartilage can become invaded in serious, advanced cases.

Lymphatic and hematogenous spread refers to the processes of transport of cancer cells from the primary tumor, to remote locations throughout the body through lymph or blood. Lymphatic spread is the most common means of metastasis and occurs