Head and Neck Squamous Cell Cancer: Approach to Staging and Surveillance

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Abstract

This chapter addresses the rising global burden of Head and Neck Squamous Cell Cancer (HNSCC), a heterogeneous group of cancers in the upper aerodigestive tract. We focus on the pivotal role of imaging modalities like CT, MRI, PET/CT, and US in the early detection, accurate staging, and management of HNSCC. The discussion includes the nuances of TNM staging, key upstaging features, and the evolving role of advanced imaging techniques such as MR/PET. The chapter highlights significant updates in the AJCC/UICC eighth edition, particularly concerning HPV-related cancers and the depth of invasion in oral cavity SCC. Special attention is given to the challenges in diagnosing Neck Cancer of Unknown Primary (NCUP), underlining the importance of integrated imaging, clinical exam, and molecular markers. Overall, the chapter emphasizes the essential role of radiologists in the comprehensive management of HNSCC, combining imaging insights with clinical findings for optimal patient care.

Keywords

Head and Neck Cancer · Extranodal extension Perineural Spread (PNS) · NI-RADS (Neck Imaging Reporting and Data System) · HPV (Human Papillomavirus) · NCUP (Neck Cancer of Unknown Primary)

Learning Objectives

- Recognize the primary imaging modalities (CT, MRI, PET/CT) used in the diagnosis, staging, and surveillance of Head and Neck Squamous Cell Cancer (HNSCC), including their advantages and limitations.
- Understand the principles and components of TNM staging according to the AJCC/UICC eighth edition for HNSCC.
- Identify the anatomic boundaries and key upstaging features for different HNSCC sites: nasopharynx, oral cavity, oropharynx, and hypopharynx/larynx.
- Appreciate the implications of cervical lymphadenopathy in HNSCC, including the size criteria and features of abnormal lymph nodes, and the concept of perineural spread.
- Understand the importance of surveillance in managing HNSCC, including the guidelines from NCCN and NI-RADS, and the role of PET/CT in this context.

Head and Neck Squamous Cell Cancer (HNSCC) remains a significant global health burden with high morbidity and mortality rates. HNSCC encompasses a heterogeneous group of neoplasms arising from the squamous epithelium of the upper aerodigestive tract, which includes the oral cavity, oropharynx, nasopharynx, hypopharynx, and larynx. It is the sixth most common cancer worldwide with 890,000 new cases and 450,000 deaths in 2018 [1, 2]. The incidence of HNSCC continues to rise and is projected to increase 30% annually by 2030 [3].

Traditionally, the highest rates of HNSCC occurred in older males due to tobacco and alcohol use [4]. However, a rising number of cases have been associated with human papillomavirus (HPV) infection in both developing and developed countries. This trend particularly affects younger and healthier patients and is often associated with oropharyngeal sites [5].

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Early detection and accurate staging of HNSCC are crucial for effective therapeutic strategy planning and prognostication. To this end, imaging plays a pivotal role. In the following sections, we will delve into the specifics of the imaging methods, the nuances of TNM (Tumor, Node, Metastasis) staging, anatomic boundaries of HNSCC, and key upstaging features. The aim of this chapter is to provide a comprehensive approach to the imaging and staging of HNSCC.

17.1 Imaging Methods

The choice of imaging modality in HNSCC is critical to accurately assess tumor extent, stage the disease, evaluate treatment response, and detect recurrence during surveillance. Computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography/computed tomography (PET/CT) are all essential tools. Each provide a unique and complementary information that guide diagnosis, staging, treatment planning, and follow-up [3]. The selection depends on the location of the primary tumor, the suspected stage of disease, the patient's clinical condition, and the available resources.

17.1.1 Computed Tomography (CT)

CT is widely used due to its accessibility, relatively low cost, and speed of acquisition. It provides excellent spatial resolution and good contrast differentiation between soft tissue, bone, and air [6]. This makes it especially ideal for detecting bony invasion.

Current advancements in multidetector CT technology permit scans with a slice thickness of under 1 mm. Ideally, a slice thickness of 3 mm is preferred. The images should be both reconstructed and viewed in bone and soft tissue windows.

For oral cavity cancers, CT scans can assist in determining how deeply a tumor has infiltrated into the tongue's deep muscles and whether it has reached the mandible. The "puffed cheek" method can enhance the assessment of lesions within the oral cavity. This method entails patients self-inflating their oral cavity with air by blowing out their cheeks which can unmask a lesion along the buccal mucosa or gingiva. Dental fillings can lead to significant beam hardening artifacts that can obscure important details within the scan plane. This issue can be rectified by re-scanning with a tilted gantry angle or using metal suppression techniques, such as dual-energy CT [7].

For other types of head and neck cancers, CT scans are generally beneficial in identifying advanced stages of cancers that have infiltrated neighboring structures that are difficult to detect clinically. For laryngeal cancers, CT scans can shed light on the invasion of the pre-epiglottic space, paraglottic space, and subglottic extension. Recent advances in dual-energy CT technology has improved the accuracy for assessing cartilage invasion compared with conventional CT, a determinant for stage T4 disease [8].

However, CT may not clearly delineate early mucosal lesions or tumoral invasion into soft tissue structures, limiting its utility in certain scenarios and necessitating the use of MRI and/or PET/CT.

17.1.2 Magnetic Resonance Imaging (MRI)

MRI is superior in demonstrating the extent of soft tissue invasion and perineural spread (Table 17.1) [9]. Its high contrast resolution makes it particularly valuable for imaging complex anatomical areas such as the skull base, nasopharynx, and parapharyngeal spaces. MRI is particularly useful for evaluating perineural tumor extension and cartilage invasion, especially when the cartilage is not ossified. MRI is also excellent for detecting early tumoral changes following treatment, distinguishing between fibrosis and recurrence. Nonetheless, obtaining a high-quality, full-neck image is more challenging with MRI than with CT due to its high susceptibility to motion artifacts. This can become particularly troublesome in post-treatment patients who might find it difficult to remain still for an extended duration.

17.1.3 Positron Emission Tomography/Computed Tomography (PET/CT)

PET/CT combines the anatomical detail of CT with the metabolic activity visualization of PET, providing both structural and functional information. It is particularly useful in initial staging, especially for nodal staging, detecting distant metastases, and identifying an unknown primary [10, 11]. Moreover, during post-treatment surveillance, PET/CT can differentiate post-treatment changes from residual or recurrent disease with a high degree of accuracy [12]. However, PET/CT is not without downsides. It is not ideal for detecting very small tumors or microinvasion due to low spatial resolution. Furthermore, considerations such as cost, availability, patient

Table 17.1 Standard MRI sequences

MRI sequence	Utility
Noncontrast T1-weighted imaging	It offers anatomical views and can help identify tumor margins and infiltration into bone, significantly contributing to staging the disease.
T2-weighted imaging with fat suppression (FS)	This is used for tumor identification and characterization and helps to identify neck lymph nodes. FS is generally used in this imaging to increase contrast although it can sometimes cause image artifacts.
Contrast-enhanced T1-weighted imaging with (FS)	This utilizes gadolinium-based contrast agents for characterizing lesions and assessing intracranial extension of disease.

preparation, extended examination time, and higher radiation dose present additional challenges that need to be weighed.

17.1.4 Ultrasound (US)

US is less frequently used for primary tumor evaluation due to its inability to penetrate bone and air-filled spaces. However, it can be valuable in specific circumstances. For instance, US is excellent for evaluating superficial structures such as thyroid and salivary glands and has high sensitivity for detecting cervical lymphadenopathy. Moreover, US is safe, cost-effective, and can be used for real-time image-guided biopsy of suspected lesions, providing a valuable adjunct.

17.1.5 Up and Coming: Magnetic Resonance/ Positron Emission Tomography (MR/ PET)

MR/PET is an emerging imaging modality that attempts to combine the strengths of MRI and PET. It offers the excellent soft tissue contrast resolution of MRI with the metabolic information of PET while reducing radiation exposure [3]. This hybrid imaging modality can potentially provide superior information for tumor characterization, staging, and treatment response evaluation. However, larger, multicenter trials are necessary to validate FDG PET/MRI's role in head and neck cancer. In addition, cost-related issues concerning purchase, maintenance, and reimbursement must also be addressed. Ultimately, practical standardized protocols are required for FDG PET/MRI to be adopted more broadly in the evaluation of head and neck cancers.

Key Point

- No single imaging modality can answer all clinical questions for HNSCC. Each method has its advantages and limitations.
- The choice of modality should be tailored to the clinical question at hand, the anatomical location of the tumor, and the resources available.

17.2 TNM Staging

The eighth edition of the AJCC/UICC TNM classification system is an internationally recognized manual that provides a standardized language for discussing HNSCC [13]. The radiologist's primary role is to provide the necessary anatomic information related to tumor assessment based on imaging characteristics that will allow the clinician to assign a correct TNM stage.

The "T" refers to the primary tumor's size and extent. Its specific classification can range from T0, indicating no evidence of a primary tumor, to T4, which suggests a significantly advanced disease in terms of size and/or invasion into adjacent structures. The T classification varies depending on the site of the cancer; therefore, having ready access to the staging table is helpful for accurate classification.

The "N" represents the degree of regional lymph node involvement. It is well recognized that cervical lymph node metastasis significantly impacts the prognosis of HNSCC patients. Identification of extranodal extension (ENE) is particularly critical in upstaging tumors.

The "M" refers to the presence (M1) or absence (M0) of distant metastasis. HNSCC typically metastasizes to the lungs, followed by bone and liver [14].

17.2.1 Key Changes in the AJCC/UICC Eighth Edition

Oropharyngeal SCC (OPSCC): In the recent years, there has been a paradigm shift in the epidemiology with an increase in HPV-related (or p16-positivity as a surrogate) cases, particularly in younger individuals with little to no history of tobacco use [15]. These typically show excellent responses to treatment, even in patients with advanced stage disease. Given the distinct clinical and biological behavior of p16-positive OPC compared to p16-negative OPC, it has been recognized as a separate entity requiring a specific staging system. One key example is that for p16-positive OPC, the ipsilateral multiplicity of lymph node involvement is no longer considered, whereas it remains a significant factor in the staging of p16-negative OPC.

Oral Cavity SCC (OCSCC): The depth of invasion (DOI) is now included as a component in the T staging as it has critical prognostic factor. While it is a pathologic measurement, studies have shown that there is good radiologic-pathologic correlation and the radiographic measurement is predictive of outcome [16].

Extranodal Extension (ENE): ENE has been incorporated in the N category, except for tumors associated with HPV. Its presence now upstages nodal disease to N3b for p16 negative and non-EBV lymph node SCC.

Key Point

- For radiologists who interpret OPC staging scans and participate in tumor boards, it is crucial to have knowledge of the p16 and HPV status.
- While the staging of ENE primarily relies on clinical assessment, radiology can supply supportive evidence especially when physical examination results are ambiguous.

17.3 Nasopharyngeal Carcinoma (NPC)

17.3.1 Anatomic Boundaries

The nasopharynx's anatomic boundaries consist of the anterior boundary (posterior nasal septum and choanae), the posterior boundary (vertebral bodies of C1-C2), and the lateral boundaries (tori tubarii, Eustachian tube orifices, and pharyngeal recess). The superior boundary is the base of the skull, specifically the undersurface of the sphenoid bone and basiocciput. The inferior boundary is the level of the soft palate, which separates the nasopharynx from the oropharynx.

This region is richly connected to adjacent critical structures like the skull base, paranasal sinuses, cavernous sinus, and the orbits. This has significant implications when it comes to the spread of malignancies and the subsequent impact on staging and treatment planning.

17.3.2 Key Upstaging Features

The involvement of the parapharyngeal space up categorizes the T classification from T1 to T2. There is considered parapharyngeal spread when the tumor invades laterally through the levator palatini muscle and pharyngobasilar fascia to involve the tensor palatini muscle and parapharyngeal fat space [17]. This can also act as a potential pathway for tumor extension from the nasopharynx to the deeper neck spaces, the skull base, and other vital structures. Tumors that invade the parapharyngeal space often present as a more advanced disease and require more aggressive management [17].

NPC often invades the skull base upon diagnosis, upgrading the disease from T2 to T3. The commonly invaded structures include the clivus, pterygoid bones, body of the sphenoid, and petrous apices. The tumor also frequently infiltrates the skull base foramina and fissures, such as the foramen rotundum, foramen ovale, foramen lacerum, vidian canal, pterygomaxillary and petroclival fissures, as well as the pterygopalatine fossa (PPF) (Fig. 17.1). This enables further spread to the orbit and intracranial structures by both direct and PNS, complicating treatment and worsening prognosis.

NPC also have a tendency for early nodal spread due to the rich lymphatic network. Cervical lymph node involvement is a common finding and can further upstage the disease. The nodal levels most frequently involved include retropharyngeal and levels II and III nodes.

17.4 Oral Cavity SCC (OCSCC)

The oral cavity includes various structures: lips, oral tongue, buccal mucosa, alveolar ridge, retromolar trigone, hard palate, and the floor of the mouth (FOM).

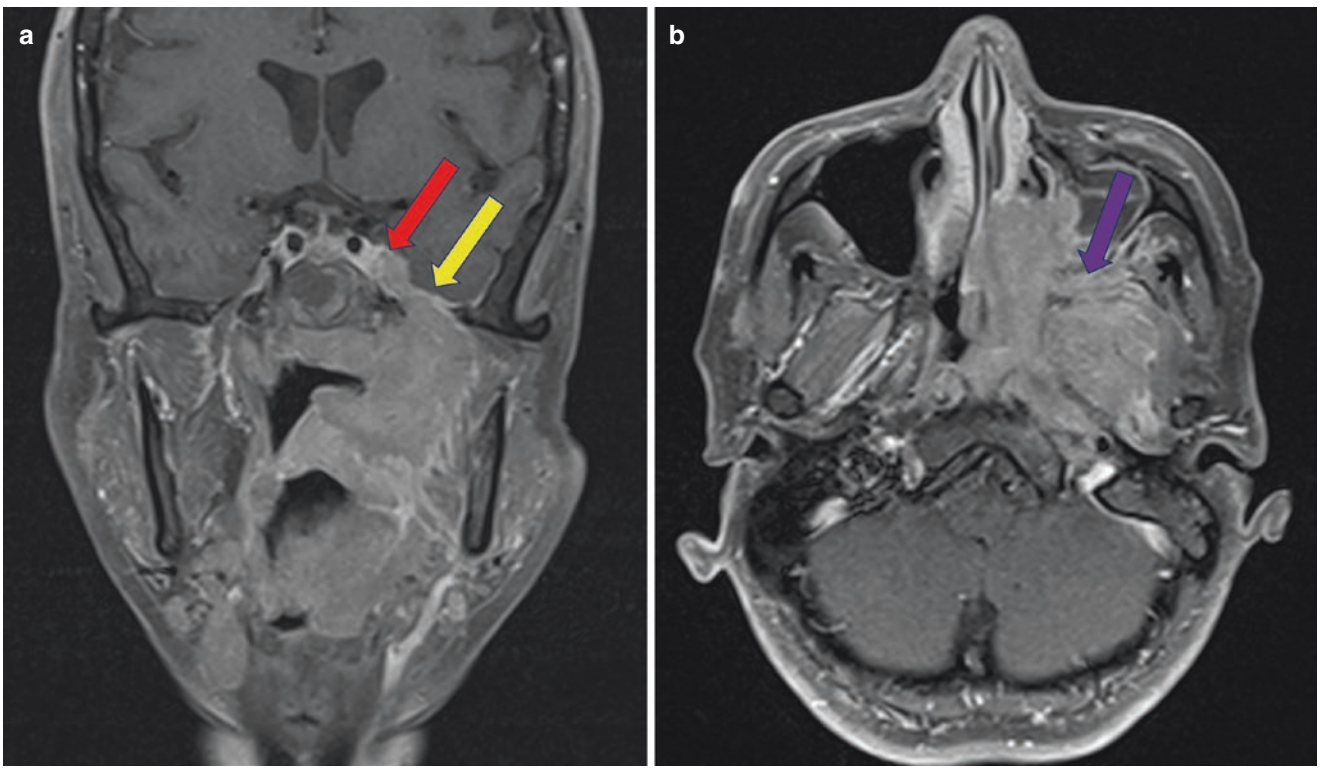

Fig. 17.1 Coronal (**a**) and axial (**b**) post-contrast T1-weighted fat-suppressed images show an enhancing left nasopharyngeal mass invading into the left pterygopalatine fossa (purple arrow), masticator space, and nasal cavity. There is perineural spread along the right V3 nerve into the left foramen ovale (yellow arrow) and cavernous sinus (red arrow)

17.4.1 Anatomic Boundaries

The oral cavity extends anteriorly from the lips to the junction of the hard and soft palate superiorly and to the line of the circumvallate papillae on the tongue inferiorly. The lateral borders are the buccal mucosa, extending posteriorly to the anterior tonsillar pillars.

The FOM, the area under the tongue, is a common site for oral cavity cancers. The hard palate, forming the roof of the mouth, divides the oral and nasal cavities. The tongue is divided into the anterior two-thirds (oral part) and the posterior one-third (base). The alveolar ridges contain the tooth sockets, and the retromolar trigone is the small area behind the wisdom teeth.

The oral cavity is richly supplied by branches of the external carotid artery, mainly the lingual artery.

17.4.2 Key Upstaging Features

Tumor thickness (TT) and the DOI are essential prognostic indicators in OCSCC [16]. Tumors that are thicker and invade deeper into the oral cavity tissues have a higher risk of metastasizing to the cervical lymph nodes and involving deep soft tissues. DOI refers to a specific pathological measurement taken during surgical resection, quantifying the extent the tumor has spread beneath the basement membrane [18]. This is distinct from TT, which measures the vertical dimension of the tumor from the surface to its deepest point. Exophytic tumors may have a large TT but can exhibit minimal DOI, as they may be broad but not deeply invasive. Conversely, endophytic tumors may demonstrate a large DOI even if the TT is smaller due to a reduced diameter. Tumors with a DOI of more than 5 mm are categorized as T2 or higher depending on other tumor characteristics. It is important to recognize that DOI is a pathologic measurement and because the primary treatment for oral cavity cancer is surgical resection, pathologic staging will typically be performed.

The inferior alveolar nerve is one of the branches of the mandibular nerve (V3), providing sensation to the lower teeth and the lower lip. It runs through the mandibular foramen and mandibular canal within the mandible and exits through the mental foramen. Its proximity makes it susceptible to invasion by OCSCC, especially those arising in the lower gingiva or the FOM (Fig. 17.2). Involvement of this nerve signifies a more advanced tumor and portends a worse prognosis. In many cases, it might escalate the category to T4, depending on other characteristics of the tumor. It also necessitates a more aggressive surgical approach, including a mandibulectomy. Damage to or resection of the inferior alveolar nerve may lead to chronic numbness or pain in the area, decreasing the patient's quality of life.

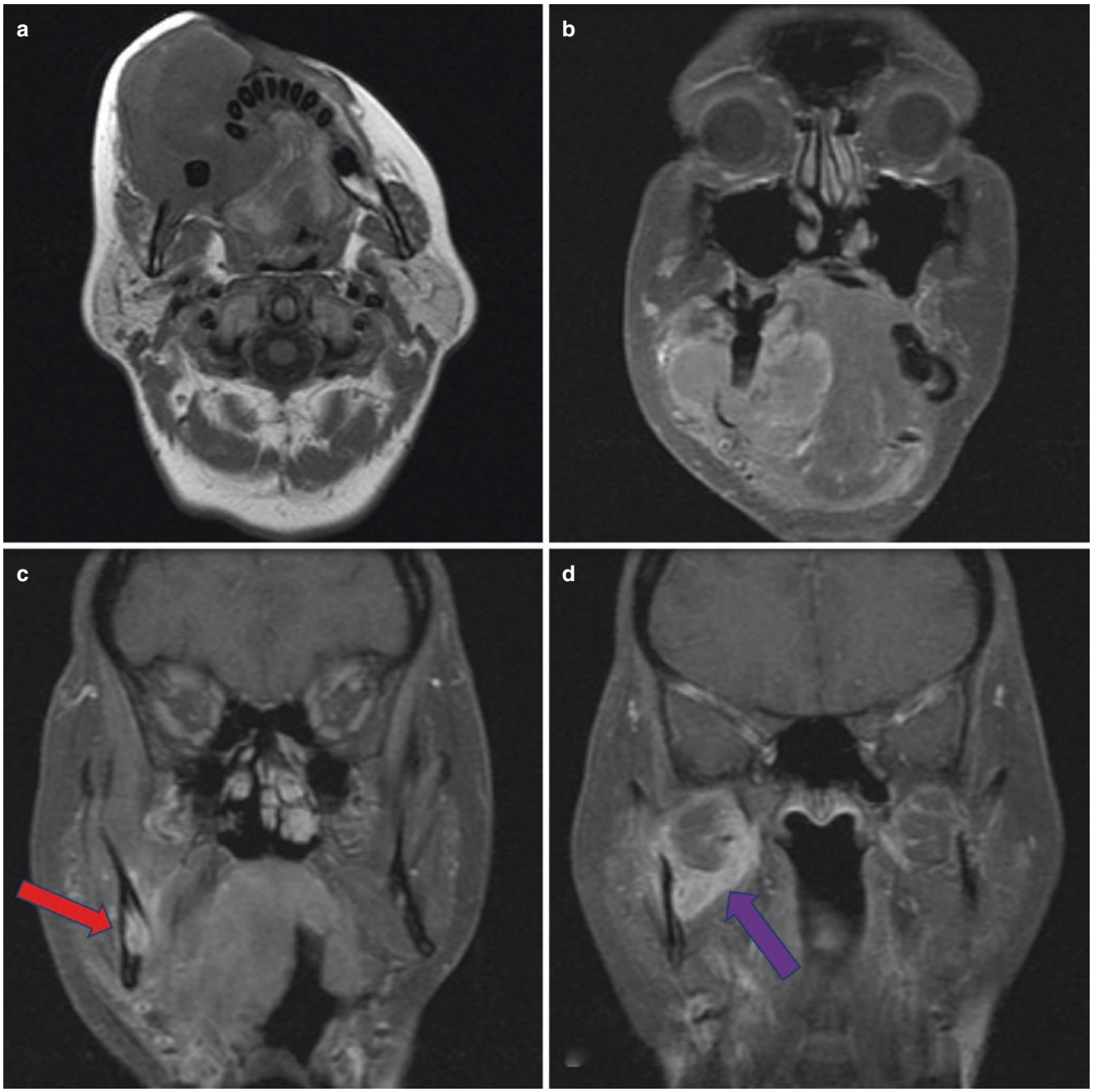

Fig. 17.2 Axial T1-weighted image (**a**) demonstrating a large T1 hypointense mass arising from the right mandibular gingiva invading into the mandible and surrounding soft tissues, including the mandibular canal. Coronal post-contrast T2-weighted fat saturated images (**b–d**) showing perineural spread of tumor along the right inferior alveolar (red arrow) and V3 nerve (purple arrow)

17.5 Oropharyngeal SCC (OPSCC)

17.5.1 Anatomic Boundaries

The oropharynx is located at the central portion of the pharynx, extending from the soft palate superiorly to the level of the hyoid bone inferiorly. It plays a vital role in speech and swallowing and is delineated by several distinct structures. It includes the base of the tongue, the palatine tonsils, and the posterior pharyngeal wall, which forms the posterior boundary. The palatine tonsils are housed in the tonsillar fossa which is the space between the anterior tonsillar pillar, or the palatoglossal arch, and the posterior tonsillar pillar, or the palatopharyngeal arch.

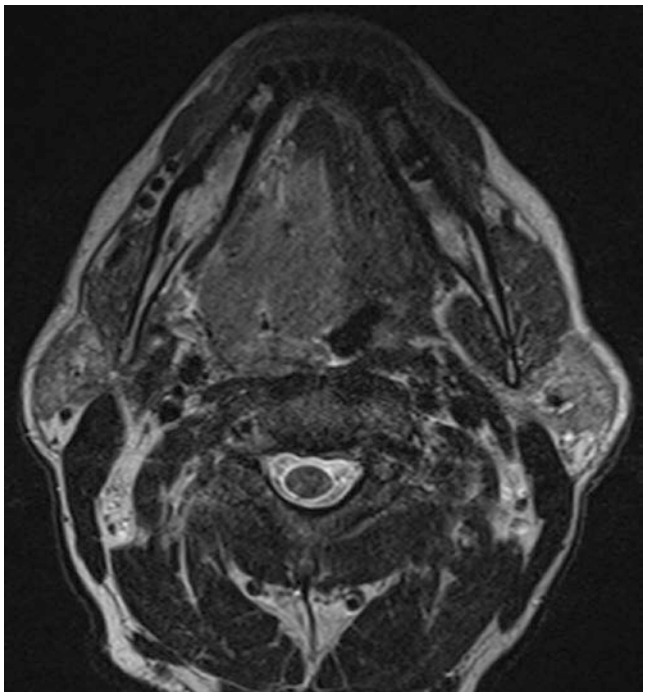

Fig. 17.3 Axial T1-weighted image shows a large right floor of mouth mass invading into the ipsilateral genioglossus and hyoglossus muscles with encasement of the right lingual artery. The tumor extends posteriorly into the right tonsil across the glossotonsillar sulcus

17.5.2 Key Upstaging Features

The extrinsic muscles of the tongue include the genioglossus, hyoglossus, styloglossus, and palatoglossus muscles. They are fundamental in orchestrating the movements of the tongue, assisting in functions like speech, mastication, and deglutition. In the context of OPSCC, the involvement of any one of the muscles serves as a sign of the tumor's spread and aggressiveness and up categorizes to T4 regardless of the p16 status. Imaging plays a particular role as it is difficult to determine their involvement clinically. CT and MRI may reveal irregularities, thickening, or a loss of symmetry that indicates malignant involvement (Fig. 17.3).

17.6 Hypopharynx/Larynx SCC

17.6.1 Anatomic Boundaries

The larynx serves as a complex organ for voice production, airway protection, and breathing. It spans from the epiglottis to the trachea and consists of three main parts: supraglottis, glottis, and subglottis. Supraglottis includes the epiglottis, aryepiglottic folds, arytenoids, and laryngeal ventricles. It is important to note that the anterior surface of the aryepiglottic folds resides in the larynx, while the posterior surface is part of the hypopharynx. Anteriorly, there is the triangular fat containing space between the epiglottis and hyoid bone called the pre-epiglottic space. The glottis is home to the true vocal cords which comes together at the anterior commissure and posterior commissure**.** On either side of the larynx exists a fat-containing space called the paraglottic space. The subglottis extends from 1 cm below the lateral margin of the ventricle to the inferior margin of the cricoid cartilage.

The hypopharynx represents the lower part of the pharynx, bridging the oropharynx to the esophagus and larynx. It extends from the hyoid bone to the cricoid cartilage, containing subsites: pyriform sinuses, posterior pharyngeal wall, and post-cricoid region.

The pyriform sinuses are pear-shaped recesses on either side of the laryngeal opening. Lying between the thyroid cartilage and thyrohyoid membrane, they are considered a common location for hypopharyngeal carcinoma. The posterior pharyngeal wall is the back wall of the pharynx, descending from the level of the soft palate to the esophagus, behind the larynx. Its muscular layer helps in swallowing. The post-cricoid region lies behind the cricoid cartilage and continues as the esophagus. Although less common, tumors can arise in this location.

17.6.2 Key Upstaging Features

Invasion into the paraglottic space for all subtypes of laryngeal SCC is a poor prognostic factor and up categorizes the tumor to a T3 lesion. MRI is usually the preferred modality due to its excellent soft tissue contrast, allowing the precise delineation of the tumor from the surrounding fatty tissue. CT can also be valuable, especially in preoperative planning.

Involvement of cartilages and extralaryngeal extension are significant factors separating between T3 and T4a categories for both laryngeal and hypopharyngeal SCC (Figs. 17.4 and 17.5). This carries significant surgical implications, as these structures maintain the structural integrity of the larynx. Their invasion usually necessitates aggressive management, including total laryngectomy, which has serious consequence for patient's quality of life. Therefore, identifying cartilage involvement through imaging is crucial although it often challenging. Typically, MRI has higher sensitivity than CT, but motion artifact poses a serious problem. CT remains a preferred method for imaging the larynx and hypopharynx, but it may miss disease involvement of a non-ossified cartilage. Dual-energy CT seems to offer promising improvements in detecting cartilage invasion, especially in reducing overestimation of cartilage invasion, thereby preventing unnecessary total laryngectomy [19].

Prevertebral space involvement, or the fixation of a tumor to the prevertebral muscles, is clinically challenging to assess. The invasion of this space signals a very advanced

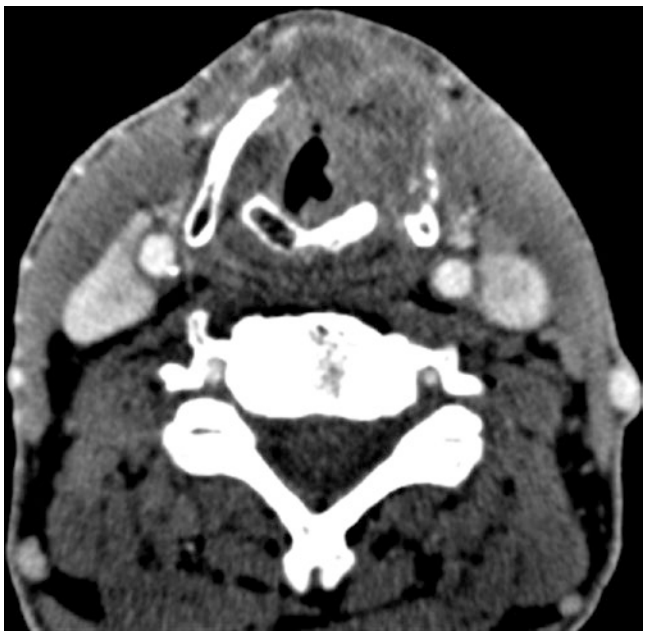

Fig. 17.4 Axial contrast-enhanced CT showing a heterogeneously enhancing left laryngeal mass invading into the overlying thyroid cartilage with infiltration of the strap musculature. The left aspect of the cricoid cartilage is sclerotic, also raising the possibility of involvement

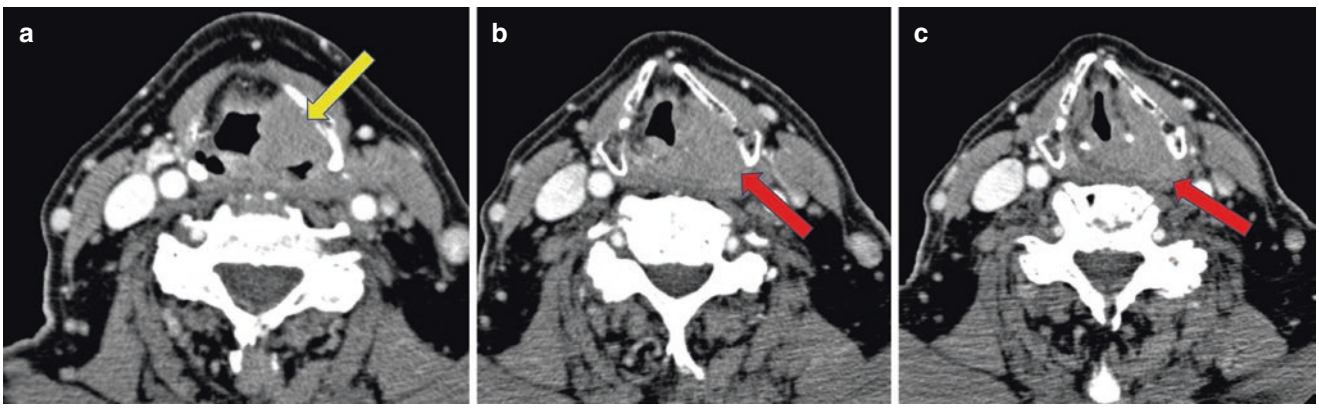

Fig. 17.5 Axial contrast-enhanced CT (**a–c**) demonstrating a left supraglottic/piriform sinus squamous cell carcinoma invading into the left paraglottic fat (yellow arrow). The tumor extends into the hypopharynx via the widened thyroarytenoid interval (red arrow)

disease, categorized as T4b, and generally indicates unresectability. The use of imaging to identify the preservation of the retropharyngeal fat plane offers a valuable diagnostic tool, as it can accurately predict the absence of direct tumor infiltration into the prevertebral space [20].

17.7 Cervical Lymphadenopathy

Identification of nodal metastases is critical in treatment and prognosis of HNSCC. A single lymph node metastasis decreases the 5-year survival rate to half. If there is an additional contralateral nodal metastasis, the survival rate is roughly halved again to 33% [21].

The mnemonic "CRISPS" can be used when assessing for cervical lymphadenopathy [14]:

Clustering: Clustering refers to a group of three or more abutting nodes without intervening fat planes measuring 8–15 mm long or 9–10 mm short axis in the jugulodigastric area and 8–9 mm elsewhere in the neck. It portends a poorer prognosis than isolated nodes.

Rounded shape: Typically, lymph nodes have an oblong or elongated shape when they are healthy. However, when

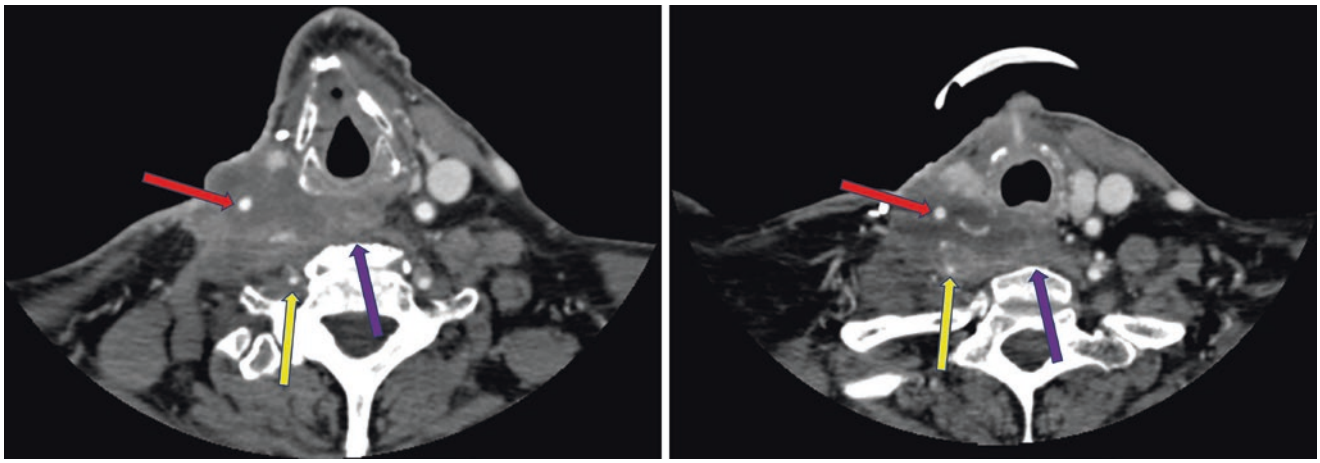

Fig. 17.6 Axial contrast enhanced CT (**a**, **b**) showing a large, necrotic, ill-defined, heterogeneously enhancing right cervical lymphadenopathy encasing the right internal carotid (red arrows) and vertebral (yellow arrows) arteries. The lesion is also inseparable from the prevertebral musculature raising the possibility of invasion (purple arrows)

they take on a more spherical or rounded shape, it often indicates a higher probability of metastasis.

Inhomogeneity: A metastatic lymph node is composed of a mix of tumor cells, native lymph node tissue, and areas of necrosis, leading to an internally heterogeneous appearance. If the heterogeneous area is larger than 3 mm, it is referred to as "central necrosis" and is one of the most reliable imaging indicators of metastatic disease.

Size: The size criteria and measurement techniques vary widely and may depend on the institution and clinicians' preference based on sensitivity and specificity. For example, at our institution, we use the largest long axis diameter on axial imaging greater than 15 mm in level I and II (jugulodigastric), and greater than 10 mm at other locations in the neck [22]. Other institutions may employ a 1-cm short axis cutoff [23]. It is important to understand that while size criteria can guide suspicion, it is not definitive. Approximately 20% of nodes larger than 1-cm short-axis diameter may show only hyperplasia, while 23% of nodes with ENE measure less than 1-cm [24]. The morphology and internal characteristics of a lymph node are arguably more reliable at identifying its pathological status.

Periphery: Any abnormalities along the borders of the lymph node can indicate underlying ENE, where the cancer cells breach the outer boundary of the lymph node. On imaging modalities, this often manifests as irregular nodal margins, capsular enhancement, and surrounding fat stranding (Fig. 17.6). Recognizing ENE is crucial at it indicates a more aggressive disease and increases the likelihood of recurrence by up to 10 times.

Sentinel node: The sentinel node is the first lymph node or group of nodes that cancer cells are most likely to spread to from the primary tumor. For majority of the oral cavity and oropharyngeal SCC, the jugulodigastric node serves as the sentinel node. Tongue-based SCC can occasionally bypass the level II nodes and spread to an ipsilateral level III or IV nodes. This information can increase the index of suspicion for nodal disease even when the appearance may be near normal.

Key Point

- Lymph node metastasis negatively impacts the prognosis in HNSCC.
- "CRISPS" mnemonic guides cervical lymphadenopathy assessment, including clustering, rounded shape, inhomogeneity, size, periphery, and sentinel nodes.
- Node morphology and internal characteristics are more telling than size alone, especially noting extracapsular spread.

17.8 Perineural Spread (PNS)

PNS involves the dissemination of the tumor along the nerve sheaths, but it is often loosely used to encompass neoplastic involvement along any or all compartments of a nerve. The significance of PNS on prognosis cannot be overstressed. It increases the probability of locoregional recurrence by 300% and decreases the 5-year survival rate by 30% [25]. Clinically, PNS can lead to functional deficits based on the nerve involved, sometimes leaving lastingdebilitation even after treatment. Therefore, the role of imaging becomes invaluable in detecting PNS.

Primary imaging features of PNS include nerve enhancement and thickening, as well as obliteration of perineural fat at foraminal openings. In advanced cases, bony erosion of the skull base foramina can be present. Secondary imaging features involve denervation atrophy of the muscles supplied by the nerves. Early on, T2-weighted MR images show muscle hyperintensity, resembling edema, and increased contrast enhancement due to increased perfusion. Over time, muscle atrophy with fatty replacement is evident.

The trigeminal nerves, particularly the maxillary and mandibular divisions, frequently become conduits for PNS due to their extensive network across the head and neck. Tumors from the facial region, as well as oropharyngeal and sinonasal cancers, can spread along the maxillary nerve. Furthermore, any skull base tumors that infiltrate the PPF can also extend to the brain through the foramen rotundum.

The mandibular nerve is often affected by masticator space and skull base tumors, such as NPC. Cancers of the submandibular gland, tongue, and mouth floor can invade the lingual or inferior alveolar nerve, and track back along the mandibular nerve and the foramen ovale, which is a portal for extending intracranially, particularly into the cavernous sinus.

Parotid gland tumors can affect the facial nerve, spreading cranially as far as the internal auditory canal. They can also infiltrate along the auriculotemporal nerve to involve the mandibular nerve. In addition, any tumors involving the PPF can also infiltrate the facial nerve along the vidian and greater superficial petrosal nerves.

Key Point

- PNS drastically affects outcomes, increasing locoregional recurrence and decreasing the 5-year survival rate.
- Primary imaging features include nerve enhancement/thickening and secondary features, such as denervation atrophy.
- The trigeminal nerves, especially the maxillary and mandibular divisions, frequently serve as pathways for PNS, affecting the course and treatment of various head and neck cancers.

17.9 Surveillance

HNSCC often recurs within the first 3 years after treatment, making this period crucial for clinical and imaging surveillance [26]. Despite development of evidence-based guidelines, none is universally accepted for surveillance timing and modality.

In general, there is a consensus that baseline post-treatment imaging should be performed within 6 months after therapy completion. This initial study could be challenging to interpret due to distorted anatomy after reconstruction flaps and radiation but will aid in reading subsequent follow-up studies. Thus, understanding the expected post-treatment findings is crucial to differentiate between treatment changes, residual tumor, and early recurrence. Ideally, the baseline scan should not show any signs of the remaining primary mass or abnormal lymph nodes.

The role of surveillance imaging for asymptomatic patients after initial post-treatment is less clear due to limited literature. However, given the high recurrence rates and difficulty identifying recurrences, many institutions routinely monitor advanced HNSCC for 2–3 years post-treatment [3].

In 2018, Neck Imaging Reporting and Data System (NI-RADS) was introduced to standardize surveillance imaging algorithm for HNSCC [27]. It offers standardized descriptions for the primary site and regional nodal basin. They include a recurrence suspicion level at each site, linked to management suggestions. NI-RADS enhances report consistency and communication, aiding clinical decisions. Studies confirm its reliability, with good interreader agreement and strong discriminatory ability in assessment categories.

Incorporating PET/CT in surveillance is increasingly popular due to its ability to detect metabolic changes before structural ones. It proves especially valuable in differentiating between post-treatment changes and tumor recurrence with studies showing specificity as high as 100% and NPV of 90–100% [3]. However, the interpretation requires caution. False positives can arise from inflammatory changes, especially when performed earlier than 12 weeks. Also, false negatives are possible with small lesions due to limited spatial resolution. Moreover, factors like cost, radiation exposure, and limited accessibility may limit its universal adoption. Regardless, in instances of clinical uncertainty, PET/CT remains a useful adjunct.

Ultimately, there is no rigid surveillance plan, and several factors must be considered. Firstly, the initial disease stage is pivotal; advanced stages necessitate more frequent monitoring. The type and intensity of treatment received play a role as well. Patients who undergo aggressive treatments, given their higher potential for complications, may be monitored more closely. The presence of residual symptoms, such as persistent pain or swelling, also directs the surveillance intensity.

Patient and clinician comfort is a nuanced yet essential aspect. Some patients may prefer more frequent check-ups for peace of mind, while others might find it anxiety-inducing. Tailoring surveillance to individual needs, balanced with evidence-based recommendations, is vital.

The overarching aim is to strike a balance between thoroughness and patient well-being. Over-surveillance may lead to unnecessary interventions, elevated healthcare costs, and undue anxiety. On the other hand, infrequent monitoring can miss early signs of recurrence. Thus, surveillance should be patient-centric, evidence-guided, and continuously evolving based on the latest research and individual patient progress.

Key Point

- HNSCC often re-emerges within 3 years, stressing early and robust post-treatment surveillance.
- The 2018 NI-RADS system standardizes HNSCC surveillance, while PET/CT is emerging as a valuable tool for differentiating post-treatment changes from recurrences.
- Surveillance must be tailored to individual patient needs and disease specifics, balancing evidence-based recommendations with patient well-being and comfort.

17.10 Neck Cancer of Unknown Primary (NCUP)

A challenging scenario in the realm of head and neck oncology is the diagnosis of cervical metastatic squamous cell carcinoma without an identifiable primary tumor, also known as NCUP. Approximately 3% of patients presenting with cervical lymphadenopathy, typically in the upper jugular chain, have no apparent primary tumor after a thorough clinical and radiographical evaluation [28].

The initial workup for NCUP involves a comprehensive clinical examination, office-based endoscopy, fine-needle aspiration (FNA) of the neck lymph node, and medical imaging. For a definitive diagnosis, operative panendoscopy with directed biopsies and palatine and/or lingual tonsillectomy are often required.

The HPV or EBV status obtained from the FNA sample is crucial, as over 90% of NCUP cases are related to HPV. Typically, HPV-related NCUP has its primary tumor in the base of the tongue and tonsillar fossa. Following this, EBV-related nasopharyngeal carcinoma is the next most common occult primary tumor. Advanced imaging, including CT, MRI, and PET/CT, often targets these areas for potential tumor detection in P16-positive cases (Fig. 17.7).

In contrast, a P16-negative status complicates the search. The primary tumor could be in numerous head and neck sites, or even more remotely in areas like the lungs. In these situations, a systematic and comprehensive evaluation is crucial.

PET/CT has a pivotal role in pinpointing unknown primaries. Particularly in the early stages, where anatomical changes may be subtle, the metabolic activity picked up by PET can guide the search.

When both advanced imaging and panendoscopy do not yield results, a "wait and watch" strategy might be adopted, especially if the lymph nodes have been surgically excised. Some primaries manifest later, while others never reveal themselves. The latter group, despite the mystery, often experiences favorable outcomes, paralleling those of known primary tumors.

Key Point

- NCUP denotes cervical metastatic squamous cell carcinoma where the primary tumor remains undetected.
- Most NCUP cases are HPV-related, often originating from the base of the tongue or tonsillar fossa.
- Advanced imaging (e.g., PET/CT) becomes instrumental in pinpointing these elusive primaries, especially given their metabolic activity.

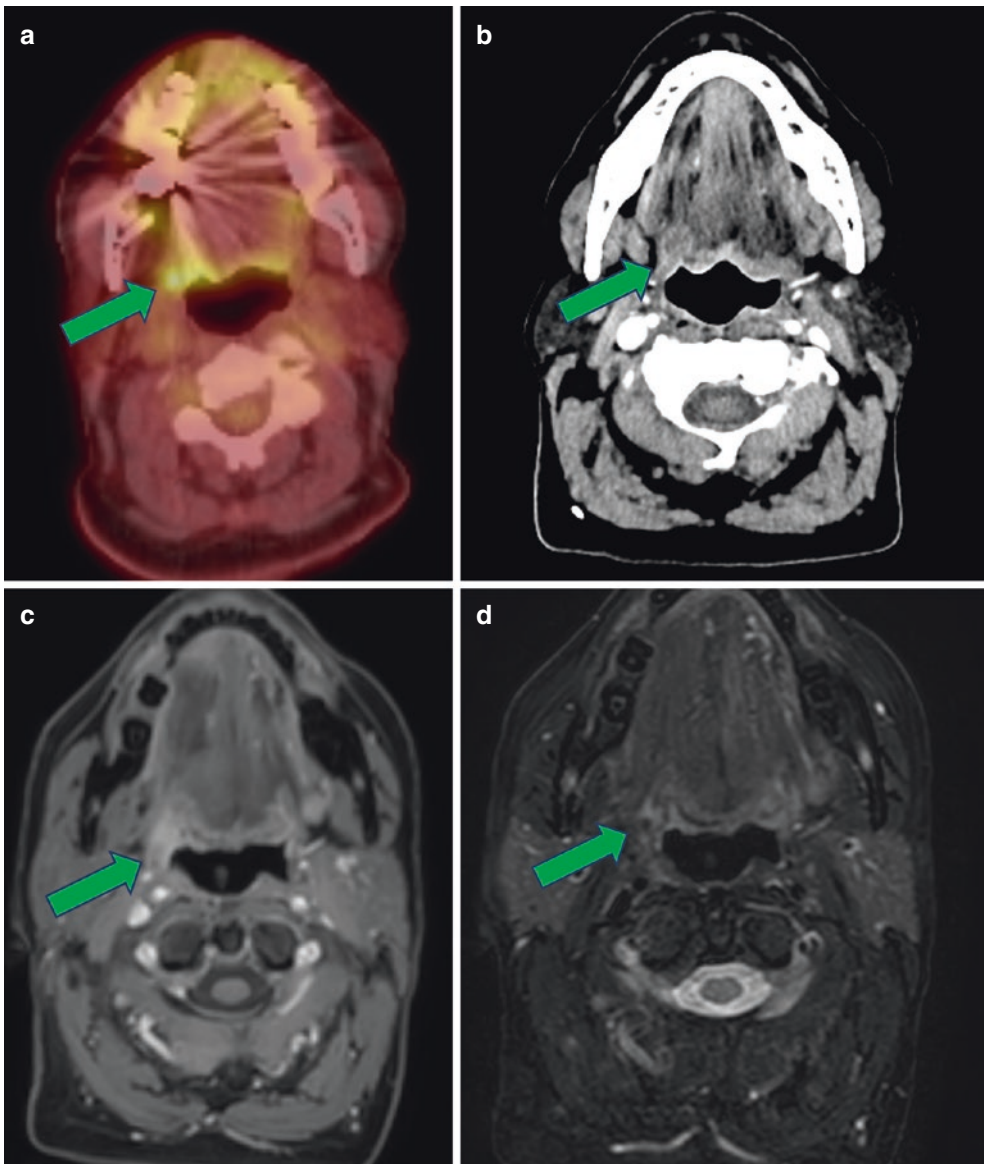

Fig. 17.7 Patient initially presented with right cervical lymphadenopathy with the biopsy showing p16-positive squamous cell carcinoma. PET-CT (**a**) shows a small focal FDG avidity at the right tongue base in keeping with the primary site of tumor. On the corresponding CT (**b**) and MRI (**c** and **d**), only subtle soft tissue thickening and enhancement are appreciated (green arrows)

17.11 Concluding Remarks

Radiologists play a central role in the management of HNSCC. Advanced imaging techniques, from PET/CT to MRI, are crucial for accurate diagnosis and staging. It is vital to recognize key upstaging features such as PNS and ENE as they have a significant bearing on treatment and outcomes. Familiarity with the AJCC/UICC eighth edition and its updates aids in consistent and accurate reporting. The challenge of HNSCC with an unknown primary highlights the importance of integrating imaging with markers like P16. Ultimately, radiologists provide essential insights that influence patient management decisions in HNSCC.

Take-Home Messages

- Advanced imaging techniques are central to the precise staging and surveillance of HNSCC, with modalities like PET/CT offering a comprehensive insight into tumor behavior and spread.
- The refined criteria in AJCC/UICC eighth edition highlight the importance of specific anatomical and molecular markers, such as P16 status, in dictating prognosis and guiding therapeutic strategies.
- Invasion into critical structures, like the paraglottic space or cartilage, significantly impacts the upstaging and prognosis of HNSCC.
- Cervical lymphadenopathy and perineural spread are pivotal factors influencing disease spread and patient outcomes, requiring meticulous evaluation.
- In the challenging realm of HNSCC with unknown primary, an integrated approach using advanced imaging, molecular markers, and endoscopy is imperative for accurate diagnosis and treatment planning.

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