Non–Squamous Cell Neoplasms of the Larynx: Radiologic-Pathologic Correlation[1]

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A variety of benign and malignant non-squamous cell neoplasms may affect the larynx. Most of these uncommon laryngeal neoplasms are located beneath an intact mucosa, making diagnosis difficult with endoscopy alone, and sampling errors may occur if only traditional superficial biopsies are performed. In some laryngeal neoplasms, radiologic evaluation allows the correct diagnosis. Hemangiomas have very high signal intensity at T2-weighted magnetic resonance (MR) imaging and strong enhancement at both computed tomography (CT) and MR imaging after administration of contrast material. Phleboliths, which are pathognomonic for hemangiomas, are easily identified at CT. Chondrogenic tumors typically manifest with coarse or stippled calcifications at CT. Because of their high water content, chondrogenic tumors have very high signal intensity on T2-weighted MR images, whereas only moderate enhancement is observed after administration of contrast material. Lipomas typically manifest at both CT and MR imaging as homogeneous nonenhancing lesions. They are isoattenuating to subcutaneous fat at CT and isointense relative to subcutaneous fat with all MR pulse sequences. Metastases from renal adenocarcinoma typically demonstrate strong contrast enhancement and flow voids at MR imaging, and metastases from melanotic melanoma usually have high signal intensity on T1-weighted MR images and low signal intensity on T2-weighted images owing to the paramagnetic properties of melanin. Although radiologic findings are nonspecific in most other non-squamous cell neoplasms of the larynx (eg, Kaposi sarcoma, hematopoietic tumors, tumors of the minor salivary glands, metastases from amelanotic melanoma), cross-sectional imaging can play an important role in the diagnostic work-up of these unusual tumors by delineating the extent of submucosal tumor spread and directing the endoscopist to the appropriate site for the deep, transmucosal biopsies needed to establish the diagnosis. In addition, CT and MR imaging are crucial for posttherapeutic monitoring and early detection of local recurrence.

Abbreviation: AIDS = acquired immunodeficiency syndrome

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■ INTRODUCTION

Although the vast majority of laryngeal neoplasms are squamous cell carcinomas, a variety of benign and malignant tumors of epithelial, neuroectodermal, and mesodermal origin may affect the larynx. Taken together, these tumors with unusual histologic features account for 2%–5% of all tumors originating from the larynx (1–5). Diagnosis and treatment of these tumors differ from those of squamous cell carcinoma in several respects. Squamous cell carcinoma usually manifests with obvious mucosal abnormalities and is therefore readily diagnosed with endoscopy, whereas many of the less common laryngeal tumors do not involve the mucosal surface and therefore necessitate deep, transmucosal biopsies at the site of the tumor mass to establish the correct diagnosis (6,7). As with squamous cell carcinoma, cross-sectional imaging is performed in these tumors to determine the extent of infiltration of the submucosal structures. In addition, cross-sectional imaging often plays a crucial role in determining the character of the tissue mass and guiding the endoscopist to the most appropriate biopsy site. Because it is usually impossible to differentiate primary mucosal from submucosal locations with imaging findings alone, clinical history and endoscopic findings should always be taken into consideration when interpreting computed tomographic (CT) and magnetic resonance (MR) images of the larynx. Normal mucosa at endoscopy and a mass at CT or MR imaging suggests either the presence of a tumor with unusual histologic features or a rare manifestation of a squamous cell carcinoma beneath intact mucosa. Squamous cell carcinoma that arises from the mucosa of the laryngeal ventricle may spread into the paraglottic space very early, invading both the supraglottic and glottic regions, and the small mucosal lesion within the ventricle may be overlooked at endoscopy (1,4,6). Thus, the tumor may manifest endoscopically as a submucosal bulge, and its true extent may be recognized only at CT or MR imaging. In our experience, however, this is the case in less than 0.5% of squamous cell carcinomas of the larynx. Therefore, when a tumor is seen at CT or MR imaging and the mucosa appears intact at endoscopy, non-squamous cell neoplasm is the most likely diagnosis. Cross-sectional imaging is also performed to evaluate for cervical metastatic adenopathy.

According to radiologic and pathologic records, 1,884 laryngeal tumors were seen at our three institutions between 1990 and 1997. Of these tumors, 1,844 (98%) were squamous cell carcinoma and 40 (2%) were uncommon histologic types. The latter were diagnosed in 33 males and seven females with a mean age of 49 years (range, 2 months to 87 years) and were malignant in 20 cases (50%) and benign in 20 cases (50%). Uncommon laryngeal neoplasms were subdivided into nine groups according to histologic type (Table).

Non–Squamous Cell Laryngeal Neoplasms Categorized by Histologic Type

Type of Neoplasm	No. of Patients
Vasoformative tumors	13 (32.5)
Chondrogenic tumors	8 (20.0)
Hematopoietic tumors	5 (12.5)
Salivary gland tumors	4 (10.0)
Tumors of fatty tissue	3 (7.5)
Metastases	3 (7.5)
Neurogenic tumors	2 (5.0)
Myogenic tumors	1 (2.5)
Fibrohistiocytic tumors	1 (2.5)
Total	40 (100.0)

Note.—Numbers in parentheses are percentages.

In this article, we describe the spectrum of imaging findings in rare laryngeal tumors, provide clinical and pathologic-anatomic correlation, and discuss the clinical role of CT and MR imaging in the pretherapeutic work-up of these unusual tumors. Because of space limitations, we discuss only the five most common groups of tumors among the non-squamous cell neoplasms encountered in our series. These include vasoformative tumors as well as tumors of the laryngeal skeleton, lymphoreticular system, minor salivary glands, and fatty tissue and metastases to the larynx. To our knowledge, the imaging features of some of these tumors have not been described in the literature.

■ VASOFORMATIVE TUMORS

According to Batsakis (5), vasoformative tumors of the head and neck may be classified as benign tumors, syndromes with vascular head and neck lesions, and malignant neoplasms. Benign tumors are classified as localized lesions (hemangioma, lymphangioma, angiofibroma), generalized or extensive lesions (angiomatosis), inflammatory lesions (granuloma pyogenicum), arteriovenous fistulas, phlebectasia, and teleangiectasia. Malignant neoplasms are classified as angiosarcoma (Kaposi sarcoma) and hemangiopericytoma. The exact nature of most benign variants, whether true neoplasms, tumorlike malformations, or responses to injury, remains controversial (1,5).

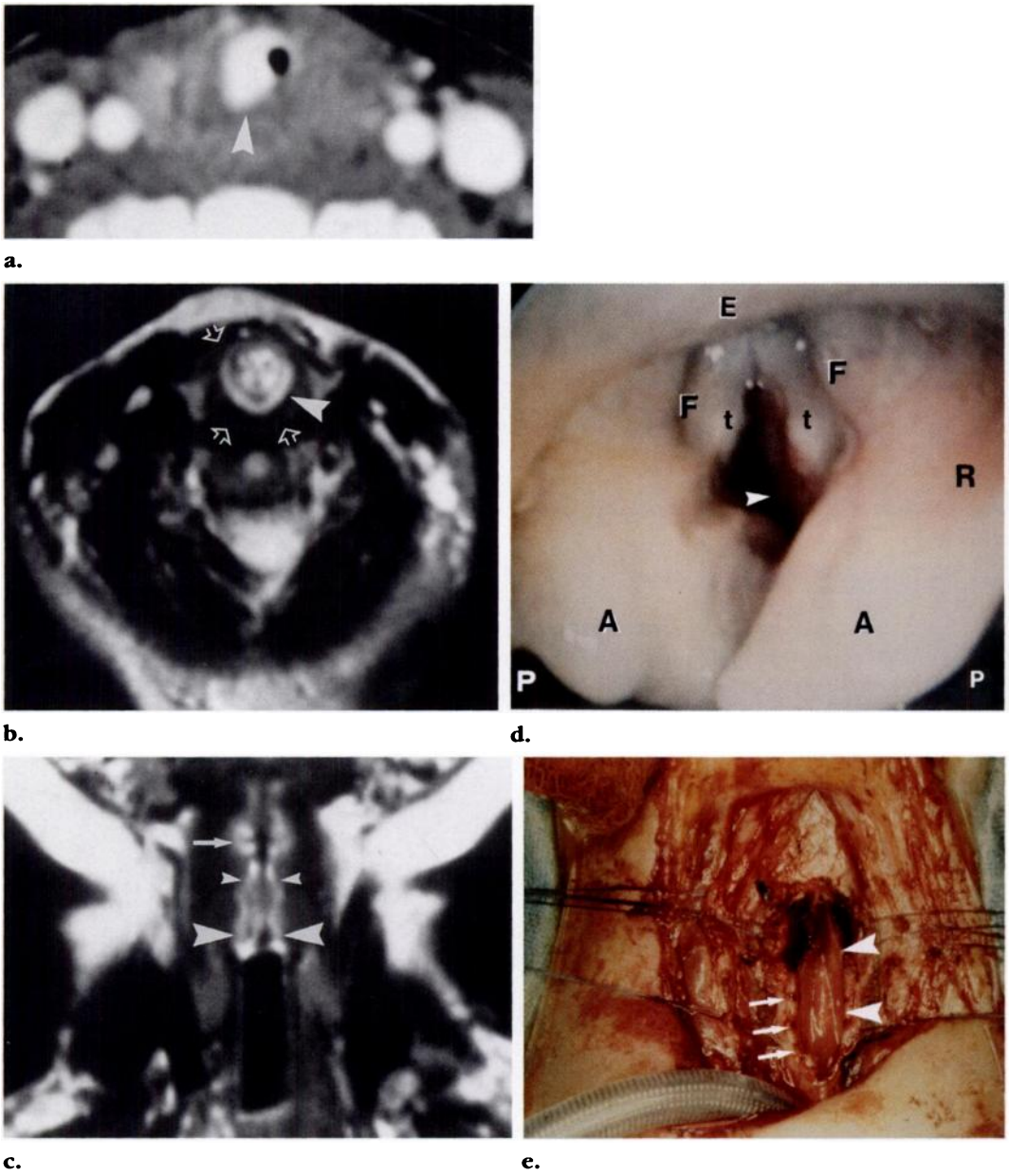
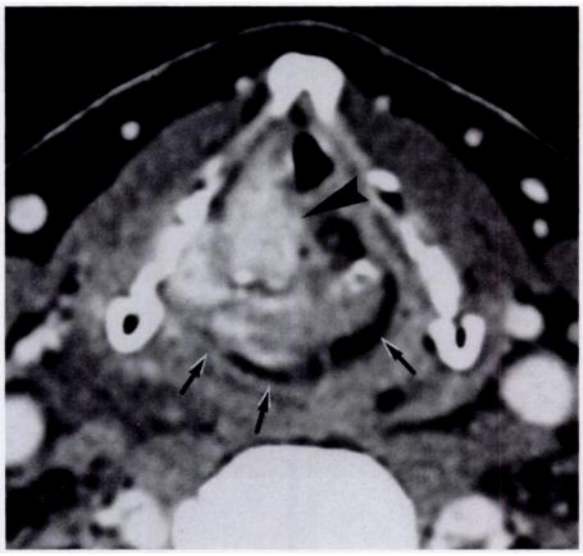


Figure 1. Infantile hemangioma in a 2-month-old girl with dyspnea. **(a)** Axial contrast material–enhanced CT scan demonstrates a strongly enhancing subglottic soft-tissue mass (arrowhead), characteristic of infantile hemangioma. **(b)** Axial T2-weighted spin-echo MR image demonstrates the high signal intensity typically observed in these lesions (arrowhead). Arrows indicate the cricoid ring. **(c)** Coronal contrast-enhanced T1-weighted MR image demonstrates involvement of the subglottis (small arrowheads) and cervical trachea (large arrowheads). Arrow indicates the right laryngeal ventricle. **(d)** Endoscopic image (rotated so that the patient's right side [*R*] is situated to the reader's right side) demonstrates a pale red subglottic mass beneath intact mucosa (arrowhead). The epiglottis (*E*) (located anteriorly) is seen at the top of the image; the piriform sinuses (*P*) (located posteriorly) are seen at the bottom of the image. *A* = aryepiglottic folds, *F* = false vocal cords, *t* = true vocal cords. **(e)** Intraoperative photograph shows extensive bilateral involvement of the subglottis and cervical trachea (arrowheads). Arrows indicate cartilaginous rings of the cervical trachea. The intraoperative findings corresponded to the craniocaudal involvement seen on the coronal MR image in **c**. Histologic analysis revealed infantile hemangioma.

• Hemangioma

Laryngeal hemangiomas have been subdivided into two groups: the infantile type and the adult type. Infantile hemangioma accounts for only 10% of all laryngeal hemangiomas, occurs in infants under the age of 6 months, and is twice as common in girls as in boys (4). It is usually located in the subglottic region (Fig 1).



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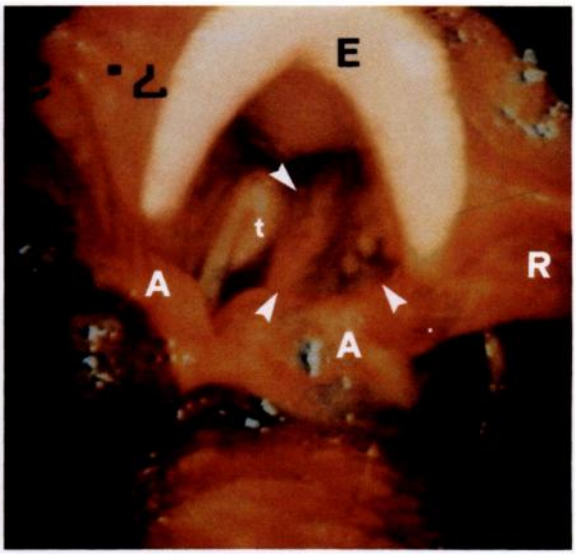
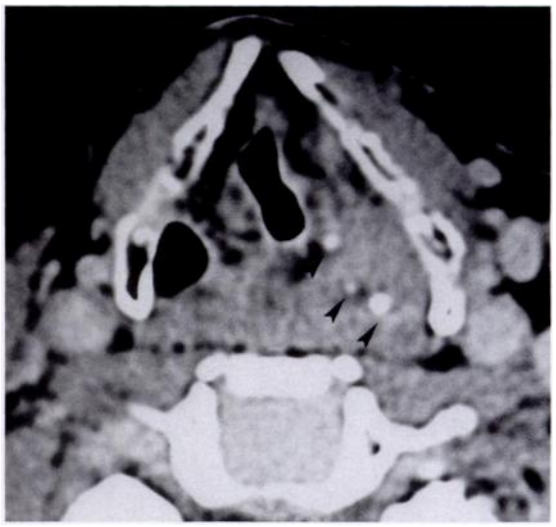


2b.

Figures 2, 3. **(2)** Localized adult hemangioma in a 58-year-old man who presented with hoarseness. **(a)** Axial CT scan obtained at the supraglottic level demonstrates a large, strongly enhancing mass involving the right false vocal cord (arrowhead). Arrows indicate the aryepiglottic folds. **(b)** Endoscopic image (rotated so that the patient's right side [*R*] is situated to the reader's right side) shows a dark red mass covered by intact mucosa (arrowheads). No treatment was administered. *A* = aryepiglottic folds, *E* = epiglottis, *t* = right true vocal cord. **(3)** Localized adult hemangioma with phleboliths in a 51-year-old man. Axial contrast-enhanced CT scan obtained at the supraglottic level demonstrates a moderately enhancing mass involving the left aryepiglottic fold and containing phleboliths (arrowheads), characteristic of hemangioma. Note the obliteration of the left piriform sinus. Findings from endoscopy and histologic analysis confirmed cavernous hemangioma. No treatment was administered.



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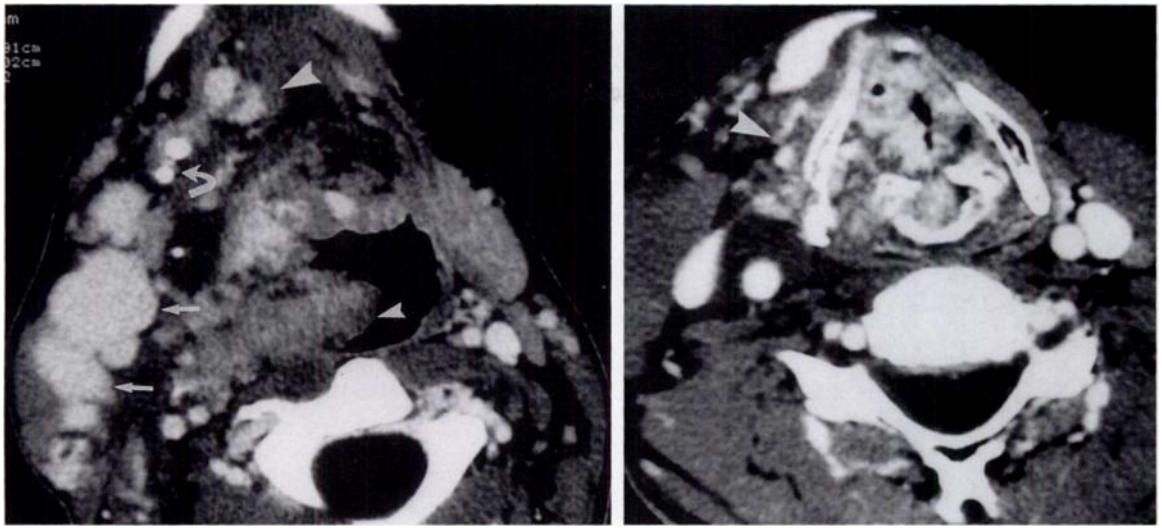
Dyspnea and stridor are the most common presenting symptoms. Adult hemangioma may manifest as an isolated, localized lesion in the supraglottic larynx (Figs 2, 3) or may be associated with extensive cervicofacial angiodysplasia (Fig 4). Men are affected more often than women.

Histologically, hemangiomas may be subdivided into cavernous and capillary types. Endoscopy shows a compressible soft swelling that is dark bluish-red or pale red in color (Figs 1, 2). The overlying mucosa is usually intact. Infantile hemangioma is treated with tracheostomy and allowed to regress spontaneously (8). Treatment options in adult hemangioma include laser excision, cryotherapy, and surgery in localized forms and selective embolization in diffuse forms (1,4).

In all 12 patients with laryngeal hemangioma in our series, the radiologic features were straightforward and allowed a correct diagnosis. At CT, hemangiomas enhance strongly after administration of contrast material, and phleboliths are pathognomonic for the cavernous type (Fig 3). At MR imaging, hemangiomas have very high signal intensity on T2-weighted images and enhance strongly after administration of gadolinium chelates, which allows a correct diagnosis in most cases. The differential diagnosis of highly vascularized laryngeal tumors includes paraganglioma and metastases of hypervascular tumors such as renal adenocarcinoma (discussed later). Laryngeal paragangliomas are neuroendocrine neoplasms arising



a. b.

Figure 4. Extensive cervicofacial angiodysplasia with laryngeal involvement in a 37-year-old man who presented with recurrent episodes of dyspnea. **(a)** Axial contrast-enhanced CT scan demonstrates cervicofacial angiodysplasia with involvement of the floor of the mouth (large arrowhead), right aryepiglottic fold (small arrowhead), and submandibular space (straight arrows). Curved arrow indicates phleboliths. **(b)** Axial contrast-enhanced CT scan obtained at a lower level shows extensive involvement of both vocal cords and strap muscles (arrowhead). The patient underwent selective embolization and partial laser excision of the endolaryngeal mass to reduce dyspnea.

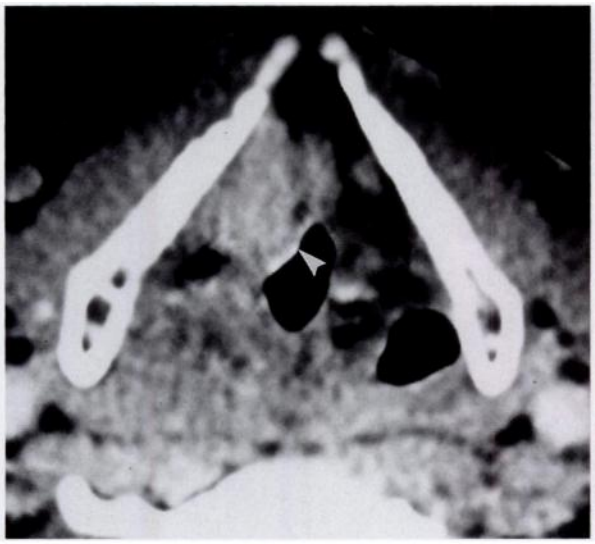
from the superior or inferior laryngeal paraganglia. These tumors are three times more common in women than in men. However, they occur only rarely in the larynx, with less than 40 cases reported to date (1). Paragangliomas typically display multiple curvilinear areas of signal void on both T1- and T2-weighted MR images. The conspicuity of these signal void areas increases with tumor size.

The characteristic histologic findings in hemangioma are hollow, blood-filled cavernous spaces with an endothelial lining (5).

• Kaposi Sarcoma

Kaposi sarcoma is considered an unusual multifocal, neoplastic disease of the vascular system (5). Rarely does it involve the larynx. The disease was rare in Europe and the United States until recently (9) but has become more common in association with acquired immunodeficiency syndrome (AIDS). Three forms of Kaposi sarcoma are recognized: classic Kaposi sarcoma affecting men of Mediterranean origin in their seventh decade, Central African Kaposi sarcoma, and AIDS-related Kaposi sarcoma. Currently, the most frequently encountered form of Kaposi sarcoma is associated with AIDS. Most patients with laryngeal Kaposi sarcoma, regardless of whether they test positive for human immunodeficiency virus, present with multiple classic skin lesions. Thus, involvement of the larynx is to be expected only in the late stages of the disease when diagnosis has been made from the skin lesions. The most common location of Kaposi sarcoma in the larynx is the epiglottis. The clinical course of Kaposi sarcoma is variable. Elderly patients with classic Kaposi sarcoma may live for many years, and rarely does death occur as a direct result of the tumor (9); complete regression of laryngeal involvement with low doses of interferon alfa-2b has been reported recently in these patients (10). Central African Kaposi sarcoma involving the larynx is usually rapidly fatal. AIDS-related Kaposi sarcoma usually affects the larynx at a late stage when lymph nodes and viscera are already involved (Fig 5). In such patients, Kaposi sarcoma is usually associated with a high prevalence of lymphomas (4,5). The prognosis is usually very poor.

At CT and MR imaging, Kaposi sarcoma may display relatively strong enhancement after administration of contrast material (Fig 5). Although radiologic findings may be nonspecific, the presence of an intensely enhancing submucosal laryngeal mass in association with multiple characteristic skin lesions strongly suggests the diagnosis of Kaposi sarcoma.



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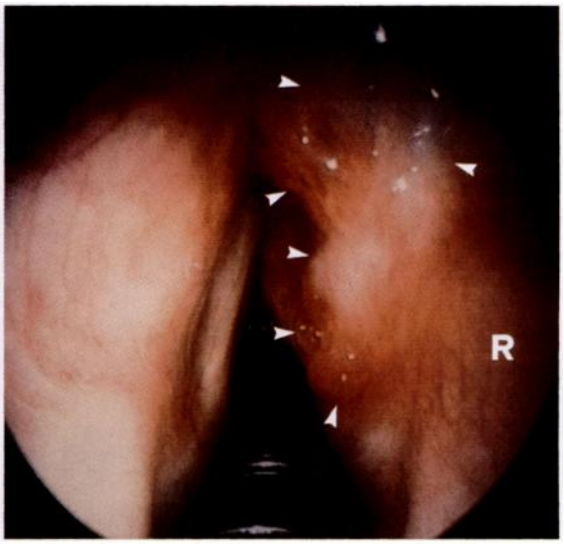

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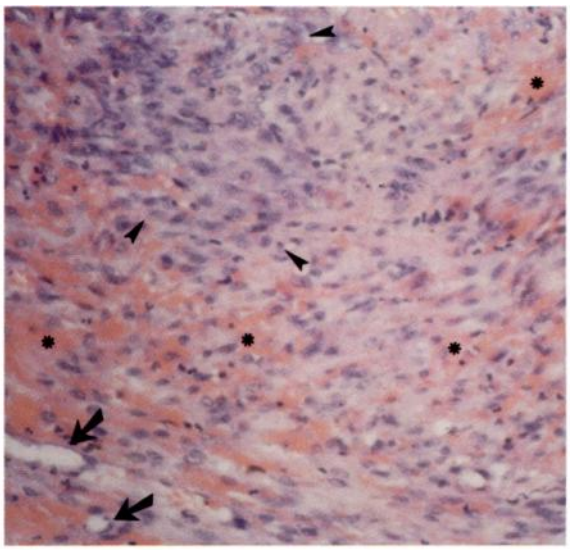
Figure 5. AIDS-related laryngeal Kaposi sarcoma in a 24-year-old man with human immunodeficiency virus who presented with dyspnea and the multiple bluish-red, slightly elevated skin lesions characteristic of cutaneous Kaposi sarcoma. **(a)** Axial contrast-enhanced CT scan obtained at the supraglottic level demonstrates a relatively strongly enhancing mass involving the right false vocal cord (arrowhead). **(b)** Endoscopic image (rotated so that the patient's right side [*R*] is situated to the reader's right side) shows a bluish-red nodular lesion involving the right false vocal cord covered by intact mucosa (arrowheads). **(c)** High-power photomicrograph (original magnification, ×100; hematoxylin-eosin stain) demonstrates the characteristic features of Kaposi sarcoma: spindle cells with considerable pleomorphism (arrowheads), vascular channels of varying size (arrows), and extensive extravasation of erythrocytes (*). The patient underwent intratumoral injection of cytotoxic drugs.

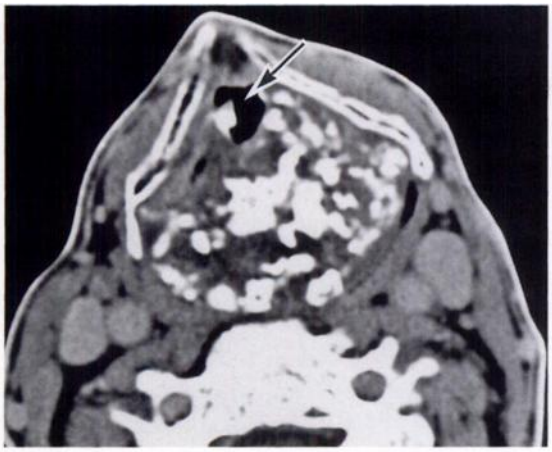


c.

At gross examination, the neoplasm appears as a nodular or pedunculated mass and is covered by intact or ulcerated mucosa. Kaposi sarcoma may be darkly stained and thus confused with melanoma. At histologic analysis, the tumor is composed of spindle cells and vascular channels lined with abnormal spindle cells (5). The stroma is infiltrated by chronic inflammatory cells and large deposits of hemosiderin pigment because of considerable hemorrhage. Extravasation of erythrocytes is frequently seen (Fig 5).

■ TUMORS OF THE LARYNGEAL SKELETON

Cartilaginous and osteogenic neoplasms of the larynx include chondroma, chondrosarcoma, and osteosarcoma. Chondrosarcoma is the most common sarcoma of the larynx (1,4). Approximately 200 cases of laryngeal chondrosarcoma have been reported in the literature (1,4,11–19), but only a few cases were documented with CT or MR imaging (15–17). Laryngeal chondrosarcoma predominantly affects men between 50 and 70 years of age. Between 50% and 70% of all laryngeal chondrosarcomas originate from the posterior lamina of the cri-



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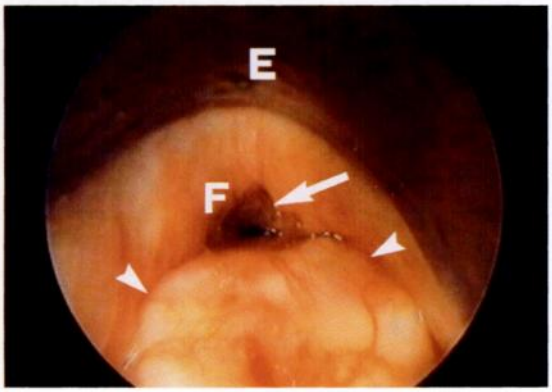

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Figure 6. Chondrosarcoma of the cricoid cartilage in a 70-year-old man who presented with dyspnea and dysphagia. **(a)** Axial contrast-enhanced CT scan shows a large, hypoattenuating mass with coarse calcifications, characteristic of chondrosarcoma. The mass arises from the cricoid cartilage and leads to significant airway obstruction (arrow). **(b)** Endoscopic image (rotated so that the patient's right side is situated to the reader's right side) shows that the large tumor mass (arrowheads) is covered by intact mucosa. Note the significant airway obstruction (arrow). The mass arising from the cricoid cartilage is seen at the bottom of the image. *E* = epiglottis, *F* = false vocal cord. Histologic analysis revealed low-grade chondrosarcoma.

coid cartilage, whereas 20%–35% originate from the thyroid cartilage (12). Laryngeal chondrosarcoma manifests as a lobulated, submucosal mass covered by intact laryngeal mucosa (Fig 6). Typically, it is locally invasive; distant metastases of this tumor are unusual. Surgery is regarded as the treatment of choice and is increasingly performed as a function-preserving laryngeal resection (19). Tumor recurrence may be seen 10 years or more after local excision or partial laryngectomy (12,14,19). Radiologic evaluation is essential for surgical planning and for monitoring those patients who have undergone function-preserving surgery for local recurrence (1,4,19).

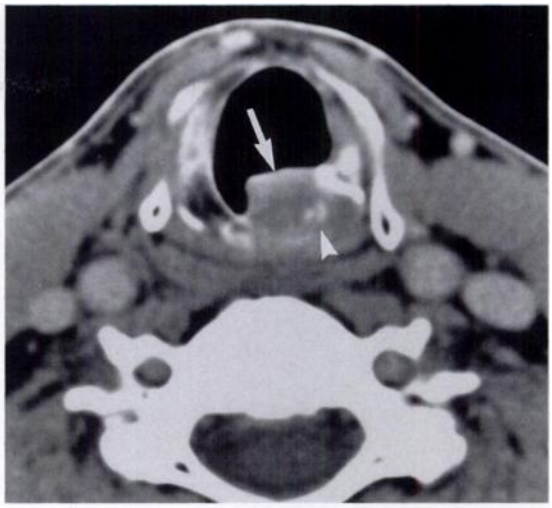
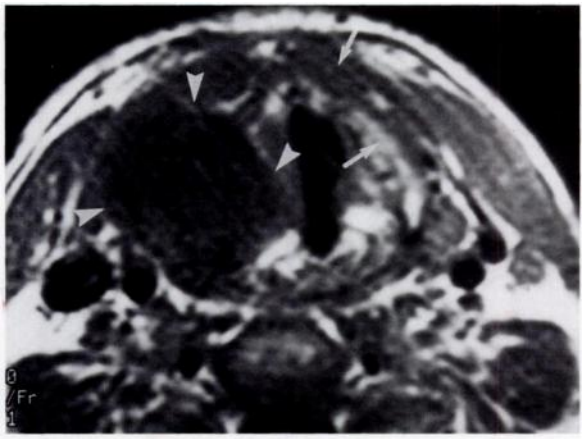


Figure 7. Chondroma of the cricoid cartilage in a 57-year-old man who presented with a foreign body sensation. Axial contrast-enhanced CT scan demonstrates a hypoattenuating tumor arising from the cricoid cartilage (arrow). The mass has stippled intratumoral calcifications (arrowhead), characteristic of a chondrogenic tumor. Histologic analysis revealed benign chondroma. The patient refused surgery and has been followed up with CT. Serial CT examinations performed over a 7-year period have shown no change.

Coarse or stippled intratumoral calcifications are highly suggestive of the chondrogenic nature of the mass (Fig 6). CT may not only show very subtle intratumoral calcifications but also helps define the exact anatomic origin of the tumor (15,17,18). However, there are no reliable CT criteria that enable differentiation between chondrosarcoma and benign chondroma (Fig 7). As in chondrogenic tumors in other locations, the tumor matrix of laryngeal chondrosarcoma has very high signal intensity on T2-weighted MR images, corresponding to hyaline cartilage with its low cellularity and high water content (Fig 8). Small areas of low



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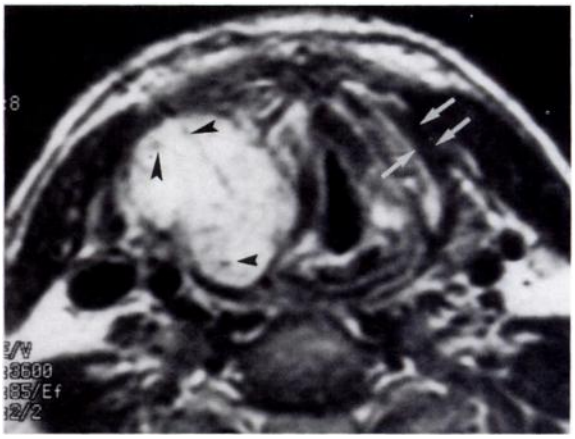

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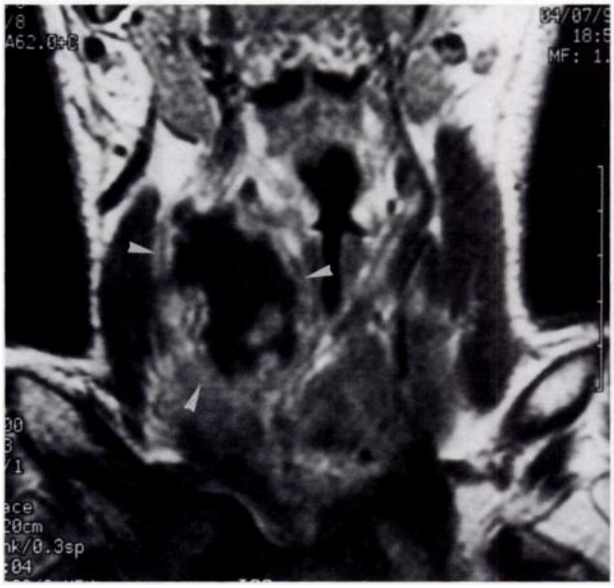

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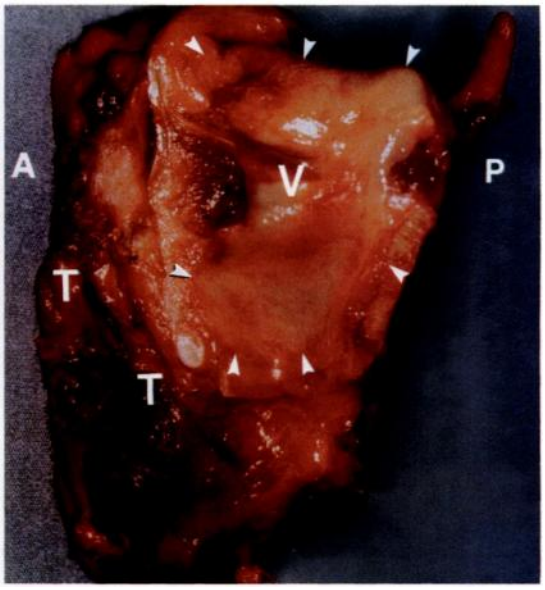

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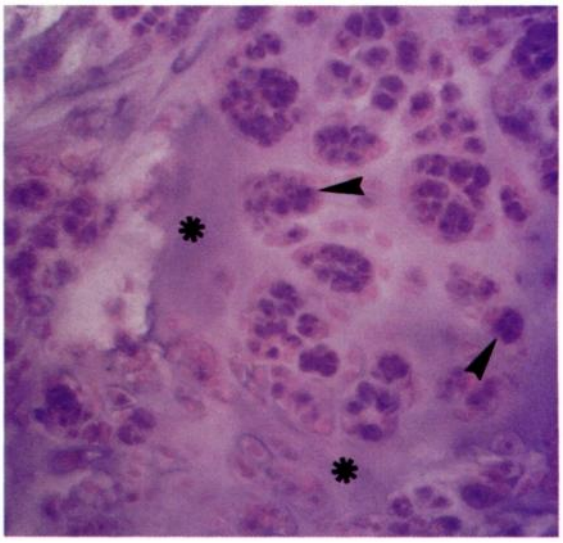

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signal intensity on T1- and T2-weighted images correspond to stippled calcifications; however, these findings are not as well demonstrated at MR imaging as at CT. Although the injection of gadolinium chelates may lead to diffuse central or peripheral enhancement, these findings are nonspecific in that they do not help differentiate low-grade chondrosarcoma from benign chondroma (16). The diagnosis of laryngeal chondrosarcoma can therefore be strongly suspected at MR imaging or CT, although it must be confirmed with deep biopsy.

Histologically, chondrosarcomas are characterized as low-grade (grade 1), medium-grade (grade 2), or high-grade (grade 3) (5). Grade 1 chondrosarcoma consists of large amounts of basophilic or metachromatic matrix and few cells with small nuclei. Binucleated and multinucleated cells may be found, but mitoses are usually absent (Fig 8). Grade 2 chondrosarcoma shows an increased cellularity, and mitoses are scarce. Grade 3 chondrosarcoma shows marked cellularity and plump binucleated and multinucleated cells, and mitoses are frequently seen. In several reported cases, differentiation between low-grade chondrosarcoma and benign chondroma has been difficult (1,2,15). This is because laryngeal chondrosarcomas often manifest as areas with varying degrees of differentiation so that only a sizable biopsy specimen provides a reliable diagnosis. Therefore, it has been suggested that the biopsy specimen be obtained with the patient under general anesthesia and a preliminary tracheotomy be performed to obtain easier access to the lesion, or that biopsy be performed under CT guidance (1,4,14).

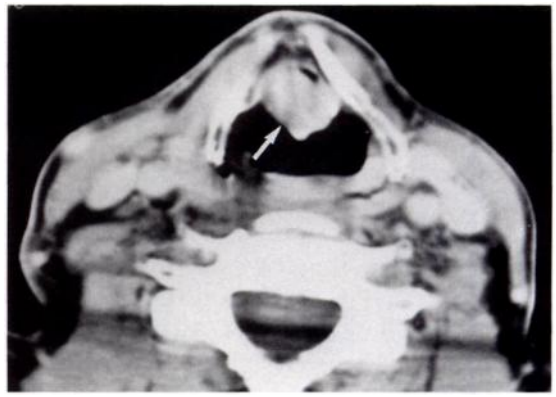
■ TUMORS OF THE LYMPHORETICULAR SYSTEM

Tumors of the lymphoreticular system include Hodgkin and non-Hodgkin lymphoma, plasmacytoma, leukemia, and pseudolymphoma. Although about 30% of all malignant lymphomas arise in the head and neck (cervical lymph nodes and Waldeyer ring), lymphomas of the larynx, either in isolation or as a manifestation of generalized disease, are rare (4).

• Plasmacytoma

Plasma cell neoplasms are characterized by monoclonal growth forming one of the two immunoglobulin light chains (κ or λ). Plasma cell neoplasms may manifest as multiple myeloma, solitary plasmacytoma of bone, or extramedullary plasmacytoma (1,2). Of the 350 reported plasmacytomas of the head and neck, about 80 were located in the larynx (1). Plasmacytoma of the larynx occurs predominantly in men between 50 and 70 years of age and involves the epiglottis and the true and false vocal cords (1,2,20–23). Endoscopy reveals a pedunculated or slightly prominent mass that bleeds easily; the mucosa above the tumor is usually intact (Fig 9). Approximately 40% of extramedullary plasmacytomas terminate in osseous and soft-tissue dissemination (22). Treatment may consist of surgical excision or radiation therapy in localized disease or chemotherapy in disseminated disease.

◀ **Figure 8.** Chondrosarcoma of the thyroid cartilage in a 47-year-old man who presented with a hard lump in the neck. **(a)** Axial T1-weighted MR image obtained at the glottic level shows a lobulated, low-signal-intensity mass arising from the right thyroid lamina (arrowheads). The left thyroid lamina (arrows) appears normal. **(b)** Axial T2-weighted MR image shows the tumor mass with very high signal intensity, indicating high water content. The hypointense areas within the tumor (arrowheads) correspond to intratumoral calcifications. The left thyroid lamina (arrows) appears normal. **(c)** Coronal contrast-enhanced T1-weighted MR image shows the tumor with moderate peripheral enhancement (arrowheads). Note the extramucosal tumor location. The patient underwent voice-preserving laryngeal resection. **(d)** Photograph of the gross specimen obtained at extended vertical hemilaryngectomy shows intact laryngeal mucosa (arrowheads). *A* = anterior, *P* = posterior, *T* = tumor, *V* = laryngeal ventricle. **(e)** High-power photomicrograph (original magnification, ×100; hematoxylin-eosin stain) shows low-grade chondrosarcoma in a lobular growth pattern with multinucleated chondrocytes (arrowheads) surrounded by chondroid intercellular substance (*). The patient is free of recurrence 5 years later.



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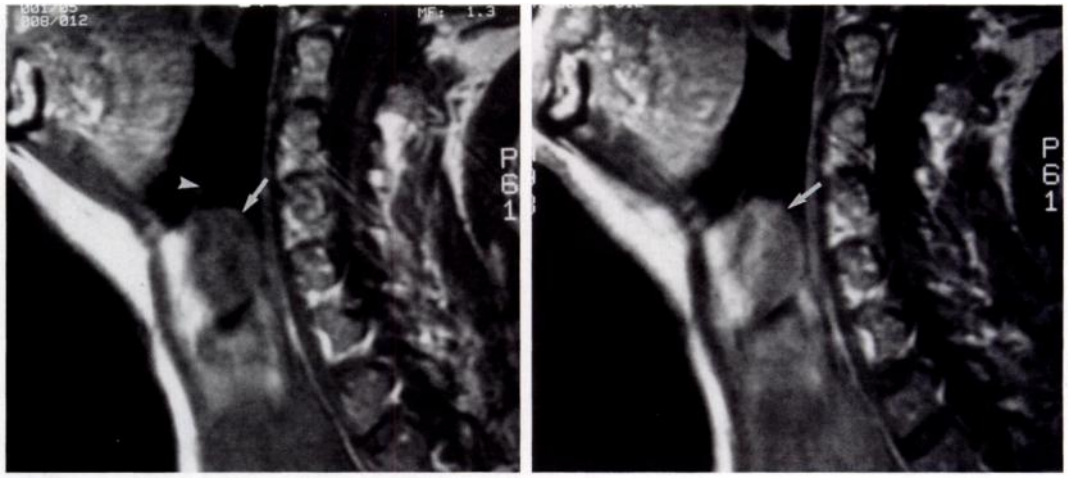

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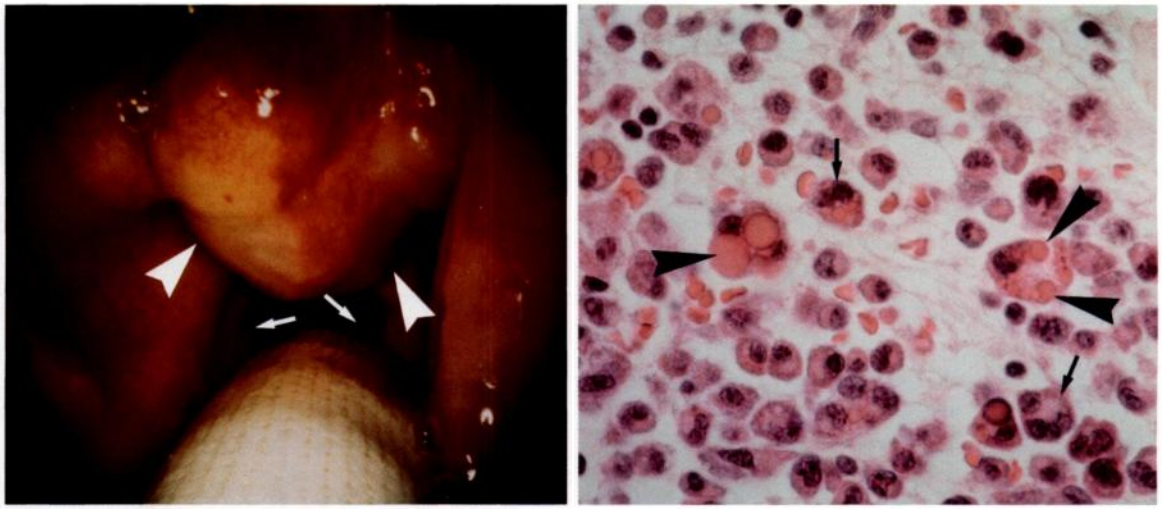
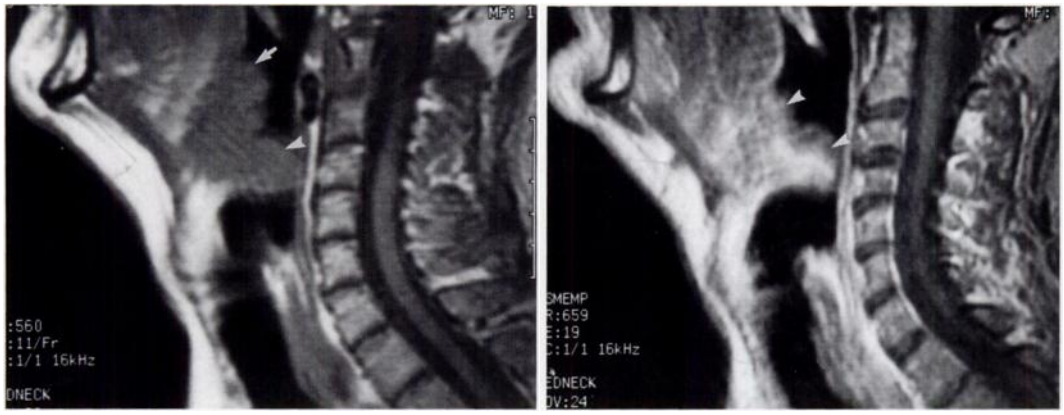


d. e.

Figure 9. Laryngeal plasmacytoma in a 71-year-old man who presented with dyspnea. **(a)** Axial contrast-enhanced CT scan shows a large, smoothly marginated epiglottic tumor without evidence of ulceration or necrosis (arrow). **(b)** Sagittal T1-weighted MR image shows an oval tumor mass with intermediate signal intensity arising from the laryngeal epiglottic surface (arrow). Arrowhead indicates the suprahyoid epiglottis. **(c)** Sagittal contrast-enhanced T1-weighted MR image shows moderate, slightly inhomogeneous enhancement of the mass (arrow). **(d)** Endoscopic image shows that the mass arising from the laryngeal surface of the epiglottis is covered by intact mucosa (arrowheads). Arrows indicate the normal-appearing true vocal cords. **(e)** High-power photomicrograph (original magnification, ×400; hematoxylin-eosin stain) shows abundant binucleated plasma cells (arrows) with mostly intracellular immunoglobulin deposits (Russell bodies) (arrowheads). The patient underwent endoscopic resection. Four years later, he developed tumor recurrence at the same site. Repeat endoscopic surgery was performed successfully, and the patient is free of recurrence 1 year later.

Figure 10. Plasma cell granuloma in a 58-year-old man who presented with dyspnea. **(a)** Sagittal T1-weighted MR image shows a large, L-shaped tumor mass with low signal intensity involving the epiglottis (arrowhead) as well as the base of the tongue (arrow). **(b)** Sagittal contrast-enhanced T1-weighted MR image obtained at the same level shows the tumor with strong, homogeneous enhancement without evidence of large necrotic areas or gross ulceration (arrowheads). At endoscopy, a large, ill-defined, yellow mass was seen arising from the epiglottis. The tumor mass was covered by intact laryngeal mucosa. The mucosa covering the base of the tongue also appeared intact. **(c)** High-power photomicrograph (original magnification, ×100; hematoxylin-eosin stain) shows plasma cell-rich tumorlike tissue with intermingled lymphocytes infiltrating the basal portion of the overlying squamous epithelium (arrows). The patient underwent radiation therapy combined with steroid therapy and is free of recurrence 4½ years later.



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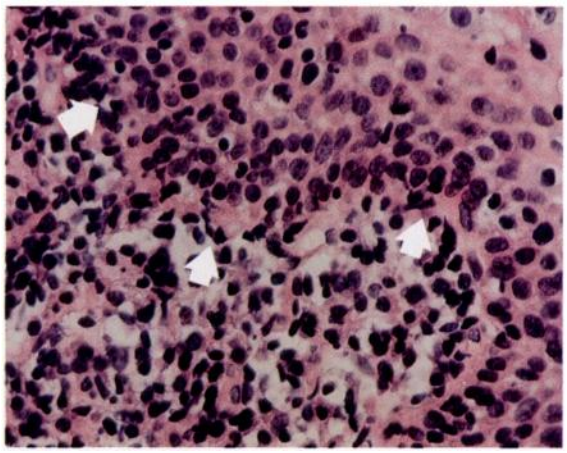


c.

At CT, the tumor manifests as a large, smoothly marginated, homogeneous mass without significant contrast enhancement or evidence of necrosis or gross ulceration (23) (Fig 9). The typical MR imaging appearance of laryngeal plasmacytoma is also demonstrated in Figure 9. Because the radiologic findings were nonspecific, the major role of CT and MR imaging in the management of the four patients in our series with plasmacytoma was to demonstrate the submucosal extent of the lesion and to follow up the patients postoperatively. One patient developed submucosal tumor recurrence, which was detected at cross-sectional imaging.

At light microscopy, the hallmark of the neoplasm is large sheets of uniform cells replacing the infiltrated tissue, many of the tumor cells being indistinguishable from normal plasma cells (Fig 9). Marked amyloid deposition is seen in over 20% of extramedullary plasmacytomas (2). Without immunohistochemical analysis, extramedullary plasmacytoma may be difficult to distinguish from plasma cell granuloma or nodular amyloidosis (2,21).

• Plasma Cell Granuloma

Plasma cell granuloma is a rare, benign pseudotumor that was first described in 1973 (24). Less than five cases of plasma cell granuloma of the larynx have been reported to date (25, 26). Plasma cell granuloma affects individuals of all ages and is most commonly encountered in the lung, gastrointestinal tract, and salivary glands (27). The cause is uncertain, although a hypersensitivity reaction has been suggested (24). In the larynx, the tumor manifests endoscopically as a submucosal mass covered by an intact laryngeal mucosa. Treatment options include steroid therapy alone or in combination with radiation therapy.

In the patient in our series with plasma cell granuloma, the tumor manifested as a large, homogeneous submucosal mass involving the epiglottis, the base of the tongue, and the aryepiglottic folds and showed significant contrast enhancement at MR imaging (Fig 10).

Histologically, plasma cell granuloma is characterized by a polyclonal infiltration of normal plasma cells mixed with other inflammatory cells such as lymphocytes, histiocytes, and neutrophils (Fig 10) and by the presence of epithelial cell granulomas of the nonnecrotizing type (27). The plasma cells show no cytologic abnormality. The differential diagnosis must be made from monoclonal neoplastic lesions such as multiple myeloma and solitary plasmacytoma (21). The use of various techniques of immunohistochemical analysis allows determination of the polyclonal nature of the plasma cells in plasma cell granuloma (21,26).

■ TUMORS OF THE MINOR SALIVARY GLANDS

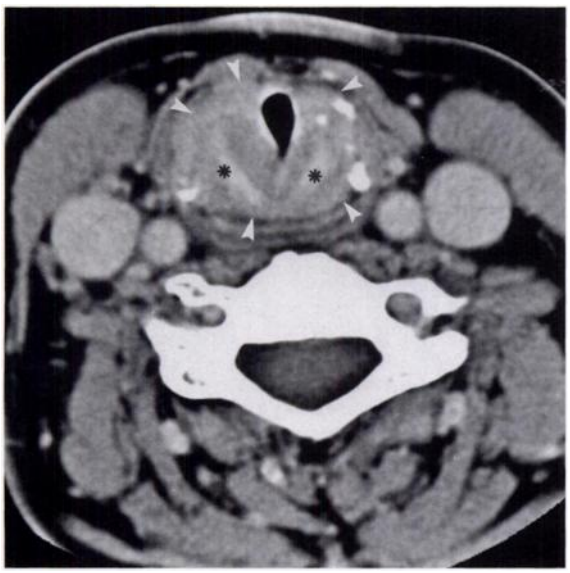
Numerous minor salivary glands are distributed throughout the larynx, particularly in the supraglottic and (to a lesser extent) the subglottic region. All known types of benign and malignant salivary gland tumors may arise from the epithelium of these glands, the most common being pleomorphic adenoma, adenoid cystic carcinoma, mucoepidermoid carcinoma, and adenocarcinoma (1,4,5).

• Adenoid Cystic Carcinoma

Adenoid cystic carcinoma (cylindroma) is the most common tumor of the minor salivary glands (1,4). In the upper air and food passages, adenoid cystic carcinoma affects (in order of decreasing frequency) the oral cavity and pharynx, the nose and paranasal sinuses, the trachea, and the larynx. Various series have shown that adenoid cystic carcinoma accounts for only 0.25%–1% of all malignant laryngeal tumors (4,28). The cause of adenoid cystic carcinoma is unknown, but the tumor is not related to smoking. Unlike most malignant laryngeal tumors seen more commonly in males, adenoid cystic carcinoma has no significant sex predilection. About 80% of adenoid cystic carcinomas of the larynx lie in the subglottis, typically at the junction with the trachea (1,4). The tumor often invades the entire larynx submucosally and infiltrates the thyroid gland and the esophagus. Symptoms of subglottic adenoid cystic carcinoma of the larynx include coughing attacks, wheezing, and occasionally hemoptysis. Pain may be a prominent symptom due to the propensity of the tumor to invade nerves. Paralysis of the recurrent laryngeal nerve is a characteristic feature and usually begins unilaterally but later affects both sides. Patients with adenoid cystic carcinoma generally survive longer than those with squamous cell carcinoma. The average survival time is 8 years but may be as long as 15–18 years (29). Regional metastases to the cervical lymph nodes are rare; however, metastases to the lungs, bone, and brain almost always occur in the terminal stage. Treatment options in laryngeal adenoid cystic carcinoma include surgery and a combination of radiation therapy and chemotherapy.

Both CT and MR imaging usually display extensive submucosal tumor spread at the time of diagnosis (Fig 11). Typically, the predominantly subglottic tumor has already invaded the cricoid cartilage and the thyroid gland, and the radiologic features of recurrent laryngeal nerve paralysis may be identified at CT or MR imaging. These features include an enlarged ventricle, ipsilateral enlargement of the piriform sinus, and a paramedian position and fatty infiltration of the true vocal cords. Signal intensity at MR imaging and patterns of contrast enhancement at CT and MR imaging are nonspecific and do not allow differentiation of adenoid cystic carcinoma from other types of tumors. Nevertheless, low signal intensity on T2-weighted MR images appears to correspond to highly cellular tumors (solid subtype, grade 3) with a poor prognosis, whereas high signal intensity on T2-weighted images appears to correspond to less cellular tumors (cribriform or tubular subtype, grades 1 and 2) with a better prognosis (30). Although the imaging findings in laryngeal adenoid cystic carcinoma are nonspecific, the diagnosis may be suspected in white women with no history of cigarette smoking who have a primary submucosal subglottic tumor and no cervical lymph node metastases.

Endoscopy typically shows a tumor beneath an intact mucosa. Histologically, the tumor is composed of uniform small, basaloid cells with large, deeply staining ovoid nuclei arranged in anastomosing cords or islands (4,5,30) (Fig 11). Sharply defined cylindrical cores of mucoid or hyaline material create a characteristic cribriform, pseudocystic appearance (cribriform subtype, grade 1). The hyaline material within and around the pseudocystic spaces consists mainly of proteoglycans. Occasionally, the tumor consists of tubules or trabeculae (tubular subtype, grade 2) or solid nests (solid or basaloid type, grade 3) (Fig 11). The tendency for perineural infiltration is a typical histologic finding in all types of adenoid cystic carcinoma (4).



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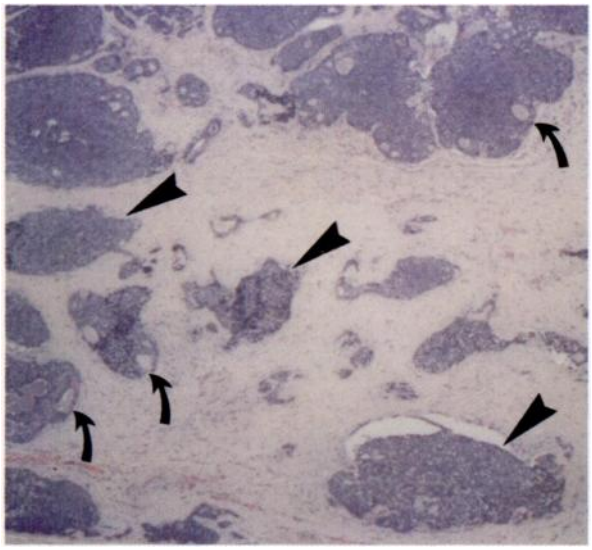

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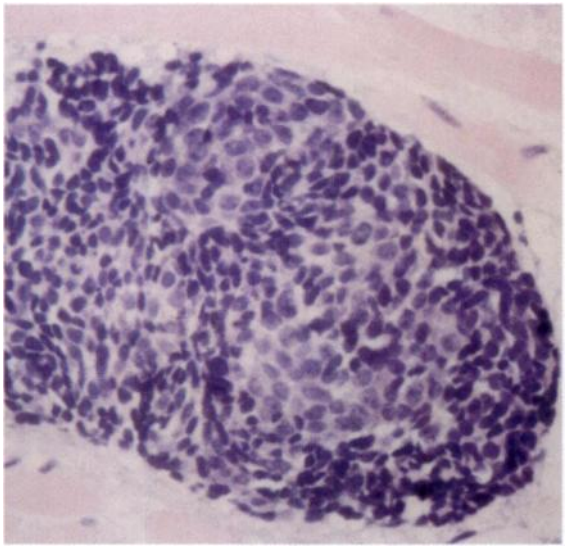
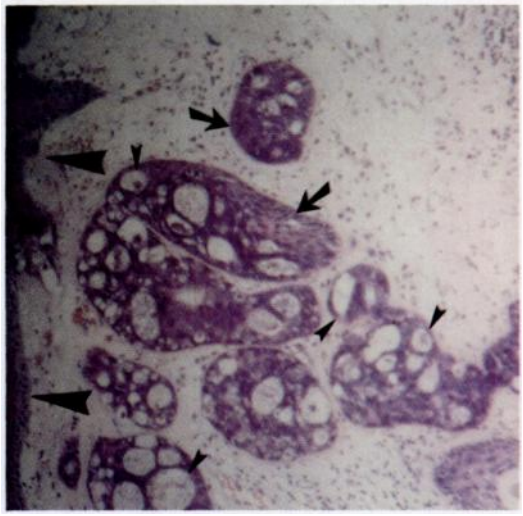


c.

Figure 11. Adenoid cystic carcinoma in a 51-year-old woman with no history of tobacco or alcohol consumption who presented with dyspnea and stridor that had been increasing over the past 3 months. Endoscopy revealed subglottic narrowing with normal-appearing mucosa. Results of endoscopic biopsy of the subglottis were negative. **(a)** Axial CT scan obtained prior to endoscopy demonstrates a large primary subglottic tumor extending beyond the larynx (arrowheads) and invading the cricoid cartilage (*). No cervical lymph node metastases were seen at CT. Because the results of repeat endoscopic biopsies were negative, external surgical biopsy was performed. **(b)** Low-power photomicrograph (original magnification, ×50; hematoxylin-eosin stain) of a biopsy specimen obtained at the subglottic level demonstrates tumor cells mainly arranged in solid nests (arrowheads), suggestive of grade 3 adenoid cystic carcinoma. Occasionally, variable-sized cribriform spaces (arrows) are seen. **(c)** High-power photomicrograph (original magnification, ×400; hematoxylin-eosin stain) of a biopsy specimen taken from the strap muscles confirms the extralaryngeal spread seen at CT and demonstrates uniform small, basaloid cells with large nuclei and scanty, indistinct cytoplasm, characteristic of grade 3 adenoid cystic carcinoma. Further radiologic investigation revealed osseous and hepatic metastases. The patient underwent palliative chemotherapy and died 1 year later of disseminated disease.

Figure 12. Mucoepidermoid carcinoma in a 59-year-old man who presented with dyspnea. The patient had undergone surgical excision of a small mucoepidermoid carcinoma of the subglottis 12 years earlier. Endoscopy revealed a subglottic bulge beneath intact mucosa. **(a)** Axial contrast-enhanced CT scan obtained at the level of the subglottis demonstrates a left-sided mass (arrowhead) with invasion of the cricoid cartilage (arrows); the lesion was radiologically indistinguishable from squamous cell carcinoma. Note also the extensive sclerosis of the cricoid cartilage caused by the proximity of the tumor. **(b)** Low-power photomicrograph (original magnification, ×50; hematoxylin-eosin stain) demonstrates tumor cells beneath intact overlying squamous epithelium (large arrowheads). The tumor has solid areas composed of squamous cells (arrows) and microcystic spaces containing mucous secretions (small arrowheads). **(c)** High-power photomicrograph (original magnification, ×400; Alcian blue stain) demonstrates a mixture of mucin-secreting cells with intracellular mucin goblets (arrowheads) and cells of intermediate type (arrows), characteristic of mucoepidermoid carcinoma. The patient underwent total laryngectomy, and histologic analysis confirmed invasion of the cricoid cartilage by mucoepidermoid carcinoma. The patient is free of recurrence 4 years later.



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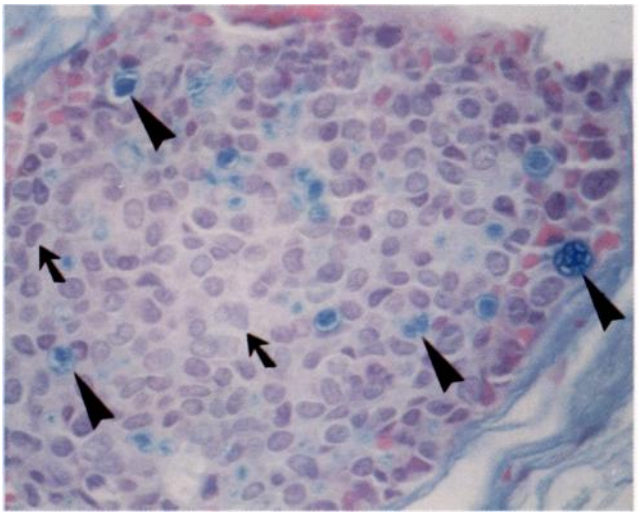

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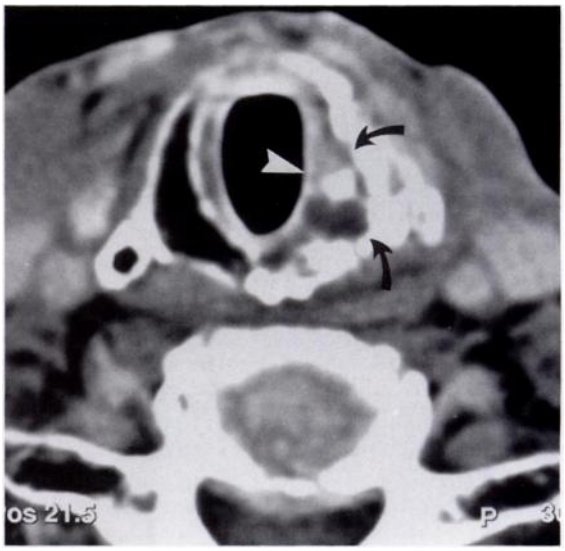


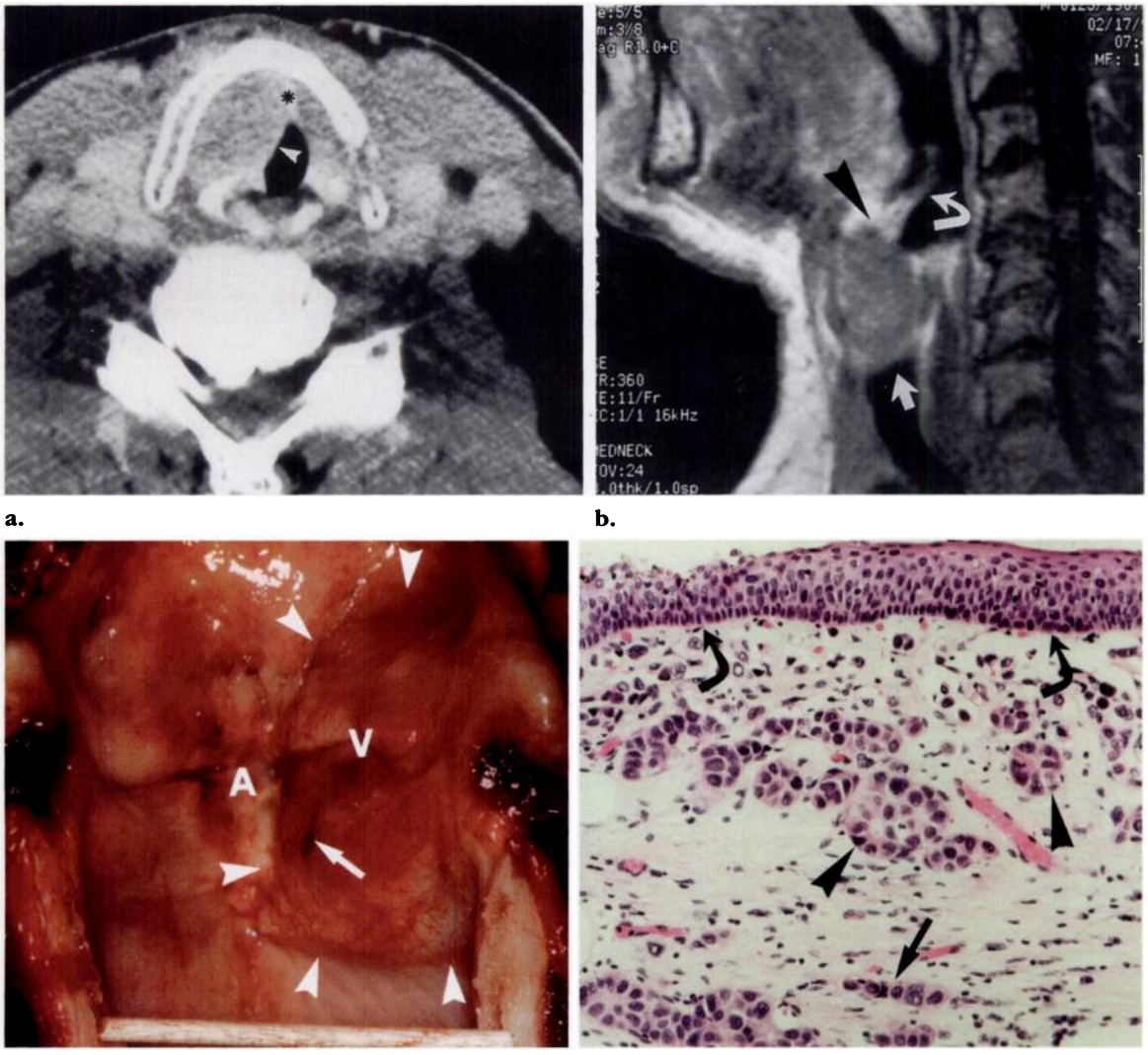
a.

• Mucoepidermoid Carcinoma

It is believed that mucoepidermoid carcinomas arise from the intercalated ducts of the seromucinous glands. Males are affected six times more often than females. Approximately 100 cases of laryngeal mucoepidermoid carcinoma have been reported to date, the most commonly affected site being the epiglottis (1,31). The biologic behavior of mucoepidermoid carcinoma is less aggressive than that of squamous cell carcinoma. Because this tumor responds only moderately well to radiation therapy, the treatment of choice is complete surgical removal.

As with other types of salivary gland tumors, the radiologic features in laryngeal mucoepidermoid carcinoma are nonspecific (Fig 12). The tumor is composed of a mixture of three cell types: mucin-secreting cells, squamous cells, and cells of intermediate type (1,31) (Fig 12). The glandular and cystic areas consist of columnar cells and mucous cells. These spaces and glands are surrounded by squamous and intermediate cells. Mucoepidermoid carcinomas are divided into low- and high-grade carcinomas. A tumor is considered to be histologically high-grade when at least 90% of its area consists of tumor cells and less than 10% consists of intracystic spaces (32). Patients with high-grade tumors have a poorer survival rate.

Figure 13. Adenocarcinoma in a 55-year-old man who presented with hoarseness. **(a)** Axial contrast-enhanced CT scan obtained at the level of the true vocal cords demonstrates a large, moderately enhancing homogeneous mass involving the right vocal cord (arrowhead) and the anterior commissure (*). **(b)** Sagittal contrast-enhanced T1-weighted MR image shows a large, moderately enhancing homogeneous mass involving the supraglottic, glottic, and subglottic regions. There is invasion of the infrahyoid preepiglottic space (arrowhead). Curved arrow indicates epiglottis, straight arrow indicates subglottic spread. The patient underwent total laryngectomy. **(c)** Photograph of the surgical specimen (posterior view; the patient's right side is to the right) shows a large transglottic tumor covered mainly by intact mucosa (arrowheads). A small area of ulceration (arrow) is also seen. *A* = anterior commissure, *V* = laryngeal ventricle. **(d)** High-power photomicrograph (original magnification, ×400; hematoxylin-eosin stain) shows intact squamous epithelium (curved arrows) with underlying carcinoma composed of cells arranged in anastomosing cords (straight arrow) and glandular-like structures (arrowheads). The patient is free of recurrence 3 years later.

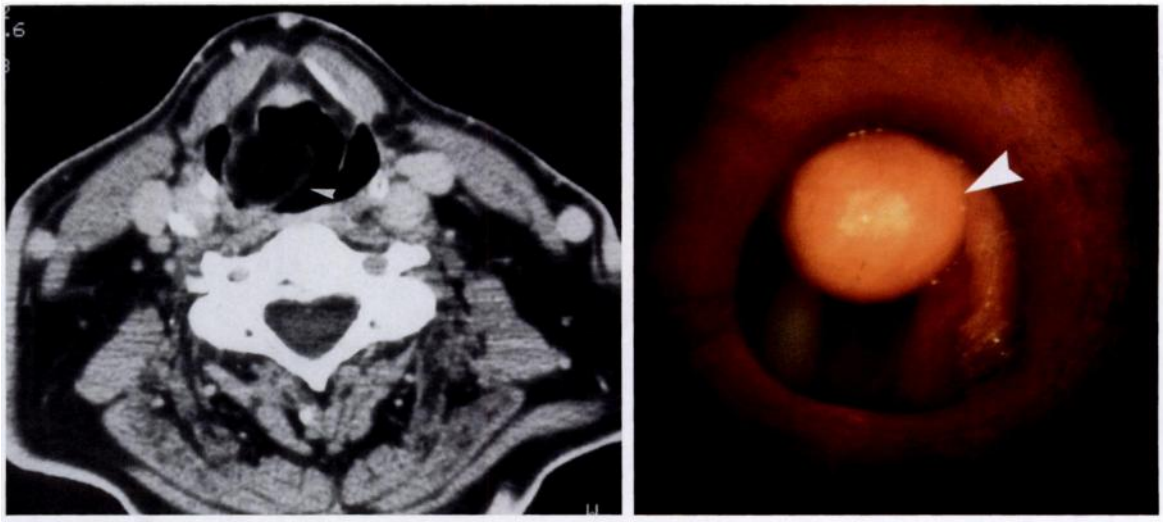


a. b.

c. d.

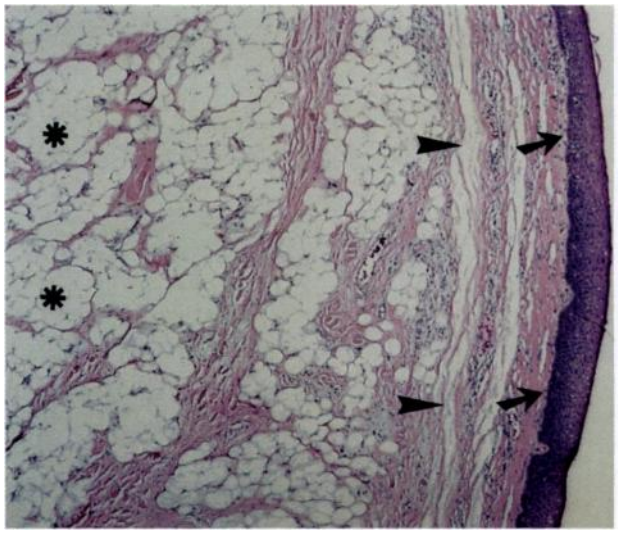
• Adenocarcinoma

Although it has been estimated that adenocarcinomas account for less than 1% of all laryngeal tumors, their true prevalence cannot be assessed accurately due to the lack of uniform terminology and varying diagnostic criteria (33,34). Adenocarcinoma is used as a generic term for those malignant gland- or duct-forming tumors that do not display characteristic features of the specific tumor types (1). Adenocarcinoma is most commonly found in patients between 40 and 60 years of age and has a male predilection. At endoscopy, adenocarcinoma may manifest as an entirely submucosal nodule or as a large, ulcerated mass (2). In both of our patients with laryngeal adenocarcinoma, the tumor was situated mainly beneath an intact mucosa (Fig 13). In one patient, however, partial necrosis of the



a. b.

Figure 14. Lipoma in a 77-year-old man with a foreign body sensation, episodes of suffocation, and change in voice quality. **(a)** Axial contrast-enhanced CT scan obtained at the supraglottic level shows a homogeneous, nonenhancing lesion isoattenuating to fat at the level of the right aryepiglottic fold (arrowhead). **(b)** Endoscopic image demonstrates a pedunculated mass covered by intact laryngeal mucosa arising from the right aryepiglottic fold (arrowhead). **(c)** Low-power photomicrograph (original magnification, ×25; hematoxylin-eosin stain) shows intact overlying squamous epithelium (arrows). Lobulated laryngeal lipoma composed of mature adipocytes (*) and a fibrous pseudocapsule (arrowheads) are also seen. The patient underwent endoscopic resection and is free of recurrence 5 years later.



c.

tumor had led to mucosal ulceration. Total or partial laryngectomy is the treatment of choice in laryngeal adenocarcinoma.

At CT and MR imaging, extensive submucosal tumor spread was observed, and in one case there was extensive invasion of the laryngeal skeleton that was later confirmed at histologic analysis. Although neither the CT nor the MR imaging features enabled differentiation of adenocarcinoma from squamous cell carcinoma, both cross-sectional imaging techniques proved useful in delineating the extent of submucosal tumor spread (Fig 13).

At histologic analysis, adenocarcinoma most often displays a typical glandular arrangement (Fig 13) and occasionally a papillary cystadenomatous architecture (2). The tumor cells are cuboidal or columnar and demonstrate low mitotic activity. Immunoreactivity against calcitonin, somatostatin, and adenocorticotropic hormone have been demonstrated (34), suggesting that these tumors are essentially expressing neuro-endocrine features even though no hormonal activity has been described clinically (2,34).

■ TUMORS OF FATTY TISSUE

Tumors of fatty tissue include lipomas and liposarcomas. Although they are the most common of all connective tissue lesions, tumors of fatty tissue are rarely found in the larynx: Only about 80 lipomas of the larynx and hypopharynx have been reported to date (1,2,35-39). It is difficult to determine the precise number of cases involving the larynx because a number of lesions originally classified as laryngeal proved to be hypopharyngeal in origin (38). Seventy percent of affected patients are men over the age of 50 (36,37), and 25% of patients present with multiple lipomas (1). Lipoma of the larynx most commonly arises in the supraglottic region. Mobile tumors may prolapse into the trachea or esophagus, leading to a foreign body sensation, dyspnea, or, occasionally, even death from suffocation (2). At endoscopy, the tumor may manifest as a sessile or polypoid submucosal mass (Fig 14). Deep biopsies are mandatory or the lesion will be overlooked at histologic analysis. Small lipomas can be removed endoscopically, whereas large lesions require an external surgical approach. The prognosis is excellent with no increased risk for recurrence.

Approximately 30 cases of laryngeal and hypopharyngeal liposarcoma have been reported to date (1,2,5). Initial clinical manifestation is very similar to that of lipoma, and surgical therapy with ample excision is the treatment of choice. Elective neck dissection is not indicated given the absence of cases of cervical metastases seen in the literature. However, local postsurgical recurrence as well as distant hematogenous metastases are common in laryngeal liposarcoma (1,2,5).

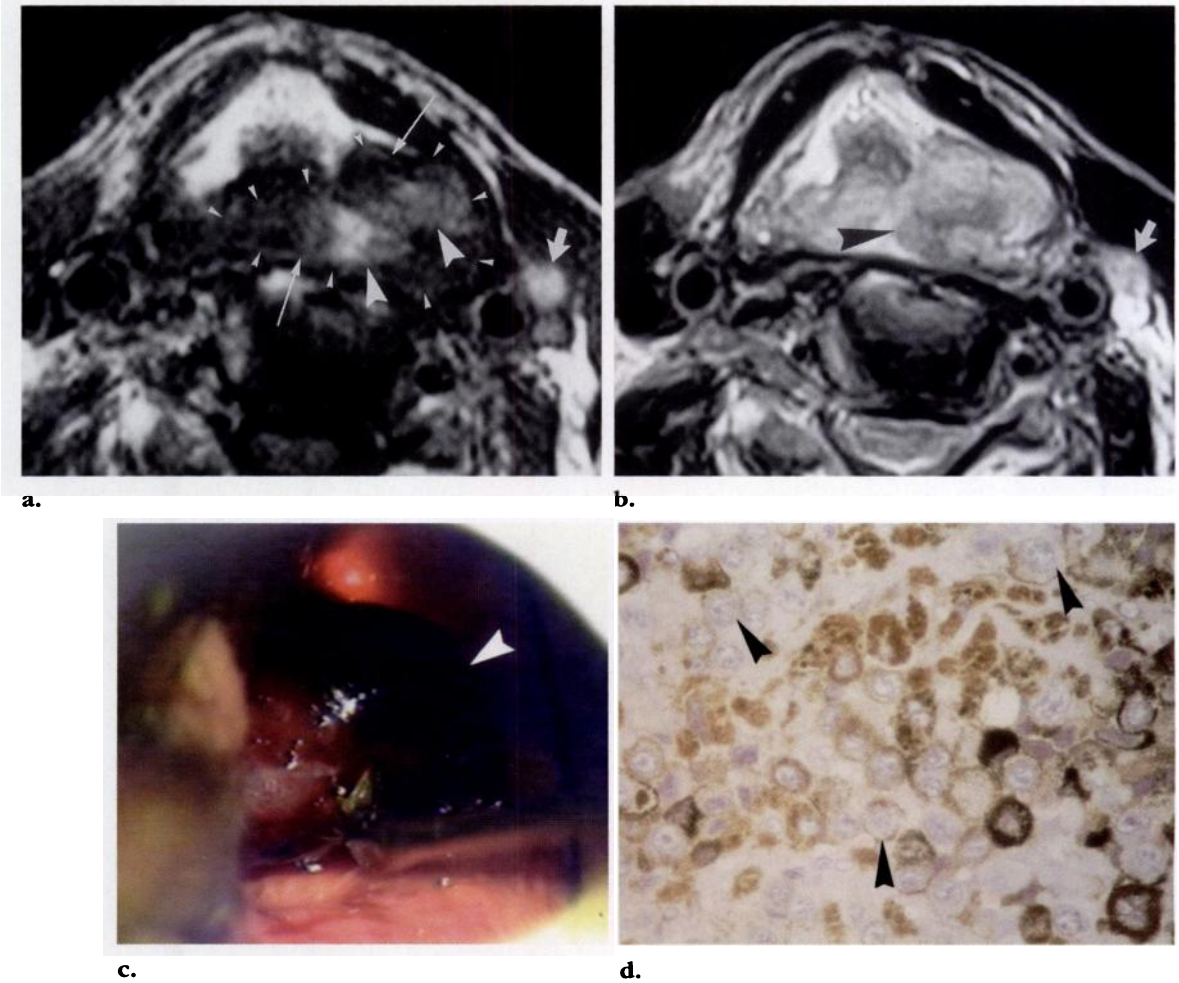
The radiologic diagnosis of lipoma is straightforward; both CT and MR imaging provide a definitive diagnosis in virtually all cases. At CT, lipoma typically manifests as a homogeneous nonenhancing lesion with attenuation values from –65 HU to –125 HU (38,39) (Fig 14). Lipoma is isointense relative to subcutaneous fat with all MR pulse sequences (ie, hyperintense on T1-weighted images, moderately intense on T2-weighted images, and hypointense on fat-suppressed T1-weighted images). As with lipomas in other parts of the body, if portions of the laryngeal lipoma are isoattenuating or isointense relative to soft tissue at CT or MR imaging and contrast enhancement is observed within these strands of connective tissue, the diagnosis of a liposarcoma should be considered. In addition, both imaging modalities reveal the exact location and extent of the neoplasm with good accuracy. In our three patients with laryngeal lipomas, CT allowed definitive diagnosis, and the tumor was removed endoscopically.

Lipoma of the larynx is composed of mature adipose tissue (Fig 14). Most tumors are well circumscribed and encapsulated, although intramuscular and infiltrating lipomas have been reported (37).

■ METASTASES TO THE LARYNX

Metastases to the larynx are rare; approximately 135 cases have been reported to date (1,40-42). The most common mechanism of metastatic spread is through the systemic circulation (ie, inferior vena cava, right side of the heart, lungs, left side of the heart, aorta, external carotid artery, upper thyroid artery, upper laryngeal artery). However, when no pulmonary involvement is observed, spread via the retrograde circulation of the paravertebral venous plexus and thoracic duct should be considered. The primary sources of metastatic tumor (in order of decreasing frequency) are skin (melanoma), kidney, breast, lung, prostate gland, colon, stomach, and ovary (1,40-42). In our series, there were three cases of metastases to the larynx: two from skin melanoma and one from renal adenocarcinoma. Metastases to the larynx are most often found in men (40). The most common sites of involvement are the supraglottic and subglottic regions. According to Glanz and Kleinsasser (40), laryngeal metastases should be divided into two groups: those that metastasize to the soft tissues, mainly the vestibular and aryepiglottic folds (eg, melanoma, renal adenocarcinoma), and those that metastasize to the marrow spaces of the ossified thyroid, cricoid, and arytenoid cartilages (eg, lung carcinoma, breast carcinoma). Symptoms of metastatic tumors to the larynx vary depending on the affected site. Hemoptysis is an important symptom of laryngeal metastases from renal adenocarcinoma because of the abundant vascularization of these tumors.

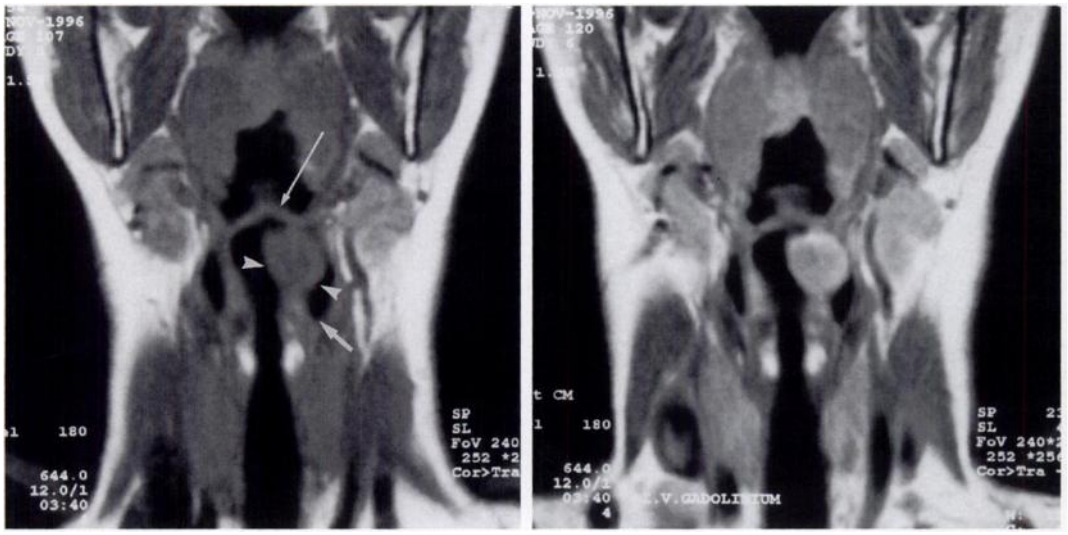
Figure 15. Metastasis from melanotic melanoma in an 81-year-old man who presented in the emergency department with severe dyspnea and a history of occasional hemoptysis. **(a)** Axial unenhanced T1-weighted MR image obtained at the supraglottic level demonstrates a large mass involving mainly the left aryepiglottic fold (small arrowheads). The mass contains areas of low signal intensity (thin arrows) and high signal intensity (large arrowheads). A left-sided lymph node with high signal intensity (thick arrow) is also seen. **(b)** On an axial T2-weighted MR image obtained at the same level, the hyperintense areas on the T1-weighted image in **a** have become slightly hypointense (arrowhead). The left-sided lymph node maintains high signal intensity (arrow). After administration of contrast material, only moderate enhancement of the tumor mass was observed. The signal intensity characteristics of the mass suggested a melanotic melanoma of the supraglottic larynx with lymph node metastasis. **(c)** Endoscopic image shows a darkly stained, polypoid supraglottic tumor involving the left aryepiglottic fold (arrowhead). **(d)** High-power photomicrograph (original magnification, ×400; hematoxylin-eosin stain) of a biopsy specimen demonstrates the typical appearance of melanotic melanoma: large round cells (arrowheads) with large hyperchromatic to vesicular nuclei. Large amounts of finely granulated, brown to black melanin are seen in the cytoplasm of neoplastic cells. The patient indicated that he had undergone removal of a small "spot" on the scalp at another institution. Inquiry at this institution revealed that their diagnosis had been melanotic melanoma of the scalp; consequently, the laryngeal tumor and the cervical lymph node metastasis were considered metastases of the melanotic melanoma of the scalp. Palliative tumor debulking was performed endoscopically to reduce dyspnea.



Treatment of a secondary tumor of the larynx is justified if it is a single metastasis. The type of treatment used—partial or total laryngectomy, radiation therapy, or chemotherapy—depends on the biologic behavior of the primary neoplasm and the quality of life of the patient. The prognosis is usually very poor; however, some well-documented cases of prolonged survival have been reported in the literature (40).

In most cases, the radiologic features of laryngeal metastases are nonspecific. However, metastases from renal adenocarcinoma and melanotic melanoma may demonstrate typical

Figure 16. Metastasis from amelanotic melanoma in a 46-year-old woman with a history of surgical excision of an amelanotic skin melanoma who presented with hoarseness and a foreign body sensation. **(a)** Coronal T1-weighted MR image shows a well-delineated mass isointense relative to muscle tissue arising from the left aryepiglottic fold (arrowheads). Long arrow indicates the epiglottis, short arrow indicates the left piriform sinus. **(b)** On a coronal contrast-enhanced T1-weighted MR image, the mass demonstrates only moderate enhancement, making differentiation of the mass from squamous cell carcinoma impossible. Endoscopy revealed an entirely submucosal mass covered by intact mucosa. The tumor was removed endoscopically, and the histologic diagnosis was amelanotic melanoma. **(c)** High-power photomicrograph (original magnification, ×100; hematoxylin-eosin stain) demonstrates large cells with large hyperchromatic to vesicular nuclei (arrowheads). Note the marked cellular pleomorphism and increased mitotic activity (arrow). Extensive examination of many sections revealed no melanin. The patient is free of recurrence 1 year later.



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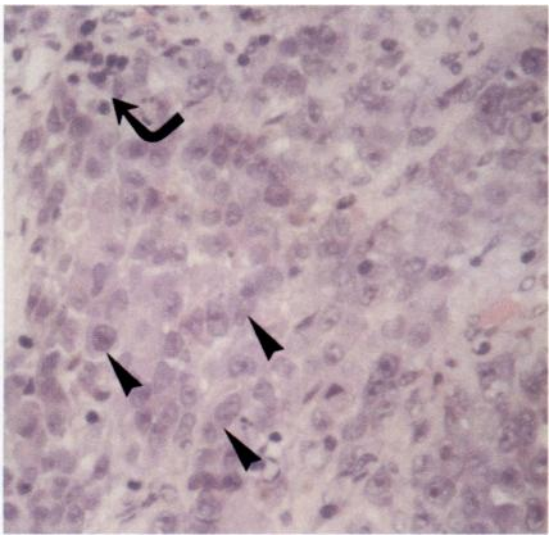

c.

features at MR imaging. Metastases from renal adenocarcinoma typically enhance strongly after administration of contrast material due to their hypervascularity and flow voids are seen on MR images, thereby suggesting a diagnosis other than squamous cell carcinoma (43). Laryngeal metastases from melanotic melanoma display the signal intensity characteristics of melanotic melanoma elsewhere in the body: high signal intensity on T1-weighted images and intermediate to low signal intensity on T2-weighted images due to the paramagnetic properties of melanin (Fig 15) (44,45). It was suggested recently that the signal intensity characteristics of melanoma may not depend on its classification as melanotic or amelanotic but on how much melanin is present at histopathologic analysis (45). The use of gray matter as the best internal standard has been recommended to differentiate between melanin-containing melanomas and hemorrhagic tumors (44). Whereas melanotic and amelanotic hemorrhagic tumors may be hyperintense relative to gray matter on T1-weighted MR images, melanotic tumors are hypointense relative to gray matter on T2-weighted images. In contrast, hemorrhagic tumors are more likely to be iso- to hyperintense. Laryngeal metastases from amelanotic melanoma have a nonspecific appearance at MR imaging (Fig 16) unless they are highly hemorrhagic. In both patients in our series with laryngeal metastases from melanoma, only moderate contrast enhancement was noted after administration of gadolinium chelates.

Metastases to the larynx have the same histologic features as the primary tumor. In the setting of a known primary tumor, the histologic diagnosis of the laryngeal neoplasm is usually straightforward. The question of whether a given laryngeal neoplasm is primary or metastatic arises particularly in patients with a solitary nodule. In such cases, a thorough clinical and radiologic evaluation should be performed to detect a possible primary neoplasm (Fig 15).

■ CONCLUSIONS

Although cross-sectional imaging alone does not allow differentiation of mucosal from submucosal laryngeal masses, both CT and MR imaging play important roles that complement clinical history and endoscopic examination. The discrepancy between an intact mucosa at endoscopy and a solid laryngeal mass at CT or MR imaging should raise suspicion of a submucosal tumor with unusual histologic characteristics. Although in many instances (eg, salivary gland tumors, hematopoietic tumors) neither CT nor MR imaging allows a specific diagnosis regarding the tissue components, the correct histologic diagnosis is often strongly suggested in cases of laryngeal lipoma, hemangioma, chondrogenic tumors, and metastases from renal adenocarcinoma and melanotic melanoma. Furthermore, CT and MR imaging are used to evaluate the extent of submucosal involvement and to direct the endoscopist to the appropriate biopsy site, thus allowing the deep biopsies needed to establish the histologic diagnosis. Thus, cross-sectional imaging plays an important role in treatment planning for these unusual tumors. In addition, CT and MR imaging are crucial for posttherapeutic monitoring and early detection of local recurrence.

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