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Larynx, Inflammatory Diseases

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Definition

Inflammatory diseases of the larynx may be of infectious or noninfectious origin. Acute infections present with a sudden onset and develop symptoms like fever and respiratory distress. Chronic infections develop over a longer period and present with hoarseness and pain.

Acute infections of the larynx are predominately relatively harmless viral infections but hazardous infections like ►laryngotracheitis (croup), ►epiglottitis, and diphtheria must be taken into consideration, because the latter can be lethal especially for children. Angioneurotic edema causing inspiratory stridor affects adolescents and adults more commonly than children.

►Chronic laryngitis develops over weeks to month and the dominant symptoms are hoarseness and pain caused by exogen factors (cigarette smoking, occupational contact with toxic fumes, voice abuse, gastroesophageal reflux disease), granulomatous and fungal infections. Systemic diseases involving the larynx are rheumatoid arthritis, sarcoidosis, Wegener's granulomatosis, and ►amyloidosis. Radiation therapy induces inflammatory changes of the laryngeal mucosa and submucosal tissue, which usually decrease within the first 6 months after completion of the therapy but may persist for years.

Pathology and Histopathology

►*Acute unspecific laryngitis* is usually caused by viruses (rhinovirus, influenza and parainfluenza virus, coxsackie virus, adenovirus, and respiratory syncytial (RS) virus), which can be associated with group A streptococcus, *Staphylococcus*, hemophilus influenzae, or *Moraxella catarrhalis*. Less common causes are thermal, allergic, or chemical inhalative substances. Serous–mucous, purulent–catarrhal, or fibrinous–purulent inflammatory changes may be observed. Pseudomembranous-necrotizing inflammation is characteristic for diphtheria.

Laryngotracheitis or croup is an infection of the subglottic larynx in the age group of 3 months to 3 years and usually is caused by a parainfluenza virus (type 1), less common are RS virus and type A influenza virus. Rapid onset of inflammatory edema of the cricovocal membrane and cranial trachea cause severe airway narrowing. *Epiglottitis* or supraglottitis occurs in an older age group (2–4 years), but can also occur in the adult population and is commonly caused by hemophilus influenza type B (HIB). In the adult population, hemophilus parainfluenzae, *Streptococcus pneumoniae*, group A streptococcus, or *Staphylococcus aureus* is also common, but there is also a high rate of negative blood cultures. Epiglottitis causes inflammation and swelling of the epiglottis, vallecula, arytenoids, and aryepiglottic folds.

Angioneurotic edema is characterized by episodes of increased capillary permeability with extravasation of intravascular fluid and subsequent edema of the cutis or mucosa of the upper airways or gastrointestinal tract. Hereditary angioneurotic edema is caused by a C1-esterase inhibitor deficiency. Allergic edema is caused by drugs (amongst others angiotensin-converting enzyme inhibitors and ionic contrast material) and food.

Tuberculosis of the larynx is rare but gained increasing importance in immunocompromised patients. The larynx is most often infected through bronchogenic spread from active lung disease but may also be affected lymphogenic or hematogenous. Mucosal hyperemia and thickening, nodules and ulcerations can be found at laryngoscopy and deep biopsy is required to exclude carcinoma. Biopsy reveals acid-fast bacilli and cultures should be performed to confirm diagnosis.

Other granulomatous diseases include Wegener's granulomatosis, sarcoid, pemphigus, leprosy, and numerous mycotic infections. Wegener's granulomatosis is characterized by necrotizing granuloma affecting the upper respiratory tract, lung, and kidneys. Laryngeal involvement is rare, mucosa ulceration and bone destruction as well as glottic and subglottic stenosis can result. Sarcoid usually affects the supraglottis, less commonly the glottis and subglottis. It may present as an isolated submucosal mass, indistinguishable from tumor.

Rheumatoid arthritis can affect the cricoarytenoid and cricothyroid joints as well as other synovial joints in the body.

Relapsing perichondritis is a rare inflammatory disease of unknown etiology. The cartilages of the ear, nose, larynx, trachea, and joints can be affected. Initially, edematous soft tissue around the cartilage is found with progression to cartilage destruction and collapse.

Amyloidosis is not a single entity but rather a group of diseases characterized by the presence of extracellular

deposition of amyloid in tissues. Less than 1% of all benign tumors in the larynx are amyloidomas. The supraglottic larynx is the most commonly involved region, amyloid deposits are located in the submucosa. Yellow-reddish tumorlike lesions with vitreous consistency can be found at inspection.

Gastroesophageal reflux disease (GERD)-related laryngitis or reflux laryngitis is common, but the prevalence varies considerably in the literature. The presence of gastric acid in the larynx can cause inflammation in the posterior larynx, especially in the interarytenoid region, aryepiglottic folds, and posterior cord area. In laryngoscopy, edema and erythema can be found as well as mucosal ulcerations in the posterior larynx.

Radiotherapy (RT) frequently induces edema and chronic inflammatory disease. Histologic findings are an acute inflammatory reaction with leukocytic infiltration, histiocyte formation, necrosis, and hemorrhage. Smaller vessels demonstrate detachment of the lining endothelial cells causing increased permeability resulting in interstitial edema. Deposition of collagenous fibers is found in the following 1–4 months, leading to sclerosis and hyalinosis of connective tissues. This inflammatory process eventually results in obstruction in the small arteries, veins, and lymphatics. By 8 months, there is advanced sclerosis, hyalinosis, and fragmentation of the collagen fibers. The formation of collateral capillary and lymphatic channels may reduce interstitial fluid.

Clinical Presentation

Acute unspecific laryngitis is characterized by dysphonia and dry cough. In advanced cases, pain and dysphagia may occur.

Laryngotracheitis has a gradual onset and typical symptoms are stridor and barking cough.

Epiglottitis or supraglottitis typically present with a sore throat and painful dysphagia/inability to swallow, along with stridor and dyspnoea. The onset is sudden with a rapid progression. Epiglottitis is a life-threatening condition because total airway obstruction may occur very rapidly.

Angioneurotic edema is characterized by recurrent edema of the face, respiratory, and gastrointestinal tract. The episodes occur spontaneous without concomitant symptoms and last for 2–3 days causing inspiratory stridor.

Tuberculosis present with dysphonia, dysphagia, and sore throat.

Wegener's granulomatosis, sarcoid, pemphigus, leprosy, mycotic infections and *rheumatoid arthritis* can present with hoarseness and dyspnoea but other organ manifestations usually cause the leading symptoms.

Relapsing perichondritis shows a prolonged course, increased subjective discomfort and typical pain on palpation.

Amyloidosis rarely affects the larynx. Symptoms are hoarseness and dyspnoea. *Gastroesophageal reflux disease* (GERD)-related laryngitis or reflux laryngitis present with chronic hoarseness, sore throat, chronic cough, dysphagia, or globus.

Radiotherapy (*RT*) frequently induces edema and mucositis leading to dyspnoea, dysphonia, and dysphagia. Delayed complications include soft tissue necrosis, osteochondronecrosis, fistula formation, pharyngeal motility dysfunction and strictures, and recurrent laryngeal nerve paralysis.

Imaging

Imaging is only occasionally performed in patients with inflammatory disease of the larynx, most patients are diagnosed clinically. Imaging may be done to exclude foreign bodies, recurrent tumor, and to localize the site of biopsy before performing laryngoscopy. Assessment of complications like abscess formation is another indication for cross-sectional imaging.

Conventional radiographs may be used in the diagnosis of laryngotracheitis (croup) or epiglottitis (supraglottitis).

CT and MRI are helpful to assess the submucosal extent of disease and to detect cartilage involvement. Imaging should be performed prior to biopsy in order to avoid misinterpretation of biopsy trauma and underlying disease.

High-resolution MRI is more sensitive to soft tissue changes than CT, but suffers from motion artefacts related to prolonged acquisition time. Fast gradient echo imaging can be performed in patients short of breath, but these patients are preferentially imaged with multislice spiral CT (MSCT) scanners.

The entire larynx can be examined with submillimeter collimation in less than 10 sec, minimizing motion artefacts and allowing phonation scans with MSCT.

Acute unspecific laryngitis is diagnosed clinically.

Laryngotracheitis causes mucosal swelling in the subglottic area and can be appreciated on a frontal radiograph as the "wine-bottle" or "steeple" sign. Paradoxical dilatation of the hypopharynx during inspiration should alert the clinician to the diagnosis.

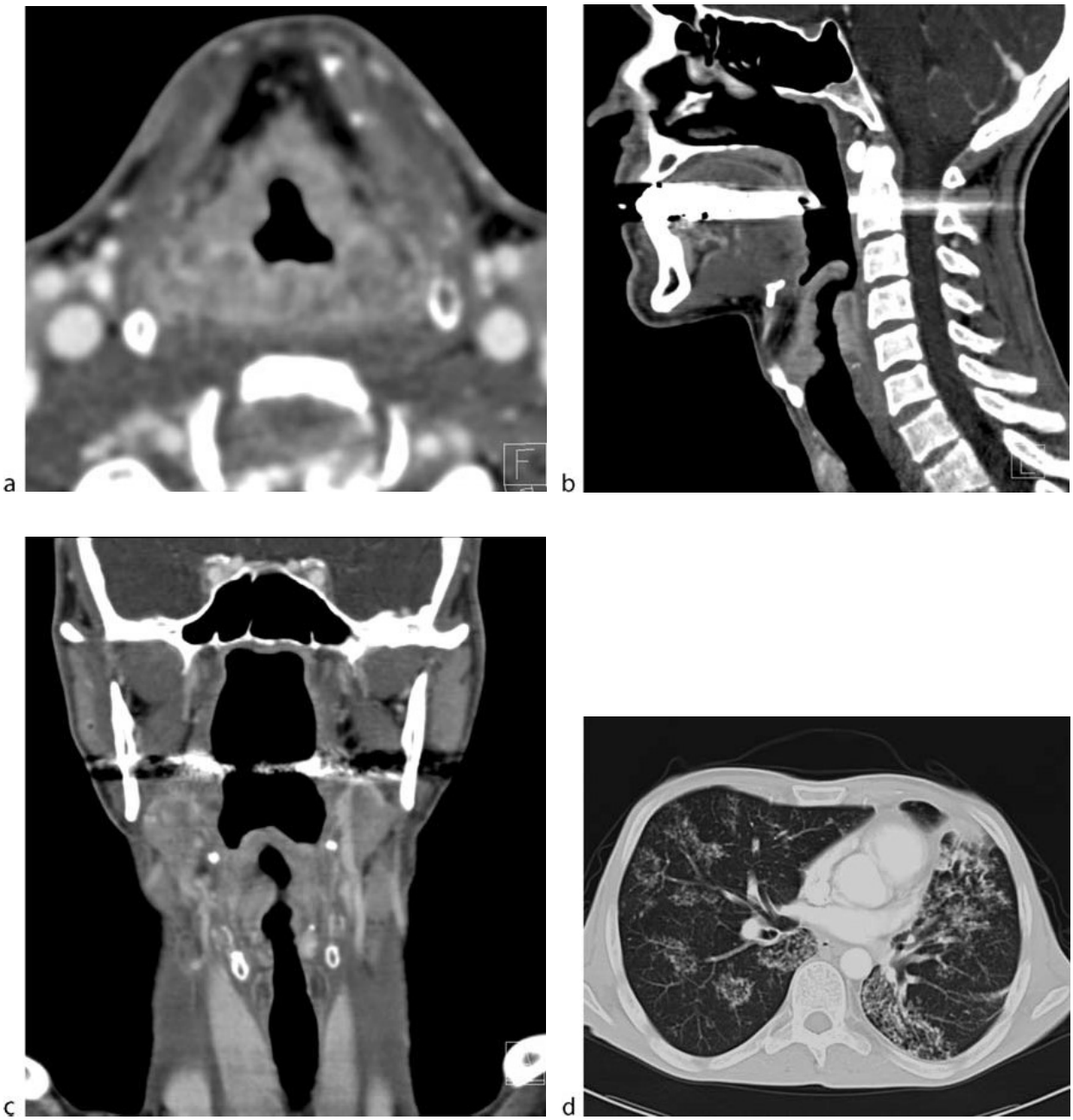
Epiglottitis or supraglottitis is a life-threatening condition because total airway obstruction may occur very rapidly. Therefore the patient must never be out of an environment where emergency tracheostomy can be performed. If imaging is performed, thickening of the epiglottis and supraglottic larynx can be seen on lateral

plain films. The thin curvilinear shape is lost ("thumb print sign"), the epiglottis bends into the enlarged aryepiglottic folds and the vallecula looses definition ("vallecula sign"). In severe cases, the arytenoids prominence may be swollen. CT or MRI can be employed in selected cases to exclude abscess formation.

Angioneurotic edema: CT or MRI demonstrates edema of the laryngeal mucosa.

Tuberculosis of the larynx: Imaging features are nonspecific and may be indistinguishable from squamous cell carcinoma. Diffuse or nodular soft tissue thickening with or without infiltration of the paraglottic and preepiglottic spaces and perichondritis can be found (1) (Fig. 1). Diffuse bilateral thickening without destruction of the laryngeal skeleton is common. The cricoarytenoid joint can be involved, causing fixation.

Wegener's granulomatosis, sarcoid, pemphigus leprosy, and mycotic infections: Radiographic findings in granulomatous disease are nonspecific soft tissue thickening and biopsy is required to establish the correct diagnosis.



Larynx, Inflammatory Diseases. Figure 1 ▶Laryngeal tuberculosis: diffuse bilateral thickening of the glottic and supraglottic larynx. (a) Axial section at the level of the false cords demonstrates nodular mucosal thickening with peripheral contrast enhancement. The extent of laryngeal involvement can be appreciated on sagittal (b) and coronal (c) images. Active pulmonary tuberculosis was present (d).

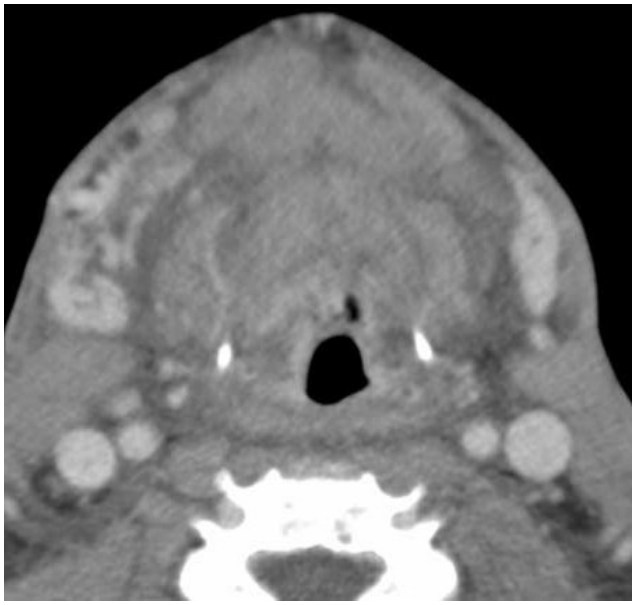
Rheumatoid arthritis: On CT irregular sclerosis or erosion of the joints can be identified.

Relapsing perichondritis: Initially, edematous soft tissue around the cartilage is found with progression to cartilage destruction and collapse. Edema and inflammation can present with high signal intensity (SI) on T2-weighted images along the margins of the cartilage. Other imaging findings are cartilage expansion, sclerosis or destruction, and soft tissue calcification.

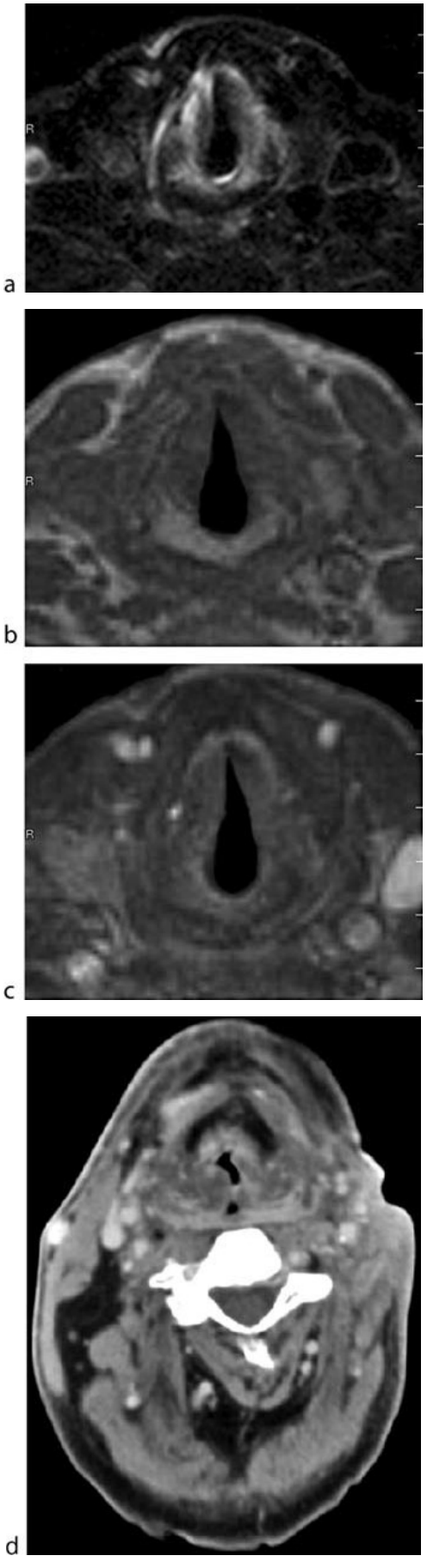
Amyloidosis: The supraglottic larynx is the most commonly involved region, amyloid deposits are submucosal. The lesions may appear as a well-defined homogeneous mass or diffuse soft tissue infiltration (Fig. 2). Although bone erosion has been described in skull base and spine lesions, cartilage or bone destructions are uncommon in the larynx. Although the amyloid itself does not enhance with contrast material administration, peripheral enhancement can be found with CT or MRI. Enhancement may be caused by the foreign body giant-cell reaction that is evoked by amyloid deposition. Calcification has been described and is best appreciated on high-resolution CT scans. Amyloidosis is isointense to muscle on T1-weighted images and can be hypointense (2) or iso- to slightly hyperintense on T2-weighted images. This may help to differentiate calcified focal amyloidoma from chondrosarcoma, which is markedly hyperintense on T2-weighted images (3).

Gastroesophageal reflux disease (GERD): Imaging findings are nonspecific, demonstrating edematous soft tissue swelling in the posterior larynx.

RT results in radiologic changes that involve both the exolaryngeal and endolaryngeal regions. In the larynx, RT



Larynx, Inflammatory Diseases. Figure 2 Amyloidosis in a patient with multiple myeloma. Extensive amyloid deposition in the supraglottic larynx.



Larynx, Inflammatory Diseases. Figure 3 (continued)

results in thickening of the epiglottis and is typically seen on CT and MRI within 3 months after RT (4). Almost all patients will show increased attenuation in the fat layers, thickening of the aryepiglottic folds and the false vocal cords (Fig. 3). Early changes at the glottic level include increased attenuation of the paraglottic fat planes, typically identified within 2 months following RT. Symmetric subglottic thickening occurs in about 80% of patients. Late changes at the glottic level include thickening of the anterior and posterior commissure. These changes occur within 7 and 14 months, respectively, and are irreversible (5). Unilateral paramedian position of the vocal cord, anteriomedial displacement of the arytenoids cartilage, ipsilateral dilatation of the pyriform sinus, laryngeal ventricle and vallecula, as well as thickening and anteromedial displacement of the aryepiglottic fold indicates recurrent laryngeal nerve paralysis. Soft tissue necrosis and chronic inflammatory disease most often observed within the first two years after RT can be focal and mimic recurrent tumor. Follow-up examinations or biopsy may be required for diagnosis.

Nuclear Medicine

Nuclear scans have a limited role in the assessment of inflammatory lesions of the larynx. Radionuclide bone scans in patients with rheumatoid and collagen vascular disease can be positive over affected joints as well as over the larynx and may be used for primary diagnosis as well as therapy follow-up.

Diagnosis

Diagnosis of inflammatory disease of the larynx is done clinically (including laryngoscopy) and imaging is rarely performed. MRI is more sensitive to inflammatory changes than CT due to better soft tissue resolution. The purpose of imaging is to exclude other causes of stridor such as foreign body aspiration or tumor and to diagnose complications like abscess formation. If abscess is suspected, CT-guided intervention can be performed in the same session. High-resolution CT is recommended in the diagnosis of perichondritis, demonstrating chondral sequestration.

Larynx, Inflammatory Diseases. Figure 3 (a–c) Patient with mild edema of the glottis 12 months after RT [(a) T2-weighted, (b) T1-weighted, and (c) T1-weighted + Gd fat suppression]. (d) Different patient with extensive supraglottic edema 6 months after postoperative radiochemotherapy and neck dissection.

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