Sore Throat: Navigating the Differential Diagnosis

Two case histories demonstrate the vital importance of staying on your toes when dealing with this routine complaint.

By Brian L. Porche, MD, and Jennifer Avegno, MD

Patients complaining of sore throats account for 1% to 2% of all visits to U.S. physicians' offices, urgent care centers, and emergency departments, adding up to at least 14 million patient encounters a year. Acute infectious pharyngitis may be caused by viral, bacterial, and fungal sources. Infection is generally transmitted through respiratory secretions and outbreaks often occur where overcrowding or close quarters exist. A localized infection primarily affects the lymphatic system of the pharyngeal structure, with tonsillar suppuration, edema, fever, and cervical lymphadenopathy as prominent findings.

Most cases of acute pharyngitis run a benign course, and sequelae have decreased significantly with the widespread use of appropriate antibiotics. However, a few life-threatening infections may have a sore throat as their main presenting symptom, so health care providers need to stay vigilant to diagnose them. The following two cases illustrate significant, emergent, alternative diagnoses to consider when evaluating the patient who complains of a sore throat.

CASE 1: EPIGLOTTITIS

Mr. P, age 33, presents to an urgent care center complaining of a scratchy throat, a fever of up to 100.5°F, and mild rhinorrhea for two days. He reports that he was seen yesterday at another facility, where he was diagnosed with an upper respiratory infection (URI) and sent home with instructions to stay well hydrated and take ibuprofen and an over-the-counter decongestant. Unfortunately, his sore throat has gotten worse and he now has odynophagia, dysphagia, a higher fever, a change in his voice, and pain in the anterior neck.

Mr. P has an unremarkable medical history with completed immunizations and no allergies, chronic medications, or surgeries. He has smoked five cigarettes a day for 10 years. His vital signs are: temperature, 102°F; heart rate, 122; blood pressure, 134/82; respiratory rate, 17, with 99% oxygen saturation on room air. He looks ill and seems anxious, is leaning forward in the sniffing position, speaks with a muffled ("hot potato") voice, and has tenderness on lateral movement of the larynx. Although no drool-

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ing or stridor is noted, the patient has become more anxious and says he is beginning to have trouble breathing.

Based on these findings, Mr. P's physicians determine that he has epiglottitis.

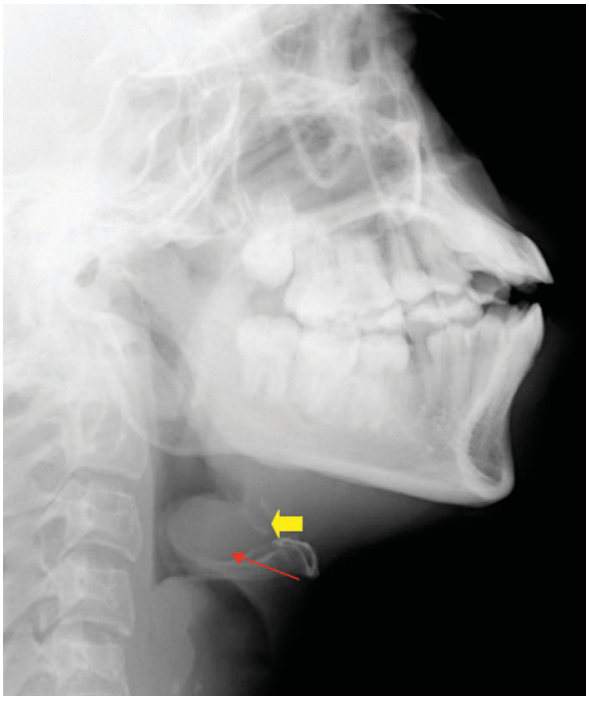
AGGRESSIVE INFECTION

Epiglottitis, also called supraglottitis, is an aggressive infection of the epiglottis and the surrounding tissues that is usually caused by bacteria. The incidence of epiglottitis is thought to be relatively low—about one patient in 100,000. In the past, the disease was most often seen in early childhood and was associated with significant morbidity and mortality. The most common organism identified was *Haemophilus influenzae* type b (HiB). However, routine infant vaccination with the HiB vaccine since 1991 has decreased the incidence of pediatric epiglottitis dramatically, making the disease rare in immunized children.

In contrast, the incidence of adult epiglottitis is increasing both in the United States and internationally. Whether because of initial misdiagnosis or undertreatment in the adult population, the mortality is higher in adults than in children. The overall mortality in all age groups is less than 7%. Because the disease is now far more common in adults than in children, this article will focus on adult epiglottitis. Male smokers are more commonly affected, and there does not seem to be an age or seasonal prevalence.

Adult epiglottitis usually starts as a localized cellulitis of the epiglottis and then spreads to the supraglottic structures, including the base of the tongue, vallecula, aryepiglottic folds, arytenoid soft tissues, and lingual tonsils. However, some patients have a normal epiglottis in the setting of severe supraglottic involvement, so many authors feel the term supraglottitis is a more accurate description of the disease process.

The histology and anatomy of the epiglottis are important in the pathogenesis of the disease. There is a large potential space that can expand as inflammatory cells and fluid from edema accumulate during infection. Inflammation and edema do not extend inferiorly to the infraglottic regions because the submucosa is densely adherent to the mucosa inferior to the vocal cords. The most commonly isolated organism causing adult epiglottis is *H. influenzae* type b, but many other organisms have been implicated. These include bacteria (*Streptococcus* and *Staphylococcus* species, *Moraxella catarrhalis*, *Klebsiella pneumoniae)*; viruses (varicella virus, adenovirus, herpesvirus, and respiratory syncytial virus); and fungi (most commonly, *Candida*).



>Radiographic red flags. Epiglottitis on lateral neck x-ray showing the thumbprint sign (red arrow) and vallecula sign (yellow arrow).

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CLINICAL PRESENTATION

Adults with acute epiglottitis typically have prodromal symptoms of a benign URI that last one to two days. However, the onset may also be insidious, lasting up to one week, or abrupt and severe. Patients usually report dysphagia, odynophagia, severe sore throat, otalgia, and a muffled voice, although hoarseness is uncommon. Fever is variable and may not be present early in the disease; in fact, it is entirely absent in up to 50% of patients.

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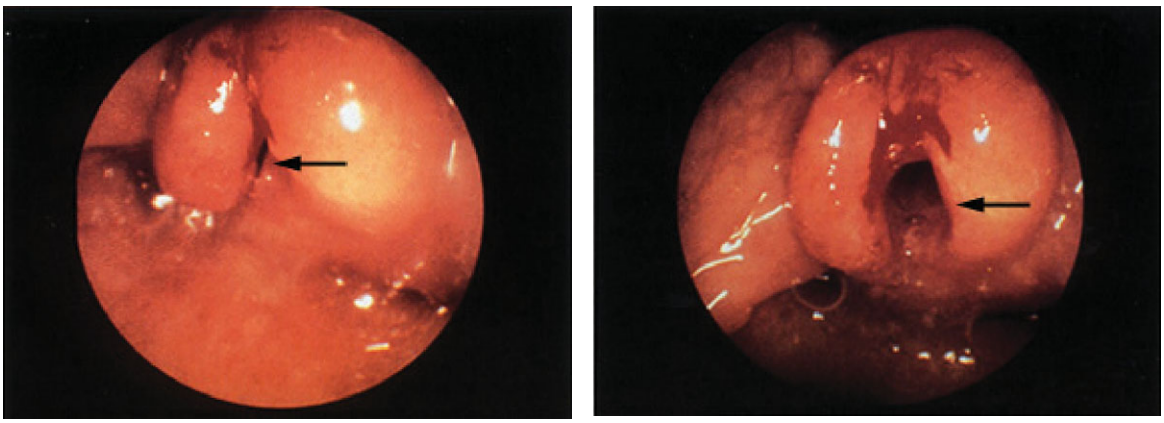
Physical examination may reveal a patient who appears ill and anxious. In patients with fever, tachycardia out of proportion to the fever may correlate



>Laryngoscopic view. Epiglottitis on direct visualization (arrows indicate airway opening).

with severe disease. A reliable finding in epiglottitis is tenderness on palpation of the anterior neck near the hyoid and on horizontal movement of the larynx. Other signs and symptoms pointing to a more severe disease process and imminent airway obstruction include respiratory distress, stridor, drooling, aphonia, and the patient assuming the sniffing position for comfort and ease of breathing.

Diagnosis of epiglottitis requires a high index of suspicion and a thorough history and physical examination, as there are many diseases with similar presenting signs and symptoms. The differential diagnosis includes the following infectious causes: deep space abscess, infectious mononucleosis, lingual tonsillitis, diphtheria, pertussis, and pharyngitis. Noninfectious causes include laryngeal trauma, angioedema, allergic reactions, foreign body aspiration, laryngospasm, tumor, and toxic inhalation or aspiration.

When the diagnosis is evident on clinical grounds alone (usually in severe cases), immediate plans should be made to admit the patient to the hospital for airway control, administration of parenteral antibiotics, and close observation, possibly with ICU admission. Act with extreme care and urgency, because these patients are at significant risk for life-threatening airway obstruction and death. When the diagnosis is unclear and the patient is stable enough for further evaluation, the tests described below may help confirm the diagnosis of acute epiglottitis.

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RADIOGRAPHIC EVIDENCE OF EPIGLOTTITIS

Lateral soft tissue neck radiographs have a sensitivity of up to 90%, but a normal or nondiagnostic film does not exclude adult epiglottitis. Patients sent to radiology should be observed closely because of the risk of acute airway obstruction. Radiographic evidence of an epiglottic width of more than 8 mm or an aryepiglottic fold width of more than 7 mm suggests epiglottitis. Other radiographic findings consistent with epiglottitis include an enlarged, thumb-shaped epiglottis, obliteration of the vallecula, swelling of the arytenoids and aryepiglottic folds, edema of the prevertebral and retropharyngeal soft tissue, and ballooning of the hypopharynx and mesopharynx.

The vallecula sign confirms a diagnosis of epiglottitis. To observe this sign, identify the base of the tongue on the radiograph and trace it inferiorly to the hyoid bone. The diagnosis is confirmed if there is no pocket of air extending almost to the hyoid bone and roughly parallel to the pharyngotracheal air column. The thumbprint sign also helps confirm the diagnosis. The swollen epiglottis looks like a thumbprint on a radiograph (see image on page 7).

Direct or indirect laryngoscopy (see image) confirms the diagnosis in stable patients. Modalities such as flexible fiberoptic laryngoscopy are ideal for this procedure, since they provide direct visualization of the epiglottis and the airway and also provides a

means to guide the intubation when indicated with direct visualization. Direct visualization may reveal a classic cherry-red epiglottis (or the epiglottis may appear pale and edematous), as well as edema surrounding the supraglottic structures. In patients with severe symptoms, including respiratory distress, stridor, drooling, and aphonia, plans for direct laryngoscopy with backup measures to obtain definitive airway control should be implemented. Ideally, this procedure should occur with an otorhinolaryngology (ENT) or anesthesia consultation and should be performed in an operating room.

AIRWAY CONTROL AND ANTIBIOTICS

The keys to therapy for epiglottitis are airway control and empiric antibiotics. After a definitive airway is obtained, antibiotics covering *H. influenzae* and other previously mentioned pathogens should be initiated. Pending cultures and sensitivities, cefotaxime or ceftriaxone are first-line agents. Alternative antibiotics include ampicillin-sulbactam and trimethoprim-sulfamethoxazole. Adjunctive therapy options include steroids to decrease the inflammation of the supraglottic structures and racemic epinephrine nebulizer treatments. The efficacy of these last two practices has not been proven, although they are frequently used in the treatment of adult acute epiglottitis.

The most significant complications of epiglottitis are airway obstruction, respiratory failure, the need for surgical procedures, and death. As the incidence of adult epiglottitis increases, so does a more common complication—epiglottic abscess. Patients with epiglottic abscesses may need incision and drainage before clinical improvement occurs. Concomitant infections are more common in the pediatric population, but extraepiglottic infections or complications may also occur in adults and include meningitis, retropharyngeal abscess, pneumothorax, empyema, pneumonia, sepsis, adult respiratory distress syndrome, and pulmonary edema.

CASE 2: RETROPHARYNGEAL ABSCESS

Ryan, age 3, is brought to an urgent care center by his parents because of a sore throat, left ear pain, and clear rhinorrhea for five days. Ryan was examined by his pediatrician, who diagnosed left otitis media and prescribed high-dose amoxicillin. However, Ryan's parents report that he has become worse over the last 24 hours with new symptoms of dysphagia, odynophagia, fever, and drooling. He also will not move his neck in any direction.

Ryan's history includes up-to-date immunizations, no known allergies or medical problems, and enrollment in day care. His vital signs are: rectal temperature, 101.7°F; heart rate, 108; blood pressure, 96/58; respiratory rate, 18, with 99% oxygen saturation on room air. The physical examination finds a well-developed toddler who is irritable, drooling, and appears ill. He refuses to move his neck to help with the examination. His tympanic membranes are clear on the right, with mild erythema and loss of landmarks on the left. His nares and oropharynx are normal, without exudate or tonsillar enlargement. Range of motion of the neck is painful, with more pain elicited on extension than on flexion. There is mild swelling of the left anterolateral aspect of the neck, with tenderness on palpation of that area.

These findings point to a diagnosis of retropharyngeal abscess.

DEEP SPACE INFECTION

Retropharyngeal abscess, a deep space neck infection, is an uncommon but significant complication of URI in children. On rare occasions, it is seen in adults who have ingested foreign bodies, had recent ENT procedures, or experienced regional trauma, or are immunocompromised. In the past, retropharyngeal abscesses caused significant morbidity and mortality secondary to complications, but advances in imaging, prompt detection, and early administration of antibiotics have reduced these complications, and long-term sequelae are rare.

The disease occurs most often in pediatric patients between six months and four years old—the peak age for numerous URIs and their complications, such as otitis media and sinusitis. The retropharyngeal lymph nodes are implicated in the development of a retropharyngeal abscess. These nodes atrophy between ages four and six, and repeated lymph node drainage after many URIs also tends to obliterate the nodes. Consequently, the incidence of retropharyngeal abscesses beyond this age group is markedly

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Retropharyngeal abscess occurs most often in pediatric patients between six months and four years old.

>Painful pressure. Retropharyngeal abscess on lateral neck x-ray.

Image courtesy Loren Yamamoto, MD, MPH

decreased, so our discussion here will focus on the pediatric population.

Keep in mind that the retropharyngeal space is a potential space in the neck between the posterior pharyngeal wall and the prevertebral fascia. The space is composed of two chains of lymph nodes that drain the nasopharnyx, adenoids, posterior paranasal sinuses, middle ear, and Eustachian tube. Therefore, infections in this area may be complications of viral or bacterial URIs that seed infection and ultimately cause abscess formation. The bacterial pathogens implicated are similar to other deep space neck abscesses and are usually polymicrobial. They include group A *Streptococcus*, *Staphylococcus aureus*, *H. influenzae*, and anaerobes, such as *Fusobacteria*, *Prevotella*, and *Veillonella* species.

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Many life-threatening airway conditions mimic retropharyngeal abscess in a toxic child with fever, sore throat, and neck pain.

CLINICAL PRESENTATION

Patients with retropharyngeal abscesses commonly complain of a preceding illness with URI symptoms or otitis media, and they are often already being treated with antibiotics. Symptoms of retropharyngeal abscess are a result of inflammation and pressure on the surrounding tissues of the airway, pharynx, or upper digestive tract. Patients appear generally ill, are febrile, and (if verbal) complain of dysphagia, odynophagia, neck swelling, or neck pain on movement. Parents often report that the child has a stiff neck, is drooling, and has some element of respiratory distress.

On physical examination, the child may appear toxic, irritable, and have a muffled voice, stridor, or tachypnea (or all three of these findings). The child may also present with torticollis or may refuse to move his neck because of the pain. Usually, neck extension is more painful than neck flexion. A midline or unilateral swelling of the posterior pharyngeal wall may be noted and may be fluctuant, but care must be taken to avoid aggressive palpation, which can result in abscess rupture. Trismus is an unusual finding when the site of infection is in the retropharyngeal space.

Occasionally, patients with retropharyngeal abscess will display classic signs and symptoms, so the diagnosis can be made on clinical grounds alone. However, it is important to consider alternative diagnoses, because many life-threatening airway conditions mimic retropharyngeal abscess in a toxic child with fever, sore throat, and neck pain. The differential diagnosis includes epiglottitis, lateral pharyngeal abscess, peritonsillar abscess, infectious mononucleosis, diphtheria, internal jugular vein thrombophlebitis, meningitis, viral pharyngitis, and streptococcal pharyngitis, among other diseases.

TAKING CARE WITH THE CHILD

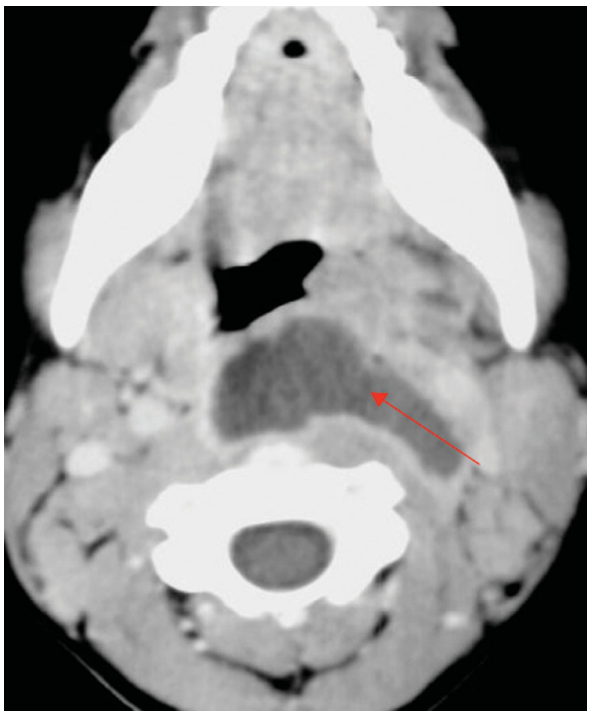
Once clinical suspicion for a retropharyngeal abscess is high, an initial workup and confirmatory testing may be performed. Close airway monitoring and definitive management should take precedence over imaging or other testing. Practitioners should take care not to upset the child and possibly worsen airway obstruction. The airway should be managed by

the most qualified physician available in a setting with multiple resources.

A lateral soft tissue neck radiograph (see image opposite) is usually performed to help delineate a retropharyngeal abscess. To avoid false positives, care must be taken to obtain an adequate film and perform the study correctly. To obtain a true lateral neck film, the neck must be kept in extension during the study, and the film should be taken during inspiration to avoid a false thickening in the retropharyngeal space. Positive findings are controversial, but 7 mm of prevertebral soft tissue width at C2 and 14 mm of prevertebral soft tissue width at C6 are considered indicative of retropharyngeal abscess. Other findings include reversal of the normal lordosis of the cervical spine, an air fluid level, foreign bodies, or vertebral body destruction in extensive cases.

When the diagnosis is unclear or the patient is uncooperative during lateral films, definitive diagnosis should be based on a computed tomography (CT) scan of the neck with intravenous contrast (see image). Although this modality is not a perfect tool, CT has been shown to have superior sensitivity and specificity in diagnosing retropharyngeal abscess. It also helps to differentiate retropharyngeal abscess from retropharyngeal cellulitis and to detect extension of the abscess to contiguous structures in the neck and surrounding tissues. Whereas complete rim enhancement is most indicative of abscess, CT findings of a low-density core, soft tissue swelling, obliterated fat planes, and mass effect may be seen in both retropharyngeal abscess and cellulitis.

When a retropharyngeal abscess is suspected or confirmed in the urgent care setting, arrangements for transfer and admission to the hospital should be made with the consultation of an ENT physician. Treatment of retropharyngeal abscess consists of airway control if indicated, empiric parenteral antibiotics, and ENT surgical consultation for possible transoral or transcervical drainage. Historically, surgical drainage and parenteral antibiotics were the mainstays of therapy. But according to many recent studies, close observation and parenteral antibiotics lead to effective resolution of symptoms and less unnecessary invasive surgeries. Empiric antibiotics should cover previously mentioned bacterial pathogens. Appropriate regimens include parenteral ampicillin-sulbactam or clindamycin. Once the patient is clinically improved and afebrile, conversion to oral antibiotics, such as amoxicillin-clavulanate or clindamycin, is recommended to complete a 14-day course of therapy.



>Diagnostic confirmation. Retropharyngeal abscess seen on computed tomography scan with intravenous contrast.

Image courtesy Loren Yamamoto, MD, MPH

Although most patients do very well with appropriate airway management, antibiotics, and surgery for complicated cases, the following life-threatening complications can occur: airway compromise; pulmonary complications from abscess rupture and aspiration, including pneumonia, empyema, and asphyxiation; direct extension along tissue planes leading to mediastinitis or mediastinal abscess, pericarditis, or pleuritis; neurologic/orthopedic complications, including atlantoaxial separation, transverse myelitis, and epidural abscess; erosion into the esophagus or auditory canal; necrotizing fasciitis; sepsis; and death. *continued*

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POTENTIAL CHALLENGES

Any patient with the chief complaint of sore throat presents a potential airway and infectious disease challenge. A thorough history, including immunization status and previous antibiotic use, is essential and should be combined with a detailed head and neck examination. Patients suspected of having epiglottitis or retropharyngeal abscess should be immediately transferred to the hospital for definitive care. □

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