Chapter 11
Laryngeal Infections

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Introduction

Laryngeal infections are caused primarily by viruses and bacteria and have important implications on the ability to swallow, phonate, and breathe. A high suspicion and timely diagnosis is important in these patients as in the most serious of circumstances airway inflammation can progress to airway obstruction; with epiglottitis being the best example of this.

The following chapter will focus on the clinical evaluation of patients with a laryngeal infection as well as the differential diagnosis, specific diagnostic tools and treatment options for each infection.

General Approach to the Clinical Evaluation

The presentation of laryngeal inflammation and infection in the pediatric patient differs drastically from that of the adult. The adult larynx has more space to accommodate inflammation while the pediatric airway is proportionally smaller and therefore more susceptible to edema and inflammation. This can lead to a rapidly progressive clinical course in children, highlighted by the presence of obstructive symptoms and impending airway compromise. The assessment of a patient with a suspected laryngeal infection should include a prompt evaluation for airway compromise focusing on stridor, increased work of breathing with retractions and accessory muscle use, and cyanosis.

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T.A. Valdez, J.G. Vallejo (eds.), *Infectious Diseases in Pediatric Otolaryngology*,
DOI 10.1007/978-3-319-21744-4_11

If the patient's airway is in stable condition, the provider should complete a history and physical exam. Information on the duration of symptoms, associated symptoms, history of exposure to ill contacts, recent travel, and any possibility of foreign body aspiration should be obtained. Commonly associated symptoms include difficulty feeding, cough, and voice changes. After a complete history, a physical exam is performed including vital signs with a focus on the patient's respiratory status. As previously mentioned, the provider needs to first determine if the patient has a stable airway. This is determined by watching the child's work of breathing as well as by listening to their breathing. Should the patient have stridor, it is important to determine if it is inspiratory, expiratory or biphasic stridor as they are each associated with different levels of obstruction.

In the stable patient, flexible laryngoscopy may provide important diagnostic information about laryngeal involvement; however the provider should take caution as laryngoscopy can exacerbate laryngeal swelling and cause acute airway obstruction, especially in a patient with epiglottitis. Additional diagnostic tools that may be helpful include neck and chest radiographs and blood work including a white blood cell count to evaluate for infection.

In general if a patient with a laryngeal infection is suspected of having severe airway obstruction, the airway should be secured in a controlled manner, with the operating room often the best option. If significant obstruction is suspected, but the patient is stable, they should be admitted for continuous monitoring with treatment targeted towards the suspected cause.

Laryngitis

Laryngitis is inflammation of the larynx and generally occurs in older children. It is most commonly caused by a viral infection or vocal strain.

Infectious Etiology

Respiratory viruses, especially adenovirus and influenza, are the most common etiology (Table 11.1). Secondary bacterial infections from *Streptococcus pyogenes* (group A streptococcus) or *Staphylococcus aureus* may also occur. Fungal infections are rare, but can occur in immunocompromised children.

Clinical Features

The most common symptom in patients with laryngitis is dysphonia with hoarseness and a change in voice at presentation. Other respiratory viral symptoms, such as rhinorrhea, low-grade fever, sore throat, and cough may also be present. Although adenovirus and influenza can be associated with high fevers, if purulent exudate or progressive pain are present, a secondary bacterial infection should be considered.

Diagnostic Evaluation

No specific laboratory testing is usually needed; some clinicians obtain a rapid influenza test or adenoviral polymerase chain reaction (PCR) for highly febrile patients. A rapid strep test and bacterial culture should be obtained if the child has purulent exudate with progressive pain.

Table 11.1 Etiologies of laryngeal infections

Laryngitis
Common
Viruses: adenovirus, influenza
Less common
Viruses: parainfluenza, coronavirus, rhinovirus, RSV, enteroviruses, HSV
Bacteria: *Streptococcus pyogenes*, *Staphylococcus aureus*
Uncommon
Viruses: mumps, measles[a], CMV, EBV
Bacteria: *Corynebacterium diphtheriae*[a]
Fungi: *Candida albicans*[b]
Croup
Common
Viruses: parainfluenza (especially type 1)
Less common
Viruses: RSV, adenovirus, coronavirus, influenza, human metapneumovirus
Uncommon
Viruses: measles[a], rhinovirus, enteroviruses, HSV
Bacteria: *Mycoplasma pneumoniae*, *S. aureus*, *S. pyogenes*, *Streptococcus pneumonia*, *Corynebacterium diphtheriae*[a]
Fungi: *Candida* species[b]
Epiglottitis
Common
Bacteria: *Haemophilus influenzae* type b
Less common
Bacteria: *H. influenzae* non-type b, *H. parainfluenzae*, *S. pyogenes*, *S. pneumoniae*
Uncommon
Bacteria: *Pseudomonas aeruginosa*[b], *Klebsiella* species
Fungi: *Candida* species[b]

[a]Important in endemic areas, but not the USA
[b]Immunocompromised patients
RSV respiratory syncytial virus, *HSV* herpes simplex virus, *CMV* cytomegalovirus, *EBV* Epstein-Barr virus

Management

Acute laryngitis is typically a self-limited illness that can be treated symptomatically with oral hydration, voice rest, and over-the-counter pain medication. Treatment with antibiotics or steroids is not usually necessary, but antibiotics are indicated in cases of secondary bacterial infection, and steroids if there is considerable concern over airway edema.

Croup (Acute Laryngotracheitis)

Croup is edema and inflammation of the subglottic airway. It is the most common cause of airway obstruction in children aged 6 months to 6 years [1].

Infectious Etiology

Parainfluenza virus accounts for two-thirds of the cases, with less common causes including respiratory syncytial virus, influenza, rhinovirus, adenovirus, enterovirus and rarely measles virus or HSV (Table 11.1) [2].

Epidemiology

Croup mainly affects patients aged 6 months to 3 years, with a peak incidence in the second year of life [3]. It occurs more commonly in males, with a male to female preponderance of 1.4/1 [3]. Patients most often develop croup in the fall or early winter.

Clinical Features

Viral croup has an incubation period of 2–6 days and typically starts with a prodrome of rhinorrhea, congestion, and low grade fever [3]. Following the prodrome, patients develop the characteristic symptoms of barky cough, hoarseness, and inspiratory stridor. The cough usually resolves after 3 days.

Diagnostic Evaluation

The diagnosis of croup is typically made based on the history and physical exam, however, an anterior-posterior (AP) and lateral radiograph of the neck may help confirm the diagnosis. The typical finding on AP imaging of the neck is the "steeple sign" which occurs secondary to the subglottic edema [4]. The radiographic findings are neither sensitive nor specific, making clinical history the most reliable diagnostic tool [5].

Management

Treatment of viral laryngotracheobronchitis varies depending on the severity of the infection. Patients with a mild episode of croup are typically treated with a single dose of intramuscular (IM) or oral corticosteroids, usually dexamethasone [0.6 mg/kg (maximum dose of 10 mg)], or inhaled budesonide (2 mg) prior to discharge home. However, should a child present with more significant symptoms, they may be admitted for observation and treated with fluids, intravenous corticosteroids, nebulized racemic epinephrine (2.25 %; 0.5 mL in 2.5 mL of saline), and oxygen supplementation if the O_2 saturation is <92 %. Nebulized racemic epinephrine can be repeated every 15–20 min if indicated, but the clinical effect only lasts 1–2 h, so children should be carefully observed for symptom return.

The benefits of corticosteroids in the treatment of viral laryngotracheitis has been established in multiple randomized placebo controlled trials demonstrating a variety of benefits including an improvement in croup scores, decreased rates of return to the emergency department (ED) or health care provider, decreased rates of hospitalization, decreased length of hospital stays, and decreased need for respiratory support [6–9]. The majority of patients will respond to treatment within the first 6–12 h [9].

In the most severe cases of croup, patients may require direct laryngoscopy, bronchoscopy and intubation, although this is typically avoided as the endotracheal tube can contribute to the development of subglottic stenosis. Children with a history of multiple episodes of croup or who are under 6 months of age at the time of their first episode should undergo elective laryngoscopy and bronchoscopy when they are healthy to evaluate for a concomitant subglottic disease process (Fig. 11.1).

Epiglottitis

Acute bacterial laryngeal infections represent a relatively rare group of conditions in the pediatric population; however it is imperative that physicians are familiar with and recognize bacterial laryngitis due to its significant potential for morbidity and mortality.

Infectious Etiology

In the post-vaccination era the bacteriology of epiglottitis has changed. Although *Haemophilus influenzae* type b continues to be the most commonly implicated organism, other organisms are now increasingly found. There have been reports of β-hemolytic streptococci, Staphylococcus *aureus*, pneumococcus, nontypable *Haemophilus influenzae*, *H. parainfluenzae*, and *Klebsiella* species (Table 11.1) [10].

Epidemiology

Epiglottitis has historically been one of the most devastating pediatric bacterial laryngeal infections. It most commonly affects children between 2 and 7 years of age [5]. Prior to the introduction of the polysaccharide vaccine to *Haemophilus influenzae* type b in 1985, epiglottitis was routinely

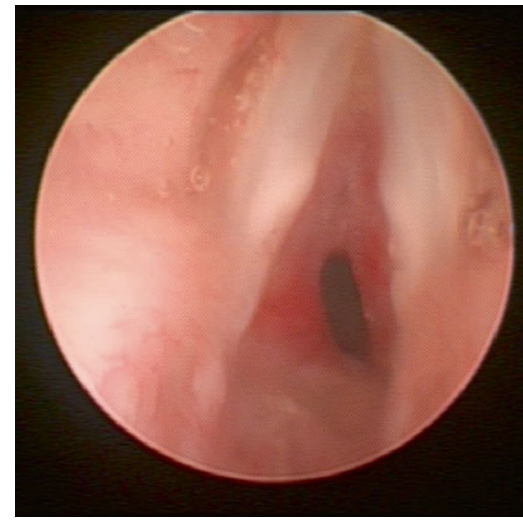

Fig. 11.1 Patient with a history of SGS and acute croup

encountered in the pediatric setting. Rates in the pre-vaccination era were reportedly between 4.9 and 6.1 cases per 100,000 children per year. These rates have dropped dramatically, and are now reported between 0.02 and 0.3 cases per 100,000 children per year [11]. Indeed, epiglottitis has become almost exclusively a condition of adults, and is often referred to as supraglottitis; however, diligence to identify epiglottitis in children remains necessary due to the potentially fatal outcomes. Contributing factors for continued *H. influenzae* type b infection are susceptibility of children under the age of 1 who have not completed their vaccination schedule, the increasing frequency of vaccination deferment, and the imperfect rate of immunity conferred by the vaccine.

Clinical Features

The classic teaching is that a child will present toxic appearing, assuming the tripod position (sitting upright, with the chin tilted upwards, and bracing themselves with an outstretched arm). There is typically a history of fever, severe odynophagia, drooling, and muffled speech. Inspiratory stridor is present at times, and signals almost complete airway obstruction. These symptoms tend to develop rapidly over the course of hours.

Diagnostic Evaluation

The diagnosis of epiglottitis is accomplished through history and a non-invasive clinical examination. The patients, having a combination of airway swelling and significant pooling of secretions, can be easily be pushed into airway collapse or laryngospasm. Anxiety provoking maneuvers should be avoided, including intraoral examination to reduce patient anxiety.

In a patient with no symptoms of airway compromise, radiographic imaging may be considered with the patient accompanied to the radiology department by an anesthesiologist or otolaryngologist. The imaging study of choice is a lateral soft tissue film of the neck. Classically patients will exhibit thickening and rounding of the epiglottis on lateral neck film, often referred to as the "thumb print" sign.

Management

The definitive treatment in patients with epiglottis is establishment of an airway, preferably in the operating room under controlled conditions. Reports from the pediatric literature indicate that institution of an artificial airway significantly reduces the number of deaths [12]. In the operating room open lines of communication between the anesthesia team and otolaryngologists is imperative. The patient should be kept spontaneously breathing and direct laryngoscopy and intubation should be performed either over a telescope or with a bronchoscope if possible (Fig. 11.2). After cannulation of the airway is accomplished, a thorough examination of the larynx takes place, cultures can be obtained, and blood may be drawn for any remaining tests. After the airway is established the patient remains intubated and is transferred to the ICU for intravenous antibiotics.

Multiple antibiotic regimens have been suggested. Traditionally chloramphenicol and ampicillin were used, but this has been replaced with third generation cephalosporins (i.e. ceftriaxone) or beta-lactamase resistant penicillins (i.e. ampicillin/sulbactam). The use of corticosteroids in reduction of airway edema is controversial. Their use has been advocated in the past; however no studies have reported any significant association with better outcome. Most data supporting their use is based on anecdotal reports [13]. Patients typically show significant improvement over the course of 2–3 days.

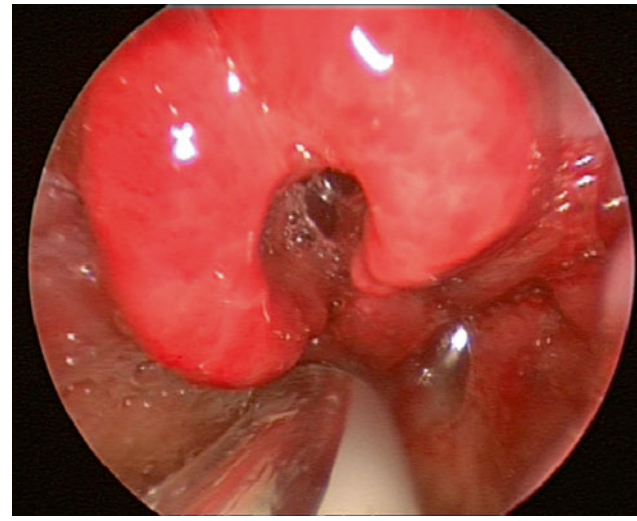

Fig. 11.2 Direct laryngoscopy findings in a 10-year-old presenting with epiglottitis

The patient is eligible for extubation when the ventilator is weaned to minimal settings and there is a free leak around an intact endotracheal tube cuff. The optimal location for extubation is the operating room, where direct laryngoscopy can be repeated prior to extubation to ensure that the inflammation has resolved. Once extubated, the patient should be monitored for an additional 24–48 h.

Recurrent Respiratory Papillomatosis

Recurrent respiratory papillomatosis (RRP) is a chronic disease caused by human papillomavirus (HPV) types 6 and 11. It is characterized by the benign growth of squamous papillomas in the aerodigestive tract and is the most common benign laryngeal neoplasm in children.

Infectious Etiology

HPV was confirmed as the causative agent in RRP in the 1990s and has been identified in nearly every case [14]. HPV 6 and HPV 11 are the most common subtypes identified in airway RRP and the disease severity and course vary depending on the identified subtype. In general, patients infected with HPV 11 have a more significant course with a higher incidence of airway obstruction, making them more likely to require a tracheotomy than those patients infected with HPV 6 [15, 16].

Epidemiology

The majority of patients (75 %) with RRP are diagnosed before their fifth birthday [17]. The youngest recorded patient to develop RRP is 1 day old, with the oldest being 84 [18]. Patients diagnosed before 3 years of age are 3.6 times more likely to require more than 4 procedures a year and 2 times more likely to have 2 anatomic sites affected [19].

The incidence of RRP in the United States is estimated to be 4.3 per 100,000 children, with between 80 and 1500 new cases of childhood-onset RRP diagnosed per year [18–20].

Clinical Features

RRP is the second most common cause of hoarseness in children, with the majority of patients presenting with hoarseness, as the vocal fold is usually the first site of lesions. The second most common presenting symptom is inspiratory stridor. Less common symptoms include cough, dyspnea, dysphagia, and acute respiratory distress. Extralaryngeal RRP is present in about 30 % of children and the oral cavity is the most common site, followed by the trachea and bronchi, and esophagus [18, 21].

RRP has a somewhat unpredictable clinical course. The majority of patients will have 1 year of symptoms prior to diagnosis [18]. Disease progression also varies greatly between patients. In some patients, the disease spontaneously regresses, while others may require surgical interventions and adjuvant therapies every few weeks to months.

Diagnostic Evaluation

RRP is diagnosed on endoscopy when the characteristic papillomatous type lesions are identified within the larynx. Once suspected, direct laryngoscopy, bronchoscopy and surgical removal with biopsy should be performed to evaluate the extent of the disease and to provide pathologic confirmation (Fig. 11.3). Histopathology demonstrates stratified squamous epithelium covering multiple finger-like projections with a central fibrovascular core. The tissue should also be sent for viral typing.

Management

The primary goal of treatment for RRP is to prevent airway obstruction while minimizing laryngeal scarring and complications. Microlaryngoscopy is performed and the papillomas are debulked using either cold steel, microdebrider, or a laser, most commonly CO2. The intervals between surgical interventions can vary greatly between patients. Adjuvant treatment is recommended in patients with four or more trips to the operating room per year, rapid regrowth of papillomas with airway compromise, or distal disease spread [14]. It is estimated that up to 20 % of patients require adjuvant treatments with intralesional cidofovir being the most widely used [21].

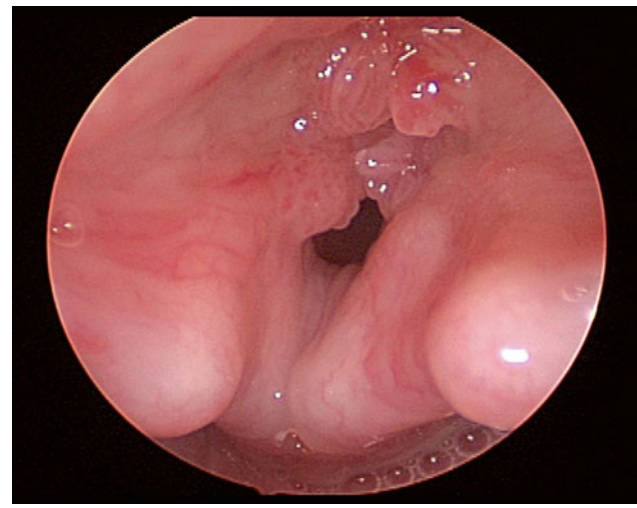

Fig. 11.3 Direct laryngoscopy on a 5-year-old patient with laryngeal recurrent respiratory papillomatosis affecting the true vocal folds

The most significant risk of surgical intervention in patients with RRP is airway stenosis. Patients with bilateral vocal cord disease extending toward the anterior or posterior commissure and patients requiring frequent surgical interventions are at the greatest risk. In some cases, complete removal should be avoided and debridement may be staged to avoid laryngeal web formation and scarring. Unless unavoidable, tracheotomy is not recommended due to the risk of disease spread into the lower airway.

Other Causes of Laryngeal Infection

There are several additional, however, less common causes of laryngeal infection that may present with airway symptoms. These include diphtheria, candidiasis, and tuberculosis.

Diphtheria

Diphtheria occurs globally and is endemic in many developing countries. It is caused by toxin-producing strains of *Corynebacterium diphtheriae*. Infected or colonized individuals transmit the organism to close contacts by respiratory droplets. Symptoms usually develop gradually, with mild fever, sore throat, and cervical lymphadenopathy. Initially, the pharynx is mildly erythematous. Up to three-fourths of patients progress to develop an adherent pseudomembrane that can involve any part of the respiratory tract.

The majority of diphtheria cases are exclusively tonsillopharyngeal. However, downward extension of infection can involve the larynx. Rarely, primary laryngeal diphtheria occurs without involvement of other anatomic sites, and presents as a nonspecific croup-like illness. A review of 1433 adult and pediatric cases from 1940 to 1950 in Los Angeles found that 276 cases (19 %) involved the larynx [22]. Twenty cases (1 %) were primary laryngeal diphtheria and all occurred in patients less than 20 years old. The mortality rate for non-laryngeal involvement was 4.7 % compared to 29.5 % for laryngeal involvement.

Diphtheria is diagnosed by culturing the nose, throat, and/or the pseudomembrane. Because special media is needed for bacterial growth, the microbiology laboratory should be notified that diphtheria is suspected. Samples should be promptly transported to the laboratory. Treatment consists of administration of antibiotics and antitoxin. Antitoxin should be administered based on clinical suspicion, and not delayed for culture results. It can be obtained from the Centers for Disease Control and Prevention (CDC) at 1-404-639-2889. Dose and frequency of antitoxin administration depends on the clinical presentation. The American Academy of Pediatrics has suggested 20,000–40,000 units for pharyngeal or laryngeal disease <48 h duration, 40,000–60,000 units for nasopharyngeal disease, and 80,000 to 120,000 units for diffuse neck swelling or extensive disease of ≥3 days duration [23]. Antibiotics stop toxin production, eradicates the infection, and reduces transmission. Recommended antibiotics include erythromycin (oral or intravenous) or penicillin G (intravenous or intramuscular) for 14 days. Repeat cultures should be obtained at 24 h intervals after completing antibiotics to confirm elimination of the organism from two consecutive negative cultures. Following treatment, patients should be immunized against diphtheria because disease does not assure immunity. The health department should be notified and close contacts identified, tested, and be considered for prophylactic antibiotics.

Candidiasis

Acute fungal infections of the larynx are uncommon among children. In the pediatric population, serious laryngeal candidiasis is seen almost exclusively in immune-compromised individuals, with only a few case reports in immune-competent children. [24]. Pediatric patients with serious laryngeal candidiasis most often present with odynophagia, dysphagia and hoarseness, however they may present as an airway emergency. A more mild clinical presentation of dysphonia has been reported among adolescents using steroid inhalers [25].

Diagnosis is made with flexible fiberoptic laryngoscopy and can be confirmed with biopsy and tissue culture. The typical appearance is erythematous and edematous mucosa with focal ulcerations and pseudomembrane-like white plaques. Exophytic lesions may also be seen, mimicking squamous cell carcinoma and respiratory papillomatosis. The lesions can involve the glottis, false cords, epiglottis, and surrounding tissue. Treatment is tailored to the individual patient depending on the underlying medical condition and extent of infection; intravenous amphotericin B, oral fluconazole, and topical nystatin have all been used. Oral antifungal agents, such as fluconazole, are the treatment of choice for laryngeal candidiasis associated with inhaled steroids [25].

Tuberculosis

Tuberculosis (TB) is a very rare laryngeal infection in the United States, and is caused by *Mycobacterium tuberculosis*. Patients typically present with severe pharyngitis with mucosal ulcerations and exudate. Patients with human immunodeficiency virus (HIV) infection are at increased risk for tuberculosis disease.

To diagnose laryngeal TB, patients must undergo a direct laryngoscopy and bronchoscopy with biopsies. The tissue is sent for culture and pathologic analysis and the diagnosis confirmed with the findings of acid-fast bacilli and caseating granulomas respectively. Due to the fastidiousness of mycobacteria, isolation by culture may take several weeks. PCR can be used to amplify the DNA and assist in diagnosis [5].

After establishment of a stable airway, laryngeal TB is treated with medical therapy with at least two antituberculous antibiotics for 6–12 months. The most commonly used antibiotics are isoniazid, rifampin, ethambutol, and pyrazinamide. In resistant cases, a 3–5 drug regimen and a longer course of therapy may be required.

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