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High risk and low prevalence diseases: Adult epiglottitis

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ABSTRACT

Introduction: Adult epiglottitis is a serious condition that carries with it a high rate of morbidity and even mortality due to airway occlusion.
Objective: This review highlights the pearls and pitfalls of epiglottitis in adult patients, including diagnosis, initial resuscitation, and management in the emergency department (ED) based on current evidence.
Discussion: Epiglottitis is a life-threatening emergency that occurs more commonly in adults in the current medical era with vaccinations. Children present more commonly with acute respiratory distress and fever, while adults present most commonly with severe dysphagia in a subacute manner. Other symptoms may include drooling, muffled voice, and dyspnea. *Streptococcus* and *Staphylococcus* bacteria are the most common etiologies, but others include viral, fungal, caustic, thermal injuries, and autoimmune. Lateral neck radiographs assist in diagnosis, but they may be falsely negative. Visualization of the epiglottis is the key to diagnosis. Airway assessment and management are paramount, which has transitioned from direct laryngoscopy to flexible intubating endoscopy and video laryngoscopy with assistance from anesthesia and/or otolaryngology if available. Along with airway assessment, antibiotics should be administered. Corticosteroids and nebulized epinephrine are controversial but should be considered. Patients should be admitted to the intensive care setting for close airway observation or ventilatory management if intubated.
Conclusions: An understanding of epiglottitis can assist emergency clinicians in diagnosing and managing this potentially deadly disease.

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1. Introduction

This article series addresses high risk and low prevalence diseases that are encountered in the emergency department (ED). Much of the primary literature evaluating these conditions is not emergency medicine focused. By their very nature, many of these disease states and clinical presentations have little useful evidence available to guide the emergency physician in diagnosis and management. The format of each article defines the disease or clinical presentation to be reviewed, provides an overview of the extent of what we currently understand, and finally discusses pearls and pitfalls using a question-and-answer format. This article will discuss epiglottitis in adults. This condition's low prevalence but high morbidity and mortality, as well as its variable atypical patient presentations and challenging diagnosis, makes it a high risk and low prevalence disease.

1.1. Definition

Epiglottitis, also known as supraglottitis, is an airway emergency defined by inflammation of the epiglottis and adjacent supraglottic structures, which may require emergent intervention to prevent airway obstruction and death [1-4]. Cellulitis and epithelial infection occur in the aryepiglottic folds and epiglottis, which can rapidly spread to surrounding tissues due to the robust lymphatic network in the supraglottic oropharynx and acutely cause supraglottic edema and decreased airway patency [2,3,5].

1.2. Epidemiology

While the incidence of pediatric epiglottitis has been declining due to the *Haemophilus influenzae b* vaccination, adult epiglottitis has been steadily increasing with an incidence of 1 per 100,000 to 4 per 100,000 in the U.S. [6-11] In comparison, the pediatric incidence has decreased to 0.5 per 100,000 [12]. This rise in epiglottitis has been attributed to increased physician recognition of this diagnosis as well as increased use of flexible endoscopy [13,14]. Despite this increase in adult patients affected, overall mortality rates approximate 1% in adults

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based on retrospective data [15,16]. A retrospective study published in 2021 found pediatric and adolescent deaths decreased from 0.064 per 100,000 individuals in 1979 to 0.001 per 100,000 individuals in 2017, while in adults, it decreased from 0.015 per 100,000 individuals in 1979 to 0.006 per 100,000 individuals in 2017 [17]. However, adults accounted for over 63% of total deaths in this study [17].

The most common presentation of epiglottitis involves males between 42 and 48 years old [18]. In adults, the most common causative bacterium is *Streptococcus* species with *Staphylococcus* species second. The infectious form of epiglottitis occurs due to direct invasion of the epithelial layer by the organism or by bacteremia. Direct invasion can occur through the posterior nasopharynx, and microscopic trauma of the epithelial surface can increase the risk of epiglottitis [1]. Other etiologies include viral or fungal infection, foreign body ingestion, thermal injury, lymphoproliferative disease or graft-versus-host disease, chronic granulomatous diseases, and caustic ingestions (e.g., hydrochloric acid and sodium hydroxide) [2,19].

These conditions result in edema and inflammatory cell accumulation in the potential space between the epiglottic cartilage and epithelial layer causing swelling of the epiglottis and supraglottic structures [20]. Infection and inflammation can worsen rapidly due to the vast lymphatic and vascular network surrounding the supraglottic region; however, the subglottic region is typically not affected due to the tightly bound epithelium at the vocal cord level [20]. This swelling of the supraglottic region decreases the upper airway caliber, which may result in airway obstruction [21].

2. Discussion

2.1. Emergency department presentation

Pediatric epiglottitis classically presents with acute progression of stridor, respiratory distress, and tripod positioning. Due to the larger airway diameter, adult epiglottitis rarely presents with the classic features associated with pediatric epiglottitis [20]. Adults most commonly present with voice changes, odynophagia, dysphagia, and drooling. While an acute progression over hours may occur in adults, the presentation is often more subacute over days. A 10-year study of 60 adult epiglottitis patients highlighted that 100% of patients complained of odynophagia; in this cohort, 85% of patients presented with dysphagia and 74% with voice changes [22]. Adult patients may have anterior neck cellulitis, toxic appearance, and anterior cervical lymphadenopathy [20]. Patients may present with cough and be in a tripod position to maximize airway diameter, but this is less common in adults due to the larger airway caliber.

2.2. Emergency department evaluation

Laboratory evaluation is nonspecific. Blood and throat cultures have limited utility, yielding an organism in 0–17% and 10–33% of cases, respectively [7,23,24]. Direct epiglottic cultures have up to a 75% bacterial yield [7,23,24]. Initial lateral neck radiography can be acquired in the upright position and may reveal the characteristic thumbprint sign or vallecula sign (Fig. 1) [25]. Point-of-care ultrasound (POCUS) may demonstrate an increased anteroposterior diameter of the epiglottis as well as acoustic shadowing of the hyoid bone and epiglottis [26,27]. The ideal modality for diagnosis of the epiglottitis includes direct visualization, typically with flexible intubating endoscopy with potential intubation and/or tracheostomy (Fig. 2) [28-30].

2.3. Emergency department management

Management focuses on evaluation for airway intervention and antibiotics [1,5]. Adult patients with epiglottitis may not present in respiratory distress, but due to the supraglottic inflammation and edema patients are at risk for airway obstruction and sudden decline.

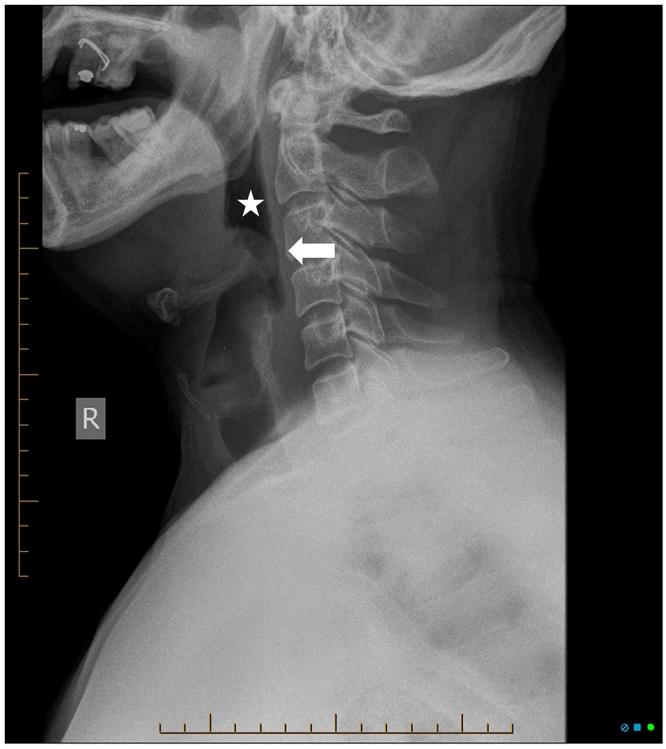

Fig. 1. Lateral radiograph demonstrating the thumbprint sign (white arrow) and vallecula sign (white star) of epiglottitis. Case courtesy of Dr. Eric Brecher, Radiopaedia.org, rID: 41935.

Consultation with otolaryngology and anesthesiology is recommended as these patients present with a challenging airway. Patients in respiratory distress are best managed in a controlled setting with anesthesia and surgery available in preparation for cricothyrotomy or tracheostomy if needed. In the ED, antibiotics should include a third-generation cephalosporin or an extended spectrum penicillin, as well as coverage for methicillin-resistant *Staphylococcus aureus* (MRSA). An appropriate regimen includes ceftriaxone (2 g intravenous [IV]) or ampicillin-sulbactam (3 g IV) with vancomycin (20 mg/kg IV) for MRSA coverage. Levofloxacin (750 mg IV) may be utilized for those with severe penicillin allergies, and cefepime (2 g IV) or piperacillin-

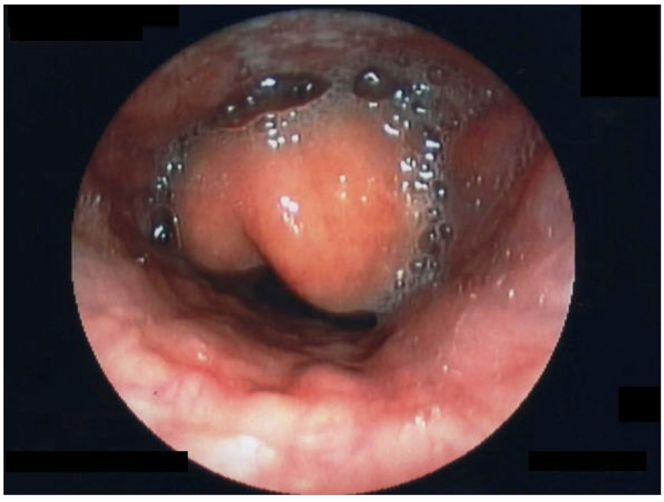

Fig. 2. Epiglottitis demonstrated on flexible intubating endoscopy. From https://commons.wikimedia.org/wiki/File:Epiglottitis_endoscopy.jpg.

tazobactam (3.375 g IV) is recommended for those with severe immunocompromise or concern for *Pseudomonas aeruginosa*. Nebulized epinephrine may reduce oropharyngeal edema and temporize the patient [31]. While corticosteroids can theoretically reduce airway edema, there is currently no evidence that corticosteroids reduce hospital or intensive care unit (ICU) length of stay, rates of intubation, or mortality [32-34]. These patients should be admitted to the ICU for close monitoring [34].

3. Pearls and pitfalls

3.1. How does the presentation of epiglottitis differ between adults and children?

Due to anatomical differences in airway shape and diameter, children and adults typically present differently with epiglottitis [5]. The pediatric epiglottis is comprised of more pliant cartilage and is more anterior and superior compared to the rigid epiglottis and airway of adults, and the narrowest portion of the pediatric airway is the subglottis compared to the glottis in adults [1,2,5,7]. Children classically present with tripod positioning, fever, and stridor progressively worsening over hours, whereas adults present with progressive odynophagia and dysphagia in a more subacute manner over days [35]. Tripod positioning and cough are present in less than 50% of adults with epiglottitis [10,36]. Children are more likely to present with stridulous breathing due to their smaller airway diameter secondary to Poiseuille's law as compared to adults, with stridor occurring in only 30% of adults [5,35]. Adult patients present most commonly in a nonspecific manner with severe sore throat, dysphagia, and drooling. Nearly all adults with epiglottitis present with pharyngitis or odynophagia (90–100% of patients) [5,7]. Fever can occur in 26–90% of cases, though only 50–65% will present with drooling or difficulty handling secretions and 50–80% with a muffled voice [5,7,10,19,23,29,37]. Adult epiglottitis is less likely to be associated with bacteremia as compared to pediatric cases, though this is not correlated to the severity of presentation [7].

3.2. What physical examination findings and maneuvers can assist in diagnosis?

Approximately 90% of adults with epiglottitis will have a normal oropharyngeal examination [37].

In patients with multiple healthcare visits for sore throat or pain out of proportion to examination, epiglottitis should be considered. Epiglottitis should also be considered in patients with severe pain with palpation of the external larynx or hyoid bone. In patients without evidence of respiratory distress, visualization of the supraglottic region can be attempted using a Macintosh laryngoscope. Nebulized lidocaine can assist with the procedure as can viscous lidocaine placed on the patient's tongue. The clinician faces the patient's face, holds the Macintosh laryngoscope in a "tomahawk" position, and places the Macintosh blade onto the patient's tongue (Fig. 3). The patient should then attempt speaking in a high-pitched tone, which will raise the supraglottic structures several centimeters. The epiglottis may be visible at that point. Video laryngoscopy may offer improved views. However, this should not be performed in patients in extremis or those who have difficulty tolerating the procedure.

3.3. What is the differential diagnosis in the patient with sore throat but an unremarkable oropharyngeal examination?

As discussed, up to 90% of adult patients with epiglottitis will present with a normal oropharynx [37]. Thus, clinicians should not exclude epiglottitis, or other dangerous conditions, based on a normal oropharyngeal examination. There are a variety of other conditions that can be airway threatening and present with a normal oropharyngeal examination (Table 1). Clinicians must consider these conditions in this setting.

Fig. 3. Tomahawk position. Reproduced from https://www.tamingthesru.com/blog/procedural-education/so-you-want-to-tomahawk-somebody?. Used with permission of Dr. Jeffery Hill, MD.

3.4. Is imaging necessary, and if so, what should be considered?

Imaging in epiglottitis is a vital component of the diagnosis. Lateral neck radiograph may assist and is performed with the patient upright [25]. The thumbprint sign (sensitivity of 89.2% and specificity of 92.2%) and the vallecula sign are radiographic evidence of epiglottitis [38]. The thumbprint sign represents a swollen epiglottis, and the vallecula sign occurs when the normal deep linear air space from the base of the tongue to the epiglottis is shallow or absent (Fig. 1) [25,38]. Additionally, an epiglottic width greater than 6.3 mm demonstrates a sensitivity of 75.8% and a specificity of 97.8% [25]. However, lateral neck radiographs have a false negative rate of 31.9% [21,25]. Thus, lateral radiographs may assist in confirming the diagnosis, but this modality should not be used to rule out the diagnosis [21]. Computed tomography (CT) requires the patient to lay supine, which may aggravate impending airway occlusion and should be pursued in those who can tolerate the positioning and to assess for complications [25]. If acquired, CT with IV contrast has a sensitivity of 88–100% and specificity of 97–96% and may demonstrate effusion, obliteration of

Table 1
Conditions causing sore throat but with normal oropharyngeal examination.

- Caustic ingestion
- Disseminated *Mycobacterium tuberculosis* with laryngeal lesions
- Epiglottitis
- Foreign body in inferior oropharynx
- Lemierre's syndrome
- Parapharyngeal space infection
- Retropharyngeal abscess
- Tracheitis
- Early Ludwig's angina

surrounding fat planes, thickening of false vocal cords, retropharyngeal enhancement and edema, and epiglottic abscess, the last of which is associated with a high likelihood of requiring airway intervention [39-41]. Due to the emergent nature of epiglottitis, POCUS presents an enticing option to evaluate the epiglottis while the patient remains in the position of comfort [26,27]. To evaluate the epiglottis using POCUS in a patient sitting with the neck extended, a linear transducer is placed in the transverse position at the level of thyrohyoid membrane halfway between the hyoid bone and the thyroid cartilage (Figs. 4–6). The epiglottic thickness and width at the thyrohyoid membrane is then measured. Preliminary studies suggest the anteroposterior diameter of the midpoint and lateral epiglottis may be larger compared to healthy controls, but further data are needed [27]. A linear transducer in the longitudinal plan may demonstrate the alphabet P sign, which is also suggestive of epiglottitis (Fig. 6) [26]. This is formed by the hyoid bone and the acoustic shadow, preepiglottic space, and swollen epiglottis, which demonstrates a P-shaped hypoechogenicity [26].

3.5. What are the treatment priorities and nuances, and what role do steroids play?

After assessment for airway intervention and management, antibiotics are a mainstay of treatment. Appropriate antibiotics include a third-generation cephalosporin or an extended spectrum penicillin, such as ceftriaxone (2 g IV) or ampicillin-sulbactam (3 g IV) with vancomycin (20 mg/kg IV) for MRSA coverage. For those with severe penicillin allergies, levofloxacin (750 mg IV) may be utilized, and for those with severe immunocompromise or concern for *Pseudomonas aeruginosa* (e.g., human immunodeficiency virus, end stage renal or liver disease, diabetes mellitus, those receiving chemotherapy or biologic agents, etc.) cefepime (2 g IV) or piperacillin-tazobactam (3.375 g IV) is recommended [2,5,28-30]. Metronidazole is not necessary based on the current literature, which suggests anaerobes are not associated with the condition [5]. In addition to antibiotics, nebulized epinephrine can be used in adults with epiglottitis to assist with airway bronchodilation and reduce edema; however, data suggesting improved patient-centered outcomes with nebulized epinephrine are lacking [28,37]. Caution is recommended in children regarding nebulized epinephrine as it may cause additional agitation, laryngospasm, and rapid deterioration without proven benefit [42-44].

The use of corticosteroids by any available route (e.g., IV, intramuscular [IM], per os [PO]) in epiglottitis remains controversial, though between 20 and 83% of epiglottitis patients receive corticosteroids [23,29]. The physiologic justification for corticosteroid use includes reduction of airway inflammation and edema to improve airway patency [5,7,45]. However, retrospective studies investigating corticosteroid administration in epiglottitis have not demonstrated an improvement in ICU length of stay, hospital length of stay, or duration of intubation [10,23,29,46]. These studies may be biased as more severely ill patients were more likely to receive corticosteroids [5]. Further data are needed before corticosteroids are recommended in the management of epiglottitis, but they should be considered in those in extremis. Several options include methylprednisolone (125 mg IV) or dexamethasone (10 mg IV or IM).

3.6. What factors on history or physical exam are predictors of patients requiring airway intervention?

Several factors are associated with need for intubation, including subjective dyspnea and a history of diabetes mellitus, based on the literature [39]. Additionally, those with rapid symptom progression over 12–24 h also more commonly require airway intervention, especially in those with stridor [47]. In addition to stridor, other presentations associated with the need for intubation include drooling, respiratory discomfort, and dyspnea [10,11,23,37]. While a variety of vital sign abnormalities and laboratory values have been evaluated as predictors for airway intervention in children, an experienced clinician's observation and impression of the child are far more predictive than clinical measures [48]. In contrast, adults with respiratory rate greater than 20 breaths per minute with subjective complaint of dyspnea required visualization of the airway, while a respiratory rate greater than 30 breaths per minute, hypercarbia (PCO_2 greater than 45 mmHg), moderate respiratory distress, stridor, or retractions were indicative of need for airway intervention [37,47]. CT demonstrating deep supraglottic effusion was found to be protective against need for intubation [39]. On visual inspection of the oropharynx, both supraglottic edema extension and presence of epiglottic abscess were associated with an increased need for airway intervention. In a multivariate regression analysis for intubation prediction factors, the combination of dyspnea and supraglottic edema extension yielded an area under the curve of 90% [39,47].

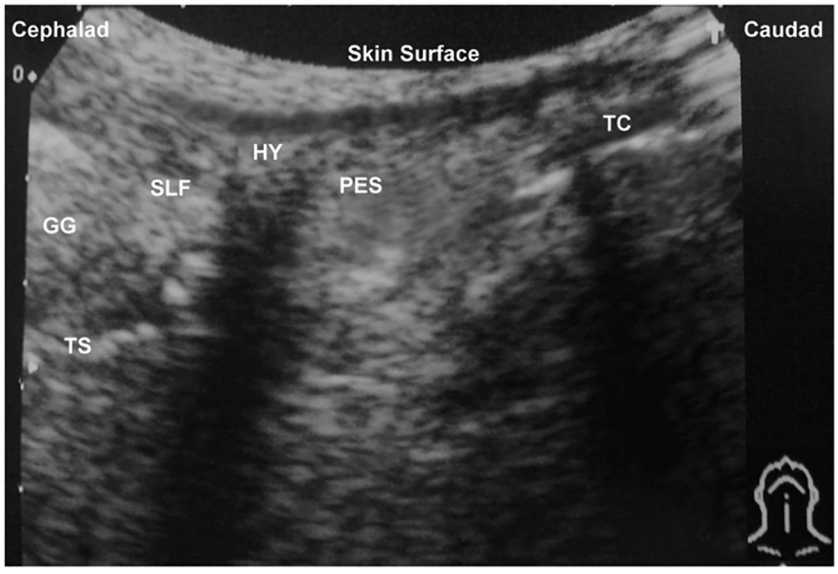

Fig. 4. Normal structure of the supraglottic region using POCUS. GG indicates genioglossus; TS, tongue surface; SLF, sublingual fat; HY, hyoid bone; PES, periepiglottic space; TC, thyroid cartilage. Obtained with permission from Dr. Tzu-Yao Hung [26].

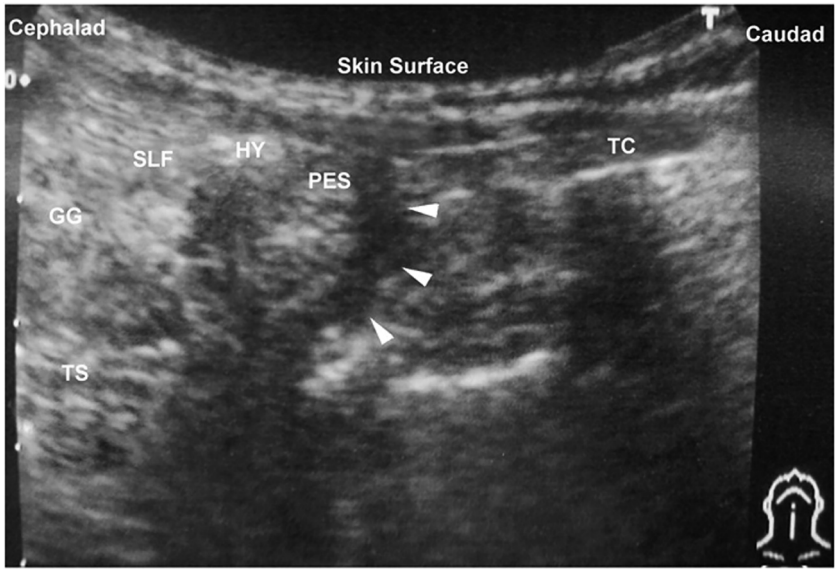

Fig. 5. Under sniffing position, the transducer is placed in linear orientation at the thyrohyoid membrane. The white arrows point at the swollen hypoechogenic epiglottis in a patient with epiglottitis. GG indicates genioglossus; TS, tongue surface; SLF, sublingual fat; HY, hyoid bone; PES, periepiglottic space; TC, thyroid cartilage. Obtained with permission from Dr. Tzu-Yao Hung [26].

3.7. How can video laryngoscopy or awake flexible endoscopic intubation be used for diagnosis and management of suspected adult epiglottitis?

Assessment for immediate airway intervention is the main priority in epiglottitis, as intubation rates range from 9 to 50% in adults with epiglottitis [19,31,39,49,50]. A 2010 review estimated intubation rates of 13.2% [15]. Historically, operative room fiberoptic bronchoscopy with potential tracheostomy in the event of failed intubation has been the airway management of choice [51]. However, this may not need to occur in the operating room with the advent of awake intubation with the use of flexible intubating endoscopy [29,47]. Flexible intubating endoscope (and less commonly video laryngoscopy) has become the preferred method of airway control over the past 20 years [29,49,52,53]. Awake nasotracheal flexible intubating endoscopy is the preferred method, though awake video laryngoscopy has also been effective [16,54-56]. Of note, supraglottic airways such as a laryngeal mask airway should not be utilized in this patient population as the device will not seat correctly and may worsen edema and precipitate impending airway occlusion [37]. In a recent retrospective review of 70 adult epiglottitis patients, 55% of airway interventions occurred in the ED. [36] In these patients, management occurred primarily by otolaryngologists as well as emergency physicians and anesthesiologists employing predominantly fiberoptic devices in 86.8% of cases and video laryngoscopy in 5.7% of cases [36].

Table 2 provides pearls concerning the presentation, evaluation, and management of epiglottitis.

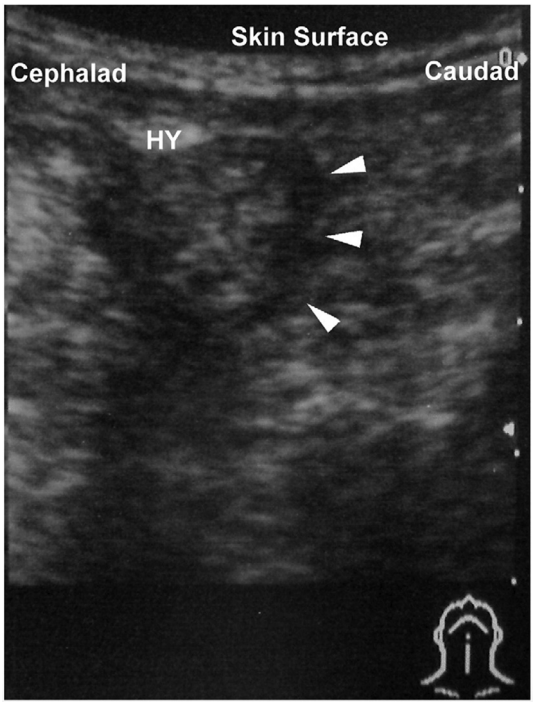

Fig. 6. "Alphabet P sign" formed by acoustic shadow of hyoid bone (HY) and swollen epiglottis (white arrows). Obtained with permission from Dr. Tzu-Yao Hung [26].

Table 2
Epiglottitis pearls.

- Epiglottitis is currently more common in adults than children.
- The presentation of pediatric epiglottitis includes fever, tripod positioning, stridor, and acute respiratory distress. This differs from adults, who present more often subacutely with severe, progressive odynophagia and dysphagia.
- Do not rely on a normal oropharyngeal examination to exclude epiglottitis.
- Lateral neck radiograph may be an initial helpful imaging test but should not be used to rule out the disease. CT is a better imaging modality, but it requires the patient to lay supine which may worsen respiratory status.
- Treatment includes airway assessment and antibiotics such as a third-generation cephalosporin or an extended-spectrum penicillin. Cefepime can be utilized if the patient is immunocompromised. Vancomycin can be used for coverage of MRSA.
- Corticosteroids and nebulized epinephrine may reduce airway edema and improve patient symptoms, but they have not demonstrated improvement in patient-centered outcomes.
- Predictive factors for airway intervention include subjective dyspnea, history of diabetes mellitus, rapid symptom progression, stridor, drooling, tachypnea, hypercapnea, and concerning imaging findings (e.g., supraglottic edema extension, epiglottic abscess).
- Airway intervention should be performed in a controlled setting with multiple airway adjuncts available. Awake intubation with nasotracheal flexible intubating endoscopy is the preferred airway tool of choice followed by video laryngoscopy.

4. Conclusion

Epiglottitis is an airway-threatening emergency that presents increasingly more in adults after *H. influenzae b* vaccination. Children present more commonly with tripod positioning and fever while adults universally complain of odynophagia, though other frequent symptoms include drooling, muffled voice, and dyspnea. *Streptococcus* and *Staphylococcus* species are the most common infectious causes of epiglottitis, but other etiologies include viral, fungal, caustic, thermal injuries, and autoimmune. Lateral neck radiographs may aid in the diagnosis, but there is a significant false-negative rate. Thus, visualization of the epiglottis is the key to diagnosis. Airway assessment and management are paramount, which has transitioned from direct laryngoscopy to fiberoptic intubation and rarely video laryngoscopy. Rapid onset of symptoms along with history of diabetes mellitus, perceived dyspnea, stridor, tachypnea, and hypercapnea are all risk factors for intubation. After airway assessment and potential intervention, antibiotics including a third-generation cephalosporin or extended beta lactamase with MRSA coverage should be administered. The use of corticosteroids and nebulized epinephrine is controversial but should be considered. Disposition for these patients should be the intensive care setting for close airway observation or ventilatory management if intubated.

CRediT authorship contribution statement

Rachel E. Bridwell: Writing – review & editing, Writing – original draft. **Alex Koyfman:** Conceptualization, Supervision, Writing – review & editing. **Brit Long:** Writing – review & editing, Writing – original draft, Supervision, Conceptualization.

Declaration of Competing Interest

None.

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