IDCases 14 (2018) xxx–xxx

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcr

Case report

A case report of serotype W135 *Neisseria meningitidis* epiglottitis in the United States and review of twelve adult cases of meningococcal epiglottitis

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ARTICLE INFO

Article history:
Received 28 September 2018
Received in revised form 30 October 2018
Accepted 30 October 2018

Introduction

Acute epiglottitis is an infection of the epiglottis and supraglottic structures. If not recognized, inflammation may lead to rapid upper airway obstruction and death [1,2]. Over the past two decades, the pattern of acute epiglottitis has evolved from being a pediatric disease caused by *H. influenzae* type B to an adult disease attributed to diverse pathogenic organisms. Acute adult epiglottitis has an incidence of 1–4 cases/100,000 people per year and the disease is reported to have a low morbidity, unless there is a delay in diagnosis [3–5]. The mortality of adult acute epiglottis has been reported to range between 0 to 53% [3–6]. Organisms identified in adult cases of acute epiglottitis include *Streptococcus pneumoniae*,*Klebsiella pneumoniae*, group A streptococci, *Staphylococcus aureus*, *Pasteurella multocida*, *Escherichia coli*, *Moraxella catarrhalis*, *Pseudomonas* species, mycobacteria, and rare reports of *Neisseria meningitidis, Candida albicans*, *Aspergillus* spp. and viral pathogens [1,7,8].

To our knowledge, there are only eleven cases in which *N. meningitidis* was the identified pathogen causing acute epiglottitis in adults between 1995 and 2015; a twelfth case was reported in 2018 in the United Kingdom at a similar time of our case [1–3,8–16]. Of these reported meningococcal epiglottitis cases, over 30% were documented in patients with diabetes and over 70% resulted in procedural airway management (oral intubation, tracheostomy or cricothyroidotomy). The average age was 67 years old (range 37–95 years, Table 1). *N. meningitidis* serotype W135 was reported in only two cases in the United Kingdom [8,16]. In our case, the state Department of Health confirmed the meningococcal strain was serotype W135, and this would be only the third reported case in literature, first in the United States. Herein, we present a case of an adult non-diabetic male with a severe case of acute epiglottitis requiring oral intubation with documented *N. meningitidis* serotype W135 bacteremia.

Case report

A 49-year-old adult male presented to an urgent care clinic complaining of increased shortness of breath, dyspnea, and difficulty swallowing due to throat tightness for the previous three days. He was immediately transferred to our hospital's Emergency Department (ED). Upon arrival to the ED, he was having difficulty forming words and was speaking with a hoarse and muffled voice. His past medical history was significant for Hashimoto's thyroiditis, Cowden's disease (Multiple Hamartoma Syndrome), gastroesophageal reflux disease, obstructive sleep apnea, and rheumatoid arthritis (RA). His RA was treated with adalimumab 14 mg subcutaneously every 14 days (last dose was six days before admission), methotrexate (MTX) 20 mg orally weekly with leucovorin 10 mg orally twelve hours after MTX (last dose was 4 days before admission), prednisone 30 mg orally daily (tapered from 40 mg daily five days before admission), and hydroxychloroquine 200 mg orally twice daily. All RA medications were held upon admission. Other pertinent home medications included fluticasone 50 mcg/actuation 2 spray each nostril daily, omeprazole 20 mg orally daily, and levothyroxine 250 mcg orally daily. The patient was up to date on pneumococcal, influenza, and tetanus-diphtheria vaccines.

His initial vital signs in the ED were a temperature of 37.8 °C, heart rate of 122 beats per minute, blood pressure of 92/59 mmHg, respiratory rate of 30 breaths per minute, and oxygen saturation of 97% on room air. Laboratory values upon presentation were

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https://doi.org/10.1016/j.idcr.2018.e00466

Table 1
Review of meningococcal epiglottitis cases reported in literature [1–3,8–16].

Reported Case Year	Patient Age (in years)	Meningococcal Serotype* (Country)	History of Diabetes Mellitus	Airway Needed (type)
2018 (this case)	49	W135 (United States)	No	Yes (oral intubation)
2018	82	W135 (United Kingdom)	No	Yes (oral intubation)
2015	65	W135 (United Kingdom)	No	Yes (oral intubation)
2011	89	Y (United Kingdom)	No	No
2009	37	C (United States)	Yes	Yes (open cricothyroidotomy)
2007	68	Y (United States)	Yes	No
2000	73	Y (United Kingdom)	No	Yes (tracheostomy)
1999	44	Y (United Kingdom)	No	Yes (oral intubation)
1998	65	Unknown (Singapore)	Yes	Yes (oral intubation)
1998	81	Y (Finland)	Yes	Yes (tracheostomy)
1997	95	B (United States)	No	No
1996	60	Y (United States)	No	Yes (oral intubation)
1995	54	B (United States)	No	Yes (tracheostomy)

*All patients had documented positive blood cultures.

significant for a white blood cell count of 37.2×10^3/uL, segmented neutrophils of 30.9×10^3/uL, bands of 4.1×10^3/uL, C-reactive protein 136.3 mg/L, and serum creatinine of 1.30 mg/dL. Two sets of blood cultures were obtained. Medications administered in the ED included methylprednisolone 125 mg intravenously, racemic epinephrine 2.25% nebulizer solution 0.5 mL, vancomycin 1000 mg intravenously, and ceftriaxone 1000 mg intravenously. A neck x-ray of the soft tissue revealed a thickened epiglottis (Fig. 1).

Over the next 5 h, he developed worsening sore throat with inspiratory stridor, worsening tachycardia and diaphoresis, tachypnea, orthopnea, and increased oxygen requirements (3 liters nasal cannula to maintain 95% O2 saturation). Based on his progressive decompensation, he was admitted to the intensive care unit (ICU). He was intubated in the operating room (OR) due to significant inflammation of the soft tissues surrounding the epiglottis. In the ICU, his antimicrobials were broadened to piperacillin-tazobactam 4.5 gm intravenously every six hours (vancomycin was not continued). Dexamethasone 10 mg intravenously every eight hours replaced methylprednisolone to account for better anti-inflammatory actions in the upper airway. He required low-dose norepinephrine to maintain mean arterial pressure (MAP) greater than 65 mmHg.

Within 24 h, the two sets of initial blood cultures resulted with gram negative coccobacilli. The infectious disease (ID) team was consulted and thought the initial report to be consistent with *H. influenzae*. No modifications to therapy were initiated. At 48 h, the blood cultures were positive for *N. meningitidis* and ID streamlined antimicrobial therapy to ceftriaxone 2 gm intravenously every 12 h for empiric treatment of meningitis since the patient remained intubated and unable to provide a clear neurological assessment. An echocardiogram (ECHO) revealed a left ventricular ejection fraction of 45–50% and no vegetations were identified.

Over hospital days five through seven, the patient was weaned off of vasopressor support and successfully extubated in the OR with no reported stridor, wheezing, laryngospasm, or other complications. His neurologic status was normal. Ceftriaxone 2 gm intravenously daily was continued to complete a total duration of 14 days. Corticosteroids were changed to prednisone 40 mg orally daily. Repeat blood cultures were negative. The patient was discharged home on day 10 with the above mentioned antibacterial therapy and a steroid taper (30 mg orally daily at discharge with a taper down to 10 mg orally daily). On outpatient follow-up with ID, an additional 10 days of oral cefuroxime axetil 500 mg twice daily was prescribed due to complaints of fever and a small elevation in WBC. Steroid therapy was continued by rheumatology with a taper of 1 mg per month until off and he was instructed to restart his RA medication regimen. The oral course of antimicrobials was completed and repeat blood cultures were negative.

Discussion

N. meningitidis is a gram-negative diplococcus that can cause a broad spectrum of clinical manifestations including rare cases of epiglottitis or supraglottitis [12]. Meningococcal disease in the United States is sporadic and most cases are in adults who are immunocompromised. Why *N. meningitidis* is not a more frequent cause of acute epiglottitis is not fully understood as this bacterium is a common colonizer of the upper airway of healthy persons [12]. *N. meningitidis* serotype Y has been increasing in the setting of meningococcal pneumonia in civilian and military populations [12]. Herein, we report a rare finding of serotype W135 as the contributory organism. This report adds to the literature of cases of adult meningococcal epiglottitis requiring oral intubation for airway protection (Table 1). The diagnosis of adult cases of acute epiglottitis is often delayed and can result in increased morbidity and mortality if symptoms are not immediately recognized and an airway established [4,5,11]. Table 2 shows the most common symptoms associated with epiglottitis.

Obtaining an airway can be difficult due to severe inflammation. Corticosteroids may assist in easing symptoms and lessening damage from passing a laryngoscope past the epiglottis. Although frequently administered in these situations, there are no studies that demonstrate corticosteroids improve outcomes. Interestingly, 8 of the 13 patients (62%) reported to have meningococcal

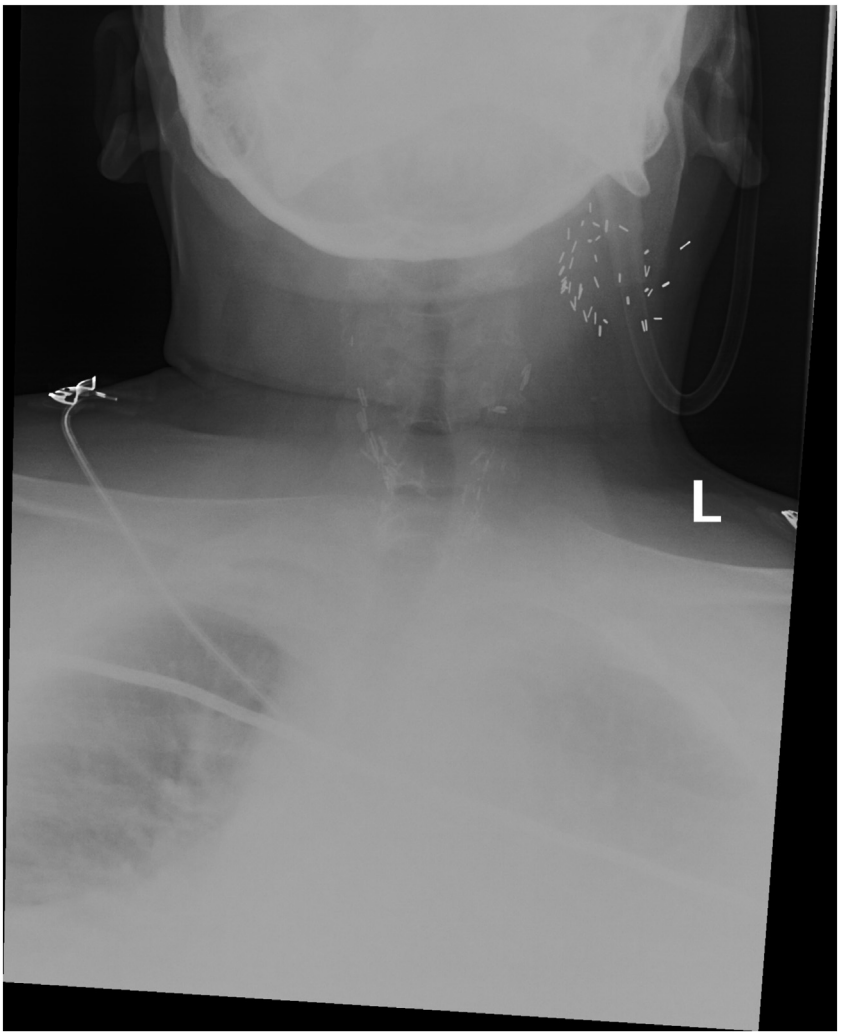

Fig. 1. Patient with thickened epiglottis.

Table 2
List of symptoms and other non-infectious causes of epiglottitis that practitioners should recognize for immediate oropharyngeal examination [2,4,5,11,20].

Symptom	Comments
Most common	Varies in duration from hours to days prior to hospital presentation.
Severe sore throat	Differential diagnosis should include other bacteria/viral infections causing sore throat and fever symptoms such as Group A Streptococcus, influenza, infectious mononucleosis, laryngitis, etc.; other causes of difficulty swallowing such as neuromuscular disorder or obstruction, etc; and other conditions such as cancer, etc.
Dysphagia/odynophagia	
Fever/chills	
Moderately common	Often short duration of symptoms prior to hospital presentation.
Hoarse or muffled voice	Differential diagnosis should include laryngeal diseases, vocal cord dysfunction, etc.; neurologic, inflammatory and neoplastic causes; and other causes such as reflux, medication use, allergies, occupational exposures to chemicals and other hazards; and many others.
Difficulty speaking	
Swollen lymph nodes	
Coughing	
Infrequent but serious	Often brief duration of symptoms prior to hospital presentation and predict airway loss in adults.
Drooling	Differential diagnosis should include presence of tumor, neurologic trauma, mechanical causes; oral or gastrointestinal causes; pulmonary and cardiac etiologies such as chronic obstructive pulmonary disease, interstitial lung disease, or congestive heart failure and other cause of airway compromise; and many others.
Stridor	
Dyspnea	
Cyanosis	
Hemoptysis	
Failure to swallow secretions	
Sepsis	
Acute decompensation with no other identifiable cause	
Other non-infectious causes of epiglottis	These mechanisms of injury should be ruled out as they are not causes of infectious epiglottitis.
Mechanical injury	
Ingestion of caustic material	
Inhalation of hot vapors or smoke	
Accidental ingestion of hot object	

epiglottitis received corticosteroids empirically and all cases resulted in positive survival outcomes [16]. In an analysis of 129 cases of adult acute epiglottitis, those that received corticosteroids had a mean hospital length of stay of 4.2 days (compared to a mean of 4.1 days in those that did not receive therapy) and demonstrated no difference in airway interventions [4]. In our case, the patient was initiated on methylprednisolone in the ED but switched to dexamethasone once intubated for postulated airway benefits. Theoretically, dexamethasone prevents post-extubation complications that require reintubation. Dexamethasone has a high anti-inflammatory potency and a long duration of action. In a study by Malhotra et al. adult patients who received dexamethasone 8 mg did not demonstrate differences compared to non-treated patients in post-extubation laryngeal edema and stridor [17]. The authors concluded that prophylactic use in every patient is unwarranted; however, therapy may be helpful in intubated high-risk patients susceptible to airway obstruction [17]. In a study by Lin et al. low-dose dexamethasone (5 mg) doses were compared to high-dose (10 mg) doses in critically ill patients with prolonged intubation and demonstrated reduction in the frequency of post-extubation airway obstruction [18]. No difference was identified between low-dose and high-dose [18]. There was not a clear role of high-dose dexamethasone therapy for epiglottitis in our case, but the patient was at risk for airway complications.

Intubation of patients with acute epiglottitis remains controversial. The proponents of intubation agree that sudden and lethal airway obstruction can occur and the airway should be secured [19]. The opposite argument maintains that most adults with epiglottitis do not have a jeopardized airway and sudden or complete obstruction is not common without preceding symptoms or signs of respiratory distress [4,18]. Predicting which patients with respiratory symptoms will progress to airway obstruction is challenging, but those with severe respiratory distress or impending arrest require immediate intubation, cricothyroidotomy, or tracheostomy in the emergency room [18]. In our case, the patient was beginning to exhibit respiratory compromise and required immediate attention in the operating room. Intubation led to a positive outcome in this case.

It is known that immunocompromised patients are more susceptible to infections and there should be a low threshold of suspicion for diagnosis of epiglottitis in those presenting with symptoms and neutropenia [20]. Chen et al. reviewed 48 cases of epiglottitis in immunocompromised hosts (age range 4 months to 70 years, with mean age of 35.5 years), in which 50% were immunocompromised secondary to cancer and/or chemotherapy, 25% had human immunodeficiency virus (HIV), and nearly 38% were neutropenic (defined as absolute neutrophil count and/or white blood cell count <1000 per cubic millimeter) [20]. None of the cases resulted from long-term corticosteroid use. It is unclear if underlying immunosuppression (from baseline RA medications) in our case played a role in developing meningococcal epiglottitis. Our case describes a patient who was not neutropenic, nor diagnosed with cancer or HIV, and not receiving traditional chemotherapy.

The pathogenicity of *N. meningitidis* has been well documented, but its role in epiglottitis is not well defined. The pharynx is the suspected portal of entry [12]. It is reported that meningococcal bacteremia can result from the invasiveness of the organism on epithelial and endothelial cells so it can cross the nasopharyngeal mucosal barrier and enter the bloodstream [12]. Thus, it is crucial that broad spectrum antimicrobials are initiated immediately once epiglottitis is suspected and narrowed based on microbiology data. Chen et al. reported organisms with >10% occurrence in immunocompromised patients was *Candida* spp., *Streptococcus* spp., *Staphylococcus* spp., and Cytomegalovirus. *Neisseria* spp. were isolated in two patients (one neutropenic and one non-neutropenic) out of the 48 reviewed [20]. Our case patient was on long-term steroid therapy for RA, but he did not have diabetes mellitus. Multiple cases of meningococcal epiglottitis have been discovered in those with underlying diabetes mellitus (Table 1). We believe that our patient developed meningococcal epiglottitis and bacteremia from community contact. Our patient was quickly initiated on broad spectrum antimicrobials in the ED, which we attribute to his positive outcome. The ID providers narrowed therapy once appropriate and followed up with the patient after discharge which was vital in preventing future morbidity, recurrence and death.

Conclusion

Neisseria meningitidis epiglottitis is a rare but important diagnosis that requires immediate recognition and antibiotic treatment. This case documents *N. meningitidis* W135 as the causative serotype and this serogroup should be considered a potential pathogen. We highlight the importance that physicians should consider epiglottitis in the adult patient who presents with dysphagia and respiratory symptoms. Epiglottitis, once a childhood illness due to *H. influenzae*, has evolved into an adult affliction with numerous possible infecting pathogens.

CRediT authorship contribution statement

Sommer D. Zarbock: Conceptualization, Visualization, Writing - original draft, Writing - review & editing. **Kirk L. DePriest**: Writing - review & editing. **Brandi M. Koepp**: Writing - review & editing.

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