

Acute Epiglottitis in the Immunocompromised Host: Case Report and Review of the Literature

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We present a case of acute epiglottitis in a 16-year-old with severe aplastic anemia. He was admitted with a history suggestive of a severe upper airway infection and an absolute neutrophil count of 0 per cubic millimeter. Despite his immunocompromised state, he presented with the classical signs and symptoms of epiglottitis. We review here the presentation and comorbidities of immunocompromised patients with epiglottitis. In addition, the appropriate choice of empirical antibiotic therapy is important for the management of epiglottitis in immunocompromised patients, especially in the post-*Haemophilus influenzae* type B vaccination era. In our patient, *Enterobacter cloacae* was isolated from endoscopically directed throat cultures, and treatment was successful without the need for intubation. The current literature suggests that in immunocompromised patients, particularly those who are neutropenic, there is a potentially wide range of organisms, both bacterial and fungal, that may play a role in the pathology of acute epiglottitis.

Keywords. aplastic anemia; *Enterobacter cloacae*; epiglottitis; immunocompromise; malignancy; neutropenia.

Epiglottitis is a life-threatening condition, characterized by acute inflammation of the supraglottic region of the oropharynx, with the potential risk of fatal airway obstruction. Effective management requires rapid diagnosis, airway management, and treatment of the causative agent. Epiglottitis is an inflammatory disease, yet it still occurs in patients whose inflammatory responses are blunted by neutropenia and immunocompromised patients. Although these patients are known to be more susceptible to infections, it has yet to be demonstrated whether epiglottitis in immunocompromised patients presents differently or follows a different clinical course. Previously, 75%–90% of cases of epiglottitis were caused by *Haemophilus influenzae* type B (Hib). Vaccination, introduced in 1985, significantly reduced the incidence of epiglottitis [1]. Cases presenting today show a mixed microbial etiology, with a relative increased incidence in older children [2]. Epiglottitis in immunocompromised patients may be caused by a wider variety of organisms than epiglottitis in immunocompetent children and adolescents. We present

here a case of acute epiglottitis with *Enterobacter cloacae* in a 16-year-old male with severe aplastic anemia with a review of the literature, exploring the clinical presentation, outcomes, and microbial etiologies in immunocompromised patients.

CASE REPORT

A 16-year-old Jamaican male presented to his local hospital with fatigue, epistaxis, and dyspnea. He had no significant past medical history or family history of serious medical illness. Initial blood tests showed a white cell count of 1900 per cubic millimeter (absolute neutrophil count 90 per cubic millimeter), hemoglobin 5.3 g per deciliter, and platelets 36 000 per cubic millimeter. He was hospitalized 3 months later, and bone marrow biopsy performed 1 month into the admission was consistent with aplastic anemia. He was discharged after receiving packed red blood cells, pooled platelet transfusions, and intravenous antibiotics of unknown type, dose, and duration.

Five months after initial presentation, he was admitted to the US National Institute of Health Clinical Center with a 1-week history of fever, dysphagia, odynophagia, cough, and scant hemoptysis. He was enrolled in an institutional review board-approved clinical research protocol, and informed consent was obtained and documented. On examination, his body temperature was 38.2°C, blood pressure 126/91 mm Hg, heart rate 88 beats per minute, respiratory rate 18 breaths per minute, and oxygen saturation 98% breathing ambient room air. He appeared thin and lethargic, but was not in acute distress, and was spitting blood-tinged saliva into a cup. He denied dyspnea and was phonating normally. He was tender diffusely around

Received 4 December 2017; editorial decision 9 February 2018; accepted 14 February 2018.

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Open Forum Infectious Diseases®

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 DOI: 10.1093/ofid/ofy038

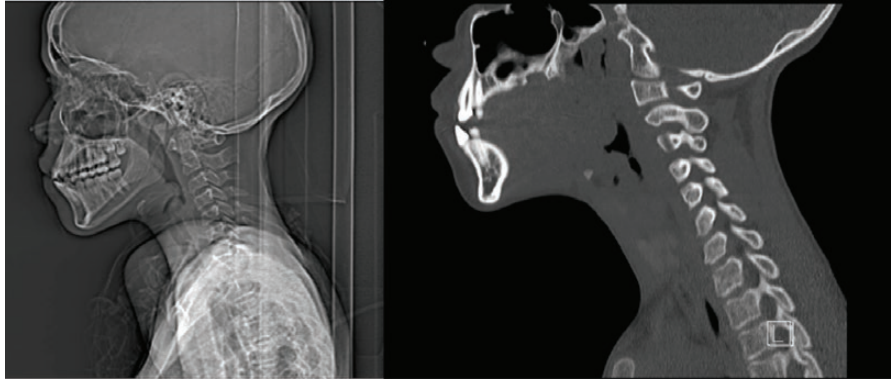


Figure 1. Topogram and sagittal view of the neck on computerized tomography scan performed on the day of presentation showing classic “thumbprint” sign due to swelling of epiglottitis.

the neck. There were no other abnormal examination findings. His laboratory findings showed a white cell count of 1430 per cubic millimeter (absolute neutrophil count 0 per cubic millimeter), hemoglobin 10.7 g per deciliter, and platelets 33 000 per cubic millimeter. Radiographic imaging showed a classic “thumbprint” sign at the site of the epiglottis (Figure 1). Direct laryngoscopy showed an erythematous, enlarged, and posteriorly ptotic epiglottitis that was not necrotic (Figure 2). The patient immediately received intravenous piperacillin/tazobactam (3.375 g, every 6 hours), vancomycin (400 mg, every 6 hours), and micafungin (100 mg, once daily), as well as intravenous dexamethasone (4 mg, every 6 hours) and nebulized racemic epinephrine (0.5 mL of 2.25%, every 6 hours). He clinically improved while being closely monitored in the intensive care unit; there was no need for definitive airway management by intubation. Blood cultures showed no growth, but endoscopically directed cultures from directly observed exudate on the

right tonsillar area isolated *Enterobacter cloacae* resistant to cefazolin, cefoxitin, ceftazidime, ceftriaxone, co-amoxiclav, ampicillin, aztreonam, and piperacillin/tazobactam; subsequently, he was prescribed meropenem (750 mg, every 8 hours). He clinically improved with this antibiotic regimen, and follow-up laryngoscopy 17 days later showed significant improvement in the appearance of the epiglottis (Figure 3).

DISCUSSION

Epiglottitis is a medical emergency, with the potential serious complication of airway compromise secondary to the inflammatory response to infection in the upper airway. It is a clinical diagnosis characterized by odynophagia, stridor, drooling, and a “hot potato” voice. The patient may also show signs of sepsis in cases of severe infection. Direct fiberoptic laryngoscopy shows an inflamed and swollen epiglottis; however, examination should be done with caution as it can lead to rapid airway compromise. Radiology, including lateral x-ray of the cervical spine or computerized tomography, may aid in diagnosis by showing a classic “thumbprint sign,” evidence of soft tissue swelling of the epiglottis. While antimicrobials are part of treatment, additional support, including steroids [3], is used to reduce the inflammation, and intubation/tracheostomy under carefully monitored conditions maintains the collapsing airway. In cases where there is abscess formation, surgical debridement may also be necessary. Isolated necrosis of the epiglottis also can occur [29].

Demographics of Epiglottitis in the Immunocompromised

We performed a literature search evaluating epiglottitis in the immunocompromised host, which yielded 48 published cases from 34 published reports (Table 1) [4–37]. Patient ages ranged from 4 months to 70 years, with a mean age of 35.5 years, with 23 male and 25 female patients. Twenty-four had immunocompromise secondary to cancer and/or chemotherapy, and 12 patients were positive for HIV. The remainder had a variety of causes of immunocompromise, including Epstein-Barr virus (EBV) mononucleosis, renal transplantation, and drug-induced



Figure 2. Laryngoscopy image of epiglottis showing erythematous and enlarged epiglottis.



Figure 3. Follow-up laryngoscopy image showing significant improvement in erythema and swelling.

neutropenia (see the footnote to Table 1). Of these 48 patients, 18 were neutropenic, defined by an absolute neutrophil count and/or total white cell count of less than 1000 per cubic millimeter. The range of underlying causes of immunocompromise in neutropenic patients was similar to that in non-neutropenics.

Clinical Presentation of Epiglottitis in the Immunocompromised

Epiglottitis has previously been reported in 1 other patient with aplastic anemia [12]. Our patient presented with typical signs and symptoms of epiglottitis similar to those observed in immunocompetent patients. Specifically, in the reviewed case reports of immunocompromised patients, patients presented with symptoms of respiratory distress, stridor, fever, drooling, sore throat, odynophagia, and dysphagia [4–37].

Table 1. Demographics of Epiglottitis in the Immunocompromised According to 48 Cases from Published Studies [4–37]

Demographic	Data for Cases	
Mean age (SD, range), y	35.5	(20.1, 4 mo–70 y)
Sex	Male	23 48%
	Female	25 52%
Underlying condition	Malignancy	24 50%
	HIV	12 25%
	Other ^a	12 25%
Neutropenia	ANC or WBC <1000	18 38%
Mortality	Neutropenic	33%
	Not neutropenic	23%

Abbreviations: ANC, absolute neutrophil count; WBC, total white blood cell count.

^aOther causes of immunocompromise included Epstein-Barr virus (EBV) mononucleosis in pregnancy, bone marrow aplasia of unknown origin, hypocellular bone marrow of unknown origin, aplastic anemia, virus-associated hemophagocytic syndrome secondary to EBV infection, renal transplantation, procainamide-induced neutropenia, infection-related hemophagocytic lymphohistiocytosis, Cytomegalovirus-related pancytopenia, systemic lupus erythematosus, and drug-induced agranulocytosis. In 1 patient, the cause of immunocompromise was not documented.

In our patient, there was no stridor or pus on laryngoscopy. Neutrophils are the key effector cells of the innate immune system, so when patients become neutropenic (<500 per cubic millimeter), they become susceptible to infections. Sore throat due to mucositis may be common in patients receiving chemotherapy for malignancy, but there should be a high index of suspicion if symptoms worsen or progress to include difficulty swallowing, clearing secretions, or breathing. We postulate that there are 3 reasons why, despite the ongoing inflammation and medical intervention, this patient’s airway remained competent without any need for airway support. First is that, anatomically, this 16-year-old’s head and neck anatomy may be different compared with younger children with Hib epiglottitis. There is more space for the swelling to expand before impinging on the airway. Second, there is an inverse correlation between patient age and risk of laryngospasm [38]. Third, the severity of his immunocompromise from aplastic anemia may have limited the extent of host response, thereby presenting a lower-than-expected degree of inflammation and swelling.

Clinical Course, Treatment, and Outcomes of Epiglottitis in the Immunocompromised

The majority of cases were empirically treated initially with broad-spectrum antibiotics. Of the 21 patients in whom fungal organisms were isolated, 7 empirically received antifungal agents, including 2 patients with concomitant neutropenia. As many of the organisms isolated are part of the normal oropharyngeal flora, especially *Candida* sp, their role in infection vs colonization often is unclear. The benefits or harms of administering antifungals empirically are unclear from this case series.

Prognosis of Epiglottitis in the Immunocompromised

Of the 48 case reports, 13 people died and 35 survived (27% overall mortality), highlighting the life-threatening nature of epiglottitis. Of the neutropenic patients, 6 died and 12 survived, giving a slightly higher mortality of 33% (Table 1). Two of 3 patients with tongue involvement were neutropenic.

Table 2 shows the interventions used in addition to antimicrobial agents and their associated mortalities in the patients who received them.

It is not possible to determine the effects of various interventions on mortality from this case series. Intubation and tracheostomy may be used in more severe cases, so higher mortality with these interventions may reflect higher baseline risk of death independent of the interventions administered.

Organisms Isolated in Immunocompromised Patients

In 29 patients, a single organism was isolated from cultures of the throat, sputum, blood, or tissue biopsy (either from an isolated site or from multiple sites), while 3 patients had either no growth on cultures or they were not done. The remaining 16 patients grew multiple organisms. A summary of organisms is shown in Table 3. The most frequent organism isolated from either cultures or biopsy was *Candida* spp, followed by *Streptococcus* spp.

Table 2. Supportive Treatments Used in Addition to Antimicrobial Therapy in the 48 Published Cases of Epiglottitis in the Immunocompromised [4–37]

Supportive Treatment	No.	Mortality, %
Intubation	30	37
Tracheostomy	10	40
Steroids	9	33
Granulocyte stimulating factor	5	20
Surgical debridement	2	0
Racemic epinephrine	2	0

Eight of the neutropenic patients grew *Candida* spp and were subsequently treated with antifungal agents (11 of 31 non-neutropenic patients grew *Candida* spp). The organisms grown from neutropenic patients showed more variety and were less predictable, such as *Prevotella* spp and *Serratia marcescens*, compared with primarily *Streptococcus pneumoniae* and *Candida albicans* in non-neutropenic patients. In 2 patients, cultures were not done, diagnosis was made on a clinical basis, and the infection resolved without intervention. There was 1 case where there was no growth from blood cultures, throat swabs, or tracheal aspirate, but the patient survived and the disease resolved after receipt of cefotaxime, erythromycin, and metronidazole.

Here we report the first documented case of acute epiglottitis associated with *Enterobacter cloacae*, a gram-negative

rod-shaped organism often found in the normal flora of the gastrointestinal tract [39]. It is also a nosocomial pathogen, with previous documentations of *E. cloacae* outbreaks [40]. Flynn et al. suggested that *Enterobacter* from patients' endogenous flora can be the source of "nosocomial" *Enterobacter* infection [41]. Our patient did recently have a hospital admission in Jamaica and receipt of prior antibiotics, so it is unclear whether the source of his infection was nosocomial or community acquired. Nonetheless, this finding has implications for the choice of empirical antimicrobial therapy for the initial management of epiglottitis in immunocompromised patients. Gram-negative and fungal infections should be considered in this setting.

CONCLUSIONS

In the immunocompromised patient, there should be a low threshold of suspicion for diagnosing acute epiglottitis, particularly in those who are neutropenic. The immunocompromised state and neutropenia do not rule out diseases caused by neutrophilic infiltration as tissue-based inflammation still may result in disease. Epiglottitis in reported cases presents similarly in immunocompromised and immunocompetent patients. Early recognition can allow prompt treatment, including administration of broad-spectrum antimicrobials and perhaps antifungals, given the wide range of organisms isolated. The impact of broad-spectrum antimicrobials with additional antifungals on outcome is unknown given that the organisms isolated also are part of the normal oropharyngeal flora, and whether they are colonizing or causing infection often is unclear. Airway management is paramount, but endotracheal intubation is not always necessary and was not necessary in our patient. Sedation, inhalers, and racemic epinephrine should be avoided [3]. Rapid treatment with steroids to reduce the immediate inflammation, along with antimicrobials to treat the underlying infection, has been associated with shorter intensive care unit and overall length of hospital stay; close monitoring and good nursing care are essential for the appropriate management of epiglottitis in the immunocompromised patient.

Acknowledgments

Financial support. This project has been funded in whole or in part with federal funds from the National Cancer Institute, National Institutes of Health, under Contract No. HHSN261200800001E. The content of this publication does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the US Government.

Potential conflicts of interest. None of the authors have any conflict of interest related to this work. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Table 3. Organisms Grown From 48 Cases of Epiglottitis in Immunocompromised Patients From Published Cases [4–37]

Organism Isolated	Neutropenic	Total	% of All Cases
<i>Candida</i> spp	8	19	40
<i>Streptococcus</i> spp	2	12	25
<i>Staphylococcus</i> spp	2	5	10
<i>Cytomegalovirus</i>	2	5	10
<i>Aspergillus</i> spp	2	4	8
<i>Serratia</i> spp	3	3	6
<i>Enterococcus</i> spp	2	2	4
<i>Corynebacterium diphtheriae</i>	1	2	4
<i>Escherichia coli</i>	1	2	4
<i>Neisseria</i> spp	1	2	4
<i>Prevotella</i> spp	2	2	4
<i>Pseudomonas</i> spp	1	2	4
<i>Klebsiella pneumoniae</i>	0	1	2
<i>Actinomyces israelii</i>	0	1	2
<i>Bacteroides</i> spp	0	1	2
<i>Diplococcus</i>	0	1	2
<i>Eikenella corrodens</i>	1	1	2
<i>Haemophilus influenzae</i>	1	1	2
<i>Kingella kingae</i>	1	1	2
<i>Mucormycosis</i>	0	1	2
<i>Stenotrophomonas maltophilia</i>	1	1	2
<i>Torulopsis glabrata</i>	0	1	2
<i>Zygomycete</i>	0	1	2
Cultures not done	0	2	4
No growth	0	1	2

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