

Case Report

Fungal Tracheitis Mimics Croup

Andrea L. Darnbrough¹, Liane B. Johnson²

¹Class of 2010, Faculty of Medicine, Dalhousie University

²Division of Otolaryngology, Department of Surgery, Dalhousie University, Halifax, Nova Scotia, Canada

Abstract

A rare case report of a 16-month-old child's survival of obstructive fungal tracheitis is presented. Atypical life-threatening croup in an immunocompromised patient often heralds very poor clinical outcomes due to underlying infection. Deep *Candida* infections are very rare, relegated to immunocompromised hosts and are often fatal due to extensive local tracheal cartilage destruction, with or without disseminated systemic disease. The literature on deep candida infections is reviewed in the context of this patient's clinical course in hospital, focusing on airway management, treatment outcome, and risks of future relapse.

Introduction

Although fungal infections of the trachea are rare, *Candida* infections in infants and children are being increasingly recognized. Risk factors for developing *Candida* infections include prolonged antimicrobial use, prematurity, and an immunocompromised host¹. There are case reports of fungal tracheitis in paediatric oncology patients. The symptoms of these infections vary depending on their location in the airway and whether or not it is invasive. The mortality rate is extremely high, particularly in cases with upper airway obstruction^{2,3}. This case report reviews the presentation of *Candida*-induced fungal tracheitis in a 16-month-old boy with newly diagnosed acute myelogenous leukemia (AML), which was initially diagnosed as croup.

Case Report

A 16-month-old boy presented to the emergency department with a one and a half-week history of upper respiratory tract infection, cough, and low-grade fever. A nasal pharyngeal aspirate was positive for respiratory syncytial virus (RSV). His complete blood count (CBC) showed peripheral blasts and he was subsequently diagnosed with acute myelogenous leukemia (AML). He received tobramycin, ticarcillin and clavulanate, and began chemotherapy. Perinatal history was unremarkable. Past medical history revealed recurrent episodes of acute otitis media requiring myringotomy and tubes at 10 months of age, recurrent wheezing, and a hospital admission for rehydration following gastroenteritis. Prior to admission, he was taking ranitidine for reflux and salbutamol and fluticasone inhalers for respiratory symptoms.

On day 10 of admission, he developed a hoarse voice, a wheeze, and increased work of breathing. Despite an initial response to salbutamol, there was further deterioration with the development of a harsh cough, inspiratory stridor, and oxygen saturations down to 80%. With a working diagnosis of croup, he was treated with dexamethasone and inhaled racemic epinephrine. White lesions were noted on his lower lip (negative for herpes simplex virus), and a *Candida* rash was identified in the diaper area (scrotal swab positive). Lateral airway and chest radiographs revealed significant subglottic narrowing, and bilaterally streaky opacities with subsegmental atelectasis and no evidence of consolidation. Over the next several days he remained neutropenic and febrile, and began requiring aerosolized racemic epinephrine every 30 minutes to control his airway symptoms.

On day 16 he had an acute deterioration, and became cyanotic with severe chest wall retractions. Urgent otolaryngology consultation led to airway endoscopy which revealed significant subglottic oedema with necrotic plaques and ulcerations throughout the subglottis and proximal trachea (Fig. 1). Airway sizing could only accommodate a 2.5 mm endotracheal tube (3.3 mm outer diameter) with force; the airway appeared at least 75% stenosed (Cotton-Myer grade III). Tracheotomy was performed to bypass the obstruction. Intravenous amphotericin B was added to the patient's treatment regimen on speculation of underlying fungal infection. Tracheal swabs and tissue cultures identified invasive *Candida albicans*, *Pseudomonas*, and *E.coli*.

A microlaryngoscopy and bronchoscopy (MLB) conducted two weeks later showed resolution of the



Figure 1. Initial diagnostic endoscopy revealing significant subglottic oedema with necrotic fungal plaques and ulcerations.



Figure 2. Resolution of fungal plaques, but significant residual subglottic oedema noted on week two of antifungal therapy.

fungal plaques with profuse subglottic and proximal trachea oedema and complete narrowing of the airway which appeared to be due to collapse of the structural framework (Fig. 2). It was not possible to determine with certainty if the underlying cartilage had been destroyed, but the probability remained great given the appearance and degree of narrowing of the subglottis and proximal trachea. Over the next 6 months the patient's clinical condition significantly improved, and serial MLBs showed gradual resolution of the oedema. The patient remained tracheotomised throughout his entire course of chemotherapy. Upon completion of chemotherapy, an MLB revealed complete normalization of the airway without evidence of fungal infection or obvious underlying destruction of cartilage (Fig. 3). The patient was successfully decannulated almost 8 months after the initial tracheotomy.

Discussion

Acute upper airway obstruction in a previously healthy child has a broad differential, however laryngotracheobronchitis (croup) is the most common infectious cause. The diagnosis of croup is primarily a clinical one. Occurring most frequently in children between three and thirty-six months of age, it is usually mild and self-limited with resolution in seven to ten days. Croup is typically of viral origin and is caused most commonly by parainfluenza viruses 1,2 and 3 and RSV⁴. Bacterial croup is uncommon although *Mycoplasma*, *Streptococcus*, *S. pneumoniae* and *H. influenzae* have occasionally been isolated⁵. Fungal causes of croup are

exceedingly rare, particularly in an immune competent host.

The few reports in the literature of paediatric fungal tracheitis are associated with immunosuppression, generally in children with leukemia. One of the first papers to evaluate the incidence of mycotic infections in hospitalized immunosuppressed patients was published in 1966; the incidence of invasive laryngeal fungal infection in this population was exceedingly rare (0.002%)⁶. A comprehensive retrospective study of invasive fungal infections in paediatric oncology patients found the rate of any type of fungal infection to be 4.9%, with the vast majority (67%) occurring in children with acute leukemia⁷. Furthermore, children with leukemia had an overall mortality rate of 21%, which increased 2.6 fold in the presence of concurrent fungal infection⁷.

Rosen *et al.* report that the majority of patients with fungal tracheitis have disseminated fungal infection, regardless of the species responsible. Yeasts were the most common type of fungal infection accounting for 66% of this 1052 patient cohort studied, while *Candida* was the most common yeast, accounting for almost half of all the fungal infections. One third of *Candida* infections affected the respiratory tract primarily, while the remaining two thirds were distributed between blood, urine, and gastrointestinal tract. Overall, this study revealed that only 0.007% of patients developed invasive laryngeal *Candida* infections⁷.



Figure 3. Complete normalization of the airway at completion of chemotherapy, six months following diagnosis.

Candida infections tend to develop shortly after the diagnosis or relapse of leukemia, with the average onset at 13 days⁸. Another review of 15 patients with leukemia with known disseminated *Candida* infection revealed that invasive laryngitis is indeed rare, occurring in only one study patient. The vast majority of these patients (75%) were found to be neutropenic at the time of diagnosis of fungal infection⁸. The current case report highlights many of the risks identified by Klingspor et al., although no convincing evidence of disseminated infection was found.

Systemic steroids are the mainstay of treatment for viral croup. A single dose of steroids promotes significant clinical improvement in respiratory symptoms and is known to decrease mortality^{9,10}. There are a few reported cases of fungal tracheitis developing in otherwise healthy children on a prolonged course of steroids for the treatment of croup^{9,11,12,13}. This risk has been shown to be even greater if the child is on antibiotics, as antibiotics disrupt the balance of normal flora^{1,6}. Despite this fact, up to 60% of children with typical croup symptoms are placed on antibiotics¹¹. For this reason, vigilant monitoring of all children receiving steroids and antibiotics for the treatment of croup is extremely important, especially children with underlying immunosuppression¹¹.

The patient in this case report was newly diagnosed with AML, and had been given both steroids and antibiotics prior to the development of fungal

tracheitis. This combined treatment has been shown to predispose to the development of fungal tracheitis, both in immunocompetent and immunocompromised patients^{11,13,14,15}. There is some evidence that empiric therapy for fungal infections with significant risk factors may be beneficial^{16,17}. The benefit of empiric therapy should be carefully considered, since amphotericin B has a notable side effect profile, including fever, chills, myalgia, nephrotoxicity and thrombocytopenia¹¹.

Invasive *Candida* infections can result in destruction of the underlying cartilage. Three cases of mortality from cartilage destruction have been previously reported^{15,18}. Another case report discusses the presence of fungal plaques and ulcerations on the first endoscopic examination. These resolved over many months, following aggressive treatment of the *Candida* infection and bypassing the obstruction with a tracheotomy¹⁸. Four other cases report successful treatment of invasive fungal tracheitis with early diagnosis, aggressive medical management, and prolonged tracheotomy^{19,20,21,22}.

Conclusion

Fungal tracheitis is a rare disease with high morbidity and mortality, however aggressive medical management can result in a positive outcome, provided the airway is secure. Physicians should be aware of the possibility of underlying fungal tracheitis in new diagnoses or recent relapses of leukemia, and the increased need for early bronchoscopy and culture in high risk patients. Prolonged use of corticosteroids in the treatment of croup is controversial. Symptoms of croup that do not respond to a single dose of steroids should be further investigated, especially when treatment is combined with antibiotics. This combined therapy may predispose to the development of fungal tracheitis, particularly in the setting of immunosuppression. A tracheotomy can provide a secure airway while a patient is undergoing medical treatment. Surgical airway reconstruction is not necessary for a positive outcome in fungal tracheitis, and should be reserved for severely damaged or stenotic airways following complete resolution of the fungal infection.

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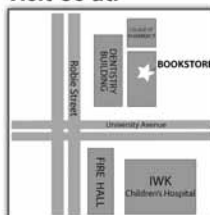


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