Lemierre syndrome presenting as acute mastoiditis in a 2-year-old girl with congenital dwarfism

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Abstract

Lemierre syndrome is defined by septic thrombophlebitis of the internal jugular vein caused by Fusobacterium. Historically, these infections originate from the oropharynx and are seen in older children, adolescents and young adults. More recently, otogenic sources in younger children have been described with increasing frequency. We present a case of a two-year-old, who initially developed otitis media with perforation of the tympanic membrane and went on to develop mastoiditis and non-occlusive thrombosis of the venous sinus and right internal jugular vein. Fusobacterium necrophorum was grown from operative cultures of the mastoid, ensuring computed tomography scan revealed occlusion of the internal jugular vein and the patient was successfully treated with clindamycin, ciprofloxacin and enoxaparin. This case demonstrates the importance of considering Fusobacterium in otogenic infections and the consideration of Lemierre syndrome when F. necrophorum is identified.

Introduction

Fusobacterium infections are potentially life-threatening illnesses that should be considered in toxic-appearing patients with pharyngitis, as well as patients with chronic suppurative otitis or other head and neck infections, including odontogenic infections. Classically, Lemierre syndrome was described as postanginal sepsis secondary to thrombosis of the tonsillar vein with a spreading septic thrombophlebitis of the internal jugular vein and the potential for sepsis and distant infectious metastasis due to Fusobacterium infection. While this syndrome was described in the pre-antibiotic era as primarily occurring in adolescents and young adults, recent case series and reports have described occurrences of this syndrome in younger pediatric patients that are increasing in frequency.

Classically, the underlying infectious etiology of Lemierre syndrome is Fusobacterium necrophorum, although cases have been reported to be associated with Streptococcus pyogenes and other organisms. Fusobacterium species have been reported to cause a variety of head and neck infections in the pediatric population, ranging from localized pharyngitis and mastoiditis to classic Lemierre syndrome with distant infectious metastases. We report a case of Fusobacterium-associated Lemierre syndrome arising as a complication of a chronic suppurative otitis media in a 2-year-old patient with an ill-defined immunodeficiency and congenital dwarfism.

Case Report

A 2-year-old girl with a past medical history of microcephalic osteodysplastic primordial dwarfism type 1 and an ill-defined immunodeficiency, manifested by selective hypogammaglobulinemia with inadequate response to the pneumococcal vaccine but no previous serious infections presented to the Emergency Department with a chief complaint of fever, dehydration, and malaise. Three weeks prior to presentation, the patient had completed a course of treatment with azithromycin for otitis media, with subsequent perforation of her tympanic membrane. The patient was prescribed a seven-day course of amoxicillin/clavulanate which was completed five days prior to presentation. Since completion, the patient had some improvement but continued to have daily fevers and ear pain. Three days prior to presentation, the patient began to have 3–5 episodes of non-bilious non-bloody emesis a day. On the day of her presentation the patient was unwilling to drink and had decreased urine output. In the emergency department the patient was initially diagnosed with severe dehydration and constipation but was subsequently admitted after interventions did not improve her condition. On admission the examination revealed a 13% loss of body weight in the previous three weeks. The exam was also significant for fever (39.1°C), tachycardia (170), severe dehydration, profound irritability and purulent drainage from the right ear. Initial laboratory evaluation was remarkable for leukocytosis with a WBC of 17.0 (93% PMNs, no bands) and a microcytic anemia with hemoglobin of 7.8 and an MCV of 71. CMP was unremarkable. Venous blood gas was notable for a respiratory alkalosis with a mildly elevated lactate (2.4).

Given the toxic appearance and a seemingly refractory otitis media with persistent fevers, a contrast computerized tomography (CT) scan of the brain was obtained prior to lumbar puncture and the patient was initiated on vancomycin and ceftriaxone. The CT scan revealed a coalescent right mastoiditis with a small underlying dural venous sinus thrombosis. Based on these findings the ceftriaxone was changed to piperacillin/tazobactam for Pseudomonas coverage and an emergent mastoidectomy was performed. Surgical specimen cultures were notable for Fusobacterium necrophorum but no additional organisms. Antimicrobial coverage was narrowed to clindamycin and ciprofloxacin. CSF gram stain was notable for PMNs but culture was negative. Blood cultures were negative for fusobacterium. Given the known association of this microorganism with Lemierre syndrome, a CT angiogram of the neck was obtained, which was notable for extensive right jugular veno-occlusive disease. There was no evidence of septic emboli in the brain or other end-organ septic embolic complications. The patient was initiated on enoxaparin for anticoagulation with significant symptomatic improvement and was discharged to complete a 6-week course of antimicrobials and anticoagulation. After completion of 6 weeks of anticoagulation therapy, she had improvement but not resolution of her dural venous sinus thrombus, and was continued on an additional 6-week course of anticoagulation, with repeat imaging pending.

Discussion

This case presents a toxic appearing toddler,
who presented after failed therapy for an otitis media. The initial differential diagnosis in a patient presenting with resistant otitis media as well as altered mental status or a toxic appearance should include mastoiditis and meningitis as well as consideration of a venous sinus thrombosis. As such head imaging followed by lumbar puncture should be performed, and broad-spectrum antibiotics should be initiated. Empiric antimicrobial choices should cover the typical organisms that cause acute otitis media (Streptococcus pneumoniae, non-typable Haemophilus influenzae, Moraxella catarrhalis, and Streptococcus pyogenes) as well as those causing chronic otitis media (most commonly Pseudomonas aeruginosa or Staphylococcus aureus). In this case, because of the prolonged course with amoxicillin/clavulanate, there was concern that the infecting organism was resistant to this therapy, P. aeruginosa and S. aureus (specifically a methicillin resistant species) were considered. The finding of a venous sinus thrombosis also brought up the possibility of a Fusobacterium infection. However, given the patient’s age Lemierre syndrome was deemed unlikely, as it typically affects older adolescents and traditionally has an oropharyngeal source. However, when operative cultures returned growing F. necrophorum a diagnosis of Lemierre syndrome was reconsidered and the internal jugular was imaged. Fusobacterium are anaerobic, non-spore forming, gram-negative bacilli, which traditionally cause primarily postanginal sepsis with suppurative thrombophlebitis stemming from an oropharyngeal source (Lemierre syndrome). However, more recently reports of Fusobacterium causing otogenic infections have occurred. Fusobacterium are often isolated from oropharyngeal specimens in healthy people and are thought to be a component of dental plaque. Alone, or in combination with other anaerobes, Fusobacterium can cause Lemierre syndrome. Lemierre syndrome is a complication of Fusobacterium that develops up to 12 days following an acute oropharyngeal infection. Lemierre syndrome is characterized by suppurative thrombophlebitis of the internal jugular vein, which can result in septic emboli, multiple organ dysfunction, meningitis, venous sinus thrombosis, disseminated intravascular coagulation, empyemas, pyogenic arthritis or osteomyelitis. Plasmaoglobin binding, platelet aggregation and hemagglutinin production by the bacteria likely play an active role in disease pathogenesis. However, it is unclear whether Fusobacterium is specifically virulent or whether it needs mucosal damage in order for invasion to occur.

In children less than five years of age Lemierre syndrome is more commonly identified after otogenic infection as in the case presented above. Three different case series from the Netherlands, France and Israel identified complicated infections with F. necrophorum which presented initially with otitis media or sinusitis and had similar complications. F. necrophorum’s emergence as an otogenic pathogen is most likely multifactorial, including alterations in the microbiome in response to the pneumococcal vaccine as well as changes in the antibiotic prescribing patterns for otitis media. Left untreated Lemierre syndrome has a mortality rate of up to 90%, survival with treatment is variable depending on complications. A French case series presented 25 cases of Fusobacterium infection, forty percent of whom presented with uncomplicated otitis media, forty percent of whom presented with acute mastoiditis and eighteen percent who presented with Lemierre syndrome with near 100% survival. In the more recent cohorts from the Netherlands and Israel, complication rates were significantly higher (~100%), and survival was far more variable, with mortality in two of the five patients in the Netherlands case series and no mortality information provided in the Israeli case series.

Fusobacterium are generally very susceptible to metronidazole, clindamycin, chloramphenicol, carbenem, cefoxitin and ceftriaxone. However, metronidazole is rarely used in isolation because of its lack of activity against other common co-infecting organisms. Gentamicin, fluoroquinolones and tetracyclines have limited activity against Fusobacterium. Some species of Fusobacterium produce beta-lactamases making penicillins and some cephalosporins ineffective; however a recent study out of the Netherlands demonstrated minimal beta-lactam production, and no resistance was reported in either the Netherlands or Israeli case series. In our patient susceptibilities were not performed; however the patient failed to improve on amoxicillin/clavulanate suggesting possible beta-lactamase production or the failure of the antibiotic to penetrate an abscess. The duration of therapy is variable and depends on the management of the thrombosis.

In our patient the thrombi were not occlusive so thrombectomy was not pursued, and she was treated with enoxaparin, as well as a minimum therapy of six weeks of antibiotics.

Conclusions

This case demonstrates the need for careful evaluation of children with otitis media who deteriorate on traditional therapy. Given the emergence of Fusobacterium in otogenic infections, it should be considered in children who present appearing toxic after failure to respond to traditional therapy for an otogenic infection. Any child with neurologic symptoms, alterations in mental status, persistent vomiting or dehydration should be evaluated for venous sinus thrombosis. Given the propensity of Fusobacterium to form septic emboli and form thrombi, careful radiographic examination of the venous sinuses as well as the internal jugular veins should be performed when identified, as this will likely impact the duration of antimicrobial therapy. A high index of suspicion must be maintained because of the unusual presentation, as many patients present after significant disease progression and complications, which can lead to poorer outcomes.

References

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