A 16-Year old with Lemierre's Syndrome and Multiple Septic Pulmonary Emboli

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Abstract

Introduction: Lemierre's syndrome, a rare complication of oropharyngeal infections, is caused by infective thrombophlebitis of the internal jugular vein and subsequent development of multisystem septic emboli. Case: A 16-year old male presented with two weeks of fever, myalgia, malaise, nausea/vomiting/diarrhea with weight loss, and a dry cough. He had previously been treated for pneumonia with three days of azithromycin. Chest imaging demonstrated bilateral cavitary lung nodules and blood cultures grew Fusobacterium necrophorum. Right jugular thrombophlebitis was later confirmed. Discussion: Lemierre's syndrome is most common among previously healthy adolescents. It often presents following mild oropharyngeal infection and may be associated with multiple pulmonary complications including septic emboli, abscesses, necrotizing pneumonia, empyema, pneumothorax, pulmonary embolism, and acute respiratory distress syndrome. Delayed diagnosis may result in life-threatening morbidity or mortality, so pediatric pulmonologists must be aware of this rare disease and maintain a high index of suspicion in cases consistent with Lemierre's syndrome.

Introduction

Lemierre's syndrome (LS) is a rare disease which results from infective thrombophlebitis of the internal jugular vein following an acute oropharyngeal infection. Following decades of decline, the incidence of LS has increased in recent years. Multiple septic pulmonary emboli are common, but all organ systems can be involved. Although LS is most often caused by *Fusobacterium necrophorum* , other pathogens have been implicated. Persistent high fever and organ-specific signs and symptoms result from the septic emboli. The diagnosis is often suspected following growth of *Fusobacterium* from blood cultures and is confirmed by head and neck imaging. Therapy includes organism-specific antimicrobial treatment, drainage of abscesses, and anticoagulation. Significant morbidity and mortality may occur if diagnosis and treatment are delayed. Pediatric pulmonologists must be aware of this rare disease and maintain a high index of suspicion in cases consistent with Lemierre's syndrome.

Case Report

A previously healthy 16-year old male was admitted to hospital following two weeks of fever, myalgia, malaise, nausea/vomiting/diarrhea associated with 10-pound weight loss, and a dry cough. He had been evaluated by his primary care provider (PCP) ten days prior to admission for complaints of sore throat and fever up to 40°C. Rapid streptococcal antigen and SARS-CoV-2 testing were negative, and he was treated with antipyretics. Continued symptoms led to reevaluation by his PCP 7 days later. A chest radiograph at that time revealed a single round pneumonia in the right lower lobe and he was treated with 3 days of oral azithromycin. He failed to improve and was referred to the emergency department 3 days later, where a computed tomography (CT) scan of the chest/abdomen/pelvis demonstrated diffuse, bilateral, cavitary, pulmonary nodules. Physical examination at the time was significant only for multiple ulcerative lesions

of the oropharynx. He was admitted for further evaluation and treatment, including empiric therapy with intravenous vancomycin and ceftriaxone.

Considerations from the admitting team included atypical infection (fungal or mycobacterial) versus e-cigarette or vaping product use associated lung injury (EVALI), so the pulmonary medicine service was consulted. EVALI was thought to be unlikely based on the radiographic appearance of the lesions (Figure 1). Additional diagnostic considerations included septic emboli, paragonimiasis, autoimmune disease with small vessel vasculitis (polyangiitis with granulomatosis), and inflammatory bowel disease. Comprehensive evaluation for the above potential diagnoses was initiated and empiric therapy with vancomycin and ceftriaxone was continued. Echocardiogram, infectious diseases testing, and rheumatic evaluation were all normal other than elevation of his C-reactive protein. The day following admission, he developed tender swelling in the right, anterior neck as well as a tender spot on his upper right back. His blood culture grew gram-negative anaerobic rods, raising concern for Lemierre's syndrome. A Doppler ultrasound of the neck demonstrated occlusive thrombus within the right external jugular vein with nonocclusive extension into the internal jugular vein. Metronidazole was added to his intravenous antimicrobial regimen and anticoagulation therapy was initiated.

Additional imaging demonstrated normal CT scan of the head with confirmation of the ultrasound findings of thrombosis of the jugular veins as well as marked inflammation over the surrounding soft tissues of the anterior right neck and a large abscess involving the posterior spinal musculature of the upper thorax. A percutaneous drain was placed, and 25 cc of purulent material was removed. Magnetic resonance imaging of the spine revealed possible extension of the abscess into the T1 spinous process concerning for osteomyelitis. The blood culture was finalized as growing *Fusobacterium necrophorum* and antibiotic coverage was changed to ampicillin/sulbactam to better treat potential polymicrobial infection. Fevers resolved, discomfort and other symptoms improved, and the percutaneous drain was removed after 3 days. He was discharged home to continue with 6 weeks of continuous infusion ampicillin/sulbactam and anticoagulation therapy.

Discussion

Lemierre's syndrome (LS) is a rare complication of infections of the head and neck, with a reported incidence of one case per million people per year.[1] Once common during the "pre-antibiotic era", LS had decreased in incidence for decades but has been increasing in incidence since the 1990s. This is thought to be secondary to better antimicrobial stewardship and decreased use of antimicrobial therapy for individuals presenting with pharyngitis.[1] Disease is attributed to infections of the palatine tonsils and peritonsillar tissue in 87% of cases and infections of the pharynx, parotid glands, sinuses, mastoids, middle ears, and teeth/gums in the remaining 13% of cases.[2] Males and females are thought to be equally affected.[3] LS has been reported in individuals aged 2 months to 78 years although it is most commonly reported among previously healthy adolescents and young adults.[2,3]

Lemierre's syndrome is thought to originate with primary infection in the head or neck.[4] This is followed by local spread of the infection through the soft tissues of the neck resulting in thrombophlebitis of the internal jugular vein. Finally, dissemination of infection through septic emboli occurs. Sites of infection include the lungs in up to 80% of cases and bones and joints in up to 27% of cases.[1-4] Additional sites of infection include cardiovascular structures, skin and muscles, central nervous system, abdominal organs including liver and spleen, and kidneys. Pulmonary involvement has included septic emboli, abscess formation, necrotizing pneumonia, empyema, pneumothorax, pulmonary embolism, and acute respiratory distress syndrome. LS is most often caused by *Fusobacterium necrophorum* , part of the normal flora of the pharynx, which may account for up to 85% of cases. Other causes include additional *Fusobacterium* species, anaerobes including *Bacteroides* , *Peptococcus* , and *Peptostreptococcus* species, and aerobes including *Streptococcus* , and *Staphylococcus* species, and others. Polymicrobial infections have been reported in up to 30% of cases.[2] Significant morbidity has been reported as a result of delayed diagnosis. Mortality rates have previously been reported as 4-18%; however, more recent reviews suggest a lower rate.[3,5]

Individuals with LS often present 4 to 12 days after the initiating oral pharyngeal infection, which may have

resolved by the time of presentation. Symptoms include high fever (up to 80% of cases), gastrointestinal complaints (50%), pharyngitis with cervical adenopathy or neck pain/swelling, myalgia/arthralgia, rigors, and respiratory symptoms, which may include cough or dyspnea.[1,2,5] Additional symptoms may be secondary to organ system dysfunction caused by septic emboli. Diagnosis is often made based on Doppler ultrasound or computed tomography imaging of the head and neck or the growth of *Fusobacterium* or other bacteria from blood or abscess cultures.

Therapy for LS typically involves long term, intravenous antibiotic therapy, surgical drainage of abscess sites, and anticoagulation.[1-6] Metronidazole is often reported as standard therapy for LS. Other antibiotic considerations include carbapenems or penicillin/beta-lactamase inhibitor combinations, which may provide broader coverage for polymicrobial infections. Duration of therapy is often 4 to 6 weeks to allow for adequate penetration of thrombi as well as treatment of secondary problems such as osteomyelitis. The role of anticoagulation therapy is more controversial. Some data suggest that the use of anticoagulation hastens overall response while others indicate adequate clinical response without additional therapy.

Lemierre's syndrome is a rare disorder of the head and neck that may be associated with significant morbidity and mortality if diagnosis and treatment are delayed. Hence, a high index of suspicion must be maintained in order to identify children with LS. Pediatric pulmonologists will most likely encounter LS in patients hospitalized with prolonged fever and multiple septic pulmonary emboli. LS must be considered as part of the differential diagnosis for any child with multiple cavitary nodules identified on chest CT imaging. This is particularly true if there is a history of proceeding oral pharyngeal infection or acute signs and symptoms suggesting pathology in the head and neck. The growth of *Fusobacterium* species from blood culture or abscesses should also suggest the possibility of LS. If LS is suspected, Doppler ultrasound examination of the neck and possible CT imaging of the head and neck should be obtained. Therapy should include long-term intravenous antibiotics directed at the treatment of specific organisms recovered. Adjuvant therapy with surgical incision and drainage of abscesses or anticoagulation therapy may be necessary in some cases.

References

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Figure 1

Axial (1A) and coronal (1B) computed tomography images of the thorax. Images demonstrate multiple, bilateral, nodules with and without thick-walled cavitation. Most lesions are peripherally located; the lesions demonstrated on the coronal images are posteriorly located.