CLINICAL VIGNETTE

Lemierre Syndrome: A Rare, Potentially Fatal Complication of Acute Pharyngitis

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"The appearance and repetition several days after the onset of a sore throat … of several pyrexial attacks with an initial rigor and still more certainly the occurrence of pulmonary infarcts and arthritic manifestations make a syndrome that is so characteristic that mistake is almost impossible." – Andre Lemierre, *Lancet* 1936

Introduction

Sore throat is a common complaint in primary care clinics, accounting for 1-2% of all ambulatory care visits in the United States.[1] Though acute pharyngitis is most commonly viral with a benign, self-limited course, other causes such as bacterial and non-infectious etiologies must be considered. We often think about streptococcal pharyngitis, but we must also suspect other unusual and dangerous causes.

Lemierre syndrome, or jugular vein suppurative thrombophlebitis is a rare and potentially lethal complication of *Fusobacterium* superinfection following acute pharyngitis. It occurs in only one in one million people but if left untreated has a greater than 90% mortality[2] and can be progressively fatal within two weeks.[3] Antibiotics lower the mortality to 2-5%,[4,5] so early diagnosis and administration of antibiotics are critical. What follows is a case of Lemierre syndrome and a description of how to recognize and treat the disease.

Case

A 32-year-old woman presented to urgent care with one day of fevers, body aches, severe sore throat, and mild nasal congestion. She was febrile to 102.5^{O}F with a heart rate of 125. Rapid strep and flu swabs were negative. Bacterial throat culture was sent, but the patient was thought to have a viral respiratory infection and was sent home without antibiotics. Her throat culture returned negative.

Six days later, the patient presented to her primary care clinic with ongoing fevers and chills. She reported improving sore throat but significant pain in her right jaw, neck, and ear. She had pain with swallowing, difficulty opening her mouth, fatigue, body aches, and dark urine. She denied shortness of breath. Initially, she was afebrile, and her vital signs were notable for a heart rate of 141. Physical exam showed asymmetric swelling in the posterior pharynx with swelling and erythema of the right tonsil. She had tenderness to palpation over the right jaw and upper lateral neck. Pulmonary exam was normal. She was given two liters of normal saline, but because she became febrile to 102.9^{O}F, had rigors, and remained tachycardic to 137 despite intravenous fluids, she was sent to the emergency room.

In the emergency room, her labs were notable for a leukocytosis of 23 and thrombocytopenia to 16. She was started on ampicillin-sulbactam empirically. Chest x-ray showed right greater than left patchy airspace opacities. CT neck showed asymmetric prominence of the right tonsil with inflammatory/phlegmonous changes extending into the right submandibular space, right masticator space, carotid sheath, and parapharyngeal fat without evidence of abscess. It also showed thrombophlebitis of the right internal jugular with nodular opacities in the right lung representing developing Lemierre syndrome. CTA chest showed no evidence of pulmonary embolism, but it did have multiple necrotic and non-necrotic nodular consolidations in the right lung consistent with septic emboli.

The patient was admitted to the hospital and continued on ampicillin-sulbactam. Infectious disease was consulted and recommended a two-to-four week course of IV antibiotics. Her final blood cultures were negative. She ultimately completed five days of ampicillin-sulbactam and then was transitioned to ertapenem for ease of outpatient antibiotic dosing, along with broad gram positive, gram negative, and *Fusobacterium* coverage. She completed an additional 10 days of ertapenem followed by a two-week course of amoxicillin-clavulanate.

For her thrombocytopenia, she received one unit of platelets. Hematology thought her severe thrombocytopenia was secondary to severe sepsis. Her platelets subsequently increased from a low of 12 to around 400 with antibiotic treatment. Her leukocytosis also resolved. Given her thrombocytopenia and the uncertain benefit of anticoagulation in Lemierre syndrome, she was not given anticoagulation.

The patient improved clinically and was discharged from the hospital. On hospital follow-up, she had persistent but improving pleuritic chest pain with small pleural effusions. These resolved over the next few weeks with completion of her antibiotic course. At follow-up six weeks after hospital discharge, she was asymptomatic.

Discussion

Lemierre syndrome occurs when mucosal damage from pharyngitis allows normal oropharyngeal flora, most commonly *Fusobacterium*, to enter through the pharyngeal mucosa, extend into the parapharyngeal space, and invade the jugular vein. As a result of this inflammation a thrombus forms, and from there bacteria may spread through the blood stream, leading to septic emboli throughout the body. Pulmonary septic emboli, as in this case, are quite common and are seen in 97% of patients.[3] It is possible to have seeding to other areas, causing empyema (10-15%), septic arthritis (13-27%), or osteomyelitis (<3%).[5] Liver or splenic abscesses, meningitis, brain abscess, skin abscess, endocarditis, renal injury, and ARDS are rare complications but have also been reported.[5-7] Other local complications can include peritonsillar abscess, parapharyngeal abscess, and paratracheal abscess.[5]

Lemierre syndrome frequently affects young, healthy adults with a mean age of 20 years. Patients typically present with initial sore throat followed by fevers, rigors, and neck or throat pain. Other symptoms can include neck swelling, dysphagia, cough, pleuritic pain, hemoptysis, respiratory distress, arthritis, or jaundice. The time between pharyngitis symptoms and onset of jugular vein thrombophlebitis is usually less than a week.

Physical exam of the throat is highly variable. It may be normal, show mild tonsillar inflammation, or have severe exudative tonsillitis with peritonsillar abscess.[5] Tenderness or swelling may be observed along the course of the jugular vein with or without cervical lymphadenopathy.

Laboratory studies show neutrophilic leukocytosis and elevated CRP. Transaminitis is present in around 50% of patients, and mild thrombocytopenia is common.[5] True confirmation of the diagnosis can be made through anaerobic blood cultures growing *Fusobacterium*. But because this organism is slow-growing, the diagnosis is mainly clinical.[3]

The best imaging method for diagnosis is a CT with contrast, which may show the actual thrombus, filling defects, or soft tissue swelling in the area. The CT scan can be extended to include the chest given the high incidence of pulmonary emboli. CT scan of the neck has higher sensitivity than ultrasound for detecting thrombus and is less expensive than MRI.[5] CT scan of the chest is more revealing than chest x-ray for demonstrating septic emboli.

Antibiotics are the main treatment for Lemierre syndrome. They should include coverage for anaerobic and beta-lactamase resistant microbes. Ampicillin-sulbactam or piperacillin-tazobactam are good choices. Carbapenems as well as metronidazole combined with ceftriaxone are also appropriate. Fluoroquinolones, macrolides, and penicillin alone are inadequate therapy because *Fusobacterium* is intrinsically resistant to them.[5] The duration of therapy is generally four weeks. Surgery is indicated only in ongoing sepsis that has not responded to antibiotics. Surgery may involve drainage of abscesses in the neck or internal jugular vein ligation or excision.[8]

Though Lemierre syndrome involves a clot, the role of anticoagulation is controversial, and no randomized controlled trials have been conducted. Some experts hypothesize that anticoagulation may prevent further septic emboli and respiratory compromise, but others suggest that the thrombosis in Lemierre syndrome will resolve spontaneously.[9] Many case reports, including this one, have demonstrated recovery without anticoagulation,[6,7,9] and a retrospective study suggests anticoagulation does not affect thrombosis outcomes.[10] Some recommend using anticoagulation only if thrombus extends into the cerebral sinuses or if there is no improvement with antibiotics alone.[8]

Conclusion

Lemierre syndrome is a rare but potentially fatal complication of pharyngitis in otherwise young, healthy adults. It should be suspected in patients with initial pharyngitis who show symptoms of sepsis, neck pain, or pulmonary involvement. Our patient was a classic example of Lemierre syndrome, presenting with acute pharyngitis complicated by fevers, rigors, trismus, and neck pain, and found to have right internal jugular thrombophlebitis complicated by septic pulmonary emboli.

Though Lemierre syndrome is uncommon, incidence rates have been rising in the last few decades.[5] This may be due to reduced antibiotic prescriptions for sore throat, improvements in anaerobic blood culture technique, and more advanced imaging modalities that can better detect internal jugular thrombus.[3,5]

Given the prevalence of sore throat in primary care clinics and the high mortality of Lemierre syndrome without treatment, it is important to look for this complication. As antibiotic use for pharyngitis continues to decline, we must be careful to consider Lemierre syndrome as a serious but treatable complication of pharyngitis.

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