Ochsner Journal 16:7–9, 2016

Lemierre Syndrome: The Forgotten Disease?

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INTRODUCTION

Lemierre syndrome occurs when an oropharyngeal infection is complicated by septic thrombophlebitis of the internal jugular vein (IJV) or one of its tributaries, leading to sepsis and metastatic infection. Here we describe a case of Lemierre syndrome and present imaging classic for the disease process.

HISTORY

An 18-year-old previously healthy female presented to the emergency department (ED) with sore throat, shortness of breath, fever to 105°F, pleuritic chest pain, weakness, and lethargy. The week prior, she had presented to her primary care physician with sore throat, fever, cervical lymphadenopathy, and vomiting. Her chest x-ray was negative at that time. She was diagnosed with mononucleosis and sent home.

RADIOGRAPHIC APPEARANCE

Upon admission to the ED, the patient's initial chest x-ray demonstrated numerous ill-defined rounded opacities throughout both lungs and a right-sided pleural effusion (Figure 1). Noncontrast computed tomography (CT) of the thorax showed numerous cavitary nodules throughout both lungs, a large encapsulated fluid lesion in the medial base of the right hemithorax, and a loculated right-sided pleural effusion in the lateral right hemithorax (Figure 2). These findings were concerning for a multifocal infectious process, and because of the patient's history of recent pharyngitis, Lemierre syndrome was suspected. CT of the neck with and without contrast showed a filling defect in the left IJV, as well as prominent tonsils and adenoids bilaterally (Figure 3). Bilateral ultrasound of the upper extremity veins also demonstrated a partially occlusive thrombus in the left IJV (Figure 4). Given the patient's history and imaging, Lemierre syndrome was diagnosed.

The patient was admitted to the pediatric intensive care unit for sepsis and respiratory failure. Numerous cultures of blood, urine, respiratory secretions, and pleural aspirations were negative. Broad-spectrum antibiotics were started: cefepime, penicillin G, azithromycin, and clindamycin. Interventional radiology was consulted to drain the right-sided pleural fluid collection (Figure 5). The patient clinically improved after 2 weeks of inpatient intravenous antibiotics. Subsequently, all lines were pulled, and she was discharged home with oral antibiotics.

DISCUSSION

Lemierre syndrome is named for André Lemierre who, in 1936, published a series of cases on throat infections associated with cervical extension, anaerobic septicemia, and pulmonary abscess formation.[1] The incidence of Lemierre syndrome decreased dramatically in the 1940s after the introduction of antibiotics to treat pharyngitis and hence became known as "the forgotten disease." During the past few decades, however, there has been an upswing in the reporting of Lemierre syndrome. Whether this increase in reporting is just a publishing trend or represents a real increase in incidence—potentially attributable to antibiotic resistance and the restricted use of antibiotics for perceived uncomplicated pharyngitis—is unclear.[2] However, studies have linked nonsteroidal antiinflammatory drugs and steroids, both commonly prescribed to treat pharyngitis, to enhanced bacterial virulence and spread.[3]

Lemierre syndrome affects mainly healthy people in the second and third decades of life. Its incidence is about one per million, with more men affected than women.[3] *Fusobacterium necrophorum* is the main culprit organism, a Gram-negative non–spore-forming obligate anaerobe. *F necrophorum* is a common component of the oral cavity

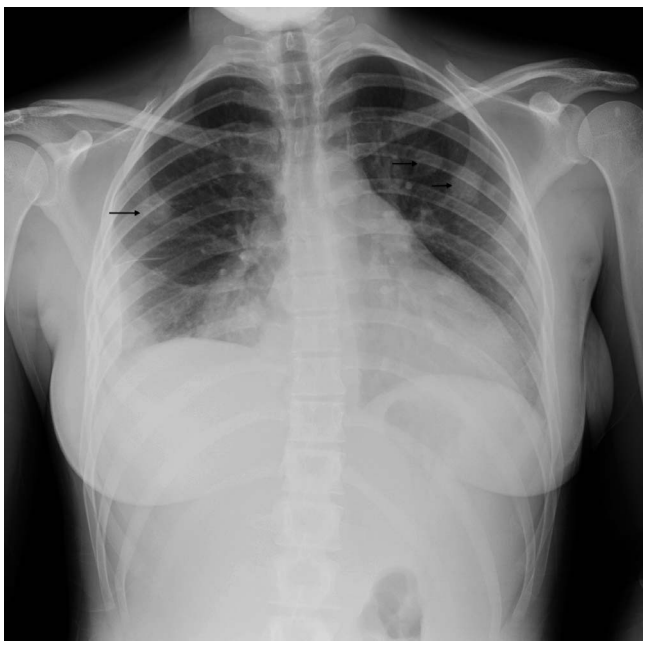

Figure 1. Posterior-anterior chest x-ray demonstrates multiple bilateral round pulmonary nodules (black arrows).

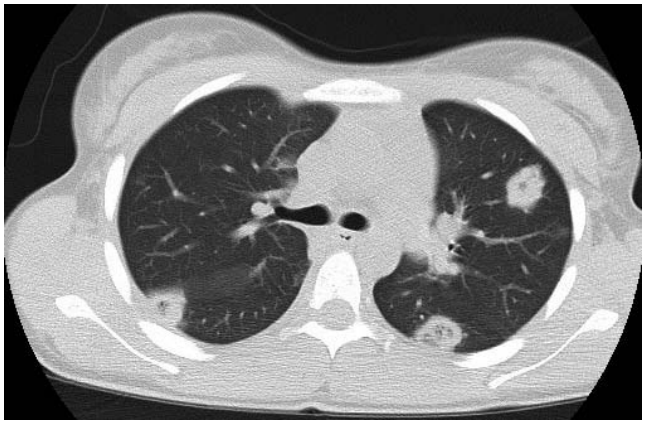

Figure 2. Chest computed tomography viewed at lung window settings shows that the bilateral pulmonary nodules have cavitation.

and is responsible for 10% of acute sore throats.[3] Other causal bacteria include streptococci, staphylococci, *Eikenella*, and bacteroides. In 10%-15% of Lemierre syndrome cases, no organism is identified, but 10%-30% of cases are polymicrobial.[3] The primary entry point of infection is peritonsillar tissue, followed by the pharynx, chest, larynx, middle ear, and odontogenic tissue. An association between Epstein-Barr virus infection and more severe cases of Lemierre syndrome has been shown, although the mechanism of this relationship is unclear.[4]

Lemierre syndrome most often begins as an oropharyngeal mucosal infection with sore throat, fever, cervical lymphadenopathy, and peritonsillar abscess. Then, 1-3 weeks later, the infection spreads to the parapharyngeal space and jugular vein, gaining access via direct extension

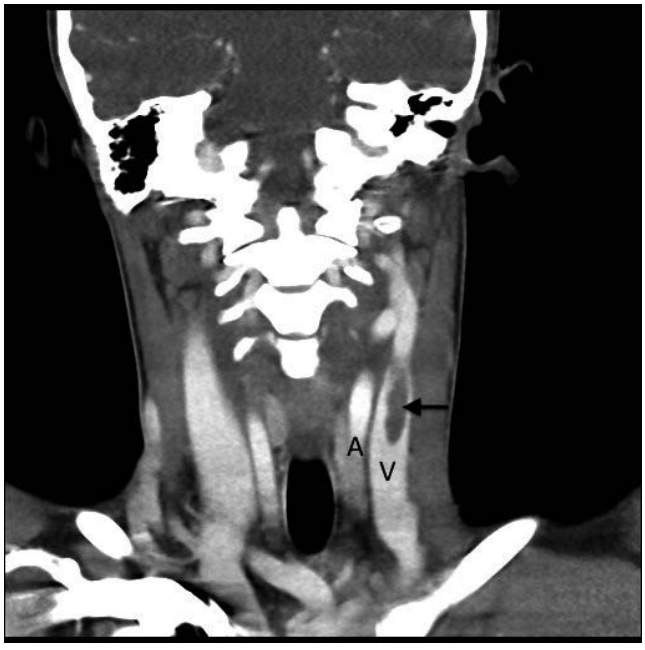

Figure 3. Coronal computed tomography of the neck with contrast reveals a soft tissue attenuation filling defect in the left internal jugular vein (black arrow). The left common carotid artery (A) and internal jugular vein (V) are indicated.

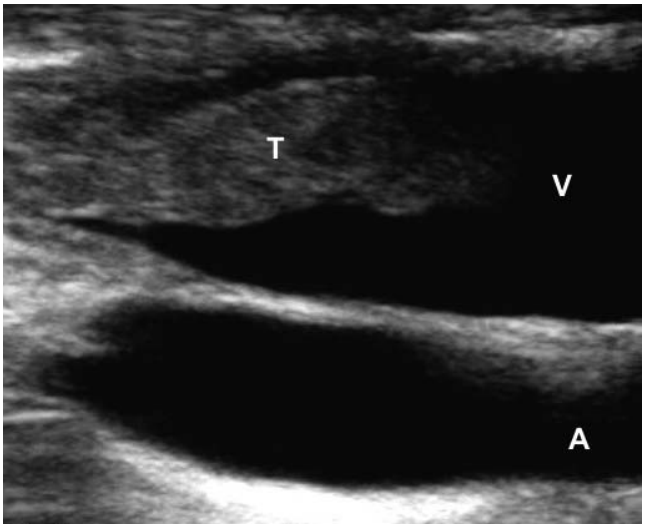

Figure 4. Longitudinal ultrasound image shows the left common carotid artery (A), left internal jugular vein (V), and thrombus (T).

or the peritonsillar venous plexus, and causes thrombosis that often manifests as a tender, swollen cord anterior to the sternocleidomastoid muscle.[5] Other complications of parapharyngeal space invasion are carotid artery rupture, Horner syndrome if the sympathetic trunk is involved, spasm or paralysis of the trapezius muscle, and dysphagia. However, 47.7% of patients have no significant neck symptoms.[6] Septic thrombophlebitis of the jugular vein is the primary source of infection that then showers septic emboli to the body, most commonly to the lungs, but also to the joints, muscle, soft tissues, liver, spleen, kidneys, and central nervous system.[2] Sepsis ensues from the stimulation of cytokines by bacterial toxins. *F necrophorum* also produces hemagglutinin that activates platelets, causing disseminated intravascular coagulation and thrombocytopenia.[2]

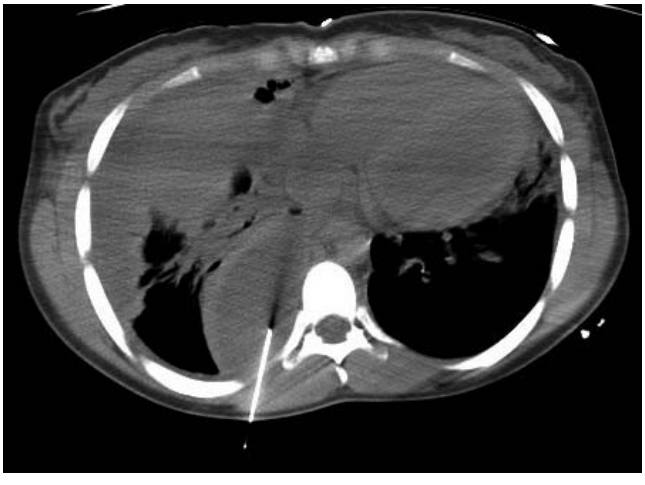

Figure 5. Computed tomography (CT) through the lower chest during CT-guided drainage catheter placement demonstrates a loculated empyema in the right posterior hemithorax. A needle has been placed from a posterior approach to access the collection during the procedure.

Demonstration of infection is crucial to the diagnosis of Lemierre syndrome. Imaging is usually the best way to identify the infection source, as blood cultures can take 5-8 days to resolve. Chest x-ray is often the primary study performed and classically demonstrates pulmonary infiltrates; however, chest x-ray appears normal in 10% of patients.[2] CT scan with contrast of the neck and chest is the test of choice for diagnosing Lemierre syndrome because it can show the classic findings of a filling defect of the IJV, as well as complications such as abscesses and septic pulmonary emboli. While the thrombus can be well demonstrated on ultrasound, visualization with this technique can be limited because of the overlying mandible and clavicle. Ultrasound is also operator dependent and less sensitive than CT with contrast to a newly formed clot.[3] Ultrasound does, however, provide a simple and inexpensive way to follow clots with serial imaging.[5] Magnetic resonance imaging can also be used to demonstrate thrombus and emboli; however, its high cost and limited availability make it a second-line study.

Antibiotics are the primary treatment for Lemierre syndrome. *F necrophorum* is usually susceptible to penicillin, clindamycin, metronidazole, chloramphenicol, and second- and third-generation cephalosporins. The most common combination used is metronidazole and ceftriaxone because they treat streptococci as well. The duration of treatment is 3-6 weeks of antibiotics.[7] Anticoagulation is used in about 30% of cases; however, reports on its efficacy conflict.[2] Minimally invasive catheter drainage is often necessary to drain parapharyngeal, cervical, or mediastinal abscesses. IJV ligation and excision are only performed in cases of persistent septic emboli despite antibiotic treatment.[2] The mean duration of hospital stay is 25 days, and approximately 58% of patients are admitted to the intensive care unit.[2] Lemierre syndrome has a mortality rate of 6%-22%.[3]

While Lemierre syndrome is still a rare disease, the number of reported cases is on the rise. This diagnosis requires awareness of the condition and a high index of suspicion, as symptoms are subtle until frank sepsis ensues. Successful management requires a multidisciplinary team approach with demonstration of septic thrombophlebitis and appropriate antibiotic treatment.

ACKNOWLEDGMENTS

The authors have no financial or proprietary interest in the subject matter of this article.

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