



REVIEW ARTICLE

Lemierre's Syndrome, A Case Report and Review of Literature

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Abstract

Lemierre's syndrome is a suppurative thrombophlebitis of the internal jugular vein. In this paper we describe a case of severe Lemierre's syndrome in a healthy 18 year-old woman. She initially presented with sore throat, and failed outpatient antibiotic therapy. She quickly progressed to septic shock, internal jugular vein septic thrombophlebitis, septic pulmonary emboli, empyema and respiratory failure. Successful treatment included intravenous antibiotics and thoracotomy. It is a rare disease that has been kept at bay with the widespread use of antibiotics for upper respiratory infections. However, in recent years there seems to be an increase in the number of cases being reported which some have attributed to increased adherence to antimicrobial stewardship.

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Introduction

Lemierre's syndrome is a pyogenic or septic thrombophlebitis of the internal jugular vein. It is a rare condition that typically starts as pharyngitis that spreads locally and leads to suppurative inflammation in and around the internal jugular vein leading to thrombosis of the vein [1]. The most commonly associated pathogen is the anaerobic gram-negative bacteria, *Fusobacterium necrophorum* [2]. However, other pathogens have been identified in this kind of infection. It is associated with significant morbidity and mortality on account of the frequently associated septic emboli from the internal jugular vein to the lungs and overwhelming anaerobic sepsis. This disease for unclear reason tends to occur in young, healthy individuals with no other identifiable risk factors. *Fusobacterium necrophorum* is a part of the normal gastrointestinal/genitourinary flora of humans. The disease is treated with a combination of IV antibiotics during inpatient treatment with continued long-term antibiotics after discharge. There is a possibility of surgery to resect the thrombus and affected vascular structures in combination with anticoagulants. The syndrome is often misdiagnosed until bacteremia is identified and the patient begins to decompensate rapidly. In this report we present the case of a young female who presented with anaerobic gram-negative sepsis and cavitary pneumonia rapidly progressing to empyema and respiratory failure requiring thoracotomy with decortication. Although there is a positive outcome in this case,

it is important to be mindful of this potentially deadly disease when evaluating any young person presenting with anaerobic sepsis.

Case Report

An 18 year old female presented to a walk-in clinic for sore throat of three days duration and was diagnosed empirically with streptococcal pharyngitis. She was sent home on five days of azithromycin. Seven days later, she presented to the emergency department with worsening symptoms of dyspnea, fever, chills, sharp left anterior chest pain, emesis, diarrhea and mental confusion. She reported some improvement in her sore throat following treatment with azithromycin. She smokes about half-pack of cigarettes every day and denies any illicit drug or alcohol use. There was no history of previous hospitalization or any major surgeries in the past, and she was not on any medications. On evaluation in the ED, patient appeared acutely ill. Her vital signs on arrival were temperature of 38.10°C, respiratory rate of 38/min, heart rate of 168 beats/min, blood pressure of 113/61 mmHg, and 92% O₂ saturation on room air. On physical examination the abnormal findings were dry oral mucous membranes, diminished breath sounds bilaterally, and a swollen left wrist that was tender to palpation. Initial chest x-ray showed a left lower lobe infiltrate.

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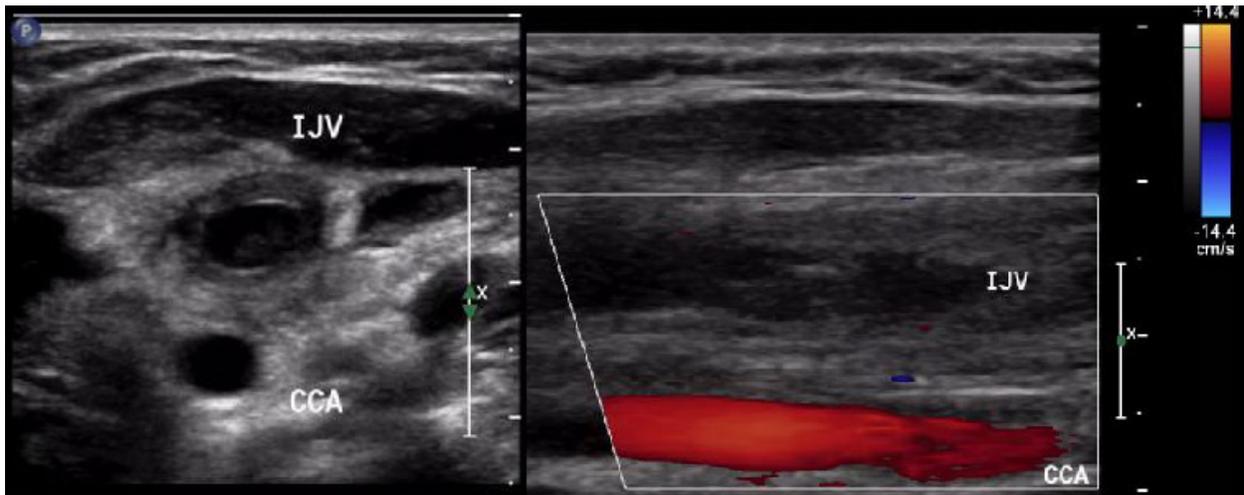


Figure 1. Ultrasound showing the thrombus in the internal jugular. Ultrasound (right) showing no flow in the internal jugular vein

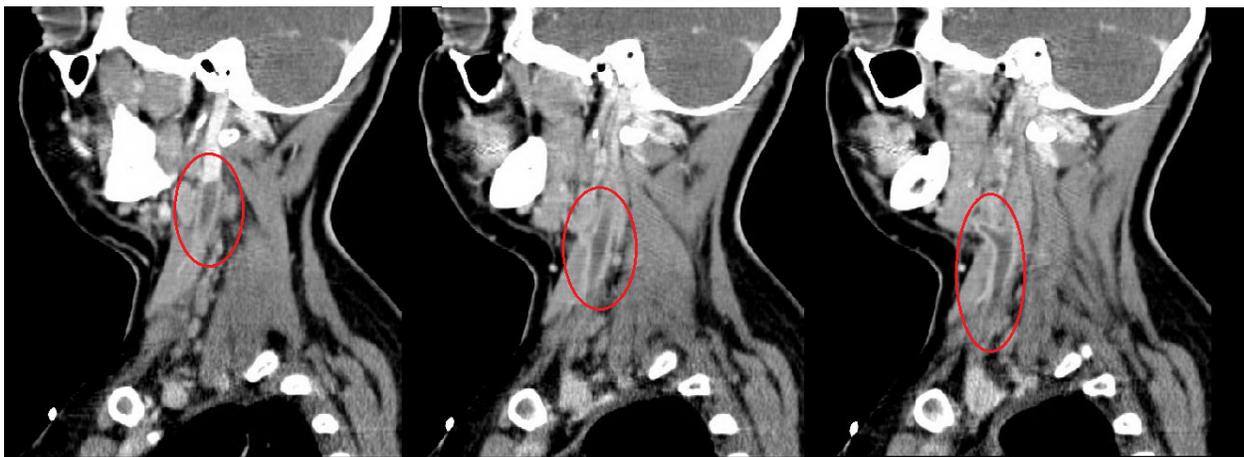


Figure 2. Progressive CT images w/ contrast showing the thrombus (in red)

Labs had normal WBC of 9.26×10^3 L with elevated neutrophils of 8.9×10^3 L and low platelets count of 79×10^3 L with lactic acid of 3.3 (venous draw). She also showed signs of liver dysfunction with ALT of 69 U/L, AST 92 U/L, Albumin 2.8 g/dL. An initial diagnosis of left lower lobe pneumonia with possible sepsis causing thrombocytopenia was made. Blood and sputum cultures were drawn and sent to lab. She was admitted to the ICU and started on intravenous fluid resuscitation, albuterol, ipratropium, ceftriaxone, ketorolac, and acetaminophen. Her CT scan showed bibasilar pneumonia with effusions and splenomegaly.

Antibiotics were changed on day two to piperacillin-tazobactam when her anaerobic blood culture bottle came up positive showing gram-negative rods. The patient continued to decline with new onset of hemoptysis, worsening dyspnea, drop in hemoglobin to 8.6 g/dL, firm and tender abdomen, undulating fevers, and further effusion in the lungs on x-ray. Thoracentesis was performed with lavage to break up loculations, and levofloxacin was added to her antibiotic management on day three. The left upper extremity swelling worsened warranting further examination. Ultrasound (**Figure 1**) found a parapharyngeal abscess about 1.5 cm in diameter, and occlusion of the left internal jugular vein was suspected and verified with

CT scan of the neck (**Figure 2**). Occlusion began at the angle of mandible and extended to the subclavian vein.

Blood cultures were later identified as *Fusobacterium necrophorum* (*F. necrophorum*) on day four, and a diagnosis

of Lemierre's syndrome was confirmed. Levofloxacin was discontinued, but piperacillin-tazobactam was continued. Anticoagulation was considered because of the extent of her vascular clotting and left upper extremity swelling but held due to inconclusive evidence it would improve the situation. However, she was on enoxaparin for DVT prophylaxis.

Chest tube lavage was done again to break up loculations, and the tube was exchanged for a larger caliber version with more drainage ports. Between day four and day five, her fever spikes worsened and she was intubated because of hypoxic respiratory failure. Repeat CT scan on day five, (**Figure 3**) showed multiple septic pulmonary emboli within the lungs.

On day six, patient underwent thoracotomy with decortication. Multiple cavitory lesions were found and unroofed during the procedure. She was kept on piperacillin-tazobactam and under sedation/ventilation until the following day. Her clinical condition began to improve on day eight, x-ray showed improvement with better lung inflation.

Her fevers subsided, and patient was transferred out of ICU. She was subsequently discharged home on IV ertapenem for 30 days on outpatient parenteral antibiotic therapy through home health and followed up at an outpatient clinic.

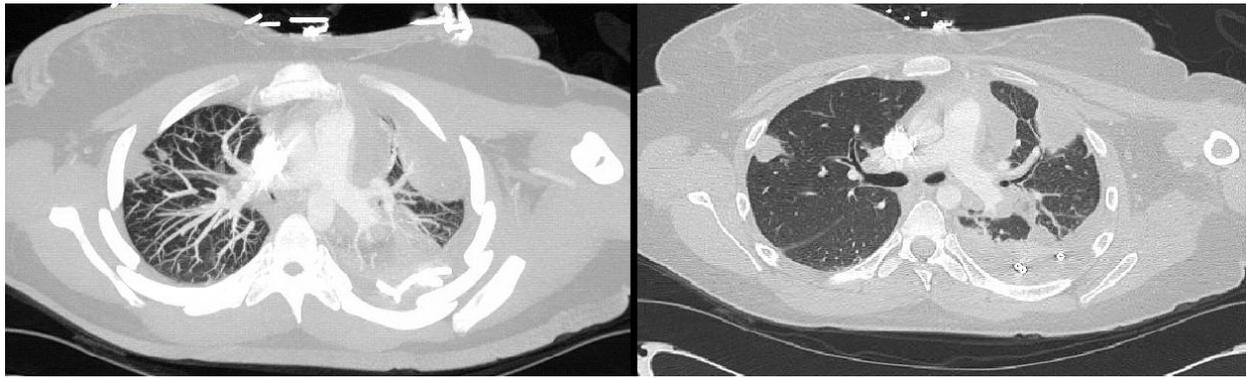


Figure 3. Angiography on left and CT on right

Review of Literature

Epidemiology

Lemierre's syndrome is described as a disease originating from the oropharynx and leading to thrombophlebitis of the internal jugular vein, anaerobic bacteremia and septic emboli to distant sites such as the lungs [2]. It was first described by Lemierre in 1936 [3]. It is a relatively rare infectious syndrome commonly found in otherwise healthy young adults. However, extensive review of 179 published papers (from 2007 to 2018) indicates that ages may range from 5 weeks to 86 years old with the median age still in the second decade of life (Figure 4). It appears to develop as a complication of an upper respiratory bacterial infection. Although it is still considered a rare disease with an incidence of less than 4 per 1 million population [4] some have noticed an uptick in cases possibly due to antibiotic resistance or changes in prescription habits [5].

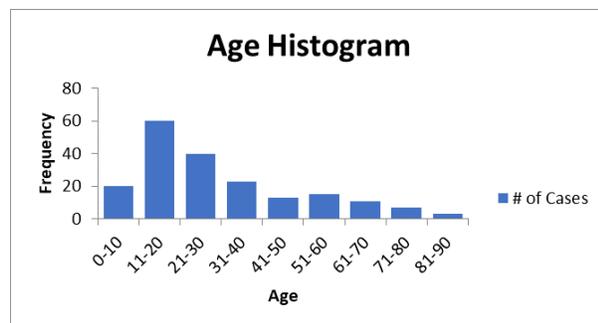


Figure 4. Histogram of cases by age 2007-2018 sampling

To date nearly 700 articles have been published related to Lemierre's Syndrome with averages of 8/year from 1950 to 1990, 81/year from 1991 to 2000, 290/year from 2001 to 2010 and 311/year since 2011 (Figure 5). It is not known whether the increase in case reports is as a result of true increase in incidence or merely an accident of more people willing to publish details of their cases. There is however some circumstantial evidence of rising incidence owing primarily to rising incidence of *F. necrophorum* bacteremia and other bacterial etiologies [6]. It has been speculated that an increase in incidence might be as a result of the hesitation of primary care providers to prescribe antibiotics for common upper respiratory tract infections due to emphasis on antimicrobial stewardship [7,8]. Also, changes in prescription patterns whereby antibiotics that are effective against *F. necrophorum* such as penicillin are no longer considered first line agents for URIs due to widespread resistance, rather other antibiotics such as azithromycin that has no activity against anaerobes are now given as first line agents when antibiotics are prescribed for pharyngitis and other URIs [9] such as was the case in our patient. The male to female

ratio is variable. Some reports put it at 1:1 [4] and a review by Kerkos reported a male to female ratio of 2:1 [5]; our summary view of the literature had a ratio of 1.8:1.

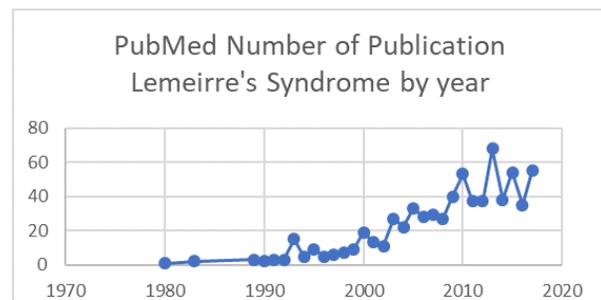


Figure 5. Search results of PubMed database for *Lemierre's Syndrome* and results broken down by year

Pathophysiology

Fusobacterium necrophorum is the most common bacterium associated with Lemierre's Syndrome [5]. *F. necrophorum* is an anaerobic gram-negative rod that is commonly found in the oropharynx. It is normal flora of the oral cavity, gastrointestinal tract and the female genital tract [2]. It has been implicated in cases of tonsillitis (87% of LS) or mastoiditis (3% of LS) [7,10]. Other bacterial etiologies include other *Fusobacterium* species, *F. nucleatum*, *Bacteroides* species, *Prevotella* species [2,5], *Streptococcus* species [11], *Staphylococcus* species [12], *Slackia* [13], *Porphyomonas* [14], methicillin-resistant *Staphylococcus epidermidis* [15], methicillin-sensitive *Staphylococcus aureus* [16], methicillin-resistant *Staphylococcus aureus* [17], *Klebsiella* [18], *Chromobacterium* [19], *Acrinobacterium* [20]. Infection usually begins in the oropharynx but spreads to peritonsillar tissue and to the parapharyngeal space via the lymphatics. This then leads to inflammation of the endothelial lining of the internal jugular vein resulting in thrombosis and later suppuration of the clotted vessel. Subsequent bacteremia leads to metastatic infection to the lungs, liver, kidney and joints [21].

Clinical Presentation

The clinical presentation of LS is variable depending on the extent of infection and distant metastasis. Lemierre's syndrome usually presents as fever, neck pain, swelling, and dyspnea about three days to four weeks after a sore throat, average seven days [2,22]. Physical symptoms may resolve at the site of original infection; however, the patient may present with sore throat, dysphagia and dysphonia, ear ache and otorrhea, pleuritic chest pain and dyspnea one week later. There may be joint pain and swelling in cases of joint involvement. Tenderness behind the ear may be noted in patients whose infections originated from mastoiditis. But by far the commonest presentations are fever,

unilateral neck pain and swelling with other signs of sepsis. Sometimes IJV thrombosis is identified incidentally during workup for neck pain or pharyngitis, and septicemia will usually begin to happen a week after onset. Spread of the infection to the lungs is common in a majority of patients [23]. Liver enzymes can be elevated, but the reason for this is not completely understood. Diagnosis should be made with positive cultures and either ultrasound or CT imaging with contrast.

Treatment

Intravenous antibiotic is the cornerstone of treatment. *F. necrophorum* can produce B-lactamase, but it is generally susceptible to penicillin, second and third generation cephalosporins, clindamycin, metronidazole, B-lactam-B-lactamase combination antibiotics such as piperacillin-tazobactam, ampicillin-sulbactam, and carbapenems [2]. Treatment can vary widely depending on the extent of infection [24]. Surgery may be required in cases of empyema or lung abscesses. Arthrotomy may be necessary in cases of septic arthritis. Even though results of treatment might not be immediate, it is important to continue IV antibiotics for up to six weeks [6]. In some cases, drainage of the abscess and/or internal jugular excision is needed if antibiotic therapy is not effective at eliminating the infection [25,26]. Ligation and excision of the IJV, which was the treatment modality in the pre-antibiotic era, is no longer being practiced. There is also some controversy on the role of anticoagulation use in this disease. The role of anticoagulation in the management of LS is limited to certain situations where thrombosis has extended to the great vessels in the chest or to intracranial venous channels [27,28,29].

Conclusion

Lemierre's syndrome is a severe suppurative intravascular infection of the neck that is associated with a high morbidity and some mortality if not identified in time. Patients with unusual neck masses with upper respiratory infections or in the week preceding that should be evaluated immediately for LS so that appropriate treatment can be promptly initiated.

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