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Case Report

Lemierre's syndrome: an evolving disease

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ABSTRACT

Lemierre's syndrome is characterized by thrombophlebitis of the internal jugular vein with resulting systemic septic emboli. Most cases occur following an oropharyngeal infection and have been historically caused by the bacterial pathogen *Fusobacterium necrophorum.* However, infection from other pathogens is becoming more common in recent years. Our case is special in the sense that Lemierre's syndrome was caused by staphylococcus aureus after influenza infection. A 23-month-old male presented with complaints of left neck swelling and recurrent fever for one week, following influenza A infection. The child was ill-appearing with fever, tachycardia, tachypnea, and erythematous swelling on the left cheek. Laboratory results revealed elevated inflammatory markers. Computed tomography (CT) scan of the neck showed loculated fluid collection suggesting an intra parotid abscess with poor visualization of the internal jugular vein (IJV). Blood cultures were positive for methicillin-sensitive *Staphylococcus aureus*. Due to high clinical suspicion of Lemierre's syndrome, a doppler ultrasound was obtained which showed a left IJV thrombus. CT scan of the chest after the clinical suspicion showed multiple bilateral pulmonary nodules suggesting septic emboli. He was treated with antibiotics and a six-week course of the anticoagulant with a resolution of his thrombus. Though historically, Lemierre's disease is caused by *Fusobacterium necrophorum*, other causative organisms such as methicillin-sensitive *Staphylococcus aureus* are increasingly being recognized. Lemierre's disease can present as a complication of influenza. A high index of clinical suspicion based on the location of the abscess helped us delineate diagnostic tests and treatment.

Keywords: Lemierre's syndrome, Methicillin-sensitive *Staphylococcus aureus*, Internal jugular vein thrombosis, Influenza

INTRODUCTION

Lemierre's syndrome is defined as thrombophlebitis of the internal jugular vein with septic emboli occurring after an oropharyngeal infection. It was first described by Andre Lemierre in 1936 as a post-anginal septicaemia. It is a rare disease with an incidence of 0.6 to 2.3 per million. The average age of diagnosis is 20 years, with young, healthy adults being the most commonly affected population.[1] Patients with Lemierre's syndrome have variable presentations including symptoms of sore throat, odynophagia, neck pain, and fever. There may be an absence of neck pain or sore throat in cases that have already progressed to sepsis. The internal jugular vein is the most often thrombosed vein, but others such as the facial vein, sinus transversus, or superior ophthalmic vein have been reported.[2]

Septic emboli are usually found in the lungs, although other organs such as the liver, spleen, joints, heart, and central nervous system can be affected. The organism classically involved is the gram-negative anaerobic bacteria *Fusobacterium necrophorum*, but other organisms are becoming more prominent in recent years.[3] Treatment involves antibiotics and anticoagulation in certain patients. The effectiveness of antibiotic treatment has made this disease less likely to present over the years.

However, Lemierre's syndrome is evolving in its presentation and bacterial etiologies and should therefore not be forgotten. This case report will review the symptoms, diagnosis, and treatment of a post-influenza case of Lemierre's syndrome caused by methicillin-sensitive *Staphylococcus aureus*.

CASE REPORT

A 23-month-old male with no significant past medical history was brought to the emergency department (ED) with left neck swelling and recurrent fever for one week. The swelling was first noted under the left jaw four days ago and since then has continued to increase in size. He was taken to the pediatrician's office when the fever started for the first time. During that visit, he was diagnosed with Influenza A via a rapid antigen test and was treated symptomatically. He did have sore throat, mouth ulcers, myalgia at that visit. Mother denied having any other symptoms like recent cold, cough, headache, trauma to the neck, or any other infections elsewhere. On arrival to the ED, the initial physical exam was positive for an ill-appearing child with swelling on the left neck extending from the left cheek to the posterior aspect of the neck. The swelling had signs of inflammation like redness, induration, and local rise of temperature. Initial laboratory results revealed elevated C-reactive protein at 12.6 mg/dl, erythrocyte sedimentation rate of 90 mm/hour, lactate dehydrogenase at 419 U/l, and lactate at 3.44 mg/dl, and white blood cells (WBC) were normal at 11.35×109/l. Computed tomography (CT) scan of the neck showed myositis, cellulitis, and fasciitis on the left neck with a collection of loculated fluid measuring approximately 1.8×1.1×0.4 cm and it was difficult to determine whether or not this collection was within or adjacent to the parotid gland (Figure 1). On the CT, we were also unable to visualize the left jugular vein.

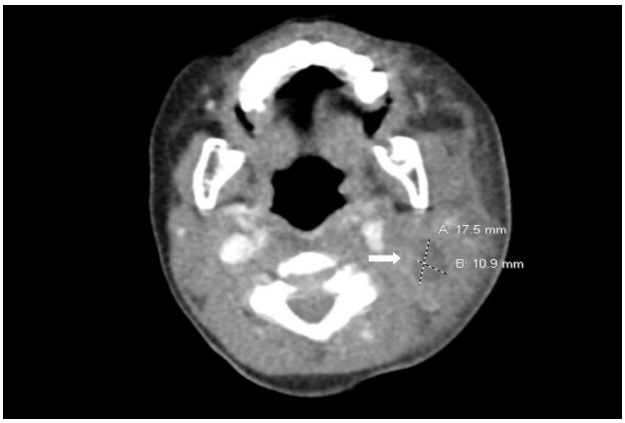

Figure 1: Axial section of neck on CT showing lobulated lesion of low density in the left neck, with peripheral enhancement measuring approximately 1.8×1.1×0.4 cm with surrounding inflammatory stranding and edema (arrow). This is surrounding cellulitis, myositis, and fasciitis, with extension to the left submandibular, parapharyngeal, and retropharyngeal spaces.

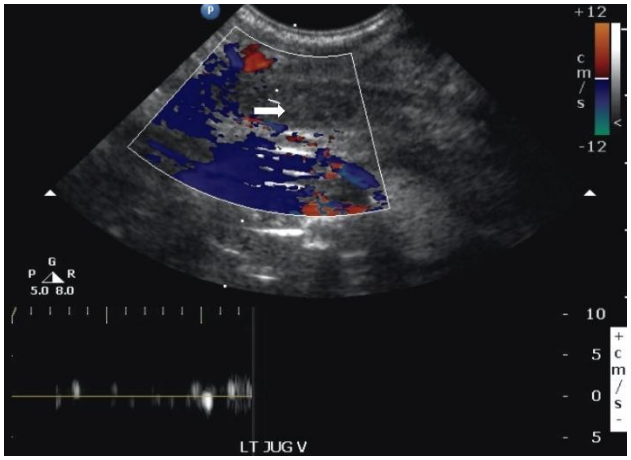

Figure 2: Venous ultrasound of the upper extremity showing occlusive left internal jugular vein thrombosis (thick arrow) and no flow was seen on Doppler study.

Blood cultures were obtained and empiric antibiotics such as vancomycin and clindamycin were started for methicillin-resistant *Staphylococcus aureus* (MRSA) and anaerobic organisms. The patient was admitted to the general pediatric floor for further investigation. Many laboratory tests were sent to identify the cause of the abscess. The tests included a rapid streptococcal antigen, Bartonella antibody titers, cytomegalovirus antibody titers, Ebstein Barr virus antibody titers, and antigen, all of which came back to be negative. Leucocytosis increased to 23.5×10^9/l after admission. On the third day of hospitalization, an incision and drainage of the cervical abscess were performed, yielding 30 ccs of purulent material whose culture grew methicillin-sensitive *Staphylococcus aureus* (MSSA). Blood cultures obtained on admission also grew MSSA within 48 hours of collection. The antibiotics were narrowed down to Oxacillin. Later Rifampin was started in addition to Oxacillin due to its synergistic effect against MSSA. It was perplexing as to why the patient was so sick by an abscess in the neck that he even had septicemia because of it. As a result, even though he only had clinical signs such as persistent fever, increasing WBC count, and a neck abscess is a preceding risk factor without other features like septic pulmonary emboli or antecedent pharyngitis we wanted to rule out Lemierre's syndrome. Consequently, a doppler ultrasound of the neck was obtained which demonstrated a left internal jugular vein thrombus (Figure 2). Given his sick clinical appearance, we obtained a chest CT to look for septic emboli in the lungs. However, the patient had no respiratory complaints and was saturating well on room air and the chest X-ray obtained before CT chest did not show any acute cardiopulmonary pathology. CT chest showed numerous bilateral pulmonary nodules suggesting septic emboli, multilobar pneumonia, trace bilateral pleural effusions, and left jugular vein thrombosis (Figures 3 and 4). A transthoracic echocardiogram was also obtained as he had septic emboli and the results were within normal limit and negative for vegetations. In the

end, taking into consideration his intra parotid abscess with left internal jugular vein thrombosis and septic emboli, the diagnosis was consistent with Lemierre's syndrome, presenting as a post-influenza MSSA infection. Following resolution of the neck swelling on hospital day five, a repeat Doppler ultrasound was completed which revealed persistence of the thrombus in the left internal jugular vein. The patient was started on subcutaneous low molecular weight heparin 1 mg/kg/dose twice daily due to the risk of clot propagation from septic emboli. The patient remained on anticoagulation with therapeutic levels for six weeks with complete resolution of the clot on repeat doppler studies. The patient completed 14 days of Oxacillin and Rifampin after negative blood culture and another 10-day course of oral cephalexin outpatient antibiotic therapy without any sequelae.

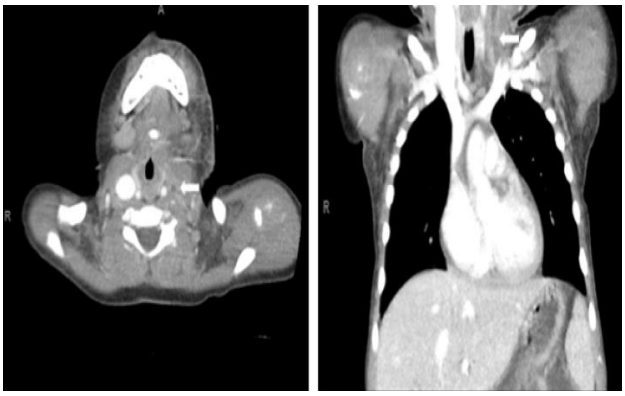

Figure 3: Axial and coronal section on CT showing complete thrombosis of the left internal jugular vein (thick arrow).

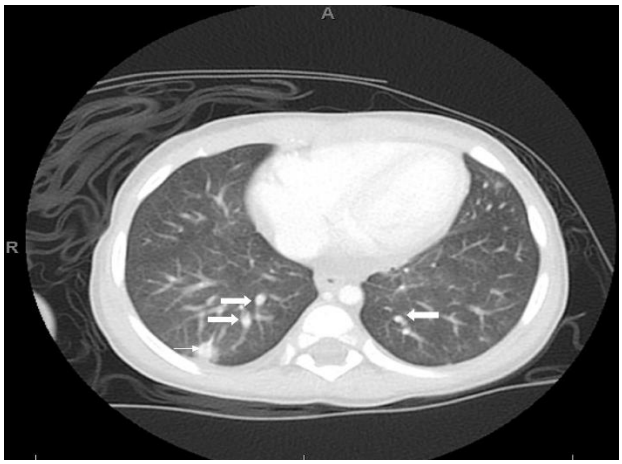

Figure 4: Numerous, predominantly peripheral based, subcentimeter bilateral infectious pulmonary nodules (thick arrows) associated with trace bilateral pleural effusion right > left (thin arrow).

DISCUSSION

This is a unique presentation of Lemeirre's syndrome because of its rare manifestation as a post-influenza complication and the presence of *Staphylococcus aureus* as a causative agent. The diagnosis of Lemeirre's syndrome should be made based on the findings of a recent pharyngeal illness, septic emboli found on imaging, and either thrombosis of the internal jugular vein or findings of *Fusobacterium necrophorum* in the blood.[2] The bacterial cause of the septic emboli in Lemierre's syndrome is classically the anaerobic Gram-negative rod *Fusobacterium necrophorum*. However, other pathogens including *Staphylococcus aureus* are becoming more common as in our patients. It is unclear as to whether this is a publication bias or if the incidence of other pathogens is actually increasing.[3] One systematic review of 137 cases from 2011-2015 found that 63% were caused by *Fusobacteria spp*. The remaining 37% of cases were caused by other bacteria, including six cases caused by MRSA and MSSA. In previous reports from 1950-2007, no cases were found to be positive for *S. aureus*.[2] The emergence of new causative bacterial pathogens may demand a re-assessment of empiric treatment guidelines.

Bacterial pneumonia is a well-known complication of viral influenza, but septic jugular thrombophlebitis as a secondary bacterial infection is not commonly diagnosed or cited in the literature. *Staphylococcus aureus* is a common cause of post-influenza bacterial pneumonia and is most often diagnosed after findings of pulmonary infiltrate on chest radiograph.[4]

The mechanism behind secondary bacterial infection in a patient with influenza is due to the virus's effects on the innate immune system. Influenza virus impairs the alveolar macrophages in respiratory epithelium. This results in depletion of macrophages, impaired neutrophil killing, and decreased extracellular mediators released in response to bacterial super-infection.[5] An impaired immune system and mucosal damage from prior infection are known risk factors of Lemeirre's syndrome.[6] These factors likely contributed to our patient's case. The mechanism by which the invasion of IJV by bacterial pathogens in Lemeirre's syndrome is not known. Proposed theories include a hematogenous spread of the pathogen via the tonsillar vein or invasion of peritonsillar tissue and spread via lymphatics to the lateral pharyngeal space. Other theories include the spread of a peritonsillar abscess through the loose connective tissue of the pharynx. Another hypothesis suggests that alteration of the pharyngeal mucosa during the primary infection allows the pathogen to invade locally and directly extend through fascial planes of the neck to the IJV.[7] Endotoxic virulence factors, such as lipopolysaccharides in *F. necrophorum*, play an important role in the progression of infection. Regardless of the pathogenesis of invasion, pneumonia or pleural empyema are the most common manifestation of septic emboli as seen on CT images of our patient.[6] The lungs are affected in 85% of patients with Lemeirre's syndrome, and lung lesions can present as infiltrates, pleural effusions, empyema, lung abscesses, and necrotizing mediastinitis.[8] If clinical suspicion is high based on high fever and neck tenderness, imaging should not be delayed. Contrast-enhanced computed tomography

of the neck is the preferred diagnostic imaging modality, although Doppler ultrasonography can also be used to visualize the internal jugular vein.

Antibiotic treatment should begin promptly once a diagnosis of Lemeirre's syndrome is made. Antibiotics have decreased the mortality rate of this disease to less than 2%.[3] Empiric coverage is traditionally focused on attacking anaerobic pathogens since the pathogen classically involved in *F. necrophorum* is *F. necrophorum* is intrinsically resistant to macrolides, fluoroquinolones, and tetracyclines which leaves Beta-lactams as the most effective antibiotic prescribed.[6] Additionally, antibiotic treatment to cover *F. necrophorum* should include a non-pseudomonas beta-lactamase inhibiting penicillin as beta-lactamase producing strains of *F. necrophorum* have been reported.[7] The increasing incidence of variable pathogens involved in Lemeirre's syndrome suggests that empiric treatment should include antibiotics that cover gram-positive organisms like *S. aureus*. Ultimately, antibiotics should be tailored to the specific pathogen involved based on blood and wound culture results. Once the causative organism is found, antibiotic therapy should be prescribed for 3-6 weeks, and clinical judgment should be used to determine when therapy can be transitioned to oral medications.[7] There is a lack of randomized studies in the literature involving treatment of Lemeirre's syndrome with anticoagulation, and it remains unclear whether anticoagulation leads to faster resolution of the thrombus.[8] Our patient's young age and extent of thrombosis prompted treatment with anticoagulation, which was beneficial in his case as the clot resolved in three months after his initial presentation. Since anticoagulation is controversial, its role without extensive thrombosis has not been clearly defined.[9]

CONCLUSION

Lemierre's syndrome is a relatively uncommon disease, yet it is an important diagnosis that should not be missed. The presentation of the disease is variable, as seen in this case it occurred as a complication of Influenza infection. High clinical suspicion based on patient history of recent oropharyngeal infection, neck tenderness, and fever should prompt imaging to confirm the diagnosis. The treatment has traditionally been focused on the coverage of anaerobic bacteria like *F. necrophorum*, but expanded coverage may be necessary as a variety of other pathogens have been found in recent cases. Lemierre's syndrome is curable in most cases when antibiotic treatment is tailored correctly, which is why the determination of the bacterial etiology and the diagnosis is crucial.

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REFERENCES

1. Alperstein A, Fertig RM, Feldman M, Watford D, Nystrom S, Delva G, Muddassir S. Septic thrombophlebitis of the internal jugular vein, a case of Lemierre's syndrome. Intractable Rare Dis Res. 2017;6(2):137-40.
2. Johannesen K, Bodtger U. Lemierre's syndrome: current perspectives on diagnosis and management. Infect Drug Resist. 2016;9:221-7.
3. Correia MS, Sadler C. Methicillin-Resistant Staphylococcus aureus Septic Internal Jugular Thrombophlebitis: Updates in the Etiology and Treatment of Lemierre's Syndrome. J Emerg Med. 2019;56(6):709-12.
4. MacIntyre CR, Chughtai AA, Barnes M, Ridda I, Seale H, Toms R, Heywood A. The role of pneumonia and secondary bacterial infection in fatal and serious outcomes of pandemic influenza a(H1N1)pdm09. BMC Infect Dis. 2018;18(1):637.
5. Robinson KM, Kolls JK, Alcorn JF. The immunology of influenza virus-associated bacterial pneumonia. Curr Opin Immunol. 2015;34:59-67.
6. Lee WS, Jean SS, Chen FL, Hsieh SM, Hsueh PR. Lemierre's syndrome: A forgotten and re-emerging infection. J Microbiol Immunol Infect. 2020;53(4):513-7.
7. Kuppalli K, Livorsi D, Talati NJ, Osborn M. Lemierres syndrome due to Fusobacterium necrophorum. Lancet Infect Dis. 2012;12(10):808-15.
8. Phua C, Chadachan V, Acharya R. Lemierre Syndrome—Should We Anticoagulate? A Case Report and Review of the Literature. Int J Angiol. 2013;22(02):137-42.
9. Lee WS, Wang FD, Shieh YH, Teng SO, Ou TY. Lemierre syndrome complicating multiple brain abscesses caused by extended-spectrum β-lactamase-producing Klebsiella pneumoniae cured by fosfomycin and meropenem combination therapy. J Microbiol Immunol Infect. 2012;45(1):72-4.

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