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Lemierre Syndrome: Not So Forgotten!

By Nishant Gupta, MD, Stephen M. Kralovic, MD, MPH, and Dennis McGraw, MD

Abstract

Lemierre syndrome is a rare and life-threatening illness. Often referred to as “the forgotten disease,” its incidence is reported to be as low as 1 in a million. The microorganism responsible for Lemierre syndrome is typically Fusobacterium necrophorum. The bacterium starts in the pharynx and peritonsillar tissue, then disseminates through lymphatic vessels. Severe sepsis rapidly develops, as does the hallmark of this syndrome: septic thrombophlebitis of the internal jugular vein. This report describes a case of Lemierre syndrome in a previously healthy 26-year-old man with life-threatening internal jugular vein thrombophlebitis following 2 weeks of an indolent course of pharyngitis. The patient’s initial presentation and extensive travel history as an Army veteran were particularly challenging aspects in establishing his diagnosis. The diagnosis of Lemierre syndrome is frequently delayed. Routine use of bedside ultrasonography may aid in rapid diagnosis of the disease. (American Journal of Critical Care. 2014;23:176-179)

Case Report

Lemierre syndrome is a complication of an acute oropharyngeal infection leading to septic thrombophlebitis of the internal jugular vein. The septic thrombophlebitis can in turn produce widespread septicemia and metastatic infections. The first clear definition of this syndrome was provided by Lemierre in 1936. The incidence of Lemierre syndrome appeared to decrease dramatically in the 1940s, and it was referred to as the “forgotten disease.” However, although it is still uncommon, the past 2 decades have seen a substantial increase in reports about Lemierre syndrome. Herein, we report a case of Lemierre syndrome and show a potential role for bedside ultrasonography to facilitate a more rapid diagnosis of the disease.

A 26-year-old white man arrived at the hospital with complaints of headache, fevers, chills, nausea, photophobia, and night sweats for 6 days. He reported severe, throbbing frontal headache along with intermittent, high-grade fever up to 102°F (39°C). His past medical and surgical histories were unremarkable, except for an emergency department visit 2 weeks prior with complaints of nausea, vomiting, diarrhea, and sore throat for which he was prescribed a course of azithromycin. The patient had past travels to Iran, Kyrgyzstan, and Germany as part of his military service, and had completed a 10-month deployment in Afghanistan 8 months before his current presentation. He was a 5-pack-year smoker but denied alcohol or drug use.

The patient’s vital signs on presentation were as follows: body temperature, 97°F (36°C); heart rate, 104/min; blood pressure, 86/54 mm Hg; respiratory rate, 20/min with 100% oxygen saturation on room air. Physical examination was unremarkable except for a palpable spleen tip with no hepatomegaly. Initial laboratory studies showed a normal white blood cell count (7300/µL) with left shift (22% bands) and prominent thrombocytopenia (platelet count,
32,000/µL). Findings on a chest radiograph and a computed tomography (CT) scan of the head were unremarkable, and an abdominal CT scan revealed mild splenomegaly.

In light of the patient’s headache, nausea, photophobia, and high fevers, a lumbar puncture was performed, which showed a normal white blood cell count and normal total protein and glucose levels with a negative Gram stain. Malaria was entertained in the differential diagnosis given the patient’s travel history, thrombocytopenia, and splenomegaly, but thin and thick blood smears for malaria were negative. Screening for infection with human immunodeficiency virus and a urine drug screen were negative.

The patient was admitted and started treatment with vancomycin and ceftriaxone after blood samples were obtained for culture. However, 36 hours into the hospital course, respiratory distress and hypoxemia developed, which prompted transfer to the intensive care unit, where he was intubated and mechanical ventilation was started. A repeat chest radiograph showed diffuse bilateral infiltrates. Subsequently, the anaerobic blood cultures returned positive for gram-negative rods. Piperacillin-tazobactam was added to his regimen to provide extended gram-negative coverage. A transthoracic echocardiogram showed no evidence of endocarditis, and the source of gram-negative bacteremia remained unclear.

The patient became hypotensive the next morning, and a central venous catheter was inserted for hemodynamic monitoring and fluid resuscitation. Notably, ultrasound examination of his neck to assist catheter placement revealed that his right internal jugular vein was noncompressible, suggestive of deep vein thrombosis (see Figure, A). A CT study of the neck with contrast material confirmed thrombosis through the entire length of the right internal jugular vein (see Figure, B). Consistent with the diagnosis of Lemierre syndrome, the gram-negative species subsequently identified as *Fusobacterium necrophorum* and treatment with piperacillin-tazobactam was continued. The patient improved clinically, was successfully extubated and subsequently discharged home with oral amoxicillin-clavulanate for 4 weeks after completion of 2 weeks of intravenous piperacillin-tazobactam.

**Figure** A, Ultrasound of neck shows thrombosis of internal jugular vein (IJV). B, Coronal views from contrast-enhanced computed tomography of the neck shows multiple areas of thrombosis (arrows) along the length of the right internal jugular vein.

**Abbreviations:** CCA, common carotid artery; INNOMIN, innominate artery.

### Discussion

Although the correlation between oropharyngeal infection and sepsis was first described by Courmont and Cade in 1900,1 Lemierre was the first to characterize the syndrome with the key elements of (1) occurrence after tonsillitis, (2) progression via thrombophlebitis of tonsillar veins to the internal jugular vein leading to septicemia and metastatic abscesses, and (3) causal association with *F necrophorum.*2 In 1936, Lemierre2 reported a series of 20 patients with antecedent infections leading to anaerobic septicemia, 18 of whom died. However, with the advent of antibiotic therapy in the 1940s, there appeared to be a gradual decline in the incidence of Lemierre syndrome. In fact, Finegold and Bartlett4 could not find a reported case of Lemierre syndrome in the 1950s and 1960s. The reported incidence of Lemierre syndrome has increased in the past 2 decades. Factors that might be responsible for this resurgence include (1) the reluctance to give antibiotics in cases of uncomplicated sore throats, (2) greater reliance on macrolides (the typical causative agent, *F necrophorum*, is not susceptible to macrolides), and (3) better radiologic techniques that enhance detection.5

Despite the recent increase in incidence, Lemierre syndrome remains an uncommon disease that occurs in approximately 1 person per million per year.7 It is primarily a disease affecting young persons. In a review by Riordan,7 the mean age at diagnosis was 19 years with 89% of patients between 10 and 35 years old.

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Classically, Lemierre syndrome is caused by monoinfection with the anaerobic bacterium *F. necrophorum*, which accounts for more than 80% of the cases. However, similar presentations with *Streptococcus* and *Staphylococcus* species have been reported. Following primary infection in the oropharynx, thrombophlebitis of the internal jugular vein develops either from direct extension or by hematogenous or lymphatic spread from peritonsillar vessels. The next phase in the pathogenesis involves seeding of septic thromboemboli to various organs. The lungs and pleura are most commonly involved (92%) but other sites may include joints (13%-27%), skin and soft tissue (0%-3%), and liver (4%).

The diagnosis of Lemierre syndrome should be suspected in a young person with antecedent pharyngitis, septic pulmonary emboli, and fever that persists despite antibiotic therapy. During invasion of the lateral pharyngeal space and septic thrombophlebitis of the internal jugular vein, a swollen and/or tender neck is the most common finding (52.2% of patients) and should be considered a “red flag” in patients with current or recent pharyngitis. This patient was unusual as he did not complain of neck pain and had no palpable neck mass or lymphadenopathy. It is possible that the 2-week delay from his symptom onset to current presentation might have led to spontaneous resolution of the aforementioned findings.

Because of its relative infrequency and the lack of awareness among treating physicians, Lemierre syndrome is often diagnosed only when the admission blood cultures return positive for *Fusobacterium* species. Recognition may therefore be delayed for several days while awaiting confirmatory culture results, although the presence of bacterial growth only on anaerobic medium may offer a potential hint to the underlying organism.

Documentation of a thrombus in the internal jugular vein remains the most reliable way of diagnosing Lemierre syndrome aside from results of blood cultures. Such documentation can be achieved with the help of ultrasound examination (with or without Doppler imaging) or a contrast-enhanced CT scan of the neck. The ability to diagnose deep venous thrombosis with compression ultrasonography alone is well established. Kory et al showed that bedside compression ultrasonography performed by critical care physicians and radiologists has similar rates of detection for deep venous thrombosis. Consistent with these reports, we found that neck vein thrombosis in our patient was readily apparent on a routine ultrasound examination performed to guide placement of a central venous catheter. Therefore, we propose that bedside ultrasonography may offer a quick means to screen patients with unexplained gram-negative bacteremia for possible septic thrombophlebitis. Ultrasound examination may also provide a simple and inexpensive way for serial imaging to assess resolution after the initial diagnosis is established. However, we recognize that not all physicians may have the training to diagnose thrombosis of the internal jugular vein by a bedside ultrasound examination, and we would recommend a formal ultrasound examination or contrast-enhanced CT until confirmatory reports or studies are performed.

The successful management of Lemierre syndrome rests on adequate dose and duration of antibiotic therapy against *Fusobacterium*. Because of the rarity of Lemierre syndrome, the antibiotic choice is based on anecdotal clinical evidence. With cases of reported penicillin resistance, most authors recommend the use of a penicillin/β-lactamase inhibitor combination. Metronidazole may be another alternative, especially in cases of penicillin allergies. Given the reports of relapses associated with the disease, most clinicians opt for a prolonged course of antibiotics (6 weeks).

Controversy still exists over the role of anticoagulation and surgery in the management of Lemierre syndrome. Because most patients with Lemierre syndrome have not been treated with anticoagulation and/or surgery; it may be prudent to treat Lemierre syndrome with a prolonged course of antibiotics and reserve the use of anticoagulation and/or surgery for cases with documented evidence of clot extension or clinical worsening despite adequate antibiotic treatment. The prognosis of patients with Lemierre syndrome is good with an overall mortality rate of 6.4%.

**Conclusion**

Lemierre syndrome is a life-threatening illness that should be suspected in a young person with antecedent pharyngitis, septic pulmonary emboli, and persistent fever despite antibiotic therapy. Although rare, the incidence of Lemierre syndrome is increasing and physicians must maintain a high index of suspicion for this disease to prevent delay in diagnosis. Our experience reported herein suggests that routine bedside ultrasonography may facilitate more rapid diagnosis of Lemierre syndrome.

**FINANCIAL DISCLOSURES**

None reported.

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