Lemierre’s Syndrome in a Young Adult

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- Fusobacterium necrophorum
- Pharyngotonsillar infections
- Bacteremia
- Cervical lymphadenopathy
- Unilateral throat pain

This case involves a diagnosis of Lemierre’s syndrome in a 18-year-old Caucasian female presenting to Christus Spohn Hospital Shoreline in Corpus Christi, TX with chief complaints of throat pain, a stiff neck, cervical lymphadenopathy, a positive monospot, left internal jugular vein thrombosis, bilateral pleural effusions, abdominal ascites, and hepatosplenomegaly. Gram-negative rods in the anaerobic blood culture from this patient were identified as F. necrophorum, and the patient was subsequently transferred to Driscoll Children’s Hospital in Corpus Christi for management of her illness.

Upon admission to Driscoll Children’s Hospital, the patient was transferred to the pediatric intensive care unit (PICU). In the unit, the patient received Demerol and a standing order for Darvocet every 4 hours to alleviate pain. Standing orders for antibiotic therapy were penicillin and metronidazole every 6 hours.

Additional laboratory testing was performed at this time. Febrile agglutinin panel and serum pregnancy tests were negative. Urinalysis was within normal limits.

Coagulation studies showed a slightly elevated prothrombin time (PT), a normal partial thromboplastin time (PTT), elevated fibrinogen level, and a positive D-Dimer. A complete blood cell count (CBC) showed leukocytosis with a left shift, normo-chronic normocytic anemia, and thrombocytopenia.

Due to the presentation of the patient, a hematology oncology consultation was requested. A factor VII, Protein C & S were ordered, and a diagnosis of partial disseminated intravascular coagulation with thrombocytopenia was made. Although the patient developed a profound anemia, no transfusions were given.

Chemistry profiles showed normal amylase and lipase, increased alkaline phosphatase, increased total and direct bilirubin, decreased total protein and albumin, and a decreased total calcium level. The patient developed a prerenal azotemia with a BUN:CREA ratio of >20:1 and an estimated fluid deficit of approximately (-)570cc. The patient’s nutritional status was poor due to decreased oral intake.

Since the patient’s oral intake remained poor, total parenteral nutrition (TPN) was initiated in the PICU. Liver enzymes of the patient remained stable, with only a slight increase in the alanine transaminase (ALT).

A MRI of the patient’s brain was normal. A CT scan of the abdomen/chest/pelvis with contrast showed bilateral pleural effusions, bilateral pulmonary emboli, and bibasilar lower lobe atelectasis.

After infectious disease consult, the patient was placed on penicillin every 4 hours and metronidazole every 4 hours. The patient also received Lovenox (low molecular weight heparin) every 12 hours for embolic prophylaxis. After several days in the PICU, the patient was transferred to the general medical floor where she continued to gradually improve.

Background on Lemierre’s Syndrome

Lemierre’s syndrome, also known as post-anginal sepsis or necrobacillosis, was initially described in 1900 by Courmont and Cade. In 1936, Lemierre subsequently reported 20 cases. This syndrome, caused by the anaerobic Gram-negative rod Fusobacterium necrophorum, is most commonly associated with acute pharyngotonsillitis but may follow acute otitis media, dental infections, appendicitis, urinary tract infection, or purulent endometritis following parturition.

Lemierre’s syndrome is encountered much less frequently due to readily available antimicrobials. Though less frequent in occurrence, Fusobacterium necrophorum remains virulent. Although this syndrome is rare, it is potentially fatal and requires quick recognition in order to institute appropriate treatment. Many clinicians are unfamiliar with the problems associated with infection from this organism.

Lemierre’s syndrome is defined as complications of infection with Fusobacterium necrophorum that include abscess formation in the peritonsillar space, internal jugular vein thrombosis, and multiple metastatic septic emboli to distant sites including lungs, liver, and joints. The throat abscess is usually unilateral.

Although exudative tonsillitis or peritonsillar abscess may be present at initial presentation of the patient, in some cases this will have subsided by the time the patient is seen. In an article published by the Massachusetts chapter of the American Society of Internal Medicine, a Lemierre’s syndrome case was identified as a rare complication of infectious mononucleosis.

In humans, F. necrophorum is part of the normal flora of mucous membranes of the oral cavity, the female genital tract, and alimentary tract. It behaves as a primary pathogen on invasion and is usually found as the sole organism when infectious material is cultured. This is in stark contrast with typical anaerobic infections, which usually show mixed flora on culture.
Rates of morbidity and mortality (4% to 18%) associated with *F. necrophorum* infection remain high because unfamiliarity with the disease leads to delays in diagnosis or under-diagnosis with concurrent delays in treatment.6

Identification of Lemierre’s syndrome is most frequently done by isolation of *F. necrophorum* in blood cultures, which can take up to 72 hours in many laboratories. Significant disease progression with septic embolization will become inevitable with delay of appropriate treatment. Also, since anaerobic blood cultures are not routinely performed in the pediatric setting, the clinician must have a strong suspicion in order to treat Lemierre’s syndrome promptly.

*Fusobacterium necrophorum*, previously known as *Bacillus funduliformis*, is a Gram-negative, pleomorphic, non-spore-forming, obligate anaerobic rod. An example is shown in I.

When isolated from blood cultures, this organism is distinctive enough to confirm a presumptive clinical diagnosis of Lemierre’s syndrome.7 On microscopic exam of Gram-stained colonies, *F. necrophorum* is highly pleomorphic. The rods may be elongated, filamentous, or curved and are often Gram-variable in appearance.

The Gram-stain may reveal spherical enlargements or large, free, round bodies. *Fusobacterium necrophorum* may be difficult to identify by laboratory methods, being most frequently mistaken for *Bacteroides* species.8

Species of *Fusobacterium* are identified presumptively on the basis of observation of Gram stain, colony morphology, pigment production, and fluorescence under long-wave ultraviolet light. Definitive species identification requires determination of biochemical activity with a battery of tests.

Toxin expression, including lipopolysaccharide endotoxin, leukocidin, hemolysin, coagulase, hemagglutinin, and adhesion may explain the propensity for vascular invasion and thrombosis exhibited by *F. necrophorum*.9

*Fusobacterium necrophorum* has recently been separated into 2 subspecies. The first, *F. necrophorum* ssp. *necrophorum*, contains the lipase (+) hemagglutinin-producing Biotype A. The second, *F. necrophorum* ssp. *funduliforme*, contains of the lipase (-) hemagglutinin (-) Biotype B.10 In a study performed by Hall and colleagues, strains of *F. necrophorum* ssp. *necrophorum*.

However, correspondence of the human strains with *F. necrophorum* ssp. *funduliforme* was less certain. Since strains of *F. necrophorum* causing human infection were clearly distinct from the Biotype A found commonly in animal infection, an assumption may be made that Biotype B, *F. necrophorum* ssp. *funduliforme*, is the etiologic agent of Lemierre’s syndrome in humans. Further research of biotype is necessary to confirm this.10

It is important to remember that antimicrobial resistance is as much a problem with anaerobes as with most other bacteria. Although problems are encountered with anaerobic susceptibility testing, the information derived from such tests does provide clinicians with some guidance for empiric therapy.3 Although susceptibility testing on anaerobes can be challenging to perform, the susceptibility and resistance patterns of these organisms must be monitored.

*Fusobacterium* as a genus is susceptible to metronidazole, clindamycin, chloramphenicol, imipenem, and some 3rd-generation cephalosporins (ceftaxime and ceftizoxime). Historically, *Fusobacterium* species have been highly sensitive to penicillin, but there appears to be an increasing prevalence of resistance to beta-lactam antibiotics among these organisms. Erythromycin, used in the treatment of many upper-respiratory tract infections, is not active against *Fusobacterium* species.2

*Fusobacterium necrophorum* may be resistant to many of the antimicrobials commonly used to treat upper respiratory tract illnesses, which allows septic embolization to occur in a patient that develops complications. However, in a patient where use of IV contrast is contraindicated, MRI is preferred due to the ability of this imaging modality to demonstrate vasculature without the need for IV contrast.
Summary

Recognizing the importance of uncovering a Gram-negative rod from an anaerobic blood culture bottle should never be underestimated. The prompt, proper identification of *Fusobacterium necrophorum* may save a patient’s life. Although it is the ultimate responsibility of the clinician to diagnose such an illness, the laboratory plays a key role in facilitating proper treatment, especially in instances where rare or unusual illnesses occur.

The patient had an excellent outcome from this illness with no long-term sequelae. She was discharged after several weeks in the hospital and continued on the prescribed antibiotic regimen for 6 weeks. Paralysis of cranial nerve XII resolved, and the thrombosed left internal jugular vein became fibrotic. The patient continued to follow up with the hematology/oncology clinic and was prescribed Plavix (clopidogrel) orally every day for thrombotic prophylaxis.

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