A 17-year-old Adolescent with Persistent Sore Throat

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A 17-year-old healthy male presented to the emergency room with sore throat, neck swelling, and fever. Throat swab was negative for group A Streptococcus antigen. A throat culture was sent and grew Streptococcus group C after 48 hours. The patient was placed on oral azithromycin and was discharged to home.

Five days later, he presented with persistent fever, sore throat, and neck pain. He developed left-sided chest pain, blood-tinged cough, vomiting that was neither bloody nor bilious, and left knee pain. He denied any drug abuse or smoking. He reported no recent travel, and immunizations were appropriate for age.

His physical examination was remarkable for a temperature of 102°F, tachypnea, retractions, and swollen knee joint with tenderness and limitation of movement. The rest of the physical examination was within normal limits. Initial laboratory blood work was significant for leukocytosis of 31 x 103/mcL and thrombocytopenia of 80 x 103/mcL with normal differential, hemoglobin, platelets, PT, PTT, liver function, kidney profile, and urinalysis.

Figure 1. Chest CT scan showed multifocal opacifications with mature peripheral nodules and cavitations representing septic emboli.

For diagnosis, see page 68.

Editor’s note: Each month, this department features a discussion of an unusual diagnosis in genetics, radiology, or dermatology. A description and images are presented, followed by the diagnosis and an explanation of how the diagnosis was determined. As always, your comments are welcome via e-mail at editor@pediatricsupersite.com.
Blood cultures were sent from two different sites. The knee joint was tapped, and synovial fluid was sent for bacterial cultures. Chest x-ray showed bilateral reticulonodular interstitial infiltrates. A chest CT scan (see Figure 1, page 67) showed multifocal opacifications with mature peripheral nodules and cavitations. An imaging study was requested and helped in making the diagnosis. The blood culture confirmed the etiology. The patient was admitted to the intensive care unit. He developed disseminated intravascular coagulopathy (DIC), septic shock, and left-lung empyema. Doppler ultrasound of the neck showed right internal jugular vein thrombosis (see Figure 2). Echocardiogram showed no evidence of endocarditis. The blood and synovial fluid cultures grew *Fusobacterium necrophorum*. He was intubated for 14 days and received supportive management for 4 weeks with chest tube insertion and surgical drainage of left knee joint. Intravenous ceftriaxone and clindamycin were started on admission and maintained for 6 weeks.

The patient developed a clot in the right basilic vein while he was on treatment. Thromboembolic investigations, including protein C, protein S, antithrombin III, plasminogen, fasting homocysteine, Factor IX, Factor VIIIC, and Factor XII were normal. Antiphospholipid antibodies and lupus anticoagulant were not detected. Low molecular weight heparin was started and was maintained for 3 months. Doppler ultrasound of the neck and the right arm was repeated and revealed complete resolution of the thrombi.

**DISCUSSION**

Lemierre’s syndrome (LS), postanginal sepsis, or necrobacillosis was best identified by Lemierre in 1936.¹ It consists classically of an acute oropharyngeal infection with secondary suppurative thrombophlebitis of the internal jugular vein (IJV), complicated by metastatic septic emboli. It can occur secondary to sinusitis, parotitis, mediastinitis, dental and middle ear infections.²,⁶ Suppurative thrombophlebitis of the external jugular vein has been documented in two patients.⁷,⁸ *F. necrophorum* subspecies funduliforme is the causative pathogen in most of the cases.⁶ It is a strictly anaerobic, nonmotile, gram-negative bacillus that might exist in the oropharyngeal cavity, the female genital tract, and the gastrointestinal tract. Oropharyngeal mucosal damage from another pathogen such as Epstein-Barr virus (EBV) can enhance its extension into the parapharyngeal spaces.⁶,⁹ Other organisms implicated as causes of LS include other *Fusobacterium* species, *Streptococcus* species, *Staphylococci*, *Eikenella corrodens*, *Peptostreptococcus* species, and *Bacteroides*.⁷,¹⁰,¹¹

The incidence of LS is not known. It has decreased since the advent of antibiotic era, but recent studies from Europe suggest a resurgence of *F. necrophorum* infections.²,⁶,¹²,¹³ A comprehensive review study estimated the median age for LS to be
Children younger than 5 years may be more prone than adolescents to have LS secondary to otogenic infections. The oropharynx is the primary site of infection in most cases. The interval between the oropharyngeal infection and the onset of the septicemia is a week or less. However, signs and symptoms of the oropharyngeal infection may disappear by the time IJV thrombosis or metastatic infection develops, regardless of antibiotic treatment. The thrombosed IJV is rarely palpable, and local findings can be minimal or absent at presentation.

Pleuropulmonary lesions and joint infections are the most common metastatic manifestations of LS. Metastatic septic emboli to muscles, bone, liver, skin, spleen, and heart were reported in the literature. Intracranial complications in the form of sinovenous thrombosis, cerebral abscess and meningitis were documented in 65.5% of otogenic *F. necrophorum* infections versus 6.2% of tonsillopharyngeal cases.

The diagnosis of LS is mainly clinical. Doppler US of the neck or CT scan with contrast will aid in the diagnosis. Isolation of *F. necrophorum* from anaerobic cultures obtained from the blood and infected sites will confirm the etiology.

LS can develop in immunocompetent individuals without any thromboembolic risk factor. However, a recent study reported five children with underlying prothrombotic risk factors who presented with otitis media and sinus venous thrombosis. Our patient did not have thromboembolic risk factor, but he developed a thrombus in the right basilic vein in the fourth week of illness. Whether it was an old thrombus or a newly developed one is unknown.

*F. necrophorum* is sensitive to penicillin in vitro. However, clinical relapses and resistance after treatment with penicillin were reported. Beta-lactamase producing isolates of *Fusobacterium* species were also documented. *F. necrophorum* is susceptible to metronidazole, clindamycin, carbapenems, penicillin/beta-lactamase inhibitor combination, and cefoxitin. Combination therapy of second- or third-generation cephalosporin with metronidazole is recommended because of the risk of coinfection with respiratory aerobic flora. It is intrinsically resistant to gentamicin and quinolones, and tetracyclines have limited activity.

Aspiration of an abscess with surgical drainage is essential for neck collections, an empyema (see Figure 3), a liver abscess, septic arthritis, and abscess in the muscle. The duration of antibiotic treatment is variable. Most of the studies recommend 6 weeks or more. Relapses have been documented with short duration of therapy, even when patients showed good clinical response initially.

Low molecular weight heparin is proposed for treatment of certain cases with prothrombotic disorders or patients with evidence of ongoing emboli. Anticoagulation therapy was studied in pediatric populations with sinus venous thrombosis secondary to different causes, and it was concluded to be...
effective and safe. However, anticoagulation use in septic patients with organ failure should be cautioned. IJV ligation is controversial but might be indicated if thromboembolism is extending, despite aggressive medical treatment.6

CONCLUSION
LS is a life-threatening illness that has a mortality rate of 6.7% if the diagnosis is missed clinically and treatment is delayed.6 It should be suspected in immunocompetent adolescents who present with persistent high fever associated with oropharyngeal infections, or in children with complicated otogenic infections.

Treatment consists of using appropriate antibiotics for a long period with surgical drainage at the site of infection if indicated. Anticoagulation is still controversial and should be based on individual risk factors.

REFERENCES