A 15-Year-Old with Sepsis and Cavitary Lung Lesions

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We report the case of a critically ill patient with Lemierre syndrome. Lemierre syndrome is characterized by septic thrombophlebitis of the internal jugular vein and metastatic abscesses in different organs, most frequently in the lungs. The disease usually occurs in young, previously healthy individuals. Most cases are caused by *Fusobacterium necrophorum*, an anaerobic gram-negative rod. Oropharyngeal infection occurring 2–3 weeks prior to septicemia is a harbinger of the syndrome. Frequently oropharyngeal symptoms and local signs are absent at the time of presentation. Computed tomography (CT) scan of the neck with contrast is the most helpful diagnostic study to identify internal jugular vein thrombosis. Treatment involves a prolonged course of intravenous antibiotics with anaerobic coverage. It is important for an intensivist to keep this syndrome in mind, especially when dealing with a young, otherwise healthy patient with sepsis. Mortality is high if the disease is not diagnosed and treated promptly. The syndrome is rare in the antibiotic era, therefore a high index of suspicion is essential.

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Case History

A 15-year-old boy was admitted to the hospital with severe headache, fever with shaking chills, nausea, vomiting, abdominal pain, pleuritic chest pain, and productive cough. He also complained of mild neck stiffness and neck pain. The symptoms started approximately 36 hours prior to admission and progressed rapidly. The patient denied confusion, mental status changes (confirmed by his parents), photophobia, diarrhea, blood per rectum, dysuria, hematuria, skin rash of any kind, or swelling, tenderness, or redness of any part of the extremities. The boy's parents recalled that 2 weeks earlier he had a sore throat and low-grade fever. He saw his doctor and had a negative throat culture at the time. The patient worked on a fishing boat, but he had not recently handled fish. He had never traveled to tropical countries. He did not recall any recent tick bite. On physical examination the patient appeared critically ill, but in no apparent distress. He was mildly lethargic but arousable, and he was alert, oriented, and cooperative.

Vital signs were as follows: respiratory rate 26 breaths/min, heart rate 140 beats/min, temperature 105.6°F, blood pressure 85/60 mmHg. There was no skin rash and no lymphadenopathy. Pupils were equal, round, and reactive to light without photophobia. The oropharynx was moist without lesions. The neck was supple, with some pain over the right neck with flexion. There was tenderness with slight swelling of the right side of the neck. There was no fluctuance.

The lungs were clear to auscultation. The cardiac examination demonstrated normal rate and rhythm without murmur. The abdomen was soft with minimal right upper quadrant and epigastric tenderness without guarding. The extremities were without cyanosis, clubbing, edema, or any areas of cellulitis.

His laboratory findings were as follows: hematocrit of 46%, white blood cell count 15,600/mm^3 with 74% polys and 20% bands, platelet count 137,000/mm^3. Serum electrolytes and renal function were normal. Urinalysis revealed trace blood, 3–5 red

blood cells/high-power field (HPF), 3–5 white blood cells/HPF, and no other abnormalities. Spinal fluid findings were: protein 29 mg/dl, glucose 72 mg/dl, white blood cells 1/HPF, lymphocyte. There were no red blood cells. Spinal fluid cultures and Gram stain were negative. Computed tomography (CT) scan of the head was within normal limits. Chest radiograph and chest CT revealed cavitary lesions in both lungs (Fig 1).

PPD was negative. Bronchoscopy revealed normal-appearing airways. All bronchial cultures including fungal, AFB, and bacterial were negative. ANCA was negative. He was admitted to the intensive care unit (ICU). With fluid resuscitation his blood pressure came up to 95/60 mmHg. The patient was empirically started on intravenous antibiotics including ceftriaxone and clindamycin. He continued to spike a fever for several days through the antibiotic course. He required pressors initially. The patient became hemodynamically stable 48 hours after admission and was transferred out of the ICU on the third hospital day. On the fourth hospital day his blood cultures grew *Fusobacterium necrophorum* and antibiotic coverage was narrowed to clindamycin. CT scan of the neck was obtained, which revealed obstruction of the right internal jugular vein by a blood clot (Fig 2). He was diagnosed with Lemierre syndrome. The patient required a total of 5 weeks of antibiotic therapy and he fully recovered from his illness.

Discussion

The Lemierre syndrome is a suppurative thrombophlebitis of the internal jugular vein secondary to oropharyngeal infection, with subsequent septic emboli affecting various organ systems. The constellation of symptoms was first mentioned by Schottmuller in 1918. In 1929 Lemierre reported a similar case and in 1936 published a review of 20 patients with "postanginal sepsis" or necrobacillosis—the syndrome that now bears his name [1]. These patients all had pharyngitis followed by a toxic syndrome with fever, rigors, septic emboli to various organs, and metastatic abscesses. In the series of patients reported by Lemierre, 18 of 20 patients died. According to Lemierre, the striking similarity of the cases permitted diagnosis of the syndrome based solely on the clinical grounds [1].

The infection is most frequently caused by *F. necrophorum*—a gram-negative rod, anaerobic microorganism, which is a commensal in the oropharynx. *Bacteroides* species and other *Fusobacterium* species including *F. nucleatum* have been less commonly implicated [2]. The pharyngitis precedes the development of septicemia by 4–8 days and has often resolved by the time septicemia develops.

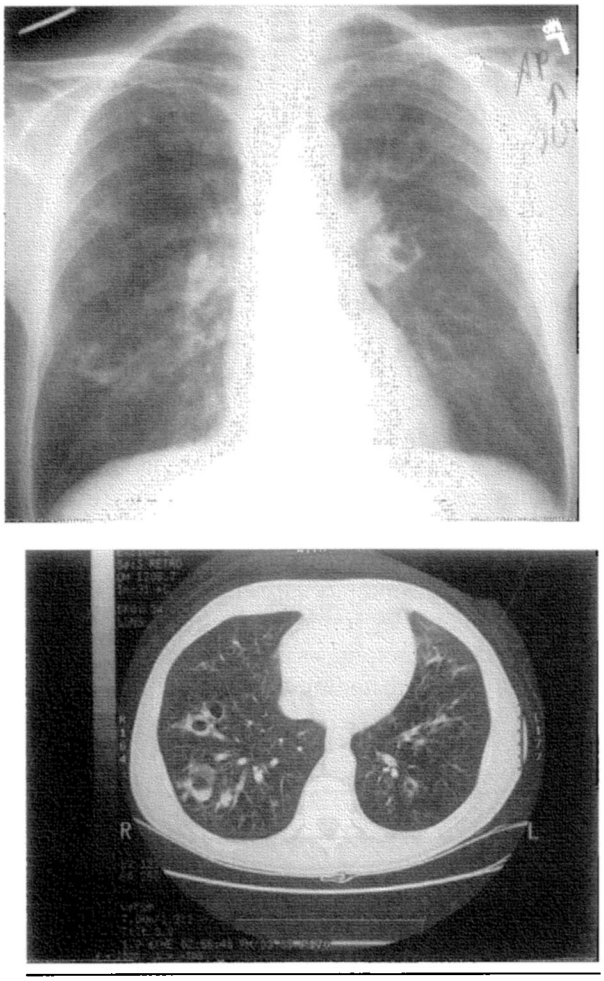

Fig 1. Chest **(A)** radiograph and **(B)** CT scan showing bilateral pulmonary cavitary lesions and lung abscesses.

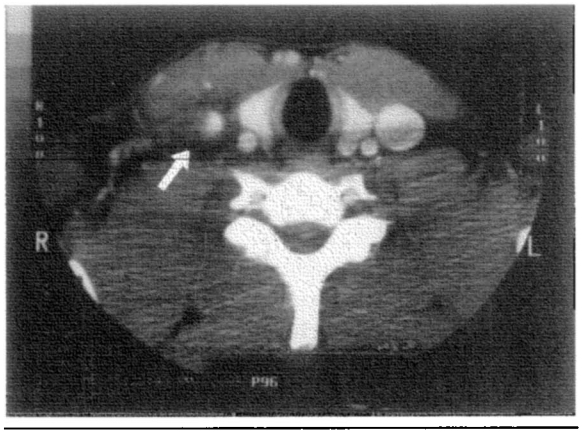

Fig 2. CT scan of the neck showing thrombus occluding the right internal jugular vein (arrow).

F. necrophorum is characterized by the ability to activate human platelets with microcirculatory thrombosis. Thrombus formation is a key in the pathophysiology of Lemierre syndrome. Pharyngeal infection causes thrombosis of the internal jugular vein (IJV) that ultimately results in embolization of the infected material and the development of metastatic foci of infection which characterize the syndrome [3].

The disease primarily affects young, previously healthy patients, usually teenagers, with boys outnumbering girls. Some have had infectious mononucleosis before postanginal septicemia. Typically pharyngitis or oropharyngeal infection precedes the onset of an acute toxic state. A history of sore throat is common, as it was in our patient. Pharyngitis or even peritonsillar abscess may be present. Not infrequently, examination of the pharynx is normal, since the finding may have resolved at the time of the patient's presentation [4]. Less frequently, anaerobic septicemia may arise as a complication of sinusitis, otitis media, mastoiditis, tooth or gingival infection, or retropharyngeal abscess. The blood supply from these areas drains into the IJV. Very high fever, chills, rigors, and a general toxic state characterize the onset of septic thrombophlebitis. Local findings include pain, swelling at the angle of the jaw, tenderness along the sternocleidomastoid muscle, dysphagia, trismus, and neck stiffness. Local findings may be absent, especially if the infection involves the posterior neck compartment [5,6]. Another feature of the syndrome is metastatic septic emboli. Pulmonary involvement is very common and was described in 90% of patients in reported series. Pulmonary abscesses and pleural effusions may develop. Those may manifest as pleuritic chest pain, dyspnea, and hemoptysis [7,8]. Septic dissemination to virtually any organ myocardium and the central nervous system (CNS) may ensue. Septic arthritis and osteomyelitis can be seen, though these are less common than in the preantibiotic era. Splenomegaly and hepatomegaly are common, but splenic and hepatic abscesses are rare [9]. Jaundice sometimes occurs. Renal involvement is relatively uncommon and when it occurs the syndrome may be confused with poststreptococcal glomerulonephritis. Septic shock may occur, more often in older patients.

Fusobacterium organisms are usually sensitive to penicillin G as well as other antibiotics with good anaerobic coverage, such as clindamycin, metronidazole, and cefoxitin. Occasionally the organism is β-lactamase productive. Because the disease is due to intravascular infection, prolonged high-dose antimicrobial therapy is needed. If localized purulent infection is present (empyema, septic arthritis, soft tissue abscess), surgical drainage is needed. Ligation and dissection of the IJV, once used in treating Lemierre syndrome, was shown to be unnecessary in the majority of cases and is rarely performed. The role of anticoagulation is somewhat controversial. Generally it is not used [10].

A high index of clinical suspicion is a key to the diagnosis. Blood cultures are positive in only 50% of cases. Fusobacteria are fastidious organisms, frequently taking 5–8 days to grow. Organisms can be cultured from other sites—abscess drainage, pleural fluid, bronchoscopy specimen, and arthritic fluid. Other nonspecific laboratory findings include leukocytosis with left shift, mild hyperbilirubinemia, elevated alkaline phosphatase, and elevated transaminases. The most useful diagnostic test is CT scan of the neck with contrast. It may reveal distended veins with enhancing walls, low attenuation intraluminal filling defects, and swelling of the adjacent soft tissues. Neck ultrasound may also be used to demonstrate IJV thrombus. Ultrasound use should be limited as an adjunct of CT to follow the evolution of the thrombus [12]. Magnetic resonance imaging (MRI) may be used. Venogram is almost obsolete. Gallium scan is sometimes used, though it is nonspecific. Differential diagnosis includes other causes of septic emboli, that is, endocarditis, mycotic aneurysm, and intravenous drug use. Poststreptococcal glomerulonephritis is in the differential in patients with kidney involvement [13].

In the preantibiotic era Lemierre syndrome was associated with a case mortality rate of 32–90%, with embolic events in 25% and endocarditis in 12.5% [2]. In the original article by A. Lemierre describing the syndrome, 18 of 20 patients died [1]. Today the mortality rate remains fairly high—up to 17% [8]—and hospital stays are frequently long. In patients with *F. necrophorum* meningitis, mortality reaches 30% despite appropriate antibiotic therapy. Half of the survivors of meningitis suffer permanent sequelae, mainly cranial nerve palsies [2].

Though rare, contemporary clinicians should remember to consider Lemierre syndrome in the appropriate clinical setting, as it still exists and remains potentially life threatening.

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