A Case Report on the Recurrence of Lemierre's Syndrome: Awareness to Diagnosis and Treatment

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Abstract

In 1936, Andrew Lemierre described a syndrome that now bears his name. He presented 20 cases of postanginal septicemia in healthy young adults that involved an acute oropharyngeal infection complicated by septic thrombophlebitis and metastatic infection.[1,2] In recent years, more cases of Lemierre's syndrome have re-emerged, thus bringing back into the spotlight the importance of prompt diagnosis and treatment.[3] Because of its previous rarity, clinicians may overlook and miss the diagnosis at the initial presentation. Mortality has been estimated at 15% to 18%, and the disease itself has been associated with significant morbidity.[4,5] It is crucial that clinicians have a high index of suspicion and heightened awareness of signs and symptoms associated with this disease. Early recognition and treatment invariably leads to optimal outcome.

Introduction

Lemierre's syndrome was common in the era before the advent of antibiotics. In the 1960s and 1970s, Lemierre's syndrome became a rare phenomenon with the proliferation of penicillin in the treatment of pharyngitis. Today, the incidence of Lemierre's syndrome is estimated to be 1 per million annually.[6] The judicious use of antibiotics has led to an increase in the incidence of Lemierre's syndrome. The main etiological agent in Lemierre's syndrome is *Bacillus fundiliformis*, now known as *Fusobacterium necrophorum*, though other species such as *Streptococcus, Bacteroides, Lactobacillus* have also been implicated.[2,7] *F. necrophorum* is a part of the normal flora of the oral cavity, GI tract and female genital tract. It is a non-motile, gram-negative, obligate anaerobic rod that is characteristically pleomorphic with filaments.[6] The oropharynx is the primary site of infection in Lemierre's syndrome, specifically the lateral pharyngeal space.[7-9] However, nasopharyngeal infection, mastoiditis, otitis media, sinusitis, and odontogenic infection as initiating sites have also been reported. [7-9] The first stage of the primary infection is usually bacterial or viral pharyngitis, such as streptococcal pharyngitis or Epstein-Barr virus mononucleosis.[6,7,9,10] It is postulated that the antecedent infection creates a favorable environment for *Fusobacterium* species to proliferate within the oropharyngeal space via immunosuppression and disruption of mucosal barriers.[11,12] The pathogenesis of septic thrombophlebitis is best understood in the context of Virchow's triad. Given the proximity of the lateral pharyngeal space to the internal jugular vein, the bacteria invade the internal jugular vein either by direct extension or lymphatic and/or hematological extension. The resultant damage to the endothelial wall of the internal jugular vein produces a change in the vessel wall that alters the pattern of blood flow, leading to hypercoagulability and development of thrombosis. Metastatic infections to other organs can then ensue.[11,12]

Case Presentation:

A 19-year-old male with relatively benign medical history presented to the emergency department with complaints of shortness of breath and right-sided abdominal pain. He had been healthy until one week prior when he initially presented to a walk-in clinic with fatigue, sore throat, and vague myalgias. At that time, he had a positive Monospot test and was diagnosed

with mononucleosis. He was released with supportive measures. He was stable for a few days but then started feeling increasingly fatigued and lethargic. He had decreased oral intake and some episodes of non-bloody emesis. The day before admission, he noticed dark colored urine as well as a change in his skin color to a yellowish hue. On the day of admission to the emergency department, he became more short of breath with increasing primarily right-sided abdominal pain. His complaints included vague abdominal pain, shortness of breath, myalgias, fever, headache, and weakness. He denied chest pain, palpitations, dysuria, melena, hematochezia or any neurologic deficits.

Figure 1A: Chest x-ray on admission indicating ARDS

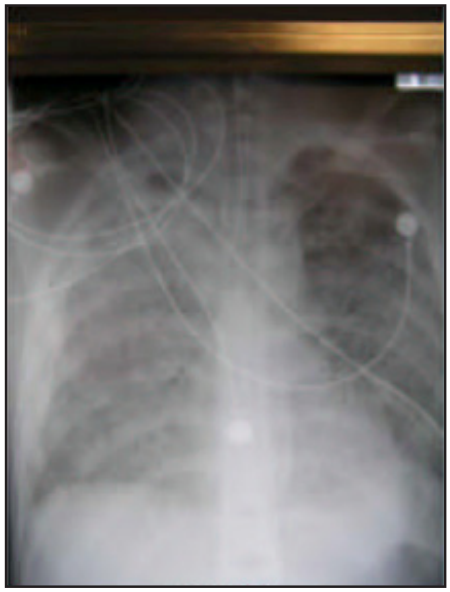
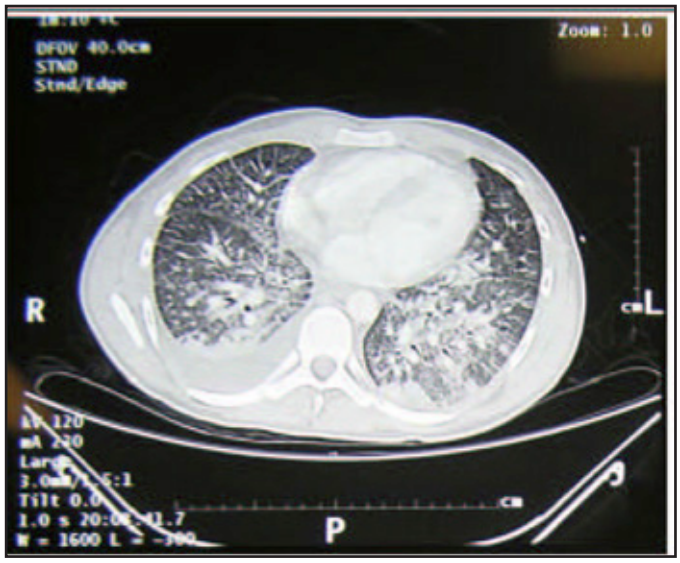
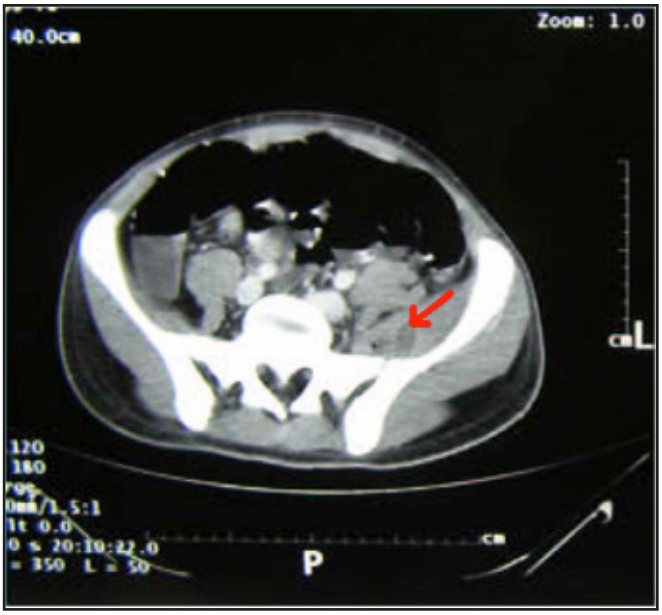


Figure 1B: CT scan of chest with contrast showing several cavitary emboli and pleural effusion



On evaluation, he had a blood pressure of 124/95, heart rate of 116, and respiratory rate was 32. Pulse oximetry reading was 94% on room air. He was thin, jaundiced, and appeared to be in mild respiratory distress. He had mild scleral icterus bilaterally. Oropharynx was dry but otherwise non-erythematous. There was no jugular venous distention. He was tachycardic but otherwise normal sinus rhythm without murmur. He had bilateral wheezes with diminished breath sounds and increased coarseness in the right lung field. Abdomen exhibited diffuse tenderness with mild rebound tenderness but was without distention or guarding. Hypoactive bowel sounds were also noted. There was no evidence of ascites or organomegaly. He had a positive heal tap and iliopsoas test. Peripheral pulses were palpable but with mildly delayed capillary refill. Cranial nerves II-XII were grossly intact bilaterally. There were no focal areas of weakness, numbness, or paresthesia.

Figure 1C: CT scan showing iliopsoas abscess – arrow



Since the patient appeared to be volume depleted in the emergency room, he was given intravenous fluids. After receiving 1200 mL of normal saline, he became increasingly short of breath and oxygen saturation by pulse oximetry subsequently dropped into the mid-80s. He was immediately given oxygen via a 100% non-rebreather mask to maintain saturation greater than 90%. A chest x-ray revealed diffuse infiltrates resembling acute respiratory distress syndrome or cardiogenic pulmonary edema (Figure 1A). Abdominal films showed mildly dilated loops of bowel consistent with possible ileus; however, no evidence of frank obstruction was noted. Chest and abdominal computed tomography (CT) scan with and without oral contrast demonstrated small, nonspecific cavitary pulmonary nodules resembling septic emboli and right pleural effusion (Figure 1B). CT scan also revealed a 3.2 cm mass and some free air within the iliopsoas consistent with an abscess cavity (Figure 1C and D), splenomegaly, and moderate degree of ascites throughout the abdomen and pelvis. The patient was admitted to the intensive care unit and started empirically on ceftriaxone and piperacillin/tazobactam. He grew increasingly hypoxic and tachypneic, with respiratory failure progressing to intubation. By the third day of hospitalization, his condition had improved and he was extubated. His blood culture grew *Fusobacterium necrophorum*. Due to mild left neck pain, a CT scan of his head and neck was obtained, revealing occlusion of

left internal jugular vein (IJV) (Figure 1E). This constellation of symptoms – respiratory distress, pulmonary cavitary nodules with pleural effusion, iliopsoas abscess, occlusion of internal jugular, and bacteremia with *Fusobacterium necrophorum* are consistent with Lemierre's syndrome. Given concerns for cerebrospinal fluid (CSF) disease (~3-4% in Lemierre's syndrome) and lack of CSF penetration from piperacillin/tazobactam, antibiotic coverage was changed to metronidazole. The patient's fever persisted for more than 96 hours, increasing concerns regarding the iliopsoas abscess. A decision was ultimately made not to drain the abscess based on the patient's elevated international normalized ratio (INR) and the potential for hematoma and/or osteomyelitis. The patient's fever resolved on day 6 of hospitalization. His condition improved and he was discharged on day 16 of hospitalization with a plan to continue antibiotics for an additional six weeks. The patient was scheduled to follow up in a week with a chest x-ray and pelvic CT scan to re-evaluate his iliopsoas abscess.

Figure 1D: CT scan showing iliopsoas abscess with some free air – arrow

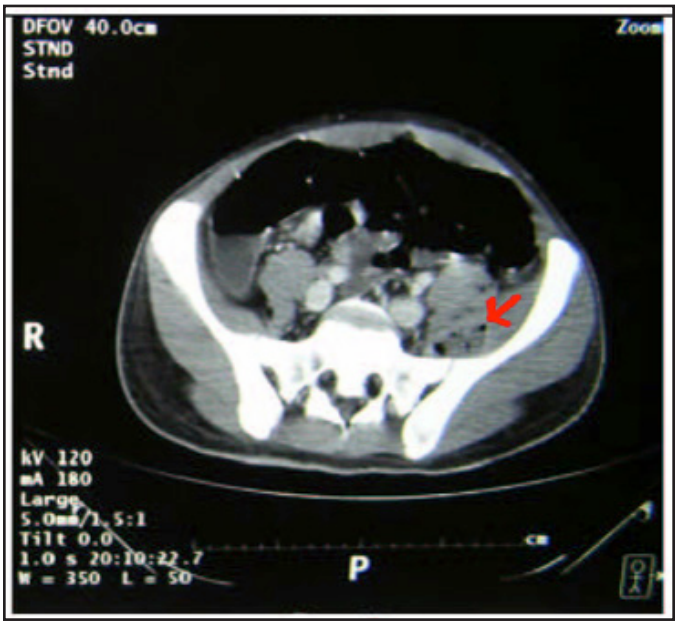
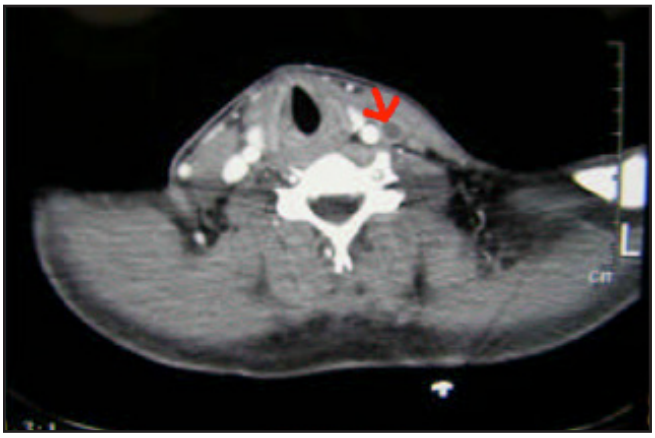


Figure 1E: CT scan of neck showing occlusion of the internal jugular vein – arrow



Diagnosis and Clinical Features

The main features of Lemierre's syndrome include: (1) primary infection of oropharynx, (2) septicemia documented by positive blood culture, (3) septic thrombophlebitis of the IJV confirmed by radiological evidence, and (4) metastatic septic emboli. The septic emboli usually consist of pulmonary foci but also can involve the joints, liver, spleen, bones, kidneys, and meninges.[8,11,13] The diagnosis is typically made on clinical grounds with high index of suspicion. However, more often than not, this is not thought of until the bacteria are isolated from culture. Patients are typically young healthy adults, although cases have been observed in all age groups.[4,11,14] Patients characteristically present within one week after onset of tonsillitis or pharyngitis with persistent fever, intense rigors, ipsilateral neck pain, and swelling along the anterior border of the sternocleidomastoid muscle. In this case report, the initial diagnosis was mononucleosis, but the patient returned a few days later with fever and respiratory failure, likely due to septic pulmonary emboli. Other associated symptoms of Lemierre's syndrome include myalgia, arthralgia, diffuse abdominal pain, and more commonly, pulmonary involvement such as productive cough, dyspnea, pleuritic chest pain, and/or hemoptysis. Laboratory findings include moderate leukocytosis with left shift, thrombocytopenia, mildly elevated liver enzymes, coagulopathy consistent with disseminated intravascular coagulation (DIC) clinical picture, and electrolyte abnormalities consistent with syndrome of inappropriate secretion of antidiuretic hormone (SIADH). In addition, the erythrocyte sedimentation rate is always elevated.[4-8,13]

Radiological studies are key in establishing the diagnosis of thrombosis to the internal jugular vein. Contrast-enhanced CT scan is the modality of choice, although others have used ultrasonography. The drawback in using ultrasound is that it provides poor imaging beneath the mandible and the clavicle and can miss fresh thrombus with low echogenicity.[8,13] In the face of pulmonary involvement, chest x-ray may show associated pleural effusion and bilateral, nodular cavitation.[8]

Treatment

The mainstay of therapy is antibiotics. The isolation of *F. necrophorum* can take up to several weeks. Antibiotic treatment should not be delayed until the blood culture results are available. *F. necrophorum* is generally susceptible to penicillin, metronidazole, and clindamycin.[8,12,14] However, treatment failures with penicillin have been reported due to B-lactamase-resistant strains of *Fusobacterium*. As such, B-lactamase-resistant antibiotics with anaerobic activity are recommended.[7] Due to the potential for polymicrobial involvement, combinations of antibiotics are often used.[13] Treatment duration is guided by clinical response. Typically, parental antibiotic treatment is required in the initial phase, usually from 1-2 weeks. This is followed by another 2-4 weeks of oral therapy.[14] Surgical drainage of abscess may be required, particularly in the face of failing medical treatment. The role of anticoagulation in the treatment of septic thrombophlebitis of the IJV remains contro-

versial.[5] The main concern with the use of anticoagulation is that it may facilitate embolic spread of the infection.[6] Others have advocated the use of anticoagulation if the thrombosis propagates to the cavernous sinus or in cases of completely vaso-occlusive jugular vein thrombosis.[15,16] Surgical ligation of thrombosed IJV or venous resection is advocated in rare cases when medical therapy has failed.[18]

Conclusion

As was rightly stated by Hall,[19] "Be not deceived by a comparatively innocent appearing pharynx, as the veins of the pharynx may be carrying the death sentence for your patient." The prognosis of Lemierre's syndrome is related to prompt initiation of therapy. A worsening of pharyngitis or mononucleosis with fever, chill, and/or respiratory failure a few days or weeks after presentation should raise a high index of suspicion for Lemierre's syndrome. Constellations of symptoms including pharyngitis (bacterial or viral), neck pain, and systemic illness are classic for this disease and should be undoubtedly included in the differential diagnosis. Once suspected, initiation of antibiotics should not be delayed until culture result is available. Anticoagulation should be considered as well as surgical drainage for metastatic abscesses.

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References

1. Lemierre A. On certain septicemias due to anaerobic organisms. *Lancet*. 1936;1:701-3.
2. Moore BA, Dekle C, Werkhaven J. Bilateral Lemierre's syndrome: A case report and literature review. *Ear Nose Throat J.* 2002;81:234-52.
3. Kushawaha A, Popalsai M, El-Charabaty E, Mobaraka N. Lemierre's syndrome, reemergence of a forgotten disease: a case report. *Cases J.* 2009;2:6397-00.
4. Karkos PD, Karkanevatos A, Panagea S, Dingle A, Davies JE. Lemierre's syndrome: how a sore throat can end in disaster. *Eur J Emerg Med*. 2004;11:228-30.
5. Bliss SJ, Flanders SA, Saint S. A pain in the neck. *N Engl J Med*. 2004;350:1037-42.
6. Chirinos JA, Lichtstein DM, Garcia J, Tamariz LJ. The evolution of Lemierre syndrome. *Medicine (Baltimore)*. 2002;81:458-65.
7. Hagelskjaer LH, Prag J. Human Necrobacillosis, with emphasis on Lemierre's syndrome. *Clin Infect Dis.* 2000;31:524-32.
8. Golpe R, Marin B, Alonso M. Lemierre's syndrome (necrobacillosis). *Postgrad Med J.* 1999;75:141-4.
9. Dool H, Soetekouw R, Van Zanten M, Grooters E. Lemierre's syndrome: three cases and a review. *Eur Arch Otorhinolaryngol.* 2005;262:651-4.
10. Love WE, Zaccheo MV. Lemierre's syndrome: More judicious antibiotic prescribing habits may lead to the clinical reappearance of this often forgotten disease. *Am J Med.* 2006;119:E7-E9.
11. Venglarcik J. Lemierre's syndrome. *Pediatr Infect Dis J.* 2003;22:921-4.
12. Venkateswaran S, Sze FKH. A case of Lemierre's syndrome presenting with multiple pulmonary abcesses associated with tension hydropneumothorax resulting in mediastinal shift. *Ann Acad Med Singapore.* 2005;34:450-3.
13. Riordan T, Wilson M. Lemierre's syndrome: more than a historical curiosa. *Postgrad Med J.* 2004;80:328-34.
14. Ochoa R, Goldstein J, Rubin R. Clinicopathological conference: Lemierre's syndrome. *Acad Emerg Med.* 2005;12:152-57.
15. Batty A, Wren MWD, Gal M. Fusobacterium necrophorum as the cause of recurrent sore throat: comparison of isolates from persistent sore throat syndrome and Lemierre's disease. *J Infect.* 2005;51:299-306.
16. Goldenberg NA, Knapp-Clevenger R, Hays T, Manco-Johnson MJ. Lemierre's and Lemierre's-like syndromes in children: survival and thromboembolic outcomes. *Pediatrics.* 2005;116:e543-e8.
17. Repanos C, Chadha NK, Griffiths MV. Sigmoid sinus thrombosis secondary to Lemierre's syndrome. *Ear Nose Throat J.* 2006;85:98-101.
18. Charles K, Flinn WR, Neschis DG. Lemierre's syndrome: A potentially fatal complication that may require vascular surgical intervention. *J Vasc Surg.* 2005;42:1023-5.
19. Hall C. Sepsis following pharyngeal infections. *Ann Otol Rhinol Laryngol.* 1939;48:905-25.