Lemierre's Syndrome Revisited: An Illustrative Case Series and Literature Review.

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ABSTRACT:

PURPOSE: Young patients with pharyngitis, odontogenic abscess, sinusitis or mastoiditis are at risk of developing thrombophlebitis of the maxillofacial and cervical veins which can be complicated by septic emboli to the lungs as well as the lungs joints, bone, soft tissues, liver, spleen, and CNS. This rare septic thrombophlebitis is known as Lemierre's syndrome. Failure to appropriately diagnose and treat patients with Lemierre's syndrome is associated with up to 98% mortality. Accurate diagnosis, prompt notification of the ordering physician and appropriate treatment reduces mortality as low as 4%. DESCRIPTION: A pictorial review of radiographic, sonographic, and cross-sectional manifestations of Lemierre's Syndrome is provided. Several cases of Lemierre's Syndrome from Tulane University Medical Center are presented and the associated epidemiological, etiological, clinical and imaging data are tabulated and analyzed. An extensive literature review was performed. The epidemiology, etiology, histopathology, clinical and imaging manifestations and treatment options of Lemierre's are discussed. SUMMARY: This image-rich case series and literature review demonstrates the clinical and multimodality imaging manifestations of Lemierre's Syndrome to reduce significant morbidity and mortality associated with delayed diagnosis and treatment.

Case Summary:

A 19-year old previously healthy male presented to the emergency department complaining of sore throat and cough for 7 days progressing to dysphagia and hemoptysis with worsening right-sided neck swelling for three days despite having been prescribed Tamiflu and Penicillin VK at a student health clinic one week prior where he had tested positive for both Influenza type A and Streptococcal pharyngitis. Review of systems was positive for headache, subjective fevers, myalgias and night sweats as well as left upper quadrant pain, nausea, vomiting and loose stools for a few days three days. He denied sick contacts, neck stiffness, photophobia, or recent dental procedure. Vitals showed tachycardia and tachypnia with low grade fever although oxygen saturation was 96% on room air. He had edematous right greater than left palatine tonsils, right-sided neck swelling without appreciable cervical lymphadenopathy, and crackles focally upon auscultation of the left lung base. Labs revealed leukocytosis of 40,000. An initial chest radiograph demonstrated a left lower lobe consolidation and small effusion. An abdominal ultrasound showed hepatosplenomegaly with periportal cuffing and confirmed the small left pleural effusion. Blood and sputum cultures were obtained, and the patient was admitted and started on broad-spectrum IV antibiotics.

The patient's fever and right neck swelling continued to worsen and oxygen saturation started to drop despite O2 nasal canula, and on day 2 of the hospital stay, a soft tissue neck CT with contrast demonstrated asymmetrical prominence of the right oropharynx with enlarged right greater than left palatine tonsils and diffuse right sided neck swelling. Narrowing and complete occlusion of the right internal jugular vein was evident. A subsequent CT of the chest with contrast demonstrated numerous pulmonary nodules and masses with multifocal areas of consolidation with varying degrees of cavitary components concerning for septic pulmonary emboli as well as the small left pleural effusion. Doppler ultrasound of the neck performed on hospital day 4 demonstrated intraluminal heterogeneous material in the distal right internal jugular vein with minimal flow and partial compressibility, confirming partial occlusion of the right IJ with thrombus. The constellation of imaging findings suggested the diagnosed of Lemierre's syndrome with septic pulmonary emboli.

The patient continued to be treated with IV Zosyn as well as Enoxaparin subcutaneously, and a left chest t ube was placed. Blood cultures drawn upon presentation to the emergency room were negative, but sputum culture grew heavy beta-hemolytic group C streptococcus. Immune compromise was suspected, but he tested negative for EBV and HIV. The patient gradually improved on IV antibiotic therapy, and the chest tube was removed. The patient was transition to PO clindamycin 450 mg po tid for two weeks on hospital day 15 and discharged in good condition to follow up with pulmonology and primary care.

Etiology/Epidemiology:

Lemierre syndrome, also known as septic thrombophlebitis, post-anginal septicemia and necrobacillosis, was first described by Dr. Andre Lemierre in 1936 in a case series of adolescents with septicemia after an oropharyngeal infection.[1] The hallmarks of the syndrome include an oropharyngeal infection that progresses to septicemia and hematogenous seeding of the internal jugular vein with subsequent thrombophlebitis and septic emboli. The most common causative agent is the bacterium Fusobacterium necrophorum, a component of normal oral flora.[2,3,4] Other species have also been described, such as Peptostreptococcus, Streptococcus, and Bacteroides species.[5] Often, pharyngitis is the inciting event, however other initial sites of infection have been noted such as sinusitis, mastoiditis, odontogenic.[6]

The incidence of Lemierre's syndrome decreased significantly after the discovery of penicillin, but appears to be on the increase beginning in the 1990's.[7,8] It is unclear whether this is due to increased antibiotic resistance, changes in antibiotic utilization, improved detection or reporting and publishing trends. Before antibiotic therapy was available, mortality rates reached 98%. However, the mortality rate has since improved to between 4% and 22%.[8] Lemierre's syndrome predominantly occurs in healthy young adults and children although it can affect all age groups.[8] The literature is unclear as to whether it is more prevalent in men or women, with one review citing a 1:1 ratio between men and women [7], and another showing a 75% male predominance.[2]

Clinical Findings:

The clinical course of Lemierre's syndrome begins with oropharyngeal infection and disruption of pharyngeal host defense.[4,9] An initial bacterial or viral pharyngitis is characterized by sore throat that may cause dysphagia. A preceding illness is thought to allow mucosal penetration by normal oral flora, Fusobacterium necrophorum, with progression to septicemia and internal jugular vein thrombophlebitis. Symptoms and signs of oropharyngeal inflammation or initial infection are frequently resolved by the time the patient is diagnosed with Lemierre's syndrome, hence the synonymous term post-anginal septicemia. [1,4] Thus, a history of sore throat is more important for diagnosis than clinically apparent tonsillitis or orpharyngitis. Fever accompanied by rigor is often the first sign of bacteremia, classically occuring four to twelve days after the initial sore throat.[1,4] The typical findings at the time of diagnosis were present in our patient, including swelling and tenderness at the anterior border of the sternocleidomastoid, tachycardia, cough, dyspnea, hemoptysis, and malaise. Leukocytosis, while extreme in our patient, may be present or absent. [10,11] Liver function abnormalities are commonly present along with hepatosplenomegaly, which was also present in our patient, and jaundice.[11] Septic emboli from the internal jugular vein in nearly all cases involve the lungs as seen in our patient, but can additionally involve joints, bone. soft tissues, liver, spleen, and CNS.[11] Retrograde thrombus extension into cerebral venous sinuses is a documented complication; and rare cases of associated pericarditis and mediastinitis have been described as well. [12,13]

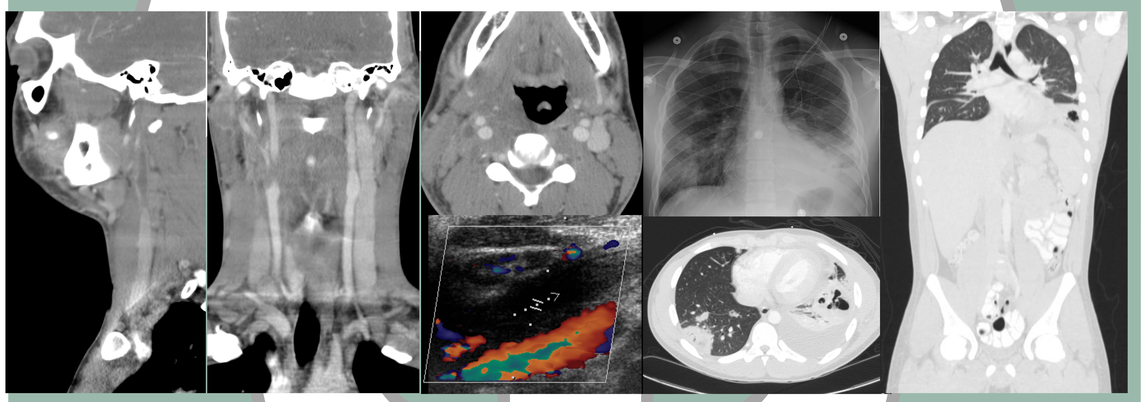
Head and Neck Findings:

Cervicofacial and particularly internal jugular venous thrombosis allows rapid colonization of highly aggressive organisms and subsequent septic emboli. The presence of internal jugular vein thrombosis in association with septic emboli in the lung suggests the diagnosis of Lemierre's syndrome. Early recognition is crucial to preventing the delay of appropriate therapy and consequently minimizing mortality and morbidity.[13]

Ultrasonongraphy (US) is considered by some the initial imaging modality of choice for diagnosis internal jugular venous thrombosis because of its widespread availability, relative ease of performance, and absence of sedation or harmful ionizing radiation exposure. For these reasons, US is particularly utilized in the pediatric population. US characteristics of internal jugular vein thrombosis include the presence of intraluminal echoes, loss of vessel compressibility, and complete or partial absence of flow although loss of vessel compressibility is the most sensitive finding.[6]

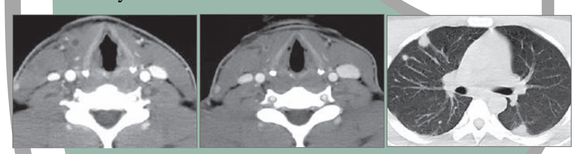
CECT is advantageous because not only can it be utilized to identify jugular venous thrombosis, but it can also delineate the source of infection, whether pharyngitis, tonsillitis, or periodontal disease. Furthermore, CECT can detect the presence of and characterize the size and location of an abscess formation, which is particularly important because the presence and size of an abscess can influence management.[14] Characteristic findings of venous thrombosis on CECT include a hypoattenuating filling defect in the lumen associated with venous distinction, thickened enhancing walls, and edema of the adjacent soft tissues.[6]

Magnetic resonance angiography has also proved useful for diagnosing jugular vein thrombosis and is advantageous because of its lack of ionizing radiation. Conventional retrograde venography is rarely performed because of its invasiveness; however, some authors believe it can be useful in the assessment of the extension of the thrombosis when jugular vein ligation is considered. Other less commonly used techniques that can lead to the diagnosis of internal jugular thombosis include gallium scan and radionuclide venography with Tc-99m-labelled RBC.[15]

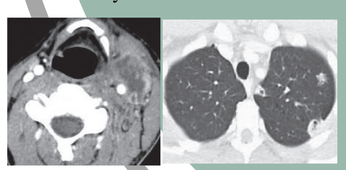


Case 1: 19 y/o Caucasian male with right-sided tonsillitis and pharyngitis develops right internal jugular thrombophlebitis and subsequent septic pulmonary emboli with cavitary consolidations and effusions bilaterally. Note also the hepatomegaly.

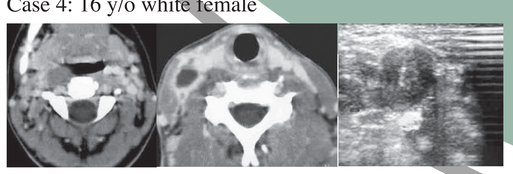
Case 2: 21 y/o AA male



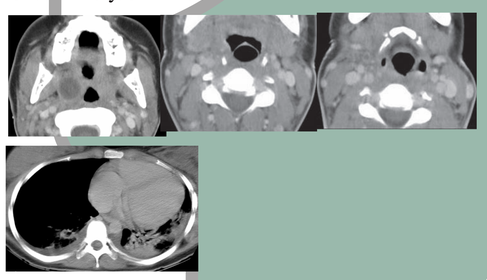
Case 3: 35 y/o white female



Case 4: 16 y/o white female



Case 5: 48 y/o AA female



Case 6: 51 y/o Caucasian male

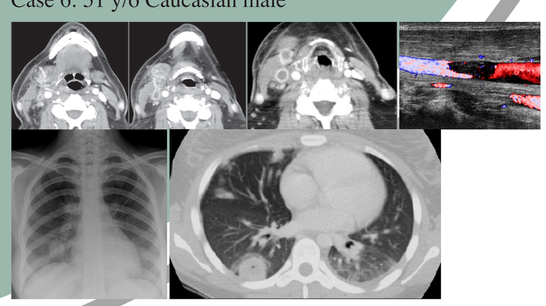


Table 1: Etiological and Epidemiological Factors with Associated Cervical Clinical and Imaging Features.

Patient	Age	Race	Gender	Origin	Cervical abscess, Location	Vessel(s) Thrombosed
1	19	Caucasian	male	R tonsillitis, Pharyngitis	No	R internal jugular
2	21	AA	male	Pharyngitis	No	R external jugular
3	35	Caucasian	female	Pharyngitis	Yes, L neck level 2/3	L internal jugular
4	16	Caucasian	female	R peritonsillar abscess	Yes, R palatine tonsil	R internal jugular
5	48	AA	female	R peritonsillar abscess	Yes, R palatine tonsil	Bilateral external jugulars,
6	51	Caucasian	male	R submandibular gland	Yes, inf margin SMG	R internal jugular

SMG = submandibular gland

Table 2: Thoracic and Abdominal Imaging Features.

Patient	Number of lesions	Shape	Unilateral/ Bilateral	Distribution	Cavitation; Number of cavitary lesions	Additional findings
1	>10	>8 nodular 2 consolidations	Bilateral	Peripheral	Yes, 2 of 2 consolidations, pleural extension	Bilateral small to mod pleural effusions (L>R); Hepatomegaly
2	>3	2 nodular 1 wedged	Bilateral	Peripheral	No	
3	>3	1 nodular 2 wedge	Unilateral, Left	Peripheral	Yes, 2 of 3, wedges, pleural extension	
4	N/A	N/A	N/A	N/A	N/A	
5	>4	1 nodular 1 wedge 2 consolidations	Bilateral	Peripheral	Yes, 1 of 3 nodules, pleural extension	Bilateral small pleural effusions (R>L)
6	>5	2 wedged 3 nodular	Unilateral	Peripheral	Yes, 1 of 5 nodules, pleural extension	Small left effusion and LLL atelectasis vs. developing consolidation

Chest Imaging Findings:

Septic emboli arising from the cervicofacial veins most commonly involve the lung, up to 97% of cases.[5,11,16] Chest radiographs are the initial study of choice if there is clinical suspicion of septic pulmonary emboli. Chest radiographs frequently demonstrate one or more areas of patchy consolidation or peripheral nodular opacities with or without cavitations in patients with septic pulmonary embolic disease. However, the radiographic findings tend to be nonspecific or the chest radiograph can appear completely normal upon presentation. A normal chest radiograph does not exclude Lemierre's syndrome with septic pulmonary emboli.[7,16]

CT is more sensitive and specific and thus better characterizes the pulmonary manifestations of septic emboli. CT demonstrates one or more focal infiltrates in the setting of pulmonary emboli, which may be nodular with peripheral distribution within one or both lungs.[16] Cavitations may or may not be present; since the advent of penicillin, cavitary embolic lesions have become less common.[5] The consolidations can rapidly increase in size, number, presence of cavitation and cavity to consolidation ratio as the disease rapidly progresses, as seen in our case. The variable number, size, and cavity to consolidation ratio upon initial imaging reflect the varying chronicity of the septic emboli. Associated findings that may be detected radiographically but are better characterized by CT include abscesses, pleural effusions, empyemas, pneumatoceles and pneumothoraces.[11,16] Hepatosplenomegaly can also be seen with CT or US, as in our case.[11]

When septic pulmonary emboli are evident on chest radiographs or CT, follow up examinations can be used to determine disease progression and response to therapy, which can be rapid as in our case. However, just as normal radiographic findings can be encountered in patients with septic pulmonary emboli diagnosed on CT, resolution on radiograph does not equate to resolution of disease. Therefore, CT is suggested as the modality of choice to confirm resolution of pulmonary manifestations even after chest radiographs are negative.[5]

Treatment:

Treatment of Lemierre's syndrome is controversial. Areas of uncertainty include antibiotic selection and duration, use and duration of anticoagulation, and the role of surgery. It is generally accepted that the presence of an abscess amenable to drainage should be drained.[10] Antibiotics should include β-lactamase coverage with broad-spectrum initial intravenous antibiotic therapy multiple agents is recommended, with subsequent narrowing of coverage dictated by culture and sensitivity.[17] The duration of intravenous and oral antibiotic therapy has ranged widely in case reports. A reasonable recommendation is to continue intravenous therapy until the patient becomes afebrile and neck tenderness abates, then to transition to oral antibiotics for an additional outpatient regimen of 3 to 4 weeks.[17] Anticoagulation can be used during inpatient therapy to decrease extension of thrombus; however, continuation to outpatient anticoagulation and optimal duration of treatment is unclear. One study reports that the risks of continued anticoagulation in a young, trauma-prone population outweigh the benefit of prevention of massive pulmonary embolism or postthrombotic syndrome.[17] Surgery is generally reserved for cases that have continued embolization despite appropriate antibiotic therapy or retrograde extension of thrombus. Resection or ligation of the internal jugular vein have been described, however it is widely accepted that vascular surgery is not a primary treatment for Lemierre's syndrome.[18]

Conclusion:

In conclusion, if a young patient with a sore throat and cough has leukocytosis and imaging demonstrates findings commensurate with internal jugular thrombophlebitis and septic pulmonary emboli, the diagnosis of Lemierre's syndrome should be made, the ordering physician notified and treatment should not be delayed. Despite the decreased mortality and morbidity associated with Lemierre's syndrome in the post antibiotic era, significant morbidity and occasionally death can still occur if the diagnosis is not readily recognized and treatment is delayed.

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