Lemierre’s syndrome: An almost forgotten clinical entity. Three case reports and Literature review


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Abstract: Lemierre’s syndrome is a rare disease that affects young adults and is mainly caused by Fusobacterium necrophorum and occasionally by other anaerobic bacteria of the species. This syndrome is characterized by a throat infection complicated with septic thrombophlebitis of the internal jugular vein and septic emboli mainly to the lungs. In the pre-antibiotic era its evolution was often fatal. Since the 1960’s this syndrome has rarely been reported given the extensive use of penicillin en pharyngeal infections. Currently the incidence of Lemierre’s syndrome is about one in a million. Currently, since imaging has a key role in the early diagnosis of this syndrome, the radiologist should be aware of and recognize its manifestations. Three cases of Lemierre’s syndrome and a literature review are presented.

Keywords (MeSH-Pubmed): Diagnostic Imaging (D003952), Lemierre Syndrome. (D057831), Pulmonary embolism (D011655).

Resumen: El síndrome de Lemierre es una enfermedad rara que afecta a adultos jóvenes y es causada principalmente por Fusobacterium necrophorum y ocasionalmente por otras bacterias anaerobias de la especie. Este síndrome se caracteriza por una infección faríngea complicada con tromboflebitis séptica de la vena jugular interna y embolias sépticas principalmente a los pulmones. En la era pre-antibióticos su evolución era frecuentemente de curso fatal. Desde los años 60 este síndrome ha sido rara vez reportado dado el extensivo uso de penicilina en infecciones faríngeas. Actualmente la incidencia del síndrome de Lemierre es de aproximadamente uno en un millón. Dado que hoy en día las imágenes tienen un rol fundamental en el diagnóstico temprano de este síndrome el radiólogo debe estar al tanto y reconocer sus manifestaciones. Se presentan tres casos de Síndrome de Lemierre y una revisión de la literatura. Palabras clave (MESH-Pubmed): Diagnóstico por imagen (D003952), Embolia pulmonar (D011655), Síndrome de Lemierre (D057831).

Introduction

Lemierre’s syndrome is a rare and potentially lethal disease, which originates as a complication of an oropharyngeal infection spreading to the carotid space. It is associated with septic thrombophlebitis of the internal jugular vein and distant septic emboli, affection of the lungs being the most frequent(1) (Figure 1).

Although initially described in 1900 by Courmont and Cade, it was the French microbiologist André Lemierre (Figure 2) who best characterized this disease in 1936. Lemierre described 20 cases of “postanginal anaerobic septicemia”, of which 18 died. This group of patients initially presented with peritonsillar or pharyngotonsillitis abscess followed by sensitivity of the sternocleidomastoid muscle,
with the subsequent development of septic emboli usually of the lung and joints. Patients usually died within 7-15 days from onset of symptoms. Lemierre postulated that this syndrome was so characteristic that it allowed for diagnosis even before bacteriological tests\(^{(1,2)}\).

The most frequent pathogen of this syndrome is Fusobacterium necrophorum, a strict anaerobic Gram-negative bacteria that form part of the normal bacterial flora of the oropharynx, gastrointestinal tract and female genital tract. Although this organism is present in 81% of Lemierre’s syndrome cases, a wide variety of other aerobic and anaerobic pathogens have been implicated including Staphylococcus, Streptococcus, Proteus, Bacteroides and Peptostreptococcus. Occasionally they can be found in isolation, but it is possible that these cases reflect the difficulty to grow strict anaerobic organisms\(^{(3,4)}\).

**Clinical symptoms**

Lemierre’s syndrome typically affects adolescent and young adult immuno-competent patients: over 70% of cases occur between 16 and 25 years. It usually presents as a sepsis characterized by fever and several days of sore throat after an apparently resolved pharyngitis, in 87% of cases the primary infection site being the palatine tonsils and peritonsillar tissue. Other early infectious foci may correspond to acute otitis media, infections of dental origin and mastoiditis\(^{(1,3)}\).

In a second stage there is invasion of the carotid space causing septic thrombophlebitis of the internal jugular vein. About 48% of patients have no cervical symptoms, however, can refer pain and increased cervical volume\(^{(5)}\). In the final stages septic thromboembolic spreading exists that reaches distant organs, the lung being the most common site of dissemination (80%)\(^{(6)}\) also with complications such as lung abscess, pneumatoceles, pleural effusion, empyema and pneumothorax being reported\(^{(1,4)}\).

Septic arthritis was part of Lemierre’s original diagnostic triad; however, it is now a rare presentation (13-27%)\(^{(5)}\). Other rare complications include osteomyelitis, splenic and hepatic abscesses, cutaneous involvement and cavernous sinus thrombosis\(^{(3,4)}\).

Establishing strict diagnostic criteria for this disease is proposed, since some authors include within Lemierre’s syndrome the presence of internal jugular vein thrombosis (for example, as a complication resulting from the use of central venous lines) even in the absence of septic emboli to the lung or other organs\(^{(1)}\) (Figure 3).

Treatment of Lemierre’s syndrome consists of prolonged antibiotic therapy with adequate coverage for anaerobes, especially directed against the Fusobacterium strain. The course of action generally includes penicillin and metronidazole or clindamycin monotherapy for at least 6 weeks. Regarding the use of systemic anticoagulation, its use is considered when accompanied by stroke or cavernous sinus thrombosis. However, there is no evidence to support its widespread use in these patients\(^{(3-5)}\).
left cervical vascular compartment underlying to the sternocleidomastoid muscle, associated with external and internal left jugular vein thrombosis. Chest AngioCT study performed later showed no pathological findings, especially, signs of septic emboli.

As the second case, is a 16 year old male patient, without morbid clinical history. Consults Emergency Services with symptoms after 12 days evolution, which are characterized by fever, trismus, odynophagia and CEG, previously treated with multiple courses of antibiotics. Physical examination highlighted fever (40° C), pharynx with purulent exudate, increased bilateral amygdala volume and painful cervical lymphadenopathy. Chest radiography on admission shows cavitated radiolucent lesion, therefore chest CT is requested which confirms the presence of cavitory nodules. Patient evolves with increase of sensitive volume in right lateral cervical region; Eco Doppler and CT with contrast of the neck is requested, which show filling defects in right internal jugular vein compatible with thrombosis.

Finally, we have a 19 year old female patient, no morbid history. Consults Emergency Services feverish, with cervicalgia and palpable mass in the left cervical region. CT of neck and CT of chest with contrast show internal left jugular vein thrombosis (IJV) and lung nodules, respectively. Favorable progress after antibiotic treatment.

**Imaging diagnosis**

The imaging study plays a key role in the diagnostic confirmation when there is adequate clinical suspicion.

In the evaluation of septic emboli it is important to mention that the radiological findings, particularly in computed tomography (CT) of the chest, may be present even before blood cultures are positive. Although the thorax Rx does not have the same sensitivity as CT, it can also display findings which suggest a septic embolism. Among those are described: small parenchymal opacities usually bilateral of peripheral distribution and toward the bases, with poorly defined edges and variable in size, looking like a normal acute pneumopathy (area of condensation prior to cavitation). When these lesions cavitate, they tend to be shown as thin walled cystic lesions (Figure 4).

In the study by multislice computed tomography (MSCT) of the thorax, septic emboli present an imaging spectrum which includes areas of ground-glass opacities, small nodular opacities (0.5 - 3 cm in diameter) and areas of condensation with air bronchogram of subpleural location, which tend to present wedge-shaped morphology (pleural based) simulating small pulmonary infarcts. These lesions may exhibit varying degrees of excavation depending on the evolution stage of the lesion, following a pe-
ipheral predominance distribution and towards the pulmonary bases\(^9\)\(^{-11}\) (Figure 5, Figure 11).

Sometimes a small pulmonary vessel that is oriented to the thickness of the lesion can be seen, corresponding to the “feeding vessel sign”, which although it is sensitive, lacks specificity as it has also been reported in lung metastases (18 – 58 %)\(^9\)^{12}. In assessing cavitated nodules, within the differential diagnosis, as well as septic emboli: pulmonary metastases, chronic granulomatous infections (fungi and TB), lymphoma (particularly in patients with HIV), rheumatoid nodules and connective tissue disease (vasculitis: necrotizing granulomatosis with polyangiitis, SLE)\(^9\) should also be considered (Figure 6).

Figure 4. Case 2. Thorax Rx on admission: Shows radiolucent image of cystoid appearance, with relatively thin walls of about 2 cm in the left lower lobe, suspicion of cavitated lesion.

Figure 5. Case 2. Chest CT pulmonary window: The study confirmed the presence of multiple small nodular subpleural opacities no greater than 10 mm in the basal posterior segment of LSD and LM (arrows a, b), small cavitated nodules being visible in the base of the left lower lobe, one of them corresponds to what was observed in previous chest Rx (arrows c, d).
### Cavitated nodule differential diagnosis

- Septic emboli (SE, CVC, pacemaker, IV drug abuse)
- Pulmonary metastasis
- chronic granulomatous infections (Fungi e.g.: angioinvasive Aspergilloma, TB)
- Lymphoma (especially en HIV patients)
- Rheumatoid nodules
- Connective tissue disease (Wegener Granulomatosis, SLE))

**Figure 6. Differential diagnosis of cavitated lung nodules.**

Identifying intraluminal images in the pulmonary artery is not an expected finding, as septic infarcts are almost invariably a consequence of small emboli that lodge in the distal pulmonary vasculature[7,8].

As for the evaluation of IJV thromboflebitis, both the MSCT with contrast as well as Doppler US are very sensitive in detecting thrombosis. Among the etiologies of thrombosis are described: neoplasms (paraneoplastic syndrome), thrombophilias, intravenous drug abuse, central venous catheterization and other infectious-suppurative processes of the head and neck (Figure 7)[13].

### IJV thrombosis differential diagnosis

- Retropharyngeal abscess
- CVC
- IV Drugs
- Neoplasms
- Thrombophilias

**Figure 7. Differential diagnosis of internal jugular vein thrombosis.**

When suspecting IJV thrombosis, the cervical Doppler US is the first-line of study with a sensitivity and specificity of 92 and 98% respectively. The absence of flow to color Doppler and the lack of vein compressibility represent findings of high sensitivity, while the most specific sign is the visualization of the thrombus. Typically an expanded vein is observed, incompressible and occupied by material inside (thrombus), usually echogenic, which reveals a certain temporality. If the thrombus is recent, a vein expanded by isoechogetic materials in relation to the lumen (soft thrombus), is usually observed. When the thrombus is occlusive we see complete absence of compressibility and flow to color Doppler, while in the case of a partially occlusive thrombus we can detect partial flow and a certain degree of vein compressibility, findings that can determine a false negative for thromboflebitis in an inexperienced operator[14-16] (Figure 8).

**Figure 8. Case 2, Eco color Doppler: Shows expanded right internal jugular vein with isoechogetic thrombus, without flow.**

MDCT allows complete visualization of the internal jugular vein, as well as the possible extension of the thrombosis to the venous vascular structures of the chest. In acute phase, we will see an expanded vein and occupied by content with soft tissue density that is not impregnated with intravenous contrast, which represents the centrally located intraluminal thrombus (Figures 9 and 10). In chronic phase when there is recanalization, an eccentric mural thrombus (organized) and IV contrast enhanced thickened walls of the vein, can be seen.

### Discussion

Lemierre’s syndrome is a clinical entity of high morbidity and mortality if not diagnosed and treated promptly. During the 60s and 70s, when penicillin was the antibiotic most commonly used to treat throat infections, this syndrome was known as the “forgotten disease” because of its low incidence. While still a rare condition, today there has been an increase in incidence probably related to the reduction in the use of antibiotics to treat symptoms of the upper respiratory tract, decrease in tonsillectomies, increased resistance to macrolides and improved diagnostic methods using images and cultures[1,17].

The prognosis for this syndrome is favorable if there is early diagnosis and treatment. Mortality has decreased since the original series of Doctor Lemierre from 90% to a rate of 4-18%[18].
Although the clinical presentation of Lemierre’s syndrome is very characteristic, currently doctors are often unfamiliar with this condition or with its form of presentation, partly because of its rarity and its differential diagnoses which are vast. It is worth noting that the presence of the classic triad for this syndrome is rare which makes diagnosis difficult.

Summary

Lemierre’s syndrome is a rare but potentially lethal clinical condition, if there is not a timely diagnosis. Special emphasis should be given to recognizing the imaging findings that suggest this syndrome, especially in the context of a young immuno-competent patient, with torpid evolution of pharyngotonsillitis
that causes IJV thrombosis and manifestations of distant septic emboli.

**Bibliography**