Lemierre's Syndrome

18

Marios Stavrakas, Petros D. Karkos, and Christos D. Karkos

Introduction

Lemierre's syndrome, sometimes called necrobacillosis or postanginal septicaemia, was first described as a clinical entity by Courmont and Cade in 1900 [1], but was named after André Lemierre, who reported 20 patients with anaerobic "septicaemia" in 1936 [2]. He divided his patients into six groups, based on the source of infection. His first group included infection of the pharynx, particularly tonsillar and peritonsillar abscesses, and he described it as "anaerobic postanginal septicaemia" ("angina" was the old term for sore throat). No formal definition for Lemierre's syndrome exits so there is confusion in the literature as to the case criteria. Most series include only those cases that have a history of recent oropharyngeal infection (pharyngotonsillitis or peritonsillar abscess), clinical or radiological evidence of internal jugular vein thrombosis, and isolation of anaerobic pathogens, mainly *Fusobacterium necrophorum*, from the blood or other sterile sites (Table 18.1) [3]. However, some authors also include cases of septic jugular thrombophlebitis arising from the ear, teeth, or other non-pharyngeal locations [4] or cases due to organisms other than anaerobes (e.g., group A streptococci) [4, 5]. Other series include only those cases that have evidence of septic emboli, in addition to meeting other criteria [5]. In this chapter, the case criteria used will be those in Table 18.1 unless otherwise noted.

Epidemiology

Following the introduction of penicillin in the 1940s and its widespread use for oropharyngeal infections, the incidence of Lemierre's syndrome decreased significantly. No cases of Lemierre's syndrome were reported in the 1950s and 1960s [6], and it was believed to be a "forgotten disease" in the 1980s and 1990s. Since the 1990s, however, there has been an increase in the number of reported cases of Lemierre's syndrome. The reason is unknown but may be related to the more judicious use of antibiotics in recent years for common oropharyngeal infections, or to a wider awareness of Lemierre's syndrome [3, 7]. The use of macrolides to treat patients with pharyngitis who are penicillin-allergic may contribute to the incidence of Lemierre's syndrome, as *F.*

M. Stavrakas
Department of Otolaryngology, Derriford Hospital, Plymouth, United Kingdom

P. D. Karkos (✉)
Department of Otolaryngology, AHEPA University Hospital, Thessaloniki, Greece

C. D. Karkos
5th Department of Surgery, Medical School, Hippocratio Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece

M. L. Durand, D. G. Deschler (eds.), *Infections of the Ears, Nose, Throat, and Sinuses*,
https://doi.org/10.1007/978-3-319-74835-1_18

Table 18.1 Characteristics typical of Lemierre's syndrome [3]

1. Oropharyngeal infection[a]
2. Clinical or radiological evidence of internal jugular vein thrombosis
3. Isolation of anaerobic pathogens, mainly *Fusobacterium necrophorum*[a]

[a]Some authors include as Lemierre's syndrome cases of septic jugular venous thrombophlebitis that have another source of infection or that are caused by non-anaerobic pathogens

necrophorum is resistant to macrolides. A review by Riodan of 222 cases of Lemierre's syndrome found that 30% of the patients had received antibiotics prior to admission, but half of these patients had received macrolides [5].

Lemierre's syndrome is rare, with an estimated annual incidence of 3.6 cases per one million population [8]. The male-to-female ratio is nearly equal (1:1.2) [3]. While patients' ages have ranged from 2 months to 78 years (median 22 years) [3], most cases occur in previously healthy adolescents or young adults. A review of nearly 60 years of published cases of Lemierre's disease found that 51% of the patients presented during adolescence, 20% presented in their 20's, and 18% presented during the first decade of life [3]. The above figures indicate that Lemierre's syndrome is predominantly a disease of young patients, but without sparing any age group [3]. The reason for the predominance of Lemierre's syndrome in adolescents and young adults may relate to the high frequency of sore throat due to *F. necrophorum* in this age group, in whom this organism may cause more cases of pharyngitis than group A *Streptococcus*. This is discussed further in Chap. 17.

Lemierre's syndrome has a significant mortality rate. According to Lemierre's study in 1936, 18 of the 20 patients that he described subsequently died [2]. This was in the pre-penicillin era, however. The current overall mortality rate is 5%, which is slightly lower compared with rates of 6–22% previously reported in the antibiotic era [3, 9].

Microbiology

The most common pathogen isolated in Lemierre's syndrome is *F. necrophorum,* a Gram-negative anaerobe. Routine throat cultures will fail to detect this organism because it is an obligate anaerobe. Cultures of any abscess should include both anaerobic and aerobic cultures. *Fusobacterium* bacteremia can be detected in blood cultures, as these include both aerobic and anaerobic bottles.

The contribution of *F. necrophorum* to Lemierre's syndrome has been assessed by several studies. Chirinos et al., in a study that included Lemierre's syndrome cases due to any organism, found that of 81.7% of the cases were due to *F. necrophorum*, including 10.1% due to *F. necrophorum* in combination with other organisms, 5.5% were due to other organisms and 12.8% had negative cultures [4]. The other organisms included several types of anaerobes (e.g., various *Bacteroides* species, *Peptostreptococcus*, *Eikenella corrodens*), *Lactobacillus* species, groups A, B, or C *Streptococcus*, viridans streptococci (e.g., *Streptococcus oralis*), and occasional unexpected organisms such as enterococci, *Proteus*, *Candida*. Which of these non-fusobacterial organisms comprised the 5.5% of cases due to "other organisms" alone was not reported. It is not unusual to find *F. necrophorum* alone as the etiology of Lemierre's syndrome [3–5, 10, 11]. Karkos et al. reviewed all cases of Lemierre's syndrome that had positive cultures for anaerobes and found that *F. necrophorum* (57% of cases), *Fusobacterium* species not further identified (30%), and *F. nucleatum* (3%) accounted for 90% of cases, while other anaerobes comprised 10% of cases [3]. The reason that *F. necrophorum* is the major cause of Lemierre's syndrome is due to the organism's virulence factors. *Fusobacterium necrophorum* possesses a lipopolysaccharide endotoxin that is lethal in animal models [12]. The inflammatory response in *F. necrophorum* infections depends on the production of a leukocidin and exotoxin [13]. *Fusobacterium necrophorum* produces more leukocidin and exotoxin than other *Fusobacterium* species and thus *F. necrophorum* is the only *Fusobacterium* species that aggregates human platelets [14].

Of interest, *F. necrophorum* is a much more common pathogen in animals than in humans. There are two subspecies of *F. necrophorum*, *F. necrophorum* subspecies *necrophorum* (seen in animal infections), and *F. necrophorum* subspecies *funduliforme* (seen in human infections) [15, 16]. Both subspecies can produce an extracellular leukotoxin [15]. *Fusobacterium necrophorum* has

been considered as being part of the normal oral flora of humans, but some recent studies question this and postulate that the organism is acquired prior to the onset of pharyngitis symptoms [16].

Pathophysiology

The parapharyngeal space anatomy and its relation with the adjacent vascular structures plays an important role in the pathophysiology of Lemierre's. The parapharyngeal space resembles an inverted cone, extending from the hyoid bone (tip of the cone) to the skull base (base of the cone). Medially lies the buccopharyngeal fascia on the superior constrictor muscle while laterally lies the internal pterygoid muscle, the parotid gland and the mandible. The parapharyngeal space is divided by the styloid process in an anterior (muscular) and a posterior (neurovascular) compartment; the latter contains the carotid artery, internal jugular vein and vagus nerve. Spread of an infection to the posterior compartment can involve the carotid artery or the internal jugular vein, leading to serious systemic complications.

Infection of the parapharyngeal space can be caused by spread of tonsillitis, pharyngitis, parotitis, otitis, mastoiditis, or dental infection. If the infection remains untreated, internal jugular vein thrombosis can occur due to compression or extension of thrombophlebitis of the peritonsillar veins into the jugular vein [10, 12, 17]. More specifically, the progress of the disease has been described in several stages: (1) primary infection (e.g., pharyngitis, tonsillitis), (2) local invasion of the parapharyngeal space (mainly via lymphatic vessels) and internal jugular vein thrombosis, and (3) metastatic complications [4].

Internal jugular vein thrombophlebitis is usually caused by virulence factors of *F. necrophorum.* These factors have been proven to trigger human platelet aggregation both in vitro and in animal models [10, 18, 19].

Clinical Presentation

> *Be not deceived by a comparatively innocent appearing pharynx as the veins of the tonsil may be carrying the death sentence of your patient.*
> *C. Hall, 1939* [20]

Table 18.2 Typical clinical presentations of Lemierre's syndrome [3]

Sore throat	33%[a]
Neck mass	23%
Neck pain	20%
Bone/joint pain	8%
Otalgia and/or otorrhoea	8%
Dental pain	5%
Orbital pain	1%
Gastrointestinal symptoms	1%
Limb weakness	1%

[a]Some authors report a much higher frequency of sore throat [4], [9], and note that dyspnea (24%) and pleuritic chest pain (31%) are common [4].

Clinical presentation is closely associated with the primary site of infection or its sequelae. Most patients have an antecedent pharyngeal infection, but rarely, other sources of infection have been described (e.g., middle ear, larynx, teeth, paranasal sinuses, and orbit) [3]. The most common initial symptom in patients with Lemierre's syndrome is sore throat, followed by neck mass and neck pain (Table 18.2) [3]. Other presenting symptoms can be otalgia, dental pain, pleuritic chest pain, dyspnea, cough, haemoptysis, joint pain, and abdominal pain [7]. Sore throat usually precedes all other symptoms by 4–5 days. The interval can be up to 12 days [14, 16]. In some cases, there is complete resolution of sore throat before the internal jugular vein becomes thrombosed. The neck pain is usually unilateral and may be aggravated, due to irritation of the sternocleidomastoid muscle, on turning the head away from the involved side. A neck mass may be palpable at the angle of the jaw or along the anterior border of the sternocleidomastoid. Patients with Lemierre's syndrome may also have cervical lymphadenitis which can either be unilateral or bilateral. Local complications may be present, such as peritonsillar abscess, parapharyngeal abscess, or paratracheal abscess [4, 21, 22].

Pulmonary symptoms are common in patients with Lemierre's syndrome, usually due to septic pulmonary emboli. One-quarter of patients have dyspnea and one-third have pleuritic chest pain on presentation [4]. The clinician may hear localized crackles and pleural rub on examination. Hemoptysis may be present [2, 4]. Pleural effusions may progress to empyema (10–15%) [8]. Progression to acute respiratory distress syn-

drome, requiring mechanical ventilation, is rare but occurs in some patients (<10%). Septic arthritis has been reported to occur in 13–27% of the patients, with the hip most commonly involved [5]. Osteomyelitis, however, is rare (3%). Abdominal wall abscess is very rare, and one case of pyomyositis has been reported [23]. Abdominal pain is common but intra-abdominal infection (abscess of the liver or spleen, peritonitis) is rare [8]. Retrograde extension of internal jugular vein thrombophlebitis into the cavernous or sigmoid sinus is a life-threatening complication of Lemierre's syndrome [5, 24, 25]. Meningitis or intracerebral abscess has been very rarely described. Other rare complications include cardiac (endocarditis, pericarditis, septic shock) [5, 22, 26], renal (abscess, acute renal failure, hemolytic uremic syndrome) [14, 27–29], and hematologic (thrombocytopenia, disseminated intravascular coagulation, subsequent peripheral ischemia and gangrene) [5, 30, 31].

Diagnosis

> *The appearance and repetition several days after the onset of sore throat (and particularly of a tonsillar abscess) of severe pyrexial attacks with an initial rigor, or still more certainly the occurrence of pulmonary infarcts and arthritic manifestations, constitute a syndrome so characteristic that mistake is almost impossible.*
> *A. Lemierre, 1936* [2]

To diagnose Lemierre's syndrome, the clinician should be aware of the existence of the syndrome and its manifestations, both localized and systemic. Clinical suspicion plays a paramount role in early diagnosis of the disease [32] (Table 18.3). It is essential to highlight that doctors rarely encounter patients with Lemierre's syndrome so there is quite frequently a significant delay in diagnosis. According to Alvarez et al., this delay may be on average 5 days from presentation [33]. Isolation of *F. necrophorum* in blood cultures should strongly suggest the diagnosis. A chest x-ray is often the first study performed (92% of cases) and demonstrates pathological findings in 75%, although it may be reported as normal in 10% [3]. In the presence of septic pulmonary emboli, the chest x-ray may reveal multiple peripheral round and wedge-shaped opacities that rapidly progress to cavitation [34].

Table 18.3 Signs and symptoms that increase the clinician's suspicion for Lemierre's syndrome [31]

Increasing suspicion for Lemierre's syndrome
• Pharyngitis that does not resolve in 3–5 days
• Pharyngitis followed by systemic or respiratory symptoms such as fevers, chills, rigors, or dyspnea
• Pharyngitis associated with lateral cervical pain and dysphagia
• Pharyngitis followed by sepsis or multiple pulmonary abscesses

The most commonly requested scan is computed tomography (CT) of the neck and chest (55%), and many authors favor contrast-enhanced CT as the imaging modality of choice (Figs. 18.1 and 18.2). Contrast-enhanced CT is superior to non-contrast CT in identifying additional pathologies, soft tissue abscesses, osteomyelitis, and septic arthritis [35–38]. The CT findings in Lemierre's syndrome include distended veins with enhancing walls, low attenuation intraluminal filling defects, and localized tissue edema [17, 39]. High resolution CT provides higher sensitivity and can contribute significantly in establishing the diagnosis [40].

Doppler ultrasound is another commonly used imaging modality. It is frequently the first step in terms of imaging as it can demonstrate internal jugular vein thrombosis and it is quick, relatively inexpensive, and does not involve exposure to radiation. However, ultrasound provides poor imaging beneath the clavicle and under the mandible and may miss a fresh thrombus because of low echogenicity. Magnetic resonance imaging (MRI) has been suggested as the imaging method of choice because of its high sensitivity, greater soft tissue contrast, and avoidance of radiation [41]. It has not yet been established as superior to CT, mainly because of the higher cost. Other radiological studies that are rarely used now include conventional retrograde angiography, gallium scan, and scintigraphic venography with Technetium (Tc) 99 [14, 42].

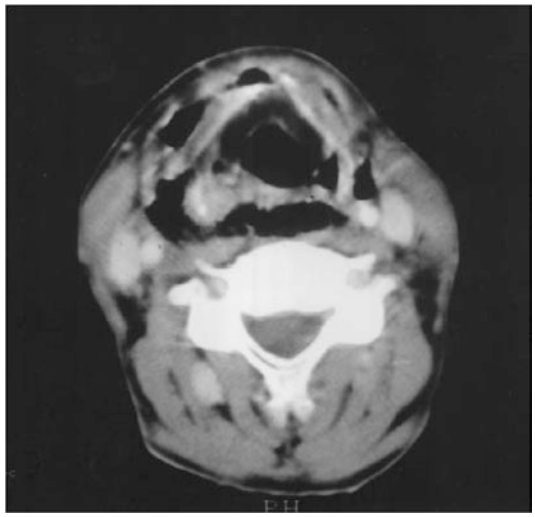

Fig. 18.1 Contrast-enhanced computed tomography scan of the neck in patient with Lemierre's syndrome. Gas is present within the anterior neck compatible with infection with gas-forming organisms. There is also a retropharyngeal space abscess. (Reproduced from Karkos PD, Karkanevatos A, Panagea S, Dingle A, Davies JE. Lemierre's syndrome: how a sore throat can end in disaster. Eur J Emerg Med 2004;11:228–30 [39], with permission from Wolters Kluwer Health)

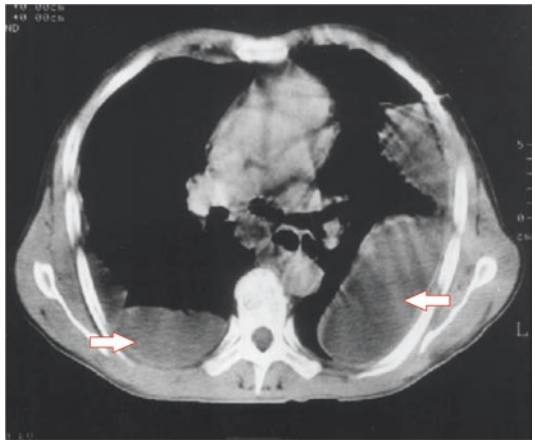

Fig. 18.2 Contrast-enhanced computed tomography scan of the chest. Bilateral empyemas are evident (arrows), and there is also gas in the mediastinum. (From Karkos PD, Karkanevatos A, Panagea S, Dingle A, Davies JE. Lemierre's syndrome: how a sore throat can end in disaster. Eur J Emerg Med 2004;11:228–30 [39], with permission from Wolters Kluwer Health)

Differential Diagnosis

Careful clinical examination, evaluation of the history and presenting symptoms, isolation of *F. necrophorum* in blood cultures, and radiological evidence of the disease can lead to the diagnosis. All the above can also help differentiate Lemierre's syndrome from other infections such as viral pharyngitis, infectious mononucleosis, and pneumonia [5].

Treatment

Antibiotic treatment is the first-line treatment for Lemierre's syndrome. *Fusobacterium necrophorum* is usually susceptible to penicillin, clindamycin, metronidazole, and chloramphenicol. There is a variable response to second and third-generation cephalosporins, and the organism is resistant to macrolides. Penicillin treatment can potentially fail due to β-lactamase production of the infecting microorganism, so a beta-lactam, beta-lactamase combination (e.g., ampicillin-sulbactam), or penicillin plus metronidazole should be prescribed, rather than penicillin alone. Based on the literature, metronidazole is associated with the most rapid response [3, 43], and the addition of metronidazole to any antibiotic regimen should be considered even in cases being treated with a beta-lactam, beta-lactamase combination (e.g., ampicillin-sulbactam). Although clindamycin has activity against most *Fusobacterium* species, up to 10% of isolates may be resistant (see Chap. 2). In addition, many cases of Lemierre's syndrome are due to mixed bacterial infections that include mouth flora streptococci that also may be resistant to clindamycin. Therefore, monotherapy with clindamycin is not recommended. Monotherapy with metronidazole is also inadvisable because of the possibility of a mixed infection; metronidazole will treat only Gram-negative anaerobes. A combination of penicillin and metronidazole is usually recommended [27, 44]. An alternative therapy for penicillin-allergic patients is a carbapenem (e.g., meropenem).

There are no available guidelines regarding the optimal duration of antibiotic treatment, but all patients should receive initial intravenous therapy. Therapy is usually given for a total of 4–6 weeks. Armstrong et al. in their literature review demonstrated that antibiotic treatment duration ranges from 7 to 84 days, with a median of 42 days of therapy [10]. Antibiotics are usually given as initial intravenous therapy (minimum 2 weeks) followed by several weeks of oral antibiotics. However, the optimal course should be individualized for each patient because there is significant variability in the severity of illness and the location and severity of any metastatic infection. Input from an infectious disease specialist in determining the optimal antibiotic choice and duration of treatment is recommended.

The role of anticoagulation in Lemierre's syndrome remains controversial. Although only a minority of patients receives anticoagulation (21%), most patients eventually do well and recover [10]. The risk of thrombosis progression or recurrence is low and this must be weighed against the risk of bleeding from anticoagulation [45]. Anticoagulation should probably be reserved for patients with evidence of retrograde progression of the internal jugular vein thrombus (e.g., to the cavernous sinus). Anticoagulation is usually continued for 3 months, once started [10].

Surgical intervention plays a significant role in the treatment of Lemierre's syndrome. Drainage of any accessible abscesses is essential. That may include neck, parapharyngeal space and peritonsillar abscesses, and distant septic complications, such as lung empyema, septic arthritis, or cerebral abscess [14, 17]. Ligation or resection of the internal jugular vein is a last resort and rarely required: it may be indicated in patients with persistent septic embolization despite aggressive antibiotic therapy [46].

Morbidity and Mortality

The mortality rate in Lemierre's report, published during the pre-penicillin era, was 90% (18 of the 20 patients included in the study group subsequently died) [2]. In more recent studies, mortality is estimated around 5%. Lemierre's syndrome leads to significant morbidity, resulting in prolonged in-hospital and/or intensive care unit stay in about 52% of the cases [3].

Conclusion

Lemierre's syndrome is rare and usually consists of the triad of recent oropharyngeal infection (e.g., pharyngitis, tonsillitis, peritonsillar abscess), septic jugular venous thrombophlebitis, and cultures of blood or abscesses positive for *F. necrophorum*. Many cases have septic pulmonary emboli and patients may present with respiratory symptoms such as dyspnea and pleuritic chest pain. Metronidazole has excellent activity against *F. necrophorum* but does not treat other organisms that may be present in a mixed infection, so an antibiotic combination such as intravenous penicillin plus metronidazole is usually given. Lemierre's syndrome has a 5% mortality even in the antibiotic era, so early diagnosis and appropriate treatment are essential.

References

1. Courmont P, Cade A. Sur une septico-pyohemie de l'homme simulant la peste et causee par un streptobacille anaerobie. Arch Med Exp Anat Pathol. 1900;12:393–418.
2. Lemierre A. On certain septicaemias due to anaerobic organisms. Lancet. 1936;227:701–3.
3. Karkos PD, Asrani S, Karkos CD, Leong SC, Theochari EG, Alexopoulou TD, et al. Lemierre's syndrome: a systematic review. Laryngoscope. 2009;119:1552–9.
4. Chirinos JA, Lichtstein DM, Garcia J, Tamariz LJ. The evolution of Lemierre syndrome: report of 2 cases and review of the literature. Medicine (Baltimore). 2002;81:458–65.
5. Riordan T, Wilson M. Lemierre's syndrome: more than a historical curiosa. Postgrad Med J. 2004;80:328–34.
6. Bartlett JG, Finegold SM. Anaerobic pleuropulmonary infections. Medicine (Baltimore). 1972;51:413–50.
7. Eilbert W, Singla N. Lemierre's syndrome. Int J Emerg Med. 2013;6:40.
8. Hagelskjaer LH, Prag J, Malczynski J, Kristensen JH. Incidence and clinical epidemiology of necrobacillosis, including Lemierre's syndrome, in Denmark 1990–1995. Eur J Clin Microbiol Infect Dis. 1998;17:561–5.

9. Vogel LC, Boyer KM. Metastatic complications of Fusobacterium necrophorum sepsis: two cases of Lemierre's postanginal septicemia. Am J Dis Child. 1980;134:356–8.
10. Armstrong AW, Spooner K, Sanders JW. Lemierre's syndrome. Curr Infect Dis Rep. 2000;2:168–73.
11. Stokroos RJ, Manni JJ, de Kruijk JR, Soudijn ER. Lemierre syndrome and acute mastoiditis. Arch Otolaryngol Head Neck Surg. 1999;125:589–91.
12. Sinave CP, Hardy GJ, Fardy PW. The Lemierre syndrome: suppurative thrombophlebitis of the internal jugular vein secondary to oropharyngeal infection. Medicine (Baltimore). 1989;68:85–94.
13. Roberts DS. The pathogenic synergy of Fusiformis necrophorus and Corynebacterium pyogenes. I. Influence of the leucocidal exotoxin of F. necrophorus. Br J Exp Pathol. 1967;48:665.
14. Leugers CM, Clover R. Lemierre syndrome: postanginal sepsis. J Am Board Fam Pract Am Board Family Med. 1995;8:384–91.
15. Tadepalli S, Stewart GC, Nagaraja TG, Narayanan SK. Human Fusobacterium necrophorum strains have a leukotoxin gene and exhibit leukotoxic activity. J Med Microbiol. 2008;57:225–31.
16. Riordan T. Human infection with Fusobacterium necrophorum (Necrobacillosis), with a focus on Lemierre's syndrome. Clin Microbiol Rev. 2007;20:622–59.
17. Lustig LR, Cusick BC, Cheung SW, Lee KC. Lemierre's syndrome: two cases of postanginal sepsis. Otolaryngol Neck Surg. 1995;112(6): 767–72.
18. Forrester LJ, Campbell BJ, Berg JN, Barrett JT. Aggregation of platelets by Fusobacterium necrophorum. J Clin Microbiol. 1985;22:245–9.
19. Kanoe M, Yamanaka M, Inoue M. Effects of Fusobacterium necrophorum on the mesenteric microcirculation of guinea pigs. Med Microbiol Immunol. 1989;178:99–104.
20. Hall C. Sepsis following pharyngeal infections. Ann Otol Rhinol Laryngol. 1939;48:905–25.
21. Cosgrove EF, Colodny SM, Pesce RR. Adult respiratory distress syndrome as a complication of postanginal sepsis. Chest. 1993;103:1628–9.
22. Møller K, Dreijer B. Post-anginal sepsis (Lemierre's disease): a persistent challenge. Presentation of 4 cases. Scand J Infect Dis. 1997;29:191–4.
23. Wolf RFE, Konings JG, Prins TR, Weits J. Fusobacterium pyomyositis of the shoulder after tonsillitis: report of a case of Lemierre's syndrome. Acta Orthop Scand. 1991;62(6):595.
24. Jones TH, Bergvall V, Bradshaw JP. Carotid artery stenoses and thrombosis secondary to cavernous sinus thromboses in Fusobacterium necrophorum meningitis. Postgrad Med J. 1990;66:747–50.
25. Agarwal R, Arunachalam PS, Bosman DA. Lemierre's syndrome: a complication of acute oropharyngitis. J Laryngol Otol. 2000;114:545–7.
26. Epstein M, Pearson AD, Hudson SJ, Bray R, Taylor M, Beesley J. Necrobacillosis with pancytopenia. Arch Dis Child. 1992;67:958–9.
27. Eykyn SJ. Necrobacillosis. Scand J Infect Dis Suppl. 1988;62:41–6.
28. Carrie S, Fenton PA. Necrobacillosis—an unusual case of pharyngotonsillitis. J Laryngol Otol. 1994;108:1097–8.
29. Chand DH, Brady RC, Bissler JJ. Hemolytic uremic syndrome in an adolescent with Fusobacterium necrophorum bacteremia. Am J Kidney Dis. 2001;37:e22–1.
30. Ellis GR, Gozzard DI, Looker DN, Green GJ. Postanginal septicaemia (Lemmiere's disease) complicated by haemophagocytosis. J Infect. 1998;36:340–1.
31. Potter MN, Drysdale HC, Price PA, Buck AC. Disseminated intravascular coagulation with Fusobacterium necrophorum septicaemia. Postgrad Med J. 1988;64:155–6.
32. Wright WF, Shiner CN, Ribes JA. Lemierre syndrome. South Med J. 2012;105:283–8.
33. Alvarez A, Schreiber JR. Lemierre's syndrome in adolescent children—anaerobic sepsis with internal jugular vein thrombophlebitis following pharyngitis. Pediatrics. 1995;96:354–9.
34. Gudinchet F, Maeder P, Neveceral P, Schnyder P. Lemierre's syndrome in children: high-resolution CT and color Doppler sonography patterns. Chest. 1997;112:271–3.
35. Carlson ER, Bergamo DF, Coccia CT. Lemierre's syndrome: two cases of a forgotten disease. J Oral Maxillofac Surg. 1994;52:74–8.
36. Gong J, Garcia J. Lemierre's syndrome. Eur Radiol. 1999;9:672–4.
37. Holzmann D, Huisman TAGM, Linder TE. Lateral dural sinus thrombosis in childhood. Laryngoscope. 1999;109:645–51.
38. Albertyn LE, Alcock MK. Diagnosis of internal jugular vein thrombosis. Radiology. 1987;162:505–8.
39. 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.
40. Screaton NJ, Ravenel JG, Lehner PJ, Heitzman ER, Flower CDR. Lemierre syndrome: forgotten but not extinct—report of four cases. Radiology. 1999;213:369–74.
41. Golpe R, Marin B, Alonso M. Lemierre's syndrome (necrobacillosis). Postgrad Med J. 1999;75:141–4.
42. Mane S, Torres M, Buges J, Rivas A, Bruno C, Rodriguez E, et al. Scintigraphic demonstration of jugular obstruction in a case of Lemierre syndrome. Clin Nucl Med. 1992;17:233–5.
43. Appelbaum PC, Spangler SK, Jacobs MR. Beta-lactamase production and susceptibilities to amoxicillin, amoxicillin-clavulanate, ticarcillin, ticarcillin-clavulanate, cefoxitin, imipenem, and metronidazole of 320 non-Bacteroides fragilis Bacteroides

isolates and 129 fusobacteria from 28 US center. Antimicrob Agents Chemother. 1990;34:1546–50.
44. Agrafiotis M, Moulara E, Chloros D, Tsara V. Lemierre syndrome and the role of modern antibiotics and therapeutic anticoagulation in its treatment. Am J Emerg Med. 2015;33:733.e3–4.
45. Cupit-Link MC, Nageswara Rao A, Warad DM, Rodriguez V. Lemierre syndrome: a retrospective study of the role of anticoagulation and thrombosis outcomes. Acta Haematol. 2016;137:59–65.
46. Venkataraman MT, Policar M. Fever, sore throat, and pulmonary infiltrates in a 20-year-old man. Chest. 1997;112:268–70.