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Complex Lemierre syndrome with multisystemic abscesses

Johan Bourgeaud [1], Benoît Delabays [1], Lorena Van den Bogaart [2], Damian Ratano [3]

[1]Internal Medicine, CHUV, Lausanne, Switzerland
[2]Infectious Diseases, CHUV, Lausanne, Switzerland
[3]Adults Intensive Care, CHUV, Lausanne, Switzerland

Correspondence to
Dr Johan Bourgeaud;
johan.bourgeaud@chuv.ch

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SUMMARY

We present here the challenging case of severe Lemierre syndrome in a healthy woman in her late twenties, whose clinical presentation was characterised by lung abscesses and disseminated systemic abscesses in the brain, the abdomen and the soft-tissues, as a likely consequence of a patent foramen ovale. Blood cultures were positive for *Fusobacterium necrophorum* and a right lingual vein thrombosis was detected at a late stage when the patient developed a septic shock. Initial antimicrobial therapy with metronidazole and ceftriaxone was modified to meropenem due to progressive worsening. The patient underwent laparoscopy and neurosurgical drainage of a cerebral abscess. She spent many days in the intensive care unit and recovered fully after 6 weeks on meropenem therapy. Although considered rare, the incidence of Lemierre syndrome, a potentially life-threatening condition, is increasing. The clinician should promptly recognise and treat it while being aware of its potential atypical presentations.

BACKGROUND

Lemierre syndrome is traditionally defined by an internal jugular vein thrombophlebitis secondary to an oropharyngeal infection caused by bacterial agents (most frequently *Fusobacterium necrophorum*), a bacteriaemia and septic emboli (typically in the lungs).[1–3] It has been called the 'forgotten disease' because of its rarity in the era of modern antibiotic therapy.[4] However, there is currently evidence of a growing incidence of the disease.[5 6] If not promptly identified and treated, Lemierre syndrome can be life-threatening and lead to lifelong consequences. There is no standard of care as evidence is based on case series.

We report here the case of complex and severe Lemierre syndrome, complicated by multiple abscesses at various extrapulmonary locations that required a multidisciplinary approach combining surgery, intensive care, internal medicine and infectious disease specialists.

CASE PRESENTATION

A previously healthy woman in her late twenties first consulted an emergency department because of a 2-day history of fever, sore throat, cough with bloody sputum, odynophagia and vomiting. She appeared well and the physical examination only showed bilateral cervical adenopathy and exudative tonsils. Rapid antigenic detection test for group A Streptococci and reverse transcription PCR for SARS-CoV-2 were negative. She was discharged home with symptomatic treatment for suspected viral pharyngitis.

Two days later, she consulted another emergency department because of persistent fever and new-onset epigastric pain despite improving sore throat. She denied past or current drug use.

On examination, she appeared very unwell, blood pressure was 100/60 mm Hg, heart rate was 110/min and body temperature was 35.8°C. Oropharyngeal examination showed a small right submandibular adenopathy, an erythematous throat and bilateral tonsillitis. Epigastric tenderness, hepatomegaly and right hypochondrium pain were present. A right gluteal pain was elicited on palpation without cutaneous lesion or palpable collection.

The patient was transferred to our tertiary referral hospital and admitted for further management of suspected abdominal sepsis (Sequential Organ Failure Assessment [SOFA] score=7 points).[7]

INVESTIGATIONS

Laboratory results on admission and on day 2 are shown in table 1. Initial workup ruled out viral hepatitis, syphilis and HIV infections. Cytomegalovirus and Epstein-Barr virus (EBV) serologies confirmed past infections. Nucleic acid amplification tests for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* (urine and vaginal swab) and for *Leptospira* spp (blood) were negative.

On admission, a contrast-enhanced CT of the chest, abdomen and pelvis showed several pulmonary nodular lesions compatible with septic emboli—the largest one in the right upper lobe—hepatosplenomegaly, periportal oedema and free abdominal fluid with a 3 cm collection in the rectouterine pouch (figures 1 and 2). A neck CT performed on the same day was negative for internal jugular thrombosis and evidenced only mild swelling of the left tonsil.

Gynaecological examination and endovaginal ultrasound were normal. Because the sepsis was suspected to be of abdominal origin, a diagnostic laparoscopy was performed on day 2. It showed fibrinous adhesions in the hepatic area (perihepatitis) as well as purulent peritonitis in the rectouterine pouch. Both 16S rRNA performed on abdominal fluid and fibrinous adhesions were negative. Blood cultures resulted positive for *F. necrophorum* in 29 hours.

Postoperatively, the patient developed acute delirium and acute pulmonary oedema, attributed to aggressive fluid resuscitation and sepsis-associated capillary leak syndrome. She was transferred to

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Table 1 Patient's blood results on admission and on day 2

	Value on admission	Value on day 2	Reference range
White cell count (10^9/L)	8.2	13.9	4–10
Lymphocytes (10^9/L)	0.7	1.3	1.5–4.0
Neutrophils (10^9/L)	7	11.4	1.8–7.5
Polynuclear neutrophils (%)	85	82	40–75
Platelets (10^9/L)	60	55	150–450
C reactive protein (mg/dL)	294	242	<5
Procalcitonin (µg/L)	37.7	6.1	If >2, compatible with bacterial infection*
Creatinine serum blood level (µg/L)	114	57	44–80
Asparate-aminotransferase (U/L)	142	17	9–32
Gamma-glutamyltransferase (U/L)	148	125	6–42
Alkaline phosphatase (U/L)	78	168	36–108
Total bilirubin (µg/L)	3	21	0–21

*According to the Department of Laboratory Medicine and Pathology, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland.

the intensive care unit for non-invasive ventilation, high-flow nasal oxygen and vasopressor support. A repeated total-body contrast-enhanced CT scan on day 3 showed a right lingual vein thrombosis (figure 3) and a right precentral cortical brain lesion (figure 4). On day 6, due to persistent fever and abdominal pain, a contrast-enhanced abdominal-CT was repeated. It showed a large right intramuscular gluteal abscess (40×80×15 mm) without evidence of connections with the collection previously described in the rectouterine pouch (figure 5). Growing pulmonary lesions were also noted at this time. The gluteal abscess was surgically drained. Broad range 16S rRNA PCR performed on drainage material returned positive for *F. necrophorum*. Brain MRI showed a right frontal abscess of 9×11 mm (figure 4). Brain MRI was repeated 8 days later because of new-onset left central facial palsy with dysarthria and showed an increase in the size brain abscess (16×18 mm). The patient underwent craniotomy and 16S rRNA confirmed *F. necrophorum* infection.

Transthoracic and transoesophageal cardiac ultrasound were performed to exclude an infectious endocarditis. Ventricular function and morphology as well as valvular apparatus were normal. A patent foramen ovale (PFO) was documented and confirmed by a bubble study.

DIFFERENTIAL DIAGNOSIS

Lemierre syndrome was considered in the differential diagnosis because of the history of sore throat, clinical signs of pharyngotonsillitis and the presence of a possible septic embolisation in the lungs. Abdominal symptoms have been commonly reported in patients with typical Lemierre syndrome initiated by a pharyngeal infection.[2 5] However, primary infection sites can be found in the liver and be associated with portal vein thrombosis (pylephlebitis),[8–10] or in gynaecological organs such as the vagina, cervix and uterus (with or without intrauterine device) and be associated with pelvic veins thrombosis.[11–16] Although not specific, thrombocytopaenia, as observed in the present case, is a common feature of Lemierre syndrome.[2 5] There was no evidence of disseminated intravascular coagulation.

The presence of a perihepatitis with periportal oedema and a 3 cm collection in the rectouterine pouch initially raised the suspicion of a pelvic inflammatory disease (PID) complicated by Fitz-Hugh-Curtis syndrome (FHCS), an inflammation of the liver capsule associated with chronic PID.[17 18] FHCS starts by ascending infection from the cervix or the vagina to the endometrium. Laparoscopy is the gold standard for FHCS diagnosis.

An infectious endocarditis was also initially considered. Endocarditis caused by *F. necrophorum* is exceptional with only 10 cases reported in the literature since 1980.[19]

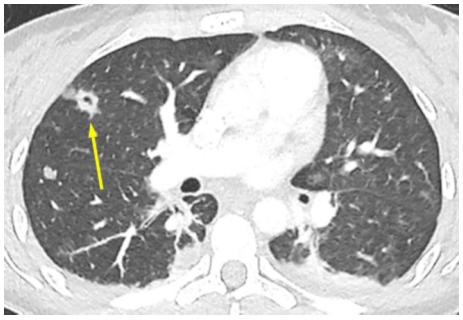

Figure 1 Chest CT scan showing pulmonary nodules, one of which in the right lung is excavated (yellow arrow), consistent with septic pulmonary emboli.

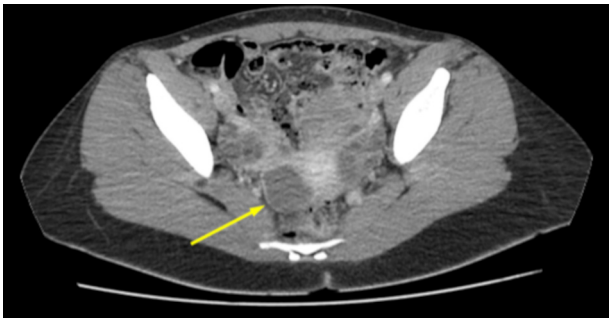

Figure 2 Contrast-enhanced abdominal CT scan showing a pelvic abscess (yellow arrow).

TREATMENT

According to our institutional guidelines and because of the suspicion of abdominal sepsis, empiric antibiotic therapy with piperacillin/tazobactam was promptly initiated on admission. As the laparoscopy suggested PID, the treatment was then modified to ceftriaxone, metronidazole and doxycycline. After identification of *F. necrophorum* in the blood cultures and exclusion of *C. trachomatis*, doxycycline was stopped. Ceftriaxone and metronidazole were continued based on susceptibility test (*F.*

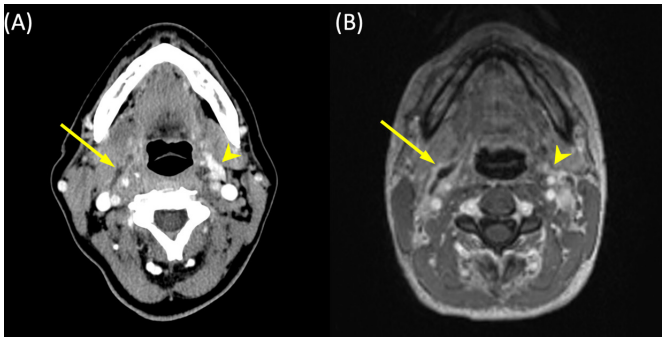

Figure 3 Contrast-enhanced neck CT scan (A) and contrast-enhanced T1-weighted MRI (B) showing a right lingual vein thrombosis (yellow arrow). In contrast, there is normal enhancement of the left lingual vein (yellow arrowhead).

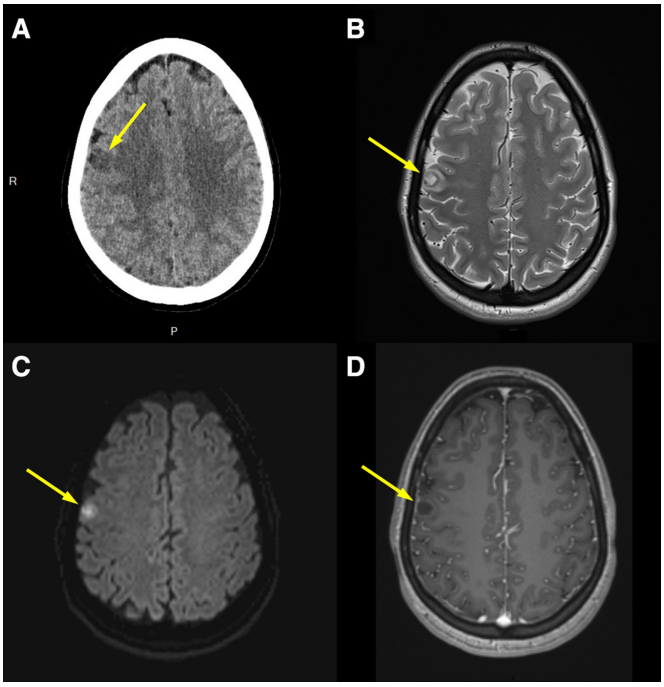

Figure 4 The typical radiological features of cerebral abscess are shown in the right frontal cortex (yellow arrows): (A) hypodensity on non-contrast CT of the brain, (B) T1-weighted with contrast MR sequence and rim enhancement, (C) diffusion-weighted MR sequence showing restricted diffusion and (D) hyperintense with a hypointense rim and peripheral oedema on T2-weighted MR sequence.

necrophorum isolate was sensitive to penicillins, carbapenems, clindamycin, moxifloxacin and metronidazole).

The pelvic and gluteal abscesses were surgically drained. Regarding the right frontal brain abscess, conservative management was initially attempted. However, due to the progression of the abscess and the onset of neurological symptoms (left facial palsy and dysarthria) on effective antibiotic therapy, a craniotomy was performed, and ceftriaxone and metronidazole were replaced by meropenem. Only a partial drainage of the abscess was possible because of the critical localisation near the motor cortex.

OUTCOME AND FOLLOW-UP

The patient was discharged home after 26 days. Meropenem was administered for 6 weeks after the neurosurgical intervention without any complications.

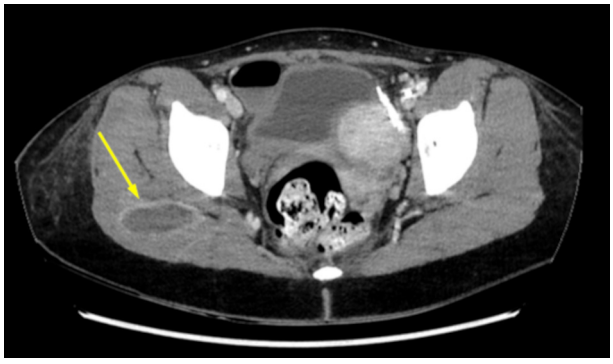

Figure 5 Contrast-enhanced abdominal CT-scan showing an abscess within the right gluteus maximus (yellow arrow).

A thorax and abdominal contrast-enhanced CT 1 week after initiation of meropenem showed a regression of the pulmonary lesions and complete regression of the gluteal abscess.

Neurological recovery was excellent after speech therapy. Cerebral MRI showed a complete regression of the abscess 1 month after surgery. At 6-month follow-up (4 months after cessation of antibiotic therapy), the patient was doing well and had no complaints. At that time, brain MRI showed complete healing of the cerebral abscess.

DISCUSSION

Local infections with anaerobic organisms leading to thrombophlebitis with distant embolisation were first described by Lemierre.[20] *F. necrophorum* is the most common aetiological agent of Lemierre syndrome, but other organisms from the oral flora can be found, such as Streptococci and less frequently *Staphylococcus aureus*.[1 3] *F. necrophorum* is classified into two subspecies: subsp. *necrophorum*, involved in most veterinary infections, and subsp. *funduliforme*, responsible for most human cases. In vitro studies show that *F. necrophorum* subsp. *funduliforme* is able to evade complement attack by binding factor H, and to activate the contact system, suggesting a potential role of these mechanisms in the virulence of the pathogen.[21 22] However, the exact mechanisms used by *F. necrophorum* subsp. *funduliforme* to escape human host defence and cause severe invasive infections remain largely unexplored. Septic clots are usually observed within 1–3 weeks after primary infection.[5 23 24]

The overall annual incidence of Lemierre syndrome, defined as a documented *F. necrophorum* infection with primary foci in the head and neck, and dissemination to a nearby region (eg, mastoiditis) and/or distal regions (eg, pulmonary septic emboli), has been reported to be 3.6 per million persons per year in the Danish general population and 14.4 cases per million in people aged 15–24 years old.[6] The reasons for the characteristic age distribution, with a predilection for young individuals, remain unclear but might be due to its possible association with EBV-related infectious mononucleosis, which presumably facilitates the entry of *Fusobacterium* inside the connective tissue.[25] Recent epidemiological data suggest an increased incidence of invasive *Fusobacterium* spp infections from 2010 to 2017.[5] This trend might be explained by several factors: a decrease in antibiotic prescriptions for upper airway tract infections, more sensitive laboratory techniques for pathogen detection and decreased rates of tonsillectomy.[26 27]

Septic thrombosis is traditionally described as occurring in the internal jugular vein. In our patient, we identified a thrombosis of the right lingual vein at a relatively late stage, after 72 hours of hospitalisation. We hypothesised that a jugular thrombosis might have occurred earlier and could have already embolised at the time the patient underwent radiologic exploration. Indeed, it has been suggested that the finding of a jugular vein thrombosis at the time of clinical presentation may not be a sensitive diagnostic criterion for Lemierre syndrome.[28] The lung is the most common site of embolisation, accounting for up to 85% of the cases.[29] Our patient presented other uncommon embolisation sites. Muscle abscesses have been reported in rare cases, resulting generally from contiguous thrombophlebitis and associated with fasciitis or arthritis.[30 31] The central nervous system is usually not affected because of downstream venous embolisation of the septic emboli in the pulmonary circulation. Only 3%–5% of patients had brain abscesses in a review of 251 infections caused by *Fusobacterium* spp (but not necessarily with

Lemierre syndrome).[1] Mechanisms causing epidural or brain abscesses in Lemierre syndrome include retrograde intracranial extension of the septic thrombosis from the internal jugular vein or contiguous dissemination from an otogenic source of infection.[2 29] In the present case, we postulated that the presence of a PFO contributed to an arterial haematogenous diffusion of *F. necrophorum* and extensive systemic embolisation, a mechanism proposed to explain septic emboli in the arterial circulation in Lemierre syndrome.[32] To the best of our knowledge, only two cases of Lemierre syndrome with brain abscess and echocardiographic evidence of right-to-left shunt through a PFO have been reported in the literature to date.[33 34] Some cases of ischaemic strokes due to arterio-arterial septic embolism from the internal carotid artery (in contiguity with the internal jugular vein) have been described.[32 35] In the present case, there was no evidence of ischaemic stroke or cervical arterial defects.

Recent studies show that *F. necrophorum* isolates are generally susceptible to penicillin with a resistance rate between 0.7% and 2% and no resistance to clindamycin or metronidazole have been identified.[5 24] Our patient demonstrated progression of cerebral abscess despite effective therapy with high doses of metronidazole. The increase in size on cerebral MRI was explained probably by the need of surgical drainage in order to control the infection rather than the development of antibiotic resistance as the negative culture on the abscess may suggest. However, the therapy was changed to meropenem with a favourable outcome after neurosurgical drainage.

The benefit of anticoagulation in Lemierre syndrome is debated in the absence of interventional studies. A post hoc analysis in a population-based observational study in Sweden found no clear indication of a benefit, nor major risks in patients with anticoagulation therapy.[36] In case series, 20%–50% of the patients with Lemierre syndrome received anticoagulant therapy.[4 37] In our case, we did not pursue anticoagulation therapy because of the cerebral abscess. There were no adverse thrombotic events during the follow-up.

Learning points

- Lemierre syndrome is a re-emerging life-threatening condition requiring early recognition. Clinical presentation can include disseminated extrapulmonary septic emboli in the presence of a patent foramen ovale.
- Empiric antibiotic therapy covering *Fusobacterium* spp and oral Streptococci (such as ceftriaxone and metronidazole) should be initiated promptly, without waiting for the identification of a thrombosis as traditionally portrayed.
- A multidisciplinary approach, including the early involvement of critical care and surgery specialists, is crucial for optimal management.

Twitter Benoît Delabays @BenDelabay and Damian Ratano @RatanoD

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ORCID iDs
Johan Bourgeaud http://orcid.org/0000-0001-9862-4652
Benoît Delabays http://orcid.org/0000-0003-1964-9099
Lorena Van den Bogaart http://orcid.org/0000-0001-8027-7218
Damian Ratano http://orcid.org/0000-0002-2556-9741

REFERENCES

1 Kuppalli K, Livorsi D, Talati NJ, *et al*. Lemierre's syndrome due to fusobacterium necrophorum. *Lancet Infect Dis* 2012;12:808–15.
2 Riordan T. Human infection with Fusobacterium necrophorum (necrobacillosis), with a focus on Lemierre's syndrome. *Clin Microbiol Rev* 2007;20:622–59.
3 Osowicki J, Kapur S, Phuong LK, *et al*. The long shadow of lemierre's syndrome. *J Infect* 2017;74 Suppl 1:S47–53.
4 Karkos PD, Asrani S, Karkos CD, *et al*. Lemierre's syndrome: a systematic review. *Laryngoscope* 2009;119:1552–9.
5 Nygren D, Holm K. Invasive infections with fusobacterium necrophorum including lemierre's syndrome: an 8-year swedish nationwide retrospective study. *Clin Microbiol Infect* 2020;26:1089.
6 Hagelskjaer Kristensen L, Prag J. Lemierre's syndrome and other disseminated Fusobacterium necrophorum infections in Denmark: a prospective epidemiological and clinical survey. *Eur J Clin Microbiol Infect Dis* 2008;27:779–89.
7 Vincent J-L, Moreno R, Takala J, *et al*. The SOFA (sepsis-related organ failure assessment) score to describe organ dysfunction/failure. *Intensive Care Med* 1996;22:707–10.
8 Mellor TE, Mitchell N, Logan J. Lemierre's syndrome variant of the gut. *BMJ Case Rep* 2017;2017:bcr2017221567.
9 Radovanovic N, Dumic I, Veselinovic M, *et al*. *fusobacterium necrophorum* subsp. *necrophorum* liver abscess with pylephlebitis: an abdominal variant of lemierre's syndrome. *Case Rep Infect Dis* 2020;2020:9237267.
10 Shahani L, Khardori N. Fusobacterium necrophorum -- beyond lemierres syndrome. *BMJ Case Rep* 2011;2011:bcr0720114527.
11 Hedengran KK, Hertz J. Lemierre's syndrome after evacuation of the uterus: a case report. *Clin Case Rep* 2014;2:60–1.
12 Huynh-Moynot S, Commandeur D, Danguy des Déserts M, *et al*. Septic shock Fusobacterium necrophorum from origin gynecological at complicated an acute respiratory distress syndrome: a variant of Lemierre's syndrome. *Ann Biol Clin (Paris)* 2011;69:202–7.
13 Pol H, Guerby P, Duazo Cassin L, *et al*. Dangerous liaisons: pelvic variant of Lemierre syndrome by right common iliac vein thrombophlebitis after sexual intercourse. *J Low Genit Tract Dis* 2017;21:e37–9.
14 Reymond B, Huette P, Roger P-A, *et al*. Fatal fusobacterium necrophorum infection with gynecological lemierre's syndrome. *Med Mal Infect* 2019;49:72–4.
15 Treszezamsky AD, Molina Boero MF, Mehta I. Cervical conization complicated by sepsis with lung and liver abscesses. *J Low Genit Tract Dis* 2010;14:130–3.
16 Thakur A, Chen W. An atypical presentation of Lemierre syndrome of urogenital source. *IDCases* 2021;26:e01314.
17 Brunham RC, Gottlieb SL, Paavonen J. Pelvic inflammatory disease. *N Engl J Med* 2015;372:2039–48.
18 Shikino K, Ikusaka M. Fitz-hugh-curtis syndrome. *BMJ Case Rep* 2019;12:e229326.
19 Sato K, Matsubara T, Imai S, *et al*. Fusobacterium necrophorum endocarditis with liver abscesses: a case report and review of the literature. *Intern Med* 2021;60:2445–9.
20 Lemierre A. On certain septicæmias due to anaerobic organisms. *The Lancet* 1936;227:701–3.
21 Friberg N, Carlson P, Kentala E, *et al*. Factor H binding as a complement evasion mechanism for an anaerobic pathogen, Fusobacterium necrophorum. *J Immunol* 2008;181:8624–32.
22 Holm K, Frick I-M, Björck L, *et al*. Activation of the contact system at the surface of Fusobacterium necrophorum represents a possible virulence mechanism in lemièrre's syndrome. *Infect Immun* 2011;79:3284–90.
23 Armstrong AW, Spooner K, Sanders JW. Lemierre's syndrome. *Curr Infect Dis Rep* 2000;2:168–73.
24 Brazier JS, Hall V, Yusuf E, *et al*. Fusobacterium necrophorum infections in England and Wales 1990-2000. *J Med Microbiol* 2002;51:269–72.

25 Chacko EM, Krilov LR, Patten W, *et al*. Lemierre's and lemierre's-like syndromes in association with infectious mononucleosis. *J Laryngol Otol* 2010;124:1257–62.
26 Schroeder AM, Lewis SS, Sahmoun AE, *et al*. Antibiotic utilization for adult acute respiratory tract infections in united states emergency departments. *Am J Emerg Med* 2021;47:66–9.
27 Sanders O, Bolton L, Nemeth Z, *et al*. A 4-year retrospective study of tonsillectomy rate and admission rate of tonsillitis and complications in the East of England and nationally. *Eur Arch Otorhinolaryngol* 2021;278:2613–8.
28 Valerio L, Corsi G, Sebastian T, *et al*. Lemierre syndrome: current evidence and rationale of the bacteria-associated thrombosis, thrombophlebitis and lemierre syndrome (battle) registry. *Thromb Res* 2020;196:494–9.
29 Lee W-S, Jean S-S, Chen F-L, *et al*. Lemierre's syndrome: a forgotten and re-emerging infection. *J Microbiol Immunol Infect* 2020;53:513–7.
30 Laurencet ME, Rosset-Zufferey S, Schrenzel J. Atypical presentation of Lemierre's syndrome: case report and literature review. *BMC Infect Dis* 2019;19:868.
31 Held MR, Kotler H, Sneller H, *et al*. Lemierre's syndrome presenting as multifocal pyomyositis in a young child. *Pediatr Infect Dis J* 2018;37:e142–4.
32 Pleming W, Barco S, Voci D, *et al*. Cardiac and cerebral arterial complications of Lemierre syndrome: results from a systematic review and individual patient data meta-analysis. *Hamostaseologie* 2022;42:261–7.
33 Aljohaney A, McCarthy A. Lemierre's syndrome with paradoxical emboli. *Intern Med* 2010;49:1433–6.
34 Howley F, O'Doherty L, McEniff N, *et al*. Late presentation of "lemierre's syndrome": how a delay in seeking healthcare and reduced access to routine services resulted in widely disseminated *fusobacterium necrophorum* infection during the global COVID-19 pandemic. *BMJ Case Rep* 2020;13:e239269.
35 Rahimi D, Langkilde AR, Iversen HK, *et al*. Lemierre's syndrome with stroke and stenosis of the internal carotid artery suggesting focal vasculitis. *J Neurol Sci* 2020;409:116632.
36 Nygren D, Elf J, Torisson G, *et al*. Jugular vein thrombosis and anticoagulation therapy in Lemierre's syndrome-a post hoc observational and population-based study of 82 patients. *Open Forum Infect Dis* 2021;8:ofaa585.
37 Valerio L, Zane F, Sacco C, *et al*. Patients with Lemierre syndrome have a high risk of new thromboembolic complications, clinical sequelae and death: an analysis of 712 cases. *J Intern Med* 2021;289:325–39.