Case Report

Wien Klin Wochenschr (2008) 120/5–6: 181–183
DOI 10.1007/s00508-008-0937-1

WIENER KLINISCHE WOCHENSCHRIFT
The Middle European Journal of Medicine
Printed in Austria

# Lemierre's syndrome following infectious mononucleosis

**Katja Garimorth**[1], **Jordan Kountchev**[2], **Romuald Bellmann**[2], **Barbara Semenitz**[1], **Günther Weiss**[1], and **Michael Joannidis**[2]

[1] Universitätsklinik für Innere Medizin, Abteilung für Allgemeine Innere Medizin, Innsbruck, Austria
[2] Universitätsklinik für Innere Medizin, Intensivstation, Abteilung für Allgemeine Innere Medizin, Innsbruck, Austria

Received April 12, 2007, accepted after revision November 8, 2007
© Springer-Verlag 2008

**Lemierre-Syndrom nach Infektiöser Mononukleose**

**Zusammenfassung.** Wir berichten über eine 18-jährige Patientin, die nach einem protrahierten Verlauf einer Infektion der oberen Atemwege (Pharyngitis, Sinusitis) mit dem Bild einer respiratorischen Insuffizienz bei septischem Schock auf die medizinische Intensivstation in Innsbruck aufgenommen wurde. Als Fokus entpuppte sich eine abszedierende Pneumonie mit massivem Pleuraempyem. Als verantwortlicher Erreger konnte *Fusobacterium necrophorum* aus dem Pleurapunktat gezüchtet werden. Neben dem Bild eines Multiorganversagens (respiratorische Insuffizienz (ALI), akutes Nierenversagen, disseminierte intravaskuläre Gerinnungsstörung) entwickelte die Patienten eine Schwellung im Bereich des Halses rechts und anschließend eine septische Arthritis des rechten Sternoclaviculargelenks. Eine genaue Anamnese und Erhebung der auswärtigen Vorbefunde erbrachte den Hinweis auf eine vorangegangene Episode einer Epstein-Barr Virus Infektion. Die zuvor gesunde Frau konnte nach einem protrahierten Verlauf nach antibiotischer Therapie und mehrfachen chirurgischen Interventionen in gutem Allgemeinzustand wieder entlassen werden.

Das Lemierre-Syndrom ist eine schwer verlaufende Infektionserkrankung, charakterisiert durch Pharyngitis, Sepsis und Thrombose der Vena Jugularis Interna. Als verantwortlicher Keim wird in der Mehrzahl der Fälle *Fusobacterium necrophorum* gefunden. Eine vorangegangene Infektion mit EBV erleichtert das Eindringen des Keimes aus dem Oropharynx in die Blutbahn.

**Summary.** We report the case of an 18-year-old woman who was admitted to the medical intensive care unit in Innsbruck with severe septic shock and respiratory insufficiency following a prolonged infection of the upper airways (pharyngitis, sinusitis). Abscessing pneumonia and bilateral pleural empyema were diagnosed as focus. Cultures of pleural fluids were positive for Fusobacterium necrophorum. In addition to multiple organ dysfunction syndrome (acute lung injury, acute renal failure, disseminated intravascular coagulation), she developed tenderness in the right neck followed by septic arthritis of the right sternoclavicular joint a few days later. Further history revealed a previous period of infectious mononucleosis (EBV infection). The previously healthy patient eventually made a complete recovery after prolonged treatment in the ICU including antibiotic therapy and multiple surgical interventions and drainage.

Lemierre's syndrome is characterized by severe infection, with pharyngitis, sepsis and thrombosis of the internal jugular vein, and is most frequently associated with upper airway infection with *Fusobacterium necrophorum,* often preceded by infection with Epstein–Barr virus which enables bacteria growing in the oral cavity to invade.

**Key words:** Infectious mononucleosis, Lemierre's syndrome, Fusobacterium necrophorum, multiple organ dysfunction syndrome, osteomyelitis.

## Introduction

Courmont and Cade were the first to publish a case of postanginal septicemia in 1900 [1]. In 1918, Schottmuller further described this syndrome [2], which is also known as necrobacillosis or, more commonly, Lemierre's syndrome [3]. The syndrome usually follows an episode of tonsillitis or pharyngitis, which impairs the mucosal barrier and allows bacteria such as *Fusobacterium necrophorum* to invade the oropharynx and lateral pharyngeal space. These anaerobic bacteria may invade further to form abcesses and penetrate neighboring veins such as the external and internal jugular veins or the peritonsillar veins. This leads to the formation of septic venous thrombi and subsequent development of distant metastatic abscesses [4]. Preceding infectious mononucleosis has been reported to occur in association with *F. necrophorum* infections. Dagan and Powell [5] observed three patients who developed post-anginal anaerobic sepsis following EBV infection. *Fusobacterium* species were isolated from all three, suggesting that the pharyngitis induced by the virus may result in an environment favorable to growth and invasion of these bacteria.

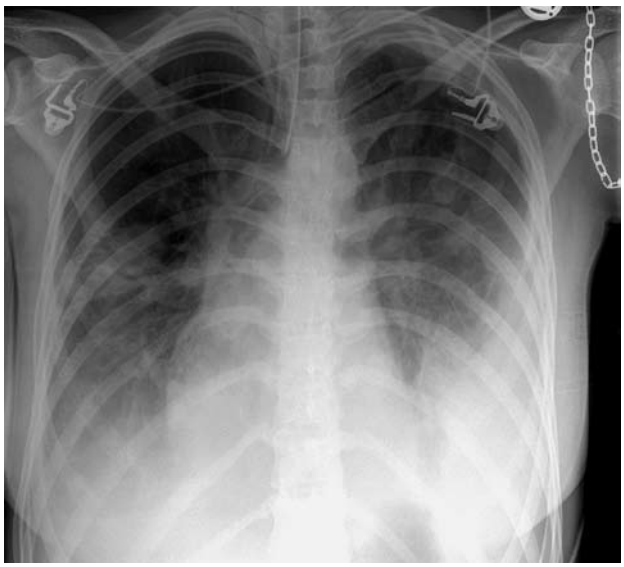

**Fig. 1.** Chest X-ray showing multiple bilateral pneumonic consolidations and pleural effusions

Before the introduction of antibiotics, Lemierre's syndrome was relatively common and had a very rapid and fatal course. Nowadays, it has become a rare disease as a result of the widespread use of antibiotics for pharyngeal infections. Nevertheless, accurate and timely diagnosis is critical because untreated disease is usually fatal and lack of familiarity with this condition may result in missing this important diagnosis [6–8].

## Case report

An 18-year-old woman was admitted to a district hospital with symptoms of malaise, sore throat, high fever, chills and recent collapse. She had a history of influenza-like symptoms lasting for more than a month. Three weeks before admission, a maxillary sinusitis had been treated with amoxicillin/clavulanic acid and rifampicin. On physical examination she presented with pharyngeal inflammation and enlarged painful lymph nodes in the neck. Physical chest examination was normal. Blood pressure was 100/80 mmHg, pulse rate 110 beats/minute, respiratory rate 16 breaths/min, and temperature 39.5 °C. A positive latex-agglutination test led to the diagnosis of Epstein–Barr virus infectious mononucleosis (serologic testing was not done) and antibiotics were withdrawn. Laboratory results at that time revealed a C-reactive protein of 25 mg/dl (normal range <0.7 mg/dl), erythrocyte sedimentation rate of 45 mm/h, platelet count 80,000/µl, white blood count 5,200/µl (90% neutrophils), hemoglobin 12 g/dl and slightly elevated liver enzymes. During the following days the patient's condition gradually worsened. She complained of increasing chest and back pain, shortness of breath, dry cough, bloody nasal discharge and severe headache. Five days after admission dyspnea deteriorated further and there was central cyanosis and nostril breathing. The chest X-ray at that point revealed bilateral pneumonic consolidations and pleural effusions (Fig. 1). There was enlargement of spleen and liver in the abdominal ultrasound examination. Antibiotic treatment was started with a single dose of moxifloxacin (400 mg) and the patient was immediately transferred to our intensive care unit (ICU). On arrival she was in septic shock (blood pressure 80/40 mmHg, pulse rate 140 beats/min, respiratory rate 38 breaths/min, temperature 40.5 °C), which rapidly deteriorated to multiple organ dysfunction syndrome. Laboratory results at that point showed C-reactive protein 27 mg/dl, platelet count 42,000/µl, white blood count 24,000/µl, hemoglobin 12 g/dl, activated partial thromboplastin time 56 sec, prothrombin time 71%, antithrombin III 36%, D-dimer 970 µg/l, arterial blood gases: $PaO_2$ 44 mmHg, $PaCO_2$ 50 mmHg, pH 7.25, $HCO_3$ 21.5 mmol/l. High doses of catecholamines with stress-dose hydrocortisone and mechanical ventilation were needed to stabilize her condition. Empiric antibiotic therapy with imipenem/cilastatin and clarithromycin was immediately started. Anuria, acidosis and uncontrollably high temperatures required continuous venovenous hemofiltration. The CT scan showed disseminated pulmonary infiltrates, multiple intrapulmonary abscesses (up to 3 cm), large bilateral pleural effusions (Fig. 2) and maxillary sinusitis. Two liters of foul-smelling empyema fluid was punctured from the left pleural space and one liter of clear effusion from the right. Gram-staining of the pleural empyema showed Gram-negative rods and raised suspicion of anaerobe organisms; metronidazole was therefore added. Two days later the organism was identified as *Fusobacterium necrophorum* (isolated from pleural empyema and two different blood cultures). Resistance testing confirmed susceptibility to imipenem and metronidazole. With increasing suspicion of Lemierre's syndrome, we examined the neck veins for thrombi; however, despite an obvious swelling around the right sternocleidomastoid region, a thrombus could not be identified in either vein, neither by ultrasound, nor by CT scanning. A superimposed nosocomial pneumonia, suspicious for methicillin-resistant *Staphylococcus aureus*, was treated with linezolid. Repeatedly increasing pleural empyema, atelectasis and recurrent pneumothoraces required three surgical interventions and multiple chest-drains. Arthritis of the right sternoclavicular joint and osteomyelitis of the sternal clavicular portion needed surgical debridement two weeks after admission. Culture remained negative. Six weeks after the first presentation to hospital the patient was discharged in good general condition and recovered without sequelae.

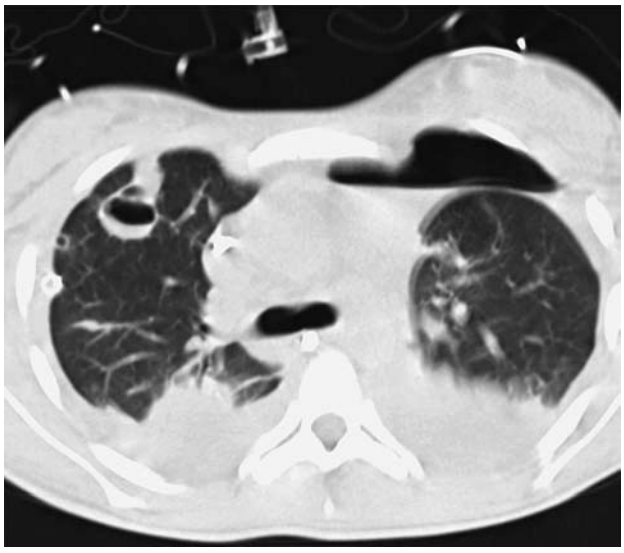

**Fig. 2.** The tomographic chest scan shows one of the large intrapulmonary abscesses, pneumothorax and large bilateral pleural effusions

## Discussion

Anaerobes are predominant components of the normal human flora of skin and mucous membranes [9], and are therefore a common cause of bacterial infections of endogenous origin. *F. necrophorum* is a strictly anaerobic, non-motile, non-spore-forming Gram-negative rod with characteristic pleomorphic morphology on Gram-stained smears, showing filaments, short rods and coccoid elements. The organism is a normal inhabitant of the oral cavity, the female genital tract and the gastrointestinal tract [10]. In contrast to other anaerobic infections, which usually show multiple anaerobic organisms, F. necrophorum is often the sole pathogen and has an unusual ability to cause severe disease as a primary pathogen in previously healthy people with intact anatomical barriers [6–8, 10–12]. Among anaerobic infections reported in children, *Fusobacterium* was responsible for 10–17% of clinically significant bacteremias [13, 14]. The invasiveness of the organism can be explained by its production of proteolytic enzymes, lipopolysaccharide endotoxin, leucocidin and hemagglutinin. Disruption of the mucosal barrier of the oropharynx leads to hypoxia and tissue destruction, which creates an oxygen-free environment [15]. Infections with bacterioidaceae, to which *F. necrophorum* belongs, have been associated with thromboembolic phenomena that are related to the lipid A moiety of their lipopolysaccharide [16]. In 1936, André Lemierre [3] gave a detailed description of septicemia secondary to an anaerobic infection of the tonsillar or peritonsillar region, based on his experience with 20 patients, of whom 18 died within two weeks. The anatomy of the lateral pharyngeal space allows invasion of the internal jugular vein either by direct penetration or by lymphatic or hematogenous spread from the peritonsillar vessels [17]. Internal jugular vein thrombosis acts as a nidus of infection that may spread hematogenously and result in septicemia and septic embolization [8].

It is now generally recognized that Lemierre's syndrome is characterised by four findings: a) primary infection of the oropharynx; b) septicemia documented by at least one positive blood culture; c) clinical or radiographic evidence of thrombosis of the internal jugular vein and d) at least one metastatic focus of infection [8, 15]. The syndrome occurs in young, otherwise healthy, persons (73.4% in patients aged 16–25 years). The major clinical symptoms are sepsis with signs of septic emboli, most commonly affecting the lungs (79.8%) and joints (16.5%) [18]. Several reports have described infected patients as having serological evidence of Epstein–Barr virus infectious mononucleosis [5, 19–21]. Chirinos et al. found that in 69.7% of all cases reviewed, diagnosis of Lemierre's syndrome was based on isolation of *F. necrophorum* in blood cultures rather than on clinical signs or symptoms [18]. Fatal outcome is still frequent [4] and a high degree of clinical suspicion is necessary for diagnosis. A swollen and/or tender neck should be regarded as a warning sign in a patient with a prolonged course of pharyngitis, fever and malaise. Nevertheless, local findings may be subtle or absent, particularly if the infection selectively affects the posterior compartment of the lateral pharyngeal space. No significant neck findings were found in 47.7% of the patients [18].

Lemierre's syndrome should still be considered a life-threatening entity in cases of serious lung infections with septicemia.

## References


1. Courmont P, Cade A (1900) Sur une septicopyahemie de l'homme simulant la peste et causée par un streptobacille anaerobic. Arch Med Exp Anat Pathol 12: 393–418
2. Schottmuller H (1918) Ueber die Pathogenität anaerober Bazillen. Dtsch Med Wochenschr 44: 1440
3. Lemierre A (1936) On certain septicaemias due to anaerobic organisms. Lancet 1: 701–703
4. Vohra A, Saiz E, Ratzan KR (1997) A young woman with a sore throat, septicaemia, and respiratory failure. Lancet 350: 928
5. Dagan R, Powell KR (1987) Postanginal sepsis following infection with mononucleosis. Arch Intern Med 147: 1581–1583
6. Henry S, DeMaria A Jr, McCabe WR (1983) Bacteremia due to Fusobacterium species. Am J Med 75: 225–232
7. Moore-Gillon J, Lee TH, Eykyn SJ, Phillips I (1984) Necrobacillosis: A forgotten disease. Br Med J (Clin Res Ed) 288: 1526–1527
8. Sinave CP, Hardy GJ, Fardy PW (1989) The Lemierre syndrome. Medicine (Baltimore) 68: 85–94
9. Finegold SM (1977) Anaerobic bacteria in human disease. Academic Press, New York
10. Hagelskjaer Kristensen L, Prag J (2000) Human necrobacillosis, with emphasis on Lemierre's syndrome. Clin Infect Dis 31: 524–532
11. Golpe R, Marin B, Alonso M (1999) Lemierre's syndrome (necrobacillosis). Postgrad Med J 75: 141–144
12. Leugers CM, Clover R (1995) Lemierre's syndrome: Post-anginal sepsis. J AM Board Fam Pract 8: 384–391
13. Dunkle LM, Brotherton TJ, Feigin RD (1976) Anaerobic infections in children. Pediatrics 57: 311–320
14. Brook I, Controni G, Rodriguez WJ, Martin WJ (1980) Anaerobic bacteremia in children. Am J Dis Child 134: 1052–1056
15. Venglarcik J (2003) Lemierre's syndrome. Ped Inf Dis 921–923
16. Bjornson HS, Hill EO (1973) Bacterioidaceae in thromboembolic disease. Infect Immun 8: 911–918
17. Moore BA, Dekle C, Werkhaven J (2002) Bilateral Lemierre's syndrome. ENT: Ear Nose Throat J 81: 234
18. Chirinos JA, Lichtstein DM, Garcia J, Tamariz LJ (2002) The evolution of Lemierre syndrome. Medicine (Baltimore) 81: 458–465
19. Moller K, Dreijer B (1997) Post-anginal sepsis (Lemierre's disease): a persistent challenge. Presentation of 4 cases. Scand J Infect Dis 29 (2): 191–194
20. Hagelskjaer LH, Prag J, Malczynski J, Kristensen JH (1998) Incidence and clinical epidemiology of necrobacillosis, including Lemierre's syndrome, in Denmark 1990–1995. Eur J Clin Microbiol Infect Dis 17: 561–565
21. Busch N, Mertens PR, Schonfelder T, Nguyen H, Marschall HU, Kierdorf H, et al (1996) Lemierre's post-tonsillitis sepsis with meningitis and intravascular consumption coagulopathy as complication of infectious mononucleosis with pansinusitis. Dtsch Med Wochenschr 121 (4): 94–98


Correspondence: Michael Joannidis, MD, Universitätsklinik für Innere Medizin, Anichstraße 35, 6020 Innsbruck, Austria, E-mail: michael.joannidis@i-med.ac.at