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Lemierre syndrome caused by Klebsiella pneumoniae complicated by epidural abscess – Case report

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ABSTRACT

Klebsiella pneumoniae is an extremely rare case of the Lemierre syndrome, which is characterized as septic thrombophlebitis of the jugular vein as a consequence of oropharyngeal infection. We present a unique case of Lemierre syndrome caused by *Klebsiella pneumoniae,* complicated by epidural abscess. The patient presented with fever, severe nuchal pain and stiffness and mild sore throat and headache. Computed tomography revealed a neck abscess localized dorsally to a left mandibular ramus and continuing caudally along the sternocleidomastoid muscle, thrombosis of the left internal jugular vein and fluid collection in the epidural space. Viewed under magnetic resonance imagining, the effusion had the character of an epidural abscess. Cultivation of oropharyngeal swab and blood cultures revealed *Klebsiella pneumoniae*. The neck abscess was surgically drained, and the patient was treated with a combination of parenteral antimicrobials until complete clinical and radiologic remission. This case highlights the importance of also covering the gram-negative facultative anaerobic rod spectrum in the empiric antimicrobial treatment of Lemierre syndrome.

Introduction

Lemierre syndrome is characterized by oropharyngeal infection resulting in septic thrombophlebitis of the jugular vein. Bacteremia and hematogenous spreading of infection via septic emboli from the jugular vein are also common components of the Lemierre syndrome [1,2]. Courmont and Cade for the first time described a case of oropharyngeal infection and jugular vein thrombosis in 1900 [3]. However, this syndrome was named much later, after Andre-Alfred Lemierre, professor of bacteriology in Claude Bernard Hospital in Paris. In 1936, Lemierre described 20 cases of young, previously healthy adults with tonsillitis or peritonsillar abscess who developed neck swelling due to septic thrombophlebitis of the internal jugular vein, metastatic abscesses, and anaerobic septicemia. In his era, the disease was almost always fatal, and 18 of these patients died [4]. In the antimicrobial era, prognosis of Lemierre syndrome is naturally much better [5]. However, severe complications still might occur. Infection may spread to distant organs by septic embolization or to nearby structures of the neck, head and thorax [1,2]. Mediastinitis or epidural abscess or spinal abscess are the most severe but rare complications [6–15]. In the vast majority of cases, Lemierre syndrome is caused by synergic infection by both aerobic and anaerobic bacteria [4,6]. A non-spore forming anaerobe, *Fusobacterium necrophorum* is regarded as the typical aetiopathogen of Lemierre syndrome [1,2]. However, other bacteria, such as *Streptococcus* species, *Staphylococcus aureus, Bacteroides* species *or Klebsiella pneumoniae*, were also isolated [1,2,16–19]. We present the first known case of Lemierre syndrome caused by *Klebsiella pneumoniae* complicated by epidural abscess.

Case report

The 19-year-old previously healthy male patient visited the emergency department of University Hospital in Bratislava. The patient complained about very severe pain in the nuchal area, mild occipital headache and mild sore throat. The headache and nuchal pain started 2 days before and worsened progressively. The sore throat had started a few days earlier. At the time of examination, the pain in the nuchal area was so excruciating that the patient was unable to perform any anteflexion or rotation of the head. At home, the patient also had a fever of up to 40 degrees Celsius and chills. Physical examination revealed only nuchal rigidity, with substantial opposition to passive anteflexion and rotation of the head and also mild redness and enlargement of tonsils. The straight leg raise maneuver was limited to 75 degrees because of severe pain in the nuchal area. The patient was afebrile and his blood pressure and heart rate was within normal range. No edema or erythema or palpable mass of the neck was present during initial examination.

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In laboratory screening, there was significant leucocytosis (25 590 cells/mL) with neutrophilia (23 180 cells/mL), elevated C-reactive protein (CRP) (179.88 mg/L) and procalcitonin (17.38 ng/mL). CT examination of the head was unremarkable, and the chest radiogram found no infiltrative or nodular changes of lung parenchyma. Neurologic examination revealed no lateralization or signs of limb paresis.

Because of nuchal rigidity, fever and headache, lumbar puncture was performed. Examination of cerebrospinal fluid revealed borderline pleocytosis (10 mononuclear cells/μL) with no apparent polymorphonuclear cells and normal proteinorhachia (15.5 mg/dL). The patient was hospitalized at the intensive care unit of The Department of Infectology and Geographical Medicine of University Hospital in Bratislava. Empiric antimicrobial therapy was started along with a combination of ceftriaxone 2 g every 12 h and vancomycin 1 g every 8 h. We also commenced parenteral rehydration by normal saline solution and analgesic therapy. The next day, the headache disappeared, but pain in the nuchal area was even more severe and also extended to the left side of the neck. In the left lateral area of the neck, the skin also had become erythematous and was tender during palpation. The patient developed generalised urticarial allergic exanthema; the antimicrobial therapy was changed to a combination of piperacillin–tazobactam 4.5 g every 8 h and clindamycin 600 mg every 8 h. On the third day, the erythema and edema of the left lateral part of the neck was even more pronounced. Also, a large palpable mass in this area became apparent. Therefore, we performed a computed tomography (CT) of the neck that revealed a well-demarcated collection of liquid of density 26 HU, localised dorsally to a left mandibular ramus and continuing caudally along the sternocleidomastoid muscle (Fig. 1). The collection was 22 mm in antero-posterior, 20 mm in latero-lateral and 58 mm in cranio-caudal diameter. In the cranial pole, it was in close proximity to the parotid gland, which was enlarged and appeared to be slightly edematous. The CT scan also revealed thrombosis of the left internal jugular vein. In the spinal canal, the CT scan revealed a hypodense collection of fluid 4.5 mm in diameter. However, there was no apparent pathologic process in the retropharyngeal space. Magnetic resonance imagining of the cervical spinal column found a 5 mm thick epidural effusion, cranially starting from the fourth cervical vertebra continuing caudally to the seventh cervical vertebra (Fig. 2). The picture of the effusion had inflammatory character. Cultivation of the oropharyngeal swab and blood cultures revealed *Klebsiella pneumoniae* which was susceptible to cefuroxime, cefotaxime, amoxicillin–clavulanate, gentamicin, ciprofloxacin and trimethoprim/sulfamethoxazole.

The patient was diagnosed with tonsillopharyngitis complicated by cervical abscess, thrombosis of left internal jugular vein and epidural abscess. He was treated for 6 days by a combination of ceftriaxone 4 g daily and clindamycin 1800 mg daily, which resulted in decline of C-reactive protein to 125 mg/L and procalcitonin to 2.50 ng/L. Pain in the neck area had become much less severe and local erythema of the skin had begun to fade. However, because of the extent of the neck abscess 7 days after admission, the patient was transferred to the Department of Otorhinolaryngology of University Hospital in Bratislava, and surgical revision and drainage of the abscess was performed. Cultivation of pus also revealed *Klebsiella pneumoniae*. Cultivation for anaerobic bacteria was negative. Antimicrobial therapy was administered in an unchanged regime and dose, and the postsurgical course was unremarkable. On the fourth day after surgery, the patient was transferred back to the intensive care unit of The Department of Infectology and Geographical Medicine. The patient was afebrile and, except for minor pain near the surgical wound, had no pain in the cervical area and had no limitations of movement in the neck. The C-reactive protein level was 26.00 mg/L. Clindamycin was stopped but continued the therapy with piperacillin–tazobactam to complete 21 days of parenteral

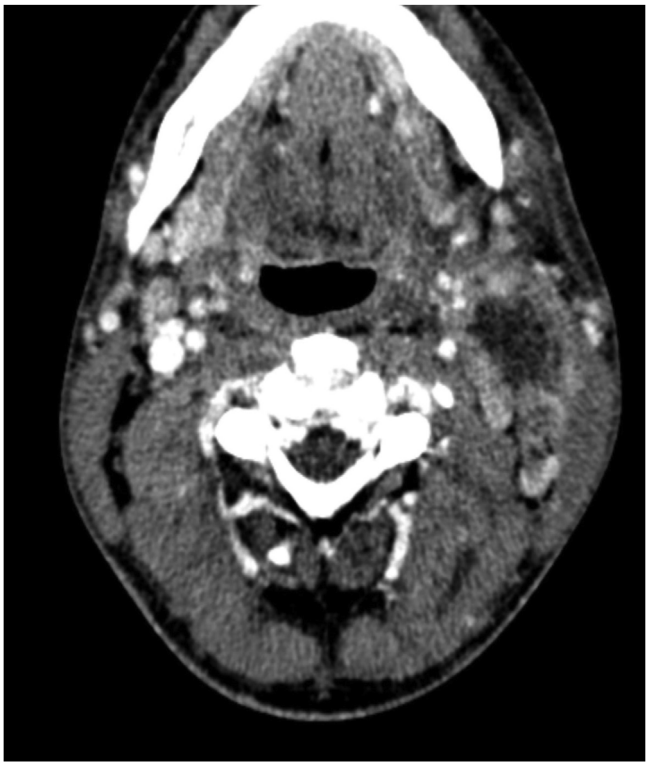

Fig. 1. Tomogram of the neck.
This is a tomogram in a late-arterial phase of the patient's neck revealing the abscess as well-demarcated collection of liquid of density 26 HU, localized dorsally to the left mandibular ramus. It is visible as hypodense area with hyperdense margins localized dorsally to a left mandibular ramus (right side of the figure).

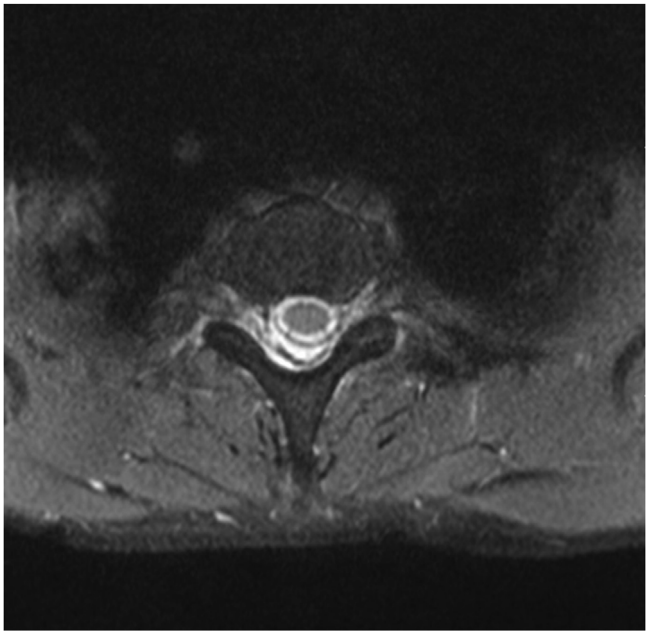

Fig. 2. Megntic resonance imagining of cervical spinal column.
Magnetic resonance imagining of the cervical spinal column found a 5 mm thick epidural effusion, cranially starting from the fourth cervical vertebra continuing caudally to the seventh cervical vertebra. This figure shows T2 weighted image revealing fluid in epidural space shown as white crescent localized dorsally from the medulla.

antimicrobial treatment. The follow-up CT scan revealed complete regression of the cervical abscess and partial recanalization of the left internal jugular vein. There was also complete regression of the epidural effusion by magnetic resonance. The C-reactive protein level was 13.26 mg/L. The antimicrobial regime was changed to one 400 mg tablet of moxifloxacin once daily, and the patient was discharged about 3 weeks after admission. Seven days after discharge, the patient was asymptomatic, CRP was below 5 mg/L and the moxifloxacin treatment was discontinued.

Discussion

Lemierre syndrome is defined as oropharyngeal infection resulting in septic thrombophlebitis of the jugular vein. Bacteremia and hematogenous spreading of infection via septic emboli from the jugular vein are also sometimes regarded as components of this syndrome [1,2]. While quite common in the pre-antimicrobial era, it is regarded as very rare nowadays. In the 90 s, the incidence of this syndrome was so low that it was regarded as an almost-forgotten condition [5,20]. In the 21 st century, the incidence of Lemierre syndrome seems to be higher [2,5]. The reason for this phenomenon might be just higher awareness and better availability of sensitive diagnostic modalities, such as computed tomography and magnetic resonance [2]. Nevertheless, it is still regarded as very rare in developed countries, with an estimated incidence of 1 case per million per year [1,2,5]. It is primarily a disease of adolescents and young adults [2,5]. The most common pathogen associated with Lemierre syndrome is *Fusobacterium necrophorum*; however, the spectrum of potential pathogens includes *Streptococcus* species, *Staphylococcus aureus* and various gram-negative bacilli [1,2].

Klebsiella pneumoniae had been identified in some cases; however, Lemierre syndrome caused by this bacterium is extremely rare. We were able to find reports of 9 cases of Lemierre syndrome caused by *Klebsiella pneumoniae* described to date, and according to available case reports, none of these cases was complicated by epidural abscess [16–19]. Chuncharunee and Khawcharoenporn described these 9 cases in 2019 including detailed description of mayor complications [17]. In these cases, the most common complications were distant metastases, mostly to the lungs (5 cases). One patient had brain metastases, and 3 patients had no signs of distant metastatic infection. In our case, the chest X-ray found no infiltrative or nodular changes of the lung parenchyma, however, our patient had an epidural abscess. In 2006, Park et al. presented the first known case of Lemierre syndrome with epidural abscess in a 43-year-old woman. Symptoms of neurologic involvement were paresis of the lower limb and confusion. In this case, *Fusobacterium necrophorum* was found in the blood culture [6]. Seven cases of Lemierre syndrome with epidural abscesses were presented since then. In some of them, neurologic involvements were very severe [7–14]. In 2017, Sinatra and Alander presented a very severe case of Lemierre syndrome with multilevel epidural abscesses in the thoracic and lumbar regions, causing progressive bilateral lower limb weakness [13]. In all but one case of Lemierre syndrome and epidural abscess, the *Fusobacterium necrophorum* was identified as etiological agent [7–14]. In 2018, Shimamoto et al. presented a case report of a 55-year-old woman with retropharyngeal abscess and epidural abscess. They identified methicillin-resistant *Staphylococcus aureus* as the most probable etiological agent. Apart from sore throat and neck pain, their patient suffered from severe upper limb weakness [14].

We present here the first case of Lemierre syndrome complicated by epidural abscess caused by *Klebsiella pneumoniae* known to date. Up to one third of patients with Lemierre syndrome had polymicrobial bacteremia and, apart from *Fusobacterium necrophorum*, various gram-negative or gram-positive bacteria might be cultivated [2]. In our case, in the blood culture, pus and pharyngeal swabs revealed a pure culture of *Klebsiella pneumoniae*. Blood and pus were also both cultivated anaerobically and were negative for *Fusobacterium* species. However, the sensitivity of standard anaerobic agar cultivation for Fusobacterium is relatively low, so coinfection with *Fusobacterium necrophorum* cannot be ruled out completely [21]. On the other hand, in none of the cases of Lemierre syndrome in which *Klebsiella* species were identified as the most probable pathogen had *Fusobacterium* species been found [16–19]. Therefore, we suppose that oropharyngeal infection by *Klebsiella pneumoniae* alone is able to induce all components of Lemierre syndrome. *Klebsiella pneumoniae* is the rare etiological agent of epidural abscess and is identified in less than 1 % of all patients [22].

Sore throat is usually the first presentation of illness and precedes the symptoms of jugular thrombophlebitis by 3–4 days. When thrombophlebitis of the internal jugular vein and inflammation of surrounding soft tissues develop, a usually painful, or at least tender, neck mass appears. Because of ongoing bacteraemia, fever with chills is usually present [1,2]. Our patient presented with fever, severe nuchal pain and mild headache and sore throat. A tender neck mass developed on the following day. Other symptoms and signs of Lemierre syndrome are caused by distant septic metastases. In most cases, these metastases are located in the lungs because of a direct route of embolization from the jugular through the right ventricle to pulmonary arteries [1,2]. Five of 9 cases of Lemierre syndrome caused by *Klebsiella pneumoniae* also had metastatic pulmonary infection. In our patient, a chest radiogram showed no signs of pulmonary involvement. Approximately one-fourth of patients with Lemierre syndrome caused by *Fusobacterium necrophorum* had symptoms of septic arthritis [1,2]. Apart from epidural abscess, we found no signs of metastatic spreading of infection. However, severe nuchal pain and stiffness caused by epidural infection were the leading symptoms and drove our patient to emergency care. Unlike other cases of Lemierre syndrome with epidural abscess, there was no paresis. That might be because of the relatively small extent of epidural involvement. The largest antero-posterior diameter of the fluid collection was just 5 mm. However, it is likely that if left untreated, the neuralgic deficit would have developed.

Prolonged antimicrobial therapy and surgical exploration and debridement if necessary are the mainstays in the treatment of Lemierre syndrome regardless of its etiology [1,2]. We treated our patient by surgical incision and drainage of the cervical abscess and potent parenteral antimicrobial therapy. Initial therapy had been chosen empirically, a combination of ceftriaxone with clindamycin. This combination had been chosen because of the possibility of meningitis, suggested by the headache and nuchal rigidity. It was later switched to piperacillin–tazobactam with clindamycin because of an allergic reaction and also because the working diagnosis was changed from meningitis to Lemierre syndrome. Aminopenicillins covered by inhibitors of beta-lactamases and clindamycin are recommended in the treatment of Lemierre syndrome because of their potent activity against anaerobic and gram-positive bacteria usually causing this disease [1,2]. After identifying the *Klebsiella pneumoniae* as the most probable aetiological pathogen, we decided not to change antimicrobial treatment because of good susceptibility of this pathogen to piperacillin–tazobactam and also the possibility of polymicrobial involvement. Most authors recommend treating the Lemierre syndrome from 2 to 6 weeks [1,2]. We treated our patient for 21 days by parenteral piperacillin–tazobactam and clindamycin, until complete regression of neck and epidural abscesses, and then 7 days by oral moxifloxacin to minimize the probability of recurrence. We chose moxifloxacin because of its known great penetration to abscesses [23]. A cultivated strain of *Klebsiella pneumoniae* also showed good susceptibility to fluoroquinolones in vitro. Possibly the most important message is that *Klebsiella pneumoniae* may also cause Lemierre syndrome with epidural abscess. Clindamycin may appear to be a great choice in the

treatment of Lemierre syndrome with epidural abscess because of its great activity against anaerobes and gram-positive cocci and also good penetration to spinal abscesses [24]. However, this case and also other cases of Lemierre syndrome caused by *Klebsiella pneumoniae* highlight the importance of also covering gram-negative aerobic rods until the final identification of the pathogen. Therefore, antimicrobials covering not just anaerobes and gram-positive bacteria but also gram-negative aerobic rods (e.g., aminopenicillins with beta-lactamase inhibitor, third generation cephalosporins or carbapenems) plus metronidazole or clindamycin should be preferred over clindamycin monotherapy in the empiric treatment.

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Consent

This case study has been conducted in accordance with the Declaration of Helsinki and has been approved by the local Ethics Committee of the University Hospital in Bratislava. Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in Chief of this journal on request.

Final statements

All author red revised manuscript and accepted all the changes to the original manuscript.

CRediT authorship contribution statement

Peter Sabaka: Writing - original draft, Conceptualization. **Mária Kachlíková:** Writing - original draft. **Matej Bendžala:** Writing - original draft, Visualization. **Helena Káčerová:** Supervision, Conceptualization.

Declaration of Competing Interest

The authors have no conflict of interest to declare.

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