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CASE REPORT

Extensive thoracolumbosacral vertebral osteomyelitis after Lemierre syndrome

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Abstract
Purpose To present a unique case of multilevel vertebral osteomyelitis after Lemierre syndrome.
Methods A previously healthy 27-year-old man presented in the Emergency Department in septic shock because of Lemierre syndrome for which he was subsequently treated with intravenous benzylpenicillin for 2 months. Two and a half months later, the patient was readmitted with severe back pain without neurological deficits or fever. Imaging revealed an extensive vertebral osteomyelitis of the complete thoracic, lumbar and sacral spine.
Results Although the blood cultures obtained at the initial admission for Lemierre syndrome revealed *Fusobacterium* species and *Streptococcus milleri*, the cultures from the spinal biopsies remained negative. Histology of the spinal biopsies showed a purulent sclerosing osteomyelitis. The patient was successfully treated with intravenous piperacillin and tazobactam. Despite persisting back pain, no recurrence of infection was seen at 3 years of follow-up.
Conclusion Lemierre syndrome and an extensive thoracolumbosacral vertebral osteomyelitis are rare but serious infections. Clinicians must maintain a high index of suspicion for infectious metastases leading to vertebral osteomyelitis when a patient presents with back pain after an episode of life-threatening septicaemia caused by Lemierre syndrome.

Keywords Lemierre syndrome · Metastatic infection · Vertebral osteomyelitis · *Fusobacterium* species

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Introduction

Pyogenic vertebral osteomyelitis is a severe pathologic condition which may be difficult to diagnose. Since it is often a complication of a distant infection causing bacteremia, the relatively non-specific array of symptoms of vertebral osteomyelitis may be initially dominated by the primary infection [1]. Consequently, a considerable delay between the onset of back pain and the diagnosis of vertebral osteomyelitis may develop [2, 3]. This report presents a patient with extensive vertebral osteomyelitis diagnosed two and a half months after admittance for Lemierre syndrome. This syndrome is a potentially lethal disease characterized by an oropharyngeal infection and an infected thrombophlebitis of the internal jugular vein with subsequent metastatic infections mainly caused by *Fusobacterium necrophorum*. The rare syndrome caused this severe case of thoracolumbosacral vertebral osteomyelitis with relative limited involvement of the intervertebral disc.

Case report

A previously healthy 27-year-old male presented to the Emergency Department with a 5-day history of sore throat,

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vomiting and fever after returning from a trip to his family in Gambia and Liberia 2-weeks earlier. During initial assessment, his throat revealed erythema of the oropharyngeal wall and cervical lymphnodes were palpable. Since he showed definitive signs of septic shock (blood pressure of 85/45 mmHg; pulse of 140/min; temperature of 39 °C (102 °F); white blood cell count 10.1×10^9/l; platelets 26×10^9/l; erythrocyte sedimentation rate >120 mm/h; C-reactive protein (CRP) 377 mg/l; serum lactate 4.4 mmol/l, signs of renal failure and liver dysfunction) and early signs of acute respiratory distress syndrome (respiratory distress and bilateral patchy consolidation on chest X-ray), he was transferred to the Intensive Care Unit for haemodynamic support, sedation and mechanically assisted ventilation. Three days after admission, a CT scan revealed a parapharyngeal abscess with a thrombotic process in the left jugulary vein which confirmed to the diagnosis of Lemierre syndrome. Additionally, the CT scan showed cavitary lung lesions; pulmonary infiltrates; bilateral psoas abscesses and prevertebral infiltrates consistent with multiple septic emboli. Blood cultures were positive for *Streptococcus milleri* and *Fusobacterium* species. Since *Fusobacterium* species were susceptible to β-lactam antibiotics, treatment was changed to intravenous benzylpenicillin. Because of the risk of β-lactamase production of *Fusobacterium* species, treatment was combined with clindamycin and metronidazol. The parapharyngeal abscess was drained surgically and cultures were positive for BRMO gram-negative rods. The psoas abscesses were drained percutaneously with positive cultures for *Enterobacter aerogenes* and *Enterococcus faecalis.* As his vital signs stabilized and his condition improved, he could be taken of mechanical ventilation and was transferred to the general internal ward on day 15.

Despite antibiotic treatment for Lemierre syndrome, a fever with temperatures up to 40 °C (104 °F) persisted. Consequently, various diagnostic tests were performed to search for a secondary infection. Skeletal scintigraphy 1 month after admission showed a slightly irregular uptake of the radionuclide in all vertebral bodies without obvious signs of osteomyelitis or spondylodiscitis. Extensive microbiological and immunological screening revealed a positive Mantoux test and positive tuberculosis-interferon gamma release assay (TBC-IGRA). A HIV test was negative. Positron-emission tomography 7 weeks after admission showed normal aspect of the psoas, jugular vein and ear-nose-throat region. However, there was an increased radionuclide uptake in the lungs, skeleton and axillary lymph nodes. Biopsies of the enlarged axillary lymph nodes and iliac crest were obtained which showed necrotizing granulomatous lymphadenitis and partial osteonecrosis with the presence of multinucleated giant cells, respectively. Cultures, polymerase chain reaction assays and Ziehl–Neelsen/auramine staining of sputum, pleural effusion and lymph nodes for mycobacterium tuberculosis were negative. Despite these negative results, there was a high index of suspicion for miliary tuberculosis considering the persisting fever, recent trip to Africa, positive Mantoux and tuberculosis-interferon gamma release assay, cavitary lung lesions and granulomatous lymphadenitis. Therefore, treatment for miliary tuberculosis with isoniazid, rifampicin and ethambutol was started. After 3 months of antibiotic treatment for Lemierre syndrome and 4 weeks of treatment for tuberculosis, his fever was gone and his condition had improved sufficiently to be discharged from the hospital.

Two and a half months later, the patient was readmitted because of severe back pain. Although mild pain was already present in the lumbar area during his first admission, it had intensified in 3 weeks time and spread throughout his complete thoracolumbosacral spine. Despite the use of acetaminophen and NSAIDs, he was notable to stand and walk because it aggravated the pain. There were no ear-nose-throat, pulmonary or abdominal complaints or abnormalities. On physical examination, his vital signs were normal. He had a limited range of motion and tenderness of the thoracic and lumbar spine without any neurologic deficits. Laboratory tests revealed an elevated WBC of 6.3×10^9/l and CRP of 45 mg/l. Plain radiographs of the thoracolumosacral spine and CT-scan revealed extensive bony changes from Th1 to the sacrum with osteolytic areas in all vertebral bodies surrounded by central and cortical sclerosis (Fig. 1). Magnetic resonance imaging (MRI) demonstrated increased signal intensity in the vertebral endplates and vertebral body on both T1 and T2-weighted sequences with limited involvement of the intervertebral disks (Fig. 2). Due to the extensive spinal involvement and a rapidly increased CRP of 447 mg/l, the patient was transferred to an infectious disease and spine center where he developed a fever of 39 °C (102 °F). Apart from the tuberculostatics, antibiotic treatment was not started before blood cultures and fluoroscopy-guided percutaneous spinal aspirates and biopsies were obtained. Although the aspirates of vertebra L1 and L2 revealed pus, microbiological cultures remained negative. Histology of the biopsies showed purulent sclerosing osteomyelitis. An echocardiogram revealed no signs of endocarditis. Since the *Fusobacterium* species were expected to be responsible for the infection, the extended spectrum β-lactam antibiotic piperacillin combined with the β-lactamase inhibitor tazobactam was started and the oral tuberculosis treatment was continued. As the patient improved clinically and CRP declined, he was mobilized with a thoracolumbar orthosis for support and comfort. After 2 weeks, antibiotic treatment was switched to ciprofloxacin and clindamycin orally.

Although his clinical condition remained unchanged upon weekly follow-up outpatient visits, he was readmitted

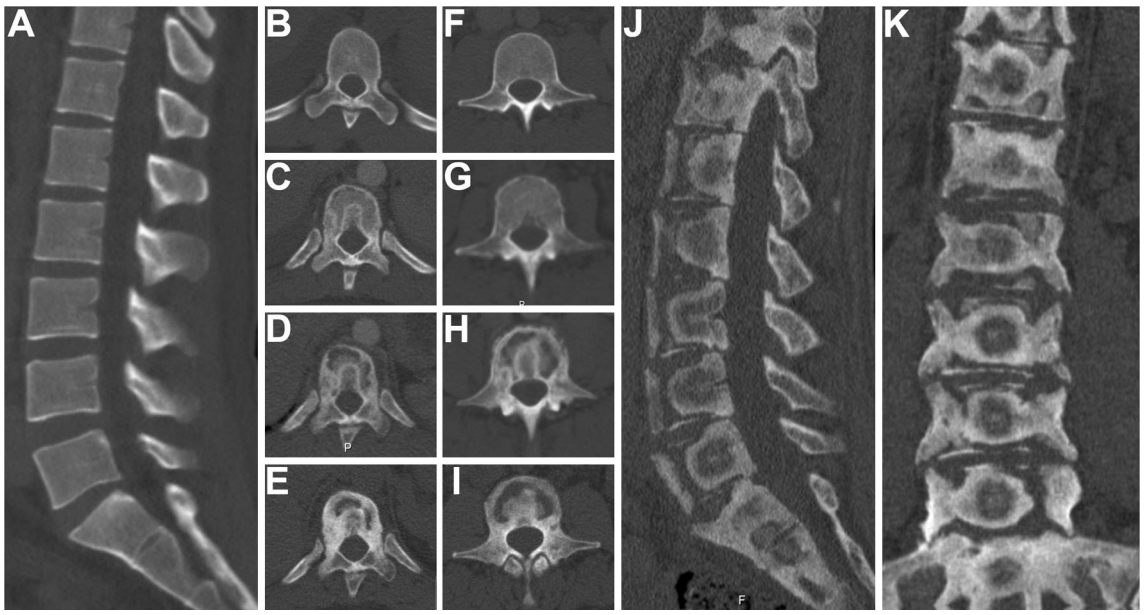

Fig. 1 Sagittal (**a**, **j**), axial (Th11, **b**–**e** and L3, **f**–**i**) and coronal (**k**) computed tomographic images showing the patient's lumbar spine in chronological order. The scans were taken 3 days after admission (**a**, **b**, **f**), 1.5 months (**c**, **g**) 6 months (**d**, **h**) and 16 months (**e**, **i**–**k**) after admission for Lemierre syndrome and show the extensive bony changes over time which resulted in an osteolytic area in the vertebral bodies surrounded by a sclerotic center and cortex

for a 6 day period because of an increase in CRP. Antibiotic treatment was switched back to intravenous piperacillin and tazobactam. The tuberculostatics were stopped 6 months after initiation. Intravenous antibiotic treatment with piperacillin and tazobactam was to be administered for 6 weeks after normalization of the CRP. However, the patient decided to stop the antibiotics prematurely 10 months after diagnosing Lemierre syndrome and 4.5 months after his re-admission for back pain. The patient was last seen 3 years after diagnosing Lemierre syndrome. Although he had improved significantly and has not had a recurrent infection, he continued to have back pain and a limited range of motion of his spine at last follow-up.

Discussion

The axial skeleton is the most frequent site of hematogenous osteomyelitis in adults [4]. Although seeding through the venous plexus from pelvic or urinary tract infections can occur, it is believed that hematogenous spinal infections are mainly the result of arterial bacterial spread [5, 6]. Bacteria are expected to arrive in the end-arteriolar arcade at the endplates of vertebral bodies through the segmental arteries where they can cause septic osseous infarctions. In approximately 95 % of cases, the infection spreads from the endplates to the avascular intervertebral disc leading to spondylodiscitis [7]. An extensive multilevel spinal infection with relative preservation of the intervertebral disc as presented in the present case report is extremely rare.

Our case of multilevel vertebral osteomyelitis started with a classical clinical case of Lemierre syndrome. This is an infection-related syndrome which starts as an oropharyngeal infection, progresses to a lateral pharyngeal space infection and finally results in a septic thrombophlebitis of the internal jugular vein with subsequent septicaemia and metastatic infections [8]. It is a rare syndrome with an estimated incidence of 0.8 per million persons per year and typically observed in previously healthy teenagers and young adults [8, 9]. Since it is a potentially lethal complication of oropharyngeal infections, early recognition and aggressive antibiotic therapy are critical. Even after early detection and intravenous antibiotic treatment, the mortality rate of Lemierre syndrome is estimated at 5–15 % [10, 11].

The organism most commonly involved in Lemierre syndrome is *Fusobacterium necrophorum* [12]. This is an anaerobic, Gram-negative bacterium which can be part of the normal oropharyngeal flora. *F. necrophorum* can cause a variety of relatively minor infections such as otitis media or sinusitis and is a common pathogen in tonsillitis and peritonsillar abscesses [13–16]. It is not known how often localized *Fusobacterium* infections progress to the life-threatening Lemierre's syndrome. In 75–82 % of Lemierre syndrome cases *F. necrophorum* was cultured [8, 11, 17]. Pathogens such as other *Fusobacterium* species and

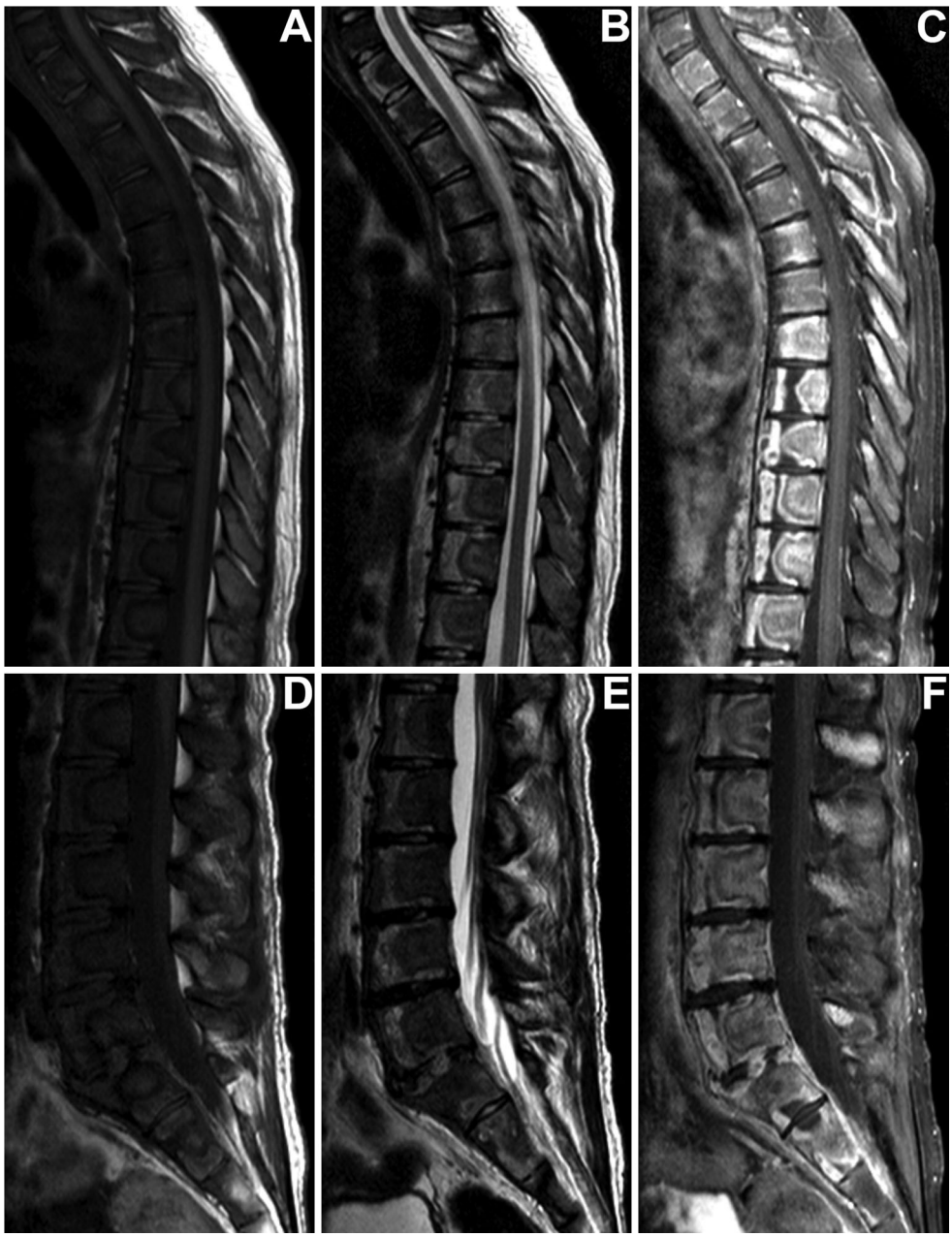

Fig. 2 Sagittal plane MRI scan of the thoracic (C7–T12, **a**–**c**) and lumbar spine (L1-sacrum, **d**–**f**) taken upon readmission in the hospital 6 months after establishing the diagnosis Lemierre syndrome. The images show the changes in the vertebral endplates and corpus on T1-weighted turbo-spin echo (TSE) (**a**, **d**), T2-weighted TSE (**b**, **e**) and gadolinium-enhanced T1 spectral persaturation with inversion recovery (SPIR) sequences

Streptococcus species have also been cultured in Lemierre syndrome. A polymicrobial bacteraemia is present in 10–30 % of the patients and in 6–12 % cultures remain sterile.

Despite 6 weeks of intravenous antibiotics for Lemierre syndrome, fever persisted in our patient. Since there was a high index of suspicion for miliary tuberculosis, tuberculostatics were started. *Mycobacterium tuberculosis* is the most common cause of vertebral osteomyelitis with prolonged preservation of the intervertebral disc and may therefore also be considered a pathogen [5, 6]. The prolonged preservation of the disc and slower destruction of the vertebral body compared to pyogenic organisms may be caused by a relative lack of protolytic enzymes produced by mycobacterium tuberculosis [6, 18]. As a result, progression of tuberculous spondylitis is often slow with minor initial clinical signs. Furthermore, destruction of the vertebral body by tuberculosis is a slow process caused by erosion due to the infection and necrosis due to obstruction of the vascular supply [19]. Due to the rapid progression of the spinal infection, the absence of a granulomatous infection in the biopsies and the continuous vertebral destruction with aggravation of the disease despite treatment for tuberculosis, the *Fusobacterium* species involved in Lemierre syndrome are a more likely pathogen in this case. However, since blood and abscess cultures were also

positive for other bacteria, the extensive vertebral osteomyelitis may have been caused by a polymicrobial infection of *Fusobacterium* with *Streptococcus milleri* or the other bacteria. Unfortunately, the exact role of these other bacteria in the etiology of this infection remains unknown since our cultures of vertebral biopsies remained negative.

Fusobacterium infections of the spine are very rare with only 15 previously reported cases in the literature [20–32]. So far, these infections were limited to two-, three- or four-level spondylodiscitis located mainly in the lumbar area. The majority of patients was over 40 years of age and presented with subacute back pain. Although preceding ear-nose-throat or paradontal infections were found in most patients, *Fusobacterium* spondylodiscitis was caused by Lemierre syndrome in only two cases. *Fusobacterium* species were isolated in blood cultures (7 patients), local biopsies (4 patients) or both (3 patients). Two polymicrobial infections have been reported: one with *F. necrophorum* and *Streptococcus constellatus* (also part of the *S. milleri* group) and the one with *F. nucleatum* and *Actinomyces israelii* [31]. Most patients were treated with penicillin, metronidazole and/or clindamycin for a period varying between 6 and 18 weeks. The case of *F. nucleatum* and *A. israelii* spondylodiscitis in combination with an epidural abscess and partial spinal cord injury was treated for 12 months. All patients were cured with antibiotic treatment and no relapse of the infection was seen upon follow-up. The long-term morbidity of these previous cases consisted of persistent muscle weakness and bowel/urinary dysfunction after a spinal cord injury in two cases and mild low back pain in one case.

In conclusion, Lemierre syndrome and *Fusobacterium* vertebral osteomyelitis are a rare occurrence. In previous cases of *Fusobacterium* vertebral osteomyelitis, average treatment duration of 13 weeks was sufficient to cure patients. However, this period was insufficient in our patient and an additional 4.5 months of antibiotics was required to treat the recurrent multi-level vertebral osteomyelitis. Since penicillin treatment failures due to β-lactamase production have been described in the past, the initial treatment was already combined with clindamycin and metronidazol which are β-lactamase-resistant antibiotics with anaerobic activity [33, 34]. Whether the initial treatment failure was due to further changes in *Fusobacterium* antibiotic resistance or due to the polymicrobial cause is unknown since the biopsie cultures remained negative. Therefore, this case should raise awareness of possible penicillin, clindamycin and metronidazol treatment failure for osteomyelitis after a life-threatening polymicrobial septicaemia in Lemierre syndrome.

Conflict of interest None.

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