CASE REPORT

Pathological fracture of the femoral neck following septic coxitis and chronic osteomyelitis: a potential complication of Lemierre's syndrome

Dominik Maximilian Vogt,¹ Ludger Tüshaus,² Martin Kaiser,² Martin Russlies¹

¹Klinik für Orthopädie und Unfallchirurgie, Universitätsklinikum Schleswig Holstein - Campus Lübeck, Lübeck, Germany

²Klinik für Kinderchirurgie, Universitätsklinikum Schleswig Holstein - Campus Lübeck, Lübeck, Germany

Correspondence to

Dr Dominik Maximilian Vogt, dominik.vogt@uksh.de

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SUMMARY

We portray the case of a 16-year-old girl who was initially admitted to the paediatric emergency department with non-specific symptoms of a severe cold and was first treated symptomatically on an ambulatory basis. Within 6 days she developed the full clinical picture of Lemierre's syndrome with the extraordinary manifestation of involvement of her right hip. Despite an interdisciplinary coordinated treatment as well as surgical therapy, a full-blown sepsis evolved within a short time period and resulted in almost 2 months of intensive care. While the primary focus could be successfully controlled, a progressive avascular necrosis of the right proximal femur developed on the basis of a chronic osteomyelitis. This finally led to a pathological fracture of the femoral neck. After excluding the possibility of an enduring bacterial infection, the fracture was treated with a total hip replacement.

BACKGROUND

Lemierre's syndrome is generally initiated by *Fusobacterium necrophorum*, which is a rod-shaped species of Gram-negative bacteria and an obligate anaerobe. It normally begins as a unilateral thrombophlebitis of the internal jugular vein following an acute oropharyngeal infection. It is often complicated by a consecutive bacteraemia with septic metastasis in various organs.^{1–3} For example, involvement of the lung has been reported in 79%–100% and an affection of joints in 13%–27%.⁴ The diagnosis must be confirmed rapidly, and an aggressive, preferably interdisciplinary, approach is required to immediately treat these commonly young and previously healthy patients, as the mortality rate of Lemierre's syndrome is still approximately 8%.⁵

We are reporting this case to raise awareness of Lemierre's syndrome and its potentially severe complications in terms of septic arthritis and osteomyelitis, which may lead to a loss of the affected joint in adolescents.

CASE PRESENTATION

A 16-year-old, previously healthy girl was initially brought to the paediatric emergency department with non-specific symptoms of severe cold and was first treated symptomatically on an ambulatory basis. Six days later she returned with a progressive, painful swelling on the left side of her neck and a painful right hip in a reduced but stable general

condition. At that time, she reported a 10-day history of sore throat, accompanied by an undulant fever of up to 41°C, and 4 days of hip pain. The antibiotic clarithromycin had been prescribed 7 days prior to this by the family physician.

INVESTIGATION

Because the patient's symptoms indicated a systemic bacterial infection, a complete sepsis work-up was undertaken, including imaging techniques: At the time of admission, the patient's white blood cell count was $17.5 \times 10^9/L$, C reactive protein (CRP) was 298 mg/L and D dimers was $2350 \mu g/L$. Her body temperature was 36.4°C. The chest X-ray showed no pathological alterations. Ultrasonography and an MRI of the patient's neck and hip revealed a unilateral parapharyngeal abscess, a thrombophlebitis of the left internal jugular vein and an effusion of the right hip joint, but neither an affection of soft tissue nor bone (figure 1). We performed an arthrocentesis of the hip joint, which revealed clear synovial fluid with a white blood cell count of $74.4 \times 10^9/L$, which we thought at that time was not high enough for a bacterial arthritis but did indicate a reactive arthritis. According with this theory, the synovial fluid cultures returned as negative. The blood cultures, which showed growth of *F. necrophorum*, finally led to the diagnosis of Lemierre's syndrome. Due to the necessary incubation time, however, this diagnosis was not confirmed until 3 days after admission.

DIFFERENTIAL DIAGNOSIS

As highlighted with our patient, the diagnosis of Lemierre's syndrome is often delayed because the clinical findings during the first stage of the disease are frequently non-specific symptoms of ordinary infections of the upper respiratory tract, such as sore throat, fatigue and fever, which can normally be treated ambulatory.⁶ Only when the patient's general condition deteriorated with signs of systemic septicaemia, despite the standard antibiotic therapy, did we initiate further investigations. At first, we believed our patient was suffering from bacterial pharyngitis, complicated by parapharyngeal abscess and reactive arthritis of her right hip. The final diagnosis was, however, achieved by the detection of a thrombophlebitis of the left internal jugular vein, combined with the growth of *F. necrophorum* in blood cultures, which is a characteristic

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Figure 1 Radiological findings on admission: (A) MRI of the neck with a contrast agent showing a left-sided parapharyngeal abscess, (B) X-ray of the right hip with normal findings and (C) MRI showing an effusion of the right hip joint.

of Lemierre's syndrome,⁷ and proof of a bacterial arthritis by a highly elevated white blood cell count in the synovial fluid of the hip joint.

TREATMENT

Initially, we believed that our therapy could remain non-invasive. Therefore, we began a calculated antibiotic therapy using ampicillin/sulbactam after drawing blood cultures. A therapeutic anticoagulation using enoxaparin was used to treat the thrombophlebitis of the left internal jugular vein. On the third day after admission, however, the patient's condition deteriorated rapidly. The patient had to be transferred to the paediatric intensive care unit and the antibiotics were escalated to meropenem and clindamycin. As the patient also reported an increasing pain of her right hip, we repeated the needle aspiration on the fourth day after admission, which then revealed an empyema with a white blood cell count of $503.3 \times 10^9/L$. Concurrently, the blood cultures showed growth of *F. necrophorum* for the first time. Following these findings, we decided to immediately drain the parapharyngeal abscess and to perform an arthroscopic intervention with the irrigation and subtotal synovectomy of the right hip joint. These measures cured the pharyngeal infection, but they only temporarily reduced the hip symptoms.

Following 2 days of amelioration, the patient again complained of increasing pain in her affected hip, which was accompanied by a rising CRP. In contrast to the initial results, a follow-up MRI of the right hip showed septic myositis, fasciitis and osteomyelitis of the proximal femur with reduced perfusion of the femoral head. An emergency arthrotomy with radical debridement of the soft tissues, osteotomy and drilling of the medullary cavity of the proximal femur with insertion of polymethyl methacrylate (PMMA) beads loaded with gentamicin was carried out on the same day (figure 2). Further, the intravenous antibiotic therapy

Figure 2 (A) MRI of the right hip showing an abscessing myositis, fasciitis and osteomyelitis of the proximal femur with reduced perfusion of the femoral head. (B) X-ray control following drilling of the medullary cavity of the proximal femur and implantation of gentamicin Polymethyl methacrylate (PMMA) chains.

was extended by ciprofloxacin, metronidazole and gentamicin to treat a potential mixed infection.

After 7 weeks of an undulant course, the patient was discharged on oral clindamycin.

OUTCOME AND FOLLOW-UP

Despite a daily therapy with oral clindamycin, in the following months the patient suffered from recurring pain in her right hip and leg accompanied by undulant elevated CRP levels, which indicated a chronic osteomyelitis. She also developed a fever up to 39°C when the PMMA beads were removed 2 months after the first open arthrotomy. Thereupon, another course of intravenous treatment with meropenem/teicoplanin was initiated because we were afraid of a secondary endocarditis by multi-drug-resistant bacteria. When the patient's condition improved and an endocarditis could finally be excluded by echocardiography, we continued with a long-term oral therapy of ampicillin/sulbactam. Repeated radiological, scintigraphic and MRI controls revealed signs of a persistent inflammation and hints of an emerging osteonecrosis of the femoral head and neck (figure 3). In spite of these radiological findings, the patient's medical condition improved. The white blood cell count and CRP showed normal levels after 7 months of continuous antibiotic treatment. Thus, increased weight bearing was allowed.

Figure 3 (A) MRI and (B) Single-photon emission computed tomography showing the persistence of inflammation and an incipient osteonecrosis of the femoral head and neck.

Figure 4 X-rays showing (A) the pathological fracture of the femoral neck, (B) the antibiotic cement spacer and (C) the total hip replacement 2 weeks after implantation.

Eight months after the onset of Lemierre's syndrome, a minimal trauma finally led to a pathological fracture of the femoral neck. At that stage, radiological evaluation showed signs of an advanced necrosis of the femoral head. Furthermore, a persistent low-grade infection could not be excluded. We therefore decided on a total hip replacement as a two-stage procedure (figure 4).

At the 8-month follow-up after a cementless hip arthroplasty and 16 months after her first admission to our hospital, the patient was pain-free, actively mobile with no sign of a persistent infection and planned to start sports again.

All the cultures of samples that we took from the hip joint and femur were negative.

DISCUSSION

In this report, we present a characteristic case of Lemierre's syndrome with septic arthritis and chronic osteomyelitis. Although we failed to detect *F. necrophorum* in the patient's hip, the clinical and radiological findings and the elevated white blood cell count in the arthrocentesis strongly suggested its presence. We can assume two possible reasons for this discrepancy: An anaerobic culture of synovial fluid is not standard at our hospital, and our own experience tells us that cultures of samples taken from joints during ongoing antibiotic therapy frequently fail to detect the bacteria.

Whereas the source of infection, the oropharynx, could be treated relatively quickly, the metastatic musculoskeletal infection was much more challenging. This seems to be a common issue in the context of Lemierre's syndrome. Even though the characteristic germ, *F. necrophorum*, is usually susceptible to a wide antibiotic spectrum, and especially to penicillin, metronidazole and clindamycin,⁸ repeated surgical procedures are often necessary. Because the patient's condition deteriorated repeatedly despite our surgical procedures and an antibiotic therapy matching the susceptibility report of *F. necrophorum*, which we detected in blood cultures, we changed the antibiotic regimen several times, assuming that another, yet undetected, bacterium may be causing the osteomyelitis. Indeed, some other bacteria

have been linked to Lemierre's syndrome in combination with *F. necrophorum* or alone.⁵

Specific circumstances may facilitate or aggravate a metastatic joint infection in Lemierre's syndrome. This may be an articular sporting injury, which occurs during an episode of a sore throat and is treated with oral steroids, as described by Harris *et al*⁹ in a 17-year-old girl, or maintaining 'a sitting position for as many as 14 hours a day' due to the patient's 'obsession with online games' as reported by Hsu *et al*.¹⁰ Whereas the short-term outcome of Harris *et al*'s patient was favourable despite high-grade chondral damage, the patient reported by Hsu *et al* developed severe sepsis and required a total hip replacement. As in most cases of Lemierre's syndrome, the infection of our patient's joint occurred spontaneously, without prior injury or disease apart from a sore throat. One could hypothesise that our first needle aspiration was an iatrogenic injury which facilitated bacterial inoculation into an aseptic reactive joint effusion. We presume, however, that we simply misjudged the result of that needle aspiration. In retrospect, the white blood cell count, which was elevated at $74.4 \times 10^9/L$, already indicated a bacterial arthritis at that time.¹¹

Hsu *et al* also reviewed five other cases of septic arthritis provoked by *F. necrophorum*. All patients were admitted to the hospital 1–5 days after the appearance of the first symptoms of a septic arthritis and were treated by a combination of surgical drainage via arthrotomy and intravenous broad-spectrum antibiotics. Whereas in one patient the limb had to be amputated due to myonecrosis, the other patients recovered entirely. Contrary to our case, none of them showed signs of osteomyelitis.^{10 12–16}

A case of Lemierre's syndrome not complicated by arthritis but rather by osteomyelitis was described by Stahlman *et al*¹⁷ in a 13-year-old boy admitted to the hospital with a 10-day history of pharyngitis, fever and chills, and a 3-day history of ankle and knee pain but no joint effusions. The needle aspirations of the fibula and femur revealed 'foul-smelling brown pus'. They debrided the infected bone marrow and achieved a complete recovery following 6 weeks of intravenous penicillin G.

While arthrotomy has been the standard treatment of septic arthritis in children and adolescents, not only in Lemierre's syndrome,¹⁸ we chose arthroscopic debridement and synovectomy as the preferred procedure. Data published over the past several years have shown that this is a reliable, minimally invasive method that can be used to successfully treat bacterial arthritis of the hip in adults and in children and adolescents.^{19–21} In addition, the average length of hospital stay is generally reduced compared with arthrotomy.²² In our case, however, the arthroscopic intervention only led to a temporary improvement and the choice of procedure had to be adjusted when an osteomyelitis of the proximal femur was identified.

In conclusion, although the involvement of joints in Lemierre's syndrome, ranging from simple arthralgia to osteomyelitis,⁵ is quite rare,²³ this possible complication should be kept in mind and must probably be treated aggressively, regardless of negative bacterial cultures. Particular attention must be paid to the specific pitfalls in the diagnosis and therapy of anaerobes, for example their intrinsic resistance to aminoglycosides, which are usually part of the standard therapy of musculoskeletal infections.²⁴ A recovery can then normally be achieved. The time interval between the first symptoms and the onset of an effective therapy may have an important impact on the outcome, as well as whether or not the arthritis is complicated by osteomyelitis.²⁵ In our case, osteomyelitis and the treatment directed thereafter led to an osteonecrosis of the proximal femur, which ultimately led to the complete destruction of the patient's hip joint.

Learning points

- ▶ Lemierre's syndrome commonly affects young and previously healthy patients.
- ▶ The first symptoms of Lemierre's syndrome are non-specific, but its course is often fulminant.
- ▶ We should bear in mind this differential diagnosis of oropharyngeal infections, especially when there are signs of a systemic infection in combination with more specific symptoms, such as unilateral swelling and neck pain.
- ▶ Metastatic joint infections are a potential complication of Lemierre's syndrome and may lead to complete articular destruction.
- ▶ If a joint infection is suspected, further investigations and an immediate, consequent therapy are obligatory, regardless of negative bacterial culture.

Contributors MR, LT and MK were responsible for the patient's treatment and also for most of the acquisition, analysis, interpretation and reporting of the patient's data in terms of imaging techniques, laboratory tests and clinical findings. MR was mainly responsible for the treatment of the patient's hip, whereas MK and LT managed the general treatment of the Lemierre's syndrome and therefore performed a systematic literature research. DMV was — supervised by MR — mainly responsible for the conception and writing of this article based on the data provided by MR, LT and MK and another systematic literature research. All authors were directly involved in the writing process by revising, discussing and modifying the article's text and content.

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