Case Report

Chronic prosthetic joint infection caused by *Listeria monocytogenes*

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We report what is to the best of our knowledge the first case of persistent human listeriosis. A housewife underwent excision of a leiomyosarcoma and implantation of a prosthetic knee device. Infection of the device with *Listeria monocytogenes* occurred and persisted for 2 years. Despite having an allergy to ampicillin, the patient was cured solely by antibiotics and without surgery.

Introduction

Prosthetic joint infections are often caused by organisms such as staphylococci, streptococci or Gram-negative bacilli. Though rarely involved in prosthetic joint infection, *Listeria monocytogenes* has recently become a topic of interest due to the spread of prosthetic joint replacements among people receiving immunosuppressive therapy (Allerberger et al., 1992). It is known that immunosuppressive therapy promotes the manifestation of listerial infections; this can be observed, for example, in cases of rheumatoid arthritis (Rocourt et al., 2000; Zimmerli, 2006). We describe a case that, to the best of our knowledge, represents the first published report of a human infection with *L. monocytogenes* lasting for more than 2 years.

Case report

A 63-year-old housewife was initially admitted to the orthopaedic polyclinic with uncharacteristic pain in the right distal lateral femur. A radiograph and magnetic resonance imaging scan of the leg raised suspicion of a malignant bone tumour in the distal lateral femur (Fig. 1). A chest radiograph was normal. The patient’s past medical history was notable for mammary carcinoma, which was treated by extirpation of the tumour, postoperative radiation therapy and tamoxifen administration for 2 years.

When the patient was admitted to the hospital for further examination of the leg, histological examination of a diagnostic biopsy identified a low-grade malignant sarcoma. No metastases were identified by abdominal sonography, computed tomography scan of the lung or bone scan. As a consequence, the patient underwent an operation that included tumour resection at the distal lateral femur and implantation of a total knee prosthesis. The histological examination of the resected tumour confirmed a low-grade, highly differentiated leiomyosarcoma. No tumour cells were detected in the resected margins suggesting complete excision of the tumour. Due to impaired wound healing and wound secretion, the patient was then operated on for a second time, 2 weeks later. In the following 4 months healing was reported as normal and the patient was free of complaints. In addition, a check-up performed at this time revealed that the knee prosthesis was in the correct position and no postoperative radiotherapy was required.

Five months after tumour resection, the patient was readmitted to the orthopaedic polyclinic, with the symptoms of fever (38.7°C), swelling and painful inflammation of the operated knee. Laboratory findings included marked leukocytosis and elevated inflammatory markers (Table 1). On physical examination, a joint effusion of the knee was verified and aspirated for further laboratory diagnostics. Culture of the aspirate yielded growth of Gram-positive rods. The biochemical profile obtained by using the dried MicroScan Pos Combo type 9 panel of the MicroScan WalkAway 96 system (Dade Behring) identified the bacteria as *L. monocytogenes*. This panel was also used for testing susceptibility towards several antibiotics (including those used for therapy) by the breakpoint method. Based on this finding and the patient’s history of ampicillin allergy, an initial therapy was started with levofloxacin and co-trimoxazole to which the pathogen was susceptible. A follow-up after several weeks revealed a reduced severity of symptoms and normalized inflammatory markers (Table 1); therefore, the therapy ended.

Abbreviation: CRP, C-reactive protein.
Over the next 18 months several episodes of swelling and painful inflammation of the knee recurred, which, as for previous episodes, were accompanied by pathological levels of C-reactive protein (CRP) (Table 1). No pathogenic bacteria were detected in several knee aspirates and wound swabs. The patient was empirically treated with courses of cefuroxime/levofloxacin, cefuroxime/clindamycin or levofloxacin/clindamycin; however, complete healing of the knee could not be achieved. It is notable that during this period the knee prosthesis broke (Fig. 2). When the patient was operated on again, the knee prosthesis was removed and the complete femur was replaced by a new prosthesis.

Seventeen months later (a total of 2 years after the first detection of *L. monocytogenes*), two further wound swabs were taken and the microbiological analysis for the second time identified *L. monocytogenes*. The patient was given another course of antibiotic therapy that, at this time, consisted of linezolid for 4 weeks, rifampicin for 3 months and co-trimoxazole for 4 months. With this antibiotic regime, the symptoms disappeared, so that the complete femur prosthesis could be preserved and the leg could be saved from amputation. The antibiotic therapy was ended due to the disappearance of symptoms, and the patient was dismissed in a satisfying condition and has remained without symptoms to the present day (3 September 2008).

**Discussion**

*L. monocytogenes* is a Gram-positive rod that can grow in food from animal sources and in decaying vegetable matter (Vazquez-Boland *et al.*, 2001). Asymptomatic human and animal carriers exist. In the vast majority of cases, infections

![Fig. 1. Primary tumour of the distal lateral femur (indicated by an arrow).](http://jmm.sgmjournals.org)

**Table 1. White blood cell count and CRP levels**

Bold entries are those where detection of *L. monocytogenes* was positive.

<table>
<thead>
<tr>
<th>Date</th>
<th>White blood cell count (cells µL⁻¹)</th>
<th>CRP (mg l⁻¹)</th>
<th>Detection of <em>L. monocytogenes</em></th>
<th>Antibiotic treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>03.01.2004</td>
<td>17 900</td>
<td>73</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>04.01.2004</td>
<td>11 300</td>
<td>194</td>
<td><strong>Pos (knee aspirate)</strong></td>
<td>L (500 mg every 24 h) + Co (480 mg every 8 h) for 6 weeks</td>
</tr>
<tr>
<td>06.01.2004</td>
<td>6 900</td>
<td>226</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>08.01.2004</td>
<td>–</td>
<td>–</td>
<td><strong>Neg (knee aspirate)</strong></td>
<td></td>
</tr>
<tr>
<td>15.01.2004</td>
<td>4 600</td>
<td>18</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>04.08.2004</td>
<td>–</td>
<td>–</td>
<td><strong>Neg (knee aspirate)</strong></td>
<td></td>
</tr>
<tr>
<td>09.08.2004</td>
<td>5 420</td>
<td>88</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>18.02.2005</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>C (500 mg every 12 h) + L (500 mg every 12 h) for 10 days</td>
</tr>
<tr>
<td>01.03.2005</td>
<td>–</td>
<td>–</td>
<td><strong>Neg (knee aspirate)</strong></td>
<td>C (1500 mg every 8 h) + Cl (600 mg every 8 h) for 2 weeks</td>
</tr>
<tr>
<td>26.04.2005</td>
<td>–</td>
<td>–</td>
<td><strong>Neg (wound swab)</strong></td>
<td></td>
</tr>
<tr>
<td>11.07.2005</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>L (500 mg every 24 h) + Cl (300 mg every 6 h) for 4 months</td>
</tr>
<tr>
<td>06.01.2006</td>
<td>4 770</td>
<td>90</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>09.01.2006</td>
<td>–</td>
<td>–</td>
<td><strong>Pos (knee aspirate)</strong></td>
<td>Li (600 mg every 12 h) for 4 weeks + Co (960 mg every 12 h) for 4 months + R (600 mg every 24 h) for 3 months</td>
</tr>
<tr>
<td>12.01.2006</td>
<td>6 080</td>
<td>49</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>23.01.2006</td>
<td>4 410</td>
<td>23</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>26.05.2006</td>
<td>–</td>
<td>–</td>
<td><strong>Neg (wound swab)</strong></td>
<td></td>
</tr>
<tr>
<td>05.01.2007</td>
<td>6 610</td>
<td>13</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>19.05.2008</td>
<td>5 900</td>
<td>&lt;5</td>
<td>–</td>
<td></td>
</tr>
</tbody>
</table>

C, Cefuroxime; Cl, clindamycin; Co, co-trimoxazole; L, levofloxacin; Li, linezolid; R, rifampicin; neg, negative; pos, positive.
with *L. monocytogenes* occur by foodborne transmission. Most of the affected patients have predisposing conditions that lower cell-mediated immunity, such as transplantation, lymphomas and AIDS (Rocourt et al., 2000). These persons often develop meningoencephalitis and sepsis. In addition, a few case reports have described focal infections caused by *L. monocytogenes* including arthritis, endocarditis and osteomyelitis (Vazquez-Boland et al., 2001).

We report here, for what is believed to be the first time, a patient with a chronic device infection with *L. monocytogenes*. The uniqueness of our case derives from the persistence of this infection for approximately 2 years, most likely due to a treatment failure. This failure may originate from the fact that there are no evaluated guidelines for the therapy of local infections with *L. monocytogenes*. Therapy for listerial infection of a prosthetic device is even more experimental, due to the rarity of cases. The generally accepted therapy consists of a combination of ampicillin and gentamicin. In the case of allergy against ampicillin (as in our case), the therapy should be changed to treatment with co-trimoxazole. All antibiotics should be given for at least 3 months. In our case, application of co-trimoxazole was stopped during the second month after the initial observation of *L. monocytogenes* due to a reduction in the severity of symptoms and a normalization of inflammatory markers (Table 1). At this time, the patient also received the oestrogen receptor modulator tamoxifen (due to a history of mammary carcinoma), which is described as being inhibitory to dendritic cells (Nalbandian et al., 2005). For this reason, the patient may have been immunocompromised making her more susceptible to *Listeria* infection.

The ensuing relapses of the infection, indicated by several episodes of swelling and painful inflammation, were treated by different combinations of cefuroxime, levofloxacin or clindamycin, which possess little or no activity against *L. monocytogenes*. These regimens were selected, because at this time there was no further detection of *L. monocytogenes* and other bacteria such as staphylococci were considered more likely as pathogen candidates.

After a total of 2 years of the disease, *L. monocytogenes* was detected for the second time in an aspirate of the affected knee. The knee aspirate was taken during another episode of swelling and painful inflammation. At this time, surgical treatment was no longer applicable without amputation of the leg. Due to the presence of *Listeria* and an allergy towards ampicillin, the patient was treated with a combination of linezolid for 4 weeks, rifampicin for 3 months and co-trimoxazole for 4 months. The considerations leading to this choice dealt with the pharmacokinetics and efficiency of the agents. In this regard linezolid, rifampicin and co-trimoxazole all reach high tissue concentrations and can be administered orally. Linezolid and rifampicin have also proven to be effective in the treatment of serious listerial infections such as rhombencephalitis and brain abscess (Leiti et al., 2005; Morosi et al., 2006). After this course of antibiotics the severity of symptoms was reduced and the leg was saved from amputation.

In the absence of surgery, cure by treatment with antibiotics alone is remarkable, given the long endurance of the disease. One possible explanation for this success might be that the causative strain of *L. monocytogenes* did not form biofilms [as revealed by measuring the optical densities of stained bacterial films adherent to the bottoms of plastic tissue culture plates (Christensen et al., 1985)]. The well known listerial pathogen factors PrfA, PlcA, Hly, Mpl, ActA, PlcB, InlA, InlB, InlC, UlpA, Bsh and PrsA were detected as described for the *L. monocytogenes* strain EGD-e (Chatterjee et al., 2006). Biofilms are composed of an adhesive matrix that protects the bacteria against antibiotics. Because of this, prostheses infected by common biofilm-producing bacteria like *Staphylococcus epidermidis* typically are not accessible to antibiotic treatment and therefore have to be surgically removed.

Our case is unique as a literature search reveals just 24 other reports of prosthetic joint infections caused by *L. monocytogenes*, all of which lasted less than 6 months. In 12 of these cases, the infection was successfully treated by the combination of surgical intervention and prolonged antibiotic therapy. Subsequently in these cases, the prostheses were preserved or replaced with full functionality during the follow-up period of at least 4 months (Chougle & Narayanaswamy, 2004; Cone et al., 2001; Gomez et al., 2006; Hansen et al., 1996; Kesteman et al., 2007; Tabib et al., 2002). In ten other cases, the authors reported successful conservative treatment regimens of prosthetic joints infected by *L. monocytogenes* predominantly with an intravenous antibiotic combination of ampicillin and gentamycin, followed by a prolonged oral administration of co-trimoxazole or ampicillin (Cone et al., 2001). In two further

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**Fig. 2.** Broken knee prosthesis (indicated by an arrow).
cases the patients died, one of them possibly secondary to an adult respiratory distress syndrome or to congestive heart failure, and the other from the underlying malignancy (Cone et al., 2001). In conclusion, this report clarifies the importance of uncommon pathogens like L. monocytogenes for prosthetic joint infections, and emphasizes the need for adequate antibiotic therapy, especially when surgical revisions are medically undesirable.

References


