ORIGINAL ARTICLE

Post-traumatic bone and/or joint limb infections due to Clostridium spp.

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Background: Clostridium spp. are saprophytic Gram-positive bacteria found in soil and capable of generating endospores. Spore germination occurs when environmental conditions are favorable. Clostridium spp. can cause infections of compound fractures and deep wounds contaminated from soil micro-organisms.

Hypothesis: Clostridium spp. infections of traffic-related injuries are particularly severe events whose outcome is uncertain even with aggressive medical and surgical treatment.

Materials and methods: We retrospectively reviewed 12 patients (median age, 45 years) with Clostridium spp. bone and/or joint infections complicating compound limb fractures with soil contamination and extensive soft-tissue damage. Prophylactic amoxicillin-clavulanic acid therapy was administrated, followed by emergency surgical wound debridement and lavage. Fracture fixation was performed immediately in nine patients (external in four and internal in five) or at a later time on three patients. The immediate outcome was unfavourable in all 12 cases, requiring early reoperation after a median of 10 days (range, 5–25 days).

Results: Median time to Clostridium strain identification was 14.5 days (range, 5–160). All infections were polymicrobial. Surgical wound excision, hardware removal (in four cases), and antibiotic therapy produced a favourable outcome in one patient, with no recurrence after 2 years of follow-up; the outcome was unfavourable in 11 cases, with delayed fracture union.

KEYWORDS
Wound infection; Bone infection; Anaerobic; Clostridium; Spores

Summary

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septic non-union, impaired healing, and/or chronic sinus tract drainage. Several second-line treatments were used in these 11 patients: intramedullary nailing without bone grafting in four patients, with three failures; decortication and grafting in two patients, with failure in both; nailing with decortication in one patient, who had a good outcome; and the induced membrane procedure described by Masquelet in four patients, all of whom had good outcomes. After a median follow-up of 24 months (range, 18–53 months), the bone infection had subsided in eight patients. The remaining four patients had septic non-union.

Discussion: *Clostridium* spp. infections are particularly severe. The diagnosis is delayed and identification of the organism is challenging. The treatment is difficult and results in unfavourable outcomes in one-third of cases. The identification of *Clostridium* in specimens from an osteoarticular infection indicates a need for extremely extensive and aggressive surgical resection, as spore resistance may impair the in vivo efficacy of antimicrobial agents.

Level of evidence: IV (retrospective cohort study).

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Introduction

*Clostridium* spp. are Gram-positive rods that are obligate anaerobes found in soil and capable of producing endospores [1]. Some species (e.g., *C. tetani*, *C. botulinum*, *C. difficile*, and *C. perfringens*) release toxins that cause acute clinical disorders (e.g., tetanus and botulism) [2]. When the environmental conditions are unfavourable, *Clostridium* spp. produce endospores that are highly resistant to physical and chemical factors in the environment (soil or water) [1,3]. In humans, the spores may result in chronic and recurrent infections [4]. Although the spores produce no clinical manifestations, they germinate when the conditions become more favourable, generating a population of actively dividing bacteria [1]. Many trauma-related injuries are at high risk for *Clostridium* spp. infection, most notably severely soiled open fractures or wounds, which may be massively contaminated with environmental micro-organisms.

Nevertheless, although *Clostridium* spp. are ubiquitous in the environment [3] and open trauma is common [5], osteoarticular infections with *Clostridium* spp. are rare. There is a paucity of published data on these infections, their treatment, and their outcomes [2,6–15].

Here, we hypothesized that post-traumatic *Clostridium* spp. infections were particularly severe whose outcome remained unpredictable despite aggressive medical and surgical treatment delivered in a specialised centre (in France, reference centre for complex osteoarticular infections, CROAC). We reviewed cases of post-traumatic osteoarticular limb infections due to *Clostridium* spp. Outcomes were assessed after a follow-up of at least 18 months following identification of the organism. Our goal was to develop suggestions about the optimal medical and surgical management.

Material and methods

We conducted a single-centre retrospective study at the Institut Locomoteur of the Toulouse Teaching Hospital in Toulouse, France. The electronic database of the hospital’s bacteriology laboratory was searched (MA, JL) for adult patients with limb trauma and at least one specimen taken in the operating room and positive for *Clostridium*. We identified 23 patients who met these criteria between April 2006 and March 2010. Among them, 11 were excluded (two with superinfected heel pressure sores and no history of trauma, one with impaired healing after treatment for a benign tibial tumour, one with hip arthritis after impaired healing complicating a closed ankle fracture with hematogenous contamination, one with surgical-site infection after a closed fracture, one with infection after finger amputation by a lawnmower, one with a compound pelvic fracture, and four with soft-tissue infections in the absence of osteoarticular involvement). The remaining 12 patients had osteoarticular infections complicating compound fractures of the limbs. There were 10 men and two women with a median age of 45 years (range, 18–77 years). Table 1 reports their main characteristics, including their initial bone and skin injuries according to the classification schemes developed by Cauchoux et al. [16] and Gustillo et al. [17].

Microbiological studies

All specimens were seeded in various enriched culture media than incubated in a CO2 atmosphere and aerobic conditions for 15 days. *Clostridium* strains were identified using standard criteria, namely, appearance of the colonies, appearance of the Gram-stained organisms, visualisation of spores, and biochemical characteristics documented using ID 32® test strips (BioMérieux SA, Marcy l’Etoile, France). Definitive identification was achieved by 16S RNA sequencing. When the same strain was recovered from several specimens collected on the same day, this strain was studied only once.

Antibiotic susceptibility was assessed using ATB ANA® test strips (BioMérieux SA) and the agar disc-diffusion method (Biorad, Marnes la Coquette, France). Other bacteria recovered in the specimens were recorded (Table 2). All microbiological studies were performed by the same team (MA, JL).

Multidisciplinary medical and surgical management

After collection of the specimens, probabilistic antibiotic therapy was given. Any changes required by the microbiologic results were made subsequently. Advice from an
infectious diseases specialist (EB) was obtained for all 12 patients. Starting on January 1, 2009, each case was discussed during a multidisciplinary meeting (with at least one physician biologist specialised in bacteriology, one infectious diseases specialist, one orthopaedic surgeon, and one pharmacist) within the framework of the CRIOAC for South-Western France. Outcomes were assessed at least 18 months after *Clostridium* was first identified, based on clinical features (e.g., fever, wound healing, and discharge), radiographic findings (fracture union); and laboratory test results (leukocyte count and C-reactive protein level) throughout follow-up and at the last evaluation.

**Results**

**Immediate management and initial course (see Appendix 1 in the online supplement)**

All 12 patients had compound fractures after high-energy trauma with soil contamination and extensive soft-tissue lesions (Gustillo 3A or 3B). Surgical wound excision and lavage was consistently performed on an emergency basis. Prophylactic antibiotic treatment was started in all but one patient (case #9); five patients also received gentamycin and 1 ofloxacin. Emergency fixation was performed in nine patients (external fixation in four and internal fixation in five); the remaining three patients underwent fixation after 18, 25, and 21 days, respectively. The initial course was unfavourable in all two patients, with a discharge (*n* = 8), delayed wound healing (*n* = 7), secondary necrosis of the skin (*n* = 2), and/or abscess formation (*n* = 2). A fever occurred in 10 patients and laboratory evidence of inflammation in nine patients. These unwanted events consistently led to early surgical revision (SR), after a median of 10 days (range, 5–25 days). Early revision usually consisted in extensive lavage and excision of necrotic tissues (Table 2). The fixation material was removed in four cases.

**Microbiology**

In 11 of the 12 patients, the microbiological studies recovered multiple organisms usually found in soil or the environment (*Clostridium, Bacillus cereus, Enterobacter cloacae, Pseudomonas aeruginosa, and Acinetobacter baumannii*) and on the skin or in the gastrointestinal tract (e.g., *Staphylococcus aureus*). *Clostridium* was recovered from SR; specimens in eight patients. In the four remaining patients, *Clostridium* was identified during subsequent
revisions performed 8 to 150 days later. Median time to the identification of *Clostridium* was 14.5 days (range, 5–160 days). *Clostridium* was always combined with other organisms, and in six of the 12 patients more than one *Clostridium* strain was recovered. In all, 23 different *Clostridium* strains were retrieved from the 12 patients, from 73 specimens, of which 56 (76%) were positive (Tables 2 and 3).

<table>
<thead>
<tr>
<th>Case #</th>
<th>Time from accident to first surgical revision (SR₁)</th>
<th>Procedures during the first surgical revision (SR₁)</th>
<th>Organisms identified in specimens taken during the first surgical revision (SR₁)</th>
<th>Outcome after the first surgical revision (SR₁)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5 days</td>
<td>Wound excision + lavage</td>
<td><em>Bacillus cereus</em></td>
<td>Unfavourable → SR₂</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Acinetobacter baumannii</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Clostridium tetani</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Pseudomonas aeruginosa</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Enterobacter cloacae</em></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>18 days</td>
<td>Wound excision + lavage + internal fixation (plate)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Clostridium beijerinckii</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Enterobacter aerogenes</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Enterobacter Cloacae</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Pseudomonas aeruginosa</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Clostridium histolyticum</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Clostridium subterminale</em></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>9 days</td>
<td>Lavage of the knee</td>
<td><em>Staphylococcus aureus</em></td>
<td>Unfavourable: resolution of the signs of infection + slow wound healing</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Staphylococcus capitis</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Staphylococcus epidermidis</em></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>16 days</td>
<td>Wound excision + lavage + removal of the plate</td>
<td><em>Pseudomonas aeruginosa</em></td>
<td>Unfavourable: delayed wound healing + purulent discharge</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Escherichia coli</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Clostridium sporogenes</em></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>10 days</td>
<td>Wound excision + lavage</td>
<td><em>Clostridium sp.</em></td>
<td>Unfavourable: initial improvement then relapse → SR₂: wound excision + lavage + drainage</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Citrobacter braakii</em></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>10 days</td>
<td>Wound excision + drainage + lavage of the elbow</td>
<td><em>Serratia marcescens</em></td>
<td>Unfavourable: septic non-union+ systemic signs of infection</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Clostridium sporogenes</em></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>10 days</td>
<td>Wound excision + lavage + nail removal + external fixation</td>
<td></td>
<td>Unfavourable: delayed wound healing + purulent discharge + persistent signs of inflammation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Clostridium sp.</em></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>13 days</td>
<td>Wound excision then vacuum-assisted closure-therapy™ then radial forearm flap for coverage</td>
<td><em>Enterococcus faecalis</em></td>
<td>Unfavourable: delayed wound healing + purulent discharge + osteoarticular infection of the elbow</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Serratia marcescens</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Clostridium sporogenes</em></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>25 days</td>
<td>Wound excision + lavage</td>
<td><em>Enterobacter aerogenes</em></td>
<td>Unfavourable: delayed wound healing + purulent discharge → SR₂: wound excision + lavage + drainage</td>
</tr>
<tr>
<td>10</td>
<td>21 days</td>
<td>Wound excision + lavage + change of external fixator</td>
<td><em>Clostridium subterminale</em></td>
<td>Unfavourable: delayed fracture union</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Pseudomonas aeruginosa</em></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>5 days</td>
<td>Wound excision + lavage</td>
<td><em>Enterobacter cloacae</em></td>
<td>Unfavourable: delayed wound healing + purulent discharge → SR₂</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Bacillus cereus</em></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>5 days</td>
<td>Wound excision + lavage + removal of the plate</td>
<td><em>Sphingomonas paucimobilis</em></td>
<td>Favourable: resolution of the signs of infection + wound healing</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Clostridium subterminale</em></td>
<td></td>
</tr>
</tbody>
</table>

SR₁: first surgical revision; SR₂: second surgical revision.

**Multidisciplinary medical and surgical management of Clostridium osteoarticular infections (Tables 3 and 4 and Appendix 2 in the online supplement)**

Median time from the accident to initiation of antibiotic treatment effective against *Clostridium* was 15.5 days
Table 3  Surgical management at the identification of Clostridium, strains identified, and early outcomes.

<table>
<thead>
<tr>
<th>Case #</th>
<th>Time from the accident to initiation of antibiotics effective against the identified Clostridium strains</th>
<th>Time from the accident to identification of Clostridium (number of the surgical revision)</th>
<th>Clostridium species identified (number of positive specimens / total number of specimens)</th>
<th>Surgical treatment of osteoarticular infection performed at identification of Clostridium</th>
<th>Initial outcome with medical and surgical treatment against Clostridium</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4 days</td>
<td>17 days (SR2)</td>
<td>Clostridium beijerinckii (4/4)</td>
<td>Wound excision + lavage + vacuum-assisted closure-therapy™ then leg skin graft</td>
<td>Unfavourable: initial resolution of the signs of infection but delayed fracture union</td>
</tr>
<tr>
<td>2</td>
<td>16 days</td>
<td>18 days (SR1)</td>
<td>Clostridium beijerinckii (1/2)</td>
<td>Wound excision + drainage of the elbow</td>
<td>Unfavourable: initial resolution of the signs of infection but delayed fracture union</td>
</tr>
<tr>
<td>3</td>
<td>3 days</td>
<td>9 days (SR1)</td>
<td>Clostridium beijerinckii (4/4)</td>
<td>Lavage of the knee</td>
<td>Unfavourable: resolution of the signs of infection but delayed wound healing</td>
</tr>
<tr>
<td>4</td>
<td>15 days</td>
<td>16 days (SR1)</td>
<td>Clostridium histolyticum (2/4)</td>
<td>Wound excision + lavage + plate removal</td>
<td>Unfavourable: delayed wound healing + purulent discharge</td>
</tr>
<tr>
<td>5</td>
<td>20 days</td>
<td>160 days (SR1)</td>
<td>Clostridium perfringens (1/3)</td>
<td>Wound excision + vacuum-assisted closure-therapy™ then skin graft</td>
<td>Unfavourable: septic non-union</td>
</tr>
<tr>
<td>6</td>
<td>9 days</td>
<td>10 days (SR1)</td>
<td>Clostridium sporogens (2/2)</td>
<td>Wound excision + drainage + lavage of the elbow</td>
<td>Unfavourable: septic non-union + systemic signs of infection</td>
</tr>
<tr>
<td>7</td>
<td>69 days</td>
<td>10 days (SR1)</td>
<td>Clostridium sporogens (2/4)</td>
<td>Wound excision + lavage + nail removal + external fixation</td>
<td>Unfavourable: delayed wound healing + purulent discharge + persistent evidence of inflammation</td>
</tr>
</tbody>
</table>

Table 3 (Continued)

<table>
<thead>
<tr>
<th>Case #</th>
<th>Time from the accident to initiation of antibiotics effective against the identified Clostridium strains(^b)</th>
<th>Time from the accident to identification of Clostridium (number of the surgical revision)</th>
<th>Clostridium species identified(^a) (number of positive specimens / total number of specimens)</th>
<th>Surgical treatment of osteoarticular infection performed at identification of Clostridium</th>
<th>Initial outcome with medical and surgical treatment against Clostridium</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>3 days</td>
<td>13 days (SR(_1))</td>
<td>Clostridium sporogenes (2/2)</td>
<td>Wound excision then vacuum-assisted closure-therapy(^\text{TM}) then Chinese flap for coverage</td>
<td>Unfavourable: delayed wound healing + purulent discharge + septic osteitis and arthritis of the elbow</td>
</tr>
<tr>
<td>9</td>
<td>72 days</td>
<td>47 days (SR(_2))</td>
<td>Clostridium sporogenes (2/2)</td>
<td>Wound excision + drainage + thigh abscess</td>
<td>Unfavourable: initial resolution of the signs of infection but delayed fracture union</td>
</tr>
<tr>
<td>10</td>
<td>24 days</td>
<td>21 days (SR(_1))</td>
<td>Clostridium subterminale (4/4)</td>
<td>Wound excision + lavage + change of the external fixator</td>
<td>Unfavourable: delayed fracture union</td>
</tr>
<tr>
<td>11</td>
<td>5 days</td>
<td>13 days (SR(_2))</td>
<td>Clostridium clostridifforme (2/2)</td>
<td>Wound excision + lavage + hyperbaric oxygen therapy</td>
<td>Unfavourable: delayed fracture union + purulent discharge</td>
</tr>
<tr>
<td>12</td>
<td>19 days</td>
<td>5 days (SR(_1))</td>
<td>Clostridium subterminale (4/5)</td>
<td>Wound excision + lavage + plate removal</td>
<td>Favourable: resolution of the signs of infection + wound healing</td>
</tr>
</tbody>
</table>

SR\(_1\): first surgical revision; SR\(_2\): second surgical revision. For ease of comprehension, the date of Clostridium identification was considered to be the date of intraoperative collection of specimens positive for Clostridium; this simplification removed variability related to the time need to obtained the identification tests (RNA 16S).

\(^a\) Definitive identification was by RNA 16S sequencing.

\(^b\) Which sometimes antedated the definitive identification of Clostridium when probabilistic or broad-spectrum antibiotics were given.
(range, 3–72 days). Concomitantly, the above-described surgical procedures were performed. Hyperbaric oxygen therapy was used in one patient (case #11). After these first-line treatments (Table 3), the outcome was favourable in a single case, with wound healing, cessation of the discharge, and fracture union; there was no recurrence during the 2-year follow-up. The remaining 11 patients had unfavourable outcomes characterized by delayed fracture union or septic non-union (n = 7), impaired wound healing (n = 4), and/or a persistent discharge (n = 1).

These unfavourable outcomes in 11 patients prompted second-line treatments (Table 4). Intramedullary nailing without bone grafting was performed in four patients (cases #1, #7, #10, and #11). This procedure was followed in three patients by reactivation of the infectious process. Two of these patients (cases #1 and #11) were managed using the induced membrane method described by Masquelet [18, 19], which ensured resolution of the infection with union of the fracture. The third patient required removal of the hardware and had septic non-union at last follow-up 25 months after the accident. Two patients (cases #2 and #6) were managed by decortication, autologous cancellous bone grafting, and internal fixation; this procedure failed in both cases. In one patient (case #5), intramedullary nailing with decortication produced a favourable outcome. The induced membrane method developed by Masquelet was used in 4 patients (cases #1, #8, #9, and #11) [18, 19] and was consistently followed by a favourable outcome. Of these four patients, one (case #11) underwent reconstruction with a vascularised fibular graft.

Table 4 reports the outcomes at last follow-up. Median follow-up was 24 months (range, 18–53) after the diagnosis of Clostridium infection; one patient was lost to follow-up. In eight patients, the outcome was favourable, with wound healing, absence of any discharge, and fracture union. The remaining two patients had septic non-union despite multiple surgical procedures; among them, two had a persistent discharge.

Discussion

Clostridium spp. account for 30% of all anaerobic organisms recovered from post-traumatic wounds [8] and 18% of those found in chronic wounds [20]. Clostridium spp. is less often found in anaerobic osteoarticular infections (5%–13%) compared to Gram-negative rods such as Bacteroides fragilis and Fusobacterium spp. (30%-50%), Gram-positive cocci (25%–58%), or Propionobacterium acnes (12%–36%) [6–8,11,21,22]. Post-traumatic osteoarticular infections due to Clostridium spp. are rare [2,6–15], with fewer than 15 cases reported in the medical literature between 2000 and 2010 [2,9–15] (Table 5). Thus, our case-series is the largest reported to date. Follow-up in our study may seem
Table 5  Literature review (2000–2010).

<table>
<thead>
<tr>
<th>Year [ref]</th>
<th>Age</th>
<th>Sex</th>
<th>Type of infection</th>
<th>Setting</th>
<th>Time from accident to Clostridium recovery</th>
<th>Species</th>
<th>Final identification method</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009 [15]</td>
<td>31</td>
<td>F</td>
<td>Osteoarticular infection</td>
<td>Hardware infection after a femoral fracture in a multiple trauma patient (car accident)</td>
<td>1 week</td>
<td>C. difficile</td>
<td>Api 20A</td>
<td>Hardware removal, amoxicillin-clavulanic acid</td>
</tr>
<tr>
<td>2004 [12]</td>
<td>39</td>
<td>M</td>
<td>Osteoarticular infection</td>
<td>Hardware infection and septicaemia after a compound tibial fracture caused by a fall</td>
<td>9 weeks</td>
<td>C. septicum</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>2004 [13]</td>
<td>50</td>
<td>M</td>
<td>Osteoarticular infection</td>
<td>Osteitis around hardware after a compound fracture of the humerus</td>
<td>4 weeks</td>
<td>C. botulinum non toxinogène</td>
<td>RNA 16S</td>
<td>Hardware removal, metronidazole</td>
</tr>
<tr>
<td>2005 [9]</td>
<td>45</td>
<td>M</td>
<td>Osteoarticular infection</td>
<td>Hardware infection after a compound femoral fracture due to a fall</td>
<td>4 weeks</td>
<td>C. celerecrescens</td>
<td>RNA 16S</td>
<td>Cotrimoxazole, clindamycin, metronidazole</td>
</tr>
<tr>
<td>2009 [10]</td>
<td>20</td>
<td>F</td>
<td>Osteoarticular infection</td>
<td>Hardware infection after a compound fracture of the radius due to a motorcycle accident</td>
<td>—</td>
<td>C. glycolicum</td>
<td>RNA 16S</td>
<td>Hardware removal, debridement, vancomycin</td>
</tr>
<tr>
<td>2006 [14]</td>
<td>34</td>
<td>M</td>
<td>Osteoarticular infection</td>
<td>Hardware infection after a compound fracture of the tibia due to a motorcycle accident</td>
<td>23 months</td>
<td>C. sporogenes. amygdalinum</td>
<td>RNA 16S</td>
<td>Hardware removal, debridement, linezolid</td>
</tr>
</tbody>
</table>

M: male; F: female; C: Clostridium. In this table, as for our study, we considered only cases of post-traumatic osteoarticular infection and we excluded infections of prostheses via haematogenous contamination at a distance from the accident.
short; however, we believe that a follow-up of at least 18 months is sufficient, despite the risk of delayed infectious relapses due to spore-producing organisms [4], because in our experience such relapses do not occur beyond 6 months after antibiotic therapy discontinuation.

No patient-related factors or other risk factors exist for these infections, which develop in young individuals with post-traumatic lesions contaminated by soil. The implantation of fixation hardware on an emergency basis is followed initially by skin necrosis, delayed wound-healing, and a seropurulent discharge. The inflammatory response is not always prominent. This unfavourable outcome occurs even when the initial management seemed satisfactory and included antibiotic therapy complying with current recommendations. Antibiotics not effective against the spores [23,24]. In addition, some Clostridium spp. strains are resistant to the antibiotics used in this situation [23,25]. When in doubt, temporary or definitive external fixation should be preferred over internal fixation to allow repeated lavage if necessary. Obtaining microbiological specimens during the initial emergent treatment seems of limited usefulness, in contrast to the collection of specimens during early revision for impaired healing. Moreover, continuing the prophylactic antibiotics for longer than 48 h is not recommended, as this strategy may put selection pressure on the bacteria, thereby inducing spore production.

The quality of the surgical treatment is paramount at all the steps of the management process. During the emergent phase, surgery seeks to prevent the development of anaerobic infections. The most important procedure at this stage for minimising the bacterial inoculate is surgical debridement [26], including extensive but accurately targeted wound excision, which may need to be repeated. The use of pulsed wound lavage is controversial: this method improves the elimination of contaminants but constitutes an additional source of trauma for the adjacent soft tissues, which may undergo focal necrosis thereby promoting spore germination and bacterial proliferation. In addition, a dreaded complication of pulsed lavage is the propulsion of bacteria and spores into deep tissues that were previously healthy [27–30]. Hyperbaric oxygen therapy may contribute to the management of anaerobic bone infections when used in combination with surgery and antibiotics [31].

In patients with bone or joint infection, the organism must be identified and the extent of the infection determined. Clostridium spp. are difficult to identify: although these organisms were present, nearly one-fourth of the specimens in our study remained negative. Every effort must be made to accurately identify the organism or organisms (surgical collection of multiple deep specimens and use of the various available microbiological tests, among which RNA 16S sequencing is the reference standard [32]). The extent of the bone infection can be determined using appropriate imaging studies. External fixation is useful in this situation, as it produces no artefacts during magnetic resonance imaging. Bone and leukocyte scintigraphy may be helpful [33].

The identification of Clostridium in a patient with an osteoarticular infection has particularly serious implications, most notably when the infectious process extends to the medullary cavity, where the spores might persist in poorly vascularized bone. In this situation, antibiotics are ineffective in vivo, although most Clostridium spp. strains are susceptible in vitro to the usual antibiotics (e.g., metronidazole and penicillin A). Identification of a Clostridium strain indicates a need for aggressive surgical treatment [26], which may require reoperation if the initial procedure is deemed suboptimal. In our experience, wound excision and lavage without extensive bone tissue resection failed in nearly every case. Thus, all the infected tissues must be excised and any internal hardware removed. The best results are obtained using the Masquelet procedure [18,19] consisting in very extensive excision of the infected tissues followed by implantation of an antibiotic-impregnated cement spacer. Before starting the excision step, deep microbiological specimens are collected to ensure documentation of the infection before antibiotic therapy initiation. We believe antibiotics should be given for 6 to 8 weeks. The second step of the Masquelet procedure is performed at least 3 weeks after antibiotic therapy discontinuation, to ensure that there is no early relapse of the infectious process. The bony defect is reconstructed using a cortical-cancellous bone graft, which should be vascularised whenever possible to improve local antibiotic diffusion [34]. In patients with septic non-union, we believe that decortication without extensive resection and bone grafting is inadequate and carries a high risk of failure. Similarly, intramedullary fixation after removal of an external fixator usually failed in our experience.

Conclusion

Osteoarticular infections due to Clostridium spp. are particularly serious. The diagnosis is often made late, after germination of the spores. The presence of a Clostridium strain should be considered in patients with soil-contaminated wounds and poor local outcomes. Clostridium spp. are difficult to identify, particularly as they are always found in conjunction with various other organisms. The treatment remains extremely challenging. Thus, despite multidisciplinary management, one-third of our patients had unfavourable outcomes. Therefore, when a Clostridium strain is identified in specimens from an osteoarticular infection, priority should be given to very extensive and aggressive surgical excision, which should be repeated if necessary, as spore resistance may impair the in vivo efficacy of antibiotics.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.otsr.2012.03.019.
Post-traumatic bone and/or joint limb infections due to *Clostridium* spp.

**References**


