

Chronic Osteomyelitis Due to *Tissierella carlieri*: First Case

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A 54-year-old woman sustained an open fracture of the right femoral shaft after a bicycle accident in 1985. Several operations were performed, the last including internal fixation using a plate and screws. In 2002, acute diverticulitis was treated with ciprofloxacin/metronidazole. In 2007, she presented with pain and swelling of the right thigh. Plain radiographs showed radiolucent femoral areas (Figure 1a and b). Treatment was with debridement and removal of orthopedic hardware except for a difficult-to-remove screw fragment. Gentamicin beads were temporarily placed along the femur. Eight intraoperative specimens showed no growth after 10 days. Because of poor wound healing, a computed tomography scan was obtained, showing a sinus tract, femoral cortical defects, and intramedullary air (Figure 1c–e). Additional debridement was done; cultures of intraoperative biopsy specimens again remained sterile. Amoxicillin/clavulanate was prescribed for 2 weeks, and ciprofloxacin/rifampin was prescribed for 10 weeks.

In 2008, local pain and swelling reappeared. Magnetic resonance imaging showed chronic osteomyelitis, contiguous with the screw fragment. This was removed, and the medullary cavity was reamed from proximal to distal [1]. Seven intraoperative specimens showed no growth after 10 days. Amoxicillin/clavulanate was prescribed for 3 months. In 2010, local swelling reappeared. Surgical bone biopsies showed no growth at 10 days. Bacterial broad-range 16S rRNA gene polymerase chain

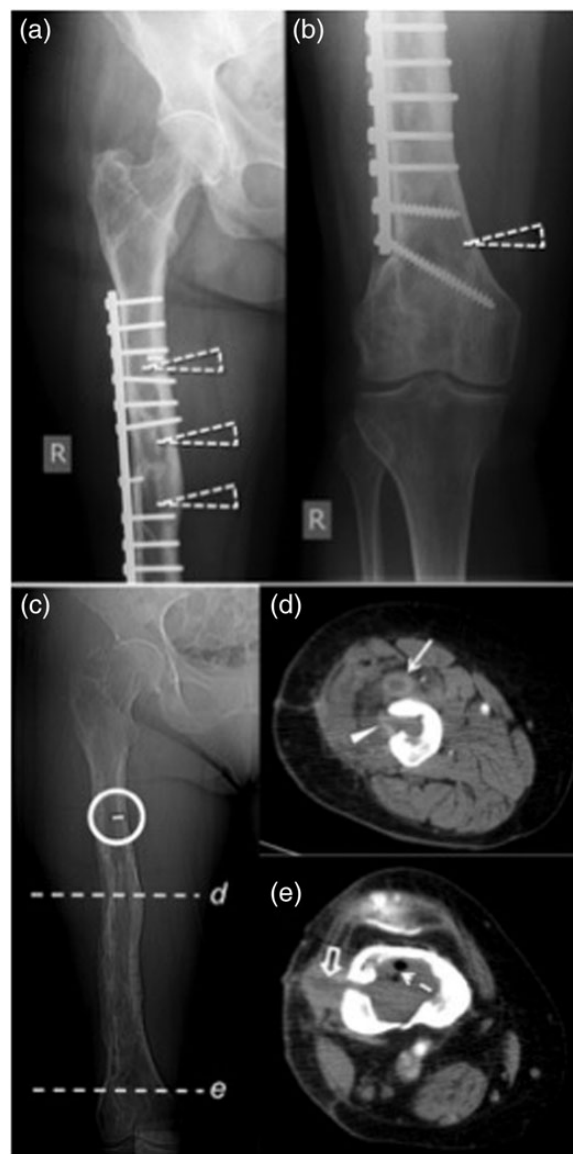


Figure 1. Chronic femoral osteomyelitis demonstrated by plain radiographs and computed tomography in 2007. Anterior-posterior plain film projections (a and b) show the orthopedic hardware and several radiolucent areas within the femur (open dashed arrowheads). Scout image of the computed tomography (c) shows the remnant of a screw (circle); location of axial images performed with intravenous contrast are marked with lines (d and e). Image (d) demonstrates an abscess formation ventral to the midportion of the femur within the vastus intermedius muscle (arrow), extending to the bone marrow (arrowhead) through a borehole defect. (e) In the distal femur, intramedullary gas (dashed arrow) within a fluid collection is shown, extending through a lateral cortical defect and a sinus tract (open arrow) to the skin.

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reaction (PCR) was done, and sequence analysis showed a *Tissierella* species. At 3 weeks, 3 of 7 biopsies showed pure anaerobic growth of a *Tissierella* species in brain-heart-infusion broth. The isolate was positive for arginine dihydrolase, alkaline

Table 1. Minimal Inhibitory Concentrations (MICs) of Clinical *Tissierella carlieri* Strain to 10 Antimicrobial Agents*

Antimicrobial Agent	MIC ($\mu\text{g/L}$)	Interpretation
Penicillin	<0.002	Susceptible
Amoxicillin-clavulanic acid	<0.016	Susceptible
Piperacillin-tazobactam	<0.016	Susceptible
Ceftriaxone	<0.016	Susceptible
Imipenem	0.002	Susceptible
Meropenem	<0.002	Susceptible
Ertapenem	<0.002	Susceptible
Clindamycin	64	Resistant
Metronidazol	<0.016	Susceptible
Moxifloxacin	0.064	Susceptible

* Susceptibility testing was done with the E-test system (bioMérieux). Interpretation of MICs was performed according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines (V5.0, 2015-01-01) using the clinical breakpoint table for Gram-positive anaerobes. Ceftriaxone and moxifloxacin susceptibility was interpreted applying CLSI standards (M100-S25 Vol. 35 No. 3).

phosphatase, and pyroglutamic acid arylamidase (rapid ID32A test strip; bioMérieux, Switzerland) and leucine arylamidase, tyrosine arylamidase, phenylalanine arylamidase, and pyroglutamic acid arylamidase (VITEK, bioMérieux, Switzerland). Identification was done by sequencing almost the entire 16S rRNA gene. The 1434 base pair (bp) sequence deposited in GenBank (accession no. KR781503) showed 1 mismatch over a 1371 bp segment compared with reference *Tissierella carlieri* strain LBN 292 (99.9% sequence similarity) that was recently described [2]. Susceptibility testing results are listed in Table 1.

No antimicrobial therapy was started because the pathogenic role of the *Tissierella* was unclear, and the wound had healed. In November 2011, local pain and discharge from the scar were noted. Imaging revealed osteomyelitis (Figure 2), including an area with sequestra in the lateral femoral condyle, an area not debrided until then. In January 2012, the distal three fifths of the medullary cavity were reached by a long cortical window from lateral. Intraoperatively, a sinus tract and several bony sequestra were found. Extensive intramedullary debridement was performed, and a cement spacer containing gentamicin/clindamycin/meropenem beads was temporarily placed. Aerobic and anaerobic cultures from 16 surgical specimens remained sterile after 6 weeks; broad-spectrum PCR again showed the *Tissierella* species in 2 of 2 specimens. The patient completed a 12-week course of amoxicillin and remains asymptomatic >3 years later (November 2015).

DISCUSSION

To our knowledge, this is the second case of monomicrobial human infection and the first reported case of chronic, orthopedic implant-associated osteomyelitis due to *Tissierella* species. The isolate was likely the causative pathogen, based on clinical, radiological, and intraoperative evidence of chronic osteomyelitis, growth in pure culture in multiple surgical bone specimens, and congruent 16S rRNA sequences in 2010 and 2012.

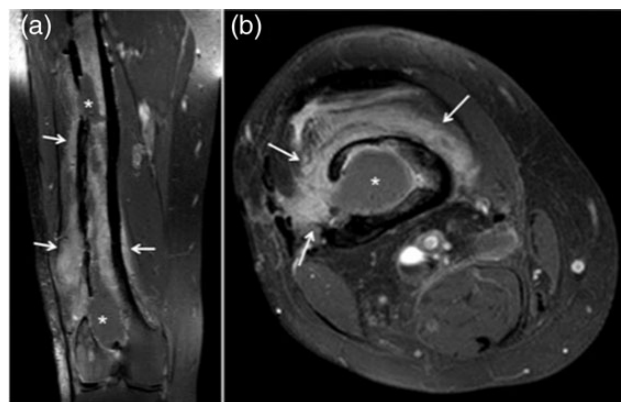


Figure 2. Chronic osteomyelitis demonstrated by magnetic resonance imaging in 2011. Coronal (a) and axial (b), T1-weighted spectral attenuated inversion recovery sequences reveal several intramedullary fluid collections (asterisks) with surrounding confluent bone marrow edema and adjacent diffuse contrast enhancement in the soft tissue (arrows).

Tissierella praeacuta (synonym: *Clostridium hastiforme* [3]) has been recovered from humans on 3 previous occasions [4–6], but in only 1 patient with eyelid necrosis [5] was there pure growth in culture. In our patient, it is unclear how *T carlieri* gained access to the femur. Prior open fracture and concomitant anaerobic infection elsewhere in the body (with presumable transient bacteremia) have been frequently noted in patients with anaerobic osteomyelitis [7–9]. The open fracture (requiring insertion of orthopedic hardware) and the diverticulitis occurred 22 and 5 years before evidence of osteomyelitis in our patient, respectively, so their pathogenic roles remain speculative. In a recent series including 61 patients with anaerobic bone and joint infections, Walter et al [10] noted several common features present in our patient, including a high proportion of implant-associated cases, delayed presentation (≥ 6 months postoperatively), and a high relapse rate.

CONCLUSIONS

Most cases of anaerobic osteomyelitis have been polymicrobial [7–10]. In our patient, monomicrobial infection with a *T carlieri* isolate might have been selected for by previous, prolonged antimicrobial treatments in the setting of persistent dead bone [7–9]. Debridement of dead bone is a key feature of successful management [11–13]. Our case also suggests that, in culture-negative osteomyelitis cases, attention should be paid to careful specimen collection and prolonged anaerobic culture. Microbiological diagnosis may require 16S rRNA gene sequence analysis based on broad-range PCR. These results can then be used to guide optimal culture method [14].

Acknowledgments

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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