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CASE REPORT

Ruminococcus gnavus Total Hip Arthroplasty Infection in a 62-Year-Old Man with Ulcerative Colitis

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We report the case of a total hip arthroplasty infection caused by *Ruminococcus gnavus* in a 62-year-old man with ulcerative colitis. The bacterium was perfectly identified by matrix-assisted laser desorption ionization–time of flight mass spectrometry.

CASE REPORT

A 62-year-old man was referred to the orthopedic surgery department of a suburban clinic with suspected prosthetic joint infection (PJI) of the right hip. This patient had undergone total right hip replacement 13 years earlier and had shown no signs of prosthesis dysfunction since surgery.

On admission, the patient presented with right hip pain and fever. Biological tests showed elevated white blood cell (18.3×10^9 cells/liter) and C-reactive protein (137 mg/liter) levels. No blood culture was collected. Radiological evaluation of the total hip arthroplasty showed a 5-mm subsidence of the femoral stem.

Three bone biopsies were performed with a notch needle, and the samples were sent to the microbiology laboratory of the Hôpitaux Universitaires Paris Ile de France Ouest, Greater Paris, for microbiological analysis. Samples were processed as previously described (1), with continuously monitored broth enrichment. Briefly, samples were topped with 17 ml sterile distilled water and bead milled for 150 s on a Retsch MM300 mixer mill (Verder, France) with 10 to 15 5-mm-diameter stainless steel beads. One hundred microliters of the resulting suspension, plated on 5% sheep blood Columbia agar medium, was incubated for 5 days at 36°C under aerobic and anaerobic conditions, and 6 ml was injected into Bactec Peds Plus and Lytic/10 Anaerobic/F blood culture vials supplemented with a fastidious organism supplement incubated for 14 days in a Bactec FX automated blood culture system (BD Diagnostics, Le Pont de Claies, France). Microscopic examination of the three biopsy samples showed an absence of erythrocytes, numerous polymorphonuclear cells, and Gram-positive cocci in short chains. No empirical antibiotic therapy was started after the biopsy. All samples yielded positive cultures on anaerobic medium, with a time to detection of 7 h 7 min for all three Lytic/10 Anaerobic/F vials. On day 1, growth was detected on anaerobic blood agar plates, with numerous translucent small colonies. The diplococci were identified by mass spectrometry (Biotyper version 3.1 on a Microflex LT mass spectrometer, Bruker Daltonics, Bremen, Germany) as *Ruminococcus gnavus*, with a score of 2.2, and later confirmed by 16S rRNA gene sequencing using previously described primers (2). A 16S rRNA gene fragment of 407 bp was amplified from the bacteria and sequenced on an Applied Biosystems genetic analyzer. GenBank database searches showed the amplified sequences to be 99% (404/407 bp) identical to the 16S rRNA gene sequence of the reference strain for *R. gnavus* ATCC 29149 (GenBank accession no. KP407134). Antimicrobial susceptibility testing by the agar disk diffusion method (Bio-Rad, Marnes-la-Coquette, France) using Comité de l'Antibiogramme de la Société Française de Microbiologie (CA-SFM 2013; http://www.sfm-microbiologie.org) guidelines and Etest (bioMérieux, Marcy l'Etoile, France) showed susceptibility to amoxicillin (MIC = 0.047 mg/liter), cefalotin (MIC unavailable), clindamycin (MIC unavailable), vancomycin (MIC = 0.38 mg/liter), rifampin (MIC < 0.002 mg/liter), and metronidazole (MIC = 0.125 mg/liter) and resistance to gentamicin (MIC unavailable) and fluoroquinolones (levofloxacin MIC > 32 mg/liter). The result for β-lactamase detection using the chromogenic nitrocefin disk assay (Mast Diagnostic, Amiens, France) was negative.

The patient was then transferred and referred to the orthopedic surgery department of the Hôpitaux Universitaires Paris Ile de France Ouest for surgical and medical management. Open irrigation and debridement with retention of the implant were performed. The macroscopic perioperative findings were compatible with the presence of purulence surrounding the prosthesis. Five intraoperative bone and tissue samples were sent to the microbiology laboratory. The samples were processed and bead milled as done for the first set of bone samples (1). Gram staining showed no organism. Four of the samples yielded cultures positive for *R. gnavus*, and the result for antimicrobial susceptibility testing was found to be identical to that for the preoperative isolates. Immediately after surgery and before the availability of the bacteriological results, empirical treatment by daptomycin (10 mg/kg of body weight/day) and piperacillin-tazobactam (4 g 3 times/day) was

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initiated. The surgical drains were cultured on the first, third, and fifth days postoperation, and the cultures were negative. On the sixth day postoperation, treatment with daptomycin and piperacillin-tazobactam was switched to a combined oral antibiotic treatment with amoxicillin (1 g 3 times/day) and metronidazole (500 mg 3 times/day) for a further 5 weeks. At the time of the patient's last examination (6 weeks postoperation), the patient was asymptomatic and showed no sign of left hip prosthesis dysfunction. The investigation of the primary focus of infection showed the patient to have been in an active phase of ulcerative colitis a few weeks before the onset of symptoms.

Anaerobic bone and joint infections (BJI) are uncommon and account for 3 to 4% of BJI (3, 4). The most frequently reported anaerobic bacterium involved in BJI is *Propionibacterium acnes*; other anaerobic bacterial species, such as *Bacteroides* spp., *Clostridium* spp., *Finegoldia magna*, or *Peptoniphilus* spp., have been reported to occur in orthopedic prosthesis infections, septic arthritis, or osteitis (4, 5, 6, 7). Little data are available on the medical and surgical management of these infections, and no clear recommendation for the treatment of BJI caused by anaerobic bacteria has been issued. Clindamycin is the most recommended antibiotic in the United States and in the French guidelines because of its bone penetration and its action against Gram-positive and Gram-negative anaerobic bacteria (IDSA recommendations and French recommendations) (8, 9). Amoxicillin and metronidazole are also recommended, but these antibiotics show no efficacy against *Bacteroides* spp. and *P. acnes*, respectively. In the case of our patient, the combination of amoxicillin and metronidazole was justified because of the severity of the infection, involving an orthopedic prosthesis, and the susceptibility of *R. gnavus*. The surgical management of our patient with debridement and implant retention was as indicated for the case of a recent acute hematogenous infection (3).

R. gnavus is an anaerobic Gram-positive non-spore-forming coccus, motile or nonmotile, that belongs to the *Clostridia* class of the *Firmicutes* division. This organism is commonly found in the intestinal flora in humans and in the rumen of animals like sheep, cattle, and goats (10). The recent sequencing of the human microbiota revealed that *R. gnavus* is widely distributed among individuals and is represented among the most common 57 species present in ≥90% of individuals (11). *R. gnavus* is among the top 15 species showing abundance in microbiota in both adults and infants, supporting the idea of adaptation of *R. gnavus* to the intestinal habitat throughout life (12). Furthermore, two studies showed that *R. gnavus* increased in normal intestinal epithelia of ulcerative colitis and Crohn's disease patients, with a decrease observed during the active phase of the bowel diseases (13, 14). These studies point toward an important role for *R. gnavus* in modulating gut inflammatory response at the mucosal surface. The only previously described human infections caused by *R. gnavus* were two cases of polymicrobial bacteremia in men with diverticulitis (15), each case associated with a Gram-negative bacillus (*Escherichia coli* in one case and *Pseudomonas aeruginosa* in the other), and a case of septic arthritis of the hip without implant (16). All three patients were immunocompromised.

In our case, the acute onset of the clinical signs on a satisfactory arthroplasty is evocative of a hematogenous infection of the implant, and the patient reported a flare of ulcerative colitis a few weeks before the onset of the hip pain, following a likely translocation from the gut during a bacteremic episode. Our patient was treated intrarectally by 5-aminosalicylic acid, which is not considered an immunosuppressive agent.

Identification of *R. gnavus* by mass spectrometry using Biotyper version 3.0 had proven to be challenging, and the use of partial 16S rRNA gene sequencing was required to reach the diagnosis, although the identification was easily reached using Biotyper version 3.1. Likewise, we had no difficulties identifying *R. gnavus* by mass spectrometry using the Biotyper version 3.1 database (Bruker Daltonics, Bremen, Germany). The advent of matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) for the routine diagnosis of bacterial infections in clinical laboratories has improved and facilitated the identification of anaerobic bacteria (4). Indeed, the database currently available has been improved, and new species are regularly included for routine identification of anaerobic bacteria. The maturation of MALDI-TOF MS techniques and the evolution of databases becoming more comprehensive can translate into deeper clinical insight into the pathogenesis of bacterial diseases.

Nucleotide sequence accession number. The 16S rRNA gene sequence for *R. gnavus* ATCC 29149 has been deposited in GenBank under accession number KP407134.

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