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. Biology showed elevated white blood cells (18.3x10⁹/L) and C-reactive protein (137 mg/liter). 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 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 beadmilled for 150 seconds on a Retsch MM300 (Verder, France) with 10-15 5mm diameter stainless steel beads. One hundred microliters of the resulting suspension plated on 5% sheep blood columbia agar medium were incubated for 5 days at 36°C in aerobic and anaerobic conditions and 6 ml injected in Bactec Peds plus and Lytic10/ Anaerobic F blood culture vials supplemented with Fastidious Organism Supplement incubated for 14 days in a Bactec FX automated blood culture system (BD Diagnostics, Le Pont de Claires, France). Microscopic examination of the three biopsies showed an absence of erythrocytes, numerous polymorphonuclear cells and Gram-positive cocci in short chains. No empiric antibiotic therapy was started after the biopsy. All samples yielded positive cultures on anaerobic media with a time to detection of 7 hours and 7 minutes for all three Lytic10/ 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 v3.1 on a Microflex LT, 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 rDNA bacterial 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 CA-SFM 2013 guidelines (Comité de l’Antibiogramme de la Société Française de Microbiologie; http://www.sfm-microbiologie.org) and Etest ( Biomérieux, Marcy l’Etoile, France) showed susceptibility to amoxicillin (MIC = 0.047 mg/L), cefalotin (MIC unavailable), clindamycin (MIC unavailable), vancomycin (MIC = 0.38 mg/L), rifampin (MIC < 0.002 mg/L), metronidazole (MIC = 0.125 mg/L) and resistance to gentamicin (MIC unavailable) and fluoroquinolones (levofloxacin MIC > 32 mg/L). 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. 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. Samples were processed and beadmilled as the first set of bone samples (1). Gram stain showed no organism. Four of them yielded positive cultures for *R. gnavus* and antimicrobial susceptibility testing was found to be identical to that of the preoperative isolates. Immediately after surgery and before the availability of the bacteriological results, empirical treatment by daptomycin (10 mg/kg/day) and piperacillin-tazobactam (4 g x3/day) was initiated. The surgical drain were cultured on first, third and fifth days post-op and were negative. On the 6th day post-op, daptomycin and piperacillin-tazobactam were switched to a combined oral antibiotic treatment of amoxicillin (1 g x3/day) and metronidazole (500 mg x3/day) for further five weeks. At the time of the patient’s last examination (six weeks post-operatively), 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 3-4% of BJI (3, 4). The most frequently reported anaerobic bacteria involved in BJI is *Propionibacterium acnes*; other anaerobic bacteria species, such as *Bacteroides* sp., *Clostridium* sp., *Finegoldia magna* or *Peptoniphilus* sp. have been reported 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
netration 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 sp. or 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 indicated in the case of a recent acute hematogenous infection (3).

R. gnavus is an anaerobic Gram-positive nonspore-forming coccus, motile or nonmotile that belongs
to the Clostridia class of the Firmicutes division. It 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 amongst individuals, and is
represented in the most common 57 species present in ≥90% of individuals (11). R. gnavus is in the
top 15 species showing abundance in both adult and infant microbiota, supporting R. gnavus
adaptation to the intestinal habitat throughout life (12). Furthermore, two studies showed that R.
gnavus increased in normal intestinal epithelium of ulcerative colitis and Crohn’s disease patients
with an observation of a decrease during active phase of the bowel diseases (13, 14). These studies
point towards an important role of 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), associated with a Gram-negative
bacillus (Escherichia coli and Pseudomonas aeruginosa respectively) 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 by 5-aminosalicylic acid in intrarectal, which is not
considered as an immunosuppressive agent.

Identification of R. gnavus by mass spectrometry using Biotyper v3.0 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 v3.1. Likewise, we had no difficulties identifying R.
gnavus by mass spectrometry using Biotyper v3.1 database (Bruker Daltonics, Bremen, Germany).

The advent of matrix assisted laser desorption ionization time-of-flight mass spectrometry 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 in the pathogenesis of bacterial diseases.

References

