

CASE REPORT

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Successful treatment of periprosthetic joint infection caused by *Granulicatella para-adiacens* with prosthesis retention: a case report

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Abstract

Background: *Granulicatella* and *Abiotrophia* spp. are difficult to detect due to their complex nutritional requirements. Infections with these organisms are associated with high treatment failure rates. We report the first implant-associated infection caused by *Granulicatella para-adiacens*, which was cured with anti-microbial treatment consisting of anti-biofilm-active rifampin and debridement, exchange of mobile parts and retention of the prosthesis.

Case presentation: Patient with a history of left hip arthroplasty presented with acute onset of fever, pain and limited range of motion of the left hip. Arthrocentesis of the affected joint yielded purulent fluid and exchange of mobile parts of the prosthesis, but retention of fixed components was performed. *Granulicatella para-adiacens* grew from preoperative and intraoperative cultures, including sonication fluid of the removed implant. The transesophageal echocardiography showed a vegetation on the mitral valve; the orthopantogram demonstrated a periapical dental abscess. The patient was treated with intravenous penicillin G and gentamicin for 4 weeks, followed by levofloxacin and rifampin for additional 2 months. At discharge and at follow-up 1, 2 and 5 years later, the patient was noted to have a functional, pain-free, and radiologically stable hip prosthesis and the serum C-reactive protein was normal.

Conclusions: Although considered a difficult-to-treat organism, we report a successful treatment of the *Granulicatella* hip prosthesis infection with prosthesis retention and a prolonged antibiofilm therapy including rifampin. The periapical dental abscess is considered the primary focus of hematogenously infected hip prosthesis, underlining the importance treatment of periodontitis prior to arthroplasty and of proper oral hygiene for prevention of hematogenous infection after arthroplasty.

Keywords: *Granulicatella*, Nutritionally variant streptococci, Prosthetic joint infection, Rifampin, Endocarditis, Prosthesis retention

Background

The genera *Granulicatella* and *Abiotrophia*, formerly known as “nutritionally variant streptococci” (NVS) are part of normal oral, urogenital and intestinal flora in humans [1, 2]. They are rarely reported as human pathogens. They can cause infective endocarditis, comprising 4.3-6 % of endocarditis and other endovascular

infections [3–7], meningitis, osteoarticular infections, endophthalmitis, keratitis and chronic sinusitis [8–11]. Due to common treatment failure in endocarditis and osteoarticular infection, NVS are considered difficult-to-treat organisms with frequent treatment failures [12–14]. Particularly in infective endocarditis relapse rates up to 41 % were reported [2, 3, 15]. Among implant-associated infections, only five cases of peri-prosthetic joint infections with *Granulicatella* or *Abiotrophia* spp. [12, 16–19] and one breast implant

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infection with *Granulicatella adiacens* have been described [20].

Since the first description of NVS by Frenkel and Hirsch in 1961 when isolated from a patient with infective endocarditis and otitis media [21], the terminology of NVS has changed several times. The species *Abiotrophia para-adiacens* was proposed on the basis of 16sRNA analysis [22]. Finally, reclassification of *Abiotrophia adiacens*, *balaenopterae* and *elegans* to a new genus *Granulicatella* was proposed in 2000 [23]. These gram-positive cocci or coccobacilli are nutritionally deficient, slow-growing and fastidious, expressing better growth around colonies of other bacteria, a microbiological phenomenon known as satellitism [14, 24]. They require blood or hemoglobin, amino acids and some vitamins to grow. These complex nutritional requirements make their detection often difficult. Because of their unique culture requirements and pleomorphic phenotypic features, misidentification or nonidentification by using commercially available phenotypic testing occur, prompting the recommendation that 16S rRNA gene sequencing be used for species-level identification of NVS infections. The Clinical and Laboratory Standards Institute (CLSI) does not recommend disk diffusion testing to determine the antimicrobial susceptibility of NVS and suggests broth microdilution MIC (minimal inhibitory concentration) testing in cation-adjusted Mueller-Hinton broth with 2.5 %–5 % lysed horse blood and 0.001 % pyridoxine hydrochloride [25].

The optimal antimicrobial treatment of NVS is not defined, especially data on implant-associated infections are scarce [12, 16–20]. In vitro antimicrobial drug susceptibility patterns do not correlate well with clinical response to treatment, and infections with NVS often respond poorly to antimicrobial treatment. Higher rates of microbiological failure and relapse rates after treatment have been observed for infection with NVS than with streptococci and related genera [2, 3, 12, 13, 15]. No experimental data are available regarding the activity of rifampin against *Granulicatella* or *Abiotrophia* spp. biofilms. Nevertheless, rifampin was used in several cases including infection of the breast implant [20], cardiac pacemaker and vertebral osteomyelitis [26] and knee periprosthetic joint infection [12]. No resistance to rifampin has been reported in NVS [24].

Case presentation

A 65-years-old man was admitted to hospital with a 3-day history of acute left hip pain accompanied by fever, chills and malaise. A non-cemented metal-on-metal hip prosthesis was implanted on the left side after a traumatic fracture 7 years ago. The postoperative course after arthroplasty was unremarkable and the joint function was satisfactory until the recent event. At

admission, the patient was febrile (38.7 °C), complaining about hip pain at mobilization with a limited range of motion. No redness, swelling, warmth or sinus tract was observed. A severe periodontitis was noticed by oral examination. Heart and lung auscultation was normal, abdominal examination was unremarkable, no skin or mucosal abnormalities were observed. At admission leukocyte count was 8.5 G/L (normal 4-10 G/L), platelet count 190 G/L (normal 150-300 G/L) and creatinine 96 mmol/L (normal 62-106 mmol/L). Liver transaminases were normal, serum C-reactive protein was 262 mg/L (normal <10 mg/L) and rheumatoid factor was negative (11 U/mL, normal <20 U/mL). Ultrasonography of the left hip showed joint effusion and 4 mL of purulent synovial fluid was aspirated. The synovial leukocyte count was 12,500 cells/ μ L with 92 % granulocytes. No microorganisms were seen in the Gram stain.

Conventional hip x-ray showed no signs of prosthesis loosening (Fig. 1). A revision hip surgery was performed on the day after admission with exchange of mobile parts (polyethylene part and head of the prosthesis) and extensive débridement, but retention of the femoral and



Fig. 1 Preoperative conventional x-ray of the hip prosthesis, imaging with intra-articular contrast medium injection (arrow)

acetabular prosthesis components. Removed mobile parts were sent for microbiological investigation for adherent biofilms by sonication. During surgery, purulent fluid was discharged after opening the joint capsule. Empiric treatment with intravenous amoxicillin/clavulanic acid (2.2 g every 8 h) was initiated.

Synovial fluid aspirate, periprosthetic tissue and sonication fluid were cultured aerobically and anaerobically for 14 days. A microorganism subsequently identified as *Granulicatella para-adiacens* grew from the sonication fluid on day 3 (>1000 colony-forming units/mL fluid), from the hip aspirate on day 9 and from one of three intraoperatively collected periprosthetic tissue samples on day 10. Blood cultures remained negative during 14 days of incubation. The identification of *Granulicatella* spp. was performed by biochemical tests and sequencing determination based on the 16S rRNA technology [27]. The minimal inhibitory concentration (MIC), performed by E-test (AB Biodisk, Solna, Sweden), was 0.19 mg/l for benzylpenicillin, 1 mg/L for ceftriaxone, 0.002 mg/L for rifampin and 0.25 mg/L for levofloxacin. According to CLSI interpretive criteria [25], the *Granulicatella para-adiacens* isolate was intermediate susceptible to penicillin (susceptible at MIC \leq 0.12 mg/L), just below the susceptible breakpoint of ceftriaxone (susceptible at MIC \leq 1 mg/L). No interpretive criteria are established by the CLSI for levofloxacin and rifampin, but the MIC values were low.

The empiric therapy was modified on day 3 to intravenous benzylpenicillin (5 million units every 6 h) plus gentamicin (80 mg every 8 h) for 4 weeks. Transesophageal echocardiography demonstrated a non-mobile vegetation on the posterior leaflet of the mitral valve (size 4 x 6 mm). Transesophageal echocardiography was repeated 4 weeks later and the size of the vegetation remained unchanged. In the orthopantomogram, 15 missing teeth and a periapical dental abscess of tooth No. 12 was noticed (Fig. 2). Tooth

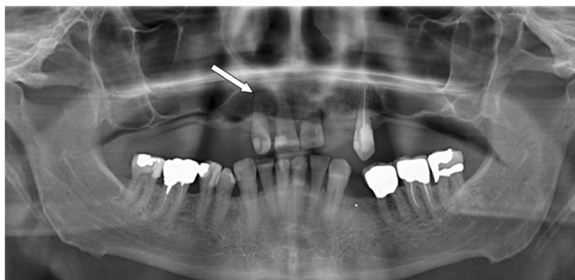


Fig. 2 Orthopantomogram at hospital admission showing severe periodontitis and periapical abscess of tooth Nr. 12 (arrow). The dental abscess is the most likely origin of hematogenous seeding of *Granulicatella* spp. to the hip prosthesis. An extraction of the tooth was performed during intravenous antibiotic treatment

extraction was performed during the intravenous antibiotic therapy.

At discharge, after completing 4 weeks of intravenous antibiotic treatment, the patient was fully mobilized, reported no pain in the hip and had a normal C-reactive protein value (3 mg/L). Treatment was continued with oral levofloxacin (500 mg every 12 h) plus rifampin (450 mg every 12 h) for additional 2 months to complete the 3 month treatment course. At follow-up visits at 1, 2 and 5 years after revision surgery, the patient presented with a functional, pain-free and radiologically stable hip prosthesis without local signs of infection and with normal serum C-reactive protein. Figure 3 shows the hip x-ray 5 years after surgery.

Discussion

We present a case of hematogenous infection of hip prosthesis caused by *Granulicatella para-adiacens* occurring 7 years after primary arthroplasty. The infection manifested acutely with fever and discrete local symptoms (joint pain at mobilization and limited range of motion). The most likely origin of the periprosthetic



Fig. 3 Native x-ray of the hip prosthesis 5 years after surgery. No signs of loosening or migration are visible

infection was the periapical dental abscess or severe periodontitis. According to modified Duke criteria [28], possible infective endocarditis was diagnosed based on one major criterion (mitral valve vegetation) and two minor criteria: fever and hematogenous seeding of the hip prosthesis. *Granulicatella* is often associated with endocarditis exhibiting affinity to the avascular cordae [29].

Interestingly, *Granulicatella para-adiacens* grew first from the sonication fluid (day 3), followed by the preoperatively aspirated synovial fluid (day 9) and periprosthetic tissue specimens (day 10), indicating the highest density of bacteria on the implant surface [30]. Only one of three periprosthetic tissues grew *Granulicatella para-adiacens* despite presence of visible pus, indicating the importance of sampling several (at least three) periprosthetic tissue specimens during surgery.

To our knowledge, this is the first case of successfully treated implant-associated infection caused by NVS without removal of the fixed components of the hip implant. All previously published cases were treated with a two-stage surgical approach, including an implant-free interval of at least four weeks [12, 17, 19]. In our patient, an acute hematogenous periprosthetic joint infection with an immature biofilm (<3 weeks of age) was diagnosed and only mobile components were exchanged according to current recommendation [31]. After initial intravenous combination of penicillin and gentamicin for 4 weeks (also sufficient for the treatment of possible infective endocarditis), an oral combination therapy with rifampin and levofloxacin was continued in order to eradicate the biofilm on the remaining foreign body.

This case report is illustrative for several reasons. First, it underlines the importance of carrying out proper preoperative and intraoperative procedures (preoperative joint puncture, multiple intraoperative periprosthetic tissue samples, sonication of removed implant parts) to diagnose prosthetic joint infections. Sonication of removed prosthetic parts is particularly useful for rapid and improved microbiological diagnosis, especially when low-burden and patchy distribution of microbial biofilms are expected [30]. Second, joint infections due to NVS occurring after dental work are well described in the literature [17, 32], which underlines the importance of the treatment of periodontitis before implantation of a prosthesis and proper oral hygiene after arthroplasty for primary and secondary prevention of prosthetic joint infection. Third, the NVS may not be needed to be classified as a difficult-to-treat-organism, if exchange of the mobile parts is followed by antimicrobial therapy that also includes biofilm-effective antibiotics such as rifampin. Current guidelines recommend for infective endocarditis due to *Granulicatella* a treatment with antibiotics that are

used for treatment of infective endocarditis due to streptococci with intermediate susceptibility to penicillin (combination of penicillins or ceftriaxon or vancomycin 4-6 weeks and gentamicin 2 weeks) [33]. In our case, we performed the combined intravenous treatment for 4 weeks taking in account the difficult-to-treat-character of *Granulicatella* and completed the recommended 12 weeks course of antibiotic therapy for periprosthetic joint infections with streptococci with a combination of levofloxacin and rifampin.

Conclusion

Although *Granulicatella* is considered a difficult-to-treat bacterial organism, we report successful treatment of a *Granulicatella* hip prosthesis infection and possible infective endocarditis with exchange of mobile parts, debridement and prosthesis retention and a prolonged course of antimicrobial therapy including biofilm-effective antibiotics. The periapical dental abscess is considered the primary focus of hematogenously infected hip prosthesis, underlining the importance of treatment of periodontitis prior to arthroplasty and of proper oral hygiene for prevention of hematogenous infection after arthroplasty.

Ethics and consent to participate

Not applicable.

Consent to publish

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images.

Availability of data and materials

All the data supporting our findings is contained within the manuscript.

Abbreviations

CLSI: clinical and laboratory standards institute; MIC: minimal inhibitory concentration; NVS: nutritionally variant streptococci.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

AT conceived of the case report, NR and FC gleaned the facts and drafted the manuscript. OB participated in the design of the study and contributed the facts from the surgical point of view. AT revised it critically and contributed substantially to the discussion. All authors read and approved the final manuscript.

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