



Case report

Granulicatella adiacens: An uncommon diagnosis of prosthetic hip joint infection. A case report with review of the literature



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ABSTRACT

We report a case of prosthetic hip infection in a 79 year old man caused by *Granulicatella adiacens*. The diagnosis was achieved using broad range 16S PCR gene analysis at an early stage, after joint aspiration and culture failed to yield a pathogen. Staged revision surgery together with administration of appropriate antibiotics resulted in cure. *Granulicatella adiacens* is a nutritionally variant streptococcus (NVS). It has been increasingly reported to cause significant morbidities involving various systems. Its insidious growth due to complex growth requirements, has made its diagnosis challenging, and often delays appropriate antibiotic administration.

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Introduction

Granulicatella adiacens is a nutritionally variant streptococcus (NVS). It has been increasingly recognised and reported to cause significant infections involving various systems. Its insidious growth due to complex growth requirements has made its diagnosis challenging, and often delays appropriate antibiotic administration.

Case report

A 79-year old man presented to hospital with sudden onset left hip pain on a background of total hip arthroplasty (THA) for osteoarthritis performed three years previously. The pain began after a period of sitting for two hours, with no clear evidence of injury or trauma. There were no systemic symptoms including fever, chills or rigors. Four days prior to presentation, the patient had a dental filling replaced. No prophylactic antibiotics were given prior to the procedure. His past medical history included a percutaneous transluminal coronary angioplasty.

On examination, he had reduced range of motion of his left hip and experienced severe pain on weight bearing. The greater trochanter of the left hip was tender to touch. Suspicion of

infection was raised when blood tests revealed a C-reactive protein (CRP) of 77 mg/L and white blood cell count of 14,000 cells/ μ l.

Attempted joint aspiration was unsuccessful, so a core biopsy was performed and sent for microscopy, culture and histology. Histology showed up to 30 neutrophils per high power field in five separate fields, suggestive of acute on chronic capsulitis of the hip. Initial microscopy and culture remained negative and given the strong clinical suspicion of infection, a broad range bacterial 16S rRNA gene analysis was performed. *Granulicatella adiacens* was identified and was subsequently isolated from broth media, indicating low numbers of organisms. The isolate was susceptible to penicillin with the minimum inhibitory concentration (MIC) by E-test (Biomérieux) at 0.03 mg/L.

The patient underwent 2-stage revision THA. A Biomet antibiotic impregnated cement spacer mould (Warsaw, Indiana USA) with 8 g Vancomycin powder mixed with 80 g Simplex P with Tobramycin bone cement (Stryker, Mahwah, NJ, USA) was used during the interval period. He was treated with intravenous Benzyl Penicillin dosed by continuous infusion for six weeks. The CRP decreased from 242 mg/L to 6 mg/L by the end of this six-week period. A core biopsy two weeks post therapy completion showed no evidence of ongoing infection. He underwent stage-2 revision THA at ten weeks after the initial operation. Smith and Nephew R3 acetabular component (Cordova, TN USA) and cementless Echelon femoral component (Memphis, TN USA) were used. His post-operative recovery was uneventful. Subsequent follow-up post revision has shown full recovery with no evidence of relapse.

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Discussion and literature review

Granulicatella species are non-motile, non-sporulating, catalase- and oxidase-negative Gram-positive cocci classified as nutritionally variant streptococci (NVS). They are facultatively anaerobic with complex growth requirements [1] and are normal flora of the oral mucosa, upper respiratory tract, intestinal and urogenital tracts. NVS were first described in cases of endocarditis and otitis media [2]. *Granulicatella* was considered a new type of viridans group Streptococcus that exhibited satellitism around colonies of *Staphylococcus aureus*. Using DNA-DNA hybridization studies, NVS were officially named *Streptococcus adiacens* and *Streptococcus defectivus* [3]. 16S rRNA sequence data demonstrated that the two NVS type strains were phylogenetically distinct from the genus Streptococcus [4], and the genus was transferred to *Abiotrophia*, with two species, *A. adiacens* and *A. defectiva*. Later the genus *Abiotrophia* was differentiated into four species, *A. defectiva* and a group consisting of *A. adiacens*, *A. balaenopterae* and *A. elegans*, and subsequently reclassified into the genus *Granulicatella* [1].

Granulicatella adiacens causes infections in a wide range of nutritionally rich tissues.

Three previous cases of *G. adiacens* prosthetic joint infection (PJI) of the hip have been published to date [5,6], of these, two were associated with recent dental intervention. In all cases, the organism was identified via 16S PCR of synovial fluid or MALDI-TOF technique. The first case [6] was cured with a two-stage exchange arthroplasty with six months of antibiotic therapy. The second case [6] underwent washout, implant retention and six months of antibiotic therapy with successful cure. The third case [5] initially underwent washout, implant retention together with intravenous antibiotics. His management was complicated by fevers and a drug reaction resulting in a further washout. No organisms were isolated from the tissue samples. A two-stage revision was planned; however, he developed a fatal community acquired pneumonia.

Granulicatella adiacens is a fastidious bacterium and diagnosis and thus treatment is often delayed. Its growth is dependent on the presence of pyridoxine, which is required for cell multiplication. *Granulicatella* can be identified by biochemical and/or molecular testing. Samples can be inoculated into blood culture bottles that contain pyridoxine and L-cysteine as growth factor, found in automated blood culture broths commonly used, such as BACTEC or BacT Alert [7]. Standard testing has been reported to lead to incorrect identification due to the extreme pleomorphic appearance of strains in direct smears. MALDI-TOF technique can assist in the identification if there is growth on solid media. Failing this, molecular testing with gene sequencing studies may help with the diagnosis as in our case.

Antibiotic susceptibility testing is problematic. Disc diffusion techniques are not recommended for *Granulicatella* isolates due to a lack of established breakpoints [8,9]. Broth microdilution and E-tests [10] using CLSI publishing guidelines 2007 or March 2017 EUCAST clinical breakpoint tables [11] may be used. These guidelines noted variable results of E-test when compared with broth microdilution in published data. In our case, E-test was performed with susceptibility to Penicillin G with MIC of 0.03 mg/L. Resistance to β -lactams including penicillin, amoxicillin, ceftriaxone and meropenem has been reported in *G. adiacens* likely as a result of penicillin binding protein mosaicism. Resistance to clindamycin, tetracycline, erythromycin and ciprofloxacin, but not to vancomycin and rifampicin has been reported [12]

Although no consensus guidelines exist, treatment duration based on published cases is dependent on the clinical site of infection but ranges from four weeks to eleven months. In previously published cases involving hip PJI, antibiotic therapy was

continued for six months. Based on current Infection Disease Society of America Prosthetic Joint Infection management guidelines [13], four to six weeks of pathogen specific antimicrobial therapy followed by long term suppression, depending on surgical procedure performed, is the recommended treatment duration for non-*Staphylococcal* prosthetic joint infection. *G. adiacens* has been shown to be a biofilm forming organism in the setting of dentures [14]. Although a literature review did not reveal any further published data on this topic, it would be reasonable to conclude that it is able to form biofilm on prosthetic material and a treatment course of six weeks of targeted antimicrobial therapy along with appropriate surgical management, depending on timing of initial implantation and patient specific factors, would seem appropriate, combined with close clinical follow up and monitoring of inflammatory markers. Our patient received penicillin for six weeks without subsequent suppressive antimicrobials with no clinical signs of relapse of infection 5 years post-surgery.

Conclusion

Granulicatella adiacens is increasingly recognised and reported to cause significant infections involving various systems as described. Management is largely dependent on the site of infection but a prolonged antibiotic course in the setting of sites of potential biofilm formation is likely warranted.

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Declaration of Competing Interest

The authors report no declarations of interest.

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