



Case report

First case of prosthetic knee infection with *Granulicatella adiacens* in the United States



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Case report

A 64 year old white male patient was referred to our infectious disease office with persistent and worsening left knee swelling for the past year. Seven years ago he underwent left total knee arthroplasty. Seven months ago he underwent root canal procedure on his left lower molars. He was not on any antimicrobial prophylaxis for this procedure. Few days after the procedure he noticed that the left knee was swollen without pain or fever. Joint swelling was slightly restricting his movements, otherwise he was totally asymptomatic. Swelling worsened day by day. Finally he saw the orthopedic surgeon who had performed his total knee arthroplasty. Knee joint was tapped in the office. The Synovial fluid was clear. Fluid analysis showed 38,255 WBC with 98% PMNs and 10000 RBC. Fluid cultures were negative. 16 s RNA study was positive for *Granulicatella adiacens*. Despite nutritional supplementation in the thiol broth we could not grow enough *organisms* to assess for sensitivities.

He underwent resection of the left knee arthroplasty with irrigation and debridement including the bone and placement of antibiotic cement articulating spacer. Synovial fluid this time showed 25926 WBC with 91% PMNs. RBC were still 10000. Fluid cultures were again negative but 16 s RNA was again positive for the same pathogen. Pathology of the joint showed severe inflammation of the synovium with giant cell granuloma formation.

Patient worked as a sales agent and opted for a single day regimen. A PICC line was placed and he was discharged home on IV ertapenem 1 gm daily for 6 weeks. Later he underwent revision left total knee arthroplasty (resection of cemented Prostalac and conversion to standard total knee arthroplasty). Peri operatively he received cefazolin for 3 days only. Repeat synovial fluid analysis showed only 286 WBC with 1000 RBC. 16 s RNA was again negative this time. The Patient was seen in the office post operatively and he remained symptomatic for the past 8 months.

Discussion

Organisms formally called nutritionally variant streptococci (NVS) require pyridoxal or L-cysteine for their growth. They are classified to a separate genus, Abiotrophia which is further classified in to Abiotrophia and Granulicatella on the basis of 16S rRNA gene sequencing. They are facultative anaerobes. The Streptococcaceae (including the genus Streptococcus), Enterococcaceae (including Enterococcus) and Aerococcaceae (including Abiotrophia) are related families [1,2]. Chromosomal DNA hybridization and 16S rRNA gene sequencing data are used in the classification of this genus [2,3]. Three species of Granulicatella have been described in human infections. *G. adiacens*, *G. elegans* and *Abiotrophia defectiva*. *G. balaenopterae* is not isolated from human samples [2]. Granulicatella species are a normal component of the oral flora and are found in dental plaques, endodontic infections, dental abscesses, GI and GU tract. They are etiological agents in a variety of visceral infections [3].

Weak metabolic activity and biochemical variability could lead to misidentification with conventional phenotypic methods. The rate of infections due to GA is probably underestimated because of difficulties encountered in both culturing and identification [2,3].

To date there are only 5 other cases of prosthetic joint infections with Granulicatella reported. We are reporting the first case from the United States [4–8]. Other infections include Intracranial infections, vertebral osteomyelitis, septic arthritis of the native joints and infective endocarditis [9,10].

This organism was difficult and slow to grow in our lab. Initial identification was possible only with the 16 s RNA study on the synovial fluid. Isolates are generally identified using a Vitec MS (bioMérieux, Craaponne, France) at a 99.9% confidence value. Species level identification of NVS isolates can be achieved by 16S rRNA gene sequencing and/or matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) [11–13]. The Clinical and Laboratory Standards Institute (CLSI) recommend broth microdilution MIC

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(minimal inhibitory concentration) testing in cation-adjusted Mueller-Hinton broth with 2.5%–5% lysed horse blood and 0.001% pyridoxine hydrochloride to determine the antimicrobial susceptibility for these organisms [3].

G. adiacens has higher MIC values for various antimicrobials than both *A. defectiva* and *G. elegans* [3]. GA is more susceptible to penicillins (PCN) than *G. defectiva* (38.9% versus 10.8%). PCN MIC = > 4 is considered resistant. Both of them are sensitive to third generation cephalosporin with latter being more sensitive. (94.6% versus 18.9% for cefotaxime and 100% versus 43.3% for ceftriaxone). The MIC₉₀ was lower for ceftaroline than for either cefotaxime or ceftriaxone (2 versus > 4 µg/ml). There is no resistance to carbapenems documented to date. Meropenem MICs were generally 2-fold higher than imipenem MICs for both species [14,15].

Isolates are usually sensitive to gentamycin, streptomycin (MICs were ≤ 4 µg/ml) and vancomycin (MICs ≤ 1 µg/ml). These organisms are also sensitive to linezolid and daptomycin but at a higher MICs. Linezolid MIC₉₀ was slightly higher for GA than for *A. defectiva* and *G. elegans* (2 versus 1 µg/ml). The daptomycin MIC₉₀s for *A. defectiva* and GA were > 4 and 4 µg/ml, respectively, whereas the MIC₉₀ for *G. elegans* was only 0.5 µg/ml. MIC ≥ 8 for levofloxacin is considered resistant [14,15].

PCN with an aminoglycoside has been the regimen of choice in the past. However PCN resistance is now documented. To date there is no documented vancomycin and aminoglycoside resistance. 83% of *A. defectiva* is sensitive to ceftriaxone compared to 63% of GA. The MIC distribution pattern differences between GA and *A. defectiva* support inherent resistance to daptomycin but are usually susceptible to linezolid [15]. *G. elegans* isolates were 100% susceptible to all antimicrobials tested, with the exception of erythromycin, to which only 20% were susceptible. 22% of erythromycin-resistant GA isolates were also resistant to clindamycin compared to only 5% and 0% of erythromycin-resistant *A. defectiva* and *G. elegans* isolates [15].

To summarize the treatment plan, penicillin with aminoglycosides can still be used as long as there is documented sensitivities. Otherwise these agents are typically sensitive to vancomycin and carbapenems. Activity of rifampin against *Granulicatella* or *Abiotrophia* spp. Biofilms is unknown at this time.

Conflict of interest

None.

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