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Case report

Development of a periprosthetic joint infection by *Abiotrophia defectiva* years after total knee arthroplasty

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ABSTRACT

A 74-year-old male presented with acute right knee pain and inability to ambulate. The patient had a total knee arthroplasty, previously complicated by a periprosthetic femur fracture requiring surgical fixation and subsequent methicillin-resistant *Staphylococcus epidermidis* periprosthetic joint infection treated via two-stage revision. Cultures from knee fluid aspiration were positive for *Abiotrophia defectiva*. Identification was confirmed using matrix-assisted laser desorption ionization–time of flight mass spectrometry. The patient underwent a two-stage revision. Between stages, the patient received intravenous ceftriaxone for six weeks with subsequent normalization of inflammatory markers. Diagnosis of periprosthetic joint infection with identification of the organism is important to guide appropriate treatment.

Introduction

Abiotrophia defectiva (*A. defectiva*), previously identified as *Streptococcus defectiva*, is one of 13 nutritional variants of the *Streptococci genus* [1]. They were separated from the *Streptococcus genus* after genetic and phylogenetic analyses (16S rRNA gene sequencing) demonstrated low resemblance to other streptococcus organisms [2]. *Abiotrophia* species are most commonly habitants of the oral cavity, urogenital mucosae, and intestinal mucosae [3]. *Abiotrophia* species are particularly difficult to culture and often require a special, complex medium with supplemental sulfhydryl compounds (eg, 1-cysteine) and pyridoxal [4]. *A. defectiva* has been cited most commonly in the context of endocarditis and otitis media [3,5]. It has only rarely been reported as the cause of osteoarticular and periprosthetic infections (Table 1). This case is only the fourth reported total knee arthroplasty (TKA) periprosthetic infection and the sixth reported infection of the knee joint due to *A. defectiva* [6-10].

Case history

A 74-year-old Caucasian male presented to the emergency department with an onset of acute right knee pain and inability to ambulate. He had a medical history significant for multiple cardiovascular comorbidities, chronic dysphagia, chronic back pain, and a past periprosthetic joint infection (PJI) of the right knee. He underwent his index TKA 11 years ago at an outside institution. This was complicated by a distal femur periprosthetic fracture five years after the operation, after a fall down an elevator shaft. The fracture was treated with open reduction and internal fixation with a medial femoral plate and screws, at the same institution as the index TKA. Prophylactic antibiotics were given at the time of surgery, and the patient recovered without immediate complications. In the following year (six years from index TKA), the patient developed a methicillin-resistant *Staphylococcus epidermidis* (MRSA) periprosthetic infection requiring a two-stage revision, including explant of the medial femoral plate, and intravaneous antibiotics (vancomycin). An antibiotic spacer containing augmentin, vancomycin, and tobramycin was used during the first stage of the revision. During the second-stage replantation, two Mitek suture anchors were placed to secure the patellar tendon to the tibial tubercle as the infrapatellar tendon had some attenuation. The patient had no further problems with his right knee prosthesis until the current encounter.

On presentation, the patient was normotensive, afebrile, and in no acute distress in the emergency center. On examination, there

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was a right knee effusion with limited flexion and extension due to pain and a well-healed midline incision without drainage. Radiographs were obtained (Fig. 1), the C-reactive protein (CRP) level was elevated at 6.8 mg/dL, and erythrocyte sedimentation rate was within normal limits at 9 mm/hr. Synovial fluid aspiration yielded a synovial white blood count of 66,512 cells/μL with 97% neutrophil differential and no crystals. Gram stain was negative, but aerobic cultures grew *A. defectiva* after five days. Identification was made using matrix-assisted laser desorption ionization–time of flight (MALDI-TOF) mass spectrometry.

The patient underwent explantation of his components and a thorough debridement. The tibial component was noted to be grossly loose with significant wear to the polyethylene insert; however, the femoral component was well fixed, and the prior fracture site was healed with callus formation present. Once the hardware was removed and after debridement, the patient was irrigated with six liters of normal saline (0.9% NaCl) and three liters of normal saline plus the bacitracin and flushed with one-liter of 0.05% chlorhexidine solution; then, an antibiotic (tobramycin/vancomycin)-impregnated static spacer was placed. The patient was placed into a knee immobilizer postoperatively. Both synovial and tissue cultures from the procedure returned positive for *A. defectiva* after five days.

The patient was administered with ceftriaxone intravenously for six weeks with weekly blood draws for CRP. At the 2-month follow-up visit, erythrocyte sedimentation rate and CRP were within normal limits and the patient underwent aspiration with no fluid obtained. At the 3-month follow-up visit, the patient underwent a right TKA with removal of the static antibiotic spacer (Fig. 2). Frozen sections of synovium and distal femoral canal and a synovial white blood cell count demonstrated no signs of infection. Synovial fluid and tissue cultures were collected and sent to the laboratory and remained negative. Antibiotic-impregnated cement, containing six packages of tobramycin and two packages of vancomycin powder (ratio of 3:1), was again used during implantation of the final components. Postoperatively, the patient was started on oral cephalexin (500 mg three times daily) for 3 months. The final cultures from the intraoperative samples resolved as negative. At the 10-month follow-up visit, the patient had completed 10 weeks of physical therapy with no signs of PJI relapse. The patient consented to the publication of this unique case.

Discussion

This patient marks only the fourth reported case of a PJI in the knee caused by *A. defectiva*. Unlike the other three studies [6-8], this case was the first to identify the organism on an aerobic culture and ultimately using MALDI-TOF mass spectrometry. The cultures took five days before being reported positive, which is corroborated by the literature that has shown *A. defectiva* to take, on average, 72 hours to culture and often requires special media to be grown in the traditional laboratory setting [4].

The use of MALDI-TOF mass spectrometry has been cited in the clinical microbiology literature as an effective laboratory test for identifying *A. defectiva* as well as a number of other fastidious, nutritionally variant streptococci organisms [11,12]. The major benefit of this laboratory technique is that it can quickly and inexpensively identify *A. defectiva* and other fastidious organisms that may otherwise be difficult to identify on cultures alone [13]. This laboratory technique uses an ionization technique that uses a laser energy–absorbing matrix to make ions from large molecules. It can be used for multiple purposes, one of which is microbial identification [14,15]. A portion of a microbial colony of the suspected organism is placed onto the sample target and overlaid with a cellular matrix. The mass spectra are assessed using a dedicated software program and compared with stored microbe-specific profiles [16]. This allows multiple suspected organisms to be tested simultaneously and also requires that the computer software organism profile be present for correct microbe identification to occur. A broad organism differential must be used for successful organism detection.

In the setting of a PJI, where organism identification is paramount, quick but accurate laboratory diagnostics is the first step in efficient treatment planning. The use of MALDI-TOF mass spectrometry should be considered in the event of a suspected PJI where the organism remains unidentified with traditional laboratory testing. MALDI-TOF mass spectrometry is becoming more mainstream for organism identification in part because of its long-term cost benefits than traditional laboratory techniques and because of its speed. A 2012 study in Greece by Vranakis *et al* [17] investigated the differences in cost and time-effectiveness of MALDI-TOF mass spectrometry compared with conventional testing, including PCR, in food and water samples containing a variety of bacteria. During the year-long study period, the laboratory spent a total of 72,675 to identify pathogens by traditional molecular and biochemical techniques and a total of 843 in using the MALDI-TOF mass spectrometry technique. In addition, in comparing the different tests, they reported equivocal diagnostic accuracy. Tran *et al* [18] in 2015 compared the use of MALDI-TOF mass spectrometry with standard laboratory techniques and found that despite high upfront purchasing costs and maintenance fees for the equipment, MALDI-TOF mass spectrometry for organism identification was about 50% cheaper overall than traditional laboratory techniques. This was mainly attributed to the cost per test and the reduction in technician costs found with the mass spectrometry. Given that the diagnostic accuracy appears equivalent, MALDI-TOF mass spectrometry offers the advantage of being less expensive and quicker, making it a viable alternative for microbial identification. It may serve as a special alternative in situations such as this case in which the organism fits an atypical picture or the initial laboratory findings are inconclusive.

This patient had no clear mechanism of inoculation and was asymptomatic for over five years after replantation after an MRSA infection. However, on presentation, there were numerous signs raising suspicion for a possible PJI. Elevated CRP testing has remained a common denominator for raising suspicions of a possible PJI in all four reported PJI cases regardless of reported negative cultures and the known fastidious nature of the organism [6-8]. Hoell *et al* [19] in 2016 looked at the use of different laboratory parameters to identify the presence of a joint infection before the second-stage revision arthroplasty in 114 patients, and the authors reported the sensitivity and specificity of serum CRP to be 42% and 84%, respectively. However, with more fastidious organisms, such as *A. defectiva*, it is important to be meticulous in the workup for a suspected PJI. To our knowledge, there is no reason to believe this infection was related to the prior MRSA infection, especially given that years of asymptomatic function occurred between the two events. However, it is possible that given the insidious nature of *Abiotrophia spp.*, the patient was seeded from another area of the body. The patient could have had an indolent bacteremia due to an event far enough removed from the presenting symptoms that it was not recalled as being relevant by the patient. This is theoretical as the true etiology of the infection remains unknown. From the literature, *Abiotrophia spp.* has been much more frequently cited in association with subacute endocarditis, and bacteremia is often connected back to a urinary tract infection or recent dental work [20,21]. All these histories were absent in this patient.

This organism should be considered in patients with clinical signs of a periprosthetic infection where the laboratory findings are either inconclusive or not congruent with the clinical picture. The previous case reports experienced both indolent symptom onset and an acute one with this organism, so it appears that the timing of symptom onset is not very reliable or unique in terms of predicting

this organism as a possible cause for periprosthetic infections [6-8]. Given that Gram staining of *Abiotrophia spp.* is unreliable and, often times, this organism is difficult to culture, *Abiotrophia spp.* must be considered as a possible cause for infection in patients with a suspected prosthetic infection so that appropriate steps are taken in the laboratory. In this particular case, the advantage of the MALDI-TOF mass spectrometry testing was that the *Abiotrophia defectiva* profile was included in the testing panel along with a number of other organisms. Given the more robust literature on *Abiotrophia spp.* and endocarditis, even in a patient with clinical signs of a prosthetic infection, it is also important to consider cardiac sources and ensure the joint is not a piece of a more systemic pathology.

This was the third out of the four studies to show successful eradication with intravenous antibiotic treatment and a two-stage revision. It is imperative to ensure there are no signs of infection before replantation. In our experience, the infection was eradicated using ceftriaxone administered intravenously for six weeks, with a prophylactic oral course of cephalexin after the revision procedure. In the other three cases that reported *A. defectiva* inoculation of a knee prosthesis, each used different antibiotic regimens as seen in Table 1. Alberti *et al* [22] analyzed the antimicrobial susceptibilities for *A. defectiva* in addition to two other nutritional variants of streptococci and found variable results. The authors reported variable susceptibilities between species with ceftriaxone, cefotaxime, carbapenems, vancomycin, and levofloxacin having the largest susceptibilities. However, the study emphasized the importance of proper organism identification as there were significant differences in susceptibility across the species studied. Third-generation cephalosporin, vancomycin, and carbopenems appear to provide the best opportunity for organism eradication. These findings were further supported by Prasidthrathsint and Fisher [23] who also described varying susceptibility across species, particularly to penicillin and ceftriaxone, and across geographical regions.

Although this case did not have any coinciding endocarditis, it is important to recognize the propensity of *A. defectiva* infections to cause endocarditis [2,5,21]. This patient was already being evaluated and cared for by cardiologists given an extensive cardiovascular history before these events. In the presence of a confirmed *A. defectiva* joint infection, it is important to ensure other, more common sites of infection, such as the heart, are properly evaluated.

Summary

There have been very few reports of *A. defectiva* and other nutritional variant of Streptococci causing musculoskeletal infections in the literature. This case adds to our understanding of this rare, fastidious organism as it pertains to PJI and highlights our institutions experience with organism identification and subsequent treatment planning.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.artd.2018.12.002.

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