Nocardia Infection Following Anterior Cruciate Ligament (ACL) Allograft Reconstruction: A Case Report and Review of Literature

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Nocardia infection following anterior cruciate ligament (ACL) allograft reconstruction is a rare occurrence. We report a case of Nocardia infection of an allograft ACL reconstruction and septic arthritis of the knee joint due to an organism most similar to the novel Nocardia species Nocardia aobensis.

CASE REPORT

Following a sporting injury, an otherwise healthy 27-year-old male mining engineer underwent revision of a hamstring tendon autograft anterior cruciate ligament (ACL) reconstruction of the left knee that had been performed 3 years earlier. Two 25-cm tibialis anterior tendon allografts were utilized and secured using fixation screws. The surgery was complicated by hemorrhaxis on the sixth postoperative day that required aspiration; however, there were no signs of infection at that time.

There was an increased range of movement in the knee and a reduction in pain during the first 2 months postoperatively. However, the patient then developed erythema and a small abscess around the inferior half of the surgical scar. He was commenced on a course of oral cephalaxin for 5 days before undergoing a left knee washout and removal of the tibial fixation screw. Postoperatively, he commenced empirical intravenous vancomycin, which he received for 1 week.

Cultures of a swab from the pointing abscess grew a Nocardia species, a light growth of Staphylococcus capitis, and Bacillus in enrichment broth. One surgical specimen taken the following day grew the Nocardia species, and Staphylococcus epidermidis from enrichment broth; the other surgical specimen grew Bacillus species, and Staphylococcus capitis from enrichment broth only. The Nocardia species exhibited two colony morphologies on chocolate agar incubated in 5% CO₂ for 7 days: one showed white substrate mycelium and was flat, while one developed dull orange substrate mycelium on Mueller-Hinton agar by 7 days of incubation in ambient air. On diagnosis of presumptive Nocardia infection, treatment was changed to sulfamethoxazole-trimethoprim. This oral antibiotic treatment was continued for 12 months, during which time there was an increased range of movement and function in the knee and a resolution of activities, including surfing, golfing, and jogging. At review 6 weeks following cessation of antibiotics, there was no evidence of recurrent infection and inflammatory markers were normal. A follow-up X-ray, computed tomography (CT), and magnetic resonance imaging (MRI) scan confirmed no evidence of osteomyelitis or soft tissue inflammation. There was no complication of the bony tunnels created in the tibia and femur.

The Nocardia species was identified by PCR and sequencing of part of the 16S rRNA gene as most closely resembling Nocardia aobensis. Primers targeting conserved areas near the 5’ end of the 16S rRNA gene (forward, 5’-CCTAACACATGCAAGTGC-3’; reverse, 5’-CGTATTACCGGCGTGCTGCT-3’) produced a 400-bp sequence (GenBank accession no. KR534216). (2) This was matched with the NCBI GenBank database (https://blast.ncbi.nlm.nih.gov) using BLAST search (3), returning 100% query coverage and 100% match to the first identified human clinical strains reported by Kageyama et al. (1) This is sufficient for identification to the species level according to CLSI guideline MM18A (4), but the validity of using only the 16S sequence has been questioned by Kong et al. as additional sequencing and matching of the secA1 gene were found to alter the identification in 16/20 cases (5). Susceptibility data are shown in Table 1.

The tissue bank that supplied the allografts performed a formal investigation, and this revealed that normal procedures had been followed in relation to procurement, irradiation, and microbiological testing, with no significant microbiological growth de-
of total knee replacement using uncemented natural por-

erana (1). After the initial report by Kageyama et al. (1), there has been no pathognomonic for infection (11,12). As there are no signs, symptoms, or radiological findings that are specific for the infection, clinical diagnosis is very difficult, and given the short period of time between surgery and presentation, intraoperative infection through environmental contamination would be one possibility. Alternatively, the presence of skin commensals and Bacillus species in swabs from the wound abscess preoperatively and tissue cultures intraoperatively raises the possibility that infection developed from a wound infection. However, isolation of these organisms may also have represented contamination during specimen collection. That none of these organisms caused relapse during prolonged follow-up (despite only receiving limited directed therapy initially) would suggest they were not the primary cause of infection.

Nocardia infections are often treated empirically, based on species identification, until results of susceptibility testing are available. Previously, species identification using 16S rRNA sequencing and phenotypic typing has shown good correlation with antibiotic susceptibility patterns (27). The emergence of new Nocardia species, for which only small numbers of isolates have been reported and thus only a small amount of susceptibility data is available, means that it is more difficult to treat infection empirically, and susceptibility testing of individual isolates is important. The present case also demonstrates the difficulties inherent in molecular identification of novel species by DNA sequencing when only small numbers of sequences are available in databases. Only 6 partial 16S rRNA gene sequences for Nocardia aobensis could be found in a public database, the Global Catalogue of Microorganisms (http://gcms.wfcc .info/speciesPage.jsp?strain_name=Nocardia aobensis [accessed 26 May 2014]).

This is the first reported case of Nocardia infection due to a novel species most closely resembling Nocardia aobensis in an ACL reconstruction using tendon allografts. This case highlights the difficulties inherent in species diagnosis by molecular methods when a novel species is concerned and the need for susceptibility testing of individual isolates.

ACKNOWLEDGMENT

The authors declare that they have no conflicts of interest.

REFERENCES


<p>| Table 1: Antibiotic susceptibility data of the Nocardia species isolated from preoperative swab |
|-------------------------------|-----------------------------------|-----------------|</p>
<table>
<thead>
<tr>
<th>MIC test and antibiotic</th>
<th>MIC (mg/liter)</th>
<th>Susceptibility interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAPMYSO</td>
<td>Co-trimoxazole</td>
<td>1/2</td>
</tr>
<tr>
<td></td>
<td>Ciprofloxacin</td>
<td>1/4</td>
</tr>
<tr>
<td></td>
<td>Amikacin</td>
<td>1/2</td>
</tr>
<tr>
<td></td>
<td>Imipenem</td>
<td>1/2</td>
</tr>
<tr>
<td></td>
<td>Augmentin</td>
<td>2/32</td>
</tr>
<tr>
<td></td>
<td>Ceftriaxone</td>
<td>1/4</td>
</tr>
<tr>
<td></td>
<td>Minocycline</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Clarithromycin</td>
<td>≤0.06</td>
</tr>
</tbody>
</table>

aMICs were determined by broth microdilution using the Sensititre RAPMYSO (Thermo Fisher Scientific) read at 96 h as per CLSI guidelines (28) or the bioMérieux Etest.

bS, susceptible; R, resistant; I, intermediate.

There has been only one previous case reported of Nocardia infection involving the ACL after reconstruction with a tibialis anterior allograft (8); however, the species identified was Nocardia nova. Nocardia nova infection has also been reported as a complication of total knee replacement using uncemented natural porous components (9). Nocardia aobensis was first identified from patients in Japan in 2004 by Kageyama et al., and was established as a unique species by DNA hybridization (1). Nocardia aobensis is most closely related to Nocardia africana, Nocardia cerradoensis, and Nocardia veterana (1). After the initial report by Kageyama et al. (1), there has been only one other reported case of human infection with a similar species: a pleuropulmonary infection in a patient with chronic hepatitis C on interferon treatment, due to a species of Nocardia with 99%16S rRNA homology to Nocardia aobensis, Nocardia africana, Nocardia veterana, and Nocardia elegans, which could not be further identified (10). This case also highlights a similar difficulty to ours in molecular identification of Nocardia species.

Nocardia species are normally found in soil, aquatic areas, and decaying vegetable matter. The route of infection is usually via inhalation or direct inoculation. Clinical diagnosis is very difficult, as there are no signs, symptoms, or radiological findings that are pathognomonic for infection (11, 12). Nocardia species are opportunistic pathogens, most commonly affecting the lungs (75%), with HIV being the most common underlying pathology (13). Nocardia is an uncommon cause of surgical site infections. To our knowledge, only 17 such cases have been reported. Fourteen cases of septic arthritis involving Nocardia species have been reported, including 10 cases of Nocardia asteroides (14–23), two cases of Nocardia nova (8, 9), and one case each of Nocardia elegans (24) and Nocardia farcinica. (25) However, it is noted that the cases previously published as Nocardia asteroides are likely to be Nocardia cyrigeoargentica based on more recent methods of identification (26).

Infection of ACL reconstructive procedures remains an uncommon occurrence (9), and the mode of infection in the present case is unclear. An investigation conducted by the tissue bank did not reveal a possible contamination event, and the allografts had been subjected to an appropriate intensity of gamma irradiation. Given the short period of time between surgery and presentation, intraoperative infection through environmental contamination would be one possibility. Alternatively, the presence of skin commensals and Bacillus species in swabs from the wound abscess preoperatively and tissue cultures intraoperatively raises the possibility that infection developed from a wound infection. However, isolation of these organisms may also have represented contamination during specimen collection. That none of these organisms caused relapse during prolonged follow-up (despite only receiving limited directed therapy initially) would suggest they were not the primary cause of infection.


