Low-grade infection after a total knee arthroplasty caused by *Actinomyces naeslundii*

J. Hedke,1 R. Skripitz,1 M. Ellenrieder,1 H. Frickmann,2,3 T. Köller,3 A. Podbielski3 and W. Mittelmeier1

1Department of Orthopedics, University Hospital Rostock, Germany
2Department of Tropical Medicine at the Bernhard Nocht Institute, German Armed Forces Hospital, Hamburg, Germany
3Institute for Medical Microbiology, Virology and Hygiene, University Hospital Rostock, Germany

Here, we present a case of an 85-year-old woman with a low-grade-infection caused by *Actinomyces naeslundii* after total-knee arthroplasty (TKA) followed by septic loosening. *Actinomyces naeslundii* was cultured from a tissue sample from the knee joint capsule/synovial tissue obtained after the initial TKA. A review of the literature revealed two cases of periprosthetic infection and another three cases of arthritis due to *Actinomyces naeslundii*. So far, no standard treatment for periprosthetic infections caused by *Actinomyces* species has been established.

Introduction

*Actinomyces naeslundii* is a Gram-positive anaerobic bacterium, residing commensally in the mammalian respiratory, gastrointestinal and female genital tracts (Persson, 1987; Wüst et al., 2000). After local trauma, it can cause infections of the oral and cervicofacial region, as well as osteomyelitis and abscesses of the lungs and the abdomen (Strazzeri & Anzel, 1986; Wüst et al., 2000). Only two cases of late endoprosthesis infections caused by *Actinomyces naeslundii* have been reported so far (Wüst et al., 2000). In three other cases, *A. naeslundii* arthritis in the absence of implant material was reported (Vandeveld et al., 1995; Quintero-Del-Rio et al., 1997). Several factors, such as dental extraction, pulmonary disease, HIV infection, intravenous drug abuse and the use of intrauterine devices, could increase risk of infection by *Actinomyces* species (Strazzeri & Anzel, 1986; Vandeveld et al., 1995; Quintero-Del-Rio et al., 1997; Zaman et al., 2002).

Case report

In October 2008 an 85-year-old women underwent a total resurfacing arthroplasty (implants: DePuy LCS, bicondylar, mobile bearing) of the right knee at a regional hospital because of osteoarthritis (Fig. 1). The post-operative course was uneventful. The patient had the following co-morbidities: high blood pressure, non-insulin-dependent diabetes mellitus and a severe chronic obstructive pulmonary disease. A left-sided total hip arthroplasty from December 1993 showed clinically good function without radiographic signs of loosening. Two months after the total knee arthroplasty (TKA) she was admitted for 2 days to the regional hospital because of swelling of the right lower limb, painful restriction of the range of motion (ROM) of the knee, a fever (38.2 °C) and elevated laboratory inflammation parameters [C-reactive protein (CRP) 48.3 mg l⁻¹; erythrocyte sedimentation rate (ESR) 52 mm h⁻¹]. An erysipela of the lower right extremity was diagnosed on the basis of clinical appearance. The patient was treated with oral sultramicillin (Unacid, 2 × 375 mg day⁻¹) for 10 days. Because of a remaining painful ROM restriction of the right knee and consistently increased inflammatory parameters, the patient was referred to our special arthroplasty consultation 4 months after the last clinical consultation.

A three-phase bone scintigraphy with 529 MBq Tc99 m- MDP indicated a loosening of the lateral femoral component of the knee endoprosthesis. For the planning of further treatment we obtained tissue samples from the knee-joint capsule and synovial membrane by minimal incision. Half of the samples were processed for histological inspection and the other half were incubated on Columbia agar supplemented with 5 % sheep’s blood and on Schaedler agar (Anoxomat, Mart Microbiology; and appropriate anaerobic jars) conditions.

The histologically inspected samples showed signs of chronic infection (Fig. 2) potentially caused by a slowly growing agent. On day 4 of incubation, tiny colonies were detected on the anaerobic culture medium exclusively. According to Gram staining and microscopic inspection, the colonies contained Gram-positive rods. The bacteria...
were subjected to biochemical differentiation using the Vitek 2 ANC card (bioMérieux) and identified as *Actinomyces naeslundii*. However, the biochemical differentiation systems API 32A (bioMérieux) and RapIDTM ANA II System (Remel, Thermo Fisher Scientific) failed to correctly identify the agent. Key biochemical reactions required for the identification of *Actinomyces naeslundii* include positive reactions for H2S production; aesculin hydrolysis; urease activity; and acid fermentation of aesculin, glucose, myo-inositol, raffinose, sucrose and trehalose; and a negative reaction for gelatin hydrolysis. Results of the catalase reaction, nitrate reduction, CAMP reaction, and fermentation of glycerol, glycogen, mannitol and xylose are inconsistent or depending on the subspecies (Moncla & Hillier, 2003).

PCR analysis and 16S rRNA gene sequencing revealed that a 466 bp portion of the 5′ end of the resulting product showed 99% sequence similarity to that of *A. naeslundii* (GenBank accession number JQ396428).

If available, rapid matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry is a suitable alternative to time-consuming biochemical differentiation or sequencing methods for the identification of *A. naeslundii*. Reference spectra for *A. naeslundii* are deposited at the SARAMIS database (AnagnosTec). However, MALDI-TOF technology was not yet established at our diagnostic institute when the strain was isolated.

Bacterial resistance to antibiotics was not tested due to the lack of standardized reference values for *Actinomyces* species. Anaerobic Gram-positive non-spore-forming rods are typically susceptible to penicillin G and chloramphenicol while clindamycin, erythromycin and tetracycline are effective in only 94, 88 and 60% of isolates, respectively (Sutter & Finegold, 1976; Wexler & Finegold, 1987, 1988a, b).

Since a suspected low-grade septic loosening was substantiated, the decision was taken to perform a two-stage knee replacement (Windsor et al., 1990; Maurer & Ochsner, 2006). On July 24 2009, a TKA was performed, combined with an extensive synovectomy and surgical debridement. Intraoperatively, there were no signs of an acute infection. A spacer, consisting of gentamicin-containing bone cement (Heraeus Palacos MV) was implanted. Clindamycin (600 mg) was added to the spacer. Preoperatively, intravenous antibiotic therapy of clindamycin (2×600 mg day−1) and penicillin G (3×2 million IU day−1) was started and continued for 2 weeks post-surgery. After the patient was discharged from hospital, antibiotic therapy was continued with orally administered clindamycin (2×600 mg day−1) and penicillin V (3×1.5 million IU day−1) for another 6 weeks. In the subsequent 4 weeks without antibiotic treatment, the patient showed no clinical or laboratory signs of recurrent infection (CRP 14.2 mg l−1, ESR 25 mm h−1, WBC 7.78×109 l−1). On October 7 2009, the patient underwent reimplantation of her TKA. Postoperatively, she was treated with clindamycin (2×600 mg) and penicillin G (3×2 million IU day−1) intravenously for 2 weeks according to a modified Liestal algorithm for implant-associated infections (Spilsbury & Johnstone, 1962; Lewis et al., 1978). Microbiological cultures and histological samples from the last surgery displayed no pathological results. After intense exercises with continuous passive motion twice daily, the patient was discharged and mobilized with partial weight bearing for 6 weeks.

On the day of discharge, the wound showed no signs of inflammation and the ROM values (Ext./Flx. 0/5/80°) were acceptable regarding the initial mobility and state of health of the patient. During a 2-year follow-up period, no clinical, laboratory or radiological signs of a persisting infection were found and good clinical function was reported.

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**Fig. 1.** Preoperative radiographs with signs of loosening in the tibial lateral compartment.

**Fig. 2.** Signs of low to moderate inflammation in the histological sample.
Discussion
Late periprosthetic infections (>3 months after surgery) are usually due to haematogenous spread from an extra-articular site, which probably applies to the present case (Maurer & Ochsner, 2006). Rare infections with Actinomyces species have been described for prosthetic hip joints and only once in association with a TKA (Zaman et al., 2002). A number of risk factors were described for invasive infections with Actinomyces naeslundii, such as haematogenous spread after infections of the oral and cervicofacial regions as well infections of the lungs and the abdomen (Windsor, 1991). In the above-mentioned cases, a prolonged antibiotic treatment with up to 18–20 million IU day\(^{-1}\) of intravenously administered penicillin for 2–6 weeks, followed by oral amoxicillin, ampicillin or penicillin V at 4 × 500 mg day\(^{-1}\) for 6–12 months was reported (Zaman et al., 2002). However, an algorithm for antibiotic and surgical treatment, especially concerning the indicated time point for reimplantation, has not yet been established.
In the present case, the decision to perform a two-stage replacement was made as described for periprosthetic infections with antibiotic-resistant or biofilm-producing bacteria (Windsor, 1991). Since we found no typical sinus tracts with pus during surgery, we administered a combined antibiotic treatment with penicillin and clindamycin according to the literature for a two-stage revision (Windsor et al., 1990; Windsor, 1991). The loss of TKA function due to soft-tissue impairment because of the ≥6 weeks interval between explantation and reimplantation is another major problem of two-stage revisions. In the present case, the combination of a moderate time span between explantation and reimplantation, an extended surgical debridement, treatment with the chosen antibiotics and intense physiotherapy resulted in a good functional outcome.

References