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Oerskovia xanthineolytica Infection of a Prosthetic Joint: Case Report and Review

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***Oerskovia* spp. are gram-positive, *Nocardia*-like bacilli which inhabit the soil and rarely cause human infections. Previously reported cases of *Oerskovia* infection have been characterized by a nonaggressive course and an association with foreign bodies. We report the first case of a patient with a prosthetic joint infection due to *Oerskovia xanthineolytica*. Our patient presented with a prolonged, indolent course and was thought to have aseptic loosening of his prosthesis until the time of surgery. He was cured of his infection by removal of the prosthesis, antibiotic therapy, and delayed reimplantation. Review of the previous 10 reported cases of *Oerskovia* infection in humans supports the recommendation that foreign-body-associated infections should be treated with a strategy that includes removal of the foreign material.**

Introduction. *Oerskovia* spp. are gram-positive bacilli which form yellow colonies and grow as branching filamentous forms resembling *Nocardia* spp. but which, unlike *Nocardia* spp., fragment into motile rod forms. The genus is composed of two species, *Oerskovia turbata* and *Oerskovia xanthineolytica*, which are soil inhabitants and have only rarely been reported to cause infection in humans (2, 5–7, 9, 10, 13–15, 18). Nine of the ten previously reported cases of *Oerskovia* infection occurred in immunocompromised patients and/or were associated with foreign bodies. In this report we describe a patient with a prosthetic knee joint infection due to *O. xanthineolytica* and we review the literature describing human infections caused by *Oerskovia* spp.

Case report. A 72-year-old man with a history of a myocardial infarction and subsequent coronary artery bypass surgery, ethanol abuse, and hypothyroidism underwent a hybrid total left knee replacement in 1991 for osteoarthritis. Approximately 2 years after his surgery he was involved in a moped accident and sustained a closed injury to his left knee, which required no immediate therapy. Later, however, he complained of intermittent pain and swelling of that joint. In September 1994 an analysis of a left-knee aspirate revealed 1,050 erythrocytes and 40,000 leukocytes per mm^3 (92% polymorphonuclear cells and 8% mononuclear cells). A Gram's stain of the joint fluid showed no organisms, and no organisms grew in culture. The sedimentation rate obtained at that time was 45 mm/h, and the patient's peripheral leukocyte count was $7.3 \times 10^3/mm^3$. A repeat left-knee aspiration, performed in January 1995, found 1,600 leukocytes per mm^3 (88% polymorphonuclear cells and 12% mononuclear cells). Again, a Gram's stain showed no organisms and the culture was sterile.

Intermittent left-knee pain and swelling persisted, presumably because of aseptic loosening of the tibial tray, and the patient was scheduled for a left-knee revision arthroplasty in March 1995. At the time of the operation, yellow fluid was found in the knee joint, along with occult loosening of both the tibial and femoral components of the prosthesis. A microscopic analysis of three frozen-section synovial tissue specimens demonstrated 2 to 10 mononuclear or polymorphonuclear cells per high-power field. A Gram's stain confirmed the presence of acute inflammatory cells and demonstrated what appeared to be gram-positive cocci in pairs and chains in the specimen obtained from the bone-prosthesis interface underlying the tibial component of the prosthesis. Therefore, the patient underwent a resection arthroplasty and complete synovectomy with insertion of a tobramycin-impregnated cement spacer. Postoperatively, he received vancomycin for 6 days followed by 5 weeks of intravenous trimethoprim-sulfamethoxazole (TMP-SMX). Cultures from two of three synovial specimens grew a gram-positive rod subsequently identified as *O. xanthineolytica*. Three months after the resection arthroplasty the patient underwent prosthesis reimplantation and now, 6 months after this latest operation, has reached independent function without evidence of recurrent joint infection. Cultures of intraoperative specimens from the patient's last surgery were sterile.

Microbiology. Two of three synovial tissue and bone specimens from the March 1995 surgery grew small, glistening, yellow, catalase-positive colonies on blood agar plates after 72 hours of incubation at 37°C in 5% CO_2. A Gram's stain of these colonies revealed gram-positive branching diphtheroid-like rods. Biochemical analysis using the API Coryne strip (BioMerieux, Hazelwood, Mo.) identified the bacterium as an *Oerskovia* sp. on the basis of its ability to reduce nitrate; hydrolyze gelatin and esculin; oxidize glucose, ribose, xylose, maltose, sucrose and glycogen; and produce pyrazinamidase, pyrrolidonyl arylamidase, alkaline phosphatase, β-galactosidase and α-galactosidase. The organism did not produce urease and did not oxidize mannitol or lactose. The isolate was identified to the species level as *O. xanthineolytica* on the basis of its ability to hydrolyze both xanthine and hypoxanthine. Antibiotic susceptibility testing using a microtiter broth assay (Sensititre, Westlake, Ohio) demonstrated susceptibility to cefazolin (MIC = 2 μg/ml), TMP-SMX (MIC < 0.25 μg/ml), and vancomycin (MIC < 0.5 μg/ml); intermediate susceptibility to

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erythromycin (MIC = 2 μg/ml); and resistance to clindamycin (MIC = 8 μg/ml) and penicillin (MIC = 0.5 μg/ml).

The Centers for Disease Control and Prevention (CDC), Atlanta, Ga., confirmed the identity of the bacterium as *O. xanthineolytica* (1a). Additional testing performed at the CDC revealed that the organism was motile; produced substrate but not aerial hyphae on heart infusion agar; hydrolyzed casein, tyrosine, and adenine; and produced acid from lactose (1). Other fermentation and hydrolysis results matched those obtained in our microbiology laboratory. Antibiotic susceptibility testing using a broth microdilution assay (11) and a different panel of antibiotics generated results that differed from those obtained in our laboratory for erythromycin and TMP-SMX. The CDC found the isolate to be susceptible to amikacin (MIC = 16 μg/ml), cefotaxime (MIC = 8 μg/ml), minocycline (MIC ≤ 0.13 μg/ml), doxycycline (MIC = 2 μg/ml), imipenem (MIC ≤ 0.25 μg/ml) and amoxicillin-clavulanic acid (MIC 1/0.5 μg/ml); moderately susceptible to ampicillin (MIC = 2 μg/ml) and ceftriaxone (MIC = 16 μg/ml); and resistant to erythromycin (MIC = 16 μg/ml), TMP-SMX (MIC = 4/76 μg/ml), and ciprofloxacin (MIC = 8 μg/ml).

Discussion. The genus *Oerskovia* was first proposed in 1970 to include those actinomycetes which were first described by Orskov in 1938 and previously called *Nocardia turbata* by Erikson (12, 17). A new genus was proposed for these bacteria since, despite resembling *Nocardia* spp. in forming branched mycelium, they broke into motile bacilli, had a cell wall different from that of *Nocardia* spp. in that it contained large amounts of galactose, and did not form aerial mycelium. The type species was named *O. turbata*, and a second species, *O. xanthineolytica*, distinguished by its ability to hydrolyze xanthine and hypoxanthine, was isolated in 1972 (8). Other nonmotile *Oerskovia*-like strains have also been identified (8).

Over a 20-year period the CDC collected 35 isolates of *Oerskovia*, of which 9 were identified as *O. turbata* and 26 were identified as *O. xanthineolytica* (16). Nine of 35 (26%) isolates were cultured from blood, 6 of 35 (17%) were cultured from heart tissue, 4 of 35 (11%) were cultured from urine, 3 of 35 (9%) were cultured from extremity wounds, and the remainder, 13 of 35 (37%), were cultured from a variety of tissues and body fluids. Bone and joint cultures yielded one isolate each. Unfortunately, accompanying case histories for these cultures were not available.

There have been 10 case reports of infection due to *Oerskovia* spp. (Table 1). Nine of these 10 cases involved patients who suffered from a variety of chronic underlying illnesses, and in 7 cases infection was associated with a foreign body. Presenting signs and symptoms varied according to the site of infection, but in general patients were febrile but nontoxic. In three cases (Table 1, cases 1, 3, and 6) the onset of symptoms was noted in relation to a probable inoculation time so that an incubation time could be estimated. This time varied from as little as 90 min in case 6, which involved a patient who was infused with contaminated total parenteral nutrition solution, to at least 4 weeks in case 1, which involved a patient who developed aortic valve endocarditis that was likely due to a contaminated homograft. Case 3 described a patient whose infection had an intermediate incubation time of 12 days and who developed endophthalmitis after suffering a penetrating injury to his left eye. A definite time of inoculation (and hence an incubation period) for the remaining 7 previous cases and the one described here cannot be determined. The *Oerskovia* species identified in the previously reported cases were *O. xanthineolytica* (five cases), *O. turbata* (three cases), and a nonmotile *Oerskovia*-like organism (one case). In one case the species was not identified. There was no correlation between the site of infection, response to initial therapy or outcome (all were cured), and the infecting species. All but two patients were treated with antibiotics; however, the choice of drug, route of administration, and duration of therapy varied. Five of the seven patients whose infections were associated with a foreign body had the foreign body removed as part of their therapy. Four of these five had failed treatment with antibiotics alone, as demonstrated by persistently positive cultures while on therapy, suggesting that foreign-body removal is often necessary for cure. The two patients treated without removal of the foreign body had central venous catheter-associated bacteremia (one case was due to contaminated total parenteral nutrition solution) which cleared with antibiotics. All patients were ultimately cured of their infections, including one patient with endocarditis (14) and another with pyonephrosis (2) whose illnesses had lasted for over 6 and 3 months, respectively. The indolent, nontoxic course of many of the reported cases and the 100% cure rate speak to the relative avirulence of *Oerskovia* spp.

Our patient is the first person reported with a prosthetic-joint infection due to *Oerskovia* spp. Most prosthetic-joint infections are caused by organisms normally found on the skin or in the gastrointestinal tract which are either directly inoculated into the wound at the time of surgery or seeded into the joint during an episode of bacteremia. Since *Oerskovia* spp. are primarily soil inhabitants and are not known to colonize humans, it seems unlikely that our patient's knee was inoculated either during his initial surgery or during a subsequent subclinical episode of *Oerskovia* bacteremia. It is possible, however, that his prosthesis was inoculated through an inapparent skin break which occurred during his moped accident.

This case reinforces the importance of careful pre- and intraoperative assessments for occult infection of painful joint prostheses, particularly in the presence of premature component loosening. This case also points out the difficulty in diagnosing prosthetic-joint infections caused by relatively avirulent and fastidious organisms like *Oerskovia* spp. In this regard, the case described in this report is similar to two previously reported cases in which negative cultures of presumably infected specimens were noted (Table 1, case 1, negative preoperative homograft cultures; case 3, negative initial foreign body and vitreous cultures). Additionally, the discordant tissue and colony Gram's stains point out the variable staining appearance of organisms in situ and emphasize the importance of culture results for obtaining an accurate diagnosis. Finally, our patient's indolent course with sterile preoperative joint aspirations is similar to that of prosthetic-joint infections caused by more commonly isolated organisms like *Staphylococcus epidermidis* (3, 4). Thus, under circumstances like those of this case, percutaneous or open-tissue biopsy may be required to establish the diagnosis.

Our patient was cured of his infection by removal of his prosthesis, complete synovectomy, prolonged antibiotic therapy, and a two-stage reimplantation procedure. The discrepancy between the antibiotic susceptibility testing results obtained at the CDC and those obtained at our own clinical microbiology laboratory points out the need for detailed studies which establish standard testing conditions for slowly growing, fastidious organisms like *Oerskovia* spp. Thus, although our patient received 5 weeks of intravenous TMP-SMX postoperatively, it is possible that he was treated with effective antibiotics for only the 6 days following removal of this prosthesis when he received vancomycin. If so, then his cure was largely due to the surgical management of this infection. While all previously reported cases of *Oerskovia* infection have also been successfully treated, a cure has usually required debride-

TABLE 1. *Oerskovia* infection case reports[a]

Case (reference)	Age (yr)/sex	Underlying condition or therapy	*Oerskovia* sp. (specimen)	Infection	Foreign body	Treatment regimen (duration and/or route of administration)	Failed antibiotic therapy alone[b]
1 (14)	68/M	Crohn's disease, ankylosing spondylitis, steroids	*O. turbata* (blood, aortic valve homograft)	Endocarditis	Aortic valve homograft	PCN, AMP, ERY, and/or TMP-SMX (6 mo); then AVR followed by TMP-SMX (12 wk, p.o.) and AMP (12 wk; i.v. and p.o.)	Yes
2 (2)	47/F	Kidney trouble	Nonmotile *Oerskovia* sp. (kidney)	Pyonephrosis	None	Nephrectomy	NA
3 (6)	47/M	None	*O. xanthineolytica* (vitreous humor)	Endophthalmitis	Metallic object	FB removal and vitrectomy followed by gent (TP), AMP (p.o.); endophthalmitis treated with GEN (s.c., i.v., and TP), cefazolin (i.v. and TP), and PCN (i.v.); relapse treated by vitrectomy, AMB (s.c.), GEN (s.c.), PCN (i.v.), and cephalexin (p.o.)[c]	NA
4 (7)	38/F	Mental retardation, astrocytoma, VP shunt	*O. xanthineolytica* (CSF)	Meningitis	VP shunt	PCN (15 days) and rifampin (13 days); shunt removal	Yes
5 (9)	3/M	AML	*O. turbata* (blood)	Bacteremia	Central venous catheter	Amikacin (7 days); catheter removal	Yes
6 (5)	40/F	Crohn's disease, short bowel syndrome	Species not specified (blood, TPN solution)	Bacteremia	Central venous catheter	Vancomycin (9 wk), GEN (5 days), and metronidazole (5 days)	No
7 (15)	70/M	Chronic renal failure, CAPD	*O. xanthineolytica* (peritoneal fluid and peritoneal catheter tip)	Peritonitis	Peritoneal catheter	Vancomycin (i.p. and i.v.) and GEN (20 days; i.m. and i.v.); catheter removal	Yes
8 (13)	23/M	AIDS	*O. turbata* (axillary abscess)	Axillary abscess	None	Debridement	NA
9 (18)	40/M	Cirrhosis, variceal bleeding, sclerotherapy	*O. xanthineolytica* (blood)	Bacteremia	None	Ceftriaxone, vancomycin, GEN, and clindamycin[b]	NA
10 (10)	54/F	Breast cancer	*O. xanthineolytica* (blood)	Bacteremia, pneumonia	Central venous catheter	Cefuroxime (3 days) and vancomycin (14 days)	No
11 (present report)	72/M	Ethanol abuse, hypothyroidism, CAD, osteoarthritis	*O. xanthineolytica* (synovial tissue)	Prosthetic knee joint infection	Prosthetic knee joint	Vancomycin (6 days) and TMP-SMX (5 wk; i.v.); prosthesis removal	NA

[a] AML, acute myelogenous leukemia; AMP, ampicillin; AMB, amphotericin; AVR, aortic valve replacement; CAD, coronary artery disease; CAPD, chronic ambulatory peritoneal dialysis; CSF, cerebrospinal fluid; ERY, erythromycin; FB, foreign body; GEN, gentimicin; i.m., intramuscular; i.p., intraperitoneal; i.v., intravenous; NA, not applicible; PCN, penicillin; p.o., oral; s.c., subconjunctival; TP, topical; TPN, total parenteral nutrition; v.p., ventriculoperitoneal.

[b] That is, foreign-body-associated infections which were not cured by antibiotic therapy alone.

[c] Duration of treatment was not specified.

ment of infected tissue and, in those cases involving a foreign body, removal of the foreign body. As previously mentioned, in four cases of infection associated with foreign material, initial therapy with antibiotics alone failed (7, 9, 14, 15). An exception to this is catheter-associated *Oerskovia* bacteremia, which may occasionally be cured with antibiotics alone (5, 10).

In summary, we present a case of a prosthetic knee joint infection due to *O. xanthineolytica*. Infection may have resulted from direct inoculation secondary to trauma. The diagnosis was elusive and eventually required culture of tissue obtained during open biopsy. Furthermore, the morphology of the organisms in situ differed significantly from their appearance in culture, making interpretation of the tissue Gram's stain problematic. Finally, our patient's indolent course and favorable

outcome are typical of previously reported cases of *Oerskovia* infection, and his cure following removal of the infected prosthesis, debridement, and antibiotics supports the notion that foreign-body removal is key to the successful management of these cases.

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