The first documented case of knee alloarthroplasty infection due to *Abiotrophia defectiva*, formerly known as nutritionally variant streptococci (NVS) and *Streptococcus defectivus*, is presented. The microbiology of this bacterium is discussed and clinical features of previously reported cases of infections by NVS are reviewed briefly.

**Introduction**

*Abiotrophia defectiva* is part of the normal human flora [1–3] and is a resident of the oral cavity [1, 4], and the genitourinary and intestinal mucosae [4, 5].

*Abiotrophia* spp. have previously been referred to as nutritionally variant streptococci (NVS) because of their fastidious nutritional growth requirements. Frenkel and Hirsch [6] first isolated these organisms from patients with endocarditis and otitis media. The organisms tend to form satellite colonies around *Staphylococcus aureus* and other bacteria, including some Enterobacteriaceae and other streptococci. They were described as ‘ungroupable’ viridans streptococci and required pyridoxal hydrochloride (vitamin B₆) analogues for growth and produced a chromophore, pyrrolidonyl arylamidase and a bacteriolytic enzyme [2–4, 7, 8].

Bouvet et al. [2] proposed two new species names for the NVS, *Streptococcus defectivus* and *S. adjacens*, on the basis of DNA–DNA hybridisation studies. Analysis of 16S ribosomal RNA (rRNA) sequences showed that these two species were not related to other members of the genus *Streptococcus*. Consequently, they were placed in the new genus *Abiotrophia* as *A. defectiva* and *A. adjacens* [9].

Recent 16S rRNA gene sequencing studies have demonstrated that the genus is not monophyletic. Phylogenetically, the genus *Abiotrophia* consists of two distinct lines, *A. defectiva* and another group consisting of *A. adjacens*, *A. balaenopterae* and *A. elegans*. Therefore, it was proposed by Collins and Lawson that the genus *Abiotrophia* be restricted to *A. defectiva* and that *A. adjacens*, *A. balaenopterae* and *A. elegans* be reclassified in a new genus, *Granulicatella* gen. nov., as *G. adjacens* comb. nov., *G. balaenopterae* comb. nov. and *G. elegans* comb. nov. [14].

To draw attention to their clinical significance and difficulties in diagnosis and treatment, this paper describes the first documented case report of an infected total knee alloarthroplasty caused by *A. defectiva*.

**Case report**

In April 2000, a 65-year-old woman was admitted to this hospital with progressive pain and swelling in her right knee, which had undergone a total knee arthroplasty (TKA) 4 years earlier. Her medical history included a nephrectomy because of glomerulonephropathy, non-insulin-dependent diabetes mellitus and alcohol abuse in the past.

She was in good general health and reported no fever. Physical examination revealed no abnormalities, in
particular no port of entry for bacteraemia nor stigmata of endocarditis. Scintigraphy showed evidence of loosening of the prosthesis, and a conventional radiograph was normal. Laboratory data showed a normal white blood count (5500 cells/ml) and elevated C-reactive protein (CRP) (41 mg/L). Aspiration of the right knee yielded 10 ml of turbid fluid. The specimen was injected into agar vials (Venturi Transsystem®, Nehren, Germany). A Gram's stain failed to reveal any micro-organisms. Nevertheless, on the basis of the clinical impression, an infection of the total knee arthroplasty was diagnosed.

The patient was taken to surgery for a radical open debridement and replacement of all polyethylene components of the prosthesis. Because no micro-organism had been isolated pre-operatively and no signs of loosening of the prosthesis were seen intra-operatively, the prosthesis was left in place.

Intra-operative aspirates were placed in Bactec plus aerobic and anaerobic culture vials (Becton Dickinson, Sparks, MD, USA). The sample was plated on to Columbia agar supplemented with defibrinated sheep blood 5% and chocolate agar and incubated aerobically and in an anaerobic atmosphere containing CO₂ 5% at 37°C. Several small α-haemolytic colonies were noted on the blood-agar plate after incubation for 24 h. Gram's stain revealed pleomorphic gram-positive coccobacilli. The bacterium was not identified with a rapid identification system for gram-positive rods (API Coryne; bioMérieux, Marcy l'Etoile, France) after incubation for 12 h, nor was it identified by rapid identification systems for streptococci (Rapid ID 32 STREP, bioMérieux) after incubation for 4 h. The bacterium was identified with a universal PCR system, with primers targeting the part of the 16S rDNA [15]. The amplified PCR product was sequenced and a BLAST search at the NCBI was performed [16]. A. defectiva was identified, with a homology of 99.9%.

Antimicrobial treatment included cefazolin i.v. for 10 days, followed by ciprofloxacin orally for 26 days until CRP levels and the physical examination returned to normal.

In July 2000 the patient presented again with pain and swelling as signs of an infected knee prosthesis. Gram's staining of the aspirated intra-articular fluid showed pleomorphic gram-positive coccobacilli and samples plated on to Columbia agar with defibrinated sheep blood 5% grew small α-haemolytic colonies.

As Abiotrophia was considered to be the possible causative agent, a rapid ID 32 STREP test (bio-Mérieux) was performed. After 12 h the biochemical reactions exhibited the characteristic patterns of A. defectiva. This prolonged incubation (12 h instead of 4 h) was necessary because of the long generation time of Abiotrophia.

A two-stage revision arthroplasty was performed. After debridement and explantation, antibiotic treatment was initiated with ciprofloxacin i.v. As the patient developed profuse diarrhoea, the regimen was changed to penicillin i.v. and subsequently to fluclaxacillin orally until the CRP level returned to normal. In December 2000 a new alloarthroplasty was implanted. At present the patient has good function of the TKA.

Discussion

A. defectiva and A. adjacens account for 5–6% of cases of streptococcal endocarditis and some authors have suggested that they are an important cause of blood culture-negative endocarditis [17–21]. Bouvet [22] isolated two strains of S. adjacens and five strains of S. defectus from 91 strains of viridans streptococci that caused endocarditis. Some authors noted that the clinical course was often more severe than in cases of endocarditis caused by other viridans streptococci or enterococci [23, 24].

Ormerod et al. [25] described four cases of infectious crystalline keratopathy caused by NVS. Recently, it has been shown that infiltrative keratitis can be associated with A. defectiva [26]. Wofsy [27] reported a case of joint infection caused by NVS as a complication of endocarditis. These organisms have also been implicated in pancreatic abscess, otitis media, wound infections and iatrogenic meningitis [28, 29].

Therapeutic failure occurred in 41% and relapse in 17% of endocarditis cases, despite treatment with antibiotics that appeared to be active in vitro [23]. Stein and Nelson [23] hypothesised that the difficulties in treatment may be caused by the slow growth rate and suggested that a longer course of antibiotic therapy may be required for successful treatment of cases of NVS endocarditis.

Exopolysaccharide production by NVS in later stages of rabbit endocarditis has been reported. It was suggested that nutrient limitation within vegetations could account for altered ultrastructural morphology and that exopolysaccharide might enhance NVS pathogenicity [4]. The frequent colonisation and infection of cardiac valves with Abiotrophia spp. suggests an affinity for avascular tissue, as found around an alloarthroplasty.

The reported incidence of knee alloarthroplasty infections ranges from 0% to 23% with an average of 5% [30] and is caused by direct spread or by haematogenous spread. Staphylococci are the major causative agents of this type of infection, followed in descending order by gram-positive aerobic streptococci, gram-negative aerobes and anaerobes [31]. The authors...
believe that, in the past, arthroplasty infections with NVS have included *Abiotrophia* spp, which were uncharacterised at that time. The treatment of arthroplasty infections includes repetitive debridements [32], removal of the prosthesis and leaving an excision arthroplasty [33] and converting to an arthrodesis [34–36]. A two-stage revision arthroplasty leaving a temporary spacer of bone cement containing antibiotics has become more common [37, 38].

In the case reported here, the isolate of *A. defectiva* was susceptible in vitro (disk diffusion tests on Mueller-Hinton agar with defibrinated sheep blood 5%) to penicillin, clindamycin, cefazolin, cefpodoxime, cefuroxime, cefotaxime, gentamicin, ciprofloxacin and imipenem and resistant to tobramycin, doxycycline and aztreonam. The susceptibility of 27 *G. adjacens* and 12 *A. defectiva* isolates was investigated by a microdilution method with pyridoxal hydrochloride and Mueller-Hinton broth supplemented with lysed horse blood. According to NCCLS interpretative criteria for *S. pneumoniae*, the susceptibilities of *G. adjacens* and *A. defectiva* strains were, respectively: penicillin, 55% and 8%; amoxicillin, 81% and 92%; ceftriaxone, 63% and 83%; meropenem, 96% and 100%; and 100% for both species with clindamycin, rifampin, levofloxacin, ofloxacin, quinupristin/dalfopristin and vancomycin [39].

High-level resistance to aminoglycosides (MIC >500 mg/L), as encountered with enterococci and viridans streptococci, has not been reported for NVS. Synergy between penicillin or vancomycin in combination with an aminoglycoside has been observed in both *in vitro* and in experimental animal models of endocarditis [40]. However, in-vitro antimicrobial susceptibility testing of *Abiotrophia* is not standardised, and the results of in-vitro susceptibility tests do not correlate well with clinical effectiveness.

In conclusion, *A. defectiva* is a relatively unknown micro-organism, which may cause serious infections including culture-negative forms of alloarthroplasty infection and endocarditis.

The extreme pleomorphic appearance of strains may be confusing and cause diagnostic problems [30], which could lead to prolonged morbidity and costly diagnostic and therapeutic procedures. If Gram's stain indicates gram-positive cocci in chains or pairs, the addition of pyridoxal-containing medium or cross-inoculation of the inoculated plate with *Staph. aureus* may increase detection of *Abiotrophia* isolates. Also, because of the slow growth rate of *Abiotrophia* spp., prolonged incubation for at least 72 h in an atmosphere containing CO₂ 5–10% is recommended.

Clinicians and microbiologists should be aware of this organism and its pathogenic potential.

### References

23. Stein DS, Nelson KE. Endocarditis due to nutritionally


