Endophthalmitis Due to *Microbacterium* Species: Case Report and Review of Microbacterium Infections

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Microbacterium **species (formerly CDC [Centers for Disease Control and Prevention] coryneform group A-4 and A-5 bacteria) are widely distributed in the environment and rarely cause infections in humans. We present a case of endophthalmitis due to *Microbacterium* species that occurred after accidental trauma and review the literature on microbacterium infections. If the infected tissue or medical device is removed and antimicrobial therapy (preferably with β-lactams or glycopeptides) is instituted, the prognosis is usually favorable for patients with microbacterium infections.**

Infections due to coryneform bacteria have been reported with increasing frequency within the last few years. The reasons for this increase may be the use of intensified and more-invasive therapy regimens, an increase in the number of immunocompromised patients, and an increased awareness regarding the pathogenic potential of coryneform bacteria. In addition, tremendous efforts have been made to clarify the taxonomy of coryneform bacteria, and thus many new genera and species have been described [1].

Strains belonging to the genus *Microbacterium* have recently been recognized as pathogens in humans; these strains were previously designated CDC (Centers for Disease Control and Prevention) coryneform groups A-4 and A-5 bacteria [2]. At present, it is almost impossible to identify individual species within the genus *Microbacterium* because the majority of descriptions of the six presently defined species that constitute the genus are based on only very few strains. *Microbacterium* strains are widely distributed in the environment (e.g., they are found in the soil and in sewage) [2, 3].

We report a case of endophthalmitis caused by a *Microbacterium* species after accidental trauma. A review of the literature revealed five other cases in which *Microbacterium* species caused severe infections.

Case Report

A 34-year-old male sustained an intraocular foreign-body injury while working with a steel hammer in an opencast mine. On admission, physical examination revealed conjunctival injection of the right eye, perforation of the cornea, a deep anterior chamber with 2+ cells, and a perforated lens with cataracts. Blood was seen in the vitreous. A roentgenogram of the right orbit showed a single intraocular foreign body (2 × 1.5 mm) with a metallic density. Subsequent ophthalmologic treatment included closing the corneal laceration; incision of the sclera, with magnetic extraction of the foreign body via pars plana; and lensectomy. Extraction of the foreign body via pars plana; and lensectomy.

Empirical antibiotic therapy with iv cefazolin (2 g t.i.d.) was started, but the drug was not applied intravitreously. Four days after this initial treatment, the patient presented with severe pain and clouding of the anterior vitreous. An anterior vitrectomy was performed to establish the diagnosis of endophthalmitis. During surgery, 0.4 mg of tobramycin were injected into the vitreous cavity, and 40 mg of gentamicin were given subconjunctivally. The patient started receiving iv therapy with gentamicin (80 mg b.i.d.), cefotiam (2 g b.i.d.), and clindamycin (300 mg t.i.d.).

The vitreous and the aspirate from the anterior chamber were both purulent (there were 5 leukocytes per high-power field), but no microorganisms were seen on direct gram stains (as reviewed by one of the authors). Within 24 hours, cultures of specimens of the aspirate and vitreous on sheep blood agar plates as well as on chocolate agar plates yielded light, pure growth of yellow-pigmented colonies (1 mm in diameter), but no growth was observed on MacConkey agar plates.

Microscopic examination revealed small gram-positive rods. They were immotile and did not reduce nitrate; they hydrolyzed esculin but not urea; they fermented glucose, maltose, sucrose, mannitol, and xylose, resulting in the production of acid but no gas (former CDC coryneform group A-4 bacteria). Additional chemotaxonomic investigations revealed that lysine was the diamino acid of the cell wall peptidoglycan and that the dominant cellular fatty acids were *ai*-C15:0 (31%) and *ai*-C17:0 (39%). On the basis of these findings, the isolate was assigned to the genus *Microbacterium* [2, 3]. Fungal cultures of the aspirate and vitreous remained negative.

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Antimicrobial susceptibility testing was performed on Mueller-Hinton agar plates with use of the Etest or broth microdilution [4]. The following MICs were obtained for the isolate: cefazolin, <0.25 μg/mL; cefotiam, <0.25 μg/mL; ciprofloxacin, 0.19 μg/mL; clindamycin, 0.19 μg/mL; gentamicin, >64 μg/mL; imipenem, 0.25 μg/mL; piperacillin, 0.032 μg/mL; tobramycin, >64 μg/mL; teicoplanin, 0.25 μg/mL; and vancomycin, 0.25 μg/mL. It remained unclear why the patient's condition deteriorated while he was receiving cefazolin.

To determine the exact phylogenetic position of the patient's isolate, we sequenced almost the entire 16S rRNA gene (European Molecular Biology Laboratory accession no. X95482) according to the method of Hiraishi [5]. Phylogenetic analysis was performed on the basis of 1,253 alignable nucleotides by using the neighbor-joining method and including bootstrap analysis with 100 resampled data sets that were compared with published sequences of the type strains of the genus *Microbacterium* [6] and phylogenetically related bacteria [7]. Methods and programs used for this analysis have previously been described in detail [8].

In the resulting phylogenetic tree (figure 1), our patient's isolate (GH 942) clustered together with *Microbacterium laevaniformans* and *Microbacterium dextranolyticum,* a finding that confirmed its place in the genus *Microbacterium.* Quantitative DNA-DNA hybridizations may reveal whether the patient's isolate represents a new species of the genus *Microbacterium.*

After surgery the patient's anterior chamber gradually cleared, and the vitreous inflammation decreased. He was discharged on the 21st day after the injury. At this time, he was able to see hand movements; no hypopyon was observed, and the vitreous was slightly hazy. Two months after the injury, ophthalmologic examination revealed that the eye was clear with no signs of infection or retinal detachment. Slight edema of the macula was noted. Three months after the accident, the best corrected visual acuity was 15/36.

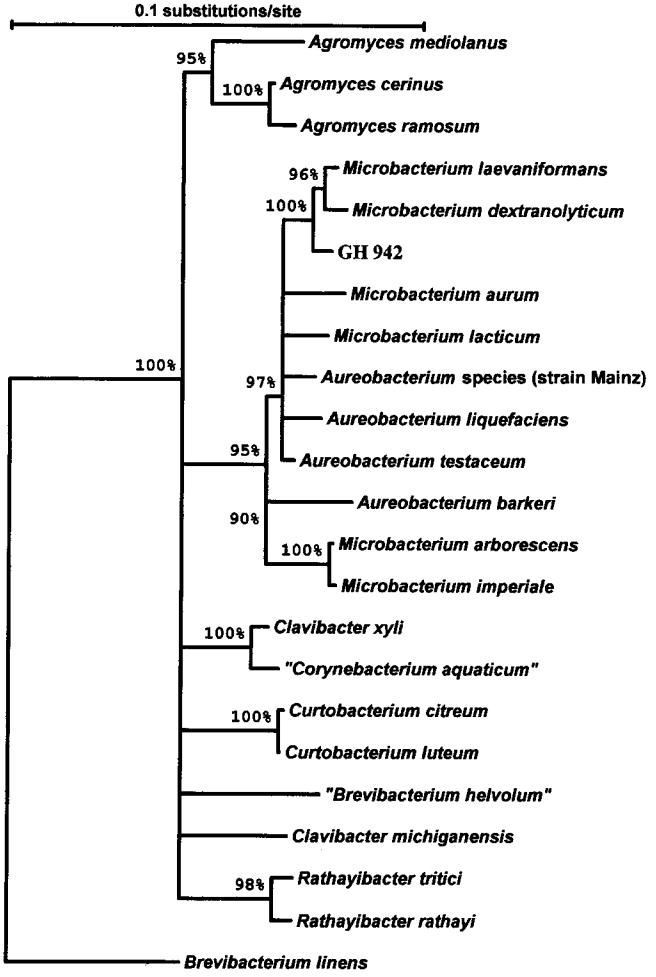

Figure 1. Phylogenetic position of an isolate (strain GH 942) from a patient with microbacterium endophthalmitis, as inferred by analysis of 16S rDNA in other actinomycetes with group B-peptidoglycan. The neighbor-joining method was used. Numbers within the tree represent bootstrap values. Statistically non-supported nodes (<90%) were not resolved.

Review and Discussion

In all of the reported cases of microbacterium infections, the patients were male (table 1). Three of the six patients had endophthalmitis (two of these cases occurred after accidental trauma, and one occurred after hematogenous spread of the organism). Gram-positive rods were seen in a direct gram stain in only one of these three cases. All three of these patients with endophthalmitis underwent at least partial vitrectomy, and all were found to have impaired vision after completing therapy, which also included treatment with antimicrobial agents (table 1).

Two of the six patients with microbacterium infections had infected catheters, and both were immunocompromised as a result of hematologic neoplasias. Because bacteremia persisted in these two patients, the catheters had to be removed to achieve cure. All six patients with microbacterium infections were cured by removal of the infected tissue or medical device and institution of antimicrobial therapy, and no other systemic manifestations of microbacterium infection were observed.

The limited experience with microbacterium infections does not allow a definitive recommendation for treatment at the present time. However, it has been our experience (as in the present report) that some *Microbacterium* strains have shown resistance in vitro to aminoglycosides when MIC values were interpreted according to the guidelines of the National Committee for Clinical Laboratory Standards [2].

Other investigators have also reported in vitro resistance to aminoglycosides in their *Microbacterium* isolates [11, 12]. Retesting of the *Microbacterium* strain described by Campbell et al. [12] revealed susceptibility to vancomycin (MIC, 2 μg/mL)

Table 1. Summary of data from six cases of microbacterium infection.

Case no. [reference]	Year	Age (y)/sex	Underlying condition	Microbacterium infection	Treatment (route, duration)	Outcome
1 [9]	1979	38/M	Penetrating metallic foreign body	Endophthalmitis	Initially, sj Gm; iv Gm, Meth; anterior vitrectomy; it Gm, Meth, corticosteroids; iv Gm, Meth, corticosteroids*	Impaired vision (12/37 visus)
2 [10]	1990	77/M	Abdominal surgery	Hematogenous endophthalmitis†	Vitrectomy; topical Ctax, Gm for 3 w; po 5-FC, Ket for 4 w	Impaired vision (6/36 visus)
3 [11]	1991	67/M	None	Mitral valve endocarditis	iv Amp for 6w	Cured
4 [12]	1994	11/M	Acute myelomonocytic leukemia	Septicemia	iv Tic/CA, Tm, Vm for 3 d; iv Ctax for 3 d; removal of infected CVC	Survived
5 [13]‡	1995	64/M	Myelodysplastic syndrome	Sepsis	iv Tic/CA, Gm, Cpfx for 2 d; iv Tic/CA, Vm;* iv Ctri for 4 d; removal of infected Hickman catheter; iv Ctri for 2 w	Survived
6 [PR]	1996	34/M	Penetrating metallic foreign body	Endophthalmitis	Initially, iv Cfaz for 3 d; anterior vitrectomy; it Tm + sj Gm; iv Gm, Cti, Cm for 3 w	Impaired vision (15/36 visus)

NOTE. Amp = ampicillin; Cfaz = cefazolin; Cm = clindamycin; Cpfx = ciprofloxacin; Ctax = cefotaxime; Cti = cefotiam; Ctri = ceftriaxone; CVC = central venous catheter; Gm = gentamicin; it = intravitreously; Ket = ketoconazole; Meth = methicillin; PR = present report; sj = subconjunctivally; Tic/CA = ticarcillin/clavulanic acid; Tm = tobramycin; Vm = vancomycin; 5-FC = 5-fluorocytosine.

* Duration not given.

† *Candida albicans* was also isolated.

‡ The biochemical reactions of the bacterial isolate recovered in this case did not clearly allow differentiation between *Cellulomonas* species and *Microbacterium* species [14].

(author's unpublished data). Nearly all *Microbacterium* strains described in the literature or tested by us were susceptible in vitro to β-lactams [2, 10, 11, 13], drugs that should always be considered for the treatment of microbacterium infections.

All *Microbacterium* strains that have been reported were susceptible to glycopeptides; thus these drugs may be used for initial empirical therapy, until the results of susceptibility testing are known, when coryneform bacteria are recovered from specimens such as blood or the vitreous.

There is no doubt that microbacterium infections are rare in humans. Three reference laboratories in Europe have received or isolated only 13 *Microbacterium* strains over nearly two decades [2]. However, it is likely that only severe infections caused by *Microbacterium* species have been reported in the literature. A series of papers described two atypical CDC coryneform group A-4 strains as causes of endophthalmitis after intraocular lens implantation and corticosteroid therapy in two female patients [15–17]. It was unclear why these strains were still referred to as CDC coryneform group A-4 [16, 17], since it was previously demonstrated that these two atypical CDC coryneform group A-4 strains were in fact CDC coryneform group 1 bacteria [18], which are now defined as *Actinomyces neuii* [19].

The pathogenic potential of *Microbacterium* species has been demonstrated in a rabbit endophthalmitis model; these bacteria fulfill the Koch postulates for an etiologic agent of an infectious process [9].

In accordance with the habitat of *Microbacterium* species, the two strains involved in cases 1 and 6 (table 1) were acquired from the environment. *Microbacterium* strains have also been isolated from the hospital environment [2], but possible nosocomial transmission of *Microbacterium* strains in cases 2, 4, and 5 (table 1) can only be suspected.

Finally, we emphasize that microbacterium infections are rare but that they have been more frequently reported within the last few years (table 1).

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