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Three Cases of Post-Cataract Surgery Endophthalmitis Due to *Rhizobium* (*Agrobacterium*) *radiobacter*

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We present three unrelated post-cataract surgery endophthalmitis cases caused by *Rhizobium radiobacter*, hospitalized in three different hospitals. Early diagnosis was obtained in two cases by bacterial DNA detection in vitreous samples. All patients recovered from infection, but pars plana vitrectomy was needed in two patients due to rapid clinical deterioration.

CASE REPORTS

Patient 1. An 81-year-old female patient complained of decreased visual acuity (20/63) 4 weeks after cataract surgery (phacoemulsification) of the right eye (Table 1). Acute postoperative endophthalmitis with severe ocular inflammation was diagnosed. Vitreous (200-μl) and aqueous humor (AH; 150- to 200-μl) samples were tested by culture using brain heart infusion broth (AES Laboratories, Combourg, France) and eubacterial PCR, as previously described (5). *Rhizobium radiobacter* was detected by culture in AH and vitreous and by eubacterial PCR in the vitreous. Species identification was confirmed by PCR amplification and sequencing of the 16S rRNA gene (GenBank accession number JQ304788) from the vitreous sample and from isolated colonies, whereas phenotypic identification of the isolated strain remained ambiguous. A 440-bp DNA fragment of the 16S rRNA gene was amplified with primers 91E and 13BS as described by Gauduchon et al. (10). The amplicon was sequenced, and the sequence obtained was compared in a phylogenetic analysis with those available in the BIBI database (http://umr5558-sud-str1.univ-lyon1.fr/lebibi/lebibi.cgi). Using an agar disk diffusion method (7), the strain was found to be intermediately susceptible to broad-spectrum cephalosporins (especially ceftazidime) but susceptible to cefepime, imipenem, and fluoroquinolones according to the interpretative criteria of the CLSI for *Pseudomonas aeruginosa*, as previously suggested (14). The patient received two intravitreal injections of vancomycin (1 mg) and ceftazidime (2 mg) on the day of admission and 4 days later, systemic antibiotics for 7 days (intravenous imipenem at 500 mg three times a day and ciprofloxacin at 500 mg orally twice a day), subconjunctival injections of dexamethasone, and topical steroid therapy. One year later, the outcome was favorable.

Patient 2. A 75-year-old male patient presented with acute endophthalmitis of moderate severity (Table 1; Fig. 1), 9 days after an uncomplicated phacoemulsification. He was followed up for obstructive sleep apnea and hypertension. Vitreous and AH were sampled, and the patient received an intravitreal injection of vancomycin plus ceftazidime, a systemic antibiotic therapy (intravenous piperacillin at 4 g three times a day and levofloxacin orally at 500 mg once a day, for 7 days), and topical steroid therapy. The following day, visual acuity was reduced to light perception, a 1-mm hypopyon appeared, and a pupillary membrane prevented fundus examination. Pars plana vitrectomy (PPV) was performed on day 3 of hospitalization, and intravitreal injections of antibiotics were repeated the same day and 2 days later. *R. radiobacter* was detected by culture in AH and vitreous samples collected on hospital admission and by eubacterial PCR in the PPV sample. Species identification was obtained by 16S rRNA gene sequencing (GenBank accession no. JQ304789), whereas the phenotypic identification of isolated colonies (API 20NE system; bioMérieux, Marcy l'Etoile, France) remained ambiguous between *Sphingomonas paucimobilis* and *R. radiobacter*. The strain was susceptible to piperacillin and broad-spectrum cephalosporins, including ceftazidime, imipenem, and fluoroquinolones, but resistant to aminoglycosides. The 6-month follow-up examination revealed optic nerve atrophy and a poor visual acuity (20/125).

Patient 3. Sixteen days after an uneventful phacoemulsification, an 84-year-old female patient presented with a severe acute endophthalmitis of the left eye (Table 1). She had type II diabetes mellitus and had received long-term steroid therapy. The patient received intravitreal injection of vancomycin plus ceftazidime, systemic antibiotics (intravenous piperacillin at 4 g three times a day and levofloxacin orally at 500 mg once a day), and topical steroid therapy. Because of clinical deterioration, a second intravitreal injection of antibiotics and PPV were performed on the 3rd and 4th days after admission, respectively.

Two clinical samples were tested by culture and eubacterial PCR: AH collected at the time of admission and vitreous collected at the time of PPV. Only culture of the PPV sample yielded *R. radiobacter*, as identified by a phenotypic method (Phoenix system; Becton Dickinson, Pont de Claix, France). Eubacterial PCR tests were negative. The strain was susceptible to piperacillin and broad-spectrum cephalosporins, including ceftazidime, cefepime,

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TABLE 1 Clinical features and microbial identification of endophthalmitis caused by *Agrobacterium radiobacter*[a]

Clinical feature or microbial identification	Data for patient:		
	1	2	3
Time of symptom onset after surgery (day)	24	9	11
VA on admission	20/63	Hand motion	Hand motion
Anterior chamber			
Conjunctival hyperemia	Moderate	Important	Important
Lid edema	None	Present	None
Tyndall	++	++	++
Hypopyon (mm)	1	0.5	1
Pupillary membrane	None	Mild	Dense
IOP (mm Hg)	20	9	10
Posterior chamber			
Red reflex	Absent	Present	Present
Visibility of the fundus	Altered	Good	Altered
Vitritis	Important	Moderate	Important
Retinal vasculitis	Not visualized	Yes	Not visualized
Culture positive	AH, VIT	AH, VIT	PPV
Eubacterial PCR positive	VIT	VIT, PPV	None
No. of intravitreal injections of antibiotics	2	2	2
Pars plana vitrectomy	No	Day 3 of hospitalization	Day 4 of hospitalization
Outcome (VA)	20/25 at 1 yr	20/125 at 6 mo	20/32 at 3 mo

[a] Abbreviations: AH and VIT, aqueous humor and vitreous samples collected at the time of hospitalization, before administration of antibiotics; PPV, vitreous sample collected at the time of pars plana vitrectomy; VA, visual acuity; IOP, intraocular pressure.

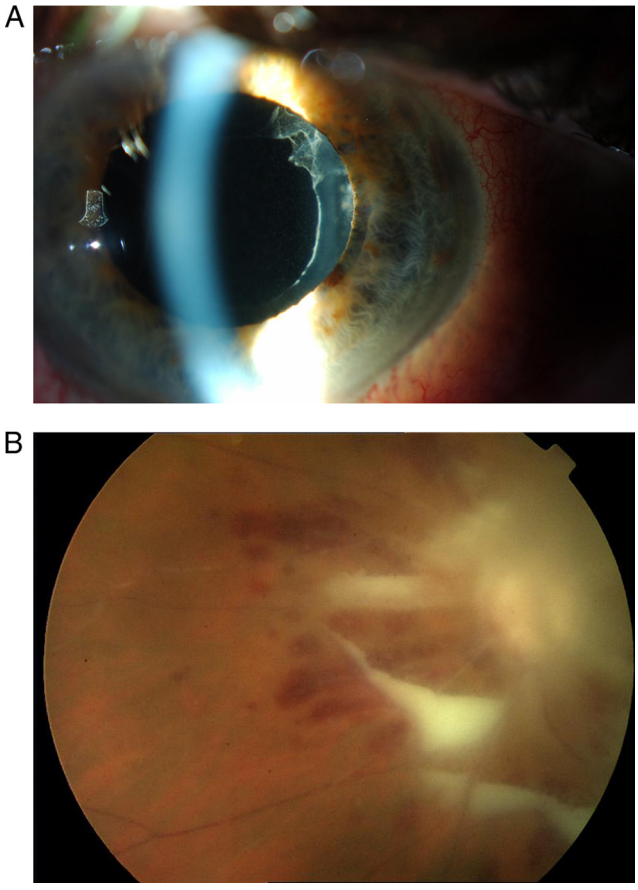

FIG 1 Ocular examination in case 2. (A) Moderate inflammation of the anterior chamber (pupillary membrane and Tyndall 1+); (B) moderate vitritis, retinal vasculitis, and preretinal infiltration.

imipenem, and fluoroquinolones, but resistant to tobramycin. Clinical improvement was obtained after PPV, and visual acuity was 20/32 at 3 months after admission of the patient.

With an incidence of 0.07 to 0.3%, postoperative bacterial endophthalmitis is one of the most feared complications of intraocular surgery, as it may result in a severe decrease of visual acuity or even blindness of the involved eye (5). Gram-positive bacteria, especially coagulase-negative staphylococci, remain the most common causative organisms, whereas Gram-negative bacteria account for only 5% of cases (5). We present three unrelated cases of postoperative endophthalmitis due to *Rhizobium radiobacter*, a Gram-negative, catalase-positive, oxidase-positive, nonfermenting bacterium predominantly found in soil (14). This species' name was proposed in 2001 by Young et al. (28), who unified the genera *Rhizobium*, *Agrobacterium*, and *Allorhizobium* into a single genus, *Rhizobium*. *R. radiobacter* includes the former synonymic species *Agrobacterium radiobacter* and *Agrobacterium tumefaciens*, which could be differentiated only by the presence of tumorigenic (Ti) plasmids. *R. radiobacter* has been occasionally associated with opportunistic infections in humans, including bacteremia (especially catheter-related bacteremia) (2, 4, 9, 11, 15, 16, 21, 22), pneumonia (17), urinary tract infections (1), peritonitis (12, 26), and endocarditis (25). Most of these infections occurred in hospital settings (14), in patients with immunosuppression (e.g., hematologic malignancies, solid-organ cancers, HIV infection, or organ transplantation) (6, 8, 13, 17), and/or in patients bearing a foreign material (e.g., central catheter) (4, 11, 14, 15, 21).

The present case series confirms that *R. radiobacter* is an opportunistic human pathogen occasionally responsible for acute postoperative endophthalmitis (18, 19, 24). The adherence of this

bacterium to the intraocular lens during cataract surgery may promote development of endophthalmitis, as has been reported for *Staphylococcus epidermidis* (20). In contrast, none of the endophthalmitis patients from our series and previous reports (18, 19, 24) had underlying malignancy or were immunocompromised. The onset of symptoms after cataract surgery varied from 4 days (18) to 4 weeks (our case series), and this may partly depend on the bacterial inoculum leading to infection. Most patients suffered from acute endophthalmitis with severe symptoms (18, 24), but a chronic endophthalmitis case was also reported (19). All patients recovered from *R. radiobacter* infection after intravitreal and systemic antibiotic therapy, but the final outcome varied from a total visual recovery to a near-complete loss of visual acuity in the affected eye (references 18, 19, and 24 and the present study). In our case series, a PPV was performed because of rapid clinical deterioration in two cases, and a poor visual outcome was observed in patient 2 because of optic nerve atrophy.

The mode of contamination in patients with *R. radiobacter* infection remains largely hypothetical. Because *R. radiobacter* is a soil organism (14), endophthalmitis may have resulted from patient contact with soil and subsequent conjunctival inoculation with this species either before or after intraocular surgery. Most patients with *R. radiobacter* endophthalmitis reported outdoor activities such as gardening or golfing that may have exposed them to soil bacteria (18, 19, 24). Because *R. radiobacter* is responsible for hospital-acquired infections (14), nosocomial transmission of the pathogen (especially in the operating room) should be considered. However, Lai et al. (14) reported that among 13 patients suffering from *R. radiobacter* infection diagnosed between 1996 and 2002 in a single hospital, the pulsed-field gel electrophoresis profiles of the 13 isolated strains were all different, indicating the absence of nosocomial spread of the bacterium. Our three endophthalmitis cases were geographically and temporally unrelated and were diagnosed and treated in three different hospitals (Grenoble, Dijon, and Lyon) in France. In addition, no series of endophthalmitis cases caused by *R. radiobacter* reported in the literature (18, 19, 24) corresponded to an epidemic situation.

Diagnosis of *R. radiobacter* infections primarily relies upon isolation of the pathogen from clinical samples (14). Although isolation of *R. radiobacter* isolates has been considered nonsignificant in some clinical situations (23, 27), its isolation from intraocular samples in a patient with clinical diagnosis of postoperative endophthalmitis should be considered evidence of true infection (18). *R. radiobacter* can be isolated on blood-enriched media but also on MacConkey agar after 2 to 3 days of incubation of cultures. However, difficulties in phenotypic identification of this species may lead to delayed reporting of results to clinicians or even erroneous identifications (19). A rapid and accurate identification of *R. radiobacter* can now be obtained by amplification and sequencing of the 16S rRNA gene (3). This technique can be applied to isolated colonies but also directly to clinical samples such as vitreous and AH to circumvent the slow growth and fastidious nature of this bacterium. In the present case series, *R. radiobacter* could be isolated from AH and/or vitreous samples in all three patients, but species identification of isolated colonies was obtained by a phenotypic method in case 3 and by 16S rRNA gene sequencing in cases 1 and 2. Eubacterial PCR allowed early detection and identification of *R. radiobacter* in intraocular samples in these two later patients.

R. radiobacter strains have been reported to be always susceptible to fluoroquinolones, cefepime (a new broad-spectrum cephalosporin), and carbapenems (e.g., imipenem and meropenem) (15, 22). Acquired resistances are common for other beta-lactam compounds (especially broad-spectrum cephalosporins such as cefotaxime and ceftazidime), aminoglycosides (gentamicin being the most frequently active compound), and other antibiotic families (14, 21). Our standard therapeutic protocol for endophthalmitis patients includes intraocular injection of vancomycin and ceftazidime. Despite the high concentrations reached in the vitreous, these drugs may not be adopted in cases of *R. radiobacter* infection both because vancomycin is not active against this Gram-negative bacterium and because of possible acquired resistance to ceftazidime. The intraocular injection of an aminoglycoside (e.g., amikacin) may be more effective. The same holds true for systemic antibiotic therapy. The combination of a carbapenem and a fluoroquinolone is probably the best choice for strains with acquired resistance mechanisms or when the antibiotic susceptibility of the involved strain cannot be assessed. This specific therapeutic strategy would be optimal in instances of early detection and identification of *R. radiobacter*. The eubacterial PCR has two advantages over culture: the possibility of rapid detection of *R. radiobacter* directly from clinical samples and reliable species identification. Culture remains, however, essential for antibiotic susceptibility testing.

In conclusion, *R. radiobacter* is a rare etiological agent of postoperative endophthalmitis. The systematic use of eubacterial PCR for the etiological diagnosis of endophthalmitis allowed rapid detection and accurate identification of this bacterium in two of the three reported cases. Although most patients presented with severe ocular symptoms, the use of local and systemic antibiotics and pars plana vitrectomy in the more severe cases allowed cure of the infection. Patients undergoing cataract surgery should avoid contact with soil in the period surrounding this surgical intervention.

Nucleotide sequence accession numbers. The 16S rRNA genes from isolates from patients 1 and 2 were assigned GenBank accession numbers JQ304788 and JQ304789, respectively.

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