Postoperative *Corynebacterium macginleyi* endophthalmitis

Consuelo Ferrer, PhD, José M. Ruiz-Moreno, MD, PhD, Alejandra Rodríguez, Javier Montero, MD, PhD, Jorge L. Alió, MD, PhD

A 72-year-old man with chronic endophthalmitis who received steroid treatment for 3 months came to our center. Sterile endophthalmitis after cataract extraction had been diagnosed. Aqueous samples including smears, classic cultures, and polymerase chain reaction were taken for microbiological study. Amplified DNA was sequenced to identify the pathogen. Polymerase chain reaction amplification was positive for bacteria. Sequence analysis showed *Corynebacterium macginleyi* as the causal agent in 48 hours. The culture and smear stains from the ocular samples were negative. The patient was successfully treated with vancomycin. Polymerase chain reaction and subsequent DNA-typing were useful in detecting the microorganisms that caused the chronic endophthalmitis.

J Cataract Refract Surg 2004; 30:2441–2444 © 2004 ASCRS and ESCRS

Infectious postoperative endophthalmitis is a serious complication of cataract surgery. It can be divided into 2 categories: (1) the acute form, usually fulminant, which occurs 2 to 7 days postoperatively and is most frequently due to *Streptococcus* species, *Staphylococcus aureus,* or gram-negative organisms; and (2) delayed postoperative infections (4 weeks to years after surgery), mainly caused by microorganisms such as *Propionibacterium acnes, Staphylococcus epidermidis, Actinomyces israelii, Corynebacterium* species, and fungi. Although these are the most commonly identified microorganisms, others not normally associated with this condition because they are difficult to grow, isolate, or identify are also encountered.

Accepted for publication April 6, 2004.

From the Departamento de Biología Molecular (Ferrer, Rodríguez), VISSUM, Instituto Oftalmológico de Alicante (Ruiz-Moreno, Montero, Alió), and Patología y Cirugía, Division Oftalmología, Universidad Miguel Hernández (Ruiz-Moreno, Alió), Alicante, Spain.

Supported by a grant from VISSUM, Instituto Oftalmológico de Alicante, Alicante, Spain.

None of the authors has a financial or proprietary interest in any material or method mentioned.

Reprint requests to Consuelo Ferrer, Departmento Biología Molecular, VISSUM, Instituto Oftalmológico de Alicante, C/ Cabanal N° 1, 03016 Alicante, Spain. E-mail: cferrer@oftalio.com.

0886-3350/04/$–see front matter
doi:10.1016/j.jcrs.2004.04.056

Recent reports have described a *Morganella morganii* endophthalmitis case,[1] *Alternaria infectoria* in posttraumatic endophthalmitis,[2] *Neisseria meningitidis,*[3] and *Rhodotorula glutinis.*[4] Some of these were diagnosed by molecular methods, as in the *Alternaria* and *Neisseria* cases. However, many delayed endophthalmitis cases have an unknown cause (negative culture) and are diagnosed as sterile endophthalmitis, although the infection improves with antimicrobial therapy.[5,6] These cases are often not reported because of a lack of data (negative culture) and uncertainty as to whether it is an infectious process.

We report a case of delayed endophthalmitis initially diagnosed as sterile endophthalmitis and treated with steroids. Later, culture-independent tests showed it was infectious endophthalmitis caused by *Corynebacterium macginleyi*. This microorganism was recently described.[7] In most cases (94%), it was isolated from patients with conjunctivitis and has not been described as a cause of endophthalmitis.

Case Report

Cataract extraction and intraocular lens (IOL) implantation were performed in the left eye of a 72-year-old man. One month later, surgery for a retinal detachment was performed in the same eye. After 15 days, the patient visited

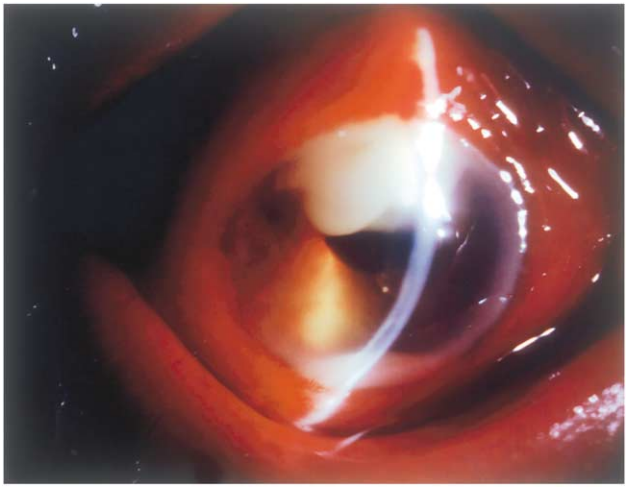

Figure 1. (Ferrer) Left eye showing conjunctival hyperemia, hypopyon, and an abscess at 12 o'clock in the anterior chamber.

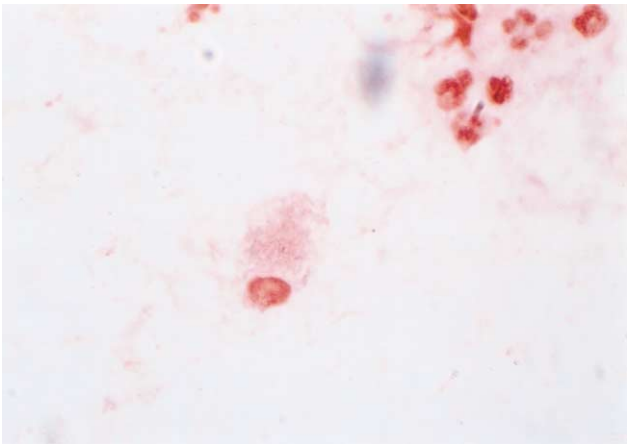

Figure 2. (Ferrer) Gram stain of the aqueous sample showing 1 macrophage and various leucocytes.

his local hospital because of problems in the left eye. Sterile endophthalmitis was diagnosed and treated with topical corticosteroids (prednisolone acetate). For more than 3 months, the patient experienced intermittent periods of pain, which were relieved with topical steroid treatment. As the eye showed no improvement by the fourth month, the patient came to our center for a second opinion.

Slitlamp examination showed conjunctival hyperemia, hypopyon, posterior synechias, and a fibrin clot at 12 o'clock in the anterior chamber (Figure 1). No view of the posterior segment was possible. The best corrected visual acuity was hand movements. An aqueous tap was done using a 30-gauge needle after the eye was examined. Diagnostic techniques included standard microbiological tests (culture and stains) and culture-independent tests (eg, polymerase chain reaction [PCR]).

The aqueous sample was cultured on several media including Columbia agar plates supplemented with 5% sheep blood, chocolate agar, MacConkey agar, and Sabouraud dextrose agar with chloramphenicol (BioMeriux) at 37°C in ambient air. The sample was also inoculated in thioglycollate and brain-heart-infusion broth (BioMeriux). Two types of detection by PCR were performed: 1 to amplify the bacteria 16S rDNA[8] and another to amplify the ITS/5.8S region of fungal DNA.[9] Amplified DNA from PCR were sequenced using both primers of the bacterial PCR.[8] The size of the amplified fragment was 954 base pairs (bp) and contained the hypervariable V3 region of the 16S rRNA gene. It was analyzed using the BLAST alignment program of the Genbank database (National Institutes of Health) and Fasta3 program of the European Molecular Biology Laboratory database.

Gram stain of the aqueous sample did not show organisms, and Giemsa stain showed an inflammatory reaction with neutrophils and lymphocytes (Figure 2). The culture remained negative after 4 weeks of incubation.

Fungal DNA amplification by PCR was negative. The 16S rDNA fragment amplification with universal bacteria primers was positive (Figure 3). The result was obtained 4 hours after the sample was taken. Bacterial identification was performed by sequencing the 954 bp fragment. Twenty-four hours later, the DNA database comparison of the sequence demonstrated that it was identical to *C macginleyi* strain CIP104099T.

Two days later, anterior chamber irrigation was performed in the abscessed area and the fibrin clot was removed. The sample was processed again by the 3 methods, and the

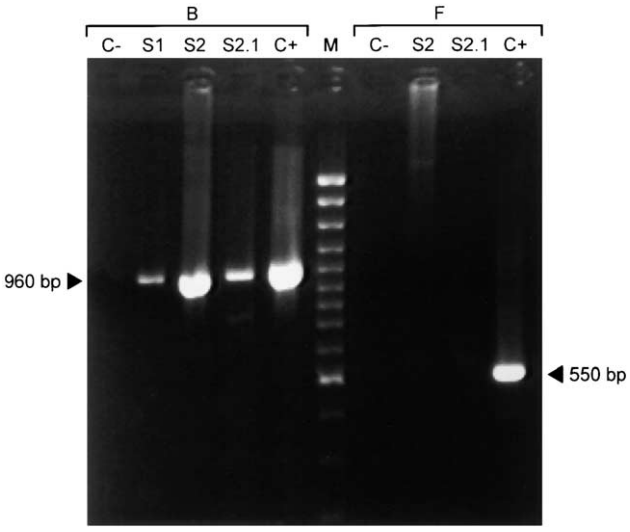

Figure 3. (Ferrer) Diagnosis by PCR. Gel showing the PCR result with bacterial (*B*) and fungal (*F*) primers. *M* = ladder marker GeneRuler 100 bp DNA Ladder Plus (500 bp = black triangle); C− = negative control (ddH2O); *S1* = aqueous sample taken the first day; *S2* = abscess sample taken the third day; *S2.1* = dilution 1:10 of the DNA extracted from S2; *C+* = positive control (*S aureus* DNA for bacterial PCR, *Candida albicans* DNA for fungal PCR).

culture and smear were negative. The smear examination results of the abscess specimen disclosed a strong inflammatory reaction consisting of neutrophils, lymphocytes, and big macrophages. However, the bacterial PCR was positive and the sequence of the amplified fragment showed the same result as the first sample, 100% homology with *C macginleyi*. The sequence was deposited in the Genbank database with the access code AJ586970.

Vancomycin (1 mg in 0.1 mL) was injected into the anterior chamber on the first day; 2 days later, intravitreal vancomycin (1 mg) and anterior chamber irrigation with vancomycin (0.1 mg/mL) were administered. Topical treatment with 0.3% ofloxacin drops (Exocin®) and tobramycin ointment (Tobrex®) was given for 1 month. Although the inflammatory signs disappeared 2 weeks after treatment, the patient's visual acuity deteriorated to no light perception and the eye, to phthisis bulbi.

Discussion

Corynebacterium macginleyi is a member of the lipophilic corynebacterial group of the genus *Corynebacterium*. It was defined and characterized by Riegel et al.,[7] who isolated 3 strains from human eye specimens. Thirty-two strains of *C macginleyi* have been isolated, comprising 30 isolates from conjunctival samples[7,10–13] and 2 from catheter-related infections, 1 intravenous and 1 bladder.[14,15] In some cases, *C macginleyi*[11,12] was the only microorganism isolated, while in most of the conjunctival samples and the 2 samples obtained from the catheters,[14,15] coagulase-negative *Staphylococci* colonies were obtained along with *C macginleyi*. In our case, only 1 sequence in both samples was obtained that corresponded to *C macginleyi*, so it seems that *C macginleyi* can cause ocular infections even when it is not associated with other microorganisms. *Corynebacterium* sp can be part of the normal conjunctival flora and since human conjunctiva corynebacterial flora is mainly lipophilic,[16] it is assumed that contamination from the patient's conjunctiva can arise during the surgery. We do not know whether contamination occurred during cataract or retinal surgery, although it is more likely to have appeared during the former since this procedure is more invasive.

Several reasons have been suggested for negative culture results in ocular infections: small sample available, the sequestration of microorganisms on solid surfaces, localization inside macrophages, and inadequate culture methods due to the fastidious nature of some microorganisms. The 2 latter reasons are especially relevant in *Corynebacterium* endophthalmitis since only one third of infections caused by this genus showed positive cultures.[6,17] Regarding inadequate culture methods, lipophilic corynebacteria are usually fastidious and grow more slowly than nonlipophilic strains,[18] and they produce small colonies unless they are grown on media enriched with a significant amount of lipids.[7] Most media routinely used in the laboratory contain at least small amounts of lipids and will support growth of lipophilic bacteria. Some of the media we used contained minimal amounts of lipids, but no growth was observed. Another explanation for negative cultures and smears is that this genus, as it occurs with *P acnes*, can be sequestrated in the capsular bag[19] or inside macrophages.[20] Results obtained by PCR suggest there is a higher concentration of microorganisms in the abscess than in the aqueous because the band obtained from the sample corresponding to the abscess has a higher intensity than that obtained from the aqueous (Figure 3). We do not know whether these microorganisms are alive or dead, but the abscess smear showed the presence of a high quantity of leucocytes and macrophages.

This species may have caused more cases of chronic endophthalmitis but has not been detected for the 2 previously mentioned reasons (unusual lipid growth requirements and bacterial sequestration). Further, *Corynebacterium* species is generally not easy to identify, especially in this recently characterized species.[7] In most cases of ocular infections caused by *Corynebacterium* species, specific identification of etiologic agents was not made. Many case reports of disease associations of coryneform bacteria were inappropriately documented, which has led to misidentifications and consequent miscitations in the literature. Funke and coauthors[18] propose a guideline to avoid these problems in future reports; they recommend the inclusion of 16S rRNA gene sequence analysis to ensure correct identification.

Detection and identification of the causative pathogens in endophthalmitis are mandatory to initiate proper therapy. Other authors[21,22] have suggested oral clarithromycin treatment for chronic endophthalmitis. Because the species in our case (*C macginleyi*) is resistant to this macrolide,[10,13,15] we decided to administer the conventional therapy with vancomycin. The infection disappeared after 2 weeks of treatment, but it was too late for the patient to recover vision in the eye. This is

an example of a delay in therapy leading to serious visual consequences. Had PCR been available in the original hospital, it is likely the infection would have been detected when the patient attended the clinic 1 month before coming to us. It is known that *C macginleyi* might cause conjunctivitis,[13] but now we know *C macginleyi* may produce endophthalmitis and that it may have serious consequences for the patient if not diagnosed in time.

Polymerase chain reaction can help discover new pathogens involved in so-called sterile chronic endophthalmitis, especially in cases caused by bacteria with unusual growth requirements or by sequestrated bacteria in macrophages.

References

1. Tsanaktsidis G, Agarwal SA, Maloof AJ, et al. Postoperative Morganella morganii endophthalmitis associated with subclinical urinary tract infection. J Cataract Refract Surg 2003; 29:1011–1013
2. Ferrer C, Montero J, Alió JL, et al. Rapid molecular diagnosis of posttraumatic keratitis and endophthalmitis caused by Alternaria infectoria. J Clin Microbiol 2003; 41:3358–3360
3. Frelich VS, Murray DL, Goei S, et al. Neisseria meningitidis endophthalmitis: use of polymerase chain reaction to support an etiologic diagnosis. Pediatr Infect Dis J 2003; 22:288–290
4. Dorey MW, Brownstein S, Kertes PJ, et al. Rhodotorula glutinis endophthalmitis. Can J Ophthalmol 2002; 37: 416–418
5. Rojo A, Ferrer E, Torrón C, et al. Capsultomía Nd-YAG antibióticos intravítreos como tratamiento de la endoftalmitis crónica. Arch Soc Esp Oftalmol 2000; 75: 109–116
6. Salvanet-Bouccara A, Serrhini A, Forestier F, Dublanchet A. Endophtalmie chronique à Corynebacterium. A propos de 3 cas. J Fr Ophtalmol 1992; 15:378–383
7. Riegel P, Ruimy R, de Briel D, et al. Genomic diversity and phylogenetic relationships among lipid-requiring diphtheroids from humans and characterization of Corynebacterium macginleyi sp. nov. Int J Syst Bacteriol 1995; 45:128–133
8. Knox CM, Cevellos V, Dean D. 16S ribosomal DNA typing for identification of pathogens in patients with bacterial keratitis. J Clin Microbiol 1998; 36:3492–3496
9. Ferrer C, Colom F, Frases S, et al. Detection and identification of fungal pathogens by PCR and by ITS2 and 5.8S ribosomal DNA typing in ocular infections. J Clin Microbiol 2001; 39:2873–2879
10. Funke G, Pagano-Niederer M, Bernauer W. Corynebacterium macginleyi has to date been isolated exclusively from conjunctival swabs. J Clin Microbiol 1998; 36: 3670–3673
11. Ortiz de la Tabla V, Martin C, Martinez C. Conjunctivitis por Corynebacterium macginleyi. Enferm Infecc Microbiol Clin 2000; 18:481–482
12. Giammanco GM, Di Marco V, Priolo I, et al. Corynebacterium macginleyi isolation from conjunctival swab in Italy. Diagn Microbiol Infect Dis 2002; 44:205–207
13. Joussen AM, Funke G, Joussen F, Herbertz G. Corynebacterium macginleyi: a conjunctiva specific pathogen. Br J Ophthalmol 2000; 84:1420–1422
14. Villanueva JL, Dominguez A, Ríos MJ, Iglesias C. Corynebacterium macginleyi isolated from urine in a patient with a permanent bladder catheter. Scand J Infect Dis 2002; 34:699–700
15. Dobler G, Braveny I. Highly resistant Corynebacterium macginleyi as cause of intravenous catheter-related infection. Eur J Clin Microbiol Infect Dis 2003; 22:72–73
16. von Graevenitz A, Schumacher U, Bernauer W. The corynebacterial flora of the normal human conjunctiva is lipophilic. Curr Microbiol 2001; 42:372–374
17. Schabereiter-Gurtner C, Maca S, Rölleke S, et al. 16S rDNA-based identification of bacteria from conjunctival swabs by PCR and DGGE fingerprinting. Invest Ophthalmol Vis Sci 2001; 42:1164–1171
18. Funke G, von Graevenitz A, Clarridge JE III, Bernard KA. Clinical microbiology of coryneform bacteria. Clin Microbiol Rev 1997; 10:125–159
19. Abreu JA, Cordovés L, Mesa CG, et al. Chronic pseudophakic endophthalmitis versus saccular endophthalmitis. J Cataract Refract Surg 1997; 23:1122–1125
20. Margo CE, Pavan PR, Groden LR. Chronic vitritis with macrophagic inclusions; a sequela of treated endophthalmitis due to a coryneform bacterium. Ophthalmology 1988; 95:156–161
21. Warheker PT, Gupta SR, Mansfield DC, Seal DV. Successful treatment of saccular endophthalmitis with clarithromycin [letter]. Eye 1998; 12:1017–1019
22. Okhravi N, Guest S, Matheson MM, et al. Assessment of the effect of oral clarithromycin on visual outcome following presumed bacterial endophthalmitis. Curr Eye Res 2000; 21:691–702