

Contact Lens-Related Infectious Keratitis with White Plaque Formation Caused by *Corynebacterium propinquum*

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We report the first case of *Corynebacterium propinquum* keratitis in the compromised cornea of a diabetic patient wearing therapeutic contact lenses. The strain was identified to the species level based on sequencing of the 16S rRNA gene and RNA polymerase β -subunit-encoding gene (*rpoB*). Ophthalmologists should be aware of nondiphtherial corynebacterial infection of compromised corneas.

CASE REPORT

This case consisted of a 44-year-old woman with a history of type 1 diabetes, hemodialysis due to diabetic nephropathy, vitrectomy in both eyes due to proliferative diabetic retinopathy, and cataract surgery in both eyes. She complained of decreased vision of the left eye without any irritation and was referred to our department because of a persistent corneal epithelial defect. The corrected vision was 0.02 in the right eye, with hand motion detectable by the left eye. Intraocular pressure was 14 mm Hg in both eyes. She had disturbance on blinking and exhibited epithelial damage in the area of the palpebral fissure in both eyes. Slit-lamp examination showed epithelial defect, pannus formation, and white plaque without obvious injection in the left cornea (Fig. 1A). To treat her left cornea, the white plaque was removed and punctal plugs were inserted; the patient was provided with therapeutic bandage contact lenses, and 0.1% hyaluronic acid was administered six times per day in both eyes. After 3 weeks, the corneal epithelial defect of the left eye improved, and the left vision recovered to 0.03. However, after an additional 3 days, hypopyon and corneal infiltration had developed in the left eye (Fig. 1B). We suspected infectious keratitis and removed the contact lens. A corneal scraping was obtained, subjected to Gram staining, and observed by light microscopy. The smear revealed numerous coryneform Gram-positive rods with phagocytosis by polymorphonuclear leukocytes (PMNs) (Fig. 1C). We suspected nondiphtherial *Corynebacterium* keratitis and switched the eye drops to gatifloxacin (GAT) and cefmenoxime administered (separately) six times per day each. Complete eye closure with eye patch was added because of poor reepithelialization, and systemic intravenous ampicillin also was added. The epithelial defect gradually healed, but complete epithelialization took about 2 months (Fig. 1D). The final visual acuity recovered to 0.02. Bacterial culture yielded *Corynebacterium* species.

Bacterial species identification. The genus of the bacterial isolate, designated MGJ001, was shown to be *Corynebacterium* by microscopic observation and biochemical tests. Identification of the isolate to the species level, performed by biochemical testing using API Coryne (1) (bioMérieux SA, Lyon, France), indicated that the strain was *Corynebacterium pseudodiphtheriticum*. The DNA sequence of the 16S rRNA gene, which was amplified by PCR with the primer pair 10F (5'-GTTTGATCCTGGCTCA-3') and 800R (5'-TACCAGGGTATCTAATCC-3'), showed 99% homol-

ogy with both *C. pseudodiphtheriticum* and *C. propinquum* by the Basic Local Alignment Search Tool (BLAST). To confirm the species identification, partial DNA sequence of the RNA polymerase β -subunit-encoding gene (*rpoB*), amplified by PCR with primer pair C2700F (CGAATGAACATCGGTCAGGT) and C3130R (TCATCTCACCGAAACGCTG), also was determined (2). The obtained DNA sequence showed 100% homology with *C. propinquum* and 94% homology with *C. pseudodiphtheriticum*. Taken together, these data permit identification of the isolate as *C. propinquum*.

Antibiotic susceptibility testing. The antibiotic susceptibilities of the isolate were determined by Etest (bioMérieux SA) on Mueller-Hinton agar according to the suppliers' instructions. The results are shown in Table 1. The strain showed macrolide and lincosamide resistance.

Nondiphtherial corynebacteria, which are rod-shaped Gram-positive bacteria, are a component of the bacterial microflora of human skin and mucosa, including ocular surfaces (3, 4). These bacteria occasionally cause conjunctivitis in aged patients, suture-related corneal infection, and on rare occasions, keratitis in compromised ocular surfaces (5–11). However, there is little information about which species are related to keratitis, because species identification is not performed routinely in most hospitals or laboratories.

It is known that *Corynebacterium macginleyi* is the dominant species among nondiphtherial corynebacteria isolated from the normal conjunctival sac and from cases of bacterial conjunctivitis

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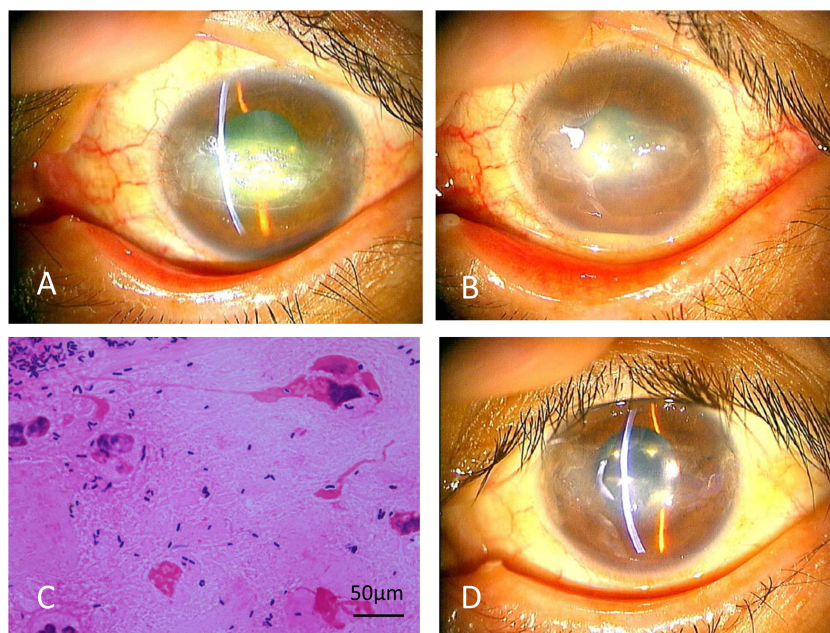


FIG 1 (A) Photograph of slit-lamp examination of the left cornea at the first visit. Observation revealed the presence of an epithelial defect accompanied by white plaque and pannus formation. (B) The cornea was treated by corneal scraping, punctal plugs, therapeutic contact lens, and topical 0.1% hyaluronic acid. However, after a further 3 days, hypopyon and corneal infiltration had developed. (C) Photograph of a Gram-stained specimen from the corneal scraping. Gram-positive rods with phagocytosis by PMNs are observed. (D) The cornea at 2 months after the first visit, following antibiotic treatment against *Corynebacterium propinquum*. The epithelial defect has healed.

(3, 5, 8–11). However, the literature contains only a few reports of corneal infection caused by *C. macginleyi* (6, 11, 12). To date, *Corynebacterium* species other than *C. macginleyi* reported to cause keratitis have included the following: *C. striatum* (13, 14), *C. xerosis* (14), *C. pseudodiphtheriticum* (15), *C. amycolatum* (T. Toi-

hana and H. Eguchi, unpublished data), and *C. propinquum* (this case). *C. macginleyi* is a lipophilic corynebacterium; the other species are nonlipophilic (16, 17). This distinction suggests that *C. macginleyi*, which requires lipids for growth, may prefer sebaceous glands to corneal surfaces. Factors contributing to colonization and virulence should be studied further.

In the present case, we first considered *C. pseudodiphtheriticum* infection because of the result of API Coryne, which differentiates between *C. pseudodiphtheriticum* and *C. propinquum* primarily on the basis of the detection of urease activity. However, a recent report reveals the existence of urease-producing strains of *C. propinquum*; this observation means that *C. propinquum* isolates may have been misidentified as *C. pseudodiphtheriticum* and that full differentiation will require sequencing of the *rpoB* locus (18). Indeed, in the case described in the present work, neither API Coryne nor the 16S rRNA gene sequence was sufficient to accurately identify the isolate to the species level; *rpoB* gene sequence was needed to demonstrate that the causative strain was *C. propinquum*.

C. propinquum is typically a harmless commensal of human nasopharynx and skin (18, 19). This species has been implicated in various opportunistic infections, such as respiratory infection (17, 20–24), bacteremia (17, 25, 26), endocarditis (27), osteitis (28), pleural effusion (29), rhino-sinusal infection (30), infection after osteosynthesis (31), trichomycosis axillaris (32), and nongonococcal urethritis (33). To date, infectious keratitis caused by *C. propinquum* has not been reported; to our knowledge, this study presents the first reported case of *C. propinquum* keratitis.

In this case, we empirically selected topical GAT and cefmenoxime; intravenous ampicillin subsequently was added in response to a previous report suggesting susceptibility of this species

TABLE 1 Antibiotic susceptibilities of *Corynebacterium propinquum* strain determined by Etest

Antibiotic ^a	MGJ001	
	MIC (μg/ml)	Interpretation ^b
CRO	0.125	S
CAZ	0.5	S
IPM	0.016	S
MEM	0.08	S
ERY	>256	R
AZM	>256	R
CLR	32	R
TOB	0.5	S
DOX	2	S
CIP	2	I
LVX	1	S
MXF	0.5	S
VAN	1	S
TEC	0.25	S
DAP	<0.016	S
Tigecycline	0.5	S

^a Abbreviations: CRO, ceftriaxone; CAZ, ceftazidime; IPM, imipenem; MEM, meropenem; ERY, erythromycin; AZM, azithromycin; CLR, clarithromycin; TOB, tobramycin; DOX, doxycycline; CIP, ciprofloxacin; LVX, levofloxacin; MXF, moxifloxacin; VAN, vancomycin; TEC, teicoplanin; and DAP, daptomycin.

^b Interpretation of susceptible (S), intermediate (I), or resistant (R) was based on the supplier's instructions.

to penicillin (4, 18). The majority of *C. propinquum* strains are constitutively resistant to the macrolides, lincosamides, and streptogramin B as a result of the presence of the *erm(X)* gene (19). The isolate MGJ001 also was resistant to macrolides and lincosamides, strongly suggesting the presence of *erm(X)*. The strain MGJ001 exhibited susceptibility to novel antibiotics, including daptomycin and tigecycline, consistent with susceptibilities observed in a previous report (18).

Keratitis is a corneal infection that usually develops after ocular trauma, contact lens wear, or various predisposing corneal diseases. Keratitis can cause severe visual disturbance, mainly by corneal scarring. In our case, infection developed in compromised cornea following the wearing of therapeutic contact lenses for a persistent epithelial defect in a patient with severe diabetes. The corneal finding was characterized by white plaques on the epithelial defects. Keratitis with white plaque is a rare corneal condition that is usually caused by less-virulent atypical microorganisms (34). Nondiphtherial corynebacteria, including *C. propinquum*, also should be considered possible causative agents of corneal white plaque, and compromised corneal surfaces (including persistent epithelial defects) might be a risk factor. As we demonstrate here, direct microscopic examination of corneal scrapings is useful for the accurate diagnosis of opportunistic corneal infection.

In summary, we report the first case of *C. propinquum* keratitis accompanied by white plaque; in this case, infection developed in an eye with a compromised cornea in a diabetic patient wearing therapeutic contact lenses. The identities of the causative agents were proven by corneal smear, bacterial culture, and DNA sequences of the 16S rRNA and *rpoB* genes. Ophthalmologists should be aware of the potential for nondiphtherial corynebacterial infection of compromised corneas.

Nucleotide sequence accession numbers. The nucleotide sequences of the rRNA gene and *rpoB* gene of MGJ001 are available in the DDBJ/EMBL/GenBank databases under accession no. LC033494 and LC063620, respectively.

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