

# Corneal ulcer caused by *nocardia brasiliensis* in a patient with diabetes

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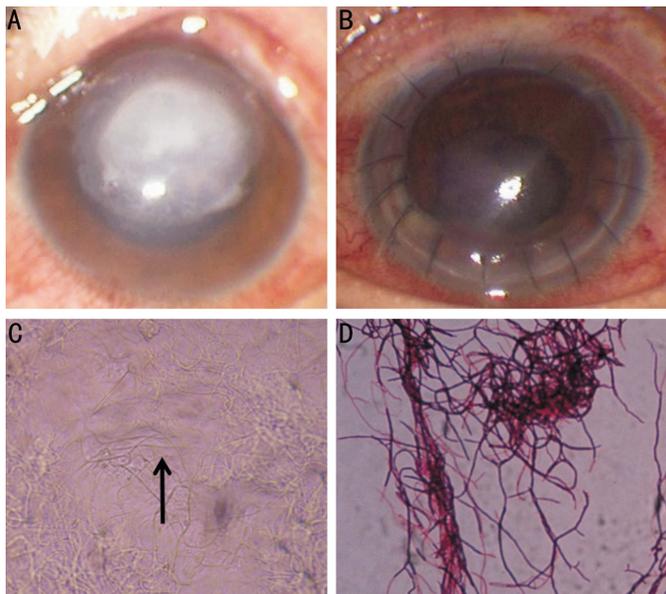
**Dear Sir,**

I am Dr. Sheng-Li Mi, from the Biomanufacturing engineering laboratory, Graduate School at Shenzhen, Tsinghua University, Shenzhen, China. I write to present a case report of *nocardia brasiliensis* in a patient with diabetes. *Nocardia* is part of a group of aerobic actinomycetes, widely distributed in soil. *Nocardia asteroides* and *nocardia brasiliensis* are the most common human pathogens. Humans infected by *nocardia asteroides* through the respiratory tract mainly suffer from primary suppurative pulmonary conditions. Infection of *nocardia brasiliensis* often occurs in the advanced stages of a progressive disease or immune disorder, especially Cushing syndrome, diabetes, or in patients using corticosteroids, immunosuppressive agents and broad-spectrum antibiotics for long time<sup>[1]</sup>. To our knowledge, the reports of *nocardia* keratitis was very rare worldwide, such a case as we stated here has not been previously reported in the literature<sup>[2-6]</sup>.

A 32-year woman was admitted to our hospital, with complaints of pain, grinding, photophobia and tearing in the

left eye, was diagnosed with "virus keratitis in the left eye" in local hospital, the patient was treated, but there was no improvement in symptoms. An eye examination demonstrated that vision in the left eye was index/front, and vision in the right eye was 0.8 (standard logarithmic vision chart check). The left eye showed mixed conjunctival hyperemia, ulcers of about 7×8-mm<sup>2</sup> at the center of the cornea, necrotic material and secretions on the surface, approximately 2 mm of pus in the anterior chamber (Figure 1). Upon admission, diagnosis indicated a corneal ulcer and endo-ophthalmitis in the left eye. Routine laboratory tests showed that fasting blood glucose was 15.79 mmol/L, demonstrating a case history of diabetes. Endocrinology consultations were subsequently invited to adjust hypoglycemic drug use for controlling blood glucose levels. Tissues at the edge of the corneal ulcer was obtained for culture, the cultural colonies were identified using Gram staining and biochemical analysis, and were tested for penicillin resistance, tetracycline sensitivity, minocycline sensitivity, cotrimoxazole sensitivity and levofloxacin sensitivity.

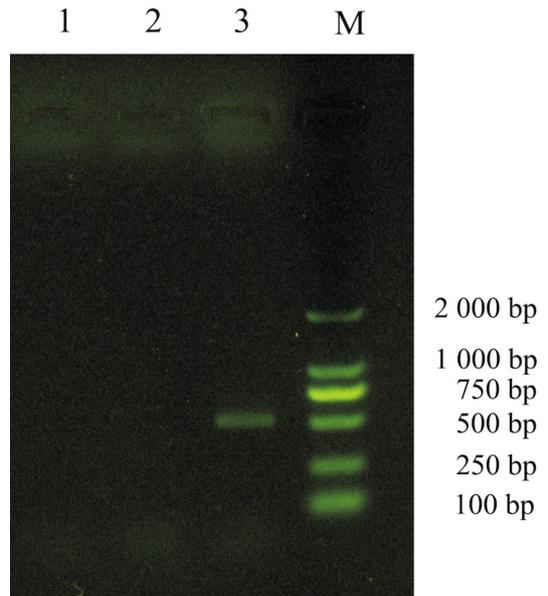
Treatment was started with local lesion debridement and the application of 4% (v/v) iodine to burn away lesions. 0.5% (v/v) levofloxacin eye drops were applied to the cornea on the first 4d, every 30min for 4h, then once each hour, and on the fifth day once each two hours, and once each four hours from the second week until surgery. Blood glucose levels were monitored according to guidelines from endocrinology diagnoses. One week after treatment, pain and grinding in the eye were significantly diminished, the size of central corneal ulcers was reduced, the attachment of hyphae on the ocular surface did not exist, and hypopyon were no longer present in the anterior chamber. After 2wk of treatment, with fasting blood glucose at 6.5 mmol/L, therapeutic penetrating keratoplasty was performed under local anesthesia. After surgery, 0.5% (v/v) levofloxacin eye drops was used for topical ocular anti-infective treatment using results from susceptibility tests as a guide, 6 times a day on the first week, 4 times on the second week; in addition to conventional immunosuppressants, prednisolone acetate ophthalmic suspension was used 3 times a day, and



**Figure 1 Ocular surface before and after treatment, and the microscopic examination of the corneal ulcer** A: The anterior segment: conjunctival hyperemia in the left eye, a corneal ulcer of approximately 7×8-mm<sup>2</sup> in the center, a large amount of necrotic material and secretions on the ocular surface and approximately 2-mm<sup>3</sup> of pus in the anterior chamber; B: The anterior segment after therapy: a transparent corneal graft with normal depth of the anterior chamber is observed; C: Microscopic examination of the corneal ulcer (KOH wet mount): The arrow indicates a large number of slender hyphae with branches among digested tissue, similar to actinomycetes are observed (magnification, ×400); D: Microscopic examination of the corneal ulcer following Gram staining: blue and purple branched filaments and unswollen hyphal ends were observed (magnification, ×1000).

tobramycin/dexamethasone ointment was used once a day; artificial tears was also used 3 times a day. The patient was discharged from hospital 2wk after surgery, while the treatment was continued: 0.5% (v/v) levofloxacin eye drops and prednisolone acetate ophthalmic suspension was used 4 times a day for 2 more weeks, tobramycin/dexamethasone ointment was used once every other day for 2 more weeks, 1% cyclosporine was used 2 times a day and artificial tears was used 3 times a day for more than 1y, intraocular pressure was also needed to monitor once every two weeks after surgery. Examination of treated eyes demonstrated that the left corneal graft was transparent and the depth of anterior chamber was normal: keratic precipitates (-), flash room (-), intraocular pressure 17 mm Hg (Figure 1). Routine immunosuppressant therapy was continued after the patient was discharged from the hospital.

**Microbiological Diagnosis** Conventional slit lamp microscope examinations were carried out, tissue at the edge of the corneal ulcer was obtained for culture and a smear of this tissue was mounted on glass slide with 10% (v/v)



**Figure 2 PCR detection by 18S rRNA** 1: The corneal ulcer tissue; 2: Negative control; 3: Positive control; M: Deoxyribonucleic acid marker.

potassium hydroxide (KOH). Microscopic examination of the mounted tissue demonstrated large amounts of thin hyphae with branches woven into a group, similar in appearance to actinomycetes (Figure 2). Tissue from the corneal ulcer was cultured for 48h. Hard, granular, sticky, gray or light brown colonies with transparent hemolytics were visible on following culture. Hyphae from cultured tissue were examined using Gram staining, blue and purple branched filaments and hyphal ends which were not swollen were observed (Figure 2). The results of biochemical analysis of cultured colonies were: casein (+), gelatin liquefaction (+), aromatic acid lipase (-), hypoxanthine (+), starchhydrolysis (-), indicating the morphology of *nocardia brasiliensis*. The result of polymerase chain reaction (PCR) detection based on 18S ribosomal ribonucleic acid (rRNA) gene sequence was negative (Figure 2), indicating it didn't belong to fungus<sup>[7]</sup>.

The characteristics of the patient described in the present study were: 1) Female, with diabetes, no history of trauma or wearing contact lens and a possible ocular endogenous infection caused by decreasing resistance to high blood glucose levels; 2) The early clinical manifestations of this patient were not critical, progressed slowly and were easily misdiagnosed as viral keratitis. The patient was treated for viral keratitis for two months at a local hospital before being admitted to Xi'an Eye Hospital; 3) Characteristics of a typical corneal ulcer caused by *nocardia keratitis* include corneal ulcers with gray and rough lower surfaces and a necrotic edge with a floral shape. Our patient had typical corneal ulcers, with approximately 2 mm<sup>3</sup> of pus in the

anterior chamber when she was admitted to Xi'an Eye Hospital; 4) Species belonging to the *nocardia* family of bacteria have been reported to vary in physical and chemical properties and the etiological diagnosis of infections caused by these microbes mainly depend on corneal scraping and subsequent microscopic examination, and rapid biochemical identification after bacterial culture. The antibacterial drug susceptibility among *nocardia* species is also quite different, therefore it is very valuable to test the sensitivity of antibacterial agents. The strain of *nocardia brasiliensis* isolated from our patient was sensitive to levofloxacin, minocycline and cotrimoxazole, and resistant to penicillin. Taking into account, results from microscopic examination of the corneal smear and the results of drug susceptibility, our patient was treated with a combination of debridement of ocular lesions, 0.5% (v/v) levofloxacin eye drops (used frequently) and corneal transplantation. This therapy successfully restored corneal clarity.

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**Conflicts of Interest:** Liu XN, None; An N, None; Wu J, None; Xu K, None; Zhu XP, None; Mi SL, None.

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