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Case Report

A Case of *Nocardia africana*-Related Keratitis

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Keywords
Nocardia africana · Keratitis · Corneal ulcer

Abstract
Nocardia spp. are gram positive, aerobic, weakly acid-fast bacteria. *Nocardia* spp. keratitis is a rare ocular infection classically described following corneal injury or vegetative and soil exposure. However, keratitis caused by *Nocardia africana* had never been reported in the literature. We first reported a 70-year-old male who had a traumatic ocular injury to his left eye a month ago. With his complaint of left eye pain, reduced vision, and light sensitivity, the slit-lamp biomicroscopy showed the superficial multi-lobulated epithelial infiltration located at the inferior cornea with a positive fluorescein stain. Microscopic workup from corneal specimens demonstrated dry and chalky white colonies on blood agar and Lowenstein-Jensen media resembling *Nocardia* spp. The MALDI-TOF MS analyses using VITEK® MS exhibited *N. africana*. The corneal lesion was treated with 2% amikacin topical eye drops and responded well. The careful history-taking, precise clinical examinations, and meticulous microscopic assessment were the cornerstones of diagnosis. Definite diagnosis and timely treatment were essential to prevention of ocular morbidity in *N. africana*.

Introduction

Nocardia spp. keratitis is an uncommon ocular infection typically described after penetrating corneal trauma or ocular contact with plants and soils [1]. For many decades, *Nocardia asteroides* had been the most common species of *Nocardia* keratitis [2]. However, *Nocardia africana* was originally discovered in a pulmonary infection in Africa [3], and

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keratitis caused by *N. africana* had not been reported. Herein, we described the first case of keratitis associated with *N. africana* following ocular trauma, including clinical characteristics, laboratory investigation, treatment, and clinical outcome.

Case Report

A 70-year-old immunocompetent male presented with a history of ocular trauma to the left eye with a small rock while mowing the grass a month prior to admission to the provincial hospital. He had severe eye pain, blurred vision, and photophobia. He denied the underlying diseases. He attended a provincial hospital, where he was admitted and treated for herpes simplex keratitis with oral acyclovir (400 mg) 5 times daily for 2 weeks. The corneal lesion had not improved. Thus, the patient was referred to the outpatient ophthalmology department.

He complained of left eye pain, reduced vision, and light sensitivity. Best corrected visual acuity (BCVA) was 6/60 with nuclear sclerosis in his right eye and hand movement, marked ciliary conjunctival injection, and superficial multi-lobulated epithelial infiltration sized 4.0 × 4.0 mm located at the inferior cornea with a positive fluorescein stain in the left eye. There was an irregular epithelial surface, mild anterior chamber inflammation with small hypopyon, and moderate ciliary injection (shown in Fig. 1a, b). Corneal sensation had diminished in the left eye. Oral acyclovir was discontinued after admission.

The corneal specimens from scraping were obtained for Gram stain, potassium hydroxide (KOH) examination, Calcoflour white stain, modified acid-fast stain, acid-fast stain, and culture prior to commencement of treatment. Microscopic examination of Gram stain revealed no bacteria, and no fungus were found in KOH mount test. Calcoflour white stain and modified acid-fast stain revealed negative results. Acid-fast stain showed no acid-fast bacilli. However, bacterial culture on blood agar after 5 days demonstrated dry and chalky white colonies (shown in Fig. 2a), and colonies of similar appearance grew on the Lowenstein-Jensen media (shown in Fig. 2b). The morphology of these colonies was compatible with *Nocardia* spp.

Gram stain and modified acid-fast stain of the specimens derived from white colonies exhibited Gram-positive branched filamentous bacilli (shown in Fig. 2c) and partial eosinophilic filamentous organisms (shown in Fig. 2d), respectively. The matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) analyses using VITEK® MS (bioMérieux SA, Marcy-l'Étoile, France) were performed to identify the organisms from the colonies and demonstrate *N. africana.* Fasting blood sugar was normal, and human immunodeficiency virus antibody test was negative.

The patient was treated with fortified amikacin (20 mg/mL) eye drops hourly. Atropine 1% eye drops were prescribed 4 times daily. Oral acetaminophen was also prescribed as required by the patient. The margin of his corneal ulcer was well demarcated after a few weeks of treatment without complication, indicating progressive improvement of the corneal lesion. As a result, the frequency of fortified amikacin eye drops with atropine 1% eye drops treatment gradually decreased to every 3 h and 2 times daily, respectively, over the next 3 weeks, according to punctate epitheliopathy, indicating drug toxicity. The edge of lesion became flat and well-demarcated infiltration, with irregular superficial corneal epithelial healing (shown in Fig. 1c, d).

After 6 weeks of treatment, the lesion was improved and replaced by a subepithelial scar without fluorescein staining. The fortified amikacin eye drops had decreased to every 6 h for 6 weeks. The overlying superficial multi-lobulated epithelial infiltration or epithelial defect was

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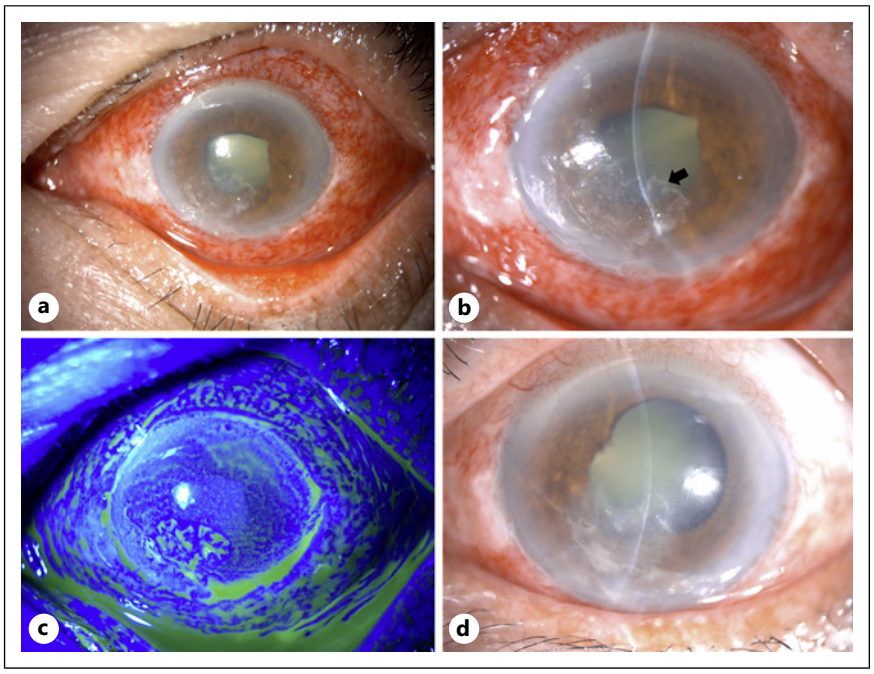

Fig. 1. Photographs of the left eye before and after treatment. **a** At the first visit, superficial multi-lobulated epithelial infiltration of 4 × 4 mm located at the inferior cornea. An irregular epithelial surface, mild anterior chamber inflammation with a small hypopyon, and moderate conjunctival injection were noted. **b** Slit beam biomicroscopy revealed irregular multi-lobulated superficial corneal infiltration (arrow). **c** Fluorescein stain picture showed positive fluorescein epithelial staining at the irregular surface of the lower cornea. **d** After 3 weeks of medical treatment, the edge of lesions became flat and well demarcated, with an irregular superficial corneal epithelial healing.

not detected eventually. All medications were discontinued after a 3-month treatment. Ocular discomfort had decreased. BCVA was improved to counting fingers at 2 feet, and intraocular pressure was normal at 6-month follow-up.

Discussion

Nocardia spp. are gram-positive, aerobic, weakly acid-fast bacteria that rarely cause ocular disease, whose corneal infection is the most common ocular morbidity [4, 5]. *Nocardia* spp., which are classified as a genus of filamentous bacteria, are ubiquitous in the environment and can be found in water, dust, soil, mud, and decomposing vegetation [6]. The most frequently reported species were *N. asteroides*, and the others were *Nocardia abscessus, Nocardia amikacinitolerans, Nocardia amamiensis, Nocardia beijingensis, Nocardia brasiliensis, Nocardia cyriacigeorgica, Nocardia exalbida, Nocardia farcinica, Nocardia kruczakiae, Nocardia otitidiscaviarum, Nocardia puris, Nocardia shinanonensis, Nocardia transvalensis, and Nocardia thailandica* [7]. Hamid et al. [3] reported the first case of pulmonary infection caused by *N. africana*. Fourteen years later, *N. africana/nova* was reported as the first causative organism in post-traumatic endophthalmitis [1].

In our study, *N. africana* keratitis was demonstrated in Thailand, whereas previous study of *N. africana* pulmonary infection had been reported in Africa [3]. The geographical distribution of Thailand and Africa were tropical countries which had the same weather; this climate condition might be prone to *N. africana* infection. The predisposing factor for

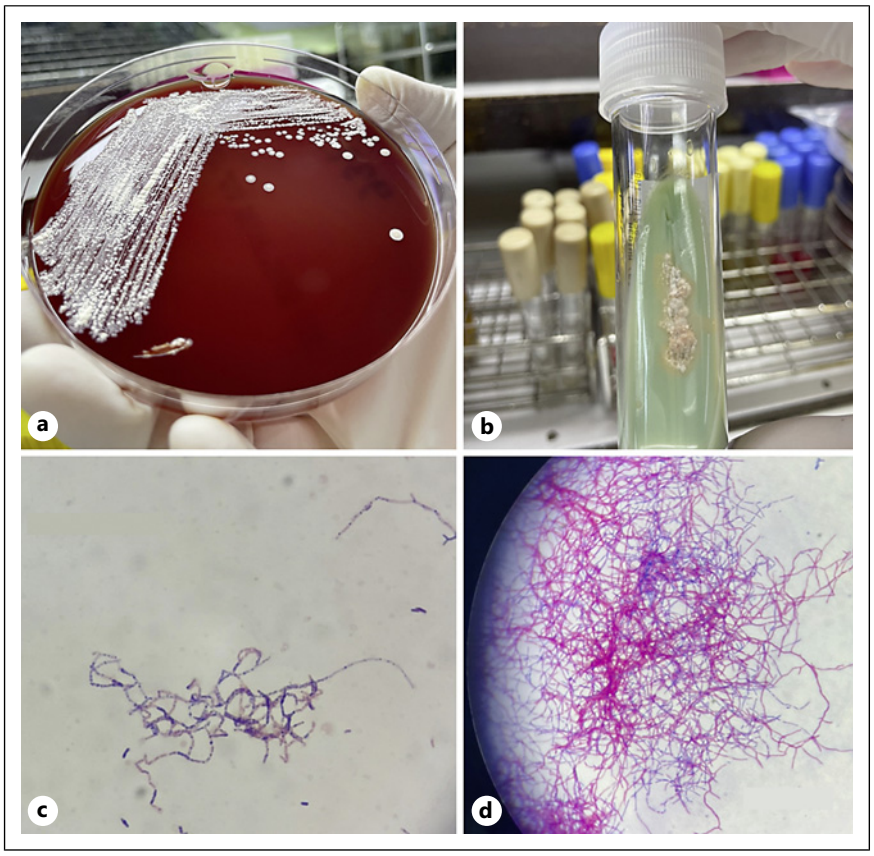

Fig. 2. a, **b** Numerous dry and chalky white colonies of *Nocardia* spp. grew up on blood agar and Lowenstein-Jensen agar. **c** Gram-positive bacilli with filamentous branching found in Gram stain ×100. **d** modified acid-fast stain demonstrated partial eosinophilic filamentous pathogens ×100.

Nocardia corneal infection in our immunocompetent patient was ocular trauma which was also similar to the study of Sridhar et al. [8]. Almost half of all *Nocardia* keratitis cases had a history of ocular exposure to soil or vegetative matter [9]. The most common risk factor for *Nocardia* keratitis was corneal injury [8]. Other known risk factors, including prior ocular surgery, chronic use of topical corticosteroid, and contact lens wears had been reported [10].

Nocardia keratitis is typically found in the mid-periphery of the cornea near the area of corneal trauma [11] and presents as patchy anterior stromal infiltrates or bead-like lesions arranged in a wreath pattern [6]. In addition, *Nocardia* keratitis isalso classically presented as a non-specific punctuate epitheliopathy, superficial corneal lesion [9]. However, full-thickness stromal infiltration with epithelial defect was also reported in an immunodeficiency patient [4].

The clinical characteristic of this patient was superficial multilobulated epithelial infiltration with mild anterior chamber reaction. An unusual clinical appearance should be suspected of *Nocardia* keratitis. In the meantime, fungal keratitis, herpetic keratitis, and topical drug toxicity had not been excluded. The microscopic work-up was started. Growth of *Nocardia* species following inoculation in culture media such as blood agar, chocolate agar, and Sabouraud agar was a gold standard diagnosis for *Nocardia* keratitis [8]. However, the organisms grew on blood agar and Lowenstein-Jensen media after 5 days and exhibited morphological colonies resembling *Nocardia* spp. *Mycobacteria* classically grew on Lowenstein-Jensen medium, but we found that *Nocardia* spp. could grow on Lowenstein-Jensen medium with typical morphological colonies of *Nocardia*.

Although, the tradition of identification of bacteria in clinical practice has depended on phenotypic identification, such as Gram stain, microscopic and unique biochemical reaction characteristics, culture media, using multiple automated and/or manual testing methods [12], an unusual and difficult-to-identify bacteria might be encountered in real-life clinical practice which may further need to be sent to a sophisticated laboratory investigation for definite diagnosis. Therefore, identification of microorganism was crucial and played a critical role for patient management and selective antimicrobial treatment. In our study, a recent technology of MALDI-TOF MS [13] was employed to identify the causal bacteria that was *N. africana*. The modified acid-fast stain demonstrated partial eosinophilic filamentous organisms, and Gram stain found positive branched filamentous bacilli that supported *Nocardia* spp. *Mycobacteria*, which were acid-fast bacteria, were best stained with the conventional acid-fast stain using 20% sulfuric acid or acid alcohol for decolorization. However, the weakly acid-fast characteristic of *Nocardia* distinguished them from *Mycobacteria* that resisted decolorization with 1% sulfuric acid on modified acid-fast stain [2, 14].

In conventional infectious keratitis, treatment comprised of dual fortified antibiotics; however, the laboratory work-up disclosed *N. Africana* that was sensitive to amikacin. In order to avoid dilutional effect and toxicity of inessential antibiotics, the patient was initially treated with 2% amikacin hourly, which was the first line of treatment [15]. Superficial multilobulated epithelial infiltration responded well after a few weeks of treatment. The edge of the lesion was gradually sharpened and eventually faded into the superficial scar within 2 months. The treatment of choice for *Nocardia* keratitis remained amikacin eye drops [14]. Others, including topical sulfonamides (10 or 30% sulfacetamide), topical aminoglycosides (1.4% tobramycin or gentamicin), and topical fluoroquinolones (0.5% moxifloxacin), were potential second-line treatments [6]. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000533906).

Conclusion

We reported a successful treatment of *N. africana* keratitis which is the first case report in the literature. The findings of ocular trauma history and multi-lobulated epithelial keratitis should be suspected for *Nocardia* corneal infection. However, meticulous microscopic assessment was the cornerstone of investigation. MALDI-TOF MS was a good instrument for the identification of specific organisms. Precise diagnosis and timely treatment were essential to prevention of ocular morbidity.

Statement of Ethics

The patient has given written informed consent, and the study protocol was approved by the Ethics Committee of the Faculty of Medicine Chiang Mai University (approval No. EXEMPTION 9205/2022). Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Study concept and design, drafting of the manuscript, and critical revision of the manuscript for important intellectual content: Winai Chaidaroon and Prangchanok Sawetwong. Acquisition, specimen analysis, interpretation of data, and approval for the final version of the manuscript: Winai Chaidaroon, Prangchanok Sawetwong, and Sirinya Manochomphu. Study supervision: Winai Chaidaroon.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

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