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CASE REPORT

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Nontuberculous mycobacterial abscess of lacrimal sac and eyelid debridement: Case report

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Key Clinical Message

It is important to stain acid-fact bacilli on the smear of abscess puncture in addition to Gram stain to detect nontuberculous and tuberculous mycobacteria in the early phase since both can cause rare and challenging extrapulmonary manifestations.

Abstract

A 56-year-old otherwise healthy woman developed abscess from dacryocystitis in the right lower eyelid. The smear of puncture fluid showed acid-fast bacilli and *Mycobacterium abscessus* was identified after a month. The early start of clarithromycin/ethambutol was switched to clarithromycin/levofloxacin. Debridement specimen after 7-month treatment showed granulomatous tissue with no bacilli.

KEYWORDS

debridement, eyelid, lacrimal sac, *Mycobacterium abscessus*, nontuberculous mycobacteria

1 | INTRODUCTION

Nontuberculous mycobacteria are free-living organisms in the environment, such as soil and water, and indicate mycobacterial species other than *Mycobacterium tuberculosis* and *Mycobacterium leprae*.[1] Two predominant groups of nontuberculous mycobacteria, which become pathogens in human are *Mycobacterium avium* complex and *Mycobacterium abscessus* complex.[2,3] A recent rise has been noted in the number of *M. abscessus* complex infection, which tends to be more resistant to treatment, and thus to be associated with poor treatment outcomes, compared with *M. avium* complex.[4,5] Three major clinical presentations of nontuberculous mycobacterial infection are pulmonary lesions, cutaneous lesions, and disseminated lesions. The disseminated infection would occur in immunocompromised hosts such as patients with acquired immunodeficiency syndrome (AIDS), while the pulmonary and cutaneous infections could occur in the otherwise healthy people. The cutaneous infection and also soft tissue infection such as lymphadenitis in children would be frequently related with skin injuries. Coinfection with human immunodeficiency virus (HIV) and nontuberculous mycobacteria is relatively uncommon in countries with a low prevalence of HIV. Nontuberculous mycobacterial infection is more common among patients in immunosuppressive therapy. The pulmonary nontuberculous mycobacterial infection is basically rare in healthy individuals, but is mainly seen in patients with chronic obstructive pulmonary diseases (COPD) such as bronchiectasis, emphysema, and other structural lung diseases.

In the field of ophthalmology, nontuberculous mycobacterial infections have been reported as extrapulmonary infections to occur as dacryocystitis (lacrimal sac infection) and also in association with trauma including surgical procedures.[6–10] Endogenous (blood-borne) endophthalmitis was reported in AIDS patients with disseminated nontuberculous mycobacterial infection.[9] In this study, we reported an otherwise healthy patient with lower eyelid abscess from lacrimal sac infection with *M. abscessus* after the intervention of lacrimal sac irrigation and nasolacrimal duct boogie, and disclosed persistent granulomatous lesions in the eyelid debridement specimen 7 months after the beginning of treatment.

2 | CASE REPORT

A 56-year-old woman had discharge in the right eye for 3 days despite repeat episodes of lacrimal sac irrigation in the first place, and thereafter she underwent nasolacrimal duct bougie on the right side to allow fluid passage at a local ophthalmologist. She then noticed the swelling of the lower eyelid and was given oral cefdinir 300 mg daily, and intravenous ampicillin-sulbactam (2:1) 1.5 g daily for a week as empirical treatment but without evident effect. She was thus referred to a University Hospital. She did not take any medication and had no past history except for having temporary medication for depression a year previously. She had a hobby of swimming in indoor pool. She did not have history of paranasal sinusitis. At the initial visit, the best-corrected visual acuity in decimals was 1.0 in the right eye and 1.5 in the left eye. The entire lower eyelid on the right side showed reddish and swollen bulging under tension and with tenderness (Figure 1A), and the upper eyelid margin on the same side was also reddish and swollen. The pupillary light reflex was normal on both sides and the eye movement appeared also normal. Ophthalmic examinations showed that both eyes had nothing particular to be noted. She did not have fever, and physical examinations detected no particular findings, including no skin rashes.

At the initial visit, her chest X-ray film as a routine screening test was normal. White blood cell count was elevated at $9.69\times10^3/\mu L$, with differentials of 30.9% lymphocytes, 3.6% monocytes, 1.2% eosinophils, 0.3% basophils, and 64% neutrophils. Red blood cell count was $3.73\times10^6/\mu L$ and platelets $398\times10^3/\mu L$. Serum C-reactive protein (CRP) was elevated to 2.49 mg/dL. The liver and kidney function tests, including proteins and electrolytes, were within normal limits. Blood glucose was 92 mg/dL and hemoglobin A1c was 5.7%. Screening tests for infectious diseases, such as serological tests for syphilis, hepatitis B virus surface antigen (HBsAg), hepatitis C virus antibody (HCV-Ab), and human immunodeficiency virus-1/2 antigen/antibodies (HIV-1/2 Ag/Ab) screening test, were all negative. Interferon-γ-releasing assay with QuantiFERON (QFT)-Plus was negative as well.

She was hospitalized and given intravenous imipenem–cilastatin sodium 0.5 mg twice daily as well as topical 0.5% levofloxacin eye drops four times daily as empirical treatment. Magnetic resonance imaging demonstrated fluid collection with 4-cm diameter in a long dimension in the entire lower eyelid, which extended to the area of the lacrimal sac on the right side (Figure 1B). The surroundings of the fluid collection were enhanced by contrast medium gadolinium diethylenetriaminepentaacetic acid (DTPA), indicative of abscess in the soft tissue of the eyelid (Figure 1C). Before the start of antibacterial drugs, she underwent puncture of the lower eyelid with an 18-gauge needle to aspirate abscess fluid in 2–3 mL. Gram stain with Victoria blue (Favor G Nissui, Shimadzu Diagnostics Co., Tokyo, Japan) of the abscess fluid smear demonstrated a small number of Gram-positive rods (Figure 1D) in the background of numerous neutrophils, suspicious of

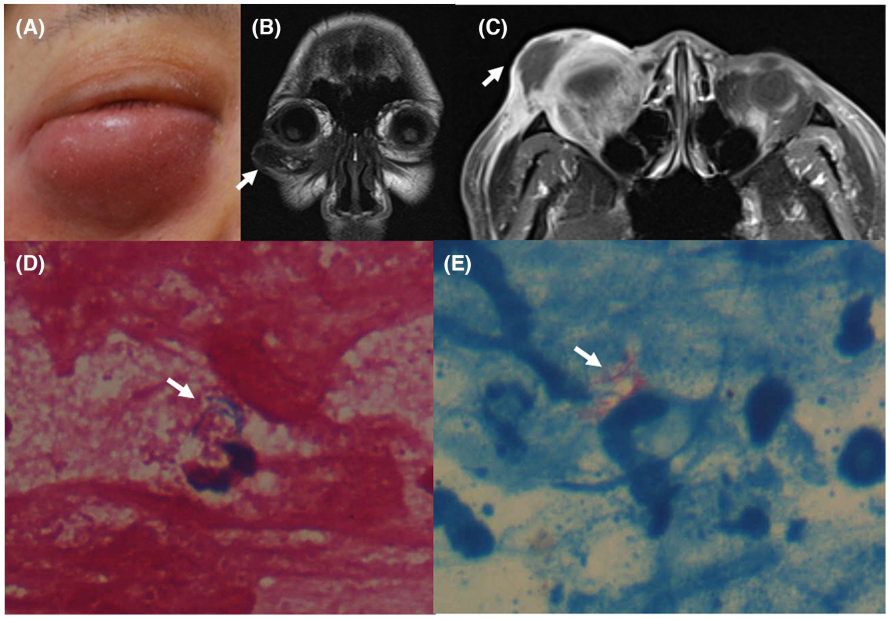

FIGURE 1 Red swollen lower eyelid bulging involving the lacrimal sac on the right side (A) at the initial visit. Magnetic resonance imaging reveals fluid collection (arrow, B) with 4-cm longest diameter in the entire lower eyelid with probable connection to the lacrimal sac on T1-weighted coronal image. Contrast enhancement in the surroundings of the fluid collection is noted on T1-weighted axial image (arrow, C), indicative of abscess. Gram-positive rods, suspicious of mycobacteria based on their configuration, are detected first by Gram stain (arrow, D), and acid-fast bacilli are then detected by Ziehl–Neelsen stain (arrow, E) in abscess fluid puncture.

mycobacteria, based on their configuration. At the next step, acid-fast bacilli were detected in smears of the abscess fluid by Ziehl–Neelsen stain (Figure 1E) and designated as 2+ on the scale (10 or more bacilli in 100 fields under ×1000 magnification), corresponding roughly to the previously used Gaffky scale of 5. *M. tuberculosis* was not detected by polymerase chain reaction of the abscess fluid while *M. avium* and *Mycobacterium intracellulare* were also not detected, supporting other nontuberculous mycobacterial infection. The abscess fluid was also negative for *M. tuberculosis* complex antigen testing, which was used basically for detecting bacilli in culture. Ten days later, mycobacterium species were cultured and detected by BD BBL TB Auramine-Rhodamine T Fluorescent Staining (Becton Dickinson and Company, Franklin Lakes, NJ, USA) in the automated microbial detection system with a CO_2 sensor (BACT/ALERT 3D, BioMerieux, Marcy l'Etoile, France).[11,12] Four weeks later in the culture, *M. abscessus* was identified by fluorometric DNA–DNA hybridization in microdilution wells (DDH Mycobacteria Kyokuto, Kyokuto Seiyaku Co., Tokyo, Japan).[13] In parallel, no other aerobic bacteria were cultured in a week on sheep blood agar plates and chocolate agar plates (Kyokuto Seiyaku Co.) in a 5% CO_2 incubator.

In the diagnosis of nontuberculous mycobacterial infection after the exclusion of *M. tuberculosis* by polymerase chain reaction at the initial visit, she began to have clarithromycin 800 mg daily and ethambutol 750 mg daily for a month. Two weeks later from the initial visit, white blood cell counts were $6.16 \times 10^3/\mu L$ and CRP became normal at 0.06 mg/dL. In the identification of *M. abscessus* as a pathogen, the medication was switched to clarithromycin 800 mg daily and levofloxacin 500 mg daily, and continued for 8 months. She continued topical 0.5% levofloxacin eye drops and gentamycin ointment for the lower eyelid skin.

She underwent debridement surgery of the lower eyelid with surface cutaneous suture 7 months after the initial visit when she was still on daily clarithromycin and levofloxacin. In the pathology of the debridement tissue, granulomatous tissue with necrotic areas and monocytic infiltration (Figure 2A) contained multinucleated cells (Figure 2B), and epithelioid cells (Figure 2C), which delineated foamy spaces in small size and large size. No acid-fast bacilli were detected on the pathological specimen. She finally underwent plastic surgery for the contracted scar in the lower eyelid on the right side by dermal fat grafting with auricular cartilage transplantation as the tarsal replacement 1.5 years later from the initial visit. The reconstructed lower eyelid appeared well in half a year after the surgery until the last visit.

3 | DISCUSSION

This case conveys a clinical message to consider rare pathogens as nontuberculous mycobacteria in atypical

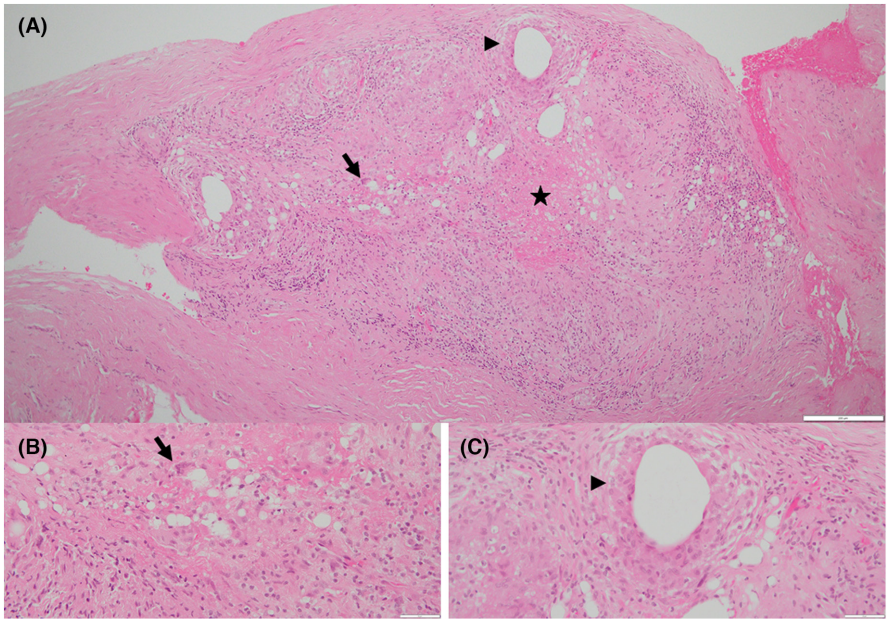

FIGURE 2 Pathology of resected lower eyelid tissue at debridement surgery 7 months after the initial visit. Low magnification image (A) shows granulomatous tissue with monocytic infiltration, multinucleated giant cells (arrow), necrotic area (asterisk), and foamy spaces. Note a large foamy space (arrowhead) surrounded by epithelioid cells. Multinucleated giant cell (arrow, B) and multiple small foamy spaces (B), and epithelioid cells (arrowhead, C) which engulf a large foamy space, in high magnification images. Hematoxylin–eosin stain. Scale bar = 200 μm in A, 50 μm in B and C.

sites of infection. A diagnostic procedure in this patient was to do the smear of abscess puncture in the lower eyelid. At the first step, Gram stain showed Gram-positive rods, suspicious of mycobacteria based on their configuration. At the next step, acid-fast bacilli were detected by Ziehl–Neelsen stain. Polymerase chain reaction of genomic DNA of *M. tuberculosis* as well as *M. avium* and *intracellulare* in the abscess fluid was then performed to exclude tuberculosis from the viewpoint of infection control. At this point, the diagnosis of a nontuberculous mycobacterial infection was established, and treatment with clarithromycin and ethambutol was started.

The extrapulmonary nontuberculous mycobacterial infection, including the cutaneous and ocular adnexal infection,[6–10] has been rare at a few percent, compared with the predominant pulmonary infection. In the cutaneous nontuberculous mycobacterial infection, *Mycobacterium marinum* was highest in number, followed by *Mycobacterium fortuitum* and *M. avium* complex at that time in the year 2012 in Japan. Since she had a hobby of swimming in indoor pool and underwent nasolacrimal duct boogie, *M. marinum* was most suspected as a candidate pathogen for the cutaneous infection. *M. marinum* likes to be present in low-salt water, such as indoor swimming pool and tropical fish water tank.

Only after the identification of *M. abscessus* in 4 weeks, the treatment was changed to the combination of clarithromycin and levofloxacin for 8 months, leading to the complete resolution. Even at present, there is no standard treatment for cutaneous infection with *M. abscessus* which is extremely rare. At that time in 2012, two or more drugs were combined as empirical treatment in the case of pulmonary *M. abscessus* infection. The drug susceptibility testing was not done in this patient. The patient wished to be treated at outpatient setting and did not wish to have intravenous administration. The patient was systemically healthy and thus, oral administration of clarithromycin and levofloxacin in combination was chosen, based on the therapeutic strategy of two or more drug combinations, which was applied to the pulmonary infection.

In this patient, repeat lacrimal sac irrigation on the right side by the former eye doctor would be a risk factor for the development of nontuberculous mycobacterial infection. Lacrimal sac or lacrimal canalicular injuries caused by irrigation with a blunt-ended needle might be a precipitating factor for the infection in this patient since cutaneous nontuberculous mycobacterial infection has been known to be predisposed by injuries. The present patient did not have any underlying factor for immunocompromised state or infection-prone condition such as diabetes mellitus or HIV infection. As illustrated in this case, extrapulmonary nontuberculous mycobacterial infection should be always considered in the list of differential diagnoses, while mortality rates of pulmonary nontuberculous mycobacterial infection have been rising in Japan.[14]

It should be noted that granulomatous tissue with monocytic infiltration still showed multinucleated giant cells and epithelioid cells in the debridement specimen 7 months after

the start of the treatment. At this time, no acid-fast bacilli were detected on the pathological specimen. Many foamy spaces would be remnants of histiocytes with foamy appearance, which have been described as a pathological feature of nontuberculous mycobacterial infection in the pulmonary lesions[15,16] and in the cutaneous lesions.[17,18] The persistent granulomatous inflammation with multinucleated giant cells and epithelioid cells would be directed against remnant antigens of dead nontuberculous mycobacteria.

In conclusion, nontuberculous mycobacterial infection in an otherwise healthy person would occur in the ocular adnexa, especially in the lacrimal sac as dacryocystitis. It is important to identify acid-fast bacilli in the smear of the abscess fluid which is obtained by puncture with a needle and then to exclude tuberculosis by polymerase chain reaction on the early phase of the infection. The granulomatous lesions with spaces of foamy appearance would be persistent many months after the beginning of the standard combination of the treatment. Repeat lacrimal sac irrigation and nasolacrimal duct boogie as a kind of surgical intervention would be a risk factor for trauma-induced nontuberculous mycobacterial infection.

AUTHOR CONTRIBUTIONS

Toshihiko Matsuo: Conceptualization; data curation; formal analysis; investigation; methodology; validation; visualization; writing – original draft. **Takehiro Tanaka:** Conceptualization; data curation; investigation; methodology; writing – review and editing. **Kiyoshi Yamada:** Data curation; investigation; writing – review and editing. **Motoko Nose:** Investigation; methodology. **Yasushi Tanimoto:** Data curation; formal analysis; investigation; methodology; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

DATA AVAILABILITY STATEMENT

Additional data are available upon reasonable request to the corresponding author.

ETHICS STATEMENT

Ethics committee review was not applicable due to the case report design, based on the Ethical Guidelines for Medical and Health Research Involving Human Subjects, issued by the Government of Japan.

CONSENT

Written consent was obtained from the patient for her anonymized information to be published in this article.

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