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Case Report

Kocuria dacryocystitis infection, caused by *kocuria ocularis* sp. Nov.

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Introduction: *Kocuria* spp. rarely cause infectious disease but can be opportunistic pathogens in immunocompromised patients. The numbers of documented infections are low but rising.

Case presentation: A 74-year-old woman presented with acute, painful swelling of the medial canthus of the left eye. The skin surface was red and acutely painful to the touch. Because of several clinical relapses despite antibiotic treatment, surgical dacryocystorhinostomy with marsupialization of the lacrimal sac into the nasal cavity was performed. Lacrimal sac drainage samples were analysed and yielded *Kocuria*. This is, to our knowledge, the first case of *Kocuria* dacryocystitis. Furthermore, the dacryocystitis was caused by a novel species of *Kocuria*, which we suggest should be named *Kocuria ocularis*.

Conclusion: *Kocuria* related to ocular infection has not yet been documented. This report expands the clinical spectrum of diseases caused by these potentially underestimated pathogens.

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Introduction

Kocuria spp. are frequently found as normal skin flora in humans and other mammals (Szczerba, 2003) and can also be present in soil and water. Clinical syndromes caused by these agents are rarely reported; however, the true prevalence of infectious disease due to *Kocuria* is presumably higher and will probably be revealed as soon as genome-based identification becomes more widely available in clinical laboratories. *Kocuria* spp. can be opportunistic pathogens in immunocompromised patients; the numbers of documented infections are low (Ma *et al.*, 2005) but rising. Indeed, it has been reported that *Kocuria* can cause bacteraemia in chronically ill patients with malignancies or in immunosuppressed states (Basaglia *et al.*, 2002; Martinaud *et al.*, 2008). *Kocuria* infection has been linked to cases of peritonitis associated with peritoneal dialysis (Altuntas *et al.*, 2004; Lee *et al.*, 2009; Meletis *et al.*, 2012), acute cholecystitis (Ma *et al.*, 2005), catheter-related bacteraemia (Dunn *et al.*, 2011; Lai *et al.*, 2011; Moissenet *et al.*, 2012), infective endocarditis (Lai *et al.*, 2011) and brain abscesses (Tsai *et al.*, 2010). Here, we describe the first known case of *Kocuria* dacryocystitis in an immunocompetent patient. Furthermore, this dacryocystitis was caused by a novel species of *Kocuria*, which we suggest should be named *Kocuria ocularis*.

The GenBank/EMBL/DDBJ accession number for the Kocuria ocularis 16S rRNA gene sequence determined in this study is KC862588

Abbreviations: MALDI-TOF MS, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry.

Case report

In April 2012, a 74-year-old woman presented at a private hospital's Ophthalmology Department with acute, painful swelling of the medial canthus of the left eye. The skin surface was red and acutely painful to the touch. The woman also displayed tearing of the left eye. There was no decrease in visual acuity. Other than hypertension, the patient's medical history was unremarkable. She was treated successfully with 1 g amoxicillin and 125 mg clavulanic acid two times daily by the oral route within 10 days for *Staphylococcus aureus* acute dacryocystitis. The dacryocystitis resolved rapidly but recurred 3 months later. The patient received another 10-day course of the same antibiotics without bacteriological analysis, and no clinical improvement was seen. Contrast-enhanced computed tomography of the lacrimal drainage system (Dacryo-Scan) was performed and revealed obstruction of the left

nasolacrimal duct (but no contrast uptake by the lacrimal sac) (Fig. 1a) and left frontal rhinosinusitis (Fig. 1b). No bacteriological analysis was performed at this time. Systemic moxifloxacin and betamethasone therapy was initiated but failed to produce any clinical improvement.

In December 2012 (i.e. 8 months after the initial consultation), she presented at our university hospital's Ophthalmology Department, and surgical dacryocystorhinostomy with marsupialization of the lacrimal sac into the nasal cavity was performed. Lacrimal sac drainage samples were analysed by the hospital's Clinical Bacteriology Department.

Further treatment with 1 g amoxicillin and 125 mg clavulanic acid two times daily by the oral route was combined with topical application of a tobramycin-dexamethasone ophthalmic ointment (Alcon). The patient's symptoms disappeared rapidly and have not recurred in the 15 months since surgery.

Diagnosis

A lacrimal sample was cultured on sheep blood Columbia agar incubated at 37 °C in both aerobic and anaerobic conditions, and on chocolate agar incubated at 37 °C in a 5 % CO_2 atmosphere. The sample was also smeared onto clean, sterile labelled glass slides for Gram staining, which revealed the presence of many pairs and clusters of Gram-positive cocci and many leucocytes. After a 48 h incubation, the lacrimal sac sample yielded pale cream, smooth, catalase-positive, coagulase-negative colonies with a diameter of 1.5 mm (under aerobic conditions only). The isolate was non-haemolytic on sheep blood agar plates. On Gram staining, the isolate was found to be Gram-positive cocci, which formed pairs and clusters. The growth was consistent with direct microscopy findings (i.e. appropriate staining and morphology with a Gram stain).

The bacterial isolate was identified as *Kocuria* using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS; Brucker Daltonics), with a very good validity score of >2 (2.3). However, MALDI-TOF MS analysis did not identify the specific *Kocuria* sp.

The strain was cultured on mannitol salt agar, and bacitracin and nitrofurantoin disks were tested on Mueller-Hinton agar. The strain grew on mannitol salt agar without acid production, and was bacitracin sensitive and nitrofurantoin resistant, as would be expected for members of the genus *Kocuria* (Savini *et al.*, 2010).

Full sequencing of the 16S rRNA gene (1474 continuous nucleotides, using the classical Sanger method as previously described by Harf-Monteil *et al.*, 2004) not only confirmed the isolate as belonging to the genus *Kocuria* but also revealed a novel *Kocuria* sp. This novel sequence was compared with all available GenBank bacterial sequences using the BLASTN (http://www.ncbi.nlm.nih.gov/blast/Blast.cgi) and the MegAlign module of the Lasergene software package (DNASTAR). By using the neighbour-joining method (Saitou & Nei, 1987), we built a phylogenetic tree depicting the novel position of this species within a subset of the genus *Kocuria* (Fig. 2). The strain was found to diverge by 0.3 % from the uncultured bacterium clone MB02E06 (GenBank accession no. FM873886) isolated recently from house dust samples (Taubel *et al.*, 2009).

The isolate's susceptibility to a range of antimicrobial agents (benzylpenicillin, oxacillin, cefoxitin, moxalactam, novobiocin, linezolid, streptomycin, kanamycin, gentamicin, tobramycin, rifampicin, tetracycline, fosfomycin,

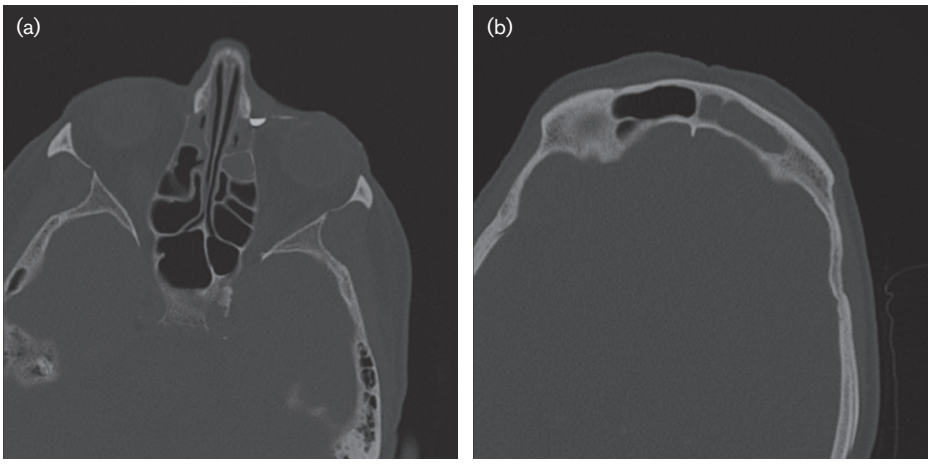

Fig. 1. Contrast-enhanced computed tomography of the lacrimal drainage system revealing left-side nasolacrimal duct obstruction (a) and left-side frontal rhinosinusitis (b)

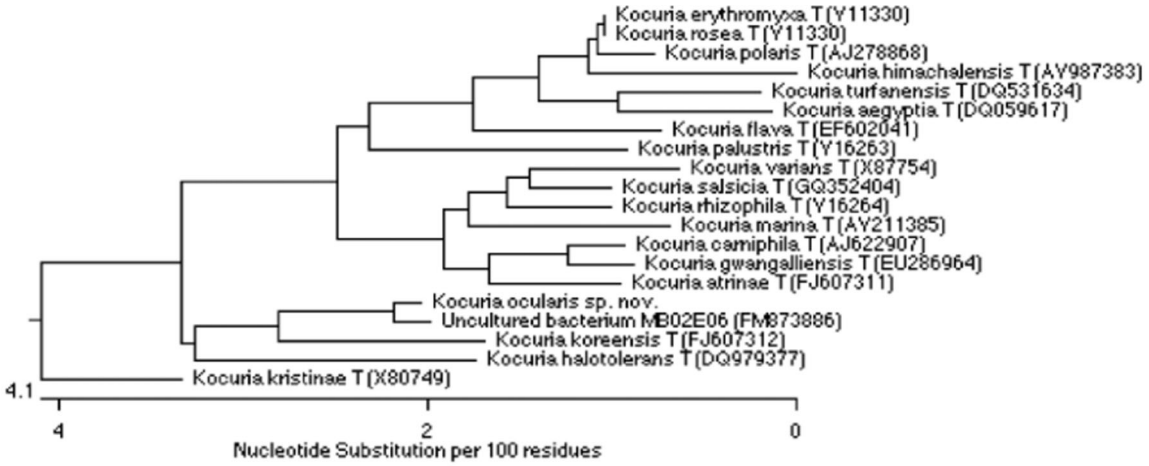

Fig. 2. A phylogenetic tree reconstructed using the neighbour-joining method and based on the 16S rRNA gene sequences of *Kocuria* species. GenBank accession numbers are given in parentheses. All sequences are from reference strains and are fully available at http://www.ncbi.nlm.nih.gov/blast/Blast.cgi.

cotrimoxazole, erythromycin, lincomycin, pristinamycin, rifampicin, ofloxacin, vancomycin, teicoplanin and fusidic acid) was analysed using the disk diffusion method, in accordance with the Comité de l'antibiogramme de la Société Française de Microbiologie (2013). We observed resistance to novobiocin, ofloxacin, fosfomycin, erythromycin and fusidic acid. The strain was susceptible to the other antibiotics tested (including β-lactams) and did not produce β-lactamase. The breakpoints used were those for *Staphylococcus* spp. To the best of our knowledge, no cases of fusidic acid resistance have ever been reported in *Kocuria* species (Savini *et al.*, 2010).

Discussion

A wide variety of aetiological agents for dacryocystitis have been identified; they include *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Haemophilus influenzae* and (more rarely) aerobic or facultative Gram-negative bacilli and anaerobes. However, *Kocuria* species as the causative agent of dacryocystitis has never been reported. Indeed, in this case patient bacterial testing of the lacrimal sac contents yielded a pure culture of Gram-positive cocci and led to the presumption of *Staphylococcus* sp. as the causative agent, but MALDI-TOF MS recognized the bacteria as *Kocuria* and the 16S rRNA gene sequencing further identified a novel *Kocuria* species: *K. ocularis* sp. nov. Gene sequencing provides more reliable information than MALDI-TOF MS and 16S rRNA gene sequencing has become the gold standard for bacterial identification (Clarridge, 2004). *K. ocularis* sp. nov was a strictly aerobic, non-motile, catalase-positive, coagulase-negative, Gram-positive coccus that occurred in tetrads. As seen for all other *Kocuria* species, it was bacitracin sensitive and nitrofurantoin resistant.

Dacryocystitis corresponds to infection and inflammation of the lacrimal sac and usually occurs because the nasolacrimal duct is obstructed. The rhinosinusitis observed in our patient's Dacryo-Scan may have contributed to the obstruction. However, a number of predisposing factors have been described in the literature as contributing to dacryocystitis. Indeed, acute dacryocystitis becomes more prevalent with age, and female gender is also a risk factor (Pinar-Sueiro *et al.*, 2012). Given that our patient responded only partially to antibiotic treatment, surgical debridement (i.e. rhinostomy of lacrimal sac in order to bypass the obstruction of the nasolacrimal duct) was ultimately necessary for complete resolution (i.e. no recurrence in the 15 months since surgery). Hence, the combination of dacryocystorhinostomy with appropriate antibiotic treatment appears to be the optimal therapy (Pinar-Sueiro *et al.*, 2010).

Accurate strain identification is essential for (i) defining the spectrum of disease caused by each species and (ii) performing epidemiological comparisons of clinical isolates.

When reviewing scientific and clinical literature in English and French, *Kocuria* related to ocular infection has not yet been documented. To the best of our knowledge, this is the first case report of *Kocuria* dacryocystitis. This case expands the clinical spectrum of disease caused by these unusual pathogens and adds to the growing body of literature on the pathogenicity of *Kocuria* in humans.

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