

Rothia prosthetic knee joint infection: report and mini-review

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Abstract

Rothia spp. are gram-positive pleomorphic bacteria that are part of the normal oral microflora. They are associated with dental and periodontal disease, although systemic infections have also been reported. We describe the case of a 75-year-old lady with rheumatoid arthritis who presented with prosthetic knee joint infection due to *Rothia aeria*. We discuss its identification and the evidence regarding association of dental disease with *Rothia* spp. joint infections based on available literature.

Keywords: Identification, infection, joint, prosthetic, *Rothia aeria*, treatment

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Introduction

Rothia spp. are gram-positive pleomorphic bacteria that are part of the normal oral microflora. They are associated with dental and periodontal disease [1,2]. The first description of disease in humans due to *Rothia* species was reported in 1975 in a case of peri-appendiceal abscess [3].

More recently a number of case reports have described *Rothia* species as causing native and prosthetic endocarditis [4,5] and other rare infections, including endophthalmitis [6,7], corneal infections [8], peritoneal infections [9] and sepsis in an immunocompromised patient [10] and a neonate [11].

Case Report

A 75-year-old lady with a history of seronegative erosive rheumatoid arthritis since 1972 presented with painful swelling of the right knee. She had bilateral knee replacements. The right knee replacement was carried out in 1993 and the left one in 2003. Her other co-morbidities included asthma,

arterial hypertension and chronic kidney disease. She was on drug therapy for treatment for the above conditions and also on methotrexate 12.5 mg once weekly and prednisolone 7.5 mg once a day, for more than 10 years. She had also undergone multiple hand and wrist surgeries. She did not have any history of trauma or previous knee infections.

On examination, body temperature was 38°C. Examination showed swelling, erythema and tenderness of the knee and upper calf. The initial blood tests showed white blood cells = $25.7 \times 10^9/L$, neutrophils = $24.4 \times 10^9/L$, C-reactive protein = 144 mg/L (normal <10 mg/L). Joint fluid aspirate contained $49\,600 \times 10^6$ white blood cells/L with 90% neutrophils. Microscopy showed gram-positive bacilli and a culture grew bacteria (Fig. 1). Identification of this isolate was performed by API Coryne (Biomérieux, Marcy l'Etoile, France). The isolate was initially identified as *Rothia dentocariosa* with a profile of 7050121. This isolate was then sent to the Health Protection Agency Regional reference laboratory in Colindale, London, UK and was identified as *Rothia aeria* by 16S rRNA sequencing.

A two-stage revision procedure was undertaken. At the first stage, all the metallic prosthetic components were extracted and spacers shaped like the prosthetic components



FIG. 1. Appearance of *Rothia aeria* on the culture plates.

(Biomet, Warsaw, IN, USA) were implanted. Vancomycin was mixed into the cement. 2 g of vancomycin was used per 40 g of cement. Four out of seven specimens grew *R. aeria*, suggesting that this was a significant organism. The patient was treated with intravenous ceftriaxone (2 g once daily) for approximately 2 weeks and then with teicoplanin (600 mg once daily) for a further 4 weeks. Inflammatory markers showed a steady decline during this period. The patient underwent a re-implantation of the metallic prostheses 12 weeks following the first stage of the revision procedure.

After 4 months following the revision the patient was doing well with good functional joint and normal blood markers. A subsequent review at the maxillofacial clinic at the hospital identified some retained roots and dental caries that were removed 5 months after surgery. Although the knee infection was successfully treated, this patient unfortunately died of *Clostridium difficile* diarrhoea 6 months after the antibiotic course.

Discussion

In 1967, Georg and Brown proposed the genus *Rothia* [12] for a group of coccoid to diphtheroid to filamentous gram-positive organisms isolated from the human oral cavity, naming the genus after Roth [13], who had performed basic studies on these organisms.

The taxonomic position of the genus *Rothia* has undergone a number of changes since Georg and Brown first assigned it to the family Actinomycetaceae and proposed *R. dentocariosa* as

the type (and only) species [12]. Possible assignments to the genera *Actinomyces* and *Nocardia* were rejected on chemotaxonomic, metabolic and biochemical grounds. More recent molecular studies placed the genus in the family Micrococcaceae, suborder Micrococccineae, order Actinomycetales, subclass Actinobacteridae, class Actinobacteria [14]. It is therefore in the same family as the genera *Micrococcus*, *Arthrobacter*, *Kocuria*, *Nesterenkonia*, *Renibacterium* and *Stomatococcus*, all of which show characteristic signature nucleotides in their 16S rDNA sequences [14]. Subsequently, *Stomatococcus mucilaginosus*, the only species in the genus *Stomatococcus*, was reclassified as *Rothia mucilaginosus* on the basis of 16S rRNA gene sequence and whole-cell protein pattern [15]. Genomic heterogeneity within *R. dentocariosa* has been observed [16].

Further, *Rothia nasimurium*, recovered from the nose of a mouse [15], and *Rothia amarae*, recovered from sludge [17], have been described and are both distinct phenotypically from *R. dentocariosa*.

More recently, phylogenetic analysis of a gram-positive bacterium strain AI-17BT isolated from Russian space station air samples showed that it grouped with unofficially named *R. dentocariosa* genomovar II, [18]. As a result of a polyphasic taxonomic study, the isolate was proposed to be classified as the novel species *Rothia aeria* sp. nov. [18].

After an extensive literature search we have been able to review six previously reported cases of *Rothia* joint infections (Table 1).

It is evident from the above mentioned cases that significant rheumatological disease and orthopaedic surgeries are a significant risk factor for joint infections. Of the seven patients studied, all but one [20] had dental disease. It is also interesting that the two patients who had *Rothia* spp. joint infections despite being immunocompetent had a history of dental problems.

Of the seven *Rothia* spp. joint infections reported to date, four were prosthetic joint infections and three were native joint infections. In three of the four prosthetic joint infections all the hardware was removed. In one of these cases [23] hardware was removed only after treatment failure with antibiotics and resection. In the fourth case [24], where hardware was not removed, amoxicillin-clavulanate was continued indefinitely.

To the best of our knowledge, our case is the first report of an *R. aeria* prosthetic joint infection. *Rothia aeria* has been identified as a rare colonizing organism in the oral cavity of healthy individuals [25].

Ko et al. [26] studied the identification of *Rothia* isolates from human patients and one of their conclusions was that two strains which had previously been supposed to be *R. dentocariosa* according to the API Coryne system, were identified as

TABLE 1. Seven reported cases of *Rothia* genus joint infections (most recent first)

First author	Organism	Age (years)	Joint	Dental disease	RA	Immunosuppression	Treatment	Duration	Outcome successful
Mahobia <i>et al.</i>	<i>Rothia aeria</i>	75	Right prosthetic knee	Yes	Yes	Methotrexate, prednisolone	Hardware removed, IV ceftriaxone 2 g once daily Teicoplanin 600 mg once daily	2 weeks 4 weeks	Yes
Trivedi <i>et al.</i> [19]	<i>Rothia</i> species not known	53	Left prosthetic knee	Yes	Yes	No	Hardware removed, ertapenem 1 g daily + amoxicillin-clavulanate Oral amoxicillin-clavulanate	8 weeks 4 months	Yes
Kaasch <i>et al.</i> [20]	<i>Rothia mucilaginoso</i>	73	Right native knee	Unknown	Yes	Prednisolone	Moxifloxacin 400 mg once daily Ampicillin plus sulbactam 375 mg twice daily	2 weeks 7 weeks	Yes
Verrall <i>et al.</i> [21]	<i>Rothia aeria</i>	88	Both native shoulders	Yes	Yes	Methotrexate, prednisolone, hydrocortisone	IV penicillin 2.4 g/day infusion	2 weeks	Yes
Favero <i>et al.</i> [22]	<i>Rothia dentocariosa</i>	46	Right native knee	Yes	Yes	Etanercept 25 mg twice weekly, oxaprozin	Levofloxacin, clarithromycin	Unknown	Yes
Michels <i>et al.</i> [23]	<i>Rothia mucilaginoso</i>	59	Right prosthetic hip	Yes	No	No	Hardware removed, vancomycin	6 weeks	Yes
Klingler <i>et al.</i> [24]	<i>Rothia dentocariosa</i>	44	Right prosthetic knee	Yes	No but OA	Zidovudine, lamivudine (HIV)	Patient declined hardware removal, IV ceftazidime Oral amoxicillin-clavulanate	6 weeks Indefinitely	Yes

IV, intravenous; OA, osteoarthritis; RA, rheumatoid arthritis.

R. aeria by 16S rRNA gene analysis. Two other case reports highlighted similar observations regarding the identification of *Rothia* spp. in their report [21,27]. This was also demonstrated in our case. This would suggest that routine biochemical tests may misidentify *R. aeria* as *R. dentocariosa*.

To date only six cases of systemic infections caused by *R. aeria* have been reported (excluding the current case). In these cases, *R. aeria* identification was performed using the 16S rRNA gene analysis [11,21,27–30].

Tarumoto *et al.* [28] reported the most recent case of *R. aeria* invasive infection. The report described a case of infective endocarditis in a 40-year-old Japanese man with a history of smoking but no history of medical problems. Unfortunately this case had a fatal outcome after cerebral haemorrhagic infarction. The other reported cases of *R. aeria* infection include a neck abscess in a patient with chronic granulomatous disease [29], multifocal nodular pneumonia [30], bronchitis [27], septic arthritis [21] and sepsis [11].

Falcone *et al.* [29] described the case of an *R. aeria* neck abscess in a patient with chronic granulomatous disease. The infection was aggressive, requiring two surgeries as well as prolonged antibiotics for complete resolution. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) using a MALDI-TOF MicroFlex LT mass spectrometer (Bruker Daltonics, Billerica, MA, USA) identified it as *Rothia* species with best match to *R. aeria*. Full 16S rRNA gene sequencing confirmed the species level identification with a 99.8% match to the *R. aeria* type strain.

We took the opportunity to run the isolate from our case (previously identified as *R. aeria* by 16S rRNA gene analysis)

through MALDI-TOF MS. The MALDI-TOF confirmed the isolate as *Rothia* spp. with best match to *R. aeria*.

Rothia aeria is susceptible to many antibiotics [11,21,27,28,30]. However, it reportedly demonstrates intermediate susceptibility to clindamycin and vancomycin [21,28]. Resistance to clindamycin [11,30], aztreonam [30] and ofloxacin [27] has also been reported.

Conclusion

Rothia spp. joint infections are rare. Genetic identification down to the level of species is important because species of *Rothia* can cause severe infections and certain species are not susceptible to some antibiotics. Evidence suggests that 16S rRNA sequencing or MALDI-TOF MS provide reliable identification of species. Failure of antibiotic treatment has been reported in the absence of complete removal of hardware.

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Conflict of Interest

None.

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