AKADÉMIAI KIADÓ

Pulmonary malakoplakia due to *Prescottella (Rhodococcus) soli* in a renal transplant recipient: First reported case

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CASE STUDY

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ABSTRACT

Prescottella (Rhodococcus) soli is a soil-dwelling organism not previously thought to be pathogenic in humans. We discuss the case of a 78-year-old male renal transplant recipient presenting with respiratory symptoms and multiple pulmonary nodules, found to be pulmonary malakoplakia secondary to infection with *Prescottella* (*Rhodococcus*) *soli*. Treatment was commenced with vancomycin, meropenem and azithromycin for an induction period of two weeks and continued with indefinite oral moxifloxacin and azithromycin with significant clinical improvement. Although rare, *Prescottella* species, including *Prescottella soli*, should be considered in the differential diagnosis of pulmonary nodules, particularly in immunocompromised patients. More data is required to inform optimal treatment.

KEYWORDS

***Prescottella soli*, *Prescottella*, *Rhodococcus*, pulmonary malakoplakia, pulmonary nodules**

INTRODUCTION

Prescottella (Rhodococcus) soli was first discovered in 2015 and has been considered a soil-dwelling, non-pathogenic organism, largely only notable for its use in bioremediation [1]. Herein, we describe the case of a 78-year-old renal transplant recipient with insidious pulmonary nodules caused by *Prescottella (Rhodococcus) soli* which is, to our knowledge, the first reported case of human disease with this organism.

CASE PRESENTATION

A 78-year-old man with a background of renal transplantation was found to have pulmonary nodules during investigation for a cough. The renal transplant had occurred 3 years prior, from a deceased donor, with a current immunosuppression regimen including mycophenolate 360 mg twice daily, prednisolone 2 mg daily and tacrolimus 1.5 mg twice daily. The native disease was presumed glomerulonephritis in a solitary kidney after nephrectomy for a benign tumour. He had had recurrent *Clostridioides difficile* infection in the past 12 months but no other infective complications. Other background history included hypertension, subclavian artery stenosis, and chronic obstructive pulmonary disease (COPD)/asthma

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overlap syndrome. He was a retired train driver who did not consume alcohol or cigarettes and resided in a rural area, though did not own or work with animals. Chest computed tomography (CT) demonstrated several pulmonary nodules in the left lower lobe (20 × 16 mm, 22 × 20 mm, and 7 mm respectively), lingula (15 mm) and right lower lobe (7 mm), which were subpleural in nature. At least one of the lesions had been noted incidentally on a CT abdomen for a different indication several months prior. The major differential diagnoses were malignancy or infection caused by an organism such as non-tuberculous mycobacteria or *Aspergillus* sp. Positron emission tomography (PET) showed the nodules to be intensely avid, suspicious for malignancy, without other significant sites of uptake (Fig. 1). Other investigations showed a normal white cell count and C-reactive protein, a baseline creatinine of approximately 400 µmol L^{-1} (reference range 60–110 µmol L^{-1}) and a therapeutic tacrolimus level. He was mildly lymphopenic at 0.9 × 10^9/L (reference range 1.0–4.0 × 10^9/L).

Endobronchial ultrasound-guided biopsy of the lingular lesion was performed with non-diagnostic cytology but pure growth of *Prescottella (Rhodococcus) soli*. Due to unclear significance, a second biopsy was obtained from a bronchoscopy, during which a friable, polypoid mass was visualised partially obstructing the left lower lobe. Histopathological examination revealed inflammation and Michaelis-Gutmann inclusion bodies, consistent with malakoplakia (Fig. 2). Giemsa and Periodic Acid-Schiff (PAS) staining highlighted granular, bacteria-like structures within the affected cells, with negative Grocott's Methenamine Silver (GMS) and Ziehl-Neelsen stains. There was no granuloma formation and no evidence of malignancy. Cultures again isolated *Prescottella (Rhodococcus) soli*, now considered the likely aetiological agent given repeated isolation in combination with malakoplakia.

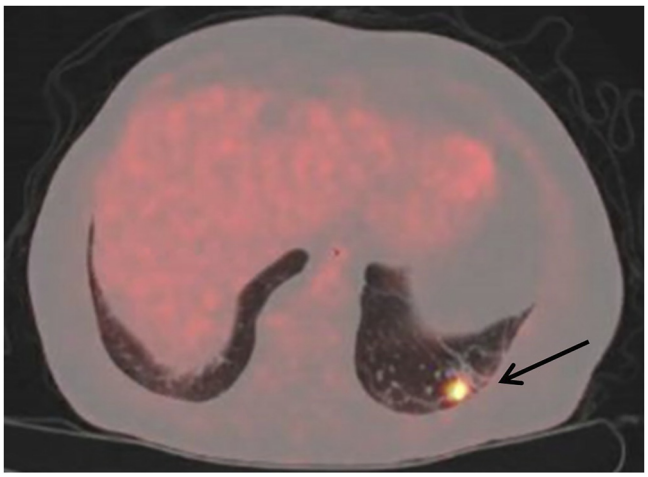

Fig. 1. Sagittal section of PET-CT showing hypermetabolic left lower lobe pulmonary nodule (arrow)

On both occasions, the samples were inoculated on a range of non-selective media both aerobically and anaerobically, as well as being inoculated into fungal and mycobacterial media, with no other organisms identified. Bacterial cultures demonstrated growth in solid media within 48 h as white, mucoid colonies, developing light pink pigmentation by day seven (Fig. 3), and additionally grew in Mycobacterial Growth Indicator Tube (MGIT) media within five days. A rod-coccus cycle was evident with Gram-positive coccobacilli and cocci appearing at 24 and 48 h on solid media respectively, and long Gram-positive rods appearing at 24 h incubation in liquid media (Fig. 3). The organisms were non-motile, catalase positive, and acid-fast with modified Ziehl-Neelsen staining. They were unable to be identified confidently with MALDI Biotyper (Bruker, MA, USA) or automated biochemical identification (VITEK2, BioMerieux, Marcy l'Etoile. France). The identification of *Prescottella (Rhodococcus) soli* was therefore achieved on each occasion by 16S rRNA polymerase chain reaction (PCR) and Sanger sequencing of the bacterial colonies. Using BLAST in NCBI, a 99.92% match was found with *Prescottella soli* reference strain NR_134799.2. Antibiotic susceptibility testing was performed using gradient diffusion method (E-test, BioMerieux, Marcy l'Etoile. France) on Mueller-Hinton blood agar with results summarised in Table 1. Clinical breakpoints are unavailable therefore categorical interpretation of Minimum Inhibitory Concentrations (MICs) was not possible. Additionally, the use of gradient diffusion method rather than a

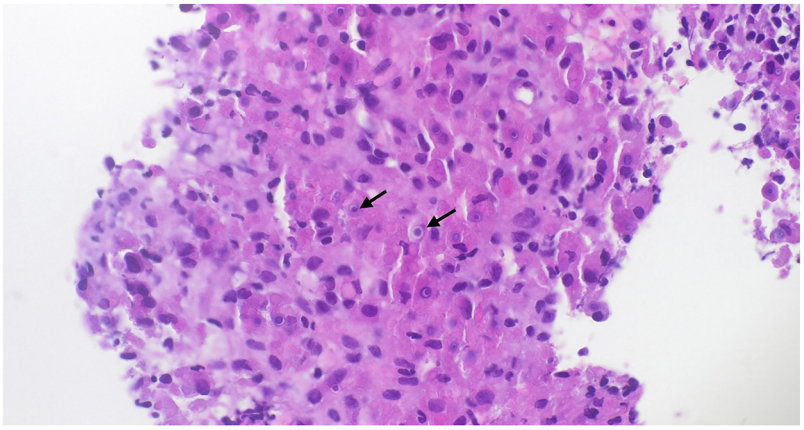

Fig. 2. High powered field with H&E staining showing target-like Michaelis-Gutmann inclusion bodies (arrows)

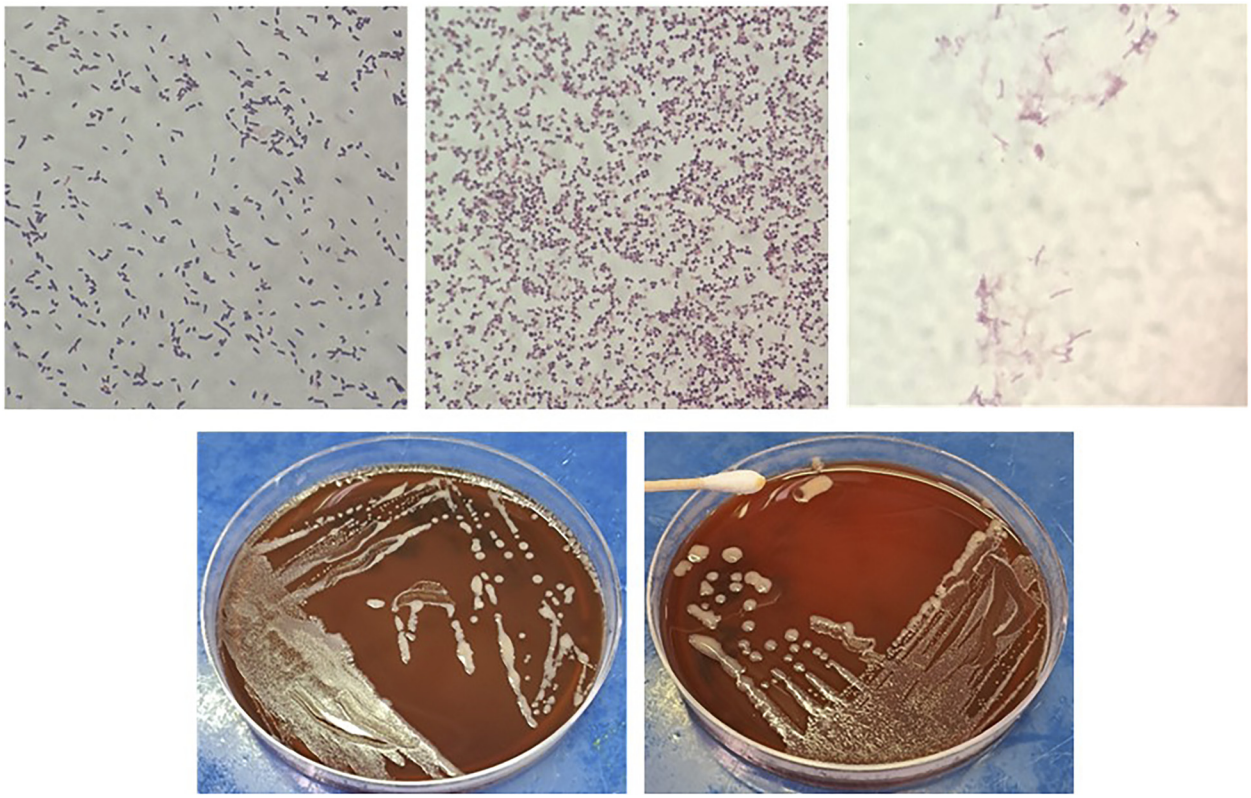

Fig. 3. Top row: Rod-coccus cycle demonstrated by Gram positive coccobacilli (left) and cocci (middle) after 24 and 48 h of incubation in solid media respectively; and rods (right) at after incubation in liquid media for 24 h.
Bottom row: Greyish white colonies at 48 h (left) and pink colonies at 7 days (right) on horse blood agar

Table 1. Antimicrobial susceptibility results

Antibiotic	Minimum Inhibitory Concentration (MIC) mg L^{-1} (E-test)
Ciprofloxacin	0.38
Cotrimoxazole	0.19
Erythromycin	1.5
Rifampicin	0.50
Vancomycin	1.0

reference method such as broth or agar dilution may limit the accuracy of the MIC data.

Our patient received treatment with two weeks of induction vancomycin adjusted to trough level, meropenem 1g 8 hourly and oral azithromycin 500 mg daily, followed by continuation therapy with moxifloxacin 400 mg and azithromycin 500 mg, both administered orally once daily. Tacrolimus and prednisolone were both reduced to 1 mg daily. Follow up bronchoscopy and PET scan after 8 weeks of treatment therapy showed significant improvement of the lesions. The oral antibiotics were continued indefinitely, to be reviewed regularly pending stable clinical and radiological resolution.

DISCUSSION

Prescottella soli was initially classified within the *Rhodococcus* genus. The *Rhodococcus* genus previously comprised more than 50 species [2], which are generally considered environmental, soil-dwelling, non-pathogenic organisms [1]. The taxonomy of *Rhodococcus* spp. has been debated since its description in 1923, and most recently there was a proposal to reclassify four species including *Rhodococcus equi*, *Rhodococcus soli*, *Rhodococcus defluvii* and *Rhodococcus subtropica* to the new genus *Prescotella* based on phylogenomic evidence [3]. For simplicity, we will refer to these species as *Prescottella* for the remainder of the report. These organisms are all aerobic actinomycetes, a group of Gram positive bacteria within the Nocardiaceae family of the order Actinomycetales [2]. They are obligately aerobic, non-spore forming, non-motile and generally oxidase negative, catalase positive [1–3]. They grow well on non-selective media producing smooth, mucoid colonies [4]. The cell wall contains mycolic acid resulting in partial acid fastness with variable detection on acid fast staining [2, 3]. *Rhodococcus* spp. were initially named for their distinct rod-coccus cycle, which *Prescottella soli* therefore shares, with a tendency to appear as cocci when isolated from solid media and rods from liquid media [2, 3]. This variation has also been seen at different phases of growth, for example cocci in the early phase (12 h) and rods at 24 h [1].

Prescottella soli was first described in 2015 from a soil sample in Kyoto [1]. It has been notable mainly in bioremediation applications due to its ability to efficiently remove the herbicide glyphosate from the environment [5] and has

not previously been considered as a human pathogen. It is closely phylogenetically related to *Prescottella equi* [1], a species most commonly associated with granulomatous bronchopneumonia in foals [2, 6]. *Prescottella equi*, while still relatively uncommon, is also the main species of *Prescottella* associated with human infection, thus the species for which the most clinical data exists [7].

Transmission of these soil-dwelling organisms is predominantly via inhalation from the environment, though inoculation is possible [2]. They are facultative intracellular organisms, specifically preferring macrophages, with infection therefore aided by inadequate phagolysosome function [8]. Given this, and that clinical disease is relatively rare despite their environmental presence, immune compromise is the main risk factor for development of clinical disease, particularly post-transplant status and advanced Human Immunodeficiency Virus (HIV) [4, 7, 9]. Most human cases of *Prescottella* infections have been seen in renal transplant patients [10]. Pulmonary disease is the most common manifestation of human infection with *Prescottella* spp., again mainly described with *Prescottella equi*, and has included pneumonia, lung abscess, and nodules, often accompanied by bacteraemia [2]. Wound infection, septic arthritis, visceral abscess, and disseminated disease have also been reported, with extra-pulmonary manifestations occurring in up to 50% of transplant patients [2]. The disease can be acute or more indolent in nature, progressing over months [4].

Malakoplakia is an uncommon inflammatory condition, diagnosed by histopathological examination and distinguished by pathognomonic Michaelis-Gutmann inclusion bodies [6], which were evident in our patient's lung nodule. These are thought to be a result of defective lysosomes, with the resulting ineffective macrophages accumulating and leading to mass-like, sometimes granulomatous, lesions that can appear like malignancy [6, 11, 12]. Factors thought to contribute to this response include abnormal immune response or exposure to atypical bacteria [11]. While most commonly associated with the urinary tract, malakoplakia can affect other organs including the lungs [6, 11]; *Prescottella equi,* the close relative of *Prescottella soli*, is the most common cause of pulmonary malakoplakia [6, 12] which is generally subclinical, appearing as pulmonary nodules that can mimic lung cancer [12].

Optimal treatment of *Prescottella* spp., including *Prescottella soli*, has not been established [2, 4, 6]. The Clinical & Laboratory Standards Institute (CLSI) provides tentative clinical breakpoints for *Prescottella (Rhodococcus) equi* only [13], while the European Committee on Antimicrobial Susceptibility Testing (EUCAST) has not yet developed clinical breakpoints. For *Prescottella equi*, combination antimicrobial therapy is recommended, as resistance has developed with monotherapy [2], with at least two agents that concentrate in macrophages such as rifampicin, macrolides, and fluoroquinolones [4, 6]. Treatment duration has varied with up to six months being used [4]. Failure with medical treatment alone requiring surgical drainage of abscesses or resection of pulmonary masses has been seen [2, 6]. Mortality has been reported up to 25% in immunocompromised patients without HIV, though other estimates have been lower [4]. There are limitations to this study. Clinical breakpoints have not been developed for this species. Our patient improved with combination antimicrobials and reduction in immunosuppression. However, the natural history of infection in this patient, therefore the efficacy of the antibiotic treatment itself versus reduction in immunosuppression, is unclear.

In conclusion, *Prescottella (Rhodococcus)* spp., including *Prescottella soli*, although rare, should be considered as an aetiological agent in cases of cavitating pneumonia or lung nodules particularly in immunocompromised hosts or where malakoplakia is present [2, 4, 6]. More data is required to inform optimal treatment.

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