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ABOUT COVER

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The primary aim of *World Journal of Clinical Cases* (WJCC, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

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Pleural empyema with endobronchial mass due to *Rhodococcus equi* infection after renal transplantation: A case report and review of literature

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Abstract

BACKGROUND

Kidney transplantation is the best option for patients with end-stage renal disease. However, the need for lifelong immunosuppression results in renal transplant recipients being susceptible to various infections. *Rhodococcus equi* (*R. equi*) is a rare opportunistic pathogen in humans, and there are limited reports of infection with *R. equi* in post-renal transplant recipients and no uniform standard of treatment. This article reports on the diagnosis and treatment of a renal transplant recipient infected with *R. equi* 21 mo postoperatively and summarizes the characteristics of infection with *R. equi* after renal transplantation, along with a detailed review of the literature.

CASE SUMMARY

Here, we present the case of a 25-year-old man who was infected with *R. equi* 21 mo after renal transplantation. Although the clinical features at the time of presentation were not specific, chest computed tomography (CT) showed a large volume of pus in the right thoracic cavity and right middle lung atelectasis, and fiberoptic bronchoscopy showed an endobronchial mass in the right middle and lower lobe orifices. Bacterial culture and metagenomic next-generation sequencing of the pus were suggestive of *R. equi* infection. The immunosuppressive drugs were immediately suspended and intravenous vancomycin and azithromycin were administered, along with adequate drainage of the abscess. The endobronchial mass was then resected. After the patient's clinical symptoms and chest CT presentation resolved, he was switched to intravenous ciprofloxacin and azithromycin, followed by oral ciprofloxacin and azithromycin. The patient

was re-hospitalized 2 wk after discharge for recurrence of *R. equi* infection. He recovered after another round of adequate abscess drainage and intravenous ciprofloxacin and azithromycin.

CONCLUSION

Infection with *R. equi* in renal transplant recipients is rare and complex, and the clinical presentation lacks specificity. Elaborate antibiotic therapy is required, and adequate abscess drainage and surgical excision are necessary. Given the recurrent nature of *R. equi*, patients need to be followed-up closely.

Key Words: Kidney transplantation; *Rhodococcus equi*; Pleural empyema; Pulmonary atelectasis; Immunosuppression; Case report

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Core Tip: Infection with *Rhodococcus equi* (*R. equi*) is rare in renal transplant recipients. To date, no cases of pleural empyema and endobronchial mass have been reported in renal transplant recipients infected with *R. equi*. We report the diagnosis and management of a renal transplant recipient infected with *R. equi* at 21 mo postoperatively and incorporate a review of the literature to illustrate the characteristics of *R. equi* infection in renal transplant recipients.

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INTRODUCTION

Kidney transplantation is an optimal choice for patients with end-stage renal disease (ESRD), which improves quality of life and prolongs life expectancy compared to other treatments[1,2]. To prevent graft rejection, kidney transplant recipients need to take immunosuppressive drugs long-term, and the use of immunosuppressive drugs can cause them to be susceptible to various infections. The development of rare, hard-to-diagnose infections after transplantation may be a serious threat to survival for kidney transplant recipients[3]. *Rhodococcus equi* (*R. equi*) is a zoonotic bacterium that causes infections in a wide variety of animals such as horses, cattle, pigs, and sheep[4]. *R. equi* is a rare opportunistic pathogen in humans that occurs mainly in immunocompromised populations such as those with human immunodeficiency virus (HIV)-infection, malignancy, and/or organ transplant recipients[5]. As immunosuppressive regimens used in organ transplantation therapy become more complex and widespread, further understanding of this pathogen is critical. We report the diagnosis and treatment of a case of pleural empyema and endobronchial mass caused by *R. equi* infection in a renal transplant recipient 21 mo after the transplantation. We also summarize the characteristics and treatment of *R. equi* infection in renal transplant recipients through a comprehensive literature review to provide clinicians with some experience in the diagnosis and treatment of this rare disease.

CASE PRESENTATION

Chief complaints

Cough and sputum for one week, and fever, chest pain, and chest tightness for one day.

History of present illness

A 25-year-old man underwent allogeneic kidney transplantation in May 2020 for ESRD secondary to chronic glomerulonephritis. The kidney was obtained from a brain-dead donor. His immune-induction regimen was basiliximab and anti-human T-cell porcine immunoglobulin, and his immunization maintenance regimen was tacrolimus (0.5 mg, bid), mycophenolate mofetil (0.5 g, bid), and methylprednisolone (16 mg, qd). One month after surgery, the patient experienced acute rejection, which improved after steroid pulse therapy, and he did not experience delayed graft function. Postoperatively, cotrimoxazole was given to prevent *Pneumocystis carinii* pneumonia, voriconazole to prevent fungal infections, and ganciclovir to prevent viral infections. The other medications he took were nifedipine and irbesartan. One week prior to admission, the patient presented with symptoms of cough and sputum; the sputum was pink and foamy, and the cough was worse at night when lying flat. He attended the local hospital, which thought it was "influenza" and gave him some medication (details unknown). The patient subsequently developed fever with chills, with a maximum temperature of 39.0 °C, followed by chest pain and chest tightness. Immediately, a chest computed tomography (CT) was performed, which revealed a right-sided fluid pneumothorax and a right lower lung abscess. The outpatient diagnosis was pleural empyema, and he was admitted to our department for treatment on February 22, 2022.

History of past illness

The patient had a history of hypertension with blood pressure levels of up to 182/90 mmHg managed through the long-term use of controlled-release nifedipine and irbesartan tablets. He denied any history of diabetes mellitus, coronary artery disease, or tuberculosis.

Personal and family history

The patient was a smoker for 5 years, but had now quit smoking and had no history of alcohol consumption. He denied any history of exposure to tuberculosis. He also denied any recent contact with farm animals such as horses, pigs, and cows and had not recently visited any farm. He did not have any clinically relevant family history.

Physical examination

The initial checkup indicated that the temperature was 38.2 °C, pulse 112/min, respiration 23/min, and blood pressure 144/112 mmHg. Physical examination showed that his general condition was poor: Respiratory movements were slightly rapid, right lower lung fibrillation was weakened, there was no pleural friction, turbidity was noted on percussion in the right lower lungs, right lung respiratory sounds were low. Cardiac and abdominal examination showed no abnormality, and both lower limbs were mildly swollen.

Laboratory examinations

White blood cell count, $9.79 \times 10^9/L$; neutrophil percentage, 77.8%; absolute lymphocyte value, 1.27; lymphocyte percentage, 13.00%; absolute monocyte value, 0.88; and monocyte percentage, 9.00%. Furthermore, serum creatinine was 526.40 $\mu\text{mol/L}$, procalcitonin was 3.40 ng/mL, and ultrasensitive C-reactive protein was $> 20 \text{ mg/L}$.

Imaging examinations

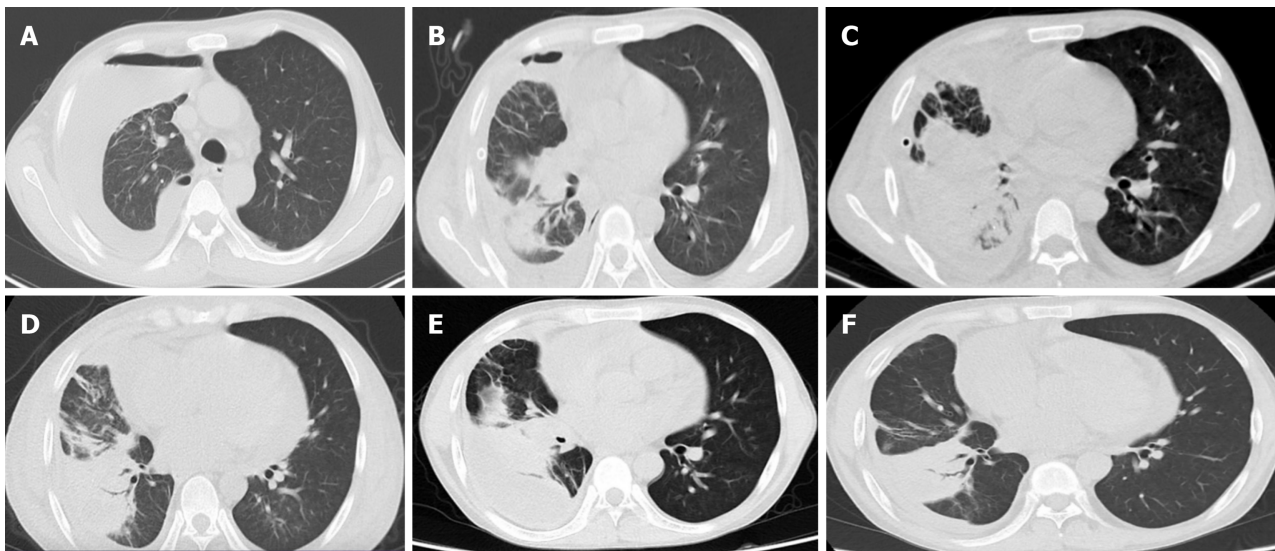
Chest CT suggested the following: Right-sided pneumothorax with multiple fluid within it; right lung with multiple exudates, and right lower lobe abscesses (Figure 1A).

FINAL DIAGNOSIS

Pleural empyema and endobronchial mass.

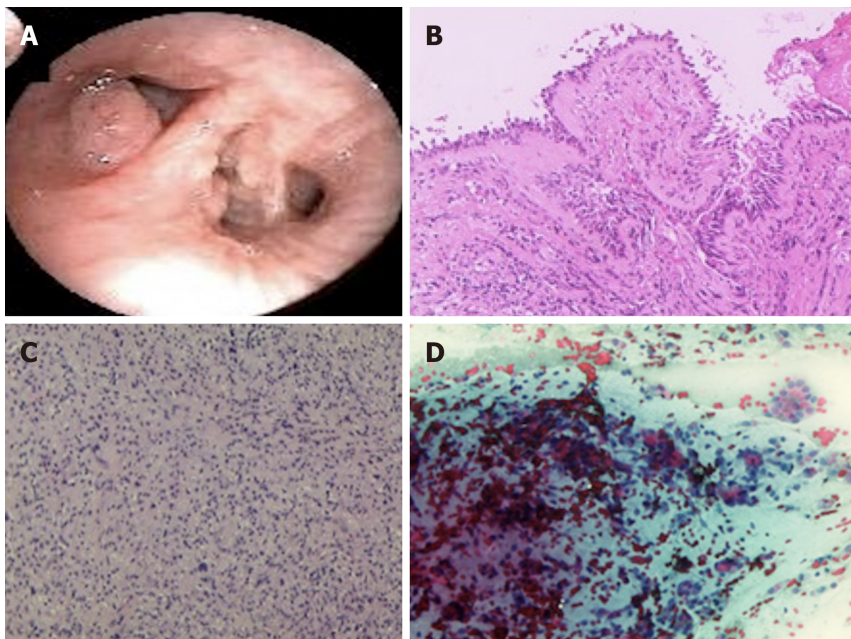
TREATMENT

Yellow pus was withdrawn during diagnostic thoracentesis at the time of the patient's admission. Combined with the chest CT findings, the patient was initially considered to have a pleural empyema, and closed thoracic drainage was performed. To analyze the pathogenic bacteria, the drainage fluid was subjected to bacterial and fungal cultures, acid-fast staining, and Gram's staining, as well as metagenomic next-generation sequencing (mNGS) sequencing. Given the severe infection, the patient was given a suspension of immunosuppressants and empirical anti-infective therapy with piperacillin-tazobactam (4.5 g, q8h). After 3 d of treatment, the patient's symptoms did not improve, his highest recorded temperature was 39.0 °C, and his cough and sputum symptoms were worse than before, with yellow mucus in the sputum. Bacterial culture and mNGS sequencing of the drainage fluid were suggestive of *R. equi* infection. Our department had no experience in the treatment of this disease owing to the rarity of this organism, and there are no relevant treatment guidelines as yet for reference. Therefore, after reviewing the literature and referring to The Sanford Guide to Antimicrobial Therapy, we adjusted the antibiotics to vancomycin (0.5 g, bid) and azithromycin (0.5 g, qd) for intravenous infusion. Afterwards, the patient's clinical symptoms improved, and the cough and sputum were better than before with only occasional fever. After 10 d of antibiotic-altered treatment, the patient's inflammatory indices and renal function improved, and the white blood cell count reduced to $5.64 \times 10^9/L$, neutrophil percentage was 83.70%, and the serum creatinine was 366.00 $\mu\text{mol/L}$. Chest CT suggested improvement of the right pleural empyema and right lower lobe abscess, but development of right middle lobe atelectasis (Figure 1B). Drainage fluid culture was performed again, and the culture result was still *R. equi*. The patient's clinical symptoms resolved, and the antibiotic regimen was switched to ciprofloxacin (200 mg, qd) and azithromycin (0.5 g, qd) for intravenous infusion. After a month of treatment, the patient's cough and sputum improved; he had no fever, chest pain, or chest tightness; and the bacterial culture of drainage fluid was negative. Therefore, the treatment plan was simplified to oral ciprofloxacin and azithromycin. The patient was restarted on low-dose immunosuppression [mycophenolate mofetil 180 mg (bid), tacrolimus 0.5 mg (qd)]. However, chest CT suggested that the right lung middle lobe atelectasis was worse than before (Figure 1C). In view of the patient's right middle lung atelectasis and right lower lung abscess, after multidisciplinary consultation with thoracic surgery, infectious disease, respiratory medicine, and clinical pharmacy, fiberoptic bronchoscopy, instead of surgery, was recommended to identify the cause of lung atelectasis. Interestingly, fiberoptic bronchoscopy revealed a nascent mass in the right middle and lower lobe orifices and symptomatic hypertrophic luminal narrowing of the right pulmonary mucosa (Figure 2A). The mass was biopsied, and histopathology suggested that the mucosa of the right middle and lower lobes of the mouth showed chronic inflammation with fibrous hyperplasia in the lamina propria, with a large number of histiocyte-like cells, but no malignant tumor cells (Figures 2B and C). Immunohistochemistry suggested chronic inflammation of the right middle and lower lobe orifice mucosa with fibrous granulation tissue proliferation (Figure 2D). Taken



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Figure 1 Chest computed tomography scan. A: Right-sided fluid pneumothorax with multiple fluid within it; right lung with multiple exudates, right lower lobe abscesses; B: After drainage of right-sided fluid pneumothorax, the right-sided encapsulated effusion was significantly reduced compared with the previous one, and the pneumoperitoneum had been largely absorbed; the right intrapulmonary exudation and right lower lobe abscess were reduced compared with the previous one; the right middle lobe of the lung was atelectatic; C: Right pleural encapsulated effusion as before; right lower lobe abscess and multiple exudates in both lungs as before; right middle lobe atelectasis was slightly worse than before; D: Right pleural encapsulated effusion absorbed more than before; right lower lobe abscess and multiple right lung exudates reduced more than before; right middle lobe atelectasis as before; E: Right pleural encapsulated effusion was significantly greater than before; right lower lobe abscess and multiple right lung exudates were lesser than before; right middle lobe atelectasis was the same as before; F: Right pleural encapsulated effusion decreased compared to before; right lower lobe abscess and multiple right lung exudates as before; right middle lobe atelectasis as before.



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Figure 2 Biopsy of endobronchial mass. A: Nascent mass at the mouth of the right middle and lower lobes with symptomatic hypertrophic luminal narrowing of the right pulmonary mucosa; B: Fibrinoscopic biopsy: The mucosa shows chronic inflammation. Fibrillar hyperplasia within the lamina propria was seen with a large number of histiocyte-like cells; C: Fiberscope brushing: A large number of erythrocytes and ciliated columnar cells and a few neutrophils and phagocytes are seen; no malignant cells are seen; D: Immunohistochemistry: Chronic inflammation of the mucosa. Fibrous granulation tissue proliferation.

together, the pulmonary atelectasis was considered to be due to this nascent mass, and a bronchoscopic right middle and lower lobe hyperplastic sarcoidectomy, balloon dilatation, and cryosurgery were performed on the 44th d after admission.

Table 1 Features of *Rhodococcus equi* infection in transplant patients in previously reported cases

Number	Year	Age	Sex	Post-transplant (mo)	Radiographic diagnosis	Bacteriological diagnosis	Treatment	Outcome	Ref.
1	2019	67	F	7	Right perihilar mass	BLA culture; TB	Abs	Improved	[17]
2	2021	60	M	108	LUL mass	BC; TB	Abs; surgery	Died	[18]
3	2014	52	F	72	RUL mass	BC, TB	Abs; surgery	Improved	[19]
4	2012	57	M	24	RUL cavity	FNAC	Abs; surgery	Relapsed and then died	[16]
5	2016	49	M	5	SA	PC	Abs	Improved	[20]
6	2015	57	M	7	LLL mass	BC	Abs	Improved	[21]
7	2009	42	F	60	SA, BA	16s rRNA sequencing	Abs	Died	[22]
8	2009	60	M	60	LUL mass	16s rRNA sequencing	Abs	Improved	[23]
9	2008	42	M	48	PA	PC, TB	Abs	Improved	[24]
10	2004	42	M	19	LLL mass	BLAC and FNAC	Abs	Improved	[25]
11	2008	52	M	228	LUL mass, LPE	SC, BLAC, BC	Abs; surgery	Improved	[26]
12	2002	38	F	108	LLL mass	FNAC	Abs	Improved	[27]
13	2000	58	M	NR	LUL mass	FNAC	Abs	Improved	[28]
14	2001	43	M	12	SPN	FNAC	Abs	Improved	[29]
15	1997	48	M	46	Left lung abscess	Blood culture	Abs	Relapsed and then improved	[30]
16	1977	45	F	120	LUL abscess	SC; bronchial brush biopsy	Abs	Died	[31]
17	1988	57	M	72	Osteomyelitis	Bone biopsy	Abs; surgery	Improved	[32]

M: Male; F: Female; BLA: Broncho-alveolar lavage; TB: Tissue biopsy; LUL: Left upper lobe; BC: Blood cultures; Abs: Antibiotics; RUL: Right upper lobe; FNAC: Fine needle aspiration cytology; SA: Subcutaneous abscesses; PC: Pus culture; LLL: Lower left lung; BA: Brain abscess; PA: Pulmonary abscess; BLAC: Broncho-alveolar lavage cultures; LPE: Left pleural effusion; SC: Sputum cultures; NR: Not reported; SPN: Small pulmonary nodules.

OUTCOME AND FOLLOW-UP

The patient's condition improved, and chest CT suggested the following: The right pleural encapsulated effusion was absorbed compared to before; right lower lobe abscess and multiple right lung exudates were reduced compared to before; and right middle lobe atelectasis was the same as before (Figure 1D). He was discharged on April 20, 2022. He was instructed to continue oral anti-infective treatment with ciprofloxacin and azithromycin for 6 months after discharge.

Two weeks after the patient was discharged from the hospital, his chest CT suggested that the right-sided encapsulated effusion was significantly larger than before (Figure 1E), and he was readmitted to the hospital on May 6, 2022. He had no symptoms of fever or cough and sputum. Closed drainage of the right thoracic cavity was performed again and yellow-green pus was drained. Bacterial cultures of the drainage fluid were negative, so mNGS of the drainage fluid was performed, which suggested that this purulent infection was still dominated by *R. equi*. Ciprofloxacin infusion and oral azithromycin were given. After treatment, the right-sided pleural encapsulated effusion was significantly reduced from the previous level (Figure 1F). The patient was discharged on May 25, 2022. His chest CT performed one month after discharge suggested a continued decrease in the right-sided pleural encapsulated effusion.

Literature review

We searched the Embase, PubMed, Web of Science, and Cochrane Library databases for articles related to infection with *R. equi* after renal transplantation in humans, from 1977 to the present. Information collected included year of publication, age, sex, time interval between kidney transplantation and *R. equi* infection, disease diagnosis, mode of diagnosis of *R. equi* infection, treatment, and outcomes. After searching, a total of 17 articles were available, all of which were case reports. Among them, 10 patients were male and 7 were female. The age distribution ranged from 38 to 67 years, and the infections occurred 5–228 mo after transplantation. Most of them had pulmonary involvement, presenting as lung masses, cavities, lung abscesses, and pleural effusions. A small number of concurrent cases presented with subcutaneous abscesses, brain abscesses, and osteomyelitis. Confirmation of the diagnosis of *R. equi* included bacterial culture of blood, sputum, pus, and broncho-alveolar lavage; fine needle aspiration cytology; biopsy of diseased tissue; and 16s rRNA sequencing. All were treated with a combination of two or more antibiotics and some cases were treated with surgical

resection. Twelve patients improved after treatment, four died (one of whom died after recurrence), and one had recurrence (which improved after treatment). Details of these cases are summarized in Table 1.

DISCUSSION

Kidney transplantation is the most effective treatment for patients with ESRD. After kidney transplantation, patients are at risk of severe illness and death due to *R. equi* infections owing to impaired immune function. *R. equi* is a gram-positive surface intracellular parasitic bacterium commonly found in farm animal feces, soil, and water[6], and is a relatively rare human pathogen. It can infect several parts of the body, with the most common being the lung, and is manifested as cavitary lung lesions, lung abscesses, pyothorax, pneumothorax, and invasion of adjacent chest structures[7]. The clinical manifestations lack specificity and mainly include cough, sputum, chest pain, dyspnea, and persistent high fever[8]. When infected with *R. equi*, the mortality rate has been reported to be about 11% in immunocompetent patients, 20%-25% in immunocompromised patients (non-HIV), and up to 50%-55% in patients with HIV infection[9]. This case, combined with literature review, showed four deaths out of 18 patients with a mortality rate of 22%, which is consistent with previous reports. Therefore, prompt diagnosis of *R. equi* infection and early treatment is crucial.

Of note, when our patient underwent fiberoptic bronchoscopy, a nascent mass was found at the mouth of the middle and lower lobes of the right lung, which was diagnosed as an inflammatory granulomatous hyperplasia on histopathologic biopsy. We hypothesized that the endobronchial mass was associated with *R. equi* infection, which has been previously reported as an associated endobronchial mass in addition to pulmonary manifestations in HIV patients infected with *R. equi*[10-12]. To our knowledge, this is the first reported case about a renal transplant recipient who developed pleural empyema combined with endobronchial mass after infection with *R. equi*. Unfortunately however, because of the rarity of the disease and clinical inexperience, the patient's endobronchial mass was detected late, and the affected lung tissue appeared to have potentially irreversible pathologic changes, resulting in poor recovery of pulmonary atelectasis even after surgical resection and treatment. The nascent endobronchial mass may lead to bronchial lumen obstruction and pulmonary atelectasis, which in turn may affect the patient's respiratory function. This emphasizes the need for prompt bronchoscopy in future renal transplant recipients infected with *R. equi*.

At present, there are no guidelines for the treatment of patients infected with *R. equi*, as *R. equi* is an intracellular parthenogenetic parasitic bacterium, in that phagocytosis into and destruction of host macrophage is the basis of its pathogenicity[13]. Therefore, treatment with antibiotics with high intracellular permeability is recommended. According to the latest Sanford Guidelines for Antimicrobial Therapy in the United States, the preferred regimen for the treatment of *R. equi* infections is a combination of at least two of the following drugs, namely azithromycin, levofloxacin, and rifampicin, and the second preferred regimen is the combination antimicrobial treatment of vancomycin or imipenem with any of the following drugs-azithromycin, levofloxacin, or rifampicin. The duration of therapy for *R. equi* depends on the site of infection, the extent of tissue involvement, and the patient's immune function. Renal transplant recipients tend to require longer antibiotic therapy because of immunosuppression, with most reports advocating a minimum of 6 mo of two or more combined antibiotic agents[14]. The initial treatment regimen for *R. equi* in this case was vancomycin combined with azithromycin infusion, and after clinical symptoms resolved, the patient was given an antibiotic regimen of ciprofloxacin combined with azithromycin infusion, which was changed to oral ciprofloxacin and azithromycin for close to one month and was scheduled to be taken orally for up to 6 mo. The patient's symptoms, signs, and chest imaging showed improvement, suggesting that the treatment regimen was feasible and effective. In addition, adequate abscess drainage and surgical resection of the lesion are necessary in addition to proper antibiotic selection[15]. It has been reported that one quarter of organ transplant recipients infected with *R. equi* have relapsed before cure during the treatment[16]. In this case, the patient experienced a relapse 2 wk after discharge from the hospital. Therefore, considering the nature of recurrence of *R. equi*, we should closely follow-up discharged patients.

CONCLUSION

We report the diagnosis and management of a renal transplant recipient with an abscessed chest and endobronchial mass due to *R. equi* infection at 21 mo postoperatively. Since this is a single case report, it is insufficient to establish treatment guidelines for those infected with *R. equi* after renal transplantation. Despite this, we believe that our case report will provide a valuable reference for transplant physicians to help identify post-transplant *R. equi* infections and guide potential treatment.

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FOOTNOTES

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