Pulmonary *Microascus cirrosus* infection in an immunocompetent patient with bronchiectasis: A case report

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**ABSTRACT**

*Microascus* species are widely distributed and rarely cause invasive infection in humans. Here we report a case of lung *Microascus cirrosus* infection in an immunocompetent patient with bronchiectasis. While on systemic voriconazole and aerosolized amphotericin B for three months, the patient’s overall condition improved. This case report highlights the possibility of rare pathogen infection occurred in a bronchiectasis patient, as well as the importance of accurate diagnosis and individualized therapy of pulmonary *Microascus* infection.

1. Introduction

Filamentous fungi *Microascus*, also as teleomorphs of some *Scopulariopsis* species, include both hyaline and dematiaceous mold forms. These genera are widely distributed in the natural environment, such as soil, animal dung and other organic matter [1,2]. In recent decades, *Microascus* species have been found to be pathogenic, particularly in immunocompromised hosts who have hematologic malignancies or those who have undergone solid organ or bone marrow transplantation (BMT) [3,4]. We describe the first case of pulmonary infection caused by *Microascus cirrosus* in an immunocompetent patient. Accurate diagnosis of the uncommon fungi and individualized therapy approaches achieved well clinical prognosis.

2. Case presentation

A 72-year-old female presented with recurrent cough, yellow phlegm and intermittent hemoptysis for over 8 years. Initially, the patient began coughing frequently after a cold with purulent sputum, occasionally with blood-tinged sputum or mild hemoptysis. She was diagnosed with bronchiectasis after a chest computed tomography (CT) examination by local hospital eight years ago. Previous medical records indicated that no fungi were detected in bronchoalveolar lavage (BAL) fluid and sputum. Pulmonary symptoms were usually reduced or alleviated by empirical broad-spectrum antibiotics (levofloxacin, ceftriaxone/tazobactam, biapenem) for about one week and hemostatic therapy (Yunnan Baiyao Capsule, a traditional Chinese medicine) as needed. However, due to progressive aggravation of cough and purulent sputum, gradually appearance of breathlessness and chest tightness for the last two years, and most importantly, increased volume of hemoptysis from less than 10ml at the beginning to occasionally 30–60ml/24h, the patient admitted for further investigation in April 2019. The main symptom on admission was cough with purulent sputum accompanied by bright red blood, about 4–8 times a day and 5–10ml each time. Fever, chills, night sweat, rash or joint pain were denied. The patient reported a history of tuberculosis 10 years ago, and recovered after one year of antituberculosis drug treatment. Beyond that, smoking or drinking were denied, nor did she have a history of hypertension, diabetes, cancers, chronic hepatitis, or blood disease.

At the time of admission, physical examination revealed a thin woman with normal vital signs. The breath sounds of both lungs were coarse, bibasilar crackles were auscultated especially in the right lung. No rhonchi or wheezes. Blood routine suggested mild anemia (hemoglobin 9.8g/dL) with normal white blood cell count. As for inflammatory markers, the level of procalcitonin (PCT) was less than 0.05ng/mL, both erythrocytes sedimentation rate (ESR, 26 mm/h) and hypersensitive C-reactive protein (hs-CRP, 2.1mg/L) were increased slightly. No significant abnormalities were found in blood coagulation function, liver and kidney function, and anti-neutrophil cytoplasmic antibody. Chest CT indicated bronchiectasis accompanied by infection in the middle and lower lobe of the right lung, multiple patchy infiltrates of both lungs with increased mediastinal lymph nodes (Fig. 1A,B,C). Fibernoptic
bronchoscopy before antibiotic administration (Fig. 2) showed a few dark red blood stains and a lot of purulent secretions in the bilateral bronchus, especially in the right middle lobe and the left superior lobar bronchus. After aspiration, the lumen was unobstructed and the mucosa was smooth. BAL fluid from the right middle bronchus was incubated on slants of Sabouraud’s dextrose agar, many white velvety and brownish-gray pigmented colonies grew after 10 days incubation (Fig. 3). Fungal PCR using 28S rDNA primers identified Microascus cirrosus. Sputum and BAL cultures grew normal flora, with no evidence of viral, mycobacterial, or additional fungal pathogens isolated; likewise, blood cultures remained negative. T-spot test and MTB/RIF GeneXpert detection assays were negative. Both galactomannan enzyme-linked immunosorbent assays and 1,3-β-D-glucan tests were negative in serum and BAL fluid.

Given these findings, the patient was diagnosed with a pulmonary fungal infection with bronchiectasis. So intravenous (oral after discharge) voriconazole 200 mg twice daily and aerosolized amphotericin B 12.5 mg twice daily were initiated for empiric treatment in April 2019. The blood concentration of voriconazole when administered orally was 2.1 μg/mL (therapeutic window: 2–6 μg/mL). While on combinational antifungal treatment, the patient presented resolution of hemoptysis, as well as remission of cough, wheezing and chest tightness. Two months later, chest CT demonstrated a slight improvement (Fig. 1D, E, F). Repeat bronchoscopy on Day 77 denoted no distinct abnormality in the visible airway are more likely to develop fungal colonization [14]. In this case we believe that the M. cirrosus infection occurred after bronchiectasis because no evidence indicted any fungi colonization or infection according the previous medical records. Therefore, in patients with bronchiectasis, significantly worsened condition should be of concern to the clinician, as there may be a rare pathogen infection rather than simply exacerbation of bronchiectasis. In addition, a regimen of multiple antibacterial drugs for an extended amount of time may be a second predisposing factor for fungal infections. BAL fluid was considered as nonsterile clinical specimen, so positive culture could still be questionable [6]. In a previous literature [4], although M. gracilis was isolated in

3. Discussion

Although Microascus is commonly found in different habitats and decaying organic matter, except for one case which was later reclassified as M. gracilis, only five publications concerning M. cirrosus infections have been reported to date [3, 5, 6]. In addition, respiratory infection was involved in just three immunosuppressed patients, with two received BMT for acute myelogenous leukemia and one underwent bilateral lung transplant for severe emphysema [7–9].

In the past, Sco/ulripis/Microascus are distinguished only by morphological characteristics [10], but different culture requirements for incubation temperature and time may affect the culture’s ability to sporulate and lead to misidentification [11]. Recently the development of molecular methods and multigene phylogenetic analysis have promoted the identification of these fungi [10, 12, 13]. Real-time PCR assay targeting 28S ribosome sequence has been recommend to detect Sco/ulripis/Microascus rapidly [8]. The combination of morphology and molecular tools would be more beneficial to the accurate and quick identification to the fungal species.

Since Microascus species have wide geographic distribution, clinicians should distinguish between infection and colonization. Patients with bronchiectasis due to irreversible anatomical distortion of the airway are more likely to develop fungal colonization [14]. In this case we believe that the M. cirrosus infection occurred after bronchiectasis because no evidence indicted any fungi colonization or infection according the previous medical records. Therefore, in patients with bronchiectasis, significantly worsened condition should be of concern to the clinician, as there may be a rare pathogen infection rather than simply exacerbation of bronchiectasis. In addition, a regimen of multiple antibacterial drugs for an extended amount of time may be a second predisposing factor for fungal infections. BAL fluid was considered as nonsterile clinical specimen, so positive culture could still be questionable [6]. In a previous literature [4], although M. gracilis was isolated in
BAL fluid from two patients with lung transplantation, they were diagnosed as colonization and did not need additional treatment due to the absence of clinical manifestations and pulmonary imaging changes. However, given our patient’s aggravated pulmonary symptoms and worsening CT with the presence of a new infiltrate, opportunistic Microascus infection was considered. All specimens from blood, sputum, and BAL fluid for pathogen detection or culture were collected prior to antibiotic administration, but no bacterial infection or colonization were
found, which might help support the likelihood of a fungal infection. This idea was also supported by the fact that symptoms and imaging scan improved after antifungal treatment. But *M. cirrosus* was still cultured positive two months later, so we assume that she might be colonized with *M. cirrosus*.

The incidence of *Microascus* is far less than *Aspergillus* and *Candida*, but because of the resistance to most common antymycotics, the overall prognosis is poor [15]. Despite the results of drug sensitivity in vitro are not ideal, several reports have also shown clinical efficacy of antifungal drugs. Multi-drug combination therapy, added with surgical resection of localized lesion and reconstitution of the immune system if necessary, may be a promising choice for *Microascus* infection [2]. In the latest report, a bilateral lung transplant recipient who developed invasive lung infection caused by *M. cirrosus* was successfully cured by a combined treatment consisting of four antifungal agents (voriconazole, terbinafine, amphotericin B, and caspofungin) and endoscopic resection of necrosed bronchial mucosa [9]. The patient in our study was given an antifungal combination therapy of voriconazole and amphotericin B. Considering the patient’s bronchiectasis, in addition to systemic voriconazole, amphotericin B was given via nebulizer twice a day to provide therapeutic dosing and sustain long enough at the site of the infection, while minimizing the side effects associated with systemic administration [16,17]. Although she was not having massive hemoptysis, Yunnan Baiyao Capsules, a traditional Chinese medicine for hemostasis was prescribed, which was discontinued after the resolution of hemoptysis. Her anemia improved although still not within the reference range. It is worth mentioning that the patient might have some vascular infiltration by *M. cirrosus*, so interventional therapy was advised by cardiothoracic surgery if the patient couldn’t achieve favorable effects with antifungal drugs or the patient developed life-threatening hemoptysis. Fortunately, the overall condition improved after antifungal therapy, so surgical treatment was not considered. Despite the patient’s transient antifungal-induced liver injury, the prognosis was good after evaluation of the patient’s pulmonary symptoms and imaging findings and withdrawal of antifungal agents. No progression during another year of follow-up. Therefore, antifungal drugs should be tailored to the individual patient with side effects be monitored such as hepatotoxicity in this case.

4. Conclusion

The case presented an experience of management and treatment of a rare but clinically significant pulmonary infection caused by *Microascus cirrosus* in an immunocompetent patient with bronchiectasis.

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**Patient consent**

The patient in this case report was well informed and signed the informed consent.

**Author contributions**

Conceptualization: Qian Liu, Shuyun Xu.

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**Declaration of competing interest**

The authors declare that they have no conflict of interest.

**References**

[1] M. Sandoval-Denis, D.A. Sutton, A.W. Forbergili, J. Cano-Lira, J. Gene, C. A. Decock, et al., Scopulariopsis, a poorly known opportunistic fungus: spectrum of species in clinical samples and in vitro responses to antifungal drugs, J. Clin. Microbiol. 51 (12) (2013) 3937–3943, https://doi.org/10.1128/JCM.01927-13.

[2] L. Yao, Z. Wan, R. Li, J. Yu, In vitro triple combination of antifungal drugs against clinical scopulariopsis and Microascus species, Antimicrob. Agents Chemother. 59 (8) (2015) 5040–5043, https://doi.org/10.1128/AAC.00145-15.

[3] L. Gao, J. Chen, D. Gao, M. Li, Primary cutaneous infection due to Microascus cirrosus: a case report, BMC Infect. Dis. 18 (1) (2018) 604, https://doi.org/10.1186/s12879-018-3555-5.

[4] L. Huang, W. Chen, L. Guo, L. Zhao, B. Cao, Y. Liu, et al., *Scopulariopsis/Microascus* isolation in lung transplant recipients: a report of three cases and a review of the literature, Mycoses 62 (10) (2019) 883–892, https://doi.org/10.1111/myc.12952.

[5] C. Miosec, F. Morio, T. Lepoivre, et al., Fatal invasive infection with fungemia due to *Microascus cirrosus* after heart and lung transplantation in a patient with cystic fibrosis, J. Clin. Microbiol. 49 (7) (2011) 2743–2747, https://doi.org/10.1128/JCM.00177-11.

[6] A. Perez-Cantero, J. Guaro, Current knowledge on the etiology and epidemiology of *Scopulariopsis* infections, Med. Mycol. 58 (2) (2020) 145–155, https://doi.org/10.1093/mmy/myz060.

[7] K.K. Keiser, N.B. Holdridge, M.M. Mustafa, M.G. Rinaldi, D.A. McGough, Disseminated *Microascus cirrosus* infection in pediatric bone marrow transplant recipient, J. Clin. Microbiol. 33 (3) (1995) 735–737, https://doi.org/10.1128/JCM.33.3.735-737.1995.

[8] C. Ustun, G. Huls, M. Stewart, K.A. Marr, Resistant *Microascus cirrosus* pneumonia can be treated with a combination of surgery, multiple anti-fungal agents and a growth factor, Mycopathologia 162 (4) (2006) 299–302, https://doi.org/10.1007/s11046-006-0067-0.

[9] O. Tatton, B. Bernier, I. Etienne, B. Bontdue, S. Lecomte, C. Knoop, et al., Necrotizing *Microascus tracheobronchitis* in a bilateral lung transplant recipient, Transpl. Infect. Dis. 20 (1) (2018), https://doi.org/10.1111/tid.12806.

[10] M. Sandoval-Denis, J. Gene, D.A. Sutton, J.F. Cano-Lira, G.S. de Hoog, C.A. Decock, et al., Redefining *Microascus*, *scopulariopsis* and allied genera, Persoonia 36 (2016) 1–36, https://doi.org/10.3767/003158516X688027.

[11] J.W. Baddeley, S.A. Moser, D.A. Sutton, P.G. Pappas, *Microascus cinereus* (Anamorph *scopulariopsis*) brain abscess in a bone marrow transplant recipient, J. Clin. Microbiol. 38 (1) (2000) 395–397, https://doi.org/10.1128/JCM.38.1.395-397.2000.

[12] T. Jagiełski, M. Sandoval-Denis, J. Yu, L. Yao, Z. Bakula, J. Kalita, et al., Molecular taxonomy of scopulariopsis-like fungi with description of new clinical and environmental species, Fungal Biol 120 (4) (2016) 586–602, https://doi.org/10.1016/j.fbi.2016.01.014.

[13] J.H.C. Woudenberg, M. Meijer, J. Houbraken, R.A. Samson, *Scopulariopsis* and *scopulariopsis*-like species from indoor environments, Stud. Mycol. 88 (2017) 1–35, https://doi.org/10.3767/003158516X688027.

[14] R. Chandrasekaran, M. Mac Aogain, J.D. Chalmers, S.J. Elborn, S.H. Chotirmall, Geographic variation in the aetiology, epidemiology and microbiology of bronchiectasis, BMC Pulm. Med. 18 (1) (2018) 83, https://doi.org/10.1186/s12890-018-0638-0.

[15] M. Skora, M. Bulanda, T. Jagiełski, In vitro activities of a wide panel of antifungal drugs against various Scopulariopsis and Microascus species, Antimicrob. Agents Chemother. 59 (9) (2015) 5827–5829, https://doi.org/10.1128/AAC.00978-15.

[16] K.E. Schoeppler, M.R. Zamora, N.M. Northcutt, G.R. Barber, G. O’Malley-Schroeder, D.M. Lyu, Invasive *Microascus* *ergonosporus* species complex pulmonary infection in a lung transplant recipient, Case Rep Transplant (2015) 2015 (2015) 745638, https://doi.org/10.1155/2015/745638.

[17] T.E. Corcoran, Aerosol drug delivery in lung transplant recipients, Expert Opin. Drug Deliv. 62 (2) (2009) 139–148, https://doi.org/10.1517/17425250802683352.