



The first case of subcutaneous mycosis caused by *Muyocopron laterale* in China

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ABSTRACT

Muyocopron laterale is a type of endophytic fungus that parasitizes monocotyledonous plants. Cases of humans and other mammals being infected by *M. laterale* are very rare around the world. We report the first case of subcutaneous mycosis caused by *M. laterale* in China. A kidney transplant recipient was admitted for *Pneumocystis carinii* pneumonia and subsequently developed left calf redness and swelling due to a *M. laterale* infection. The patient was treated with sulfamethoxazole and voriconazole and underwent five surgical debridements and vacuum sealing drainage (VSD) applications with the left leg. The patient was eventually cured and discharged from the hospital.

1. Introduction

Endophytic fungi have gained attention as a novel microbial resource for new bioactive products. Many studies now concentrate on utilizing endophytic fungi for their ability to produce bioactive compounds and as biocontrol agents. Most research on endophytic fungi has focused on their pathogenic or beneficial relationships with plants. Reports of endophytic fungi infecting humans are exceedingly rare.

Muyocopron laterale is a dematiaceous, endophytic fungus that parasitizes monocotyledonous plants [1] and has rarely been reported from human infections. We report a case of a 52-year-old man with kidney transplantation and diabetes mellitus who was admitted to the hospital with *Pneumocystis carinii* pneumonia and was infected with *M. laterale* in his left calf, which is the first report of *M. laterale* infection in humans in China.

2. Case

The patient, a 52-year-old man, was admitted with stable vital signs and symptoms of a pulmonary infection on day 0 after working on a vegetable farm and in a pig slaughterhouse for a long time. On day 1, laboratory test results revealed the following: white blood cell count was $5.99 \times 10^9/L$, neutrophil percentage was 93.9 %, fungal D-glucan test result was 210.63 pg/ml, and high-sensitivity C-reactive protein was 88.98 mg/L. On day 2, the patient's blood metagenomics next-generation sequencing (mNGS) revealed *Pneumocystis carinii* and

Cytomegalovirus (CMV). Upon admission, the patient was treated with a combination of medications including sulfamethoxazole for *P. carinii* therapy, caspofungin for antifungal treatment, and methylprednisolone for immunomodulation. The medical professional administered piperacillin sodium-tazobactam and cefuroxime antibiotics consecutively, while also providing antiviral treatment with acyclovir to the patient. On the 15th day of admission, the patient's respiratory symptoms significantly improved, and a CT scan showed a marked decrease in lung infection compared to the previous scan (Fig. 1). On the 11th day, the patient developed redness, a small ulcer, and black spots on the lateral aspect of his lower left leg. The ulcer was treated with disinfection and saline irrigation, and silver ion dressings were applied. The culture of ulcer secretions yielded negative results. On the 24th day, a first surgical repair of the chronic ulcer on the left lower leg was performed, with deep soft tissue debridement and drainage, and was given vacuum sealing drainage (VSD) after the operation. Tissue and pus samples from the lower leg were sent to the laboratory for detection during the operation (Fig. 2). The samples were incubated at 35 °C for 7 days, and filamentous fungi were observed on Columbia blood agar and Sabouraud agar (Fig. 3). The cultured organisms were stained with lactophenol cotton blue and fluorophores (Fig. 4). Under the microscope, the hyphae were transparent, smooth, and septate with thick walls. The conidia had a variety of shapes and sizes, ranging from single round cells to large clusters of conidia, and had unbranched appendages at each end. We performed ITS sequence analysis since Maldi-tof failed to identify the cultured organism. The amplification was performed using the fungal

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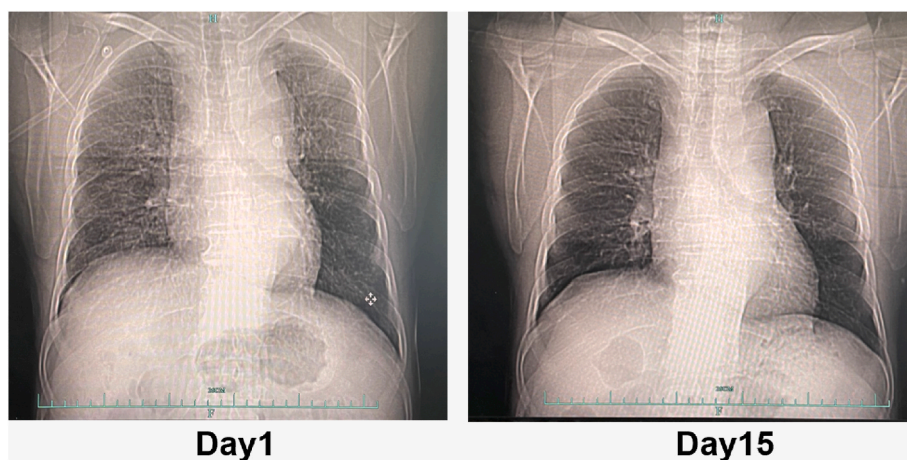


Fig. 1. The CT-thorax showing a marked decrease in infiltrative abnormalities after 14 days of treatment.

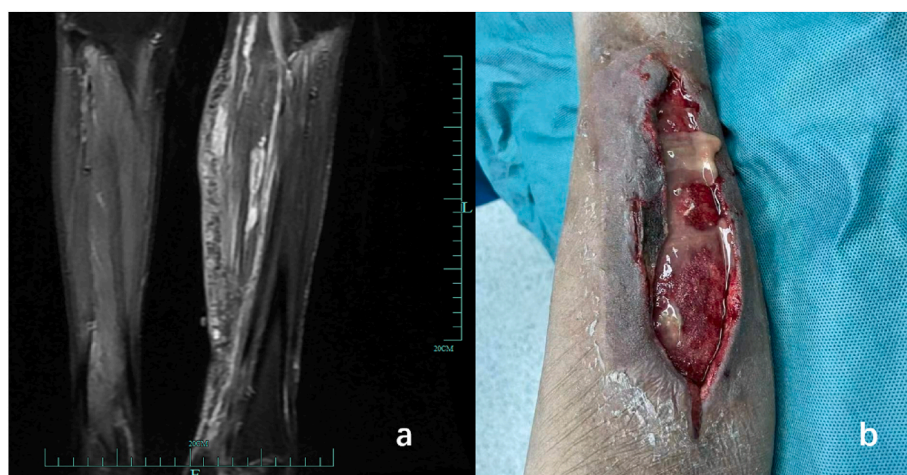


Fig. 2. (a) The CT scan of the left lower leg showing infiltrative abnormalities. (b) During surgery, the incision of a long-lasting ulcer on the lower left leg shows a significant presence of yellow pus. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

ITS1 primer (5'-TCCGTAGGTGAACCTGCGG-3'). The sequence analysis indicated a 100 % match with *M. laterale* strain IMI 324533 (GenBank: MK487739.1). We registered the measured sequence in GenBank with accession number OR616707. After analyzing the culture results, we suspected a mixed infection and modified the antibiotic treatment plan to incorporate daptomycin and voriconazole. Additional surgical repair of the chronic ulcer on the left lower leg was performed, involving deep tissue debridement with drainage, and VSD on day 26, day 33, and day 40, respectively. On the 47th day, a final leg surgery was conducted. The surgical team observed an intraoperative granulomatous hyperplasia in the wound, and there was less pus exudation than before on the medial extrusion of the wound. We proceeded to remove the necrotic inactivated tissues, trim the wound margins, perform intramuscular interspace debridement, and inserted a drainage tube. Copious saline rinses and iodophor flushes were carried out, and an artificial dermis was implanted. After five rounds of removing tissue (debridement), we took samples of the pus and tissues from the wound to test for bacteria and fungi. During the first detection, we observed some smooth hyphae of filamentous fungi under KOH smear (Fig. 4). We used Gram stains of the pus, which revealed fungal hyphae and numerous polymorphonuclear cells (Fig. 4). In the first four detections, we isolated filamentous fungi from the pus and tissue samples. However, no filamentous fungi were found in the samples from the last surgery. On the 50th day, the patient's symptoms of *Pneumocystis pneumonia* (PCP) significantly improved, and the leg wound healed without exudate. The patient was discharged

home with instructions for regular wound care and a prescription for oral voriconazole 400 mg daily for two months, which was changed to 200 mg/day until the second hospitalization for leg problems.

The patient was readmitted to the hospital due to several lipomas on his left lower leg, more than four months after he was discharged. Following admission, the patient had surgery to remove the soft tissue growth on his left lower leg. During the procedure, the mass was found to be necroinflammatory but was successfully removed and sent for culturing. Cultures of the tissue were negative. Histopathology showed adipose tissue with fibrous tissue hyperplasia, acute and chronic inflammatory cell infiltration, granulation tissue hyperplasia, and focal necrosis (Fig. 5). He was hospitalized for 20 days and was discharged with a fair recovery of the lower leg after the operation. The patient's condition remains stable with no leg infection recurrence during follow-up.

3. Discussion

PCP is a severe and difficult-to-diagnose fungal infection that may occur after renal transplantation and is often accompanied by multiple complications and has poor prognosis [2]. The clinical diagnosis of PCP was primarily based on the patient's history, clinical manifestations, and chest CT imaging. Although microbiology is the gold standard for diagnosis, its detection rate is relatively low. Our patient had undergone renal transplantation and was on long-term immunosuppressants. A

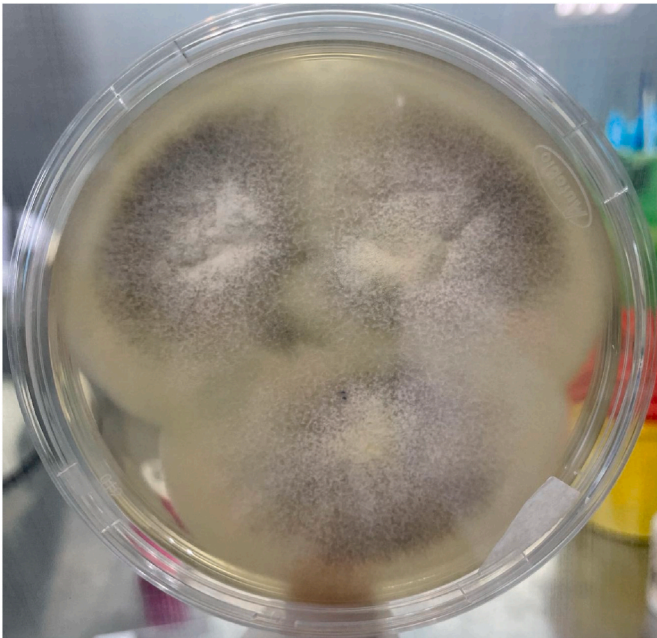


Fig. 3. Morphology of filamentous fungal colonies on Sabouraud agar after 7 days of incubation at 35 °C.

lung CT revealed the presence of diffuse ground glass foci and exudative changes in both lungs. But the patient's general condition was poor, and he was not able to undergo fiber bronchoscopy. Therefore, we obtained the patient's permission and sent the blood for mNGS to determine the

underlying cause. mNGS enables the identification and genomic characterization of bacteria, fungi, parasites and viruses from clinical specimens without prior knowledge of specific pathogens [3]. It is a powerful tool for detecting pathogens and shortens the time needed to find the target pathogen. mNGS test results of the patient indicated coinfection with *P. carinii* and *CMV*. *CMV* infection and allograft rejection are independent predictors of PCP [4]. Sulfamethoxazole is commonly used as the first-line drug for treating PCP. In this case, after the patient was treated with sulfamethoxazole, his lung symptoms were significantly

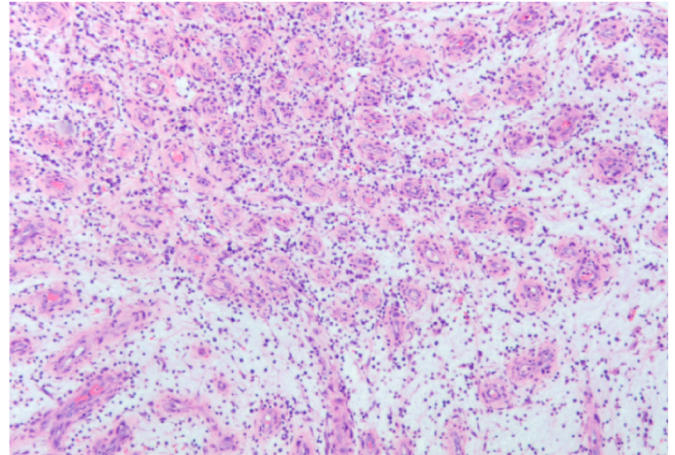


Fig. 5. Histopathology revealed adipose tissue with fibrous and granulation tissue hyperplasia, and acute and chronic inflammatory cell infiltration, as well as focal necrosis.

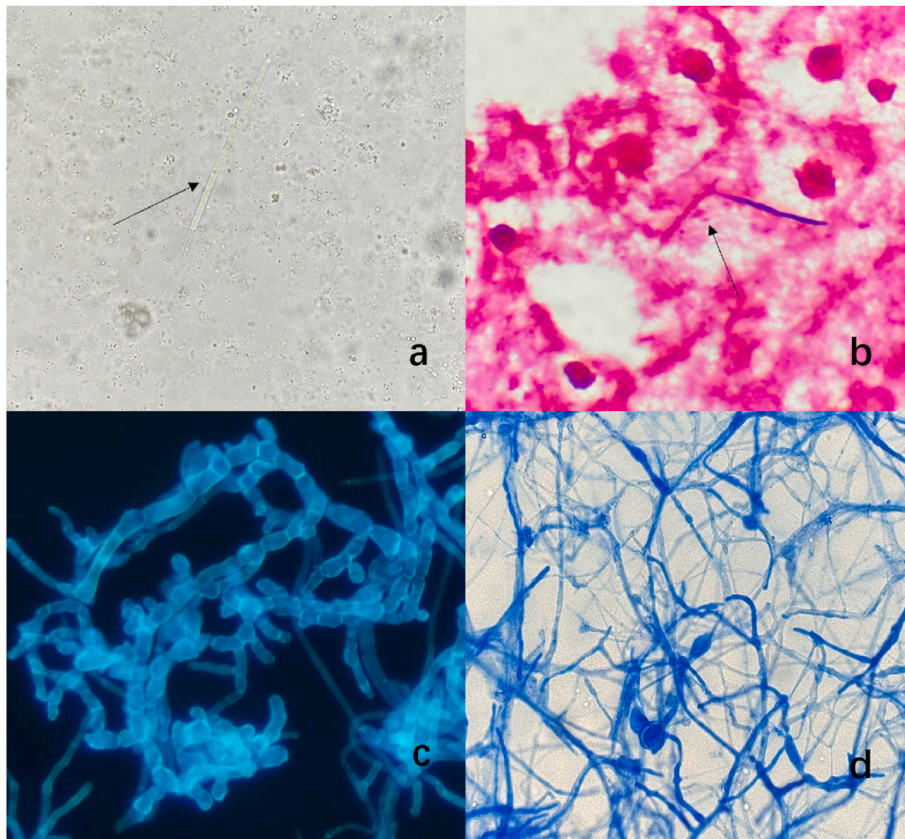


Fig. 4. Microscopic morphologies of the filamentous fungal isolate (a) KOH smear of the pus. (b) Gram staining of the pus. (c) Fluorescence staining of the isolates. (d) Lactophenol cotton blue staining of the isolates. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

reduced and improved. The patient continued taking sulfamethoxazole for a year after being discharged from the hospital.

Endophytic fungi have been widely reported for their ability to aid in the defense of their host plants [5]. Some have specialized, irregularly shaped appressoria to attach to plant surfaces and invade host cells, promoting fungal infection [6]. Such fungi rarely cause infections in humans. *M. laterale* previously incorrectly referred to as *Mycocleptodiscus indicus*, is one kind of endophytic fungi that can cause phaeohyphomycosis [1]. Human and animal infections have been published under both names [7–10].

Jiang et al. reported the first instance of *Muyocopron laterale* infection in plants in China [11], while Lye et al. reported the first case of infection in an immunocompromised patient [12]. Unfortunately, the patient's outcome was poor despite limb amputation. We are pleased to report the first successful treatment and cure of *M. laterale* infection in an immunocompromised human in China.

Infections caused by filamentous fungi of the skin and soft tissues can be challenging and require prolonged treatment. The first-line antifungal treatment recommendations for subcutaneous mycoses caused by phaeohyphomycosis are itraconazole or voriconazole [13]. Long-term surgical and management therapy is necessary for treating filamentous fungal infections of skin tissues. Our patient had undergone renal transplantation and was diagnosed with diabetes mellitus, both of which increased the risk of developing fungal infections. After detecting filamentous fungi in the initial surgical culture, the patient was prescribed voriconazole as part of the antifungal treatment. Additionally, the patient underwent five surgical debridements and VSD application, which likely played a crucial role in controlling the fungal infection in his leg.

When filamentous fungi invade the skin and muscle tissue of immunocompromised patients, it can lead to fatal infections that require urgent attention. It is crucial to identify the type of fungal infection accurately and early, to begin the appropriate therapy to control the condition. Therefore, we require improved surveillance and diagnostic tests to detect infections and potential sources of infection sooner.

CRediT author contribution

TingtingYang: Responsible for case collection and analysis, draft writing.

YikaiDing: Responsible for the culture and identification of samples.

YajieFu: Helped perform the analysis with constructive discussions and was responsible for patient follow-up.

HongchaoChen: Writing - Review & Editing.

Conflict of interest

The authors declare no conflict of interest.

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Ethical approval statement

Written informed consent was obtained from the patient for

publication of this case report and accompanying images. A copy of the written consent is available for review by the editor of this journal on request.

Ethical form

TingtingYang, YikaiDing, YajieFu, HongchaoChen.

Funding source

There are none.

Consent

Written informed consent was obtained from the patient or legal guardian(s) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Declaration of competing interest

We declare that they have no competing interests.

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