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ABOUT COVER

Peer Reviewer of *World Journal of Clinical Cases*, Sanjeet Singh Avtaar Singh, MBChB, MSc, PhD, Department of Cardiothoracic Surgery, Royal Infirmary of Edinburgh, Edinburgh EH16 4SA, United Kingdom. sanjeetsinghtoor@gmail.com

AIMS AND SCOPE

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.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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CASE REPORT

Successful treatment of *Purpureocillium lilacinum* pulmonary infection with isavuconazole: A case report

Xue-Lin Yang, Jun-Yu Zhang, Jian-Min Ren

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Xue-Lin Yang, Department of Emergency Medicine, Lishui Central Hospital, Lishui 323000, Zhejiang Province, China

Jun-Yu Zhang, Department of Hematology, Lishui Central Hospital, Lishui 323000, Zhejiang Province, China

Jian-Min Ren, Department of Clinical Laboratory, The Fifth Affiliated Hospital of Wenzhou Medical University, Lishui 323000, Zhejiang Province, China

Corresponding author: Jun-Yu Zhang, MD, MM, Associate Chief Physician, Chief Doctor, Department of Hematology, Lishui Central Hospital, No. 289 Kuocang Road, Lishui 323000, Zhejiang Province, China. zhangjunyu815@163.com

Abstract

BACKGROUND

Purpureocillium lilacinum (*P. lilacinum*) is a saprophytic fungus widespread in soil and vegetation. As a causative agent, it is very rarely detected in humans, most commonly in the skin.

CASE SUMMARY

In this article, we reported the case of a 72-year-old patient with chronic lymphocytic leukemia who was admitted with cough and fever. Computed tomography revealed an infection in the right lower lobe. Bronchoalveolar lavage fluid culture and metagenomic next-generation sequencing were ultimately confirmed to have a pulmonary infection with *P. lilacinum*. She was eventually discharged with good outcomes after treatment with isavuconazole.

CONCLUSION

Pulmonary infection with *P. lilacinum* was exceedingly rare. While currently there are no definitive therapeutic agents, there are reports of high resistance to amphotericin B and fluconazole and good sensitivity to second-generation triazoles. The present report is the first known use of isavuconazole for pulmonary *P. lilacinum* infection. It provides new evidence for the characterization and treatment of clinical *P. lilacinum* lung infections.

Key Words: *Purpureocillium lilacinum*; Pulmonary infection; Isavuconazole; Case report

Core Tip: Pulmonary infection caused by *Purpureocillium lilacinum* (*P. lilacinum*) is exceedingly rare, with uncharacteristic clinical symptoms, signs, and imaging findings. In this case, we reported an older woman with chronic lymphocytic leukemia, long-standing ibrutinib, poor immune function, and fever and cough was admitted to a hematologic department. The patient was diagnosed with *P. lilacinum* pulmonary infection based on bronchoalveolar lavage fluid culture and metagenomic next-generation sequencing. Conventional antifungal agents often have inherent resistance. Isavuconazole was found to have good safety and efficacy. This is the first known use of isavuconazole for pulmonary *P. lilacinum* infection. After treatment with isavuconazole, the clinical symptoms of cough and fever improved, and the patient was discharged from the hospital.

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INTRODUCTION

Purpureocillium lilacinum (*P. lilacinum*) is a saprophytic fungus widely found in soil and vegetation and a common contaminant detected in laboratories and instruments. In 1977, Takayasu *et al*[1] first reported that *P. lilacinum* causes skin infections in humans[1]. However, since then, only a few sporadic cases of infection have been reported worldwide. These cases were found in both immunocompetent and immunocompromised populations, most commonly in the skin but exceedingly rarely in the lungs[2,3]. While there are no standardized treatments for *P. lilacinum* infection, there are reports of high resistance to amphotericin B and fluconazole and good sensitivity to second-generation triazoles[4,5]. Herein, we reported a case of pulmonary infection caused by *P. lilacinum* successfully treated with isavuconazole, and reviewed the relevant literature.

CASE PRESENTATION

Chief complaints

A 72-year-old female with fever and chest tightness coughing sputum for 1 month presented at our emergency department.

History of present illness

The patient had no history of present illness.

History of past illness

She had an 11-month history of chronic lymphocytic leukemia and was treated with long-term, regular ibrutinib antitumor therapy.

Personal and family history

The patient had no notable personal or family history.

Physical examination

Her physical examination was as follows: Clear consciousness, blood pressure 112/63 mmHg (14.896/8.379 kPa), respiratory rate 24/min, heart rate 102/min, body temperature 38.2 °C, fingertip oxygen saturation 98%, and moist rales in the right lung.

Laboratory examinations

White blood cell 10.6 × 10^9/L (Normal range: 3.5 × 10^9/L to 9.5 × 10^9/L), neutrophils percentage 70.2% (Normal range: 40% to 75%), hemoglobin 98 g/L (Normal range: 115 g/L to 150 g/L), platelets 310 × 10^9/L (Normal range: 125 × 10^9/L to 350 × 10^9/L), and C-reactive protein 67 mg/L (Normal range: 0 mg/L to 8 mg/L). Procalcitonin 0.35 ng/mL (Normal range: 0 ng/mL to 0.05 ng/mL). Fungal D-glucan, galactomannan test and aspergillus IgG antibodies were all normal.

Imaging examinations

Computed tomography (CT) revealed an infection in the right lower lobe (Figure 1A and B).

Additional diagnostic work-up

After admission to the hospital, the patient was given oxygen, and because her etiology was unknown, we administered empiric cefoperazone-sulbactam for anti-infection. Three d post-treatment, the patient remained feverish and chest

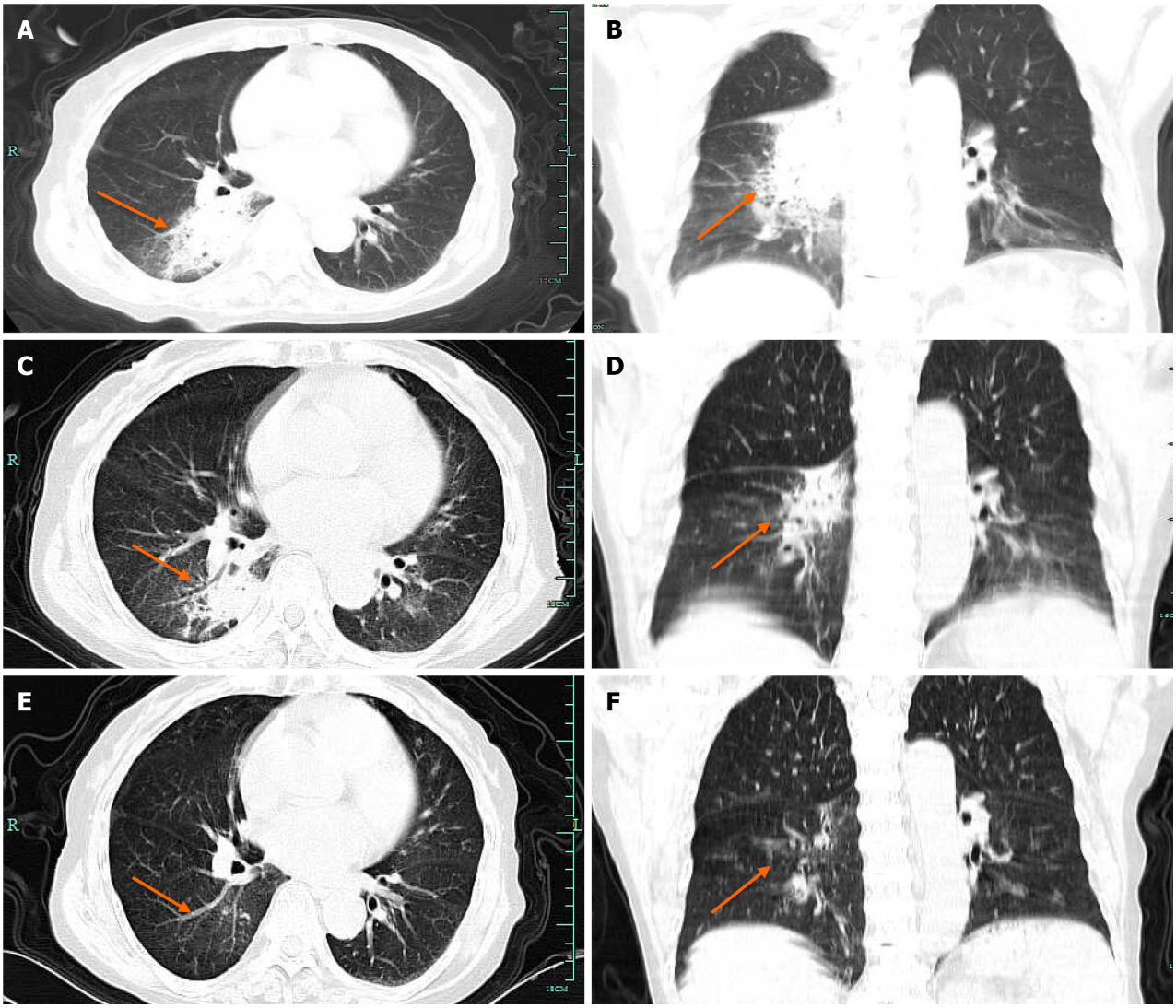

Figure 1 Chest computed tomography on admission and post-treatment. A: Pulmonary consolidation in the posterior segment of the right lower lobe at admission [axial thorax computed tomography (CT) view); B: Mass consolidation in the posterior segment of the right lower lobe at admission (coronal thorax CT view); C: Lesion reduction in pulmonary consolidation in the posterior segment of the right lower lobe after 2 wk of isavuconazole treatment (axial thorax CT view); D: Lesion reduction in pulmonary consolidation in the posterior segment of the right lower lobe after 2 wk of isavuconazole treatment (coronal thorax CT view); E: Significant absorption of pulmonary consolidation in the posterior segment of the right lower lobe at 6 wk of discharge (axial thorax CT view); F: Significant absorption of pulmonary consolidation in the posterior segment of the right lower lobe at 6 wk of discharge (coronal thorax CT view).

tightness remained unresolved. Bronchoscopy was performed to identify the causative agent. On day 7, the colonies were approximately 3.0 cm in diameter, and the purplish colony were concentric (Figure 2A and B). Microscopic examination of the microbiota was performed, and clear, colorless, branching hyphae were observed, and the spores were infarct (Figure 2C). *P. lilacinum* was identified by the Vitek® MS Full Automated Rapid Microbiota Spectrometry System with a confidence interval of 99.9%. *In vitro* drug susceptibility for *P. lilacinum* was as follows: Amphotericin B = 8 μg/mL, fluconazole = 16 μg/mL, voriconazole = 1 μg/mL, and isavuconazolezole = 1 μg/mL. A sample of 1.5-3 mL of bronchoalveolar lavage fluid (BALF) from the patient was submitted for metagenomic next-generation sequencing (mNGS) analysis, which showed 100% homology with ATCC10114 (AY213665.1) from the GenBank database, and was classified as *P. lilacinum*.

FINAL DIAGNOSIS

The patient was diagnosed with *P. lilacinum* pulmonary infection and chronic lymphocytic leukemia based on medical history, physical examination, laboratory tests, imaging, BALF culture, and mNGS.

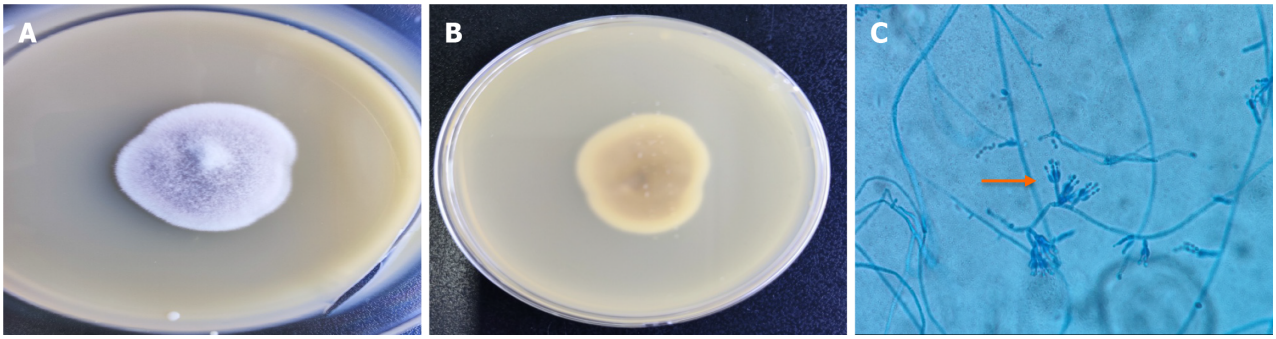

Figure 2 Culture and microscopic examination of the microorganisms. A: Salmonella glucose agar, 28 °C, culture for 7 d, the purplish colony were concentric on the front; B: Yellowish-pale colonies on the back; C: Colorless hyaline branching filaments were observed under light microscopy, and the spores were erect, with a broomy tip and a cone-shaped, fine bony tip at the base of the flask. The spores were mainly oval or near-spherical in shape, and the chains were cylindrical or discrete.

TREATMENT

Based on pathogenic studies and *in vitro* drug sensitivity, we used voriconazole 200 mg tablets every 12 h for antifungal therapy. After 3 d, the patient presented with hallucinations and involuntary tremors of the hands and feet, which were considered adverse events associated with voriconazole. The patient stopped using voriconazole and was given isavuconazole tablets (200 mg every 8 h for the first 48 h, 200 mg once daily after 48 h) followed by antifungal therapy. The hallucinations and tremors of the hands and feet disappeared after 12 h of voriconazole. After 72 h of administration, her body temperature returned to normal, and cough and chest tightness improved after 1 wk.

OUTCOME AND FOLLOW-UP

The patient was discharged from the hospital on day 14, continuing to take isavuconazole for 3 wk, during which time she experienced no significant adverse effects. At one week after discharge, re-examination using chest CT revealed reduced lung lesions (Figure 1C and D). At 6 wk after discharge, chest CT was performed again, and the pulmonary lesions were essentially absorbed (Figure 1E and F).

DISCUSSION

P. lilacinum is a fungus found in a wide range of habitats. In 1974, Samson classified it as a penicillium-like genus based on the characteristic cone-shaped distortion of the top of the flask[6]. Cultural identification of *P. lilacinum* is based on its pale-violet colony color and characteristic flask morphology, and genetic sequencing of the strain may provide a more accurate identification method for clinicians[7]. *P. lilacinum* is rarely found in humans and is generally not considered a pathogenic mold. However, sporadic cases have been reported worldwide since 1977, when it was first described as a skin infection. It predominantly presents as a skin infection, posing the highest threat for immunocompromised patients. Sprute *et al*[8] analyzed 101 cases of invasive *P. lilacinum* infection, found that the youngest patient was 31, and the oldest was 64; male accounted for 61.1%; 31 cases (30.7%) with hematologic and neoplastic disease, 27 (26.7%) with steroid therapy, 26 (25.7%) with solid organ transplantation, and 19 (18.8%) with diabetes mellitus, with the skin being the most common site of infection (36.6%); fever, cough, and dyspnoea were the most common clinical symptoms of pulmonary infection; overall mortality was 21.8%[8].

In the present case, an older woman with chronic lymphocytic leukemia, long-standing ibrutinib, poor immune function, and fever and cough was admitted to a hematologic department and initially considered to be infected with bacteria. She was injected with cefoperazone-sulbactam as an anti-infection therapy, with no good effect.

Identifying *P. lilacinum* is challenging, and its histomorphology is very similar to that of *Aspergillus* and other hyaluro-cephalus pathogens[9]. There are no characteristic imaging findings. In chest CT, nodular infiltrates and cavitary lesions were common findings[8]. In our case, there was a probability of progression from pulmonary consolidation to cavitary lesions without any treatment. To further identify the causative organisms, we cultured BALF on the medium for 7 d, observed the growth of a violet-colored colony on the dishes, and observed the microscopically characteristic infarct morphology of the bottle. Microbiome profiling and BALF mNGS further identified *P. lilacinum*, which provided laboratory evidence for diagnosing the pathogen.

There are only a few clinical cases of *P. lilacinum*, so no standard antifungal regimens exist[10]. Aguilar *et al*[11] showed early on that amphotericin B, miconazole, itraconazole, fluconazole, and flucytosine are less active against penicillium [11]. González performed *in vitro* drug susceptibility assays on 22 strains of *Aspergillus pallidus*, revealing that isavuconazole had a minimum inhibitory concentration of 0.2 to 2 μg/mL, amphotericin B 4 to 16 μg/mL, itraconazole 1 to 16 μg/mL, fluxonazole 16 to 64 μg/mL, voriconazole 0.5 to 4 μg/mL, posaconazole 0.5 to 2 μg/mL, and ravuconazole

0.25 to 2 μg/mL[12]. By analyzing clinical isolates of infected cases, Sprute *et al*[8] showed high resistance to amphotericin B and excellent *in vitro* activity against second-generation triazole[8]. In this case, we also performed *in vitro* drug susceptibility assays on isolates showing poor antifungal activity of amphotericin B and fluconazole, and excellent antifungal activity of voriconazole and isavuconazole, which is consistent with the previous literature. Our patient was administered voriconazole tablets, but on day 3 she developed hallucinations and involuntary tremors of the hands and feet, so the treatment was stopped. Isavuconazole is a second-generation triazole antifungal approved by the United States Food and Drug Administration in 2015 for treating invasive aspergillosis and mold diseases. It inhibits cytochrome woolly steroid 14 alpha-demethylation enzyme (CYP51), disrupts the structure and function of the fungal cell membrane by blocking the synthesis of ergosterol on the fungal cell membrane, has a higher affinity for fungal side chain CYP51 protein in its structural molecules, has a broad antifungal spectrum, and includes fungi resistant to other triazole antifungals[13]. In their study, Maertens *et al*[14] conducted an international multicenter, randomized, double-blind, phase III Secure clinical trial involving patients with a clinical diagnosis of invasive mold disease who were initially treated with isavuconazole and voriconazole, finding similar overall response rates ($P > 0.05$), with adverse drug reaction rates of 42% and 60%, respectively ($P < 0.001$), and lower visual, psychiatric, and liver toxicity associated with isavuconazole than with voriconazole[14]. In the vital study, Thompson *et al*[15] found that 38 patients with rare fungal diseases (including cryptococcosis, 9 cases of paracoccosis, 9 cases of coccidiosis, 7 cases of histoplasmosis, and 3 cases of blastomycosis) were treated with isavuconazole, with an overall response rate of 63.2% and stable disease progression in 21.1%, suggesting that isavuconazole is also an effective drug for rare invasive fungal diseases[15]. Moreover, compared with posaconazole, isavuconazole has a cost-effective option for treating invasive mold diseases in high-risk hematological patients[16]. We could identify only one case of a cutaneous infection caused by *P. lilacinum* used to treat a patient who was successfully cured by PubMed[17]. Huang *et al*[18] conducted a pharmacokinetic study of intravenous isavuconazole in healthy subjects, finding that lung tissue/plasma concentration was 1.438[18]. Caballero-Bermejo *et al*[19] found that isavuconazole was a drug with a tolerable safety profile that achieved adequate concentrations in the lung[19]. The bioavailability of isavuconazole tablets was 98%. Therefore, we switched to oral isavuconazole to continue antifungal therapy. To the best of our knowledge, this is the first known use of isavuconazole for pulmonary *P. lilacinum* infection.

After 12 h of voriconazole discontinuation, the patient's hallucinations and autonomic tremor disappeared, further confirming voriconazole-associated adverse effects. After 1 wk of treatment with isavuconazole, the clinical symptoms of cough and fever improved, and the patient was discharged from the hospital on day 14, continuing to take isavuconazole for 3 wk, during which time she experienced no significant adverse effects. At 6 wk after discharge, chest CT was performed again, and the pulmonary lesions were essentially absorbed.

CONCLUSION

Pulmonary infection caused by *P. lilacinum* is exceedingly rare, with uncharacteristic clinical symptoms, signs, and imaging findings. Pathogenic detection is complex, and conventional antifungal agents often have inherent resistance. In our patient infected with *P. lilacinum*, isavuconazole was found to have good safety and efficacy, but due to the small number of patients, more studies are needed to determine the optimal treatment strategy.

FOOTNOTES

Author contributions: Zhang JY conceived and designed the experiments, was responsible for the revision of the manuscript for important content; Yang XL collected information of case and drafted the manuscript; Ren JM performed the microbiological analyses. All authors critically reviewed and approved the final manuscript.

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ORCID number: Xue-Lin Yang 0009-0002-0384-3997; Jun-Yu Zhang 0000-0002-1013-8172; Jian-Min Ren 0000-0001-6005-0374.

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