


Voriconazole treatment of pulmonary mycosis caused by *Chrysosporium zonatum* after treatment for pulmonary tuberculosis

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Keywords

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Abstract

Chrysosporium zonatum is a soil-dwelling fungus that rarely causes pulmonary infections, and a small number of cases have been reported to date. A 74-year-old man, who had previously been treated for tuberculosis, presented with symptoms of low-grade fever, anorexia, cough, and bloody sputum. Chest computed tomography (CT) showed a thick-walled cavitary lesion in the right upper lobe, in which there was a suspected mycotic mass. Initially, the patient was suspected to have chronic aspergillosis due to positive serum anti-*Aspergillus* antibodies. However, bronchoscopic culture revealed the growth of *C. zonatum*. Symptoms and imaging findings improved with administration of voriconazole for 18 months. Infection by *C. zonatum* is very rare and is difficult to differentiate from aspergillosis by clinical features. Clinicians should be aware of the possibility of coinfection with *C. zonatum* and *Aspergillus* sp. Voriconazole may be an effective treatment option.

Introduction

The genus *Chrysosporium* is a keratinophilic filamentous fungus isolated from the soil, which has been reported to cause skin and some deep infections [1]. Immunodeficiency is a risk factor for infection, and systemic dissemination is typically fatal [2]. *Chrysosporium zonatum* was first described in Kuwait and has now been found globally [1]. There have been a few reported cases of human respiratory infections [1–4]. Due to the limited reports, the clinical features and treatment are unclear. We present a case of pulmonary mycosis caused by *C. zonatum* after the completion of treatment for pulmonary tuberculosis.

Case Report

A 74-year-old male presented with complaints of a slight fever, appetite loss, and haemoptysis, and was admitted for evaluation. Nineteen months before this admission, he was

referred with cough and sputum and an abnormal shadow on his chest X-ray. At that time, chest computed tomography (CT) revealed traction bronchiectasis and consolidation at the right pulmonary apex. Although pulmonary tuberculosis and pulmonary mycosis were suspected, sputum examination showed no remarkable findings. On follow-up four months later, the imaging findings had worsened, and pulmonary tuberculosis was diagnosed due to a positive tuberculosis polymerase chain reaction test of the sputum (Fig. 1A). Isoniazid, rifampicin, ethambutol, and pyrazinamide were administered for six months (Fig. 1B).

At this admission, he was seven months post-treatment for tuberculosis. His weight and height were 48.8 kg and 165 cm, respectively. His blood pressure was 120/89 mmHg; pulse rate 72 beats/min, pulse oximetry 98% in room air, and body temperature was 36.2°C. Chest auscultation revealed decreased breath sounds in the right lung. Chest X-ray

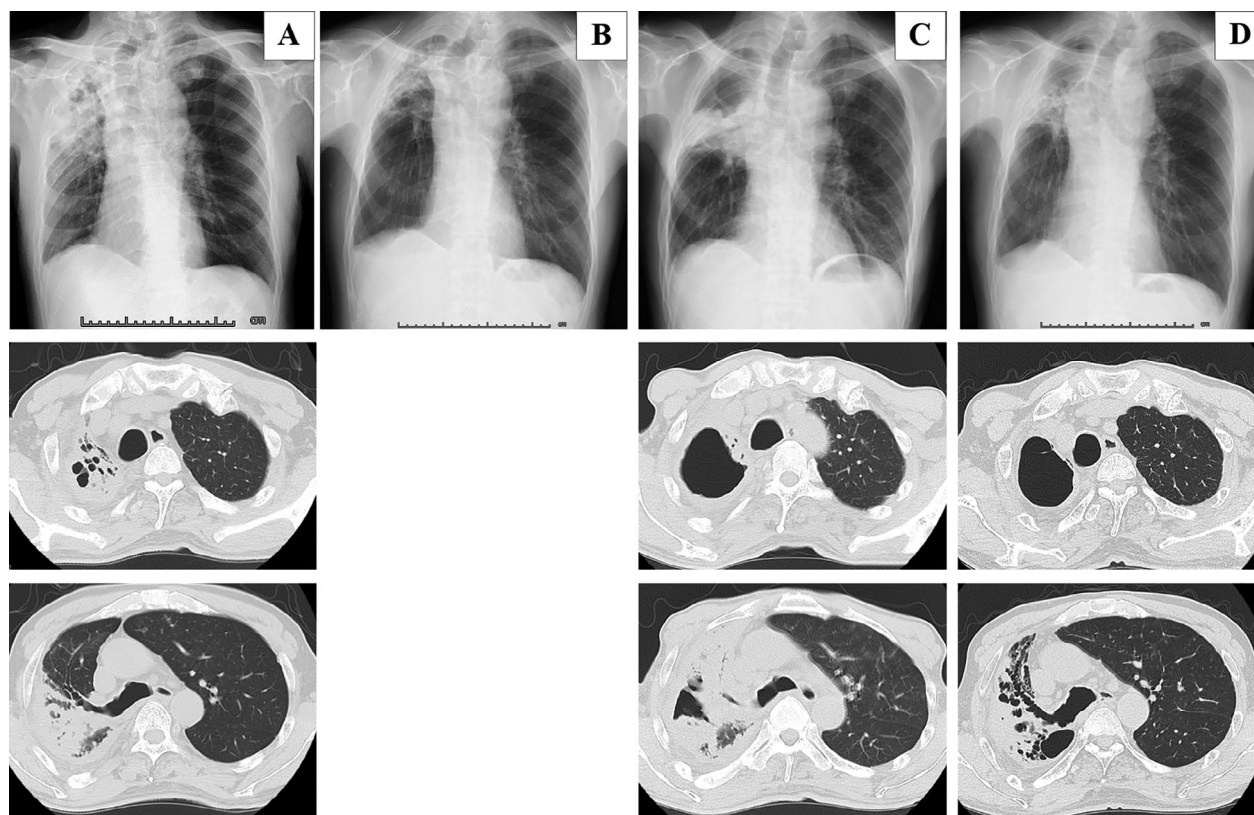


Figure 1. Chest X-ray and computed tomography (CT) findings over time. (A) Traction bronchiectasis and consolidation that worsened over time at the right pulmonary apex were seen at the time of tuberculosis diagnosis. (B) X-ray showed improvement after six months of tuberculosis treatment. (C) X-ray at the time of admission shows right upper lobe consolidation. CT showed a thick-walled cavitary lesion with a suspected mycotic mass. (D) Imaging 10 months after completing voriconazole treatment showed improvement.

demonstrated a consolidation with cavities in the right upper lung field consistent with the shadow after the treatment for pulmonary tuberculosis (Fig. 1C). Chest CT showed a thick-walled cavitary lesion in the right upper lobe with a suspected mycotic mass (Fig. 1C). Laboratory examinations showed inflammatory findings associated with infection. The serum (1-3)- β -D-glucan (BDG) levels were elevated (25.1 pg/mL) and *Aspergillus* antibodies were positive (Table 1). Bronchoscopy showed an accumulation of purulent bronchial secretion around the right upper lobe branch. The bronchial aspirate smear showed Gram-positive cocci, Gram-negative cocci, and no mycelium. After bronchoscopy, voriconazole was administered because of suspected chronic pulmonary aspergillosis (CPA). The patient responded well and was discharged after a week of voriconazole treatment. The effective voriconazole trough level was maintained within 1–2 μ g/mL. The culture showed filamentous fungi, which had branched hyphae with constant vertical width and irregular direction of growth (Fig. 2). On the other hand, there was no evidence of malignancy or mycobacterial infection. While the morphology of the filamentous fungi was different from *Aspergillus*, the

species could not be identified by mass spectrometry. The fungus was identified as *C. zonatum* by sequencing of the D1/D2 domains of the 28S rRNA gene seven months after the patient was discharged. Because the symptoms and imaging findings improved, voriconazole was continued for 18 months. There was no recurrence for about two years after voriconazole discontinuation (Fig. 1D).

Discussion

This case demonstrates the presentation and treatment of pulmonary mycosis caused by *C. zonatum*. In addition, this case suggests the possibility of coinfection with *C. zonatum* and *Aspergillus*. Although a pulmonary mycosis was suspected from the first visit onwards, tuberculosis was subsequently diagnosed. Pulmonary mycosis caused by *C. zonatum* was diagnosed 19 months after the first visit.

A small number of previous reports have described pulmonary infection with *C. zonatum*. In two cases, infection developed after the treatment of pulmonary tuberculosis,

Table 1. Laboratory data on admission.

Complete blood count		Blood chemistry		Immunology	
White blood cell count	7000/ μ g	Aspartate aminotransferase	29 U/L	C-reactive protein	9.75 mg/dL
Neutrophil	68.9%	Alanine aminotransferase	23 U/L	Procalcitonin	0.13 ng/mL
Eosinophil	3.4%	Lactate dehydrogenase	99 U/L	Carcinoembryonic antigen	1.2 ng/mL
Monocyte	0.7%	Alkaline phosphatase	232 U/L	Cytokeratin 19 fragment	0.84 ng/mL
Lymphocyte	17.5%	γ -Glutamyl transferase	22 U/L	Gastrin-releasing peptide	57.2 pg/mL
Red blood cell count	$377 \times 10^4/\mu$ L	Total bilirubin	0.5 mg/dL	<i>Aspergillus</i> antigen	Negative
Haemoglobin	10.8 g/dL	Total protein	6.2 g/dL	<i>Aspergillus</i> antibodies	Positive
Haematocrit	33.3%	Albumin	2.5 g/dL	(1 \rightarrow 3)- β -D-glucan	25.1 pg/mL
Platelet count	$31.7 \times 10^4/\mu$ L	Urea nitrogen	10.6 mg/dL		
		Creatinine	0.64 mg/dL		
Coagulation system		Sodium	135 mmol/L		
APTT	39.4 sec	Potassium	4.4 mmol/L		
PT activity	80.0%	Chlorine	106 mmol/L		
D-dimer	1.75 μ g/dL				

APTT, activated partial thromboplastin time; PT, prothrombin time.

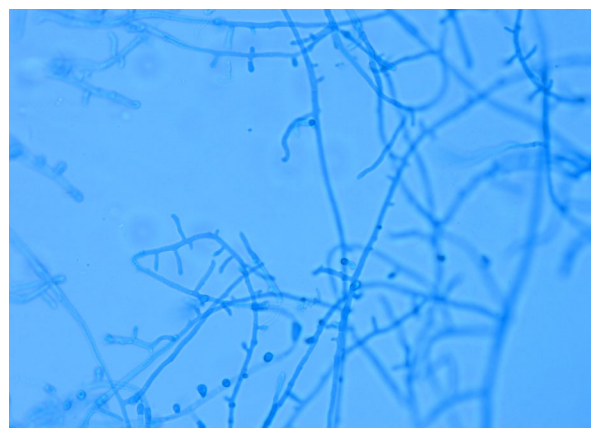


Figure 2. Microscopical findings of fungal culture. The branched hyphae have constant vertical width, and the direction of growth is irregular. The morphology differs from *Aspergillus* spp. (lactophenol cotton blue, 400 \times).

and the remaining cases developed in chronic granulomatosis and chronic obstructive pulmonary disease [1–3]. In addition, a case of pulmonary mycosis caused by the *Chryso sporium* species after the treatment for pulmonary tuberculosis was reported [4]. However, in the case, the species of *Chryso sporium* was not identified. In this case, *C. zonatum* subsequently developed within the pulmonary tuberculosis cavity. However, it is not clear whether the pulmonary mycosis caused by *C. zonatum* developed concurrently or after pulmonary tuberculosis. In previous cases, the imaging findings from the onset of the disease were not clearly described, and this case was significant for demonstrating the imaging changes over the entire clinical course (Fig. 1).

Voriconazole was initially administered because CPA was suspected. The medication was continued after the identification of the fungus because of the positive response and proved to be effective against pulmonary mycosis caused by *C. zonatum*. In general, surgery would be regarded as a treatment option for mycetoma/aspergilloma in suitable cases. In our case, as the right upper lung was dilapidated, surgical resection of the lesion was considered difficult. In addition, voriconazole treatment was limited to 18 months in consideration of the potential adverse events with prolonged administration of the drug. There was no relapse for about two years after voriconazole discontinuation. This clinical course suggested that the drug response of *C. zonatum* may be better than *Aspergillus*. Furthermore, previous reports have shown good responses to amphotericin B and voriconazole. However, as there have been a small number of reported cases in addition to our case, a clear treatment strategy has not been established. Accumulation of further cases is needed to establish a treatment strategy.

The clinical diagnosis of CPA is based on imaging findings and serodiagnosis, but the definitive diagnosis is by a

culture of *Aspergillus* [5]. Therefore, this case was first diagnosed as CPA. However, *C. zonatum* grew on the culture of bronchoscopic specimens. The previously reported *C. zonatum* cases have no mention of *Aspergillus*. Because the *Aspergillus* antibody test (IgG) has a sensitivity of 78.6% and a specificity of 94.4% [6], false-positive results are unlikely. Therefore, a mixed infection or cross-reaction between *C. zonatum* and *Aspergillus* was probable in this case. Because the clinical picture and prognosis for *C. zonatum* infection may differ from that of *Aspergillus* infection, it is important to identify the causative fungus by aggressive specimen collection, even in cases of clinically suspected CPA.

Chrysosporium zonatum is a very rare fungus and it is difficult to differentiate from *Aspergillus* with clinical features. As *C. zonatum* is found in the environment (soil), it may be considered a possible commensal organism, growing within the cavity/airways, after the treatment for tuberculosis. Furthermore, *C. zonatum* may also be present in confirmed cases of *Aspergillus* infection. Voriconazole may be an effective treatment option. Further cases are needed to establish the clinical features and optimal treatment strategy for pulmonary infection with *C. zonatum*.

Disclosure Statement

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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Author Contribution Statement

Dr Takuya Matsuzaki is the guarantor of this manuscript and contributed to the writing and review of the entire manuscript. Drs Hajime Kasai and Takashi Urushibara contributed to the critical review of the manuscript. Drs Hideki Ikeda, Yuki Tajiri, Akira Watanabe, and Katsuhiko Kamei collected and analysed the clinical data for the patient and contributed to critical review of the manuscript.

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