Case report

Exophiala dermatitidis, 'the real black fungus' fungemia in a patient with COVID-19

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A B S T R A C T

The second wave of the COVID-19 pandemic in India had brought with it a surge of ‘black fungus’ co-infection, which is a misnomer for mucormycosis. The present case illustrates the ‘real black fungus’ infection in a 50-year old male patient with COVID-19 pneumonia, who otherwise had no significant previous medical history. He was admitted on day 8 of COVID-19 illness and was intubated due to persistently low oxygen saturation. Blood cultures were positive for flask-shaped dematiaceous budding yeasts with pseudohyphae formation, which grew as brown-black fuzzy colonies on Sabouraud dextrose agar. The isolate was identified as Exophiala dermatitidis based on phenotypic characterization. Despite antifungal therapy with amphotericin B and itraconazole, the patient deteriorated rapidly and succumbed to acute respiratory distress syndrome and multiorgan failure. A review of reported cases of Exophiala dermatitidis fungemia over the last 5-years is discussed.

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Introduction

Coronavirus disease 2019 (COVID-19), a respiratory infection caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has been shown to cause immunological dysfunction [1,2]. This predisposes the host to fungal infections including those caused by dematiaceous (melanin producing or black) fungi. Exophiala dermatitidis, a dematiaceous fungus, was first isolated from a lesion on the cheek of a Japanese woman [3]. It is a type of black yeast which can be found in many extreme natural habitats, whether in hot or wet environment or in decaying organic matter. Among Exophiala species, Exophiala dermatitidis is frequently associated with systemic infection and has poorer outcome [4]. To the best of our knowledge, we report the first case of fatal Exophiala dermatitidis fungemia in a male patient diagnosed with COVID-19 pneumonia.

Case report

A 50-year old male with no known underlying medical illness was found in his room in a poorly responsive state. He had a history of fever, shortness of breath and lethargy and tested positive for COVID-19 antigen one week prior to presentation. He was brought to the emergency department with a low-grade fever of 37.4 °C, and tachypnea with a respiratory rate of 40 breaths per minute. His capillary blood sugar was 200 mg/dL, blood pressure 110/60 mmHg and pulse rate 105 beats per minute. Since his oxygen saturation was persistently low, he was intubated.

On examination, pulmonary crepitations were heard bilaterally up to the midzone with occasional rhonchi. Abdomen and cardiovascular examinations were unremarkable. ECG showed sinus tachycardia and chest X-ray revealed diffuse lung haziness bilaterally with consolidation. Total WBC was 11,100/µL, C-reactive protein 6.43 mg/dL and D-dimer 1.23 µg/mL. The clinical impression was COVID-19 pneumonia with severe acute respiratory distress syndrome.

Blood drawn on day 2 of admission for culture became positive after 4 days of incubation in the aerobic BACTEC bottle. Gram stain revealed flask-shaped budding yeast with pseudohyphae formation. Hence, an empiric intravenous amphotericin B was started. Culture on Sabouraud dextrose agar grew brown-black, velvety colonies with black pigment on the reverse side of the plate. Microscopic examination of the mould with lactophenol cotton blue dye showed dematiaceous septate hyphae with numerous cylindrical to oval conidiogenous cells produced along the hyphae. Based on the macroscopic and microscopic phenotypic features, the isolate was identified as Exophiala dermatitidis.

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In view of poor response to amphotericin B, the antifungal agent was changed to itraconazole 200 mg 12-hourly. Unfortunately, the patient condition continued to deteriorate and after 12 days of intensive care therapy, the patient eventually succumbed due to severe COVID-19 pneumonia with fungemia and multiorgan failure.

**Discussion**

COVID-19 infection has been shown to induce some degree of immunological dysfunction, such as diffuse alveolar damage with severe inflammatory exudates and reduced amount of absolute T lymphocytes, CD4 + T cells and CD8 + T cells [1]. The surviving T cells among patients with severe COVID-19 were also shown to be functionally exhausted [2]. During severe active COVID-19 infection, markedly increased level of cytokines such as IL-2R, IL-6, IL-10, and TNF-alpha further result in an immunosuppressed state [5]. Highly aggressive features of SARS-CoV-2 virus on the lung tissue give rise to large bilateral alveo-interstitial lesions, making the occurrence of fungal infection very likely, especially infection through inhalation including Exophiala dermatitidis [6].

Our case is the first reported case of *Exophiala dermatitidis* fungemia-co-infection in COVID-19 pneumonia in a previously healthy individual. Review of reported cases of *Exophiala dermatitidis* fungemia over the last five years (2017–2021) found one reported outbreak at an outpatient oncology clinic in New York, USA [7] and eight other individual cases throughout the world; mainly from Japan (5 cases) [8–12] and one case each from Argentina [13], India [14] and the United States [15]. For cases that were reported between 2019 and 2021, none of the authors mentioned any association of SARS-CoV-2 or COVID-19 disease with *Exophiala dermatitidis* fungemia (Table 1).

In terms of management of *Exophiala dermatitidis* fungemia, all patients in the New York outbreak had their central venous catheters (CVCs) removed and antifungal agents started. Despite being in immunocompromised states, the majority of patients (11/14, 78.6%) who received voriconazole during this outbreak survived [7]. This is in stark contrast to other individual cases reported later including the present case, where only three out of nine (33.3%) patients in stark contrast to other individual cases reported later including the present case, where only three out of nine (33.3%) patients presented 5-year data on antifungal susceptibility testing performed on *Exophiala dermatitidis* isolates (Table 1) showed the following minimum inhibitory concentrations (MICs): liposomal amphotericin B 0.5 µg/mL, conventional amphotericin B 0.125 – 0.25 µg/mL, anidulafungin 0.008 µg/mL, caspofungin 0.008–0.16 µg/mL, micafungin 4 – > 16 µg/mL, fluconazole 4–16 µg/mL, flucytosine 2 – > 64 µg/mL, itraconazole 0.03–0.5 µg/mL, voriconazole 0.03–2 µg/mL, posaconazole 0.06 µg/mL, and miconazole 0.25 µg/mL. Although amphotericin B (whether liposomal or conventional) appeared to have low MICs, patients treated with them did not fare well as compared to other antifungal agents/s (2/5) survived. In comparison, only 1/5 (20%) patients who received amphotericin B formulations survived. Similarly, only 1/6 (16.7%) patients who received micafungin survived (Table 1). Even though these observations are intriguing,
clearly there were other factors at play that could influence the outcomes in these patients. Therefore, more studies are needed to better correlate in vitro antifungal susceptibility with clinical response, especially for moulds.

Conclusions

Severe COVID-19 pneumonia can lead to immunosuppression which increases the risk for infection by inhaled fungi including invasive *Exophiala dermatitidis*. Review of previous cases of *Exophiala dermatitidis* fungemia suggests that complete removal of CVC and voriconazole therapy seemed to produce the best survival outcome.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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