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Geotrichum infection in an immunocompetent host with SARS-CoV-2 infection

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ABSTRACT

Geotrichum infection in an immunocompetent host with SARS-CoV-2 infection

There has been increasing reports of secondary bacterial and fungal infections associated with COVID-19. Following the initial reports of infection with *Aspergillus* spp., and *Candida* spp. there has been a significant rise in infections with *Mucorales* spp. In this case report, we present a case of *Geotrichum* spp. infection in an immunocompetent host with COVID-19. To our knowledge, this is the first case of *Geotrichum* infection in COVID-19. *Geotrichum* is a rare emerging pathogen that causes invasive disease, termed geotrichosis, which occurs in immunocompromised adult hosts with neutropenia. The development of invasive fungal infection such as *Geotrichum* in patients with SARS-CoV-2 infection requires a high degree of clinical suspicion and should be considered particularly in those who have an underlying immunocompromised state and those receiving corticosteroids or other immunosuppressive agents.

Key words: COVID-19; SARS-CoV-2; immunosuppressive agents; fungal; *Geotrichum*

ÖZ

SARS-CoV-2 enfeksiyonlu bağışıklığı sağlam bir hastada *Geotrichum* enfeksiyonu

COVID-19 ile ilişkili sekonder bakteriyel ve fungal enfeksiyonlara ilişkin raporlar gün geçtikçe artmaktadır. *Aspergillus* spp. ve *Candida* spp. ile enfeksiyonların, olguların tarif edildiği ilk raporlarının ardından *Mucorales* spp. ile enfeksiyonlarda önemli bir artış olmuştur. Bu olgu sunumunda COVID-19 olan bağışıklığı sağlam bir hastada *Geotrichum* spp.'ye bağlı enfeksiyonu bildiriyoruz. Bildiğimiz kadarıyla, bu COVID-19'daki ilk *Geotrichum* enfeksiyonu vakasıdır. *Geotrichum*, bağışıklığı baskılanmış ve özellikle nötropenili hastalarda ortaya çıkan, geotrikoz olarak adlandırılan invaziv hastalığa neden olan, nadir ortaya çıkan bir patojendir. SARS-CoV-2 enfeksiyonlu hastalarda *Geotrichum* gibi invaziv mantar enfeksiyonu gelişimi, yüksek derecede klinik şüphe gerektirir ve özellikle altta yatan bir bağışıklık sistemi baskılanmış durumu olanlarda ve kortikosteroidler veya diğer bağışıklık bastırıcı ajanlar alan hastalarda düşünülmelidir.

Anahtar kelimeler: COVID-19; SARS-CoV-2; bağışıklık baskılayıcı ilaçlar; fungal; *Geotrichum*

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INTRODUCTION

There has been an increasing number of fungal infections reported in patients with COVID-19 (1-3). The most commonly reported pathogens include *Aspergillus* spp., *Candida* spp., and more recently, *Mucorales* spp. (1,2). In fact, during the second wave of COVID-19 in India, there has been a significant rise in cases of mucormycosis (3). While it is not clear whether these fungal infections are due to COVID-19 or occur as a complication of treatment with immunosuppressive agents, the development of fungal infections represent another challenge complicating the management and likely outcome of patients with COVID-19. Here, we present a case of *Geotrichum* spp. infection in an immunocompetent host with COVID-19.

CASE

A 50-year-old man with history of type 2 diabetes mellitus presented as a transfer to the medical intensive care unit (MICU) of a tertiary care center with acute respiratory distress syndrome (ARDS). He initially presented to a local emergency department 22 days prior to transfer with fevers, chills, and muscle aches and was found to be PCR positive for SARS-CoV-2. He was admitted to a general medicine service and started on dexamethasone and remdesivir. Due to progressive hypoxemic respiratory failure, he required transfer to the MICU and was ultimately intubated on hospital day 17. Over the course of his hospitalization, he received treatment with convalescent plasma, tocilizumab, baricitinib, anakinra, N-acetylcysteine, vitamin C, and zinc. Despite these

therapies, he remained severely hypoxemic and was transferred to our institution for consideration of extracorporeal membrane oxygenation (ECMO).

Upon arrival to our MICU, he was afebrile and hemodynamically stable, mechanically ventilated on assist-control volume-control (AC-VC) with the following settings: tidal volume 330 cc (6 cc/kg IBW), respiratory rate 30 breaths/minute, fraction of inspired oxygen (FiO_2) 0.6, positive end-expiratory pressure (PEEP) 5 cm H_2O . Arterial blood gas showed pH 7.37, pCO_2 82 mmHg, and pO_2 88 mmHg. An endotracheal aspirate was collected on admission.

Four days after arrival, he developed fever and was empirically started on vancomycin and cefepime. Five days after arrival, his admission endotracheal aspirate returned positive for filamentous fungi that ultimately speciated to *Geotrichum* spp., and voriconazole was initiated. Antimicrobial sensitivity testing showed sensitivity to both azoles and polyenes (Table 1). Despite aggressive fluid resuscitation and treatment with antimicrobial drugs, the patient did not improve and developed refractory septic shock requiring treatment with multiple vasopressors and severe mixed acidosis requiring continuous renal

Table 1. *Geotrichum* spp. sensitivities

Antifungal	Concentration ($\mu\text{g/ml}$)
Amphotericin B	1
Fluconazole	32
Voriconazole	0.5
Posaconazole	1

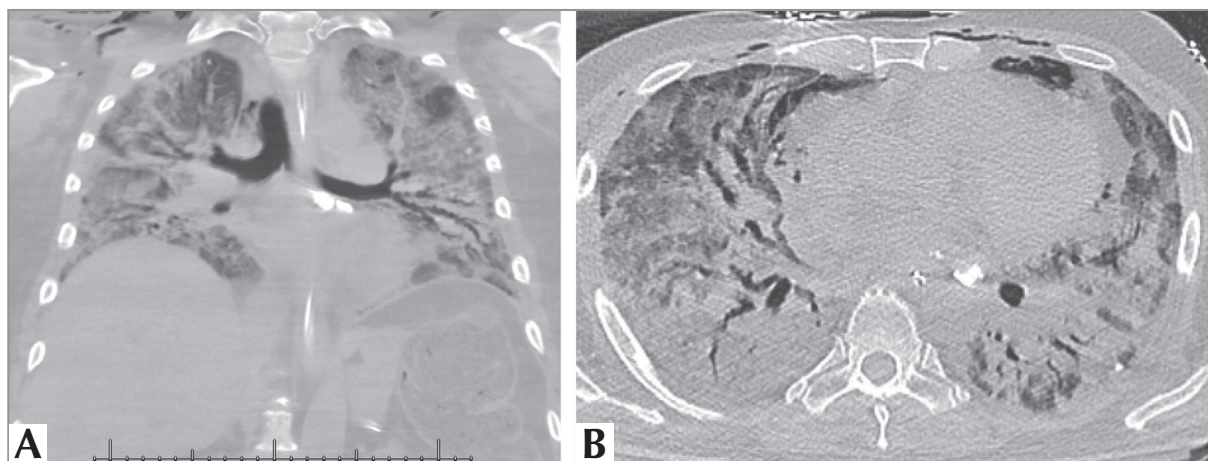


Figure 1. A. High-resolution CT (HRCT) images in coronal and B. Axial planes showing bilateral ground glass opacities with traction bronchiectasis.

replacement therapy (CRRT). After discussion with family, the decision was made to transition to comfort-focused care, and the patient ultimately passed away 11 days after arrival.

DISCUSSION

There has been a growing body of literature describing fungal infection in patients with COVID-19. A 2020 study from China reported five cases of fungal infection (one case of *Aspergillus flavus* and four cases of *Candida* spp.) identified in a cohort of 99 patients with SARS-CoV-2 infection, and more recent studies have reported increased rates of coronavirus-associated pulmonary aspergillosis in severely-ill, mechanically ventilated patients, ranging from 3.8 to 34% (1,2). More recently, India has reported an alarming number of COVID-19-associated mucormycosis cases, accounting for approximately 71% of global cases reported between December 2019 and April 2021 (3). Risk factors identified for the development of invasive fungal disease include advanced age, hypertension, underlying pulmonary disease, uncontrolled diabetes, use of corticosteroids, prolonged ICU stays, and severe SARS-CoV-2 infection (2-5). Additionally, the use of non-corticosteroid immunosuppressive agents may also represent a risk factor for invasive fungal infection (6,7). An observational cohort study found that tocilizumab, an IL-6 receptor antagonist, was associated with an increased risk of invasive fungal infection in patients with severe COVID-19 receiving renal replacement therapy, prompting the American Thoracic Society to publish a practice update urging caution with its use (6).

Here, we described a case of *Geotrichum* spp. infection in a middle-aged man with SARS-CoV-2 infection. To our knowledge, this is the first case of *Geotrichum* infection in COVID-19. The genus *Geotrichum* encompasses several species of saprophytic yeast that are found in nature and colonize the human skin, respiratory, and gastrointestinal tracts (8). It is a rare emerging pathogen that causes invasive disease, termed geotrichosis, in immunocompromised adult hosts, and infection is most commonly associated with neutropenia secondary to the administration of chemotherapy (9). Even more rare is the development of bronchopulmonary geotrichosis, of which there are only a handful of case reports described in the literature, all of which occurring in patients with underlying chronic lung disease or cancer (10).

Trauma and burn injuries are the only predisposing factors that have been described in the literature for the development of geotrichosis in immunocompetent individuals (11-13).

While our patient was not classically immunocompromised, he did have several risk factors that may have contributed to the development of pulmonary geotrichosis. On admission, his HbA1c was 9.1% indicating poor control of his diabetes mellitus; however, the majority of reported cases of geotrichosis in this population have been limited to oral, urinary, or rarely, cutaneous involvement (14-16). Additionally, he received multiple immunosuppressive agents during his hospitalization as part of his treatment for severe SARS-CoV-2 infection, including high-dose corticosteroids and tocilizumab, both of which may have led to increased susceptibility to fungal infection. Lastly, there is emerging evidence that in hospitalized COVID-19 patients develop dysbiosis characterized by alterations in fecal bacterial and fungal microbiota with enrichment of *Candida* and *Aspergillus* species (17,18) which may lead to an increased susceptibility for fungal infections. Further studies are needed to determine whether changes in microbiota may play a role in the increased fungal infection in patients with COVID-19.

The development of invasive fungal infection in patients with SARS-CoV-2 infection can be difficult to identify and requires a high degree of clinical suspicion. Bronchopulmonary geotrichosis should be considered in patients with severe COVID-19, particularly in those who have an underlying immunocompromised state and those receiving corticosteroids or other immunosuppressive agents.

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: KS, GMM

Analysis/Interpretation: KS, GMM

Data Acquisition: KS

Writing: KS, GMM

Critical Revision: KS, GMM

Final Approval: KS, GMM

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