Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Case report

Coronavirus disease and candidemia infection: A case report

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Introduction

In patients infected with the severe acute respiratory syndrome coronavirus (SARS-CoV-2), organ damage develops due to the excessive or uncontrolled release of proinflammatory cytokines and inflammatory processes after viral replication [1]. At the same time, bacterial and fungal co-infections can occur among these patients [2,3]. Limited data are available for bacterial and fungal co-infections associated with COVID-19 caused by the novel coronavirus (SARS-CoV-2). As the pandemic proceeds, epidemiological, microbiological, and clinical features of co-infections will be collated through prospective studies.

Candidemia, one of the most prominent fungal infections, is an opportunistic infection associated with high mortality in patients admitted to intensive care units (ICU) in hospitals. The most frequently identified risk factors for the development of candidemia in patients are: advanced age, prolonged hospital stay, broad spectrum antibiotics, central vascular catheters, parenteral nutrition, mechanical ventilation, colonization, antifungal prophylaxis, long-term antibiotic therapy, severe sepsis, and corticosteroids and chemotherapy [4,5].

In this paper, we present a case of candidemia in an 81-year-old woman with COVID-19, who underwent surgery for squamous cell carcinoma.

Case

On April 16, 2020, the patient diagnosed with squamous cell carcinoma was operated on and admitted to the ICU due to post-op general condition disorder. The patient had no history of travel abroad and contact with a foreign individual. She had hypertension. Laboratory tests showed her white blood cell count to be 16.37 x 10^3 / μL, C-reactive protein (CRP) to be 117 mg/L, procalcitonin to be 2.47 μg/L, fibrinogen to be 84,200 mg/dl, and ferritin to be 377 ng/ml. Blood culture and urine culture were taken from the patient and sent to the laboratory, and negative culture results were reported. The prognostic value of the components of the Glasgow Coma Scale (GCS) was evaluated at 14 points. Piperacillin-tazobactam and clarithromycin were added her treatment. On April 17, 2020, the general condition of the patient began to deteriorate, and the GCS was calculated at 3 points. She had fever and dyspnea. The patient was intubated. In the thorax computerized tomography, there was fibrosis and pleural retractions and a flagstone appearance in the right lung. This infiltration was compatible with COVID-19. Favipiravir was added to combination antibiotic therapy. The patient had received parenteral nutrition during hospitalization. SARS-CoV-2 RT-PCR (Bioeksen, Turkey) was studied from the nasopharyngeal swab sample, and the result was reported to be positive. On April 22, 2020, fungal growth was detected in the blood culture. A positive signal was obtained from the BACTEC automatic blood culture system inoculation was performed from the bottles in which yeast cells had been detected by gram staining, in Sabouraud Dextrose Agar (SDA, Oxoid, England) culture media with or without antibiotics. The *Candida* isolate was

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defined as *C. albicans* by using VITEK® 2 (bioMérieux, France) commercial methods. On April 23, 2020, Antifungal susceptibility of fluconazole (FLC), caspofungin (CAS), voriconazole (VRC), and amphotericin B (AMB) was performed by the E-test method. For the antifungal susceptibility testing RPMI 1640 (Sigma Chemical Co, St Louis, Mo, USA) medium was used. The inoculum suspensions were adjusted spectrophotometrically at 530 nm to match the turbidity of a 0.5 McFarland standard. Agar plates were inoculated with a cotton swab and allowed to dry for at least 15 min before the E-test strips were applied. E-test agar plates were incubated at 35 °C and read at 24 h. Azole MICs were read as the lowest concentrations producing an 80% reduction of growth. The AMB MIC was determined as the lowest concentration inhibiting any growth. The MICs of amphotericin B, fluconazole, voriconazole, and caspofungin Used were 0,125 μg/mL,1.00 μg/mL, 0.032 μg/mL, and 0.250 μg/mL, respectively. On the same day, the patient's condition worsened, and she died. Kayseri city hospital has a capacity of 1600 beds, 38 operating rooms and 289 beds in the intensive care unit. A total of 1500 patients are followed in hospital with the virus, either confirmed or suspected. Now we're doing approximately 1000 SARS-CoV-2 PCR tests per day.

Discussion

The first case of COVID-19, which has infected 4.5 million people, was diagnosed in Turkey on March 11, 2020. Along with the measures taken worldwide, immensely effective measures were adopted in our country and our hospital was authorized as a pandemic hospital. Although we have little information regarding the relationship between COVID-19 and fungal infections, secondary fungal infections are increasingly being presented in COVID-19 patients. Koehler et al. [6] reported that COVID-19-associated invasive pulmonary aspergillosis was diagnosed in 5 of 19 consecutive critically ill patients with moderate to severe acute respiratory distress syndrome. Blaizeet al. [7] presented a case of invasive pulmonary aspergillosis associated with coronavirus in an immunocompetent patient in France. In our case, *C albicans* related candidemia was presented in the patient with COVID-19. The pathogenesis of bacterial and fungal co-infections in patients with COVID-19 are still unclear, but it also appears plausible from the explanations provided on this topic. Previous virus-related co-infection studies have explained that the severe COVID-19 infection is associated with immune dysregulation, including viral-induced overexpression of anti-inflammatory cytokines, dysregulation of T helper cell differentiation, and impaired cell-mediated immune response [8,9]. Cytokines are predominant modulators secreted from the human body in response to various fungal pathogen infections. An imbalance between pro- inflammatory and anti-inflammatory cytokines is a triggering factor for fungal infections in critically ill patients. The pattern of immune dysregulation in COVID-19 patients is defined by the uncontrolled release of pro-inflammatory cytokines and chemokines (TNF-α, IL-1β, IL-1Ra, sIL-2Rα, IL-6, IL-10, IL-17, IL-18, IFN-γ, MCP-3, M-CSF, MIP-1a, G-CSF, IP-10, and MCP-1) and lymphopenia [10,11]. Underlying diseases (particularly chronic respiratory diseases), corticosteroid therapy, intubation/mechanical ventilation, and cytokine storm were the risk factors for invasive fungal infection in COVID-19 patients hospitalized in intensive care units [12,13] . Broad-spectrum antimicrobial use is likely to be widely practiced in hospitalized patients, both as directed and empiric therapy. These antibiotics lead to the depletion of the normal bacterial flora, which, in turn, leads to an overgrowth of opportunistic fungal pathogens [14]. Limiting the use of broad-spectrum antimicrobial treatment is important in hospitalized patients for the development of resistant bacteria and fungi. For the patient in this study, antiviral therapy and broad-spectrum antibiotics were applied for the treatment of the COVID-19 infection. There are no FDA-approved therapeutic drugs or vaccines for SARS-CoV-2. Since the current management strategies of COVID-19 involve supportive treatment, vital supportive applications can be used for patients admitted to intensive care units. Invasive surgical procedures such as intravenous catheter use, total parenteral nutrition, and tracheal intubation can lead to Candida colonization and fungal infection in patients in intensive care [15]. Our patient remained in the intensive care unit for four days, and she was connected to the mechanical ventilator as a supportive treatment measure. In addition, the patient was fed parenterally, as her general condition had worsened. The patient's illness took a rapid and fatal turn, and we did not have time to initiate the process of appropriate antifungal treatment.

Consequently, Fungal infections may occur in critically ill COVID-19 patients. Co-infections can develop due to certain medical practices during the intensive care treatment of these patients. Therefore, while optimizing the treatment of the COVID-19 infection, fungal and bacterial co-infections should not be forgotten. COVID-19 patients need to be tested for bacteria and fungi, not just the Coronavirus.

Consent for publication

The authors agreed to publish this article in Journal de Mycologie Médicale

Ethical considerations

Written informed consent was obtained from the ethics committee of Kayseri city hospital for the publication of this case report

Declaration of Competing Interest

The authors declare no conflict of interest.

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