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Case Report

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Fatal Mucormycosis Infection with Coronavirus Disease 2019 in a Kidney Transplant Patient

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ABSTRACT

Mucormycosis is a life-threatening infection, especially seen in individuals with diabetes mellitus and immunosuppression, in which the vast majority of cases result in death. Early diagnosis is vital for treatment. Coronavirus disease 2019 infection can also lead to the development of mucormycosis infection. Only few cases have been reported in the literature. A 35-year-old kidney transplant patient was hospitalized for coronavirus disease 2019 infection with lung involvement and was further examined upon complaint of headache and visual impairment during follow-up, which was later diagnosed as mucormycosis infection. The patient died despite the initiation of emergent surgical debridement and amphotericin B therapy.

Keywords: Clinical nephrology, pathology, renal transplantation, renal transplantation, COVID, mucormycosis

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CASE PRESENTATION

Mucormycosis infection is a fulminant, aggressive, and angio-invasive fungal infection caused by a fungus of the class of Zygomycetes,[1] ranking the third most common following candidiasis and aspergillosis. Its incidence is about 1.7 per million.[2,3]

Although fungi are common in nature, they only cause disease in people with low immune systems.[4] Facilitating factors include hematological malignancy (acute leukemia and lymphoma), long-term neutropenia associated with disease or chemotherapy, transplantation, diabetes mellitus–diabetic ketoacidosis, high-dose steroid use, desferrioxamine therapy, iron overload, acquired immunodeficiency syndrome, intravenous drug use, trauma/burns, and malnutrition.[5-8]

The rate of bacterial and fungal co-infection increases with high-dose corticosteroid use in the treatment of coronavirus disease 2019 (COVID-19) infection as well as the use of broad-spectrum antibiotics during prolonged hospitalization due to severe acute respiratory distress syndrome (ARDS). Cases of mucormycosis infection developing during or after COVID-19 infection have been reported very rarely in the literature.[9]

In this case, we wanted to present a kidney transplant patient who developed COVID-19 infection and rhino-facial mucormycosis infection and died despite effective treatment.

CASE REPORT

A 35-year-old female patient with Alport syndrome who received a kidney transplant from her father in 2017 was admitted to the COVID-19 infection unit in February 2022 following a positive COVID-19 polymerase chain reaction test result with 25% lung involvement on thorax computer tomography (CT). The patient was followed

up with chronic humoral rejection and had a serum baseline creatinine level of 4 mg/dL at the last outpatient follow-up. She was on tacrolimus (1 mg in the morning and 0.5 mg in the evening) and prednisolone (10 mg/day) treatment.

She had a cough, a body temperature of 38.7°C, and malaise for several days. Her general condition was moderate, and she looked sluggish and tired. She had rhonchi in the lung on physical examination. There was diffuse infiltration on thorax CT (25% lung involvement), and her oxygen saturation was 92%. At the time of hospitalization, her creatinine level was 5.2 mg/dL, leukocyte count was 7.620 per mm^3, and lymphocyte count was 530 per mm^3. Following hospitalization, due to pneumonia, empirical ceftriaxone (2 × 1 g) and levofloxacin (1 × 500 mg) therapy were initiated by the department of infectious diseases. Antiviral treatment was not started for COVID-19 infection, and 10 mg prednisolone treatment continued. The tacrolimus level was measured as 12 µg/L, and the drug dose was reduced to 2 × 0.5 mg/day. Antibiotic therapy was adjusted to 1 × 500 mg of meropenem and 2 × 50 mg of tigecycline after elevated C-reactive protein, and procalcitonin was detected on the third day of treatment. Fungostatin drops and 1 × 100 mg of fluconazole were started for the candida-like plaques on the tongue.

The patient was consulted with the departments of ophthalmology and neurology due to diffuse headache prominent in the frontal region and pain in the left eye. No pathology was detected on brain CT. Blood pressure was 120/70 mmHg and body temperature was 36.8°C. On the seventh day of hospitalization, the headache continued, oral intake decreased, and urine output decreased followed by ascites development, and the patient was taken to intensive care. The blood urea nitrogen was 167 mg/dL and creatinine increased to 7.4 mg/dL. Hemodialysis treatment was started in the patient with renal failure and hypervolemia.

The departments of neurology and ophthalmology were consulted again upon the exacerbation of headache, eyelid edema, and sudden loss of vision in the left eye (Figure 1), and cranial and orbital CT scans were scheduled (Figure 2). In CT, septation and inflammation were detected in the maxillary, frontal, and ethmoidal sinuses, nasal cavity, and paranasal sinuses. Defects in bone structures were detected, and there was edema under

MAIN POINTS

- Duringcoronavirus disease 2019 (COVID-19) one should be alert aboutopportunistic infections.
- Since mucormycosis is a rare disease, it receives a late diagnosis.
- As mucormycosis has a mortal course, it should be treated quickly.
- COVID-19 19 can be mortal in kidney transplant patients.

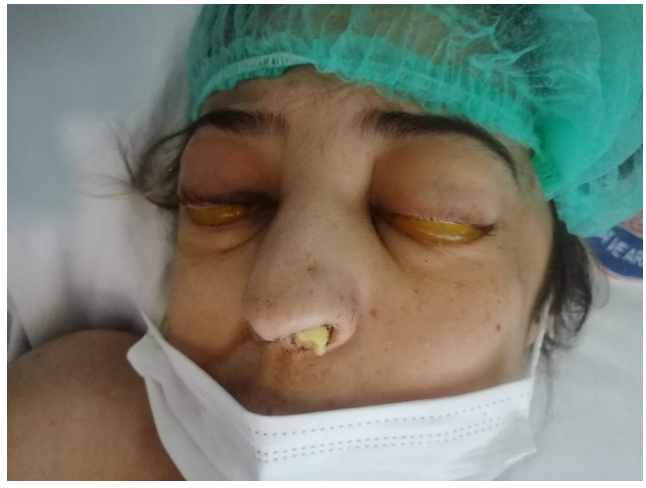

Figure 1. Eyelid edema and sudden loss of vision in the left eye.

the skin. The patient was consulted with the department of eye–nose–throat. Mucormycosis infection was considered as a preliminary diagnosis, and emergent debridement was performed. Liposomal amphotericin B therapy was started at 5 mg/kg/day. Pathology report confirmed mucormycosis infection (Figures 3 and 4). The patient who progressed rapidly died on postoperative day 10.

DISCUSSION

Although fungi are commonly found in nature, they often cause opportunistic infections in humans. These pathogens enter the sinuses and nasal cavity by inhalation of fungal spores and localize in the upper respiratory tract. The immune system keeps fungal growth under control, but fungi present as opportunistic pathogens in a few cases that disrupt the immune system.[14] They may cause acute fulminant invasive infection in

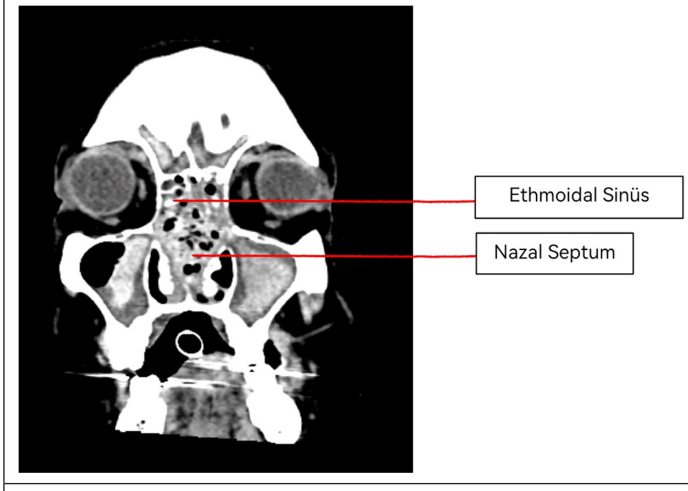

Figure 2. Widespread defective appearance—inflammation in the nasal septum bone structure, ethmoidal cells, and bone structures in the medial of both orbits.

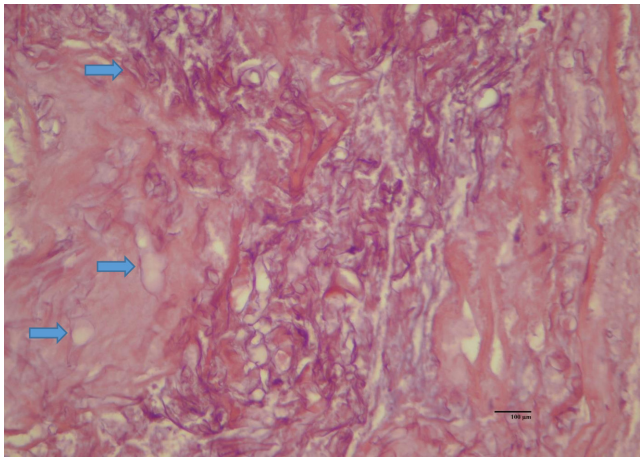

Figure 3. Numerous fungal structures are widely distributed and irregularly distributed. A few septa are indicated by arrows. (we need details about thispicture in terms of dyesetc) (H/E X 400 [hematoksilen eozin])

cases of secondary immunodeficiency such as uncontrolled diabetes mellitus (especially those associated with ketoacidosis), long-term steroid use or immunosuppressive therapy, AIDS, and drug addiction.[15]

The most common presentations of mucormycosis infection include rhino-orbital-cerebral (27%), pulmonary (30%), cutaneous (26%), and disseminated (15%) forms.[10] Although less frequent, gastrointestinal, renal, and isolated central nervous system involvement can also be seen. A definitive diagnosis of mucormycosis infection is based on the identification of organisms in tissue by histopathology with culture confirmation. Like aspergillus, mucormycosis also causes vascular invasion and necrosis of the infected tissue, leading to hemorrhage and necrotic lesions. It exhibits a very poor prognosis.[11-13]

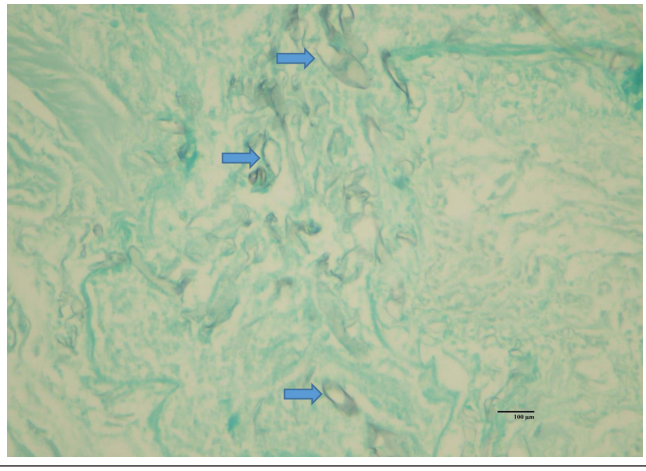

Figure 4. Fungal structures belonging to mucormycosis staining positive for histochemical Gomori methenamine silver. (GMS X 400 [gomorinin gümüş boyası])

Rhinocerebral mucormycosis (RSM) presents with black necrotic lesions in the nasal vestibule and oral mucosa in 80% of patients, but the definitive diagnosis is made histologically upon the presence of a large number of septate-free fungal hyphae with a primary culture of the fungus.[19,20] Direct spread may first infect the orbits and paranasal sinuses, while hematogenous spread infects intracranial structures. Perinasal and periorbital edema, cellulitis, and paresthesia may be early symptoms of RSM.[15,16] Cranial nerve involvement can be isolated or include all cranial nerves.[17] Cranial nerves V and VII are affected in most cases, resulting in ipsilateral loss of facial sensation, ptosis, and pupillary dilation. Involvement of the oral cavity may result in painful ulcerated lesions and perforations in the palate.[18]

Coronavirus disease 2019 infection causes excessive cytokine response and decreased cellular immune response, which consequently increases susceptibility to fungal co-infection. In addition, high-dose use of steroids in the treatment of COVID-19 infection causes uncontrolled blood sugar, increasing the susceptibility to diabetic ketoacidosis, which may also increase the risk of mucormycosis infection. However, our case received no high-dose steroid therapy and exhibited regulated blood glucose during the follow-up. Few cases of post-COVID-19 infection mucormycosis among kidney transplant patients and other patients with immunosuppression, all of which, resulted in death are reported. In our case, the patient did not respond well to the treatment, although debridement and antifungal therapy were initiated in the early period.

Rhinoorbital mucormycosis infection therapy includes systemic administration of high-dose amphotericin B with radical surgical debridement of infected tissues. However, assessment and early diagnosis are vital for this rare and fatal condition since it is an obstinate infection with high mortality despite treatment.

Meshram et al[21] published a series of 11 cases of mucormycosis. They reported the mortality rate as 27%. Bansal et al[22] published a series of 11 cases, and 2 patients died. Our case also showed similar clinical features with these cases.

CONCLUSION

In conclusion, mucormycosis infection should be taken into consideration in kidney transplant patients who develop headache and visual impairment concurrently with the COVID-19 infection, and treatment should be planned urgently.

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Analysis and/or interpretation – F.B.G., İ.Ö., Ö.G.; Literature review – S.N., İ.Ö., F.B.G.; Writer – F.B.G., İ.Ö., Ö.G., O.A.; Critival review – F.B.G., Ö.G., O.A., S.N.

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