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CASE REPORT

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Fatal rhinocerebral mucormycosis under the shade of hepatic encephalopathy

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ABSTRACT

Mucormycosis is an acutely fatal infection that occurs in immuncompromised patients. Cirrhosis is an acquired immune deficiency state and those patients are more prone to develop opportunistic infections. A 42-years-old cirrhotic man was admitted to our gastroenterology clinic with hepatic encephalopathy. Although he recovered from encephalopathy with supportive measurements, he developed paresthesia on the face. He was diagnosed with rhinocerebral mucormycosis and antifungal therapy was administered. Surgical treatment couldn't be performed because of his bleeding diathesis and poor general condition. He succumbed on the 12th day of his admission.

Key words. Mucormycosis. Cirrhosis. Fatal Infection.

INTRODUCTION

Mucormycosis is a rare, fatal infection, affecting mostly diabetic and immuncompromised patients.[1] Other risk factors include the use of systemic steroids, the presence of neutropenia, malnutrition, immunodeficiency, hematological malignancy and solid organ or bone marrow transplantation. Patients with cirrhosis are prone to opportunistic infections. Rhinocerebral mucormycosis in patients with hepatic cirrhosis (with or without hepatic encephalopathy) is very rare in current literature.[1,2] Herein, we report a case of rhinocerebral mucormycosis in a patient with hepatic cirrhosis.

CASE REPORT

A 42-year-old man, with decompensated liver cirrhosis due to hepatitis B virus infection, was admitted to our gastroenterology department with symptoms of hepatic encephalopathy. He had a history of recurrent episodes of hepatic encephalopathy. There was no history of gastrointestinal bleeding or spontaneous bacterial peritonitis. He had been diagnosed with hepatitis B-associated chronic liver disease 2.5 years ago, while undergoing cholecystectomy and he was since on 100 mg/day lamivudine. He denied alcohol use/misuse. His general condition was poor and he was lethargic. He had deeply icteric skin and sclera and there were palmar erythema, gynecomastia and spider nevi. Asterixis was noted. His laboratory findings were shown in table 1. HBV DNA and anti-delta antibodies were negative. Abdominal sonography was compatible with cirrhosis, portal hypertension, splenomegaly and ascites.

He was hospitalized in intensive care unit and supportive measurements for hepatic encephalopathy were initiated. He became conscious and oriented on the 2nd day of his admission. Because of severe pruritus, plasmapheresis was performed and the symptom was decreased gradually. Liver transplantation was planned, but while waiting, he developed paraesthesia on the left side of his face. Other neurologic examination was normal. There was an approximately 3 x 2 cm necrotic lesion in the upper palatine that completely eroding the mucosa and causing bone destruction beneath the lesion. The patient was referred to ear-nose-throat surgeons. A computerized tomography (CT) scan was performed and a biopsy was taken from the lesion. Fungal hyphi were detected on histology. The CT documen-

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Table 1. Laboratory findings of the patient.

Hemoglobin 10.9 g/dL	ALT 161 U/L	Direct bilirubin: 29.88 mg/dL
Hematocrit 30.5%	GGT 130 U/L	Fibrinogen 1.07 g/dL
Platelet 81.000/mm^3	ALP 563 U/L	AFP 8.86 IU/mL
WBC 7800/mm^3	Glucose 100 mg/dL	HBsAg 73.31 IU/mL
INR 3.23	Total protein 6.2 g/dL	HBeAg: Negative
aPTT 68.6 sec	Albumin 3.6 g/dL	Anti HBe: Positive
AST 367 U/L	Total bilirubin: 49.83 mg/dL	Anti HBc IgM: Negative

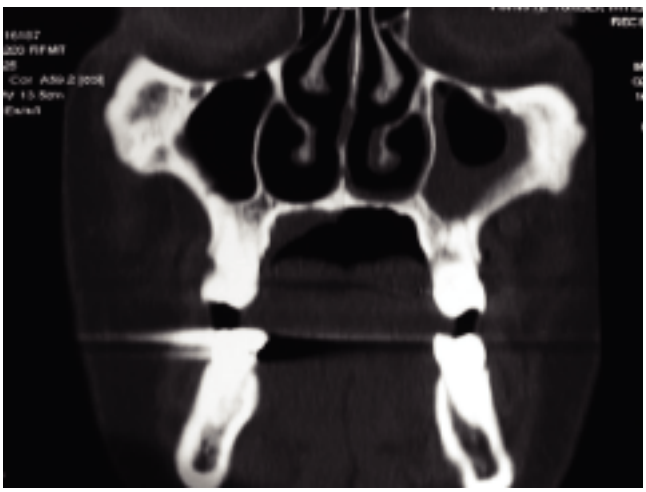

Figure 1. *Computerized tomography showed nodular mucosal thickening in left maxillary and ethmoid sinusoids and focal destruction on left palatine osseous.*

ted soft tissue thickening within the sphenoid, ethmoid and maxillary sinuses. Moreover there was significant soft tissue loss on the left side of the upper palatine and some erosive areas of the maxillary bone (Figure 1).

Overall, the CT and histology findings were consistent with mucormycosis. Intravenous amphotericin B (5 mg/kg/day) and teicoplanin (1,200 mg induction and 400 mg/day maintenance) was initiated. Surgical debridement could not be performed because of his general condition and risk of bleeding. Unfortunately, he succumbed 9 days later.

DISCUSSION

Mucormycosis is extremely rare, opportunistic and highly fatal fungal infection caused by Mucorales, which belongs to class Zygomycetes. A recent review of mucormycosis cases at one US cancer center found that 0.7% of patients were found to have mucormycosis at autopsy and that 20 patients per 100,000 admissions had the disease. The organism has an affinity to paranasal sinuses. The most frequent type is rhinocerebral mucormycosis, which may eventually affect the orbit and brain. Lungs, skin, gastrointestinal system and central nervous system are other probable sites of infection.[1,3]

Risk factors of mucormycosis are diabetes mellitus, use of systemic steroids, neutropenia, malnutrition, immunodeficiency, hematological malignancy, solid organ and bone marrow transplantation.[4,5] Although there are only few reported cases of rhinocerebral mucormycosis in cirrhotic patients, both pre- and post- liver transplantation, they have increased risk of developing this infection. Hepatic cirrhosis is an acquired immune deficiency state and these groups of patients are more prone to develop opportunistic infections.[6]

Spores of mucormycosis are transmitted through inhalation. The nasal clearance system transports these spores out of the nasal cavity, down to the pharynx, to be cleared out by the gastrointestinal tract. Spores are pahagocyted but never result with any disease state. However, when immunodeficiency occurs, these organisms become a candidate to be a causative agent of severe disease.[7,8] Contributing factors of mucormycosis in patients with cirrhosis are immune deficiency, dysfunction of reticuloendothelial system, malnutrition and taking prophylactic antibiotics for spontaneous bacterial peritonitis.[2] Anemia, hypovolemia, hypotension and porto-systemic by-pass of splanchnic blood may further deteriorate the poor condition. Moreover, disorders of cellular immunity, complement level, monocyte and neutrophil function, fibronectin and opsonic activity and invasive procedures during hospitalization may facilitate the the opportunistic infections in patients with cirrhosis. Four of 6 cases reported by Abbas, *et al*., had diabetes mellitus and the rest had hepatocellular carcinoma.[2] In contrast, our case had none of those predisposing factors. Hence, cirrhosis itself may be the only contributing factor to develop such an opportunistic infection.

Fever, nasal ulceration and necrosis, periorbital or facial swelling, ptosis, decreased vision, ophtalmoplegia, headache and decrease in mental status are

main presenting clinical features in the first 72 hrs.[9] As in our case, Dhiwakar, *et al.*, reported that paraesthesia or spreading cellulitis of the perinasal area is an early and typical sign. Periorbital oedema, mucopurulent rhinorrhoea and nasal crusting are other early signs.[10] As in our case, clinical signs and symptoms of mucormycosis may be masked by underlying hepatic failure. Therefore, early diagnosis and treatment have extreme importance in those cases.

CT as an initial investigation of choice is considered vital for the early detection of mucormycosis. Typical findings are diffuse thickening of the mucosa of involved sinuses. This is frequently accompanied by erosion or destruction of the bony sinus wall and extra sinusoidal spread of infection.[10] Morphologic feature of the class Zygomycetes is broad, nonseptate hyphae showing irregular, right-angled branching.[11]

The main stay of therapy is reversal of the source of immune-compromisation, early institution of systemic high dose amphotericin B and surgical debridement of non-viable tissue.[10] The combination of strict metabolic control, systemically and locally liposomal amphotericin B therapy, aggressive surgical intervention, repeated surgical debridement play an important factor in the outcome of those cases.[7] In our patient we couldn't perform surgical debridement because of bleeding diathesis and thrombocytopenia.

CONCLUSION

Mucormycosis is a rare infection in patients with hepatic cirrhosis. Some signs of mucormycosis can be concealed in patients with cirrhosis because of hepatic encephalopathy as in our case. It is a life threatening infection when the diagnosis and treatment are delayed. For early diagnosis and treatment, clinician must suspect and consider infection. Moreover, mucormycosis may cause decompensation of chronic liver disease and it can be a risk factor for hepatic encephalopathy.

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