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HEPATIC MUCORMYCOSIS IN A CHILD WITH FULMINANT HEPATIC FAILURE*

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Mucormycosis is an uncommon, opportunistic infection in children. We present a case of fulminant hepatic failure with hepatic mucormycosis. Although the suggested defects and pathogenic mechanisms in infections related to hepatic failure and mucormycosis are similar, few cases with both mucormycosis and liver failure have been reported.
Key words: mucormycosis, liver, hepatic failure.

We report a postmortem-diagnosed case of mucormycosis with fulminant hepatic failure (FHF) due to hepatitis A infection. Mucormycosis appears in tissue as irregularly shaped, broad hyphae with right-angle branching in the midst of acute neutrophilic infiltrate and vascular invasion. Vascular invasion and tissue necrosis are the hallmarks of the disease[1]. Antemortem diagnosis has been made infrequently in mucormycosis, and tissue cultures give variable results[1,2].

Case Report

A five-year-old girl was admitted with a two-week history of jaundice. On admission she was conscious, icteric, and her liver was palpable eight cm from the right costal margin. Routine laboratory investigations were all normal except for mild bilirubinuria. Her transaminase levels were increased; SGOT was 1065 IU/L and SGPT was 632 IU/L; total bilirubin was 23.7 mg/dl with a direct fraction of 13.4 mg/dl. The alkaline phosphatase level was 310 IU/L, total protein was 9.5 g/dl and albumin was 3.8 g/dl. On admission she had a positive anti-HAV IgM.

During the follow-up period of four days, the patient became irritable and lethargic. Although inpatient treatment for hepatic encephalopathy was begun immediately, she lost consciousness completely within two days and developed coma with anisocoria. Her transaminase levels continued to decline during the hospitalization

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period, with a decrease in liver size and extreme increase in bilirubin levels (total bilirubin: 43.8 mg/dl; direct fraction: 17.4 mg/dl). Her blood ammonia and prothrombin times were within normal limits. On the eighth day of hospitalization she had a sudden cardiopulmonary arrest and did not respond to resuscitative efforts.

On postmortem examination the incisional tissue specimen from the liver was firm with a brownish-green color. On cut surface, nodular lesions of 0.2-0.3 cm in diameter were observed. Histopathological examination revealed necrosis of the hepatocytes around the central veins and dilation of the sinusoids. Intracellular cholestasis was evident. In areas of diffuse necrosis, the vessels of portal triads were filled with necrotic debris infiltrated by numerous broad, aseptate hyphae (Fig. 1). Hyphae with nearly 45-degree-angle branching were less condensed in the surrounding parenchyma and were stained positively with methenamine silver stain (Fig. 2). Cultures for mucormycosis were negative. Tissue specimens were obtained from the brain, kidney, and lungs, and no hyphae was seen in these organs.

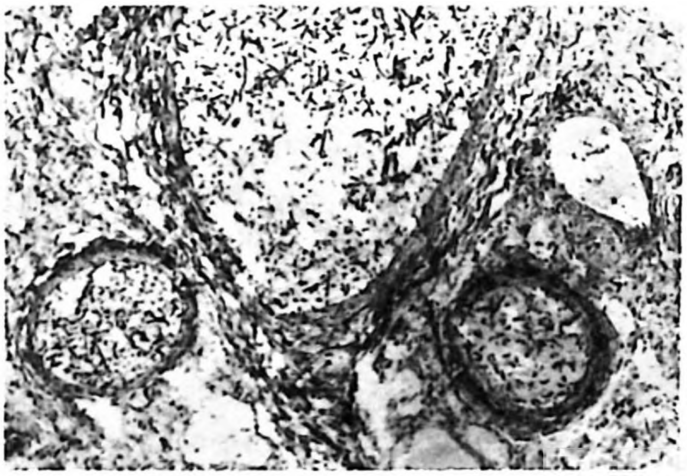

Fig. 1: The portal area and hyphae in the postmortem liver tissue sample (Methenamine silver stain 4 x 13).

Fig. 2: Broad nonseptate hyphae in liver tissue; branching is shown by an arrow (Methenamine silver stain 20 x 66).

Discussion

Viral hepatitis is the most common cause of FHF, which is complicated by infections in up to 40 percent of cases[3, 4]. Besides bacterial and viral infections, opportunistic fungal infections occur in most of these patients[3]. In a clinical study of 35 patients with FHF, fungi, especially the candida species, were cultured from 14 patients[5]. The increased risk of bacterial and fungal infections in these patients is thought to be due to a reversible immune suppression, including impaired neutrophil and Kupffer cell functions and deficiency of opsonins such as complement components and fibronectin[6-8].

The mucormycoses are an important class of opportunistic fungal pathogens in mostly immunocompromised hosts, but the underlying immunologic defects responsible for the development of mucormycoses are not well understood[9, 10].

Delayed chemotaxis of neutrophils seen in infected rabbits, defects in alternate complement pathway activation, generation of oxidative metabolites, defensins and cationic proteins may all contribute to the pathogenesis of mucormycosis[2, 11].

Although factors contributing to both mucormycosis and infections in FHF are still unclear, most of the accused defects in neutrophil and macrophage functions are similar. Immunologic studies were unfortunately not available in our case due to postmortem diagnosis. It is difficult to explain why mucormycosis is so rare in patients with hepatic failure. It may be due to the fact that most patients die from other complications of FHF before the development of fungal infections. The infrequency of reported cases of mucormycosis does not indicate low frequency of disease but rather decreased reportability of the condition[12]. Of the 34 reports of mucormycosis in children reported since 1954, only one patient with viral hepatitis developed mucormycosis with a perirenal abscess and total renal infarct without gastrointestinal tract involvement[12, 13]. In an adult patient with oliguric renal failure and renal mucormycosis, FHF was found to be the preceding disease[14].

Gastrointestinal mucormycosis is rare, and intrinsic abnormalities of the gastrointestinal tract, such as amebic colitis, thyphoid, pellegra and kwashiorkor generally have preceded the infection[9]. Those abnormalities were not present in our case. The organ most frequently involved is the stomach, with the large bowel next in frequency. The liver is involved secondary to a widespread dissemination from a primary site[10, 11]. It is interesting that in our case there were no hypae in the lungs, kidney or brain. Hyphae were only demonstrated in the liver tissue specimen.

To our knowledge, this is the first child with hepatic mucormycosis in FHF. The definitions of the underlying defects in both mucormycosis and in infections of patients with FHF may shed light on the rarity of mucormycosis in patients with hepatic failure.

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