Primary gastrointestinal mucormycosis in an immunocompetent person

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ABSTRACT

In the past decade, mucormycosis has emerged as an important lethal infection in diabetics and other immunocompromised hosts. Rhinosinusitis, pansinusitis, rhino-orbital and rhinocerebral are the common classical manifestations of mucormycosis. However, primary gastrointestinal (GI) mucormycosis is an uncommon disease associated with a high mortality rate. Stomach is the most common site involved in GI mucormycosis. Reported cases of GI mucormycosis in an immunocompetent host are very few in the literature. Here we present a case of a young male with fungal sepsis secondary to GI mucormycosis in an immunocompetent person.

KEY WORDS: Amphotericin B, gastric ulcer, gastrointestinal mucormycosis, immunocompetent

Mucormycosis is the second most common mold after aspergillus in culture-proven invasive infections in hematological malignancies and recipients of stem cell transplants. In mucormycosis, *Rhizopus* species (47%) account for the majority of isolates followed by mucor, cunninghamella, apophysomyces, absidia, saksenaea, and *Rhizomucor* species.[1,2] The spectrum of disease ranges from localized cutaneous to disseminated disease. Rhinocerebral and pulmonary disease are the most common forms followed by gastrointestinal (GI) infections. All portions of the alimentary tract are vulnerable to infection, with the stomach, ileum, and colon most commonly affected. Mortality of patients with GI mucormycosis is very high. In a meta-analysis study of 929 cases of mucormycosis, 7% (66) patients had GI mucormycosis and mortality was 85% (56).[3] Gastrointestinal mucormycosis is an uncommon disease most often occurring in patients with predisposing conditions. We report this case of primary GI mucormycosis in a patient with no predisposing factors.

Case History

A 28-year-old male presented with 10 days of fever, abdominal pain and bloody diarrhea. He was initially treated at a local hospital as a case of gastroenteritis and referred to our center when he developed altered sensorium and decreased urine output. Past medical history was negative and he wasn't taking any prior medications. General examination revealed bilateral subconjunctival hemorrhages and anasarca. His systemic examination was normal except for diffuse abdominal tenderness. Investigations revealed a serum hemoglobin 13.6 gm/dl, total leukocytes 29,500/cmm, platelets-80,000/cmm, aspartate transaminase-583 IU/L, alanine transaminase-1798 IU/L, alkaline phosphatase-234U/L, urea nitrogen-126 mg/dL, creatinine-6.2 mg/dL, sodium-128 meq/L, potassium-3.9 meq L, amylase-387 IU/L, lipase-404 IU/L, bleeding time-4 min, clotting time 8 min, prothrombin time 30.9 sec (control-12 sec.), Activated partial thromboplastin time >120 sec (control-27.6 sec.), random blood sugar-124 mg/dL. Fibrin degradation products were positive. His microbiological evaluation for malaria, bacterial (blood culture and serology), HIV and hepatitis B and C serology were negative. He was started on crystalline penicillin, tazobactum-piperacillin and with the provisional diagnosis of leptospirosis. He later required mechanical ventilation and dialysis. Hematochezia of 150 ml daily was observed for which he underwent colonoscopy. Colonoscopy revealed multiple small bleeding ulcers in the ascending colon which were managed with local epinephrine injections. The patient later developed epigastric tenderness and coffee ground gastric aspirate. Subsequent gastroscopy revealed an unusually large ulcer (5 cm) with necrotic base on the lesser curvature of the stomach. Biopsy from the ulcer revealed extensive necrosis of the gastric mucosa with polymorphonuclear infiltration, hemorrhage and thrombosed blood vessels, and numerous broad aseptate hyaline fungal hyphae branching at right angles suggestive of mucormycosis [Figures 1, 2]. The patient received two weeks of amphotericin B (deoxycholate), 50 mg/day (1 mg/kg/day) with minimal improvement. Conservative management was advised by surgical team as there was no perforation. The patient succumbed to the infection in spite of antifungal and

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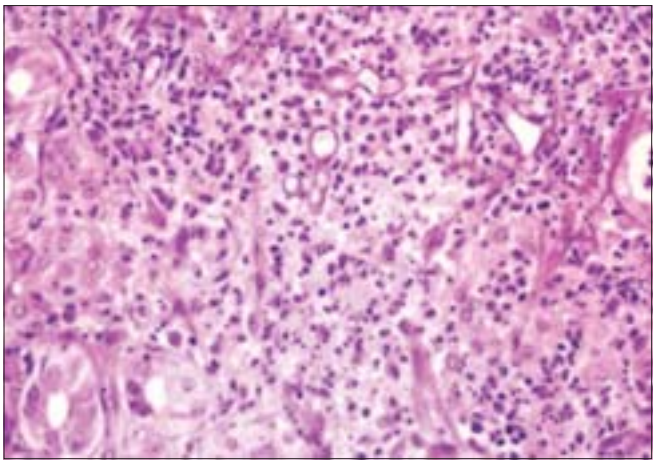

Figure 1: Gastric biopsy showing gastric mucosa and mucormycosis. (H&E, x10)

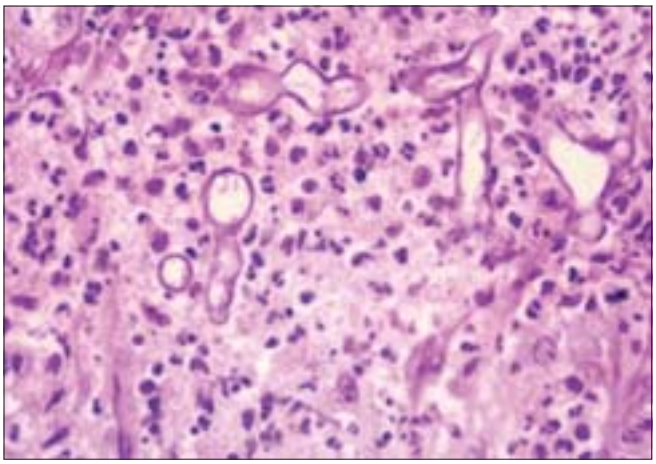

Figure 2: Gastric biopsy showing gastric mucosa and mucormycosis, with magnification (H&E, x40)

supportive management because of secondary nosocomial infection.

Discussion

The first case of mucormycosis was reported by Paultauf in 1885.[4] Mucormycosis (phycomycosis, zygomycosis) is an uncommon infection, largely confined to immunocompromised patients. Sporangiospores are typical infective forms while angioinvasive hyphal forms are responsible for tissue invasion and dissemination.[1] Two major hallmarks of the histopathology are direct penetration and growth through the blood vessel wall explains the propensity for thrombosis and tissue necrosis with black eschar and discharge pathogenesis of mucormycosis. The ability to scavenge free iron from the host is essential for the pathogenesis. Fungi can acquire iron from the host using low molecular weight iron chelators (siderophores) or high affinity iron permeases such as ferrizoferrin.[5] Interactions between iron and fungal spores appear to be important in the rate of replication and survival of fungi in the human host.

Six different manifestations of mucormycosis based on clinical presentation and involvement of a particular body site, are: (1) rhinocerebral, (2) pulmonary, (3) cutaneous, (4) gastrointestinal, (5) central nervous system, and (6) disseminated/miscellaneous.[1,2]

Malnutrition, persistent ingestion of non-nutritional substances (pica), gastric ulcers, severe systemic illness, age extremes and systemic immunosuppression are the typical predisposing conditions for GI mucormycosis.[2] Only 25% of cases of GI mucormycosis are diagnosed antemortem.[3] Gastrointestinal mucormycosis is thought to be due to ingestion of contaminated food materials. Initial manifestations may be abdominal pain and distension, fever and hematochezia. In premature neonates mucormycosis may present as necrotizing enterocolitis.[3] Gastric mucormycosis can be categorized into three forms: colonization, infiltration and vascular invasion. The most frequent presentation is perforation, bleeding or epigastric distention.

Diagnosis depends on demonstration of the organism in the tissue. Newer diagnostic modalities include serology and multiplex PCR system. Systemic amphotericin B is the mainstay of treatment. Liposomal amphotericin B may be more efficacious, less toxic allowing higher dosages (up to 10 mg/kg/day). Reversal of underlying medical disease and surgical debridement is necessary for successful management. Newer therapies for mucormycosis include posaconazole and deferiprone which inhibit iron uptake by rhizopus and adjunctive hyperbaric oxygen therapy.

Various sites of infection have been reported from the Indian subcontinent in immunocompetent individuals, the most common being cutaneous, paranasal and rhinofascial. Jain *et al.*, reported 18 cases of mucormycosis presenting as necrotizing fascitis in immunocompetent persons.[6] Involvement of the pericardium has also been reported in immunocompetent persons.[7]

A review of the literature revealed GI mucormycosis after traumatic brain injury also. Kamat *et al.* and Verma *et al.*, have described disseminated mucormycosis in healthy individuals.[8,9] Shahapure has also reported gastric mucormycosis in an immunocompetent person that was treated successfully with amphotericin.[10] Sharma *et al.*, also reported isolated GI mucormycosis in eight patients of which two were middle-aged without predisposing factors.[11] Virk *et al.*, also reported massive upper GI bleed due to mucormycosis.[12]

To conclude, it was a case of fungal sepsis secondary to GI mucormycosis which was diagnosed very late due to unsuspected fungal infection in an immunocompetent person. We believe that the primary site of infection was the stomach. An initial biopsy of the colonic ulcer or a fungal culture could have clinched the diagnosis. Rare diagnosis to be considered when common causes have been ruled out. Fungal septicemia is a well-known entity, so should be kept as a differential when repeated blood cultures are negative for the common organisms even in an immunocompetent individual.

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