Gastric Angioinvasive Mucormycosis in Immunocompetent Adult, A Rare Occurrence

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Abstract
Mucormycosis is a rare, opportunistic fungal infection that occurs almost exclusively in immunocompromised hosts such as patients with diabetes mellitus, leukemia, lymphoma, renal disease, septicemia, burns, malnutrition, and following long-term treatment with steroids and antibiotics. Based on the clinical presentation and involvement, mucormycosis is classified as six major forms, namely, rhinocerebral, pulmonary, cutaneous, gastrointestinal (GI), disseminated and miscellaneous, with rhinocerebral and pulmonary being the common forms. GI mucormycosis is rare, accounting for only 7% of all cases; however, the mortality rate is as high as 85%. Here we report a case of a young immunocompetent male who developed gastric invasive mucormycosis during an acute illness and succumbed to it despite all supportive care.

Introduction
Gastric Mucormycosis is a rare, usually fatal fungal infection. It is commonly associated in immunocompromised conditions. Very rarely it can present in immunocompetent patients also as shown in the current case report. Surgical and medical management combined together works best for favourable outcomes. Despite all the advances like better intensive care, optimized treatment regimens, understanding of pharmacokinetics and newer anti-fungals, the overall outcomes remain poor.

Case Report
A 31 year old male, known case of mood disorder, was admitted with complaints of alleged drug overdose with olanzapine. Patient had one episode of tonic clonic seizures prior to admission. He was non diabetic, and not on any immune suppressants. He had history of malaena. Patient was admitted under Neurology in intensive care unit.

Investigations
On evaluation, he was found to have acute kidney injury with oliguria and acidosis, requiring dialysis. Contrast enhanced MRI of brain showed a progressively enhancing lesion in the left premotor cortex with surrounding cerebral edema. He also underwent PET-CT Brain without contrast which suggested possibility of multifocal primary cerebral neoplasm such as oligodendroglialoma or grade 2 oligoastrocytoma. Histopathological diagnosis could not be done due to poor general condition of the patient. He was negative for HIV 1 and 2, hepatitis antigen and hepatitis C antibody. During admission, he developed abdominal distension and started spiking fever. He also had leucocytosis. He underwent esophago-gastro-duodenoscopy which showed multiple esophageal and gastric ulcerations. Biopsy was taken from the edge of the ulcerations.

The histopathology showed angioinvasive mucormycosis (Figures 1 and 2). He was started on intravenous amphotericin B. In view of abdominal pain, a CT scan of abdomen was done. It showed presence of free peritoneal air and perforation in the stomach wall.

Treatment
Patient was taken up for exploratory laparotomy. Amphotericin was continued in the postoperative period.

Outcome and Follow-Up
Repeat CT Scan of brain showed worsening cerebral edema despite all the medical care. Despite the best supportive care, the patient continued to deteriorate and developed multi-organ failure, sepsis and succumbed to the disease.

Discussion
Angioinvasive mucormycosis is a life threatening fungal infection caused by Rhizopus (Zygomycetes). It is common in immunocompromised and diabetic patients. Its is rarely reported with immunocompetent patients. The usual areas of involvement include, rhinocerebral, followed by pulmonary and skin involvement.¹ In a published case series, gastrointestinal mucormycosis accounts for only around 7% of cases. The gastrointestinal organ most frequently involved is the stomach, followed by colon, small intestine, and esophagus. Widespread dissemination from a primary gastrointestinal site may occur.²

Mortality of gastric mucormycosis is very high.³ Thomson et al,⁴ in their case series of gastrointestinal mucormycosis, described 21 patients with the disease and vascular invasion in 8 cases. In 10 patients, mucormycosis complicated peptic ulcer disease. They concluded that when there was histological evidence of vascular invasion by the fungus, the outcome was usually fatal, irrespective of the gut site.

The most common mode of spread of gastrointestinal mucormycosis is through ingestion of spores. The usual risk factors include, diabetes, hematological malignancies, immunocompromised status, defects of phagocytes action, corticosteroid use, post organ transplantation and availability of iron stores as a result of acidosis. Sequestration of iron by serum is a major host defense mechanism against R. oryzae in particular. The organism grows poorly in serum and this growth inhibition is reversed when

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exogenous iron is added. The patient in the case report was also in acidosis due to acute kidney injury, as one of the risk factors for developing mucormycosis.

When they invade, the lesion extends and marked surrounding induration develops, with a shaggy, velvety discolored surface or large plaque-like areas of green and blacked eschar. They also invade blood vessels and thus tend to cause extensive thrombosis, necrosis, and, ultimately, dissemination. Clinically, the lesion mimics ulcer or carcinoma.

The patients usually present with abdominal pain and distension. Gastrointestinal bleed in the form of melaena and hematochezia may present. Usually gastric mucormycosis can be divided into colonization, infiltration and vascular invasion. The most common presentation of vascular invasion is gut perforation which is invariably fatal.

Patients may also present with non-specific symptoms such as fever and diarrhoea. Persistent severe abdominal pain in a patient with neutropenia should alert the clinician to the possibility of a fungal infection such as zygomycosis especially in appropriate clinical setting. In our case, the clinical suspicion of invasive fungal infection was low, as the patient was immunocompetent and there was no neutropenia. A high index of suspicion is usually required as early intervention, both medical and surgical can improve the outcomes of these patients. Image guided biopsies or endoscopic biopsies should be obtained if feasible.

Histology characteristically shows hyphae that are wide, non-septate, branch at right angles, and look empty when haematoxylin and eosin stained. Polymerase Chain reaction (PCR) based tests for mucormycosis are currently not routinely available. Identification of species using molecular methods are usually for epidemiological studies.

In medical management, currently amphotericin B is the approved agent. Liposomal or other lipid formulations may be better agents than conventional amphotericin B. Posaconazole is also effective for mucormycosis but is currently not the drug of first choice. It has been compared with amphotericin B, voriconazole, and itraconazole in in vitro studies. Posaconazole was significantly more active than voriconazole and other agents. It is now known that R. oryzae expresses the target enzyme for echinocandins. In DKA mice infected with R. oryzae, combination caspofungin plus ABLC therapy markedly improved survival compared to either monotherapy or placebo. Further randomized controlled trials are necessary to evaluate role of echinocandins as a combination therapy.

Surgical resection of the involved area along with medical management does improve survival. However, the surgical option may not be feasible because of involvement at multiple sites, low platelet and neutrophil counts, and poor performance status. The outcome in these individuals is less favourable. Studies have shown that without surgical resection, this infection is inevitably fatal.

**Learning Points**

- **Gastric Mucormycosis** is a life threatening infection in immunocompromised and can also occur in immunocompetent individuals.
- Prompt identification and treatment, preferably with combined medical and surgical therapy may improve survival.

**References**