Case Report

Gastric mucormycosis in an immunocompetent patient with fatal outcome
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ABSTRACT
Mucormycosis is being reported as a serious fungal infection with grave outcomes among patients recovering from corona virus disease 2019 (COVID-19). This condition is a new challenge for the physicians in this pandemic situation. Mucormycosis predominantly occurs among patients with immunosuppression but immunocompetent patients are not immune. Here, we report a case of gastric mucormycosis occurring in an immunocompetent patient during the pre-COVID era. Patient presented with fever and upper gastro-intestinal bleeding. Diagnostic work-up confirmed gastric mucormycosis. His response to medical management was unsatisfactory and he died while awaiting a gastric resection.

Key words: gastric mucormycosis, immunocompetent patient, mucormycosis.

INTRODUCTION
Mucormycosis is an opportunistic infection which represents the third most common angio-invasive fungal infection and is considered as one of the most important medical complications in immunocompromised patients.1 The majority of patients are either treated with immunosuppressants like steroids or have underlying conditions, such as diabetes mellitus, hematologic malignancies, trauma and/or transplant recipients.2 Though common in immunocompromised patients, few cases of mucormycosis have been described in immunocompetent patients without any identifiable predisposing cause in the last thirty years.3 It is caused by Mucorales of class Zygomycetes.4 Mucoraceae are moulds in the environment that transform into hyphal forms in tissues and invade blood vessels producing tissue infarction, necrosis and thrombosis.5 Rhinocerebral and pulmonary involvements are the two most common forms; less often followed by cutaneous, gastrointestinal (GI) and disseminated infections.6 Cases of GI mucormycosis in immunocompetent hosts are rare and the mortality rate due to GI mucormycosis is as high as 85%.7 Management of mucormycosis is a big challenge. Rapid diagnosis, removal or control of risk factors and initiation of anti-fungal drugs (polyenes) with or without surgical debridements are the mainstay of treatment. Though mucormycosis has been diagnosed since many years, recently large numbers of cases are being identified in patients recovered from coronavirus disease-2019 (COVID-19).8 Patients with COVID-19 present with high levels of inflammatory cytokines and associated with impaired cell-mediated immune response, which lead to increased susceptibility to fungal co-infections.9 Also, the use of corticosteroids and other immunosuppressive agents and oxygen delivery devices

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have posed mucormycosis as an emerging threat for patients with COVID-19. Here we present case history of a young physician diagnosed with gastric mucormycosis.

CASE REPORT

A 32-year-old male physician presented with history of high grade intermittent fever for five days, repeated vomiting for two days and passage of loose stool three times for one day. His past medical history included chronic headache.

After getting hospital admission, he was initially treated as a case of malaria on the basis of clinical findings and relevant travel history to malaria endemic zone. On the 4th day of hospital admission, patient developed hypotension and his oxygen saturation was falling. He was immediately shifted to Intensive Care Unit (ICU) and mechanical ventilator support was required. Electrocardiogram, echocardiography and troponin-I levels were normal. Chest radiograph showed bilateral consolidation involving the mid zones of both lung fields. Ultrasound of abdomen showed mild hepatomegaly. Blood glucose, thyroid function tests, prothrombin time, activated partial thromboplastin time and liver function tests were normal. Hepatic viral markers were negative. During his ICU stay, he developed haematemesis and melaena for several times. Upper GI endoscopy showed whole mucosa of stomach was severely congested and ulcerated, active oozing of blood was noted all over the ulcerated area (Figure 1). Human immunodeficiency virus (I & II) (antigen & antibody test) and triple antigen tests were negative. Three samples of tracheal aspirate (TA) smears and broncho-alveolar lavage (BAL) for acid fast bacilli (AFB) were negative. BAL was negative for malignant cells and no fungus was found on direct microscopic examinations. As the haematemesis and melaena persisted even after one week, repeat upper GI endoscopy was done which revealed that there was thick slough and ulcers involving the body, fundus and cardiac end of the stomach and endoscopic biopsy was taken.

Patient had persistent fever. His TA culture showed growth of Acinetobacter susceptible to colistin only and it was initiated. Tracheostomy was done for prolonged mechanical ventilation support. Later report of endoscopic biopsy from gastric body revealed ulcer with fungal infection which was morphologically consistent with mucormycosis (Figure 2). After receiving histopathology report, intravenous amphotericin-B was started. But, his condition did not improve. Rather he developed septic shock and acute respiratory distress syndrome (ARDS). Inotropes were started and mechanical ventilation set-up was adjusted. As his condition was deteriorating despite getting maximum medical management, gastrectomy was planned after consulting with surgical team. Details were discussed with his family and they also agreed for surgical intervention despite possible fatal outcome. Unfortunately, he developed cardiac arrest before surgery and expired inspite of all resuscitative measures.

Figure 1 Upper GI endoscopy showing severely congested and ulcerated mucosa of the stomach with active oozing of blood involving the (a) fundus, (b) body and (c)the antrum. There was ulcer in the 2nd part of duodenum (d)
DISCUSSION
The GI tract mucormycosis occurs as a result of the ingestion of the spores of the fungus. The predisposing factors include malignancy, transplantations, metabolic diseases, malnutrition, chemo-, radio- and/or immuno-suppressive therapy. All parts of the alimentary tract are vulnerable to infection. Stomach is the most common site of GI involvement, followed by the colon and ileum. The presentation of GI mucormycosis is non-specific, with abdominal pain, distension, fever, diarrhoea, constipation and haematochezia. The common presentations of gastric mucormycosis are perforation, bleeding and/or peritonitis. The endoscopic appearance of gastric mucormycosis is usually a large ulcer with necrosis, presenting an adherent, thick, green exudates. Diagnosis of gastrointestinal mucormycosis is established by obtaining a biopsy and cultures. The biopsy demonstrates the characteristic wide, ribbon-like, aseptate branched hyphal elements, as was seen in the present case. Two major hallmarks of histopathology are direct penetration and growth through the blood vessel wall, which explains the propensity for thrombosis and tissue necrosis with black eschar and discharge that are pathognomonic of this infection. Anti-fungal therapy alone is typically inadequate to control mucormycosis and surgery to debulk the fungal infection and/or resection of all infected tissues are often required for effective cure. Systemic amphotericin B is the mainstay of treatment. Newer therapies include posaconazole and deferiprone. Surgical debridement and reversal of underlying medical disease is mandatory for successful management.

At least 212 cases of mucormycosis has been described among immunocompetent individuals without underlying risk factors. Infection in immunocompetent patients are rare because mucosal/cutaneous epithelium and endothelium provide an effective barrier against tissue invasion and angio invasion. A chronic local insult, such as, peptic ulcer disease may be considered as a predisposing factor for development of mucormycosis infection in this case. Use of antibiotic and immune-based therapies like corticosteroids, interleukin inhibitors to modulate the immune response of COVID-19 patients leads to immune suppression and invite opportunistic fungal infection. Many reports have been published on opportunistic fungal infection among COVID-19 patients including gastric mucormycosis and considered as a new treatment challenge for physicians. Most patients develop mucormycosis after recovering from COVID-19. Though rare, gastric mucormycosis should be considered if suspicious gastric ulcer is identified in COVID-19 patients.

Figure 2 Endoscopic biopsy and histopathology of gastric mucosa. Macroscopic description: sections showed necrotic and ulcerated pieces of gastric mucosa. Microscopic description: fungal hyphae were present in the surface and also invaded the gastric glands. These fungal hyphae were broad, irregular, aseptate and morphologically compatible with mucor (a). There was infiltration of polymorph and lymphocyte (b)
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or they present with hematemesis, melaena or other GI symptoms. Early clinical suspicion and prompt initiation of treatment may save the life of a patient.

In conclusion, mucormycosis is an under-reported disease. Though, most often it affects immunocompromised patients, it can also occur among immunocompetent individuals. Early diagnosis and prompt treatment requires strong clinical suspicion, specially, when patient become unresponsive to conventional treatment in this COVID-19 era.

Authors’ contribution: MMHC, KF, FA planned publication and drafted manuscript. All authors were involved in evaluation and management of the case. All authors read and approved the final manuscript for publication.

Conflicts of interest: Nothing to declare.

REFERENCES