Gastrointestinal mucormycosis: Rare presentation and review of literature

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ABSTRACT

Mucormycosis is an emerging life-threatening opportunistic infection. It is commonly seen in immunocompromised patients. Gastrointestinal mucormycosis is rare and only 25% of cases of gastrointestinal mucormycosis are reported antemortem. The stomach is the common site of gastrointestinal mucormycosis. In this study, three cases of gastrointestinal mucormycosis were diagnosed in 1 year. One was a gastric endoscopic biopsy. Two cases were diagnosed in the small intestine, one in the jejunum and one in the ileum. The diagnosis was made on hematoxylin and eosin stains. Gomori Methenamine Silver staining was done to confirm the morphology in all the cases. Mucormycosis shows broad non-septate filamentous hyphae with irregular branching. It is associated with angioinvasion with necrosis and acute inflammation. Cultures were not done as the diagnosis was not suspected.

Key words: *Chronic liver disease, Gastrointestinal tract, Mucormycosis*

Mucormycosis is a rare opportunistic fungal infection of the order Mucorales and class Zygomycetes. It was first described by Plaultauf in 1885 [1]. Depending on the site of occurrence, mucormycosis is divided into rhinocerebral, pulmonary, cutaneous, gastrointestinal, disseminated, and uncommon presentation. Gastrointestinal mucormycosis is rare with an incidence of 7% [2]. It is usually seen in immunosuppressed patients. Only 12 cases of gastrointestinal mucormycosis are reported in immunocompetent patients in the literature. Mucormycosis is rare in cirrhosis of the liver. Only 17 cases are reported. Rhinocerebral infections and peripheral infections are common in patients with cirrhosis; only one case of gastric mucormycosis in cirrhosis was reported in the literature. We report a case series of gastric mucormycosis in cirrhosis because of its rarity.

CASE SERIES

Case 1

A 36-year-old male patient presented with dyspeptic symptoms of 2 weeks duration. He gave a history of vomiting on and off and mild epigastric pain. It was not radiating. No associated systemic symptoms were present. He was a known alcoholic with cirrhosis. The vital parameters were normal. His routine hematological parameters revealed Hb of 11.2 gm/dl. His viral screening for HIV, HbsAg, and HCV was negative. His liver functions revealed total bilirubin of 0.7 mg/dl, direct bilirubin of 0.5 mg/dl, alanine aminotransferase (ALT) – 16 U/L, aspartate transaminase (AST) – 45 U/L, and serum alkaline phosphatase of 140 U/L. His total proteins were decreased total proteins – 6.1 g/dl with decreased serum albumin of 2.2 g/dl. Prothrombin time with international normalized ratio (INR) was 2.0.

Ultrasound abdomen revealed a shrunken liver with portal vein dilatation of 13 mm. There was associated splenomegaly with moderate ascites. As part of investigations for dyspepsia, he underwent upper gastrointestinal endoscopy after adequate preparation. Endoscopy revealed candidiasis of the esophagus. The stomach revealed an ulcerated lesion in the antrum. Ulcer measured 4 × 3 cm with elevated margins and the surface of the ulcer had blackish slough (Fig. 1a). There was no significant bleed after the biopsy.

Two endoscopic biopsy bits from the ulcer edge were submitted. Histological examination revealed antral type gastric mucosa with ulceration. Ulcer surface had fibrin with irregular, broad, branching filamentous hyphae (Fig. 1b). These hyphal forms were seen in the entire thickness of the biopsy (Fig. 1c). There was dense neutrophilic infiltration. Gomori Methenamine Silver (GMS) stains revealed fungal hyphae with similar morphology (Fig. 1d). The patient came for review to the outpatient 3 days after endoscopy. He was advised admission and treatment with antifungal agents. He refused treatment and was lost to follow-up.

Case 2

A 16-year-old boy presented with fever of 4 days duration. He complained of pain and distention of the abdomen of 2 days duration. Fever was high grade not associated with chills and rigors. It was partially responding to paracetamol. The pain was diffuse and non-radiating in nature. He gave a history of loose stools for a day followed by constipation. No significant medical history was present, and he was not on any medication. The vitals were stable. His routine hematological investigations revealed mild anemia with hemoglobin (Hb) of 10.8 gm/dl. Total leukocyte count was 13,000/mm^3 with 79% neutrophils and platelets were 120,000/mm^3. Viral markers were negative. Chest X-ray revealed gas under the domes of the diaphragm. With a diagnosis of perforation of hollow viscera, he was taken up for laparotomy.

Intraoperatively, 5.5 cm of distal jejunum appeared dull with perforation and exudate on the serosa. It was resected and end-to-end anastomosis was done. There was free fluid in the abdomen. It revealed 3200 cells/mm^3 with 90% neutrophils. The culture and Gram stain of the fluid were negative. Postoperatively, he developed metabolic acidosis, anuria, and seizures. He expired on the 10th post-operative day.

Gross examination revealed a perforation which was 1.5 cm from one resected end, present at the segment of the intestine measuring 6.0 cm. The serosal surface was dull with exudate. Cut section of the intestine revealed an ulcer with perforation. Histological examination revealed jejunal mucosa with ulceration. The ulcer surface had fibrin. Wall had diffused neutrophilic infiltration. There were focal collections of epithelioid cells and multinucleate giant cells (Fig. 2a). GMS stains revealed similar morphology (Fig. 2b). Over the ulcer and in the wall were seen broad septate filamentous hyphae with branching. There was a vascular invasion of the fungal filaments with areas of necrosis (Fig. 2c).

Case 3

A 28-year-old male presented with pain and distension of the abdomen of 24 h duration. It was associated with constipation and fever. Fever was low grade and associated with chills. He gave a history of decreased urine output for the past 2 days. There was no significant medical history. There was no history of any medication in the past or for present illness. On examination, the vitals were stable. There were guarding and tenderness with the rigidity of the abdomen. There was no organomegaly. His hematological investigations revealed hemoglobin of 11.2 g/dl, total leukocyte count of 22,000/mm^3 with 94% neutrophils, and platelet count of 140,000/mm^3.

The chest X-ray revealed mild pleural effusion. Ultrasound abdomen revealed grade two parenchymal changes in both kidneys and minimal ascites. Procalcitonin was 200 ng/ml. He was initiated on meropenem 500 mg intravenously twice a day and vancomycin 1 g intravenously once a day. He was also put on intravenous fluids and paracetamol. On the evening of admission to the hospital, he complained of an increase in pain and distention of the abdomen. His X-ray abdomen in erect

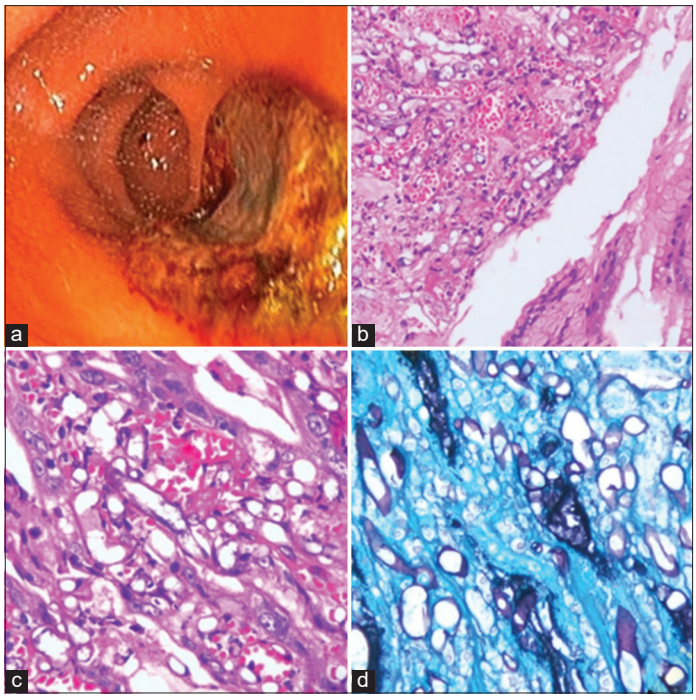

Figure 1: (a) Endoscopic picture showing gastric ulcer with elevated margins with blackish slough on the surface; (b) gastric mucosal tissue showing ulceration. Surface of the ulcer shows broad branching hyphal forms (H&E, ×100); (c) gastric biopsy showing hyphal forms in the lamina propria. (H&E ×400); (d) Gomori Methenamine Silver stain highlighting the morphology of the fungus. (×400)

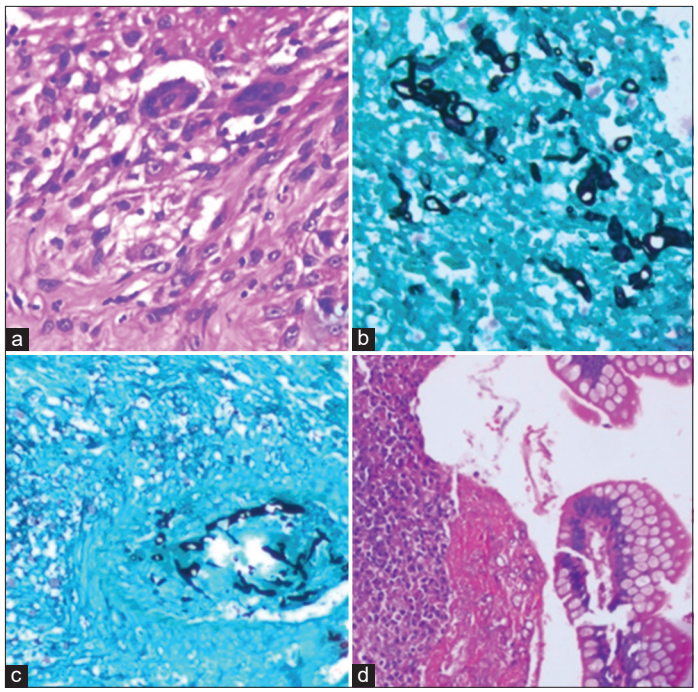

Figure 2: (a) Jejunal tissue showing granulomatous inflammation with epithelioid cells and giant cells along with broad fungal hyphae. (H&E ×400); (b) Gomori Methenamine Silver staining showing morphology of the fungus (×400); (c) Methenamine Silver stain showing vascular invasion of the fungal hyphae (×200); (d ileal tissue showing ulceration with fibrinous exudates containing broad filamentous hyphae (H&E ×100)

posture revealed gas under the domes of the diaphragm. As there were features of perforation, an exploratory laparotomy was done.

On opening the abdomen, 30 cm from the ileocecal valve, ileum revealed perforation. The rest of the organs were normal. A small segment of perforated ileum was excised and anastomosis was done. Postoperatively, he developed bilateral pneumonia. His counts further increased to 34,000/mm^3. Platelets dropped to 12,000/mm^3. He developed anuria and dialysis was initiated. He developed multiorgan failure and expired on the 6th post-operative day.

Grossly, the specimen was a 2.0 cm segment of the intestine. The serosal surface had blood and purulent material. Cut section revealed a dull mucosal surface with an area of perforation. Histological examination revealed ulceration with dense acute inflammation. There was focal granulomatous inflammation associated with dense diffuse neutrophilic infiltration. Broad branching non-septate fungal filaments were seen in the exudate (Fig. 2d). GMS staining also revealed similar morphology. There was exudate on the serosa with fungal hyphae. Tissue was not available for culture studies.

DISCUSSION

Mucormycosis is a rare opportunistic fungal infection of the order Mucorales and class Zygomycetes. It was first reported in 1885 by Paultauf. It is a ubiquitous filamentous fungus. Human infections occur as a result of inhalation of fungal sporangiospores or direct inoculation of organisms into the skin or mucosa. Depending on the anatomic site of infection, mucormycosis is classified as rhinocerebral, pulmonary, cutaneous, gastrointestinal, disseminated, and uncommon presentations.

Gastrointestinal mucormycosis is uncommon, usually diagnosed at autopsy. Only 25% of cases are diagnosed antemortem. The stomach is involved in 67% of cases, colon in 21%, small intestine in 4%, and the esophagus in 2% [3]. In the small intestine, the ileum is more commonly involved than the jejunum. In our case series of three cases, one is from the jejunum. In a literature review, nine cases of gastrointestinal mucormycosis were studied in immunocompetent patients. Male-to-female ratio was 7:2. The youngest patient was a 26-year-old male [4] and the oldest patient was a 70-year-old male [5]. The survival rate was 22.2%. They commonly occurred in the stomach and colon [6]. In our case series, both the immunocompetent patients had mucormycosis of the small intestine, namely, jejunum and ileum. Small intestinal mucormycosis is very rare.

A small percentage of patients with mucormycosis do not have any predisposing factors. In such patients, cutaneous and rhinocerebral infections are common. Pre-disposing factors for mucormycosis include diabetes 36%, hematological malignancy 17%, and solid organ transplant in 12% of cases [7]. The diagnosis of gastrointestinal mucormycosis is usually delayed because of non-specific symptoms. They include abdominal pain, distention, nausea, vomiting, hematemesis, and hematochezia.

Seventeen cases of mucormycosis were reported in patients with cirrhosis of the liver [7]. Only one case of gastric mucormycosis in association with cirrhosis is reported in the literature [8]. In the present study, one patient with gastric mucormycosis had cirrhosis of the liver. This case is rare because of its rare association with cirrhosis and rare site of occurrence. Prognosis is very poor and survival rates are 11.7% [7]. Other sites of mucormycosis include sinuses 39%, lungs 24%, skin 19%, brain 9%, and kidneys 3% [9]. Less common sites include endocardium and bone presenting as endocarditis and osteomyelitis.

Gastrointestinal mucormycosis has a very poor prognosis. The survival rates for mucormycosis in diabetes are 60–90%. It is 20–50% in hematological malignancies and in cirrhosis, it is 11.7%.

CONCLUSION

Gastrointestinal mucormycosis is a rare disease with high mortality. Its occurrence in cirrhosis and immunocompetent cases is even rarer. We report three unusual presentations of gastrointestinal mucormycosis, one was in a patient with cirrhosis and two in immune-competent patients. Presenting features are non-specific and there are no specific clinical or radiological features of this disease, hence the delay in diagnosis. A high index of suspicion and prompt diagnosis are the key factors to improve survival rates.

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