CASE REPORT

A Rare Case Report of Intra-abdominal Mucormycosis Complicating Acute Pancreatitis

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Abstract

Intra-abdominal infections are known to complicate the course of acute pancreatitis. Invasive fungal infections (*Candida* spp.) are not the uncommon microorganisms which isolate from intra-abdominal specimen in acute necrotizing pancreatitis. However, we are reporting first case of invasive gastric mucormycosis in a postpartum acute pancreatitis patient.

Keywords: Acute pancreatitis, Invasive fungal infection, Mucormycosis, Postpartum.

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Introduction

Acute pancreatitis course is complicated by intra-abdominal sepsis, leading to increase in morbidity and mortality.[1] Although bacterial infections are more commonly isolated from pancreatic infections, fungal infections are increasingly been found to complicate course of the disease.[2] Fungal pancreatic infections (*Candida* spp.) are found in up to 17% of patients at the time of the initial intervention (primary infection) and in up to one-third of patients during the course of the disease (secondary infections).[1–4] Gastrointestinal (GI) mucormycosis is a rare and life-threatening invasive fungal infection and mainly reported in patients having immune-deficiency states like hematologic malignancies, solid organ transplantation, diabetes mellitus, and glucocorticoid therapy.[4,5] Here, we are reporting first case of gastric mucormycosis in a young female of postpartum acute pancreatitis.

Case Description

A 22-year-old female, 2 months postpartum after uneventful pregnancy (Para-2, Living-2) presented with acute abdominal pain on Day 1 of her illness. She was admitted in medical gastroenterology ward, initial work-up revealed amylase 172 (30–110 Unit/L), lipase 178 (0–160 Unit/L), serum alanine transaminase 109 (7–56 Units/L), aspartate transaminase 172 (5–40 Units/L), alkaline phosphatase 320 (44–147 Unit/L), and triglyceride 139 (<150 mg/dL). Abdominal ultrasonography showed edematous pancreas and normal biliary radicals. Two days later, she developed headache and left eye proptosis with ptosis, and fundoscopy showed papilledema suggestive of cavernous venous sinus thrombosis. Therapeutic anticoagulation with unfractionated heparin was started with targeted activated partial thromboplastin time (aPTT) of 60–85 seconds. On fourth day of illness, she had increased blood sugar readings ranging from 550 to 750 mg/dL, further work-up showed blood ketone of 6 (<0.5) mmol/L and urinary ketone bodies of >1.6 (normal <0.6) mmol/L, and HbA_1C of 6.2%; arterial blood gas revealed pH of 7.15, bicarbonate of 7 mmol/L, and anion gap of 25 mmol/L. She had worsening respiratory failure. She was managed with fluids and insulin, and she was shifted to ICU for further management (Pancreatitis Day 5). Admission acute physiology and chronic health evaluation-II (APACHE II) and sequential organ failure assessment (SOFA) scores were 20 and 9, respectively. Management with fluid, electrolyte, and insulin therapy continued, along with noninvasive ventilation support, and empirical antimicrobial coverage was started with meropenem, teicoplanin, and fluconazole. Over 36 hours of ICU admission, diabetic ketoacidosis (DKA) resolved with decrease in blood ketone bodies (β-hydroxy butyrate—0.2 mmol/L). Therapeutic anticoagulation was continued. Magnetic resonance venography of brain showed bulging of eyeball and left cavernous sinus thrombosis with presence of a nonenhancing T1/T2 isointense filling defect within, with prominent left superior ophthalmic vein. Time-of-flight (TOF) image showed filling defect in left cavernous sinus region (not shown here). On Day 14 of illness, contrast-enhanced computed tomography (CECT) abdomen (Fig. 1A) was done as she had fever, abdominal pain, and increased gastric residual volume. Contrast-enhanced computed tomography (CECT) abdomen showed no contrast enhancement of pancreas with modified computed tomography severity index score of 10/10 with peripancreatic collections compressing the posterior wall of stomach and moderate

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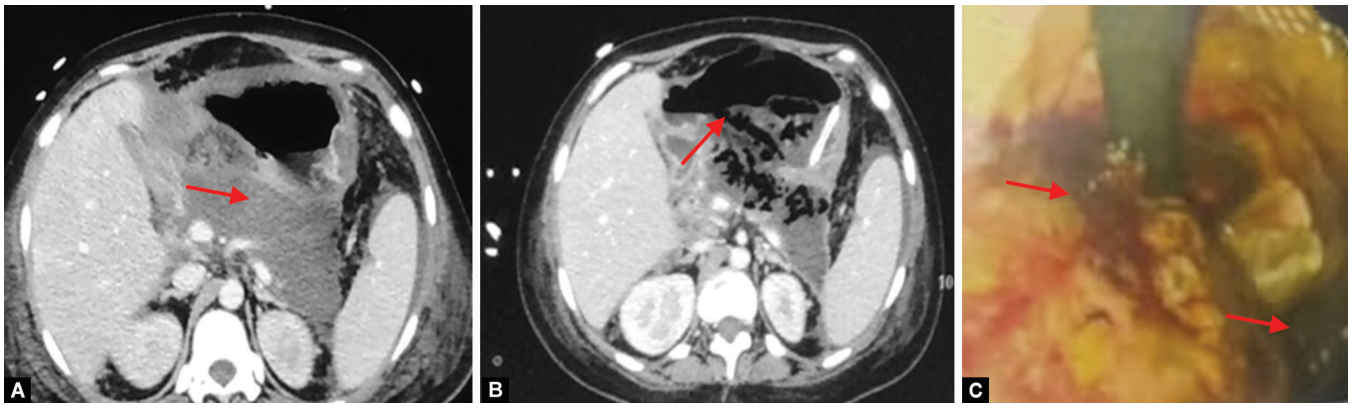
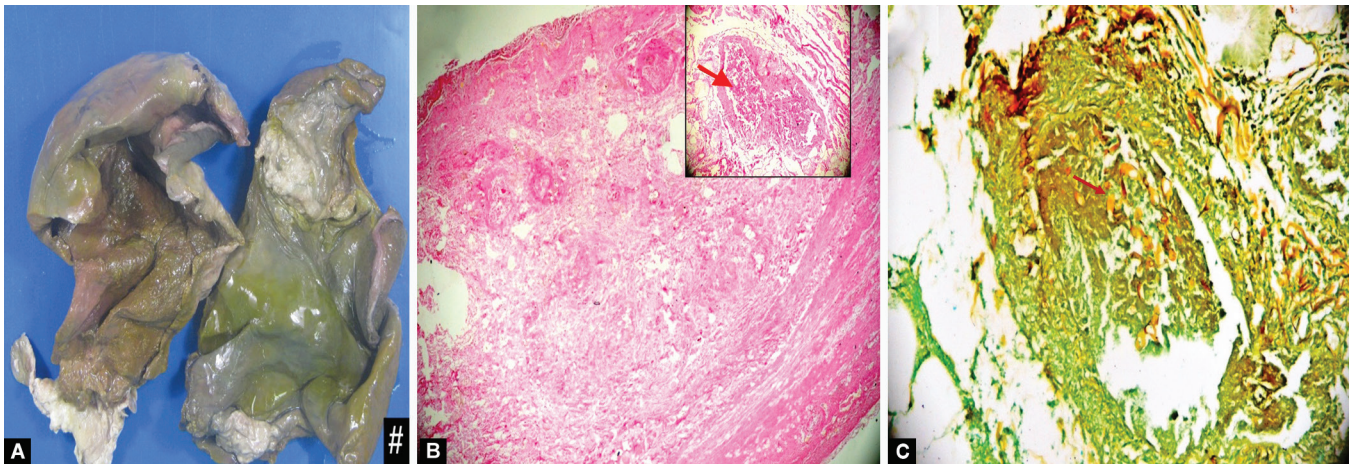


Figs 1A to C: (A) Initial CECT abdomen showing nonenhancement of entire pancreas with normal stomach cavity; (B) CECT abdomen showing rent in the posterior wall of stomach, air-filled necrotic collections draining into stomach cavity; (C) Upper GI endoscopy showing ulcerated gastric mucosa involving lesser curvature, intervening area covered with brown-black exudates



Figs 2A to C: (A) Macroscopic photograph of total gastrectomy specimen showing exudate covered areas (formalin preserved); (B) Transmural necrosis of the stomach wall (H-E stain, x40) with vessel wall invasion (inset, x40); (C) Silver stain highlighting the broad nonseptate fungal hyphae (x40)

ascites. Naso-jejunal tube was placed endoscopically for enteral feeding. On Day 18 of illness, there was clinically significant upper gastrointestinal bleed, at that time PT-14.2 seconds (control 12.3) and aPTT—45 seconds (control 30.8 seconds). Anticoagulation was stopped and diagnostic endoscopy was done, which showed large ulcerated area involving lesser curvature of stomach (Fig. 1C). Contrast-enhanced computed tomography (CECT) abdomen done subsequently showed complete defect of posterior wall of stomach and communication with necrotic collection and sigmoid colon perforation (Fig. 1B). Exploratory laparotomy was done, and subtotal gastrectomy, feeding jejunostomy, and ileostomy were performed. Stomach specimen—formalin preserved (Fig. 2A)—was sent to histopathologic examination (Figs 2B and C) which shows necrotic stomach wall with small foci of acute inflammatory cells and plenty of broad-based aseptate fungal profiles suggestive of Mucorales, and angioinvasion is also seen. Sections from rest of the specimen show necrotic tissue with few ghost outlines of pancreatic acini. Further culture and species identification could not be done as the specimen was kept in formalin solution. Patient was already receiving amphotericin B (7 days prior to surgery); subsequently, posaconazole oral suspension was also added. Effective anticoagulation for left eye cavernous venous thrombosis could not be instituted due to recent surgery and GI bleed. Despite surgical debridement and antifungal therapy, her clinical condition continued to worsen with disseminated intra-abdominal mucormycosis and she finally succumbed to her illness after 6 weeks of ICU stay.

Discussion

About 20% of acute pancreatitis complicate to severe grade with pancreatic necrosis and organ dysfunction.[1,3] Gastric perforation in acute pancreatitis is rarely reported.[6]

Mucor species belong to family zygomycetes found as mold or hyphae are the part of normal commensal in gastrointestinal tract, which can be lethal as opportunistic pathogens.[7] Mucormycosis generally complicates immunodeficiency states like uncontrolled diabetes, hematologic malignancies, solid organ transplantation, and glucocorticoid therapy.[7] Neutrophil or macrophage dysfunction, especially when associated with acidosis and hyperglycemia, predisposes to mucormycosis.[5] Definitive diagnosis is by direct microscopy under fluorescent brighteners, hematoxylin–eosin, periodic acid-Schiff, and/or Gomori's methenamine silver. Microscopy shows hyphae with variable width of 6–16 µm, nonseptate to pauci-septate, branching at 90° angles. Acute lesions show hemorrhagic infarct,

coagulation necrosis, angioinvasion, infiltration by neutrophils (in non-neutropenic hosts), and perineural invasion. Chronic lesion showed pyogranulomatous inflammation with presence of giant cells and sometimes hyphae. Serological markers for mucormycosis are currently not in routine use.[7,8]

As in this case, antifungal therapy alone is typically inadequate to control mucormycosis. The surgery to resect the infected tissue is often required. Aside from the resistance of some fungal strains to amphotericin B, several hallmark features of mucormycosis including angioinvasion, thrombosis, and tissue necrosis result in poor penetration of anti-infective agents to the site of infection.[7] Control of predisposing factors for infection, like hyperglycemia, metabolic acidosis, deferoxamine administration, immunosuppressive drugs, and neutropenia, is important. Liposomal amphotericin B is the drug of choice for initial therapy rather than amphotericin B deoxycholate in order to deliver a high dose with less nephrotoxicity.[4] The usual starting dose is 5–10 mg/kg (start at high dose). Isavuconazole is a new FDA-approved drug into armamentarium for the treatment of mucormycosis, also for salvage therapy. There are reports of using combination therapy with amphotericin B and either posaconazole or echinocandin.[4] However, due to lack of evidence, combination therapy is not recommended by major treatment guidelines.[4] Patients can be switched from a lipid formulation of amphotericin B to delayed-release posaconazole tablets for oral step-down therapy once a favorable clinical response is achieved after several weeks. Therapy should continue until there is clinical resolution of the signs and symptoms of infection, as well as resolution of radiographic signs of active disease, until reversal of underlying immunosuppression is achieved.[4]

This case highlights that clinician should keep suspicion of mucormycosis in a patient of pancreatitis, especially when associated with immunocompromised states like diabetic-ketoacidosis, as mucormycosis patients have high mortality due to its angioinvasive nature, which requires early surgical intervention along with antifungal therapy.

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