COVID-19 Associated Gastric Mucormycosis: A Case Report

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Abstract

Mucormycosis is a rare and opportunistic fungal infection caused by the order Mucorales. The onset of the coronavirus disease 2019 (COVID-19) has led to re-merging of this opportunistic infection. COVID-19 and its management protocols have been implicated to cause this surge due to sequential impaired immunity of those patients. High-index of suspicion with prompt evaluation and management is advisable for best clinical outcome.

Keywords: coronavirus disease 2019, COVID-19, SARS CoV 2 Infection, Mucormycosis.

Introduction

Mucormycosis is a rare and opportunistic fungal infection caused by the order Mucorales. Common sites of infection are rhino-orbito-cerebral, pulmonary, cutaneous, and the rarest location being gastric mucosa.[1] Symptoms of gastrointestinal (GI) mucormycosis vary and range from fever, nausea, vomiting, abdominal pain, GI bleeding to perforation. Definitive diagnosis of mucormycosis is dependent on the histopathological demonstration of fungal hyphae typical of mucormycetes in affected tissue biopsies. Tissue culture is considered essential for diagnosis and treatment, as it help finding sensitive anti-fungal medication through identifying the genus and species of the fungus.[2]

Mucormycosis is a dangerous infection that needs to be treated aggressively. Medical management consists of supportive care, elimination of predisposing factors and antifungals; such as liposomal Amphotericin B, Isavuconazole, or Posaconazole. However, surgical debridement of devitalized necrotic tissue and debulking of infection is frequently found to be needed.[3]

Mucormycosis is one of the rare opportunistic co-infections that have emerged with the onset of the coronavirus disease 2019 (COVID-19). The largest number were reported in India and most common site reported was rhino-orbital, followed by rhino-orbital cerebral.[4] This merge is thought to be related to infection related factors and treatment related factors.

Gastric mucormycosis is a lethal fungal infection caused by the invasion of Mucorales into gastric tissues. Gastrointestinal mucormycosis is very rare and present 7% of all reported cases, with the stomach as the most commonly affected organ (67%). Mortality rates in immunocompromised patients is more than 50%.[5]

In this paper, we are reporting this case of an unfortunate patient with COVID-19 pneumonia developing gastric mucormycosis.

Case Report

In April of 2021, a sixty-six-year-old lady presented to our institute with shortness of breath, malaise and sore-throat. At time of presentation, she was drowsy and hypoxemic. Her respiratory rate was 24 breath/minute with an oxygen saturation of 55% on room air, pulse rate 84 beats/min, blood pressure 140/69mmHg. Patient's oxygen saturation picked up to 92% after starting her on 15 litres/min of oxygen via non-rebreather mask. Her laboratory workup was remarkable for raised inflammatory markers (WCC 13.81 x10^9/L, absolute neutrophil count 10.6 x 10^9/L, C-reactive protein 269mg/L), acute kidney injury (creatinine 608 micromol/L, potassium 6.7mmol/L, sodium 126mmol/L, urea 23.1mmol/L), normal hemoglobin (11g/dL), Troponin T 28.4 ng/L, LFTs unremarkable (ALT 34 IU/L, AST 49 IU/L, ALP 185 IU/L). A semi-erect anteroposterior (AP) portable chest X-Ray showed bilateral infiltrates suggestive of COVID pneumonia (figure 1), and with the evidence of raised inflammatory markers she was immediately isolated and tested for COVID-19. She resulted positive and was started on IV dexamethasone, ceftriaxone, frusemide, and gentle hydration. She was admitted with the impression of acute respiratory distress syndrome secondary to COVID-19. Patient remained in need of aggressive respiratory support and so she was intubated and shifted to the intensive care unit (ICU). Upon further enquiry to her family members, she was also found to have a two-day history of vomiting and loose stools which they did not seek treatment to prior to this admission. Her past medical history was positive for hypertension on oral antihypertensive, chronic lower back pain taking diclofenac sodium regularly, and a psychiatric disorder.

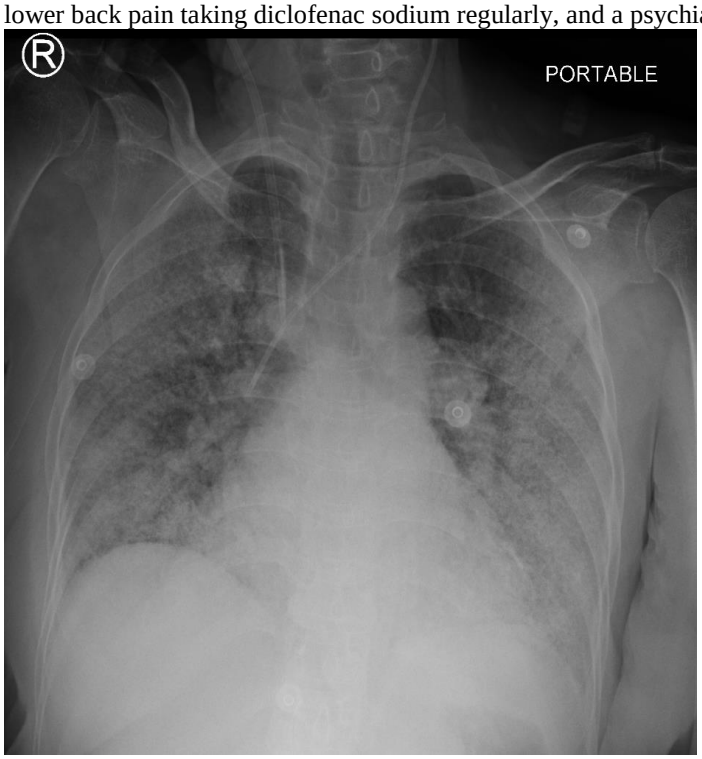

Figure 1: A semi-erect anteroposterior (AP) portable chest X-Ray showing bilateral infiltrates, suggestive of COVID pneumonia.

In COVID ICU, the patient was kept on ceftriaxone, azithromycin, and dexamethasone 10mg BID. Anticoagulated with low-molecular weight heparin with 5000iu BID. Patient showed steady recovery over her ICU admission. On day 9, coffee-ground material was aspirated through her NGT despite being on a proton pump inhibitor, so the dose was increased. Her hemoglobin was found to be unstable, dropping to 8.4 g/dL (was 11 on admission). On day 11 of ICU admission, she was extubated and shifted to the general ward. On the following day, she was again found coffee-ground nasogastric aspirate with continuous drop of her hemoglobin to 6.8g/dL and received two units of packed red blood cells. Patient was further investigated with computed tomography (CT) scan of the chest, abdomen and pelvis, which showed a significant thickening of stomach wall with specks of air along it suggestive of a possible sealed perforation or emphysematous gastritis, indicating an inflammatory or infective etiology (figure 2). As a result, steroids were stopped and her antibiotics were upgraded with the impression of hollow viscous perforation. This was followed by an upper gastrointestinal endoscopy that showed antral ulcer suspicious for malignancy, for which a biopsy was taken.

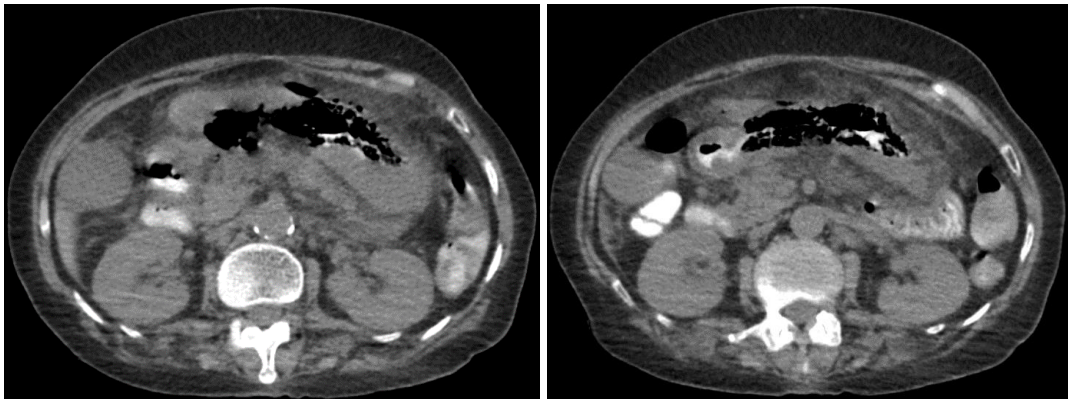

Figure 2: A computed tomography (CT) showing a significant thickening of stomach wall with specks of air along the stomach, suggestive of a possible sealed perforation or emphysematous gastritis.

Following these findings, the patient was referred to general surgery. Surgical review found tenderness in the epigastrium and right iliac fossa but no signs of peritonitis. Impression was sealed perforation due to inflammatory/neoplastic gastric ulcer. The patient was treated conservatively by keeping her nil-per-oral, on nasogastric tube with free drainage, continuing antibiotics, monitoring the patient and considering a repeat CT if the patient's condition worsens. At that time, she was on meropenem and vancomycin, which was guided by previous positive blood cultures since her ICU admission. Five days later her gastric biopsy has resulted. The Histopathology showed gastric mucosa with extensive ulceration. Many fragments of necrotic slough contain abundant fungal hyphae morphology consistent with mucormycosis. The fungal elements show numerous broad irregular non-septate and pauciseptate ribbon like hyphae branching at 90-degree angles suggestive of mucormycosis. Angioinvasion was present. There is no evidence of malignancy (Figure 3). Infectious disease team was involved and she was started on a regime of liposomal Amphotericin B while continuing other antibiotics. A non-contrast enhanced CT scan of the brain was done to rule out rhinocerebral mucormycosis and was found to be unremarkable.

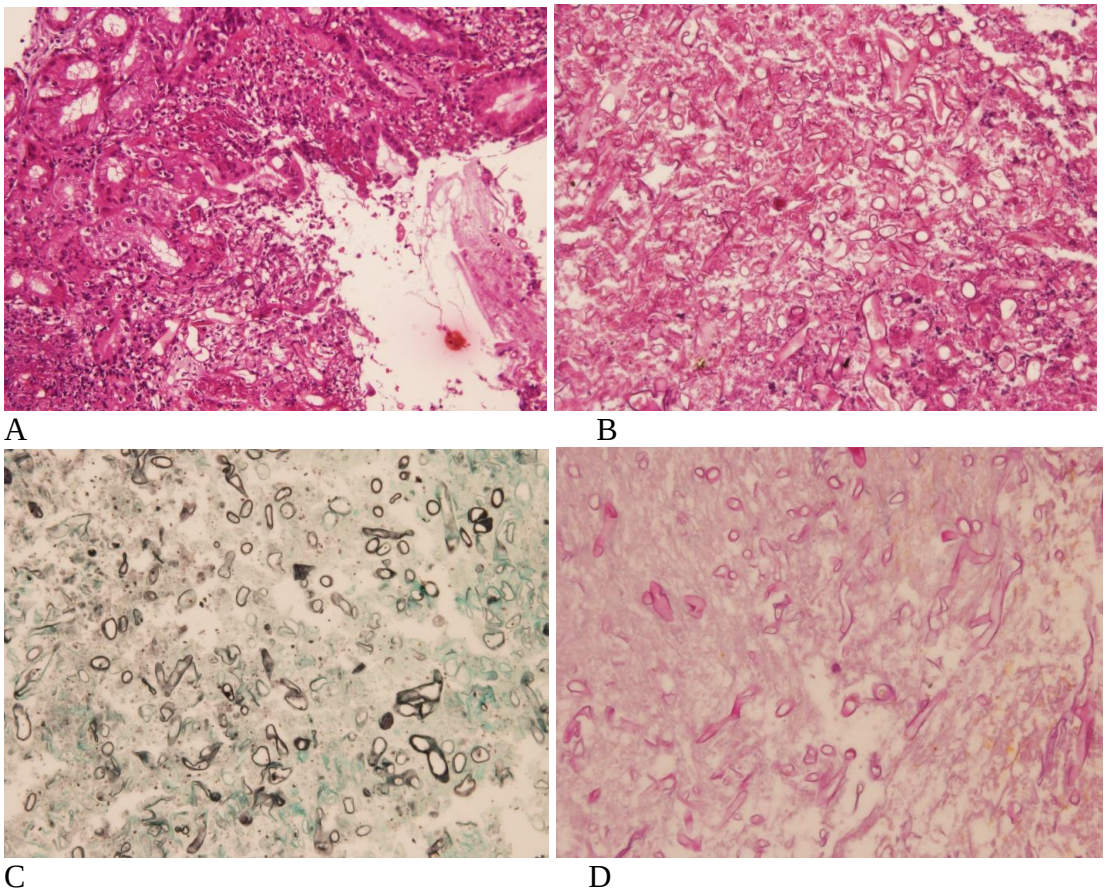

Figure 3: A: H&E section showed gastric mucosa with ulceration and necroinflammatory debris, fungal hyphae present. B: H&E section showed numerous broad based irregular pauciseptate ribbon like fungal hyphae consistent with mucormycosis. C: GMS stain highlights the fungal hyphae. D: PAS stain highlights the fungal hyphae.

On day 20 her condition shows features of worsening infection with white cell count rising to 24 x10^9/L, absolute neutrophil count rising to 22.9 x10^9/L and platelets dropping to 80 x10^6/L and so a repeat abdominal CT scan was obtained, with findings showing a significant increase in free fluid in the perihepatic area likely infected, increased abdominal fat stranding, posterior stomach wall showing increased thickness, anterior gastric emphysema as well as findings of COVID pneumonia (figure 4). The family was counselled extensively for surgical intervention due to her worsening prognosis despite appropriate medical management. Unfortunately, they vehemently refused any surgical options and decided to continue conservatively. They refused partially because they were in denial and partially because believed she was too frail for major surgery. Patient was shifted back to the ICU and gradually her condition deteriorated. Eventually it was decided not to resuscitate her due to her grave prognosis and failure to respond to treatment. On day 30 the patient passed away due to ongoing severe septic shock leading to multi-organ failure.

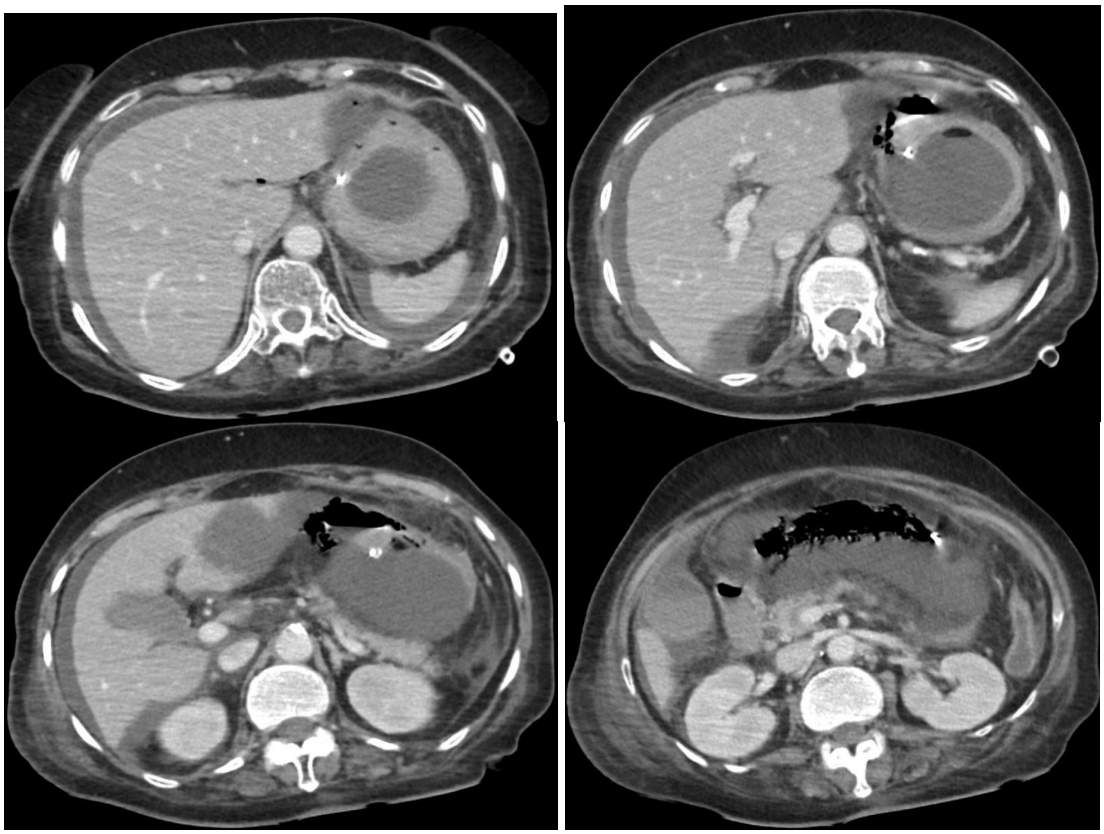

Figure 4: A computed tomography (CT) showing significant free fluid in the perihepatic area with increased abdominal fat stranding and gastric emphysema.

Discussion

Mucormycosis is a rare and dangerous opportunistic infection caused by the subphylum Mucoromycotina, order Mucorales, also colloquially known as the "black fungus". The most common organism to be isolated from patients is Rhizopus oryzae. The disease most often occurs in immunocompromised patients, with predisposing factors such as uncontrolled diabetes mellitus, solid organ or stem cell transplantation, underlying hematological malignancy, major trauma or burns, use of steroids, iron overload states, severe neutropenia, and disseminated chronic infections.[6]

Mucormycosis can affect any organ system, but most commonly presents as rhino-cerebral, followed by pulmonary and cutaneous. Primary gastrointestinal infection is uncommon, accounting for approximately 7% of all cases, with the stomach being the most common (67%) followed by the colon (21%), small intestine (4%), and esophagus (2%). Mucormycosis is characterized by hyphae invading the vasculature leading to infarction and necrosis of the host's tissues. Symptoms of GI mucormycosis may vary but range from fever, nausea, vomiting, abdominal pain, GI bleeding and perforation.[7]

The true incidence/prevalence of mucormycosis is unknown, as many of the cases remain undiagnosed due to difficulty in collecting the sample from deep tissue and low sensitivity of diagnostic tests. The Leading International Fungal Education (LIFE) portal has estimated the annual incidence of acute invasive mucormycosis might be around 10,000 cases.[8] With the ongoing pandemic of coronavirus disease 2019 caused by SARS-CoV-2, several cases of mucormycosis in COVID-19 positive patients have been reported globally, with India recording the highest number of COVID-19 associated Mucormycosis (CAM).[9] The hypothesis being that COVID-19 provides an ideal environment for the germination of Mucorales spores, which are hypoxia, hyperglycaemia (steroid-induced, new onset, or diabetes), acidosis (metabolic, diabetic), high iron levels and decreased phagocytic activity due to immunosuppression (SARS-CoV-2 mediated, steroid-mediated, or background co-morbidities).[10]

The diagnosis of mucormycosis is challenging, especially when it's in rare a site. However, it starts with having a high index of suspicion in un immunocompromised patients who is COVID-19 positive with known risk factors. Once diagnosis is suspected appropriate imaging and confirmatory biopsy for culture if possible is advised. The management of this condition require the combination of aggressive surgical debridement and appropriate antifungal medications with supportive care. Finally, steroids use in COVID-19 patients should be tailed based on sound clinical judgement to reduce incidence of CAM.

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