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Case Report

A Case of Gastrointestinal Mucormycosis in an Immunocompetent Patient with Comorbidities and Alcohol Use Disorder

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Abstract

Gastrointestinal mucormycosis (GIMM) is a rare and aggressive opportunistic fungal infection that is most reported in patients who are immunocompromised or immunosuppressed. GIMM accounts for about 7% of all mucormycosis cases and carries mortality rates up to 85%. GIMM mimics common causes of gastrointestinal bleeding, and diagnosis is made through endoscopic evaluation with histopathologic confirmation. We present a case of an immunocompetent 79-year-old male with chronic kidney disease and alcohol use disorder who presented with hematemesis. The patient rapidly deteriorated, requiring intensive care for hypoxia and suspected aspiration. Endoscopy revealed esophageal ulcerations and a large necrotic gastric ulcer. Histopathologic evaluation demonstrated findings consistent with herpes esophagitis as well as tissue-invasive fungal elements characterized by broad, ribbon-like hyphae consistent with mucormycosis, later confirmed by culture. The patient was treated with isavuconazonium and underwent proximal gastric resection. A repeat endoscopy 4 weeks later showed no evidence of mucormycosis. This case underscores the importance of maintaining a high index of clinical suspicion for GIMM in patients presenting with upper gastrointestinal bleeding, even in the absence of classic immunosuppressive states.

Keywords: *Mucormycosis; Gastrointestinal mucormycosis; Alcohol related immunomodulation; immunocompetent host.*

Introduction

Mucormycosis is a rare, aggressive fungal infection caused by fungi of the order Mucorales. It is found ubiquitously in nature but it rarely a concern in immunocompetent patients.[1] It is most reported in patients who are immunocompromised or immunosuppressed. This can include patients with uncontrolled diabetes mellitus, hematologic malignancies, solid organ transplantation, intravenous drug abuse, or HIV.[2] Angioinvasion is the most prominent feature of mucor pathogenesis. The fungus penetrates and damages endothelial cells and arteries to cause ulceration, and forms thrombi which can cause infarction and lead to hemorrhage.[3]

Mucormycosis is known to affect various systems; however, gastrointestinal mucormycosis (GIMM) is the least common and while it only accounts for about 7% of all mucormycosis cases, it has a mortality as high as 85%.[2] The stomach is considered the most common site of GIMM.[4] It is mostly prevalent in patients undergoing solid- organ transplant. Furthermore, due to the angioinvasive nature of mucor, pain and bleeding are the most common presenting symptoms for GIMM, especially of the stomach.[5]

The diagnosis of GIMM is challenging due to its nonspecific presentation of pain and bleeding. It mimics more common causes of upper gastrointestinal bleeding like peptic ulcer disease or variceal hemorrhage. This is particularly true for immunocompetent patients because the suspicion of GIMM is already low. An endoscopic evaluation with histopathologic confirmation is required to definitively diagnose GIMM.[6] Furthermore, given the angioinvasive nature of the organism, a delay in recognition can lead to rapid clinical deterioration.[6]

Historically, case reports have highlighted the challenges of diagnosing GIMM due to its rarity, atypical presentations, and prevalence mostly in immunocompromised patients.[7,8] However, cases describing GIMM infection in immunocompetent patients is exceedingly limited. This case demonstrates severe presentation of gastric GIMM in an immunocompetent patient with multiple comorbidities and alcohol use disorder, which led to rapid clinical deterioration requiring intensive care management and proximal gastric resection.

Case

This case presents a 79-year-old male with a past medical history of hypertension, chronic kidney disease, hyperlipidemia, peripheral arterial disease, gastroesophageal reflux disease, cerebrovascular disease, and alcohol use disorder who presented to the emergency department with a two-day history of hematemesis. The emesis initially began as non-bloody but progressively evolved to a bloody, coffee-ground appearance. He reported associated nausea and weakness but denied abdominal pain, fever, chills, myalgias, hematochezia, diarrhea, constipation, or reflux symptoms. His last alcohol intake was two days prior to presentation, and he reported daily consumption of liquor (approximately three to four shots per night).

The patient was admitted to the general medicine service; however, his clinical status deteriorated overnight. He developed hypoxia requiring high-flow oxygen support. In the setting of an episode of projectile vomiting and concern for aspiration, he was transferred to the intensive care unit for management of acute respiratory distress.

Empiric broad-spectrum antibiotic therapy with vancomycin and meropenem was initiated for suspected aspiration pneumonia, and the patient was made nil per os. Pulmonology and gastroenterology services were consulted. Given his significant smoking history (100 pack-years, quit seven years prior), pulmonology recommended initiation of systemic corticosteroids and bronchodilators for possible concomitant chronic obstructive pulmonary disease exacerbation along with antibiotics for aspiration pneumonia. Concurrently, gastroenterology planned endoscopic evaluation once the patient stabilizes. In light of laboratory findings notable for transaminitis and hyperbilirubinemia, a comprehensive hepatic workup was also pursued which all came back negative.

Patient's esophagogastroduodenoscopy revealed multiple dispersed and clustered ulcerations in the middle third of the esophagus suggestive of healing HSV esophagitis. Furthermore, a large, irregular-appearing 4 cm ulceration with red to purple discoloration, fungating borders, and exudate was found in the proximal gastric body and fundus. Otherwise, the rest of stomach and esophagus was normal. Histopathologic evaluation of biopsy specimens was negative for Helicobacter pylori but demonstrated findings consistent with herpes esophagitis as well as tissue-invasive fungal elements characterized by broad, ribbon-like hyphae (Figure 1 and 2).

Infectious disease consultation was obtained, with concern for mucormycosis prompting recommendation for repeat endoscopic biopsy and culture. Empiric antifungal therapy with isavuconazonium was initiated for suspected mucormycosis, along with famciclovir for herpes simplex virus esophagitis. Subsequent fungal cultures and polymerase chain reaction testing returned positive for Rhizopus species.

Given the extent of disease, the patient underwent proximal gastric resection (Figure 3 and 4). He was continued on isavuconazonium therapy for six weeks with weekly monitoring for hepatotoxicity. He is currently doing well and is trying to cut back on alcohol. A repeat esophagogastroduodenoscopy done 4 weeks post cresemba initiation showed no evidence of mucormycosis.

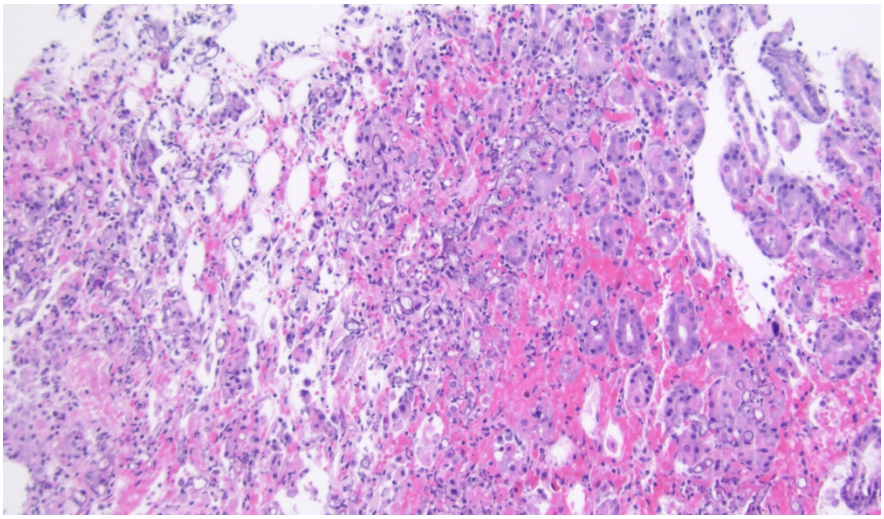

Figure 1: Fragment of necrotic, ulcerated, and inflamed gastric mucosa with detached and tissue-invasive fungal hyphae. The fungal organisms are broad and ribbon-like without obvious septations

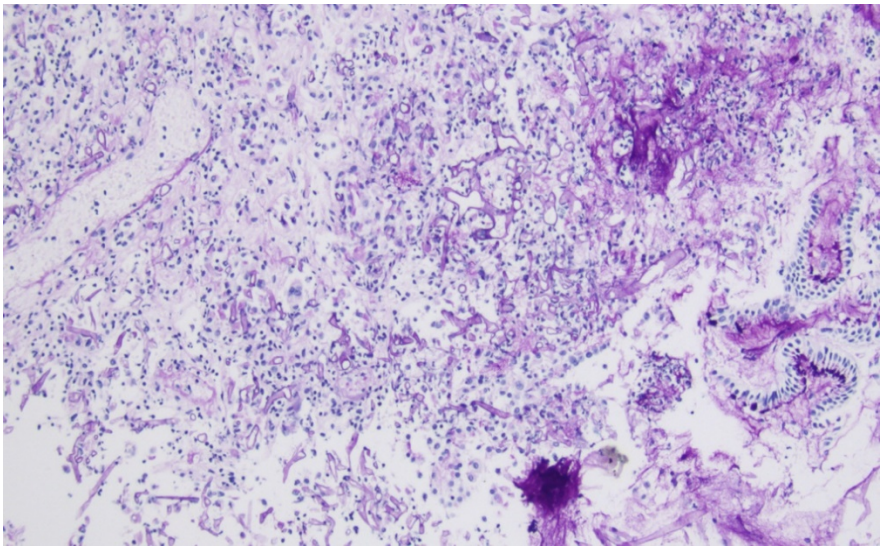

Figure 2: The fungal organisms from figure 1 highlighted by a DPAS special stain

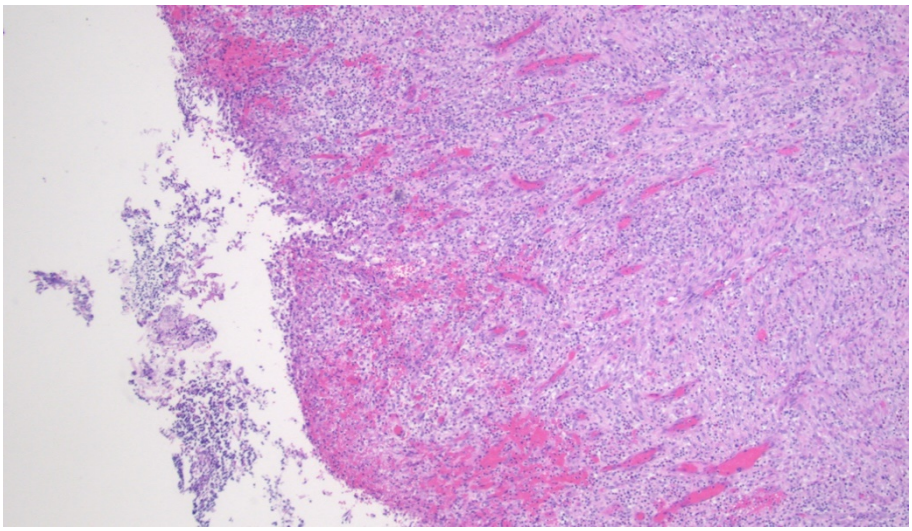

Figure 3: Gastrectomy specimen showing sections of stomach with ulcerated and inflamed gastric mucosa demonstrating focal, detached, ribbon-like fungal hyphae.

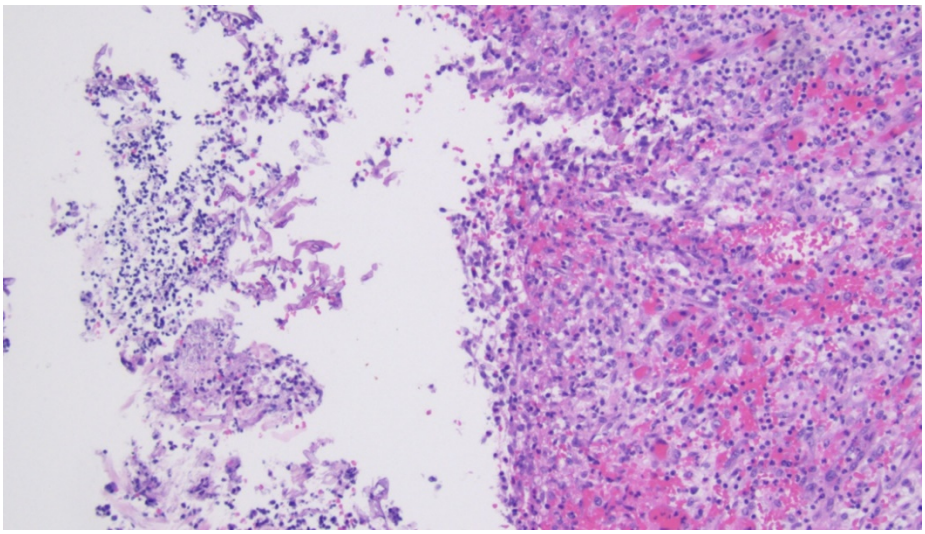

Figure 4: Another gastrectomy specimen showing sections of stomach with ulcerated and inflamed gastric mucosa demonstrating focal, detached, ribbon-like fungal hyphae

Discussion

Gastrointestinal mucormycosis (GIMM) is a rare and aggressive opportunistic fungal infection, which comprises of about 7% of all mucormycosis cases but carries a disproportionately high mortality rate of about 85% secondary to its rapid progression and the diagnostic challenges.[2] The stomach is cited as the most common site for GIMM and the infection typically targets those with profound immunosuppression.[4]

However, a review article by Kaur et al. 2018 demonstrated the rise in GIMM cases among immunocompetent patients with stomach being the second most common affected site for the disease. It also highlighted multiple factors like uncontrollable diabetes, hemodialysis/peritoneal dialysis, acute renal failure, and malnourishment being the classic associations of GIMM in immunocompetent population.[10]

This particular case showcases an immunocompetent patient who lacks the ideal immunocompromised risk factors associated with fungal infections. However, given his history of alcohol use disorder and chronic kidney disease, a state of "functional" immunosuppression was likely created in the patient. Chronic alcohol consumption impairs neutrophil chemotaxis and dysregulates the systemic immune response.[11] Furthermore, his alcohol use disorder also puts him at a higher risk of malnutrition, one of the risk factors mentioned in Kaur et al. 2018. Due to his chronic kidney disease, uremic toxins also impair the classic response of neutrophils and monocytes to fungal cells.[12] Lastly, the diagnostic process was further complicated by the patient's non-specific presentation and concomitant HSV esophagitis, which could have easily been mistaken as the sole source of his clinical deterioration.

The successful management of this patient highlights the necessity of a multi-modal therapeutic approach to manage GIMM. Antifungal medications alone are often insufficient to treat GIMM because of the fungus's intrinsic resistance to short-tailed azoles.[13] The only two drugs which has shown efficacy in treating mucormycosis is amphotericin B and extended spectrum azoles like isavuconazonium.[14] Furthermore, Isavuconazonium was selected as the antifungal agent not only due to its broad-spectrum efficacy but also relatively favorable side-effect profile regarding hepatotoxicity and nephrotoxicity, an important thing to consider given the patient's underlying chronic kidney disease.[14] Lastly, as a part of a multi-modal therapeutic approach, surgical debridement, in this case proximal gastric resection, should be performed whenever feasible concomitantly with antifungal therapies because of a combination of both is usually better than either alone in improving mortality.[1]

In conclusion, this case highlights the importance of having a high index of clinical suspicion for GIMM, even in immunocompetent patients, who present with symptoms of gastrointestinal bleeding. Early endoscopic evaluation with histopathologic confirmation is the gold standard for diagnosis. Furthermore, prompt initiation of broad-spectrum azole therapy in combination with timely surgical debridement remains the most effective strategy for overcoming the high mortality associated with GIMM.

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