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# Invasive gastric mucormycosis: A case report of a deadly complication in an immunocompromised patient after penetrating trauma

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## 1. Introduction

Mucormycosis is a rare life-threatening fungal infection that typically involves the rhino-cerebral area. It is the third most common invasive fungal infection, after aspergillosis and candidiasis, and can affect any organ system, with the most common presentations involving the nasal sinuses, orbit, brain or the lung. Invasive gastrointestinal Mucormycosis is a rare form of the disease that affects the stomach, colon and ileum, in descending order of incidence [1]. Previous case reports describe Mucormycosis primarily in premature neonates; neutropenic adults; and those with immunocompromising conditions such as diabetes, AIDS, SLE, corticosteroid use, transplantation, and increased levels of serum iron [1–7]. Treatment involves a combination of early antifungal therapy and surgical debridement [3,4,8,9]. We report the first case of primary gastric Mucormycosis in an immunocompromised patient after penetrating abdominal trauma, which presented post-operatively as a gastropleural fistula from a gastric perforation. We report in line with the SCARE criteria [10].

## 2. Case report

The patient is a 34-year-old HIV positive African American male with a history of gastrointestinal CMV, CNS mycobacterium avium infection(MAC), and immune reconstitution inflammatory syndrome(IRIS) on prednisone who initially presented to our level I trauma center with eight gunshot wounds to the abdomen (Fig. 1). He presented with peritonitis on examination, was taken for an emergency laparotomy by a trauma surgeon, and was found to have a grade IV splenic laceration; grade III left kidney laceration; injury to the colon at the splenic flexure, and injuries to the duodenum and stomach. He underwent a splenectomy, segmental colon resection, left partial nephrectomy, and repair of the pylorus and duodenum. Due to hemorrhage and the large amount of resuscitative fluid received, the edema precluded wound closure. His operation was a damage controlled operation, he was left in discontinuity, and his abdomen was left open with a temporary vacuum-assisted closure device with the plan to return to the operating room for definitive reconstruction of the injuries. The patient was monitored in the Intensive Care Unit(ICU) post-operatively and required vasopressor support in addition to stress dose steroids for ongoing hypotension in the face of chronic steroid use. On subse-

*Abbreviations:* AIDS, acquired immune deficiency syndrome; BID, twice a day; CMV, cytomegalovirus; CNS, central nervous system; CT, computed tomography; GE, gastroesophageal; GI, gastrointestinal; Hgb, hemoglobin; ICU, intensive care unit; IRIS, immune reconstitution inflammatory syndrome; MAC, mycobacterium avium complex; POD, postoperative day; SLE, systemic lupus erythematosus.

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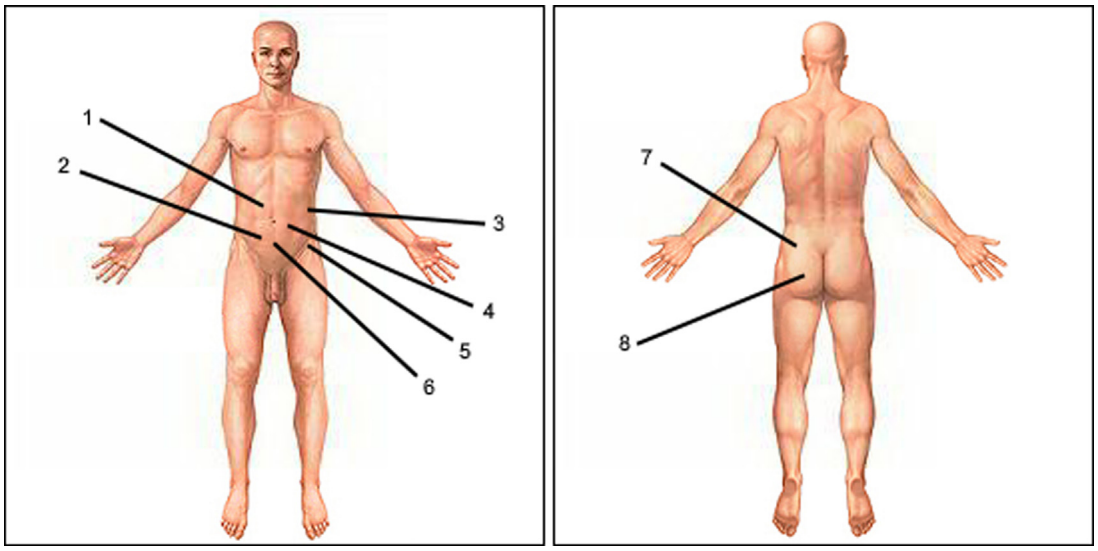


**Fig. 1.** Diagram representing location of 8 gunshot wounds upon initial presentation.

quent laparotomy, a left diaphragmatic injury was repaired and an end transverse colostomy was created as there was a suspected rectal injury distally. His antiretroviral medication, CMV maintenance therapy, and CNS MAC treatment were held in the acute trauma setting. He was initially started on piperacillin/tazobactam for colonic flora and resumed azithromycin, moxifloxacin, rifampin, amikacin, and ganciclovir maintenance therapy once stabilized on post-operative day(POD) #4. After the abdomen was closed POD #11, he resumed his home anti-retroviral therapy including emtricitabine, darunavir, and tenofovir. His CD4 count at that time was 137/mm$^3$. He was then transferred to inpatient acute rehabilitation.

While in rehabilitation on POD #18, he developed bleeding from his midline wound and dropped to a hemoglobin(Hgb) 3.6 g/dL. This required transfer back for transfusions and surgical management of a bleeding arterial vessel from his abdominal wound. On POD #29, he was transferred to the ICU after complaints of chest pain with tachycardia, hypoxia, and hypotension requiring vasopressors. Workup revealed a large left-sided hydropneumothorax with right-sided mediastinal shift. A chest tube was placed on the left side with immediate return of dark blood. A CT scan with oral contrast revealed a communication between the stomach and the left pleural space correlating with high chest tube output (Fig. 2). Endoscopic evaluation found a 2–3 cm patch of necrosis in the posterior of the stomach along with linear erosions. He was subsequently taken to the OR for gastropleural fistula repair.

On exploration, there was a large area of necrosis of the fundus and cardia of the stomach and extension into the gastroesophageal (GE) junction and an adjacent portion of the diaphragm. The grossly devitalized areas were resected and the decision was made to perform a planned second look with reconstruction after further resuscitation. The patient continued to have high output from his chest tube, which required multiple transfusions. Urine cultures were positive for enterococcus and chest tube cultures were positive for vancomycin resistant enterococci. Findings during the second look laparotomy revealed extension of the necrosis. The fundus was necrotic and did not bleed when cut. The body of the stomach showed hemorrhagic mucosa, and devitalized serosa with thrombosed veins on the exterior surface (Fig. 3). The previously repaired area of the diaphragm was perforated and necrotic with a 10 cm defect. A subtotal gastrectomy with reconstruction was performed and drains were placed. In the ICU, the patient's condition deteriorated with multiorgan failure and after a discussion with the family, the decision was made to withdraw care on POD #3.

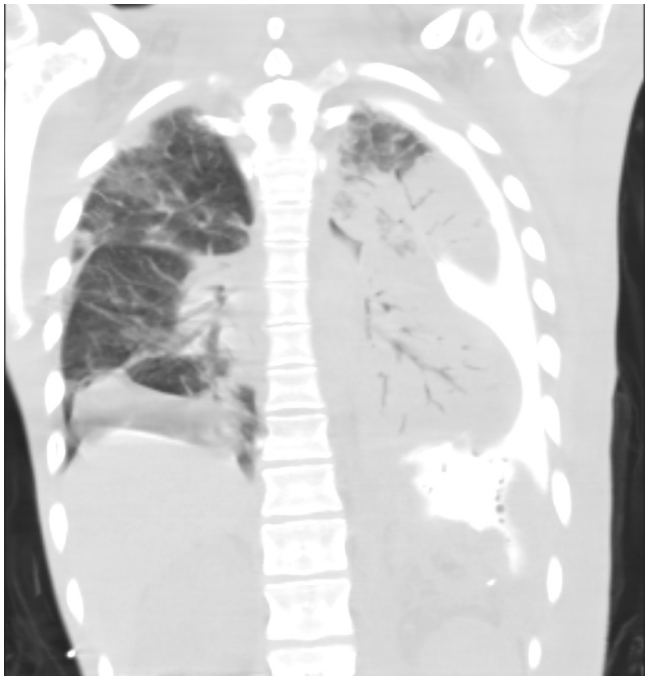

**Fig. 2.** CT scan with oral contrast: enteric contrast within the left pleural space with an apparent open communication between the stomach and pleura. There is also continued collapse/consolidation in the left to right mediastinal shift after the placement of a chest tube.

## 3. Pathology

Three specimens including the stomach, GE junction, and the diaphragm were sent for evaluation (Fig. 3). The serosa was dusky in appearance with sub-serosal petechial hemorrhages. The gastric mucosa showed regular rugae with a well-defined area of hemorrhage involving the mucosa and muscularis. Adjacent to the hemorrhage was an area of red-brown discoloration consistent with necrosis. Similar findings of hemorrhage and necrosis were observed at the GE junction. The diaphragm consisted of congested and necrotic muscle. Microscopic sections showed invasive fungal hyphae, described as broad, non-septate, with branching consistent

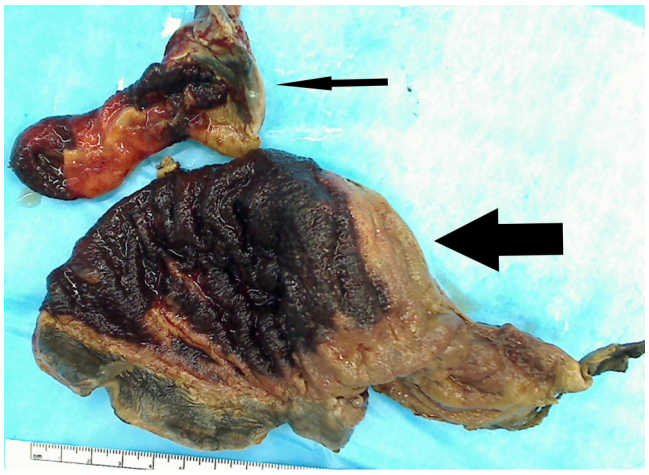

**Fig. 3.** Gross specimen of stomach (wide arrow) and GE junction (narrow arrow). Demonstrating hemorrhage and necrosis involving the mucosa and muscularis.

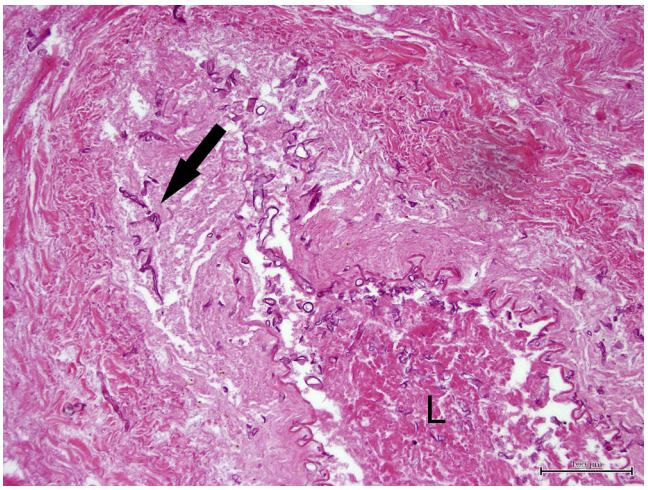


**Fig. 5.** Hematoxylin & Eosin Stain of the stomach. L – vessel lumen. Thick arrow – demonstrating angioinvasion by Mucor sp.

with the Mucor genus (Fig. 4). Angioinvasion, thrombosis, hemorrhage, and necrosis were also seen (Fig. 5).

## 4. Discussion

Mucormycosis is an opportunistic angioinvasive fungal infection considered to be a zygomycosis (infection caused by the class Zygomycetes). Zygomycetes are divided into two orders: the Entophthorales and the Mucorales. The Entomophthorales contain rarely pathogenic species, whereas the Mucorales contain the most common human pathogens, specifically *Rhizopus*, *Mucor*, *Absidia*, and *Cunninghamellacae*. These organisms with low virulence rarely cause disease and usually present in immunocompromised individuals. The *Rhizopus* species is the most pathogenic and significantly more virulent than other fungi in that order [11,12].

Like *Aspergillus*, the pathogenesis of *Rhizopus* may be attributed to its tendency towards angioinvasion (vasculotropism) because blood vessels provide a source of oxygen. Results of angioinvasion include local ischemia, tissue infarction, necrosis, and provides a pathway for hematogenous spread [12]. The risk factors for infection were described in a review of 929 patients: diabetes (36%), malignancy (17%), transplantation (12%), and deferoxamine therapy (6%) [4]. Steroid exposure has also been associated with worse outcomes [13]. In a broader context, these conditions are associated with impairment of normal immune function, specifically in white cell counts, which is associated with increased risk for invasive fungal infections.

Mucormycosis results from either the inhalation or direct inoculation of sporangiospores onto a disrupted epithelium, such as skin or mucosa [1]. It can manifest anywhere in the body, namely the rhinocerebral (21%), pulmonary (24%), cutaneous (19%), gastrointestinal (7%), CNS, and disseminated forms. Within the GI tract, the stomach is most commonly involved (57.5%), followed by the colon (32.3%), then ileum (6.9%) [1,4].

The initial presentation of a gastrointestinal lesions consists of abdominal pain, distention, fever, and diarrhea. If the infection extends from the lumen of the gut, it can lead to obstruction, ulceration, bleeding, or perforation [11]. As this disease typically affects immunocompromised individuals with a variety of co-morbidities and progresses rapidly to be potentially fatal, a high degree of clinical suspicion is needed to diagnose this rare condition.

The principles of treatment are early diagnosis, reversal of underlying risk factors, surgical debridement, and prompt antifungal therapy. Diagnosis is achieved most rapidly by a tissue diagnosis with direct microscopy and histopathology from biopsies or surgical specimens [8]. Cultures are considered essential, despite low sensitivity, allowing for identification and susceptibility testing [8]. Prompt initiation of antifungal therapies within 5 days of diagnosis has been associated with improved survival compared to later initiation (83% vs 49%) [3].

Based on the most recent guidelines from the European Society for Clinical Microbiology and Infectious Diseases, the use of liposomal amphotericin B at 5–10 mg/kg and amphotericin B lipid complex at 5–7.5 mg/kg are recommended as grade BII and BIII evidence. Amphotericin B deoxycholate and amphotericin B

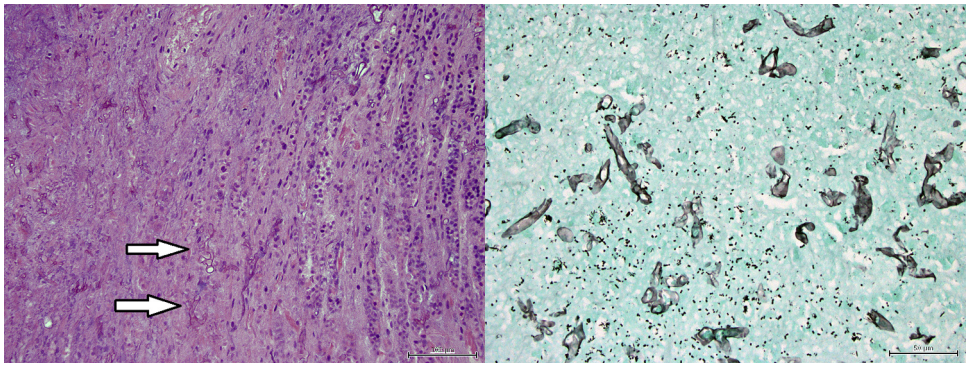

**Fig. 4.** (Left) Hematoxylin & Eosin Stain of the stomach. Arrows pointing to broad, nonpigmeneted, non-septated hyphae with right angle branching consistent with Mucor. (Right) Gomori methenamine-silver stain demonstrating Mucor.

colloidal dispersion are both grade CII recommendations Posaconazole 400 mg BID or the use of combination therapy are grade CIII recommendations [8,9]. In addition to antifungal therapy, early surgical debridement has been associated with improved survival (62% with antifungal alone, 57% with surgery alone, and 70% with both) [4]. Vascular invasion with thrombosis results in necrosis and poor tissue penetration by antifungal therapies. Therefore, debridement of necrotic tissues is necessary for the complete treatment of invasive Mucormycosis [3].

## 5. Conclusion

We describe a catastrophic case of an immunocompromised patient with penetrating abdominal trauma who developed invasive gastrointestinal Mucormycosis and a gastropleural fistula. He had predisposing conditions, including AIDS, steroid use, penetrating abdominal injury, and gastric mucosal trauma. It was not until later in his rehabilitation that the Mucormycosis infection had invaded through the wall of the stomach, as well as the adjacent diaphragm to cause a gastropleural fistula. Unfortunately, the tissue diagnosis was not obtained until after the patient's condition had deteriorated. To date, there have only been four case reports of invasive Mucormycosis involving trauma patients that presented either as a cutaneous lesion or as a GI bleed [14–17]. We emphasize the importance of having a high clinical suspicion to obtain early histopathologic diagnosis of this rare disease to initiate the proper treatment of surgical debridement, intravenous antifungals, and improve outcomes from this deadly infection.

## Conflicts of interest

The authors have no conflict of interest.

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## Ethical approval

The Institutional Review Board (IRB) of our institution was consulted and appropriate ethical approval was granted.

## Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

## Author contribution

Kevin L. Chow, MD – data collection, wrote the paper.

David P. McElmeel, DO – data collection, reviewed paper.

Henry G. Brown, MD PhD – provided pathology consultation, reviewed paper.

Muhammad S. Tabriz, MD – provided infectious disease consultation, reviewed paper.

Ellen C. Omi, MD – study concept, paper writing and review.

## Guarantor

Kevin L. Chow, MD.

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