

# Emphysematous Gastritis Secondary to Gastric Mucormycosis in A COVID-19 Positive Patient: Case Report

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## ABSTRACT

Mucormycosis is an invasive fungal infection with high mortality, which occurs mostly in immunocompromised patients. It is characterized by necrotizing vasculitis and the presence of branching wide-angle hyphae. The gastrointestinal form is one of the rarest, symptoms are nonspecific and only 25% are diagnosed pre-mortem. Treatment consists of antifungal therapy and urgent surgical debridement. Case report: 69-year-old male with a history of type 2 diabetes mellitus presents with dyspnea, SARS CoV2 rapid antigen test turns out positive. During his hospital stay he presents sepsis, gastrointestinal bleeding and pneumoperitoneum on abdominal CT. The patient underwent exploratory laparotomy, necrosis of the greater curvature of the stomach was found, therefore vertical gastrectomy was performed. The histopathological report revealed panmural necrosis associated with arterial thrombosis secondary to *Mucor* spp, liposomal amphotericin B was started, however, the patient developed nosocomial urinary tract and pulmonary infections, decease was documented 29 days after admission. Conclusion: Mucormycosis is an emerging fungal infection that requires high suspicion for its diagnosis. Antifungals and urgent surgical debridement by the general surgeon are the cornerstone treatment for this entity.

**Keywords:** *Gastrointestinal Mucormycosis, Emphysematous Gastritis, Vertical Gastrectomy, COVID, Case Report*

## Introduction

Mucormycosis is an emerging infection caused by fungi belonging to the order Mucorales (Serris *et al.*, 2019). It occurs mainly in patients with immunosuppression, such as hematological malignancies, hematopoietic stem cell or solid organ transplantation and diabetes mellitus (Dioverti *et al.*, 2015). In this context, patients with COVID-19 may present an altered cell-mediated immune response and increased susceptibility for fungal co-infections (Monte Junior *et al.*, 2020). The disease is characterized by extensive necrotizing vasculitis, resulting in thrombosis and subsequent tissue infarction. Primary gastrointestinal disease is the rarest form, the stomach being the most common site of infection. It can be

acquired by ingestion of contaminated food, but can also be associated with contaminated healthcare-associated devices or equipment (Monte Junior *et al.*, 2020). Diagnosis may be suspected by endoscopic findings showing a fungal mass or necrotic lesions overlying an ulcerated area; radiological findings are nonspecific (Monte Junior *et al.*, 2020). Early diagnosis helps to accelerate antifungal therapy and improve survival, being liposomal amphotericin B the treatment of choice (Chamilos *et al.*, 2008). Surgical debridement or complete resection of the affected organ is of utmost importance to eliminate necrosis and improve penetration of antifungal agents at the targeted site. These patients present a high risk of perforation and hemorrhage, which requires extensive surgical resection (Chamilos *et al.*, 2008). We performed a literature review in databases such as "wiley" and "pub med" using the keywords "mucormycosis, covid, infection" finding very few case reports of fungal disease associated with covid19 and no reports searching for association between the words "gastric, mucormycosis, covid".

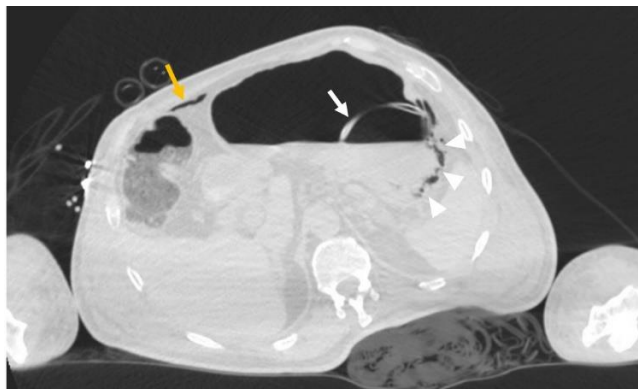
## Case Report

A 69-year-old male with a history of type 2 diabetes mellitus on Metformin and Clopropramide, arterial hypertension under treatment with Losartan and Amlodipine arrived to the emergency department with headache, chest pain, cough, myalgias, arthralgias and dyspnea of one week of onset. On admission he presented heart rate of 114 bpm, respiratory rate of 24 rpm, oxygen saturation 80% without supplemental oxygen support, glucose 587 mg/dl, leukocytes 25,690 cells/mm<sup>3</sup>, neutrophils 85% Lymphocytes 1. 2%, hemoglobin 16.3 g/dl, procalcitonin 3.78 ng/dl, arterial blood gas with pH 7.41, PCO<sub>2</sub> 21 mmHg, PO<sub>2</sub> 35 mmHg, HCO<sub>3</sub> 13 mmol/L, oxygen saturation of 62%. A rapid antigen test for SARS Cov2 was performed and the result turned out positive. Chest CT scan (Fig. 1) showed radiological data suggestive of SARS-Cov2 infection, and management with supplemental oxygen, insulin infusion pump, carbapenemics, antihypertensive drugs, dexamethasone and antithrombotic prophylaxis with enoxaparin was started. 48 hours after admission the patient developed septic shock and went on vasopressor amines, orotracheal intubation and invasive mechanical ventilation, nasogastric tube (NGT) was placed, which, 24 hours after its placement, revealed hematemesis accompanied by abdominal distension and leukocytosis of 40,000 cells/mm<sup>3</sup>. Gastric pneumatosis and pneumoperitoneum were observed on simple abdominal CT scan (Fig. 2) therefore urgent exploratory laparotomy was performed, necrosis of the greater curvature of the stomach was found and vertical gastrectomy was performed with GIA stapler, 45 and 60mm purple cartridges (Fig. 3). The staple line was reinforced with continuous suture with prolene 00, a feeding jejunostomy tube was placed at 60cm distal from the Treitz angle and Saratoga drains were placed. At 24 hours postoperatively the patient presented hemodynamic stability, vasopressor amines were suspended, and enteral nutrition with elemental diet was initiated. On the fifth postoperative day the patient showed adequate tolerance to enteral diet by jejunostomy, methylene blue

was administered through NGT without evidence of leaks through drains and leukocytes decreased to 24,000 cells/mm<sup>3</sup>. Histopathology results showed panmural necrosis associated with arterial thrombosis secondary to microorganisms compatible with *Mucor* sp (Fig. 4 and 5), amphotericin B was started. During follow up, he presented good evolution, an abdominopelvic CT scan with contrast through the nasogastric tube as performed, which showed gastric wall integrity and ruled out leaks or intra-abdominal collections so drains were removed and he was discharged from general surgery on day 9 post-surgery, continuing inpatient care by internal medicine department. During the following days of hospitalization, the patient presented cardiovascular and pulmonary deterioration, a urine culture revealed growth of *Candida tropicalis*, a CT scan of head, thorax and abdomen and pelvis with oral contrast was performed (Fig. 6, 7 and 8) which showed no evidence of enteric leaks. Also, rhinocerebral and pulmonary mucormycosis was ruled out, reporting probable bacterial pneumonia and interstitial pneumopathy secondary to COVID 19. Clinical deterioration and refractory shock persisted, leading to the patient's death 29 days after admission.



**Figure 1:** Chest CT scan. Ground glass opacities associated with septal thickening, a cobblestone pattern with bilateral central and peripheral distribution are observed, compatible with SARS-Cov2 infection.



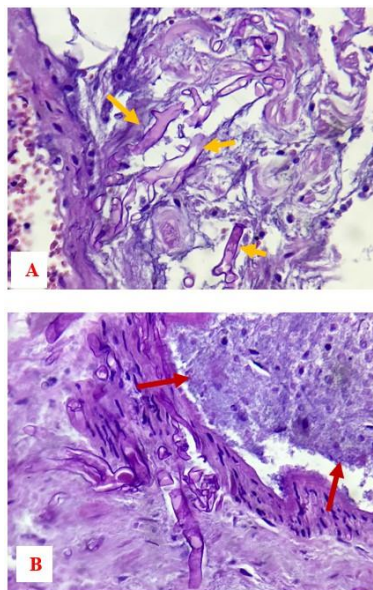
**Figure 2:** Simple abdominal CT, pulmonary window. Gastric pneumatosis (arrowheads) and Pneumoperitoneum (yellow arrow). NGS in gastric chamber (White arrow).



**Figure 3:** Vertical gastrectomy specimen showing extensive necrosis of the greater curvature and stapling line (arrowheads).



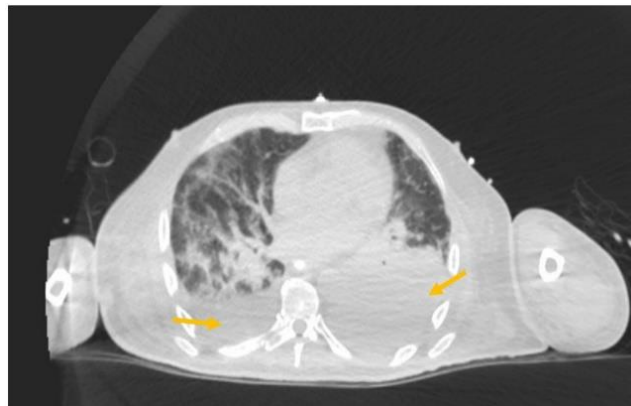
**Figure 4:** Vertical partial gastrectomy surgical specimen. Transition between normal mucosa and panmural necrosis associated with thrombosis is observed (white arrows).



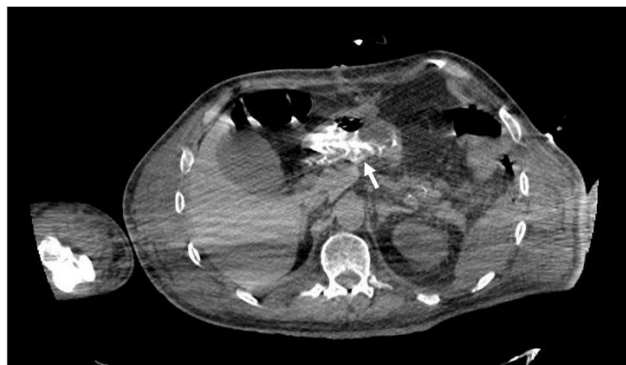
**Figure 5:** Histological section: A) Short and thick paucisegmented hyphae not pigmented hyaline, morphologically compatible with Mucor sp (yellow arrows). B) Vascular invasion with thrombosis and inflammatory infiltrate (red arrows).



**Figure 6:** Skull CT without data suggestive of mucormycosis at the rhinocerebral level.



**Figure 7:** Chest CT scan. Superimposed bacterial pneumonia and bilateral pleural effusion are observed.



**Figure 8:** CT abdomen. Intraluminal water-soluble contrast is observed in the stomach (white arrow), with no evidence of leakage or intra-abdominal collections.

## Discussion

Mucormycosis is an invasive mycotic infection with high mortality. Its incidence has increased in recent years due to the increase of population at risk of infection and improved diagnostic tools<sup>1</sup>. It was first described as pulmonary form in 1876 by Furbringer (Jung *et al.*, 2007). It occurs mostly in the context of an immunocompromised patient<sup>1</sup>. Mortality varies from 32% to 70%, and localized infection is associated with better survival (Lanternier *et al.*, 2012). It is diagnosed premortem in only 25% of cases.



In their review of 31 cases, Dioverti, *et al.* (2015) reported a predominance of males (61%) and a mean age of 47 years, 52% of the cases were post-transplanted solid organ patients and 35% were patients undergoing chemotherapy for hematological malignancy, 100% of the patients had at least one comorbidity, with neutropenia being the most common. It has been described in patients with severe malnutrition, use of corticosteroids, but also in patients without any predisposing factor (Martinello *et al.*, 2012). In our case, the patient had multiple risk factors already described, decompensated type 2 diabetes mellitus, acute coronavirus infection and steroid therapy initiated for the management of COVID-19, being the only factor that improved prognosis focal infection in the stomach. The disease is characterized by extensive necrotizing vasculitis with arterial thrombosis, tissue infarction (Serris *et al.*, 2019) and pathognomonic presence of non-septate right-angled branching hyphae within the tissues (Alvarado-Lezama *et al.*, 2015). The genus *Rhizopus* is the most frequently isolated (Rammaert *et al.*, 2012). Known risk factors include hyperglycemia and acidosis as they cause leukocyte dysfunction of neutrophils and/or macrophages, affecting their chemotaxis (Spellberg, 2012). Six different clinical syndromes can occur, with rhino-orbito-cerebral and pulmonary infection being the most frequent, and gastrointestinal infection the least common. Gastrointestinal infection is acquired through ingestion of contaminated food or, in case of associated health care, through contaminated devices (Serris *et al.*, 2019). The stomach is the most common site of involvement, followed by the colon, small intestine and esophagus (Agha *et al.*, 1985). Most symptoms are non-specific which delays diagnosis and increases mortality (Dioverti *et al.*, 2015). Clinical presentation may include abdominal pain (68%), gastrointestinal bleeding (48%), fever (19%) or changes of defecation patterns (10%) (Dioverti *et al.*, 2015). On admission, the patient did not report any abdominal symptoms, so there was no suspicion of gastrointestinal involvement. Subsequently, intravenous sedation and orotracheal intubation were performed, making it impossible for the patient to manifest gastric involvement. The only sign the patient presented was hematemesis 24 hours after the NGT placement, which ruled out the possibility of a Mucormycosis associated with health care, since 24 hours are not enough to achieve the introduction, inoculation and growth of the fungus. This previous statement opens the hypothesis that the patient acquired the mycotic infection in his community. The diagnosis may be suspected by endoscopic findings which may be a fungal mass or necrotic lesions covering ulcerated areas that may perforate and cause peritonitis (Dioverti *et al.*, 2015). Often, the study protocol is initiated in the presence of an intra-abdominal abscess, and the diagnosis can be made by biopsy of the suspicious area during surgery or endoscopy (Alvarado-Lezama *et al.*, 2015), few samples are sent for culture (Dioverti *et al.*, 2015) and those that are sent are positive in only 30%. In addition, specialized culture media, such as potato dextrose agar, are required to promote fungal growth (Quiroz *et al.*, 2017). Confirmatory molecular tests are further required which can detect surface antigens, which are not available yet (Dioverti *et al.*, 2015).

CT findings may be as follows: focal or diffuse thickening of the gastric wall, pneumatosis with decreased wall enhancement on contrast administration (Emphysematous gastritis) secondary to ischemia and necrosis, adjacent collections, wall necrosis with focal disruption or perforation, and rarely pneumoperitoneum (Ghuman *et al.*, 2021). Upon the presence of hematemesis we are aware that the subsequent diagnostic step could have been an upper endoscopy, nevertheless the abdominal distension presented by the patient suggested a high probability of perforation of hollow viscus, so initially CT of the abdomen was performed, and after reporting gastric pneumatosis and pneumoperitoneum, surgical emergency was considered, ruling out endoscopy at the time (Ghuman *et al.*, 2021). The laparotomy allowed direct exploration of the stomach and partial resection of the stomach as a diagnostic and therapeutic measure. Medical treatment consists of antifungal agents and urgent surgical debridement, since the presence of necrotic tissue will affect the penetration of the antifungal agent into the tissues, in addition to which aggressive medical support for comorbidities must be provided (Ho and Singh, 2011). Intravenous liposomal amphotericin B is the treatment of choice as it has been shown to be more effective than conventional amphotericin B (Cornely *et al.*, 2014). Delaying the initiation of amphotericin for more than 6 days doubles mortality (Chamilos *et al.*, 2008). Although most of the literature suggests aggressive surgical treatment (Jung *et al.*, 2007; Martinello *et al.*, 2012; Alvarado-Lezama *et al.*, 2015), we opted for a more conservative treatment by preserving a portion of the stomach and performing only a vertical gastrectomy, since macroscopic inspection showed clear delimitation between necrotic tissue and viable tissue. The patient presented good evolution, the methylene blue test, for enteric leaks, and the two abdominal CT scans with contrast in the stomach through the nasogastric tube allowed us to verify the integrity of the suture line from the first day post-surgery until the day of his death. The sample sent to pathology allowed us to make the diagnosis and thus initiate targeted therapy with amphotericin B and since no fungal infection by *Mucor* sp was demonstrated at another organic level, the cause of death is attributed to nosocomial infectious complications at pulmonary and urinary level.

## Conclusion

Mucormycosis is a life-threatening fungal infection. The diagnosis requires a high index of suspicion, especially in cases with intestinal involvement and should be suspected in all patients with risk factors and imaging studies suggestive of ischemia and/or unexplained gastrointestinal necrosis. The role of the general surgeon in the success of the treatment consists of urgent surgical debridement, who, based on the trans-surgical findings, should opt for aggressive management or preserve as far as possible the integrity and functionality of the affected organ.

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