Journal of Bacteriology and Mycology

Open Access

Austin Publishing Group

Case Report

A Rare Case of Gastric Zygomycosis Mimicking Malignancy: Case Report with Review of Literature

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Received: April 13, 2020; **Accepted:** May 06, 2020; **Published:** May 13, 2020

Abstract

Gastrointestinal mucormycosis, is an extremely rare, angioinvasive fungal function most commonly encountered in immunocompromised patients and associated with catastrophic outcomes. It can affect any part of alimentary tract with stomach being most common site followed by large intestine. The diagnosis of gastric mucormycosis is often delayed due to its vague symptomatology and a need for invasive investigations. It usually presents as ulcers in the stomach, however mass forming lesions mimicking malignancy are extremely rare. Despite aggressive treatment with anti-fungals and surgical debridement of the affected portion the mortality rates in these cases remain quite high. We report a case of gastric mucormycosis mimicking malignancy in a young, diabetic patient, who was successfully treated with timely diagnosis, aggressive anti-fungal regimen and radical gastrectomy.

Keywords: Gastrointestinal; Diabetes; Invasive Gastric Mucormycsosis; Mimicking Malignancy

Introduction

Mucormycosis, a lethal fungal infection has been steadily gaining interest in recent decades due to its increasing incidence in immunocompromised patients [1,2]. It is an aggressive angio-invasive infection caused by the subphylum Mucormycotina belonging to the Zygomatica phylum and is associated with an extremely dismal prognosis [1-4]. The most important predisposing factor for this infection is an immunocompromised state, seen in patients with neutropenia, hematological malignancies, diabetes mellitus, transplant recipients and in patients with severe malnutrition [1,2,4-8]. Mucormycosis has a varied clinical presentation ranging from localized cutaneous to fatal disseminated disease with rhino-orbito-cerebral and pulmonary mucormycosis accounting for the majority of the cases [6-9]. Gastrointestinal mucormycosis is the least common form of this disease and any portion of the alimentary tract can be affected [10-12]. However, the stomach has been identified as the most vulnerable site followed by ileum and colon [2,3,9]. The diagnosis of gastric mucormycosis is often delayed due to its non-specific clinical presentation resulting in extremely high mortality rates. Despite several advances in diagnostic modalities, an alarmingly small percentage of cases are diagnosed antemortem [3,8-14]. Mass forming fungal infection in GI tract is a rarity. We report a case of gastric mucormycosis in a young male with diabetes mimicking a malignancy.

Case Presentation

A 28-year-old, male presented with retrosternal pain, nausea, and malena since two weeks. He was both a smoker and alcoholic and was diagnosed with Type II diabetes mellitus one year back. He was taking a combination of Metformin and Tenogliptun for diabetes. On examination, the patient was afebrile with mild abdominal tenderness and distension. The other systemic examination was unremarkable. The routine investigations including hemogram, urine examination, renal and liver function tests were within normal limits. The random blood sugar level was 150mg/dl. The urine sugar and ketone bodies were not detected. Cardiac evaluation revealed no abnormalities and lab investigations were negative for viral markers. The computed tomography of abdomen showed a heterogeneously enhancing polypoid growth in the fundus with perigastric lymphadenopathy.

An endoscopy was performed which revealed an ulceroproliferative, friable growth in the fundus of the stomach which was also thought to be malignant.

The biopsy from the mass revealed only necrotic mucosal bits however malignancy was not identified. The patient underwent a proximal gastrectomy which was sent for further histopathological examination. The gross examination revealed a large ulcer proliferative growth measuring 10.5x4.8x1.5cm in the fundus of the stomach. The microscopic sections showed extensive ulceration of the mucosa and dense eosinophilic infiltrate. Multiple granulomas were seen in all the layers of the wall of stomach which were mainly comprised of epithelioid cells and foreign body giant cells. Many broad, a septate hyphae were seen within the giant cells as well as extracellularly which were highlighted by silver meth enamine stain. The radiology, gross features and microscopy has been highlighted in (Figure 1). Nine lymph nodes isolated showed only reactive changes. Unfortunately, culture could not be submitted since the tissue was formalin fixed and there was no preoperative suspicion of fungal infection. The patient was started on Amphotericin (50mg) and Posaconazole (300mg). After two months postsurgery, patient is doing well.

Discussion

Since the first case report of Mucormycosis in 1885 by Paltauf, it has emerged as the third most common form of angioinvasive fungal infection after Candidiasis and Aspergillus [1,8,10,11]. Mucormycosis is most commonly encountered in patients with an infringement of the immune system [1-5]. Although there has been

Citation: Madireddy N, Patil R, Uppin SG and Uppin MS. A Rare Case of Gastric Zygomycosis Mimicking Malignancy: Case Report with Review of Literature. J Bacteriol Mycol. 2020; 7(2): 1126.

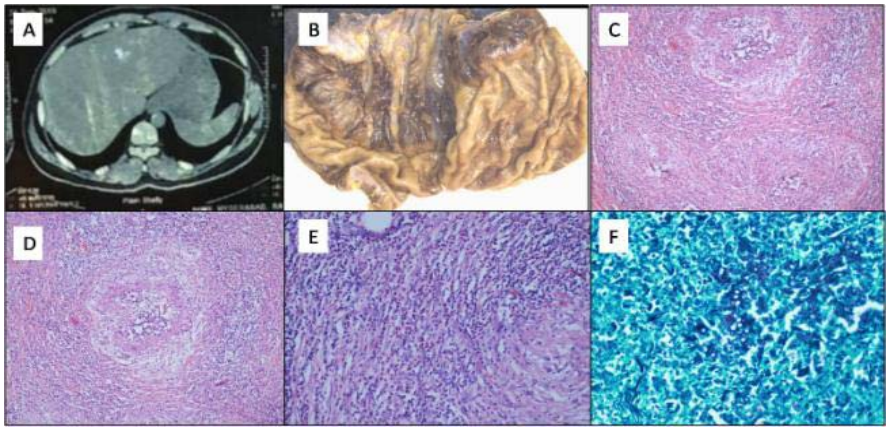

Figure 1: (A): CT scan images showing a heterogeneously enhancing polypoid growth in the fundus. **(B):** Proximal gastrectomy showing a large ulceroproliferative growth in the fundus of stomach. **(C and D):** Well-formed epithelioid cell granulomas in the gastric wall. **(E):** The broad aseptate hyphal structures highlighted on silver methanamine. GMSX100.

a global increase in the incidence of mucormycosis, an exceptionally high rise has been observed in Asia, more so in India and China [2,3,12]. While transplantation and hematological malignancies are the major predisposing factors in the Unites States and European countries, Diabetes Mellitus especially associated with ketoacidosis overshadows all other causes in the Asian continent [2,3].

Mucorales are universally present in the environment and are classified into two classes, zygomycosis, and phycomycosis [1-4]. These fungal organisms are saprophytic and commonly encountered in decaying organic material and soil [2-5,15]. Thermotolerance, inhibition of Interferon-Gamma, ability to attach to endothelial cells and rapid growth contribute to the aggressive nature of these organisms [1]. Sporangiospores, the infective forms invade the hosts either by inhalation or ingestion of contaminated food and rarely through inoculation into the skin [1,2,6]. The spores have the ability to evade phagocytosis by macrophages and neutrophils and germinate into hyphal forms [1,4]. Ketoacidosis, iron overload, hyperglycemia, and neutropenia provide a favorable milieu for the organisms to thrive and increase their virulence. Interaction with free iron in the host seems to be an important mechanism in aiding the rate of replication and survival of the fungal spores [1,2,6]. The angioinvasive hyphal forms have the ability to attach to the endothelial cells and induce endocytosis. This endothelial injury leads to hemorrhage, thrombosis, tissue necrosis and eventual hematogenous dissemination resulting in lethal multiorgan involvement [6-9].

Mucormycosis is more frequently seen in the male population however the reason behind this finding has not been elucidated [9,13]. Mucormycosis can invade any organ and shows a varied presentation, including rhinocerebral, pulmonary, renal, cutaneous, gastrointestinal and disseminated forms six in rhino-orbit-cerebral, pulmonary, cutaneous, renal, gastrointestinal and soft tissue disease [3-5,11-14]. Rhinocerebral is the most common manifestation followed by pulmonary mucormycosis. [1-5,15] Gastrointestinal mucormycosis is the least prevalent form and accounted for just 7% in a meta-analytic study of 929 cases conducted by Roden et al. [9] Stomach has been reported as the most common site of infection in the gastrointestinal tract by several studies. [5,9,11] However Kaur H et al reviewed 200 cases gastrointestinal mucormycosis in immunocompetent patients from 1948 to 2017 and identified large intestine as the most common and stomach as the second most common site of infection. [12] Likewise, Dioverti et al who reviewed 31 cases of gastrointestinal mucormycosis between 1991 and 2013 also reported intestine as the most common site in the gastrointestinal tract and also stated that gastric mucormycosis is more common in post-transplant patients, while large intestinal involvement is more commonly seen in patients with hematological manifestations [14].

Gastric mucormycosis is both rare and a challenging diagnosis due to its non-specific presentation and the need for invasive investigations [2,12]. Ingestion of contaminated food, herbal medications and corn based alcoholic drinks have all been identified as sources of infective spores. [12,16,17] The patients may initially present with non-specific symptoms like fever, abdominal discomfort, gastritis, gastric ulcers, and hematochezia, however, it is not uncommon to see patients with perforation which is an acute emergency. [6-8,12] Although non-specific, abdominal pain is the most common presentation, followed by gastrointestinal bleeding and fever. [14] Necrotizing colitis is the most frequent form of presentation in premature neonates. [6] Our patient presented with nausea, malena and retrosternal pain. Irrespective of the clinical presentation aggressive vascular invasion resulting in vasculitis, thrombosis and tissue necrosis are the hallmark features of this disease. [1,3,14].

Endoscopic findings in these cases are quite ambiguous ranging from ulcers to solid masses and can be easily mistaken for bezoars, abscess, or even malignancy. [8,13,18] However mass forming lesions are extraordinarily rare in stomach and to this day only a handful of cases have been reported. [8,18-21] These lesions mimic malignancy as was the scenario in our patient. Grossly gastrointestinal mucormycosis commonly present as necrosis, gangrene and as large ulcers with rolled margins often mimicking malignancy. [11,12,15,18] The definitive diagnosis usually depends on the histopathological examination as was done in our case. Microscopically the hyphae are broad ribbon-like with a diameter of 5-20um. They are pauciseptate, obtuse, randomly branching organisms and need to differentiate from Aspergillus hyphae which shows separation and acute angled

branching. [4,22] They appear to have a thinner wall as compared to other fungal hyphae which probably is because of weaker staining by Periodic Acid-Schiff and Gomorri-Methanamine stain [4,7] These hyphae are also prone to folding which can be mistaken for septations and thus should be careful not to misinterpret it as Aspergillus. [11] Although the inflammatory response is variable neutrophilic infiltration has been identified as the most common type. [4,11] However this observation is not concordance with the findings in our case wherein we observed an extensive eosinophilic infiltrate.

Traditionally mucormycosis was almost always seen in association with immunocompromised however the past decade has also seen a steady increase in incidence even in patients with no predisposing factors. [7,9,12] Cutaneous mucormycosis is the most common manifestation in immunocompetent patients, however several authors have now reported cases of gastric mucormycosis in immunocompetent patients. [2,7,19,20] Kaur H et al also reviewed 176 cases of gastrointestinal mucormycosis and identified intestine as the most common site to be affected followed by the stomach [12].

Effective management of gastrointestinal mucormycosis includes timely diagnosis and immediate administration of aggressive anti-fungal regimen [19,23]. Chamilos et al retrospectively reviewed 70 cases of Mucormycosis and stated that a delay beyond 6 days has doubled the rate of mortality [24].

Liposomal formulation of Amphotericin -B is the most effective choice of anti-fungal in mucormycosis [6,24,25]. This formulation shows relatively lesser renal toxicity in diabetics as compared to the deoxycholate and lipid complex forms [7,20]. Fluconazole and Itraconazole have been found to be ineffective against these fungi [26]. Posaconazole and Deferiprone which act by inhibiting the uptake of iron by the spores required for replication are the new class of anti-fungals being used in therapy and seem to be effective in cases resistant to Amphotericin [26,27]. Isavuconazole is the other drug which was found to act efficiently against mucormycosis while minimizing the toxicity associated with Amphotericin [28]. However, despite the success of the new class of antifungals, several studies have now proven beyond doubt that monotherapy with antifungals is insufficient and complete and aggressive surgical debridement or excision of the affected area is of supreme importance [3,15,22,29] The need for surgery outweighs the postoperative surgical morbidity. A comprehensive treatment that combines reversal of the underlying predisposing factors, aggressive anti-fungal therapy and surgery is the only chance of complete cure [12-14,22,29].

Conclusion

We report an extremely rare case of a form of gastric mucormycosis in a 28-year-old male patient who was a known diabetic. The case highlights problems in diagnosis of gastric fungal infections, uncommon presentation mimicking a malignancy and importance of histopathology for a definite diagnosis.

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