

CASE REPORT

Gastric perforation due to mucormycosis infection in a kidney-pancreas transplant patient. A fatal complication

Perforación gástrica secundaria a infección por mucormicosis en un paciente con trasplante reno-pancreático. Una complicación fatal

Franco R. Pascual*, Rodrigo Figueroa, Julieta Zanatta-Scattolini, Maximiliano Yance, Carlos Valenzuela, Rogelio Traverso, and Octavio Gil

Servicio de Trasplante Hepático y Renopancreático, Sanatorio Allende, Córdoba, Argentina

Abstract

Mucormycosis is a rare deep fungal infection that develops mainly in immunosuppressed patients, being unusual the gastro-intestinal presentation. The adequate treatment consists in rapid and aggressive surgical debridement, along with initial adjuvant treatment with liposomal amphotericin B. Despite recent advances in the management of this disease, the prognosis is poor, with a high mortality rate. We will present a case of a 37-year-old male patient, who underwent a combined pancreas and kidney transplant, with gastric perforation secondary to deep mucormycosis.

Keywords: Mucormycosis. Pancreas Transplantation. Kidney Transplantation. Gastrectomy.

Resumen

La mucormicosis es una infección micótica profunda poco común que se desarrolla principalmente en pacientes inmunodeprimidos, siendo la presentación gastrointestinal inusual. El tratamiento adecuado consiste en el desbridamiento quirúrgico rápido y agresivo, junto con el tratamiento coadyuvante inicial con anfotericina B liposomal. A pesar de los avances, el pronóstico es malo, con una alta tasa de mortalidad. Presentamos el caso de un paciente de 37 años sometido a un trasplante combinado de páncreas y riñón, que se presenta con perforación gástrica secundaria a infección por mucormicosis.

Palabras clave: Mucormicosis. Trasplante de páncreas. Trasplante de riñón. Gastrectomía.

*Correspondence:

Franco R. Pascual

E-mail: francopascual23@gmail.com

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Introduction

Mucormycosis is a deep fungal infection (DFI) that develops in immunocompromised patients. Its incidence has increased in recent years¹, especially in patients with diabetes mellitus, hematologic malignancy, solid organ transplants (SOT), and corticoid therapy^{1,2}. The most common sites of infection are the paranasal sinuses, brain, lungs, and skin³. GI locations are rare.

Given that the most common fungal infections in SOT recipients are candidiasis, aspergillosis, and cryptococcosis⁴, mucormycosis is a rare complication in this subset of patients, representing around 2% of all DFIs⁵.

Despite adequate antifungal treatment and aggressive surgical intervention, mortality is high vs other common infectious diseases such as candidiasis and aspergillosis, ranging from 50% up to 90%, depending on the location⁶.

A complicated case of gastric mucormycosis is described in an immunocompromised patient who presented with acute gastric perforation.

Case report

A 37-year-old male with a past medical history of diabetes mellitus since childhood and terminal chronic kidney disease on thrice-weekly dialysis underwent a combined pancreas and kidney transplant at the age of 32. Four years after the transplant, he lost the pancreatic graft due to multiple complications. The kidney graft was currently functioning normally, and the patient was on a standard immunosuppressive regimen consisting of tacrolimus, mycophenolate mofetil, and prednisone.

The patient presented to the emergency department with diarrhea and fever. On physical examination, his temperature was 38°C, and the rest of his vital signs were within normal parameters. His abdomen was moderately distended, with absence of bowel sounds, and no signs of peritonitis.

Lab test results showed a normal white blood cell count, metabolic acidosis, and acute renal failure. Due to his immunocompromised condition, he was initially admitted to the intensive care unit and treated with fluid resuscitation and broad-spectrum IV antibiotics, including piperacillin-tazobactam 2.25 mg 3 times/day. Two days after admission, the patient experienced a sudden deterioration in his clinical condition, with the onset of severe abdominal pain.

Given the symptoms and findings on physical examination, an abdominal CT with oral and IV contrast was

ordered, which showed an edematous gastric wall with the presence of air in the posterior wall, pneumoperitoneum, and free contrast material, indicating a perforation of a hollow viscera (Fig. 1).

The patient was quickly subjected to an exploratory laparotomy, during which a small amount of seropurulent fluid was found, along with a full-thickness gastric perforation on the anterior surface of the stomach, associated with transmural gastric necrosis (Fig. 2).

The rest of the intestine appeared normal. A total gastrectomy was performed without restoration of the tract, and a feeding tube was inserted into the distal end of the esophagus, which was exteriorized, forming an esophagostomy. The abdomen was left open and packed, due to the presence of purulent material and to allow for subsequent exploration of the abdominal cavity to assess the progression of necrosis. Two days after the initial surgery, a revision surgery was performed, during which no evidence of perforation, necrosis, or purulent material was found at any level; consequently, a Witzel-type jejunostomy was performed, and the abdominal wall was closed.

Histological examination of the stomach showed extensive necrosis of the gastric wall. Numerous fungal microorganisms were present, with angulated budding hyphae and angioinvasion found in the ulcer bed. The histological findings were consistent with gastric mucormycosis (Fig. 3).

The early postoperative course was satisfactory. The patient was treated with broad-spectrum antibiotics, including meropenem 500 mg once daily, tigecycline 50 mg twice daily, and fluconazole 200 mg once daily. However, the patient began to show progressive clinical deterioration. On postoperative day 15, as the pathological report confirmed the diagnosis of mucormycosis, liposomal amphotericin B 150 mg once daily was added to the treatment regimen. Despite timely surgical intervention and specific antifungal medication, the patient died on postoperative day 19 due to sepsis and multiple organ failure.

Discussion

We report the case of an immunocompromised patient who presented with an acute gastric perforation due to mucormycosis. What is unusual in our case is not only the location and presentation of this infection but also the time elapsed since the transplant (5 years).

Mucormycosis is caused by fungi belonging to the order Mucorales. Humans predominantly acquire the

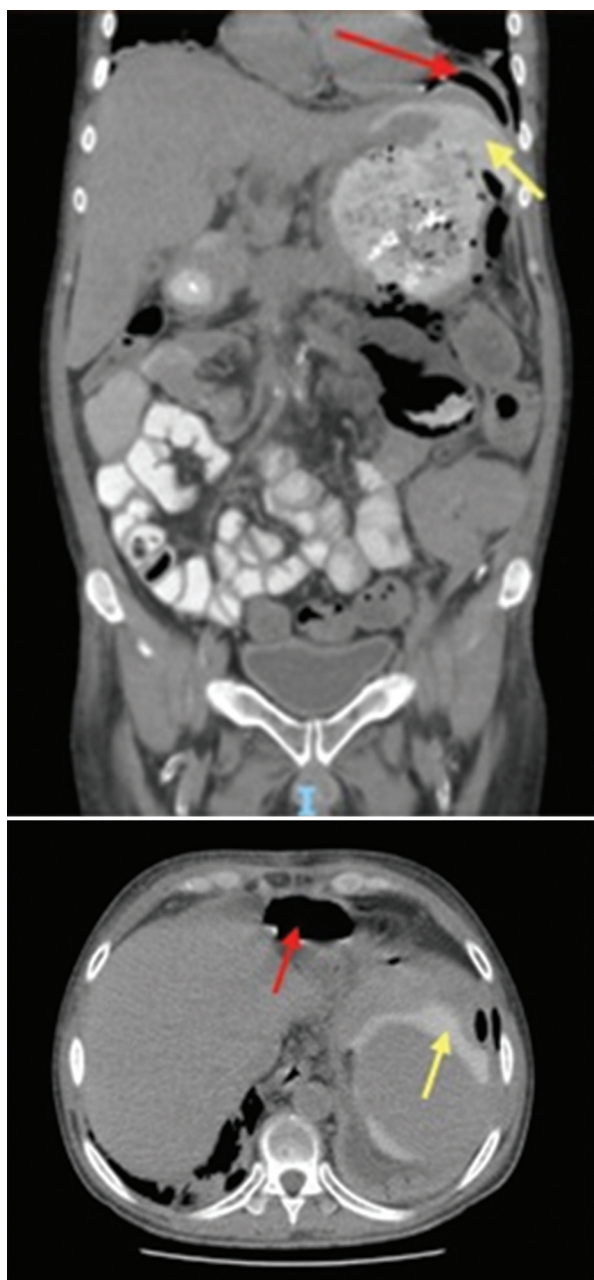


Figure 1. Abdominal CT showing free air (red arrows) and free contrast material (yellow arrows) in the abdominal cavity, indicating a hollow viscera perforation.

infection through the inhalation of sporangiospores, occasionally by ingestion of contaminated food, or through traumatic inoculation⁷. Regardless of the route of infection (inhalation of spores from the air, ingestion, or direct inoculation to the skin), the spores germinate into hyphae and develop rapidly, invading blood vessels and causing thrombosis, infarction, and necrosis⁸.

The clinical presentation varies greatly and can involve a specific organ or be disseminated. In a



Figure 2. Macroscopic appearance of the anterior gastric wall showing extensive transmurular necrosis.

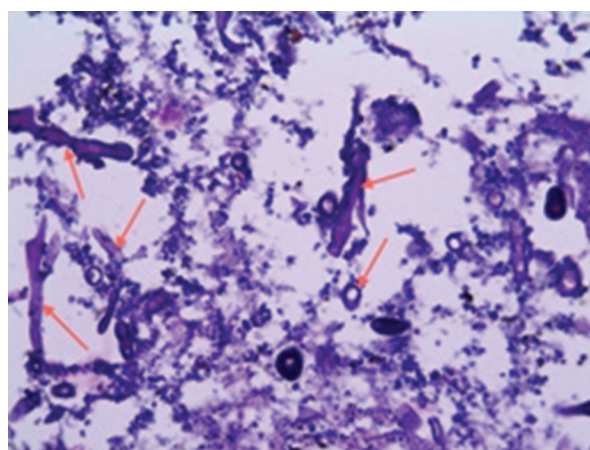


Figure 3. Histological appearance of mucormycosis ($\times 10$). PAS stain showing the characteristic hyphae in clusters (arrows).

review of 851 cases, Jeong et al.⁹ found that the rhino-orbital-cerebral region was the most common site of fungal infection (34%), followed by the skin (22%) and the lungs (20%).

As for GI involvement, the most common form is intestinal mucormycosis (52%), followed by gastric disease (42%)¹⁰. Gastric mucormycosis is commonly associated with SOT10. However, this infection can also be observed in immunocompetent hosts¹¹.

Regarding the clinical presentation, abdominal pain is the most frequent symptom (68%) of GI mucormycosis in this patient population, followed by GI bleeding (48%) and abdominal distension¹⁰. Diarrhea, one of the initial symptoms in our patient, represents < 10% of the clinical signs¹. Gastric perforation is a very unusual presentation. To date, we have found 11 case reports

of patients who presented with gastric perforation due to mucormycosis. In this particular presentation, the mechanism could be a perforated ulcer (with or without bleeding) or gastric necrosis, as in our case. Reviewing the literature, the latter form of presentation is associated with a higher mortality rate (66% vs 33%).

The optimal management of DFI includes surgical debridement and effective antifungal treatment, as well as control of underlying risk factors, such as neutropenia, reduction or cessation of steroids, and reduction of immunosuppression when possible. Current treatment guidelines for DFI recommend combination therapy with an IV formulation of amphotericin B and surgery¹², as observed in our case and in most of the reports reviewed. Modern antifungal agents, such as posaconazole, have a good safety profile and in vitro activity vs mucormycosis. In one study³, the results for patients on posaconazole were favorable, making it an alternative treatment option.

Early diagnosis or suspicion is of utmost importance, as early initiation of antifungal therapy is strongly associated with better patient survival¹³.

However, our patient presented to the emergency department with fever and diarrhea, and initially, no severe abdominal complication was suspected. The sudden gastric perforation later and the histological examination were what ultimately led to the diagnosis of gastric mucormycosis. The delay in appropriate antifungal therapy in this case, on postoperative day 15, could explain the fatal outcome despite adequate surgical debridement.

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Conflicts of interest

None declared.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed their workplace protocols regarding the publication of patient data.

Right to privacy and informed consent. The authors have obtained informed consent from the patient referenced in the article. This document is held by the corresponding author.

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