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Fatal invasive gastric mucormycosis: 2 case reports

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Abstract

Mucormycosis affects most commonly immunocompromised patients. We report two cases: a 61-year old female with diabetes whose the upper gastrointestinal endoscopy showed a budding greyish process which corresponded with an invasive mycormucosis in histology and a 59-year old man who presented with worsening of general state. No patients survived.

Introduction :

Mucormycosis is an uncommon fungal infection that occures usually in immunocompromised patients such as patients with diabetes, renal dysfunction, cancer or under immunosupressive therapy. It often affects sinuses , lungs or skin and less commonly the gastrointestinal tract ; the stomach being on the top of the list. It is associated with poor prognosis and high rates of mortality.

Cases presentation :

Case one:

A 61-year old Tunisian female patient with type 2 diabetes mellitus, hypertension, dyslipidemia and family history of peptic ulcer presented to our gastoenterology department with a 7-day history of vomiting preceded by a 4-month history of dry cough for which she took inhaled corticosteroids. On physical examination, she had no fever. Her body mass index (BMI) was 29.8 kg/m^2. Her blood pressure was 120/70 mmHg. Her abdominal exam was normal. Initial laboratory studies showed renal dysfunction with creatinine 163 µmol/L and clearance 60 ml/min, Hemoglobin 11.5 g/dL, white blood cell count (WBC) 11100 cells/µL, C-reactive protein (CRP) 132 g/L and blood sugar 20 mmol/L (table1).

Upper gastrointestinal endoscopy revealed budding and infiltrating greyish process resting on an ulcerated fundic mucosa (figure 1).

Anatomopathological exam concluded to an invasive mucormycosis by demonstrating zygomycosis hyphae without any malignant signs (figure 2).

These findings were confirmed by parasitological examination (figure 3).

A brain-face-chest-abdomen and pelvis computed tomography (CT) scan without contrast was practiced to search other sites of mucormycosis (figure 4). It revealed a fundic mucosal thickening without any other infection site confirmed by an ENT exam.

Since the liposomal form of amphotericin B which is less nephrotoxic was not available in our country, therapy based on conventional amphotericin B was started on the fifth day of diagnosis at progressive dose 5mg/day

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on day one until 25 mg/day (0.4 mg/kg/d) on day 5. The evolution was marked by an aggravation of renal dysfunction: creatinine 208 µmol/L and clearance 25 ml/min.Thus we stopped the antifungal therapy but though creatinine levels were still high. In day 19, she was programed for a total gastrectomy but presented a respiratory distress due to pulmonary embolism. The patient underwent total gastrectomy two months after diagnosis. The examination of the stomach showed 2 digging ulcers in the fundus (figure 5).The patient died 10 days after surgery.

Case two:

A 59 year old man originally from Cango living in Tunisia without any medical history presented to the hospital with gastric pain and vomiting and a fast worsening of the general state. At admission, he had fever with a temperature at 39°C. His blood pressure was low : 80/45 mmHg and his pulse was 110 BPM. Abdominal exam showed epigastric tenderness and a moderate ascites.Laboratory findings revealed severe normocytic anemia with 7.1 g/dL hemoglobin, elevated white blood cell count (WBC) 24 900 cells/µL (93% neutrophils) and thrombopenia at 72 000/mm^3.He had high C-reactive protein (CRP) 231 g/L with a positive procalcitonin test (2.53 ng/ml). We concluded to a septic shock and the patient had broad-spectrum antibiotherapy and vascular filling with vasoactive drugs.

Upper gastrointestinal endoscopy revealed a very fragile mucosa and a gastric ulcer with bleeding stigmata (figure 6). Abdominal ultrasound was normal besides moderate ascites.

Anatomopathological exam showed typical broad zygomycetes hyphae (figure 7).

Six days later, the patient developped an hemophagocytic syndrome confirmed by cytological examination of the bone marrow. The evolution was rapidly fatal with continuous decrease in hemoglobin level despite transfusions and the patient died within 8 days after admission.

Discussion:

Zygomycosis was first described as a cause of human disease in 1885 [1].Unlike other fungal opportunist infections which affect patients with cancer, recipients of organ transplant or with compromised immunity, mucormycosis can touch patients with diabetes mellitus [1-3], renal insufficiency, alcoholism [4-6]or even with an intact immunity system [7-9]. These underlying conditions not only predispose to the disease but also worsen the outcome of patients. Our first patient had diabetes and renal insufficiency as a risk factors of mucormycosis [9].

The mode of transmission of mucormycosis involves inhalation or ingestion of spores and direct inoculation into damaged mucocutaneous surfaces [8].

The common sites of infection are sinuses(39%) which constitue the predilected infection site in diabetic patients, skin (19%) in particular in patients with no risk factor and lungs (24%) in patients with cancer [1,10].

The gastrointestinal tract is less commonlyaffected (7%) with67% of stomach infection and 25% of intestine infection [1,9].Factors predisposing for gastrointestinal mucormycosis (GIM) include malnutrition, typhoid fever, uremia and penetrating trauma [8,11].

The clinical manifestations of GIM include fever, abdominal pain, nausea, vomiting, diarrhea, hemorrhage, or gastrointestinal perforation [8,12]. Our first patient presented only vomiting and the second patient presented withfever, abdominal pain and vomiting. The confirmation of diagnosis is based on anatomopathological examination of tissue samples showing fungal hyphae [8,13].

GIM is usually fatal with 85% of mortality [1,10,14],.The mainstay of therapy in GIM is a combination of surgical debridement and intravenous antifungal therapy. Early initiation of antifungal therapy improves survival and can even exempt the patient from surgery in case of non-invasive form of the disease [10].A delayintreatmentgreaterthan6daysworsens the prognosis and seems to double the mortality rates [8]. The cornerstone of drug-therapy is amphotericin B which constitutes the first line treatment at a daily dose of

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1 to 1.5 mg/kg for a duration of 4-6 weeks [4,8,15]. The liposomal form is prefered for its lower risk of nephrotoxicity and the possibility to administrate higher doses : 5 to 10 mg/kg/day [1,16,17]. Posaconazole and isavuconazole are also effective agents and can be used as second line therapy. Surgical debridement of necrotic tissue is often required for invasive mucormycosis [17]. In our first patient, liposomal form of amphotericin B was not available in our country thus we started treatment with conventional amphotericin B at low doses which was stopped at day 5 because of worsening of renal dysfunction and we opted for the surgical debridment. As for the second patient, he did not receive this treatment since he was in a septic shock.

Conclusion :

Gastric mucormycosis is a rare entity that affects usually predisposed patients such as immunocompromised, alcoholic and diabetic patients but sometimes immunocompetent ones. Its treatment is based on amphotericin B and surgical debridment of all necrotic tissues. The mortality rates remain high up to 85%. However, an early diagnosis and prompt therapy can improve prognosis.

Ethical approval:

Patient personal data have been respected.

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3. Given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content : Mohamed Moussaddek Azouz

4. Agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved : Amal Khsiba, Manel Moalla, Mohamed Moussaddek Azouz

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Table 1 : laboratory test results on admission

Figure 1: Upper gastrointestinal endoscopy showingbudding and infiltrating greyish process

Figure 2: A, B: necrotic and inflammatory material comprising mycelial filaments suggesting mucormycosis

Figure 3. A: microscopic exam in lactophenol showing large, irregular and non-septatehyphae

B :microscopicexam after culture showing the rhizoids and the columella specific for the species Rhizopus arrhizus.

Figure 4 . CT scan of abdomen showing fundic mucosal thickening

Figure 5: resected stomach showing 2 ulcers in the fundus

Figure 6: endoscopy showing fragile mucosa and a gastric ulcer with bleeding stigmata

Figure 7: A: Typical broad zygomycetes hyphae branching at right angle (PAS, 400x).

B: Zygomycetes hyphae within the gastric mucosa.

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