Jejunal mucormycosis in a patient with Hodgkin’s lymphoma

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ABSTRACT

We report a case of intestinal mucormycosis in a 46-year-old male diagnosed with classical Hodgkin’s disease, IV-B. During the first phase of chemotherapy he had a massive digestive bleeding event secondary to a jejunal ulcer, and zygomycosis mucor-type was diagnosed by endoscopic biopsy. The patient was treated with antifungal drugs and surgical resection of the intestine involved. At surgery a double covered perforation of the jejunum was seen. Pathological examination confirmed the previous diagnosis. After one year of follow-up the patient is doing well, and his lymphoma is in remission. To our best knowledge this is the second case of intestinal mucormycosis in a patient with Hodgkin’s lymphoma reported in the medical literature.

Key words: Intestinal mucormycosis. Hodgkin’s disease. Lymphoma. Intestinal ulcer.


INTRODUCTION

Mucormycosis is a systemic opportunistic, often fatal infection caused by fungi of the Mucoral order, class Zygomycetos, that affects immunocompromised patients, especially those with hematological diseases such as acute leukemia and lymphoma. The three most frequent clinical forms are rhinocerebral, maxillofacial, and pulmonary (1), with the most common locations being the paranasal sinuses (39%), lungs (24%), skin (19%), and more rarely the brain (9%) and gastrointestinal tract (7%) (1-4).

We report a case of intestinal mucormycosis in a 46-year-old male diagnosed with classic Hodgkin’s disease, IV-B. During the induction phase of chemotherapy he suffered from massive digestive bleeding secondary to a jejunal ulcer diagnosed as zygomycosis of the Mucor type. The patient was treated with antifungal drugs and surgical resection of the intestine involved. After a year of follow-up he recovered, and his Hodgkin’s lymphoma is in remission. As far as we know, this is the second case of intestinal mucormycosis in a patient with Hodgkin’s lymphoma in the medical literature that was diagnosed by endoscopic biopsy and with survival for more than 1 year.
CASE REPORT

A 46-year-old male who was diagnosed with classic Hodgkin’s lymphoma -- IV-B stage, mixed cellularity -- with marrow, liver, and splenic affection under chemotherapy (BEACOPP). In the induction phase of chemotherapy (day 11) he showed a clinical picture of fever, shivering, and blood in the stools. Blood tests revealed neutropenia (100 WBCs/mm³) and thrombopenia. The patient was admitted to the intensive care unit with acute respiratory failure. Afterwards he suffered from gastrointestinal bleeding with hypovolemic shock, which needed intubation and blood replacement. A large jejunal ulcer 2-3 cm in size, with smooth edges, a necrotic base and no active bleeding was identified by endoscopy. A pathological exam of the biopsy sample from the ulcer edges showed a dense mixed inflammatory infiltrate and foreign-body granulomas with multinucleated giant cells. Inside the cytoplasms and among infiltrate cells abundant gross, non-septed hyphaes compatible with mucormycosis could be identified. A CT scan showed a thickening of the jejunal wall 4.5 cm in diameter, multiple hypodense lesions in both hepatic lobes, and lytic affection of the vertebral bodies at dorsal and lumbar levels. Treatment with amphotericin B was started with control of glycemia and surgery scheduled. At surgery a plastron consisting of three jejunal loops and transverse mesocolon with a double covered perforation was observed (Fig. 1). An en bloc resection of the affected jejunum was performed. Pathological examination revealed a double ulceration with intense acute and chronic inflammation secondary to infection by *Zygomicetum mucor*-type, with extensive fibrin necrosis of medium-size vessel walls in the sub-serosal layer. Hyphaes were thick, variable in diameter, branched at right angles, and showing a sharp, strengthened membrane. Hyphaes were positive for PAS and methenamine-silver staining for fungi (Figs. 2 and 3). There were no surgery-related complications, and after a year of follow-up the patient is still alive with a complete remission of his hematological disease.
DISCUSSION

Mucormycosis represents the third cause of invasive fungal infection after *Aspergillus* and *Candida* (1), and is presently considered an emergent disease. Gastrointestinal mucormycosis is a non-frequent opportunistic systemic infection, often fatal, caused by fungi of the Mucorales order, *Zygomycetum* class, saprophytic aeroebes that are sub-divided into the genres *Absidia*, *Rhizopus*, and *Mucor*, and that usually affect immunocompromised patients (1). Increased susceptibility to infection has been observed in patients with neutropenia and T cell dysfunction (1,5,6), fundamentally in patients with malignant hematological disease, especially acute leukemia and lymphoma, in relation to neutropenia secondary to the disease itself or induced by chemotherapy (1,2,4-7).

In the Pagano et al series (1) 78% of patients had acute leukemia (acute myeloid leukemia or acute lymphoblastic leukemia). Non-Hodgkin’s lymphoma represents 10%, and only one case of Hodgkin’s lymphoma was identified (3%). To our best knowledge this is the second case of intestinal mucormycosis reported in the medical literature in a patient with Hodgkin’s lymphoma.

Cases of mucormycosis associated with diabetic ketoacidosis have also been described. Ketoacidosis induces an acid environment rich in glucose that facilitates fungal growth. In the same way, it has been associated with states of immunosuppression secondary to steroids, transplantation, and AIDS. It has also been reported when using catheters that break de muco-cutaneous barrier, and in patients under treatment with deferoxamine as a chelating agent used for iron overload such as when on dialysis (1,2,4-7).

The three most frequent presentation forms are: rhinocerebral, maxillofacial and pulmonary (1), with paranasal sinuses (39%), lung (24%), skin (19%), and more rarely the brain (9%) and gastrointestinal tract (7%) (4), most particularly the stomach, being most commonly involved. In the intestinal form there is predilection for the colon, cecum, and terminal ileum (1,2,3,8). Only one third of the 60 cases of intestinal mucormycosis described in the literature involve the small bowel as in the present case (9). When this occurs a necrotizing ulceration ensues (10). Most cases of gastrointestinal mucormycosis are associated with malignant hematological diseases (1,3,5,8,11-13), and with treatment with deferoxamine for dialyzed patients (10,14,15).

Gastrointestinal mucormycosis occurs after the ingestion of spores in the food or contaminated mucus (2). In immunocompetent people spores are eliminated by humoral mechanisms. In immunosuppressed patients, the germinated hyphae of the fungus enter the tissues, with a high capacity for vascular invasion, especially of arteries (2,3,8), which results in fast vascular thrombosis that leads to ischemic infarctions and necrosis in any organ (4,6,7,10,13). The intestinal form has been described in adults, but particularly in neonates and premature babies, mimicking a necrotizing enterocolitis (5,16,17). Abdominal CT scans show a diffuse thickening of the intestinal wall, together with areas intensely or sparsely enhanced by radiological contrast. (8).

The diagnosis of mucormycosis is not difficult for rhino-orbital or mucocutaneous forms. Nonetheless, when the infection affects deep organs such as the lungs or gastrointestinal tract, diagnosis is difficult and often made post-mortem. In the present case the diagnosis was made by endoscopic biopsy, which allowed fast treatment. For a definitive diagnosis, a pathological examination of the ulcerated areas showing the characteristic hyphae is necessary (3,5,8), with a subsequent culture for fungal categorization (7).

In all cases, an early diagnosis and the use of aggressive treatment with both antifungal therapy using high doses of liposomal amphotericin B and extensive surgical eradication, together with a correction of all predisposing factors, are essential. In hematological patients, a transfusion of granulocytes or growth factors to induce an increase in endogenous neutrophils is used to correct neutropenia (1-3,6,7).

A significant decrease in mucormycosis-related mortality has been seen in patients treated with amphotericin B, which is the most relevant factor for survival (1,2). Deoxycholate AmB is the first-choice antifungal against mucormycosis, given that most zygomycetes have demonstrated resistance to fluconazole, itraconazole, and 5-fluorocytosine (1,5,7). Posaconazole and ravuconazole have good in vitro activity (7). Mortality rate in this kind of infection is over 70% (1), and reaches 96% in some series (2,5,6,9). The diagnosis is made post mortem in many cases. In the present case the patient is alive after one year of follow-up. This was possible due to early diagnosis together with antifungal treatment and aggressive surgery.

In conclusion, an early diagnosis of zygomycosis in hematological patients permits a fast, aggressive therapeutic attitude that is crucial to save the patient’s life, as happened in this unusual case of intestinal mucormycosis in a patient with Hodgkin’s lymphoma.

REFERENCES


