Gastrointestinal mucormycosis in a renal transplant patient

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CASE PRESENTATION

A 57-year-old man, who had undergone cadaveric renal transplantation for end-stage renal disease secondary to hypertension two months earlier, presented with complaints of generalized abdominal pain, distention and constipation. Acetaminophen with codeine had recently been started for pleuritic chest pain secondary to Escherichia coli pneumonia. At renal transplantation, the patient was initially immunosuppressed with cyclosporine and steroids. However, acute rejection developed requiring high dose pulse steroids and thyroglobulin infusion. Antilymphocyte globulin was not used. The immunosuppressive agents were changed to tacrolimus, prednisone and mycophenolate mofetil (MMF). Steroid-induced diabetes, controlled by oral hypoglycemic agents, was developed after this regimen was instituted. One week before admission, the MMF was stopped because of gastrointestinal complaints. Past medical history also included hypertension and non-cirrhotic hepatitis C. On admission, medications included ciprofloxacin, clarithromycin, tacrolimus 4 mg every 12 h; prednisone 15 mg/day, glyburide, diltiazem hydrochloride.

Although it is relatively uncommon, mucormycosis, a fungus of the order Mucorales, may cause opportunistic infection in patients with diabetic ketoacidosis and neoplastic diseases, and in patients who have undergone organ transplantation. The present report describes a rare case of gastrointestinal mucormycosis in a solid organ transplant patient. The pathophysiology, incidence and prognosis of this disease are discussed.

Key Words: Diabetes; Gastrointestinal disease; Immunosuppression; Mucormycosis; Renal allograft; Transplantation

Mucormycose gastro-intestinale chez un receveur de greffe rénale

RÉSUMÉ : On présente ici l’évolution clinique et le traitement d’un cas rare de mucormycose gastro-intestinale chez un receveur de greffe rénale. Le diagnostic a été posé à partir d’un examen pathologique des tissus réséqués chirurgicalement au niveau du côlon, de la rate et du l'estomac. Le patient n’a pas survécu à l’infection. À notre connaissance, il s’agit du onzième cas rapporté de mucormycose gastro-intestinale dans un organe solide chez un receveur de greffe. La physiopathologie, l’incidence et le pronostic de cette maladie sont abordées.
(Cardizem, Aventis Pharmaceuticals, Canada) and acebutolol.

Initial investigations revealed a white blood cell count of $7.2 \times 10^9/L$, a hemoglobin concentration of 97 g/L and a platelet count of $153 \times 10^9/L$. Random blood sugar concentration was 4.6 mmol/L. Creatinine was 160, unchanged after transplantation. Plain films of the abdomen showed mild dilation of the large bowel, a few air-fluid levels, air in the rectum, and stool in the ascending and transverse colon. The abdominal complaints were attributed to constipation secondary to the codeine, and laxative treatment was undertaken. At admission, the patient’s tacrolimus concentrations were elevated at 18.8 µg/L; the concentrations fell into the target range (10 to 15 µg/L) within two days without adjusting the tacrolimus dose.

The gastrointestinal symptoms persisted and colonoscopy was performed but failed to show pathology. The patient underwent gastroscopy several days later, and two large duodenal ulcers (Figure 1) and one large gastric ulcer (located in the body) were seen. The ulcers had elevated mucosa at the margins and black, necrotic centres. Mucosal biopsies revealed nonspecific ulceration.

During hospitalization, the patient had daily spiking fevers, and pulmonary Aspergillus fumigatus was diagnosed by sputum culture. Itraconazole was started and was subsequently changed to amphotericin B. While on itraconazole, tacrolimus concentrations rose significantly to 27.5 µg/L and the tacrolimus was held. The concentrations normalized within several days.

The fevers continued and the patient’s white cell count climbed to $51.6 \times 10^9/L$. Abdominal computer-assisted tomography (CAT) scan revealed a splenic abscess. Despite percutaneous catheter drainage, the patient’s condition worsened clinically and he was taken to the operating room for splenectomy.

Operative findings were more extensive than those from the CAT imaging. Widespread necrosis was found encompassing the spleen, the fundus of the stomach, the diaphragm, the splenic flexure and the descending colon. The affected areas were debrided. Pathological examination of the resected stomach revealed ulceration and vascular invasion by abundant, broad, nonseptate, irregularly branching hyphae (Figure 2) consistent with mucormycosis. These fungi were culture-confirmed on blood and Sabouraud agar plates as Rhizopus rhizopodiformis. Despite having all immunosuppressive medications withheld and being treated aggressively surgically and with amphotericin B, the patient became progressively more septic and died eight days after surgery.

**DISCUSSION**

Although mucormycosis is commonly found in soil and decaying organic matter, including food, clinical infection is rare. Therefore, host factors are critical determinants of disease. Immunocompromised patients, such as transplant recipients, patients with lymphoproliferative disorders and diabetic patients, are particularly susceptible. Predisposing factors in our patient included immunosuppression and possibly diabetes and hemodialysis. In mice infected with Absidia species, a member of the mucor family, cortisone increased susceptibility to infection and promoted disseminated infection, while azathioprine, cyclophosphamide and antithymocyte serum did not (1). In a review of transplant recipients infected with mucor, 76% received augmented immunosuppression, like the patient in the present case, mainly in the form of corticosteroids (2). During hospitalization, the patient’s tacrolimus concentrations were elevated on several occasions, likely secondary to the interaction with clarithromycin and itraconazole (3,4); however, the clinical importance of these elevated concen-
gastrointestinal mucormycosis infections are pulmonary or rhinocerebral. Other forms of the disease include cutaneous, isolated neurological, gastrointestinal and disseminated infections. Gastrointestinal mucor is a rare entity, accounting for only 7% of all cases of mucormycosis. The stomach is the most common site of gastrointestinal infection, followed by the colon and small bowel (8).

Endoscopically, mucormycosis presents as a shaggy, velvety and discoloured mucosa or, as in the present case, as giant ulcers with necrotic, black centres. Biopsies from the centre of the ulcer are thought to be more diagnostic than ulcer margin biopsies. Tissue necrosis associated with mucor is also a substrate for secondary bacterial infection and recently, a case of emphysematous gastritis associated with invasive mucormycosis was reported (9).

In recent years, the prognosis of mucormycosis has improved, but the overall mortality rate of 27% remains significant (10). Solid organ transplant patients tend to do worse, having a reported mortality of 56% for all forms of mucor (2). Patients with invasive gastrointestinal disease have a poor outcome, with mortality ranging from 46% to 98% (5,8). We reviewed the literature using Grateful Med and the search terms, ‘gastrointestinal disease’, ‘mucormycosis’ and ‘transplantation’. Including the present case, there were 11 cases of gastrointestinal mucor in organ transplantation patients in the literature. Of these patients, five (45%) survived (11-15) and six (55%) died, including the patient in the present case (2,12,16-18).

Outcomes from mucormycosis have improved since the 1970s (10). This is attributable to earlier diagnosis leading to aggressive and early surgical debridement with adjunct amphotericin B treatment. Gastroenterologists must have a high index of suspicion for mucormycosis when evaluating gastrointestinal ulcers in susceptible patients such as organ transplant recipients so that appropriate interventions may be instituted early in the course of the illness.

REFERENCES

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