Colonic Mucormycosis Mimicking Ischemic Colitis in Kidney Transplant Recipient

Hyun Woo Kim, M.D.¹, Young Min Yoon, M.D.¹, Mi Ja Lee, M.D.², Nam Gyu Choi, M.D.³, Sung Pyo Moon, M.D.³, Na Ra Yoon, M.D.¹, Sun Ae Han, M.D.¹, Hyung Nam Kim, M.D.¹, Jun Hyung Lee, M.D.¹, Da Yeong Kang, M.D.¹, Hee Jung Ahn, M.D.¹, Byung Chul Shin, M.D.¹, Hyun Lee Kim, M.D.¹ and Jong Hoon Chung, M.D.¹

Departments of Internal Medicine¹, Pathology² and Surgery³, Chosun University School of Medicine, Gwangju, Korea

Mucormycosis is an extremely rare but potentially life-threatening fungal infection. Mucormycosis of the gastrointestinal tract manifests with features similar to ischemic colitis. A 48-year-old man with end-stage renal disease due to diabetic nephropathy underwent deceased donor kidney transplantation. He complained of abdominal pain and distension on postoperative day 17. A computed tomography (CT) scan revealed symmetrical wall thickening of the ascending colon, which was consistent with ischemic colitis. However, a follow-up CT scan showed a localized wall-off colon perforation in the hepatic flexure and segmental mural gas in the ascending colon. Microscopic examination obtained from a surgical specimen demonstrated numerous fungal hyphae and spores in the mucosa and submucosa. A total colectomy was performed, but the patient died 36 days later due to multiple organ failure, despite antifungal agents. Clinicians should be informed about fungal infection, such as colonic mucormycosis mimicking ischemic colitis, in kidney transplant patients with diabetes mellitus, and treatment should be initiated at the earliest.

Key Words: Mucormycosis, Kidney transplantation, Ischemic colitis

INTRODUCTION

Mucormycosis is an extremely rare, but potentially life-threatening fungal infection, that occurs in 0.4% to 16% of solid organ transplantation recipients and results in a high mortality rate(1). Mucormycosis can manifest with different clinical presentations, particularly in solid organ transplantation recipients, among whom the most common type of infection is parasal sinus (39%) followed by pulmonary (24%), cutaneous (19%), cerebral (9%), and gastrointestinal forms (7%)(2). Mucormycosis of the gastrointestinal tract manifests with features similar to those of ischemic colitis(3).

Mucor, one of the fungi that cause mucormycosis, has a special affinity for blood vessels, which may explain the clinical presentation of colonic infection as an ischemic colitis pattern(4).

Several cases of mucormycosis were reported in disseminated form after chemotherapy in patient with acute lymphocytic leukemia, allogenic bone marrow transplantation and small bowel transplantation in Korea(5-7). We describe a case of colonic mucormycosis mimicking ischemic colitis in deceased donor kidney transplantation (DDKT) recipient with diabetes mellitus.
CASE REPORT

A 48-year-old man with end-stage renal disease due to diabetic nephropathy underwent DDKT. He suffered from diabetes mellitus for 10 years and was treated with insulin. He was maintained on hemodialysis for 6 years prior to the transplant. His general condition was good after transplantation and there were no immediate complications such as acute rejection or infection. The patient received immunosuppressive agents along with methylprednisolone, myco-

Fig. 1. Abdominopelvic computed tomography scan. Ascites and (A) mild to (B) moderate symmetrical wall thickening (arrows) was observed on the ascending colon.

Fig. 2. Follow-up abdominopelvic computed tomography scan revealed (A) localized wall-off colon perforation in the hepatic flexure (hollow arrow) and (B, C) segmental mural gas in the ascending colon (arrows) and (D) symmetrical wall thickening (arrow) was observed in the descending colon.
phenolate mofetil, and tacrolimus.

On the 17th day after DDKT, the patient complained of abdominal pain. A physical examination indicated a blood pressure of 130/80 mmHg, a pulse rate of 98 beats per minute, and a body temperature of 37.2°C. His abdomen was soft but diffusely tender without signs of peritoneal irritation. The laboratory findings were as follows: leukocyte count 14,890/mm³ with 96% segment form, hemoglobin 7.6 g/dL, platelet count 93,000/mm³, serum fasting glucose 204 mg/dL, 2-hour postprandial glucose 283 mg/dL, hemoglobin A₁c 7.7%, C-reactive protein 6.70 mg/dL, cytomegalovirus (CMV) immunoglobulin M was negative, CMV antigemia was negative, aspergillus antigen was negative, and *Clostridium difficile* toxin assay was negative. A computed tomography (CT) scan of the abdomen revealed ascites and mild to moderate symmetrical wall thickening of the ascending colon (Fig. 1). Ischemic colitis was suspected from the CT scan. The patient was treated with bowel rest, intravenous fluid replacement, and antibiotics. However, the patient’s condition continued to deteriorate. On the 23rd day after DDKT, a follow-up CT scan revealed localized wall-off colon perforation in the hepatic flexure and segmental mural gas in the ascending colon, and symmetrical wall thickening was observed on the descending colon (Fig. 2). Therefore, he underwent emergency operation. Surgical findings were ischemic colitis from the cecum to the proximal transverse colon and necrotizing colitis from the distal transverse colon to the descending colon. Therefore, we resected from the terminal ileum to the mid-sigmoid colon (Fig. 3). Microscopic examination demonstrated numerous fungal hyphae and spores were noted in the mucosa and submucosa characterized by large non-septated hyphae with acute angle branching (Fig. 4). On the basis of clinical findings and morphological features of the fungal organisms, mucormycosis was diagnosed. Antifungal treatment was initiated with intravenous amphotericin B (1 mg/kg/day). Mycophenolate and tacrolimus were discontinued and the dose of methylprednisolone was reduced. On the 29th hospital day, the patient developed progressive dyspnea, tachycardia, and jaundice. Despite maximal vasopressor and mechanical ventilator support, the patient died on the 36th hospital day.

**DISCUSSION**

Infection is a major cause of morbidity among solid organ transplant recipients and the incidence of fungal infections is in the range 6% to 38% (1,2). The risk factors of mucormycosis include hematologic malignancies, diabetes mellitus, steroids, and immunosuppressive agents used in bone marrow, solid organ transplantation, broad-spectrum antibiotics, cytotoxic chemotherapy, burns, and dialysis (3,4). Augmented immunosuppression for the treatment of rejection, mainly in the form of steroids, may accelerate the course of infection. An important characteristic feature of *Mucor* hyphae is their propensity to invade the blood vessels, causing thrombosis, multiple infarctions, and hemorrhages of the visceral organs. Vessel thrombosis by *Mucor* fungi and tissue necrosis are two major hallmarks of mucormycosis (8).

Our patient was diagnosed with end-stage renal disease due to diabetic nephropathy and received postoperative immunosuppressive agents after kidney transplantation. A review of 116 solid organ transplant recipients with mucormycosis found that the site of involvement of gastrointestinal mucormycosis (n=13, 11.2%), included the stomach in nine (69.2%), the colon in one (7.6%), the esophagus in one (7.6%), and the liver in one (7.6%) (9). The symptoms are varied and depend on the site affected, non-specific abdominal pain and distention associated with nausea and vomiting are the most common symptoms (10).
The diagnosis is based on the history, clinical examination, diagnostic radiography, and biopsy(11). Because mucormycosis is a rare disease in transplant recipients, a high index of suspicion is required, which should be followed by an aggressive attempt to obtain tissue for histologic and bacteriologic studies from the affected organs.

The current treatment for mucormycosis involves a combined approach: rapidity of diagnosis, control of the underlying predisposing illness, appropriate surgical debridement of the infected tissue and prompt initiation of antifungal therapy(12). Till date, only the polyene class of drugs, including amphotericin B deoxycholate and its lipid derivatives, demonstrated activity against the agents of mucormycosis(10). Surgery is essential in decreasing the fungal burden by removing infarcted tissues, where amphotericin B cannot be distributed. Nonetheless, mucormycosis is generally a severe infection with an overall patient survival rate of approximately 50%(10).

In this case, the patient with diabetic nephropathy had received immunosuppressive agents after kidney transplantation and ischemic colitis was initially suspected. The patient was treated with supportive care including bowel rest, intravenous fluid replacement, and antibiotics. However, the patient’s symptoms showed a deteriorating condition. He was finally diagnosed by operative biopsy and was treated with antifungal agents. Nevertheless, he died. Uncontrolled...
diabetes mellitus and augmented immunosuppression, particularly with methylprednisolone, are the risk factors of mucormycosis in kidney transplant recipients. Early diagnosis by endoscopic biopsies and treatment with antifungal agent are essential for managing the invasive colonic mucormycosis after kidney transplantation. The clinician should be informed about fungal infection, such as colonic mucormycosis mimicking ischemic colitis in kidney transplant patient with diabetes mellitus and treatment should be started at the earliest.

REFERENCES