

## Acute Appendicitis Associated with Aspergillosis in a Leukemia Patient – A Case Report–

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Herein we describe a rare case of acute appendicitis associated with localized aspergillosis in an 8-year-old boy with acute lymphoblastic leukemia. During chemotherapy, the patient complained of mild abdominal pain in the peri-umbilical area and displayed an increased C-reactive protein level. Abdominal ultrasonography disclosed appendicitis and consequently an appendectomy was done. Histologically, acute appendicitis and *Aspergillus* hyphae were identified in the lumen and necrotic mucosa. However, there was no evidence of systemic aspergillosis. While aspergillosis is a common fungal infection in immunocompromised patients treated with chemotherapy, acute appendicitis associated with localized aspergillosis without systemic infection is a very rare occurrence.

**Key Words :** Appendicitis; Aspergillosis; Leukemia

Aspergillosis may be a fatal infection in immunocompromised patients, such as patients undergoing therapy for lymphoma, leukemia, carcinoma, or transplantation.<sup>1</sup> The prevalence of aspergillosis has increased due to the accumulating number of immunocompromised cases associated with transplantation, cytotoxic chemotherapy and increased immunodeficiencies including human immunodeficiency virus (HIV) infection. However, the incidence of aspergillosis of the intestine is low.<sup>1</sup> Furthermore, acute appendicitis associated with localized aspergillosis is very uncommon. We recently encountered a rare case of leukemia with acute appendicitis presenting with aspergillosis.

### CASE REPORT

The patient was an 8-year-old boy diagnosed with acute lymphoblastic leukemia in September 2003. Until December 2006, he had been in a state of remission following chemotherapeutic regimens administered according to the Children's Cancer Group

(CCG) 1952 protocol (vincristine, L-asparaginase, prednisolone, intrathecal methotrexate). However, he had a relapse in March 29, 2007, and received additional chemotherapy.

Then, on June 20, 2008, the patient was readmitted to our hospital for a scheduled intensification chemotherapy. There was no evidence of specific abnormal findings on physical examination. The laboratory findings were as follows: white blood cell count (WBC),  $1.89 \times 10^3/\text{mm}^3$  (normal, 4.0 to 10.0); absolute neutrophil count (ANC),  $1,190/\text{mm}^3$ . On day 4 after admission, he complained of an intermittent cough and his C-reactive protein (CRP) level increased to 8.05 mg/dL (normal, 0.00 to 0.50). However, no other symptoms or signs were found. The patient received ceftazidime as empiric therapy. After 10 days, because he still complained of abdominal pain with tenderness in the peri-umbilical area and intermittent fever, an additional antibiotic, amikacin, was used. Laboratory findings were as follows: WBC  $6.0 \times 10^3/\text{mm}^3$ , ANC  $12/\text{mm}^3$  and CRP 10.27 mg/dL. Since intermittent fever and abdominal pain persisted and CRP did not normalize despite empiric antibiotic treat-

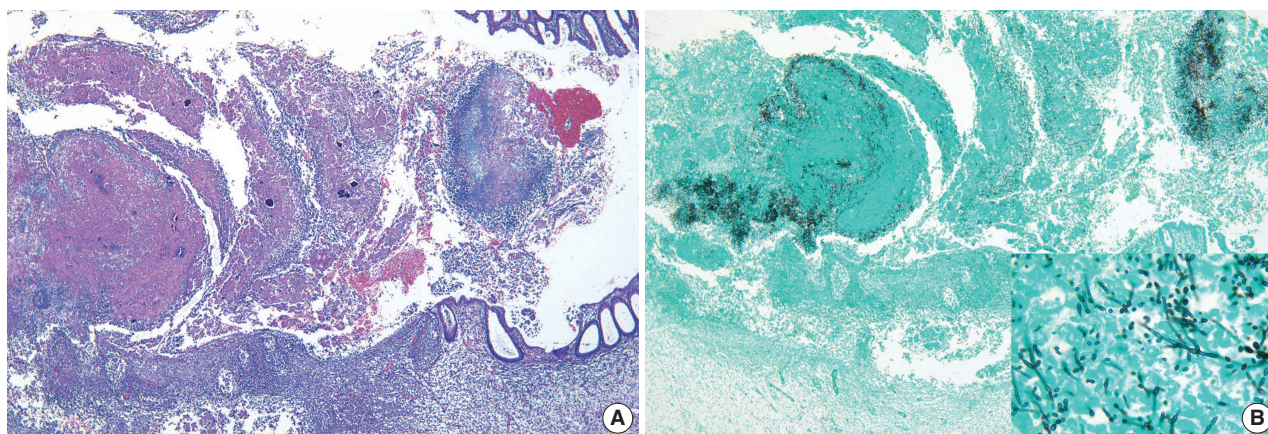


Fig. 1. (A) Histologic sections display dense neutrophilic infiltration in necrotic mucosa and muscularis propria. (B) *Aspergillus* fungi (inset) are stained with Gomori methenamine-silver stain. Fungal hyphae are present in necrotic mucosa and ulcerative areas.

ment, an abdominal ultrasonographic examination was done. The findings suggested appendicitis with enlargement of the appendix, bowel wall thickening of the cecum, and the collection of a small amount of fluid at the peri-appendiceal area. Appendectomy was done and histological findings revealed necrotic and inflammatory changes in the mucosa and muscle coat consistent with acute appendicitis, as well as many septate fungal hyphae with acute-angle branching characteristic of *Aspergillus* (Fig. 1). Fungal hyphae were predominantly present in necrotic inflammatory exudates and ulcerative areas of the mucosa and were focally observed in the submucosal layer. Abdominal computed tomography and serologic tests and culture for aspergillosis disclosed no evidence of systemic *Aspergillus* infection. No postoperative complications occurred. The patient was discharged on postoperative day 10, and the scheduled chemotherapy was continued.

## DISCUSSION

*Aspergillus* is a causative factor in various disorders including allergic diseases, pulmonary aspergillosis, and fatal opportunistic infection in immunocompromised patients.<sup>2</sup> Since *Aspergillus* spores are usually ingested by inhalation through a respiratory route, lung and cranial sinuses are common target organs. Moreover, organisms may invade adjacent vasculatures, resulting in hematogenous secondary dissemination to diverse organs, including brain, heart, eye, intestine, and bone.<sup>3</sup>

While pulmonary aspergillosis is a common clinical manifestation, primary *Aspergillus* infection of the intestine is relatively rare. Several reports have described intestinal aspergillosis asso-

ciated with chemotherapy in leukemic patients.<sup>4,5</sup> In particular, acute appendicitis associated with localized aspergillosis is very uncommon in immunocompromised patients and only two cases have been documented in the English language literature.<sup>4,6</sup> Two patients with acute myelogenous leukemia exhibited septic fever and clinical signs of acute appendicitis during induction therapy. Despite surgical management and antifungal therapy, both patients died of septic shock associated with disseminated aspergillosis.<sup>4,6</sup>

When intestinal aspergillosis develops in patients with persistent neutropenia, early diagnosis is very difficult, and may be delayed or even overlooked due to nonspecific and ambiguous symptoms and clinical signs.<sup>3</sup> Therefore, delayed diagnosis and management may contribute to dissemination of *Aspergillus* and perforation of the bowel wall.

In conclusion, although a surgical abdomen such as appendicitis is a well-described infectious complication in neutropenic patients with hematologic malignancies,<sup>7</sup> it is extremely rare that acute appendicitis is associated with aspergillosis. Thus, it is important to recognize the possibility of fungal infection and to consider such an infection in the differential diagnosis, especially with the development of nonspecific or ambiguous clinical symptoms and signs, including persistent fever, increased CRP and abdominal pain in immunocompromised patients with prolonged neutropenia during chemotherapy.

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