

Case Report

Primary Gastrointestinal *Aspergillosis* Presenting as Multiple Ulcerated Colonic Masses: a Case Report

Atoosa Gharib¹, Azadeh Rakhshan¹, Farzaneh Jadali¹, Bibi Shahin Shamsian²

1. Dept. of Pathology, Mofid Children Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

2. Dept. of Hematology-oncology, Mofid Children Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

ABSTRACT

Gastrointestinal *aspergillosis* most often occurs in the setting of disseminated infection from a primary pulmonary site and primary gastrointestinal *aspergillosis* is an unusual presentation.

We report a 7 year old female child with aplastic anemia, who was under treatment but experienced periods of neutropenia. She had no evidence of respiratory *aspergillosis* before the onset of abdominal symptoms including severe abdominal pain and rectorrhagia. The patient died of septic shock two weeks after emergency surgery for rectal bleeding.

Although a rare condition, primary gastrointestinal *aspergillosis* should be considered in differential diagnosis of gastrointestinal symptoms in neutropenic patients.

Key words: *Aspergillosis*, Gastrointestinal Tract

Introduction

Aspergillus is a saprophytic fungus that has rarely any adverse effect in immunocompetent individuals, since the inhaled conidia are eliminated relatively efficiently by innate immune mechanisms but can cause severe invasive infections in immunocompromised hosts (1). Invasive pulmonary *aspergillosis* accounts for 90-98% of invasive infections. Extra-pulmonary *aspergillosis* may be present in 25-60% of these cases and is most often described in the setting of disseminated disease. Isolated extra-pulmonary *aspergillosis* located in the central nervous system, the skin, the liver, the urinary tract and the digestive tract has only been mentioned in

case reports. Primary invasive *aspergillosis* has been rarely reported in the literature and the presentations varied from persisting fever to bloody diarrhea and peritonitis (2).

Case report

A 7 year-old female child was admitted to the hospital due to watery diarrhea for one week. The child was a known case of aplastic anemia since 3 months before admission and was under treatment with cyclosporine, G-CSF, prednisolone, oxymetholone and broad spectrum antibiotics. On examination, the patient was slightly ill and had fever. There was no tenderness and organomegaly on abdominal examination. Blood

Received: 7 April 2008

Accepted: 23 May 2008

Address Communications to: Dr. Atoosa Gharib, Department of Pathology, Mofid Children Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Email: atoosagharib@yahoo.com

count revealed anemia (Hb: 11.2 g/dl), neutropenia (126/cumm) and thrombocytopenia (9000/cumm).

In the hospital, the patient developed rectorrhagia. Upper GI endoscopy revealed severe gastritis and esophagitis with bile reflux, lacking ulcer and active bleeding site. No biopsy was taken due to bleeding tendency of the patient. Stool exams revealed bloody mucoid stool with 8-10 WBC/HPF and no entropathogenic bacteria, other relevant investigations including chest X-ray and abdominal sonography were normal.

Colonoscopy was also performed but because of the patient's severe rectorrhagia, she was quickly transferred to the operating room. During surgery, multiple masses in the cecum, transverse colon, and rectosigmoid were seen and a near total colectomy was performed.

The colon contained blood clots and multiple masses, measuring up to 2.5 cm in diameter, some of which had umbilicated ulcer on surface (Figure 1). H&E-stained sections revealed infiltration of lymphoplasmacelles, histiocytes, and langhan's type giant cells with foci of ulceration and necrosis (Figure 2). In H&E and PAS staining, dichotomously branching septate hyphae with vascular invasion were seen (Figure 3).

Two weeks after surgery the patient died following atelectasis, bronchopneumonia and sepsis.



Figure 1: Ulcerated mass in the resected segment of colon

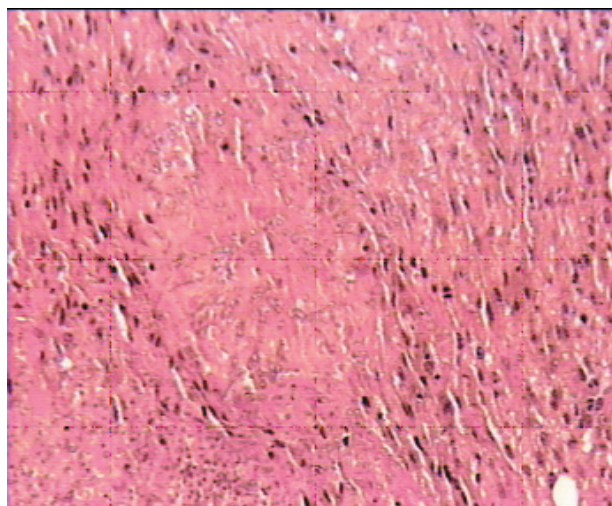


Figure 2: Fungal hyphae obliterating a vessel. (H&E × 100)

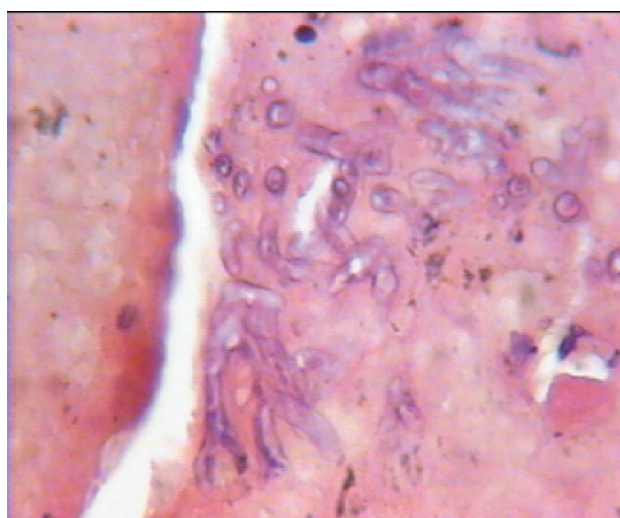


Figure 3: Septate, branching hyphae of *Aspergillus* spp. (PAS, × 400)

Discussion

Invasive gastrointestinal *aspergillosis* is a highly lethal and rapidly progressive opportunistic infection that characteristically affects the immunocompromised host, resulting in high degree of morbidity and mortality (3). Risk factors for invasive aspergillosis are categorized into 5 major groups: 1) neutropenia, 2) hematopoietic stem cell transplantation, 3) solid organ transplantation, 4) AIDS, and 5) chronic granulomatous disease. In neutropenic patients including aplastic anemia the risk of invasive aspergillosis is strongly related to the duration and degree of neutropenia (4). Severe (polymorphonuclear leukocytes = 500 mm^{-3} and especially 100 mm^{-3}) and prolonged (>12 to 15 days) neutropenia are associated with the greatest risk for invasive aspergillosis (1).

Almost one quarter of patients with invasive pulmonary aspergillosis develop disseminated infection via hematogenous spread (5) and of these patients there is a reported incidence of gastrointestinal involvement of 41-47% (5;6). Thus,

gastrointestinal involvement of *aspergillosis* mainly describes the dissemination following a primary pulmonary infection and primary digestive tract aspergillosis is really rare. P.Eggimann et al reported 2 cases and reviewed 23 cases of primary invasive aspergillosis of digestive tract from 1960 to 2005. Abdominal symptoms suggestive of typhlitis were the main clinical presentation of them (2). In other reported cases, the disease presented with appendicitis, abdominal mass, and bowel infarction (7-10).

Our case showed normal chest radiographs and had no respiratory symptoms before surgery, which proved that she had not pulmonary *aspergillosis* as a primary source of infection and that most probably the digestive tract had been the initial portal of entry. It has been proposed that chemotherapeutic toxicity may alter normal gastrointestinal immunity and allow entry of *Aspergillus* by disrupting mucosal barriers (5). High mortality of these patients despite antifungal therapy is a well-recognized outcome according to the literature (2) and also ante mortem diagnosis remains difficult .

The combination of predisposing factors in the host , compatible clinical and radiologic findings and two consecutive positive serum galactomannan assays (fungal cell wall constituent as detected by double sandwich ELISA) can be equated with “probable invasive aspergillosis” and obviate the need for an invasive procedure for definite diagnosis (4). Invasive aspergillosis is defined histologically by the presence of *Aspergillus* hyphae in the bowel biopsy with mucosal alteration and tissue destruction and/or tissue invasion with microvascular involvement (2).

Despite significant progress in the serological diagnosis of invasive *aspergillosis* by antigen detection, the sensitivity of detection must be improved (1). We hope that by being aware of the significance

of the clinical symptoms and setting up serological assays for early detection, the survival of these patients will improve in future.

References

1. Latge JP. *Aspergillus fumigatus* and aspergillosis. Clin Microbiol Rev 1999 Apr;12(2):310-50.
2. Eggimann P, Chevreton JC, Starobinski M, Majno P, Totsch M, Chapuis B, et al. Primary invasive *aspergillosis* of the digestive tract: report of two cases and review of the literature. Infection 2006 Dec;34(6):333-8.
3. Shah SS, Birnbaum BA, Jacobs JE. Disseminated *aspergillosis* inciting intestinal ischaemia and obstruction. Br J Radiol 2001 Dec;74(888):1145-7.
4. Segal BH, Walsh TJ. Current approaches to diagnosis and treatment of invasive *aspergillosis*. Am J Respir Crit Care Med 2006 Apr 1;173(7):707-17.
5. Young RC, Bennett JE, Vogel CL, Carbone PP, DeVita VT. Aspergillosis. The spectrum of the disease in 98 patients. Medicine (Baltimore) 1970 Mar;49(2):147-73.
6. Prescott RJ, Harris M, Banerjee SS. Fungal infections of the small and large intestine. J Clin Pathol 1992 Sep;45(9):806-11.
7. Tzankov A, Haberer O, Pall J, Kreczy A, Mairinger T. Intraappendicular Aspergilloma with catarrhalic appendicitis after neoadjuvant radiotherapy for rectal adenocarcinoma. Electronic J of Pathol and Histol 2001;(7):7.
8. Ibrahim AH, al Malki TA, Morad N. Primary locally infiltrative gastrointestinal aspergilloma in a non-neutropenic child. J R Coll Surg Edinb 2000 Oct;45(5):335-8.
9. Gonzalez-Vicent M, Diaz MA, Colmenero I, Sevilla J, Madero L. Primary gastrointestinal *aspergillosis* after autologous peripheral blood progenitor cell transplantation: an unusual presentation of invasive aspergillosis. Transpl Infect Dis 2008 Jun;10(3):193-6.
10. Kami M, Hori A, Takaue Y, Mutou Y. The gastrointestinal tract is a common target of invasive *aspergillosis* in patients receiving cytotoxic chemotherapy for hematological malignancy. Clin Infect Dis 2002 Jul 1;35(1):105-6.