

Emergency emicolectomy for intestinal primary Aspergillosis in acute myeloid leukemia

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SUMMARY: Emergency emicolectomy for intestinal primary aspergillosis in acute myeloid leukemia.

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Intestinal aspergillosis is an infection with a very high death rate especially in leukemic patients.

Here we describe a case of a 46 years old woman with acute myeloid leukemia (LAM M5) who developed intestinal primary aspergillosis. This patient was diagnosed with LAM M5 through bone marrow aspiration and bone biopsy in March 2004. Symptoms of the disease were slight persistent fever, weight loss, asthenia, anemia, thrombocytopenia, and leukocytosis with high number of blasts in peripheral blood. After induction chemotherapy with ICE (Ifosfamide, Carboplatin, Etoposide), she developed neutropenia and high fever without apparent infective foci. She was treated with empiric antibiotic therapy, nevertheless she developed an intense diarrhea and ileo-cecal distention. Diagnostic exams didn't show signs of a focal lesion. Despite the change in antibiotic treatment and the transfusions of granulocytes and blood cells, the patient developed extremely critical conditions with persistence of neutropenia and abdominal distention. A surgical treatment was decided at the time.

We treated the patient with a two steps surgical procedure. The first step was a right abdominal ileostomy followed by improvement of general conditions and then the second step a right colectomy. The histological morphology confirmed necrotizing colitis with Aspergillus ife. At that time, treatment with voriconazole was started. The general conditions of the patient improved rapidly and we were able to treat the patient with other medical anti-leukemic therapies. The patient is now cured and in healthy state. We obtained a good clinical result as only in other few cases described in literature.

RIASSUNTO: Emicolectomia in emergenza per Aspergillosi intestinale in paziente con leuemia mieloide acuta.

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L'aspergillosi intestinale è un'infezione ad alta mortalità in particolare nei pazienti leucemici.

Il nostro paziente è una donna di 46 anni con leucemia acuta M5 diagnosticata con aspirato e biopsia midollare. La sintomatologia era rappresentata da febbre persistente, perdita di peso, astenia, anemia, trombocitopenia con alto numero di blasti nel sangue periferico. La paziente è stata sottoposta a terapia di induzione con ICE (ifosfamide, carboplatino e etoposide), con conseguente sviluppo di neutropenia con febbre elevata senza apparenti foci infettivi. La paziente è stata quindi sottoposta a terapia antibiotica di tipo empirico senza risultato, con comparsa di intensa diarrea e distensione ileo-ciecale. Nonostante la modifica della terapia e l'utilizzo di trasfusioni di granulociti le condizioni cliniche peggiorarono con persistente neutropenia e distensione addominale.

La paziente è stata pertanto sottoposta a chirurgia in due steps. La prima procedura è stata una ileostomia, con miglioramento delle condizioni cliniche, la seconda l'emicolectomia destra. L'istologia confermava una colite necrotizzante con presenza di ife di Aspergillus. La paziente è stata quindi sottoposta a terapia con voriconazolo. Le condizioni generali migliorarono rapidamente. In seguito si sono copplete le terapie antileucemiche. La paziente è in remissione completa persistente. Il nostro è uno dei pochi casi in letteratura con risultati favorevoli.

KEY WORDS: Aspergillosis - Acute leukemia - Emicolectomy.
Aspergillosi - Leucemia acuta - Emicolectomia.

Introduction

Fungal infections are frequent in patients treated with chemotherapy in oncologic and haematologic departments (1,2). Immunodeficiency is the main reason for these complications and dissemination in the body of

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multiple infectious foci is the main clinical presentation. *Aspergillus fumigatus* is one of the many frequent pathogens observed, with different clinical presentation. In these patients the incidence of disseminated aspergillosis can be observed in about 20% of the cases (3). In those patients with prolonged neutropenia the death rate is around 80-90% (1).

Generally the most common site of infection is represented by the respiratory tract, with consequent lung colonization. In these patients, *Aspergillus* can disseminate through the vascular system and in 41% of the patients intestinal disease is observed (3).

In a limited number of cases, the intestine is the only site of infectious localization. In this situation *Aspergillus* makes its way through the intestinal mucosa eventually disrupted by chemotherapy's toxicity with consequent deterioration of gastro-intestinal immunity (4). Also this solitary clinical presentation can have a high death rate.

Case report

A white woman, aged 46 years, was diagnosed with acute myeloid leukemia during her hospitalization in the Oncological Department. At the beginning of the disease, symptoms were represented by a slight persistent fever, weight loss, asthenia, anemia, thrombocytopenia and leucocytosis with a high number of blasts in peripheral blood. The diagnosis of LAM M5 was done in March 2004 by bone marrow aspiration and bone biopsy.

A cycle of induction chemotherapy with the ICE scheme (Ifosfamide, Carboplatin, Etoposide) was started. After eight days neutropenia G4 was observed and after few days a high fever appeared without evident infective foci. Empiric antibiotic therapy with piperacillin/tazobactam, amikacin and antifungal therapy with fluconazole was administered. Two days after the beginning of the antibiotic therapy we observed intense diarrhea and ileo-cecal distention without signs of bowel perforation. Blood culture, urine culture, feces-culture, oral and pharyngeal samples were all negative. High resolution CT scan, abdominal ultrasound, and cardiac ultrasound didn't show focal lesions.

For the persistence of high fever we administered a new antibiotic treatment with Meropenem, Caspofungin and Vancomycin and we added G-CSF (Granulocyte Colony-Stimulating Factor), granulocyte transfusions, blood cell transfusions and Octreotide therapy. Nevertheless the general conditions of the patient worsened and she developed an acute abdomen, septic shock and cardiac-respiratory failure. A CT scan was performed at that time (day +23 from the beginning of ICE) showing bilateral pleural effusion, abdominal ascitis and conspicuous thickening of descendent colon and sigma walls with the suspicion of endoluminal bleeding (Fig. 1, 2).

The patient was in extremely critical conditions with persistent neutropenia; for this reason, after a surgical consultation the decision was to perform a right abdominal ileostomy (first step). After a few days (day +26 from ICE), taking advantage of granulocyte partial recovery, a right colectomy enlarged to left colon and ileum was performed with lateral-lateral ileo-colostomy. The macroscopic appearance of the colon was that of necrotic colitis of all the colon walls' width up to the pericolic adipous tissue, with clottings and abdominal material outside the intestine. The histologic morphology was that of a necrotizing colitis with numerous fungal life with the

typical appearance of aspergillosis (5).

At that time (day +40 from ICE) a treatment with Voriconazole was started. The patient's clinical conditions improved rapidly after surgery. During the following months we performed the left over cycles of consolidation chemotherapy with associated Voriconazole treatment with good tolerance. Ten months after, at the end of 2004, the treatment ended. The patient obtained a complete haematological remission with no signs of intestinal aspergillosis and good general conditions.

The duration of remission was one year and after this period a relapse of the disease occurred. Therefore the patient underwent allogenic transplantation and at present is in good clinical conditions.

Discussion

Intestinal aspergillosis is one of the typical infectious diseases in many immune-compromised or severely neutropenic patients (6). In 41% of cases this "characteristic" clinical feature occurs in patients with disseminated aspergillosis, with the lung being the way of entrance. In some cases a localized intestinal infection may appear (3), with very few symptoms at the beginning of the disease. Typical clinical signs are very rare at the beginning and so are clinical findings at instrumental examination.

Rarely antigenic evidence can be demonstrated (7), and the typical radiologic appearance of the *Aspergillus* can be detected, with sub-obstruction, colon distention and also characteristic CT colon features with thickening of the bowel walls (8,9). In this phase of the disease rapid decision should be done for the high rate of mortality in these patients. Also with intensive an-

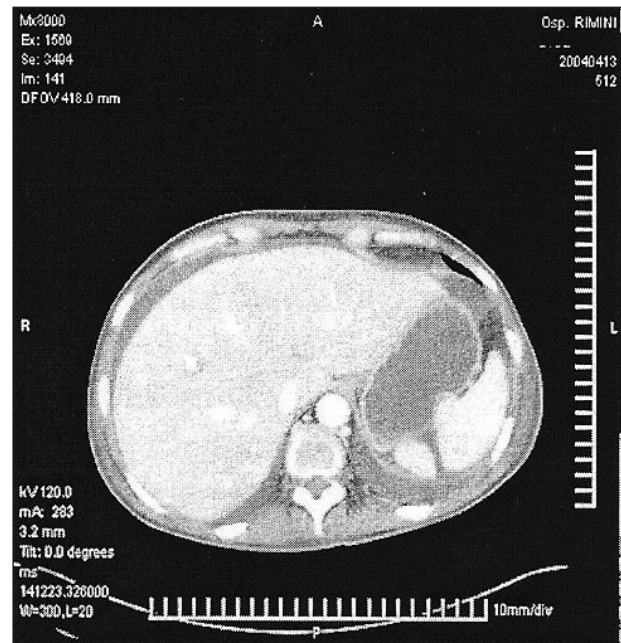


Fig. 1 - Abdominal CT scan - Ascitis and conspicuous thickening of descendent colon and sigma walls with the suspicion of endoluminal bleeding.

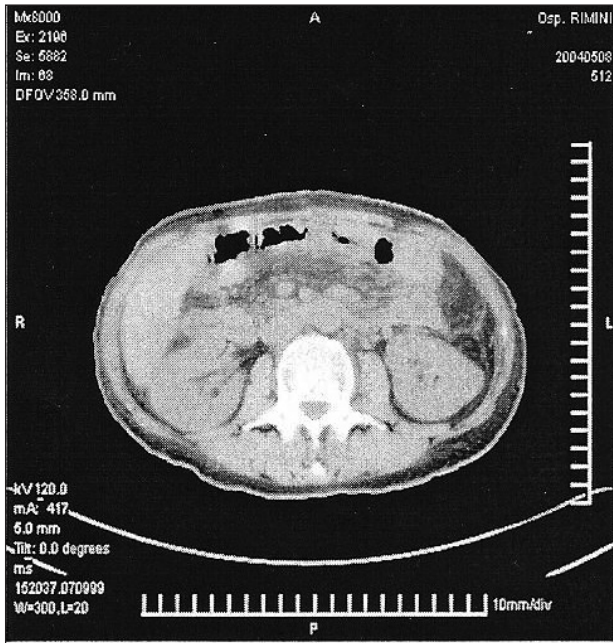


Fig. 2 - Abdominal CT scan - Ascitis.

tifungal therapy the evolution of the infection is fatal.

Surgery is essential for the treatment of intestinal aspergillosis to avoid perforation or obstruction. In these severely neutropenic patients this surgical procedure only in some cases can improve and solve the situation (10).

In our patient we tried as a first step, during the neutropenic period, "to deflate" the small bowel, with a right ileostomy. This first procedure allowed us to resolve temporarily the obstruction and to perform a definitive colectomy in a less severe neutropenic situation. Our patient promptly recovered, without signs of aspergillosis.

Conclusion

Generally intestinal aspergillosis in severely immune-compromised patient is a fatal complication. A careful and prompt surgical and medical treatment can solve this life-threatening condition.

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