

Concomitant invasive pulmonary aspergillosis and *Aspergillus* sinusitis in a patient with acute leukaemia

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Abstract. A 67 years old male otherwise healthy who had undergone surgery for nasal polyposis ten years earlier was recently diagnosed with B-cell acute lymphoblastic leukaemia. During induction treatment the patient developed sino-pulmonary aspergillosis caused by *Aspergillus flavus*. The patient developed severe reactions against amphotericin-B and thereafter Abelcet[®], whereas he tolerated treatment with AmBisome[®]. Surgery of the nasal cavities was performed whereas surgery of the pulmonary infiltrates was not possible. During subsequent treatment for his leukaemia and long periods of neutropenia, the patient was on AmBisome[®] treatment and there were no signs of progression of the *Aspergillus* infection. The antifungal treatment was considered to be successful. The patient was referred back to his local hospital and antifungal treatment was switched to oral itraconazole. (www.actabiomedica.it)

Key words: *Aspergillus* infection, sinusitis, pneumonia, leukaemia, AmBisome[®]

Case report

A 67 years old male who had recently been diagnosed with B-cell acute lymphoblastic leukaemia was referred to the Uppsala University Hospital for treatment. Before the diagnosis of leukaemia he was otherwise healthy except for surgery for nasal polyposis approximately ten years before.

The induction treatment for leukaemia was started on the 4th of May 2000 according to the standard protocol and consisted of vincristin 2 mg, amsakrin 200 mg/m², cytarabin 3 g/m², and corticosteroids (betamethason) 20 mg/m². Prophylaxis consisted of ciprofloxacin 0.5x2 and acyclovir 400 mgx2.

On the 6th May he developed fever. He received i.v. cefuroxime and initially improved. On the 13th May he was still neutropenic and fever increased. The C-reactive protein (CRP) increased to 146 mg/l. The antibiotic treatment was changed to meropenem and on the 16th May vancomycin was added. However, the fever increased and a CT-scan of the thorax that was performed on the 17th May showed

five nodular infiltrates, suggesting *Aspergillus* infection (1-9). A bronchoalveolar lavage (BAL) was performed on the 18th May and antifungal treatment with amphotericin-B was initiated. The BAL was cultured but was negative. The Platelia ELISA test for *Aspergillus* galactomannan carried out on serum showed an increased titre of 3.56 (reference index < 1.0) (1-3).

When the dose of amphotericin B was increased to 0.75 mg/kg bodyweight on the 21st May, the patient had a severe adverse reaction with fever, shivering and developed atrial fibrillation. Treatment was changed to Abelcet[®] 350 mg/day. However, during the second infusion of Abelcet[®] the patient developed pulmonary oedema and the infusion was stopped. Because of suspected severe adverse reactions to amphotericin-B, treatment was changed to oral itraconazole 400 mg/day (4).

During the following week a CT-scan of the sinuses was performed that showed thickening of the right maxillary sinus with some infiltrates, suspected destructions within the cavity and nasal septum and in-

filtrates in two other sinuses (5, 6). However, he was previously operated on for nasal polyposis. A biopsy from the right maxillaris sinus was performed that was culture-positive for *Aspergillus flavus*.

A CT-scan of thorax on the 31st May showed progression of the infiltrates with pleural effusion, pericarditis and two cavitations in the lung, one in the right and one in the left lung. Thoracic surgery was not possible. Because of these findings antifungal treatment was switched to AmBisome®, an initial dose of 3 mg/kg bodyweight which was then increased to 5mg/kg the day after (7-9). No adverse reaction was observed.

The patient improved, but a new investigation of the nasal septae and sinuses showed necrotic debris and a progression of the destruction of the nasal wall (6, 10). Surgery was performed on the 9th June. Samples taken during the operation showed further growth of *Aspergillus flavus*. An Aspergillus antigen test showed a titre of 2.63 (strongly positive) (2, 3, 9). At the time of surgery the leucocytes had recovered and the patient was in remission of his leukaemia. Thereafter the patient improved and the pleural effusions and pericarditis resolved. No growth of Aspergillus was found from the pericardial fluid.

On the 30th June further anti-leukaemia treatment was given with vincristin, amsakrin cytarabine and corticosteroids. Flucytosine was added as an adjunctive antifungal to AmBisome® during this neutropenic period.

During the following month he had a variety of severe adverse reactions to the leukaemia treatment with prolonged fever and an elevated CRP that was not related to the antifungal treatment. Flucytosine concentrations were frequently measured in serum and the dose was adjusted thereafter, but no adverse reactions were reported. A CT-scan of the sinuses on the 8th August showed a new thickening of the right maxillaris sinus with infiltrates. The AmBisome® dose was increased to 7 mg/kg (6, 8-10). A biopsy did not reveal Aspergillus and the ELISA Aspergillus-antigen test was negative (titre of 0.45) and there was no sign of progression. A CT-scan of the thorax showed no progression of infiltrates (1, 11).

Because of the patient's bad health related to treatment of his leukaemia with severe thrombocyte-

mia he was started on maintenance therapy with Purinethol.

Antifungal treatment was also switched to oral treatment with itraconazole and serum levels were frequently measured to monitor absorption (7). Thereafter he was transferred to his local hospital for further antifungal and leukaemia treatment.

This case illustrates that patients can tolerate amphotericin B lipid formulations although several adverse reactions to amphotericin B lipic complex may be experienced.

There was also a good correlation with the ELISA aspergillus-antigen test and the Aspergillus infection. The importance of surgery was also shown. There was no sign of progression of invasive Aspergillus infections during leukaemia treatment when the patient was being treated with AmBisome®.

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