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Case reports

Invasive pulmonary aspergillosis after near-drowning

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Abstract. After near-drowning following a car accident, a 27-year-old man developed servere ARDS. Six days later *Aspergillus fumigatus* was isolated in his sputum, and invasive pulmonary aspergillosis developed thereafter. Aspergillus titre increased, and chest tomograms revealed cavities in both lungs. The treatment consisted essentially of Amphotericin B and 5 fluorocytosine, intravenously and by inhalation, intensive postural drainage and mechnical ventilation with PEEP. After 41 days he was cured and discharged from the ICU. Six months later he returned to his job and clinical examination was normal.

Key words: Near-drowning – Aspergillosis – Respiratory failure

Aspergillus species are ubiquitous fungi found in soil, sewage and air [2].

Serious Aspergillosis infections with high mortality have been reported in several immunocompromised hosts. The patient presented in this case developed a clinical and radiological picture of invasive pulmonary aspergillosis (IPA), with remission of the clinical signs after a therapeutic course with Amphotericin B (Am B) and 5 fluorocytosine (5 FC) both intravenously and by inhalation. This complication appeared as a solitary infection after severe near-drowning.

Case report

A 27-year-old man was admitted to our University Hospital on 23 December 1982, after near-drowning in a ditch following a car accident.

On admission his arterial blood gas analysis showed pH 7,32; P_aO_2 3 kPa; p_aCO_2 5,9 kPA; S_aO_2 53%. The patient was intubated and ventilated with high level of PEEP, and treated with steroids, diuretics and cardiotonics. The first chest X-ray showed a picture of severe ARDS rapidly worsening on the following radiograms. After this phase of lung edema and extreme impairment of gas exchange, there was progressive improvement of the ARDS.

For infection prevention, selective decontamination of the digestive tract (SDD) [4] was instituted, together with a cefalosporine (Cefotaxime). The leucocyte count was within the normal range ($5-10 \times 10^3$), but core temperature was high (39 °C to 40.2 °C). A skin test (multitest IMC) showed an anergic reaction.

Chest physiotherapy was performed every 3 hours, and lung nebulization with 2-mercapto-etanosulfonate and salbutamol every 6 hours.

Six days after admission *Aspergillus fumigatus* (A. fumigatus) was isolated from the sputum. Antimycotic treatment was started with miconazole intravenously (600 mg 3 × day) and in nebulization (8 × 50 mg/day). More intensive physiotherapy was instituted including postural drainage.

Aspergillus serology (ELISA) was performed at 12/1, 18/1, 27/1, 27/2 and 1/3/83. IgG was positive in all samples. IgA and IgM were both negative in the first and in the last two samples. In the samples from 18/1 and 27/1 IgA and IgM were present in high concentrations (Ext. > 0.268).

The leucocyte count increased suddenly on the 6th day after admission (13×10^3) and rose to 22×10^3 on the 9th day, decreasing gradually thereafter. The sputum cultures remained positive for *A. fumigatus* and the clinical condition deteriorated, with increasing fever reaching 40.5 °C.

The chest X-rays showed increasing infiltrates in the right and left lower lobes and left upper lobe. Tomograms revealed the presence of cavities in the right lower lobe and left upper lobe.

Fourteen days after admission the sputum cultures were still positive for *A. fumigatus*. The antimycotic treatment with miconazole was stopped and a combination of Am B and 5FC was started intravenously

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and by inhalation. The inhalation therapy consisted of the administration by nebulization of Am B 10 mg and 5FC 50 mg every 4 h.

The reason for this change was the ineffectiveness of therapy (chest X-ray, fever, poor clinical condition) and the diminished sensitivity of the strain to miconazole ($\geqslant$125 μg/ml).

Under this therapy the clinical and radiological picture improved progressively with remission of the fever and decrease of lung infiltrates which became more localized to the right lower lobe.

Tomograms, 36 days after admission showed persistence of cavities localized in the left upper lobe and right lower lobe.

Levels of Am B and 5 FC were determined weekly They ranged, respectively, from 3.4 μg/ml – 61 μg/ml and from 31.6 μg/ml – 44.7 μg/ml. The minimal inhibitory concentrations (M.I.C.) are for Am B 0.16 – 0.32 μg/ml and for 5FC 312 – 625 μg/ml.

The mean doses of Am B and 5FC were respectively 45 mg/day (total dose 1,240 mg) and 12,2 g/day (total dose 300 g).

To identify a possible source of contamination *A. fumigatus* from the patient was inoculated into brain heart infusion (broth), 0.9% saline, and sterile water. The fungus grew at high concentrations. Ditch water samples collected at the site of accident were free from *A. fumigatus*. The inspiratory and expiratory assembly parts of the ventilator (Servo 900B) were sterile. The nutritional state of the patient was good.

On the 41th day the patient was discharged from the ICU without fever and in good clinical condition. Presently, May 1983, he has resumed his work and is doing well. Radiologic studies are normal.

Discussion

In the literature, cases of fatal disseminated aspergillosis are reported in leukemia, lymphoma and other hematological malignancies and in patients receiving corticosteroids.

After near-drowning, respiratory tract infections are generally caused by gram negative bacteria. Pulmonary aspergillosis is rare. The literature from the last twenty years reports two cases of fungal infections after near-drowning; both were fatal [1, 5].

In our case the *A. fumigatus* could have been aspirated into the lungs during submersion but the samples of ditch water did not yield *A. fumigatus*. A possible explanation could be the high concentrations of an adsorbing agent (Ekoperl) added to ditch water after the accident. We have shown that this agent has fungicidal activity.

For the last ten years the patient was known to suffer from bronchiectasias. Nevertheless *A. fumigatus* was never isolated from his sputum.

It is therefore impossible to establish if he was already a carrier of *A. fumigatus,* or if colonization occured during submersion.

Trauma, ARDS mechanical ventilation, together with high doses of corticosteroids decreased the immune defense system of our patient and made him susceptible to aspergillus infection. He received 50 mg Dexamethason on the 1st day and then the administration of corticosteroids was prolonged up to the 19th day (total prednisolone dose, 340 mg). According to Pennington [3] a proper clinical setting is very important to establish the diagnosis of IPA.

In our case the diagnosis was based on the following: (1) Pneumonia with high fever, (2) Bilateral patchy infiltration on X-ray, (3) Repeated isolates of *A. fumigatus,* (4) Strongly positive serology tests, and (5) Favourable reaction to Am B/5FC treatment. An open lung biopsy was not performed.

Very high doses of miconazole both intravenously and via nebulization proved to be ineffective. The minimal inhibitory concentrations of miconazole became higher (>125 μg/ml) suggesting a decreasing sensitivity of *A. fumigatus*. Amphotericin B associated with 5 Fluorocytosine was thus the chosen alternative. Because of doubt whether these drugs given intravenously would reach lung cavities in therapeutic concentrations, they were also administered via a nebulizer. In order to transport the nebulized substances into the cavities, and to facilitate grainage, the lungs were mechanically ventilated, and the airways and cavities kept under the influence of continuous positive pressure.

This case of IPA was succesfully treated after 41 days. The early recognition of the disease, the treatment with Am B and 5FC i.v. and by inhalation, the aggressive physiotherapy and mechanical ventilation prolonged up to the moment when the sputum cultures were negative have been, in our opinion, the most important contributors to the good result.

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