ANSWER TO PHOTO QUIZ (PAGE 187)

A PATIENT WITH FLANK PAIN AND HAEMATURIA AFTER ALLOGENEIC STEM CELL TRANSPLANTATION

DIAGNOSIS

Direct microscopy of bronchoalveolar lavage (BAL) showed leukocytes, but no fungal elements. However, fungal culture was positive, and macroscopic and microscopic morphology was consistent with *Rhizopus microsporus*. The galactomannan index in the BAL was increased (3.5, cut-off value ≥ 0.5) suggesting an *Aspergillus* co-infection. No other microorganisms were found. The minimum inhibitory concentration (MIC) using the EUCAST reference method was performed, and showed a MIC of 0.5 mg/l for both amphotericin B and posaconazole.

A kidney biopsy was performed and histological examination showed focal necrosis with neutrophil accumulation and extensive proliferation of fungal hyphae, morphologically consistent with mucormycosis. Fungal cultures remained negative, and a species-specific mucormycetes polymerase chain reaction (PCR) detected *R. microsporus*, while the aspergillus species-specific PCR remained negative. A diagnosis of probable pulmonary aspergillosis and proven disseminated mucormycosis was made and treatment with liposomal amphotericin B (5 mg/kg/day) was started. Because the graft-versus-host-disease was not very active, cyclosporine was discontinued and the daily dose of prednisolone was decreased to 30 mg and thereafter gradually tapered by 5 mg per month and finally stopped.

During admission, the clinical situation deteriorated with the development of haemoptysis and anaemia. Follow-up CT scan showed progression of the pulmonary and renal lesion.

Unfortunately surgical removal of the fungal lesions was not possible and because there was evidence of fungal disease progression despite intravenous antifungal therapy and reduction of immunosuppression, it was decided to discharge the patient for outpatient palliative care. Treatment with liposomal amphotericin B, which the patient had received for approximately one month, was also discontinued. However, above expectations the patient recuperated and follow-up X-ray showed regression of the pulmonary lesion. Ultrasound of the right kidney three months after presentation showed complete regression. Posaconazole oral suspension was started (200 mg 4 times a day) and a trough level of 0.8 mg/l was achieved (target value > 0.7mg/l).

Eleven months after presentation and continued posaconazole therapy, our patient is in a stable condition. The ability to reduce the immunosuppressive therapy was believed to be the main determinant for this favourable outcome. Probably, the initial radiological deterioration which had been attributed to progression of the fungal infection was in fact a result of immune reconstitution after tapering of immunosuppressants, which caused a temporary aggravation of signs and symptoms.

Invasive mould infections are a common complication in patients after alloSCT, with an annual incidence of approximately 8.8%. The most common causative mould is *Aspergillus fumigatus*. Mucormycosis is less common with a reported incidence of approximately 3.7%.[1]

Although our patient exhibited well-recognised risk factors, i.e. acute myeloid leukaemia, alloSCT, treatment for graft-versus-host disease and diabetes mellitus, the clinical presentation was quite remarkable.

Despite the presence of a pulmonary cavity, the patient presented with flank pain. Kidney involvement is uncommon and presents in only 2% of cases, and probably results from haematogenous dissemination from the primary infection site, in this case the lung.[2]

For treatment of invasive mucormycosis, liposomal amphotericin B is the drug of first choice, and if possible, resection of infected tissue and waning of immunosuppressive drugs. Second-line or maintenance therapy may consist of posaconazole.[3,4]

Mortality depends on several factors including control over the fungus by the mentioned treatments and the ability to improve the immune status of the patient, for instance by decreasing the use of immunosuppressants. Mortality, however, remains high in patients after stem cell transplantation, with a case fatality rate of 76% in localised disease but approaching 100% in disseminated cases.[2]

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