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Myelodysplastic Syndrome with Monosomy 7 and Pulmonary Aspergillosis

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ABSTRACT

A 43-year-old man with no past history presented with symptoms of fever, cough and dyspnoea arising from invasive pulmonary aspergillosis and was found to have myelodysplastic syndrome with monosomy 7. Before initiation of chemotherapy, he deteriorated rapidly, developing multi-organ failure requiring mechanical ventilation, and he eventually succumbed despite amphotericin B treatment. The importance of monosomy 7 in determining immune function in patients with myelodysplastic syndrome is emphasised.

Keywords: myelodysplastic syndrome, monosomy 7, aspergillosis, neutrophil

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Patients with myelodysplastic syndrome often develop sepsis, with the lungs being an important source. Bacterial infections are the commonest cause[1], while fungal infections are uncommon and occur in the context of treated myelodysplastic syndrome. We report a patient with untreated myelodysplastic syndrome with monosomy 7, who presented with fever, cough and dyspnoea arising from invasive pulmonary aspergillosis.

CASE REPORT

A 43-year-old man from Bangladesh presented with a 10 day history of right hypochondrial pain, fever, cough and dyspnoea. He had no past medical history of note, and was previously well till 10 days before presentation. He was found to be febrile with crepitations in both lungs. Hepatomegaly, measuring 8 centimetres, was present clinically; splenomegaly was noted on CT scan of the abdomen. Haematological profile showed leucocytosis with anaemia and thrombocytopaenia. A blood film showed nucleated red blood cells, prominent monocytosis, a few blasts, occasional myelocytes and metamyelocytes, and some neutrophils showed the Pelget-Huet abnormality. Platelets showed abnormal granulation and shape. Marrow examination revealed dysplastic changes in all three cell lines. Erythroid maturation was megaloblastoid, some abnormal megakaryocytes and approximately 15-20% blasts. Cytogenetic studies confirmed monosomy 7. He was diagnosed with myelodysplastic syndrome based on the clinical and haematological findings.

The chest X-ray showed diffuse interstitial shadowing (Fig. 1), and a CT thorax showed widespread interstitial and airspace disease in both lungs (Fig. 2). HIV serology was negative. He was started empirically on day one of hospitalisation on ceftazidime, with addition of cotrimoxazole (day two), clarithromycin (day three) and acyclovir (day four) when he deteriorated both clinically and radiologically. Bronchoscopy and lavage showed *Aspergillus* with branching hyphae. He was started on lipsomal amphotericin B (Ambisone®)

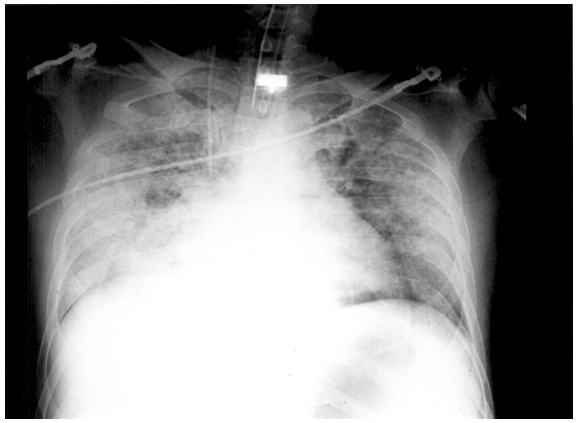

Fig. 1 Chest radiograph in ICU.

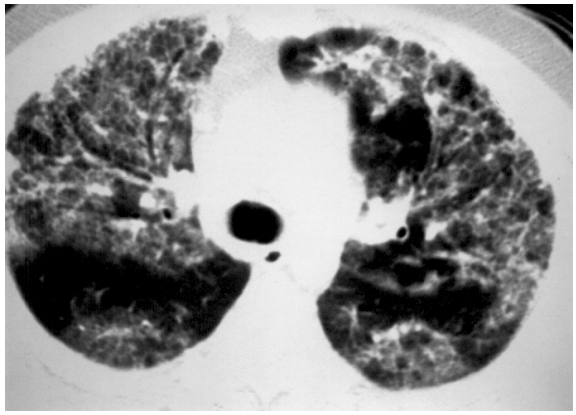

Fig. 2 Computed tomography of the lungs.

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on day nine. Before initiation of treatment for his myelodysplastic syndrome, he developed acute respiratory failure requiring mechanical ventilation and ICU care, renal failure and disseminated intravascular coagulation. Despite continued aggressive support, he died twelve days after hospital admission.

DISCUSSION

Invasive pulmonary aspergillosis is well recognised in immunocompromised hosts, often pursuing a rapidly progressive course resulting in death. Invasive aspergillosis in immunocompetent hosts is in contrast much rarer. A recent review[2] of twelve presumably immunocompetent cases who presented with *Aspergillus* community-acquired pneumonia showed that in all patients, diagnosis was delayed, with a third of the patients having the diagnosis made only postmortem. Amphotericin B was only used in half of the cases. There was 100% mortality in this series, illustrating the diagnostic and therapeutic difficulties encountered in treatment of invasive pulmonary aspergillosis.

Intact neutrophil function, including neutrophil migration, is essential for host defence against *Aspergillus*. Patients with myelodysplastic syndrome have impaired neutrophil function[3,4]. Neutrophils may be poorly granulated[2] or have decreased myeloperoxidase activity despite normal numbers of granules. They may also have abnormal esterase content, defective adhesion, decreased phagocytosis and impaired microbicidal activity. In particular, patients with monosomy 7 and partial deletions of long arm of chromosome 7 also have been demonstrated to have defective neutrophil migration[5].

One Japanese study[6] reported that the frequency of infectious episodes is highest immediately after diagnosis of myelodysplastic syndrome, when more than 4 episodes per 1000 patient days occurred, declining thereafter. The majority of infections in patients with myelodysplastic syndrome are bacterial[1], with the lungs being the most common site; fungal infections are uncommon and occur mainly in patients receiving immunosuppressive therapy. The important risk factors associated with invasive aspergillosis include neutropenia, corticosteroid use, organ transplant patients, collagen vascular diseases and HIV-positive patients[7].

In contrast, our patient had not received any chemotherapy, and in fact presented with symptoms arising from invasive pulmonary aspergillosis, which had hitherto not been reported in association with untreated myelodysplastic syndrome. Immune dysfunction associated with monosomy 7 has been described above. We believe that his atypical presentation may reflect the importance of monosomy 7 in determining the immune function of patients with myelodysplastic syndrome, especially with regards to fungal infections.

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