CASE REPORT

Aspergillus fumigatus endophthalmitis in a patient with acute myeloid leukaemia

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Summary
A 55-year-old patient developed progressive loss of vision in one eye following induction chemotherapy for acute myeloid leukaemia (AML). Aspergillus fumigatus was cultured from vitreal aspirates. The patient was treated with intravenous and intravitreal amphotericin B but suffered complete loss of vision in her right eye. We believe this is the first report of culture-proven Aspergillus fumigatus endophthalmitis in a patient treated for a hematological malignancy.

Keywords
Aspergillus fumigatus, endophthalmitis, acute myeloid leukaemia

Case report

A 55-year-old woman was found to have monocytoid blasts in her peripheral blood film when investigated for symptoms of lethargy and recurring mouth ulceration. Bone marrow aspiration and trephine biopsy confirmed the diagnosis of AML M5 with an apparently normal female karyotype and she was entered into the current Medical Research Council AML 12 trial. At presentation her blood count showed Hb 9.1 g/dl, WBC 6.15 × 10⁹/l, neutrophils 0.93 × 10⁹/l and platelets 200 × 10⁹/l. She received full dose mitozantrone, cytosine arabinoside and etoposide according to the trial protocol.

Remission induction was particularly difficult. Fourteen days after commencing chemotherapy (D + 14) the patient developed an acute abdomen with a small bowel ileus. She required red cell and platelet support and became septic with E. coli and Enterococcus species being grown from blood cultures. She was managed with nasogastric suction and intravenous antibiotics. G-CSF was added at D + 15 and the small bowel ileus resolved over a 12-day period during which time she received 10 days of intravenous nutrition. The peripheral blood count regenerated by D + 24 and the G-CSF was stopped.

Despite a marked improvement in her general condition, on D + 30 the patient alerted us to a progressive loss of vision and discomfort in her right eye which had developed over the preceding week. Ophthalmic examination revealed almost complete loss of vision with only a perception of light in her right temporal field but 6/9 vision on the left. There was no red reflex on the right with chemosis and injection of the conjunctiva. The cornea was oedematous and there was a hypopyon with extensive posterior synechiae. B-scan ultrasonography of the eye showed gross thickening of the choroid and multiple fine echoes from the vitreous. An initial diagnosis of metastatic bacterial endophthalmitis was made and following a vitreal biopsy, intravitreal and intravenous ceftazidine and vancomycin were commenced empirically. Vitreal material was inoculated directly onto chocolate and sabourd agar plates. Four to five distinct colonies grew on each plate. They had a flat spreading blue/green appearance with a powdery texture and microscopy revealed characteristic appearances of Aspergillus fumigatus. The patient was changed to intravenous colloidal amphotericin B (Amphocil) commencing at 3 mg/kg/day, increasing to 6 mg/kg/day over a few days. Intravitreal amphotericin B was given (0.01 mg initially followed by 0.005 mg) twice a week for 3 weeks and prednisolone was commenced (40 mg/day). After one week of treatment Aspergillus fumigatus was again cultured from a repeat vitreal sample. Furthermore, heavy growth of Aspergillus fumigatus was obtained from three sequential sputum samples at this time, although the patient had minimal respiratory symptoms or signs and an unremarkable chest radiograph.

The corneal oedema and conjunctival injection settled rapidly with treatment but there was no improvement in visual acuity. Bone marrow examination confirmed remission with < 2% blasts on flow cytometry and a 6
A week course of intravenous amphotericin B was completed uneventfully. Following extensive discussion, the patient declined further consolidation chemotherapy, and at the time of writing she remains in remission on no further treatment. Her left eye remains unaffected but her right eye is now completely blind.

Discussion

Opportunistic fungal infections are a significant cause of morbidity and mortality in patients treated for haematological malignancies. While disseminated aspergillosis due to *Aspergillus fumigatus* is not uncommon in such patients (Richardson & Kokki 1998), we have found no reports of culture-proven *Aspergillus fumigatus* endophthalmitis in patients treated in haematological practice. Sporadic cases have been reported in ophthalmology journals where infection is often metastatic from another primary source and has been associated with long-term placement of intravenous lines, general debilitation and intravenous drug abuse (Gross 1992; Essman et al. 1997). It seems likely, however, that the majority of cases in seriously ill patients remain undiagnosed. A recent autopsy series of liver transplant recipients found six of 85 post-mortem patients had Aspergillus endophthalmitis on histological examination, yet in only one case was the diagnosis made before death (Hunt & Glasgow 1996). In this series, the eye was the second most common site for Aspergillus infection.

Evidence-based treatment strategies are difficult for such a rare condition and therefore the combination of intravitreal and intravenous amphotericin B appears to be the best empirical treatment available. While isolated treatment successes have been documented (Gross 1992), in the vast majority of reported cases, complete or almost complete blindness is the end result. One patient required enucleation of the infected eye due to persisting pain with a poor response to treatment (Oxford et al. 1995).

Our case emphasizes the importance of taking and performing frequent ophthalmic histories and examinations in patients treated for haematological malignancies with intensive chemotherapy protocols, even following bone marrow regeneration as the risk period for deep Aspergillus infection extends well beyond neutrophil recovery. In such patients, symptoms of pain and redness of the eye, particularly in association with reduction of vision, may have grave significance. Early recognition and treatment of Aspergillus endophthalmitis could potentially improve the ophthalmic outcome for the patient. The prolonged treatment required for eradication of Aspergillus from the eye makes decisions regarding the choice and timing of further chemotherapy difficult. Evidence for the most appropriate strategies to follow under these circumstances appears to be lacking at present.

References