Aspergillus endophthalmitis following orthotopic heart transplant

Opportunistic systemic infections with Aspergillus species are common following orthotopic heart transplant (OHT). However, ocular infections are rare. To date, few cases of Aspergillus endophthalmitis following OHT have been reported; all showed evidence of disseminated aspergillosis and died within a few days of treatment. We report a patient with invasive Aspergillus endophthalmitis who survived for 16 years.

A 70-year-old male presented in 1992 with a 3-day history of a painful left eye associated with blurred vision. He had undergone an OHT 80 days earlier and was immunosuppressed with azathioprine, 75 mg, prednisolone, 12.5 mg, and cyclosporine, 250 mg, daily. Differential white blood count (5.9 × 10^9/L) showed a neutrophilia (88%) and lymphopenia (10%). Two months previously, he had been investigated for pyrexia and shortness of breath. Chest computerized tomography showed a left lower lobe cavitated lesion, and bronchoalveolar lavage cultured Aspergillus fumigatus. No organism was grown on repeated blood culture, and echocardiography excluded any vegetations. At presentation to the eye department, systemic antifungal treatment included itraconazole, 400 mg, intravenous amphotericin B, 200 mg, and nebulized amphotericin.

His visual acuity was 6/5 right and hand movements left. Examination revealed left iridocyclitis with hypopyon restricting posterior segment view. A provisional diagnosis of endogenous endophthalmitis was made, urgent vitreous biopsy was performed, and intravitreal amphotericin, 5 µg, miconazole, 10 µg, gentamicin, 0.1 mg, and vancomycin, 1 mg, were administered. A large white retinal exudate was observed superotemporally; however, the retina was attached.

Light microscopy of the vitreous aspirate identified neutrophils but no organisms. Subsequent cultures were negative. Electron microscopy revealed organisms measuring 2 to 4 µm, with features suggestive of either Aspergillus or Candida (Fig. 1). Unfortunately, the patient’s left eye became blind and painful, requiring enucleation 1 month after presentation.

The enucleation specimen showed a vitreous abscess, adjacent choroidal thickening, and retinal detachment (Fig. 1A). Histological examination confirmed a vitreous abscess (Fig. 1B) containing necrotic fungal elements centrally, with viable septate branching organisms peripherally. Mycological assessment confirmed A. fumigatus. Fungal hyphae penetrated the internal limiting membrane of the detached retina and invaded the inner nuclear layer. The retina was necrotic at the equator because of thrombosis of peripheral retinal vessels. Subretinal
fungal hyphae invaded Bruch’s membrane through to the inner choroid (Figs. 1C and 1D). A massive inflammatory cell infiltration destroyed the choriocapillaris.

The use of new selective immunosuppressive drugs has enabled the long-term survival of transplanted organs, while creating an increasing patient population at risk for invasive infections. Invasive aspergillosis is the most important cause of life-threatening fungal infection, affecting up to 13% of OHT recipients. A. fumigatus causes up to 90% of invasive aspergillosis in OHT recipients; Aspergillus flavus and Aspergillus niger are rare. A. fumigatus can bind specifically to different host tissue components, releases toxins that have a significant generalized immunosuppressive effect on host defences, and produces proteolytic enzymes that seem to be the main factor responsible for tissue invasion. The lungs are the main portal of entry. Once tissue infection develops, invasion of blood vessels ensues, resulting in tissue infarction and dissemination with metastatic seeding, which is almost uniformly fatal.

Ocular complications following OHT are well described; however, endophthalmitis is rare and is usually associated with disseminated infection. Previous reports describe patients who had preceding aspergillus pneumonia or infective endocarditis and died within a few days despite treatment. Retinal and choroidal vascular invasion with thrombosis and subsequent infarction is a predominant feature in Aspergillus endophthalmitis. Mycelia extend through the vessel walls and accumulate in tissue spaces, characteristically the subretinal and subretinal pigment epithelial spaces, which may explain why vitreous biopsy yielded no growth.

Endogenous Aspergillus endophthalmitis is a rare, sight-threatening complication following OHT, typically associated with systemic infection and high mortality. Physicians managing transplant recipients should be aware of the risk and implications of fungal endophthalmitis and seek urgent ophthalmic assessment of any patient with visual symptoms because prompt systemic treatment may reduce morbidity and mortality.

**References**


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