

Retinal seeding from anterior segment coccidioidomycosis after vitrectomy

Coccidioidomycosis is usually localised in the eye either to the anterior or to the posterior segment, but only rarely to both.¹⁻⁸ We present a case in which the initial infection involved the anterior segment, but was followed by extensive superficial retinal seeding after vitrectomy. Retinal involvement after vitrectomy raises the possibility of the anterior hyaloid face acting as a barrier to spread of the fungus posteriorly. A review of prior cases indicates that, in the absence of vitrectomy, retinal involvement does not occur in anterior segment coccidioidomycosis.

Case report

A 64-year-old man had been treated 3 years previously for iritis and secondary ocular hypertension with topical prednisolone acetate 1% and timolol 0.5%, with alleviation of symptoms. He presented with recurrence of similar symptoms that did not resolve with topical, retroseptal, and systemic corticosteroids and glaucoma drugs. A detailed systemic evaluation was negative.

On examination, the right eye was unremarkable. Visual acuity of the left eye was perception of hand motion at 5 feet. Keratic precipitates and a white mass in the anterior chamber were seen (fig 1A, inset). An iris biopsy and anterior chamber aspiration showed numerous spherules.

After treatment with oral fluconazole, intravenous amphotericin B, pars plana vitrectomy and lensectomy, the vitreous humor, retina and choroid appeared normal, but an infiltrate reformed in the anterior chamber soon after. Tissue plasminogen activator and intracameral amphotericin B were given, followed by another pars plana vitrectomy. At 1 month after the second vitrectomy, the eye was enucleated for intractable pain.

Examination of the eye showed granulomata with spherules on the retinal surface (fig 1B, inset), posterior chamber cornea, iris, ciliary body, and in the vitreous space (fig 1).

Comment

This case shows that retinal seeding may follow vitrectomy for anterior segment coccidioidomycosis. There are only two other reports of vitrectomy for anterior segment coccidioidomycosis.^{1,8,9} In each case, the eye was enucleated within weeks of the vitrectomy.^{1,9} Pathological sections from both cases were reviewed. One of the cases was subsequently shown to have superficial seeding of the retina after vitrectomy.^{9,10} The other was reported from our files and showed a tractional retinal detachment with granulomatous inflammation and adjacent cysts, but with no direct retinal involvement (fig 2B).¹

The prognosis for anterior segment coccidioidomycosis is poor. Of the 10 histologically proved cases, seven did not have vitrectomy. Four of these seven cases were not enucleated and at least two retained vision.^{1,4,11,12} None of these four eyes had evidence of posterior segment involvement after treatment. In contrast, all three eyes that underwent vitrectomy were enucleated within months of the procedure, despite the extended course of the disease before the operation in two of the cases. The histological findings of superficial retinal involvement in our case suggest spread

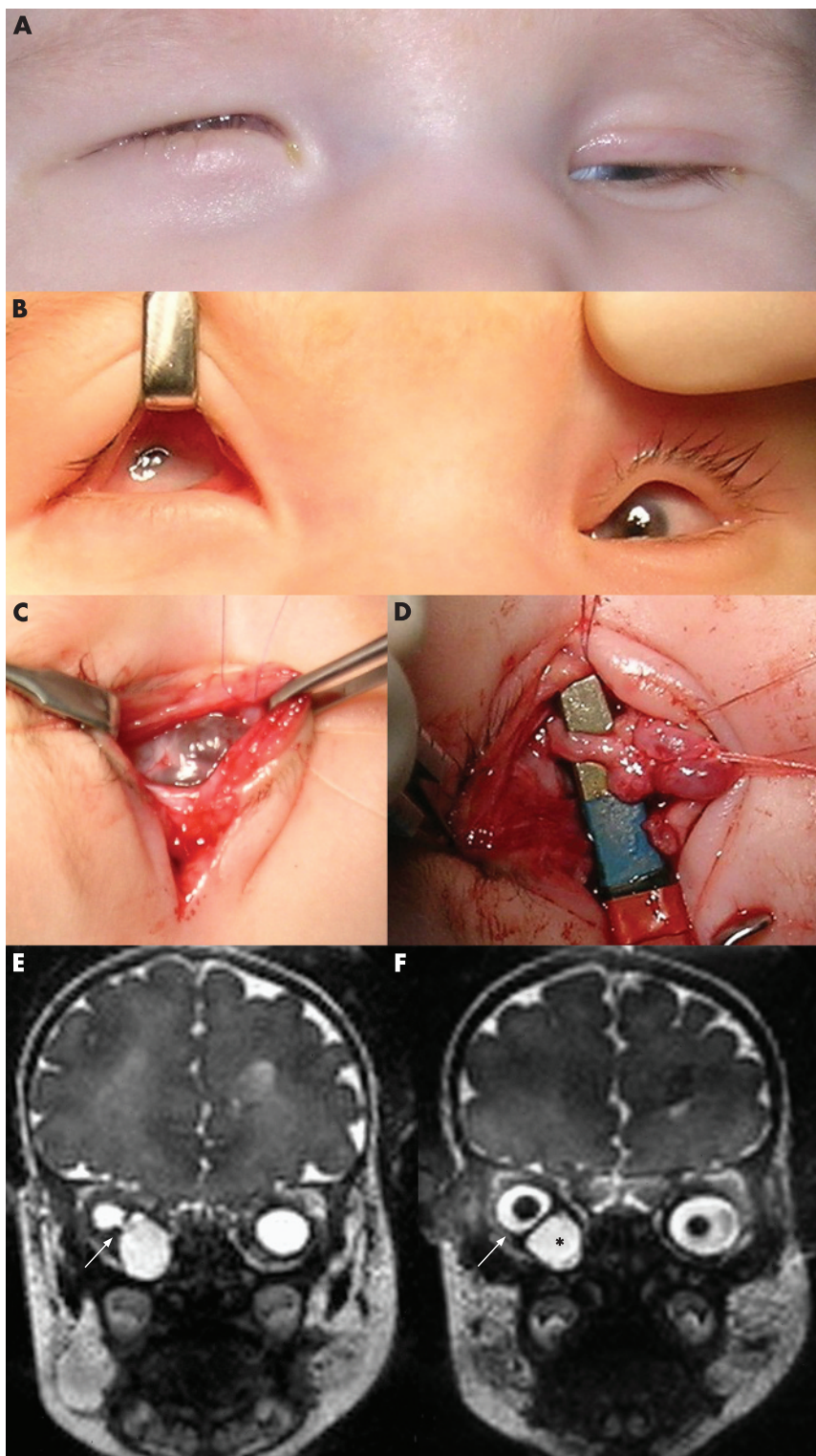


Figure 1 (A) External appearance of newborn with bilateral colobomatous microphthalmos with right orbital cyst. Note the bluish bulge in the right lower eyelid; (B) preoperative presentation of both eyes; (C) peroperative dissection of right orbital cyst; (D) intraoperative view of connective stalk between cyst and right microphthalmic eye; (E, F) Orbital T₂-weighted magnetic resonance imaging shows bilateral microphthalmos and large cyst in right orbit; (E) coronal view, demonstrating a connective stalk between microphthalmic eyeball and cyst (arrow); (F) coronal view, showing hyperintense cystic mass (black asterisk) causing superotemporal displacement of right microphthalmic eye (arrow).

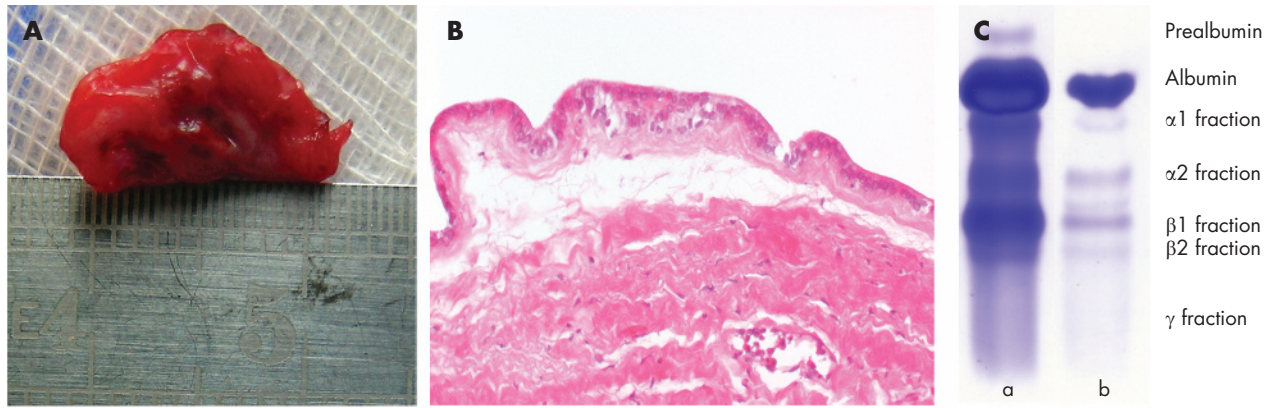


Figure 2 (A) Excised orbital cyst; (B) haematoxylin and eosin-stained section of cyst wall (at magnification $\times 200$), demonstrating the inner layer of neuroectodermal-like cylindrical cells without any organisation, and outer layer of dense fibrous tissue; (C) electrophoresis of (a) cyst fluid and (b) serum sample as negative control.

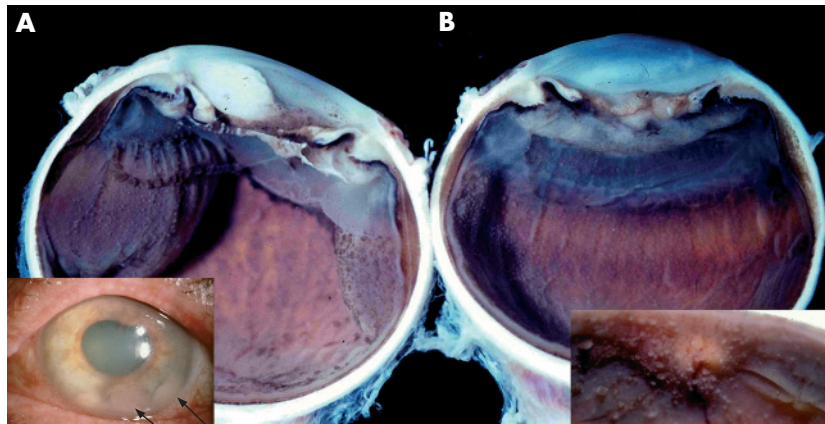


Figure 1 The present case (Mondino–Glasgow–Holland). (A, B) Macro photograph of the enucleated eye showing multiple rows of superficial granulomata lying on the surface of the retina. The inset in (A) shows hypopyon, iris synechiae and large fluffy masses in the inferior portion of the anterior chamber. The inset in (B) shows numerous granulomata coating the surface of the optic nerve head.

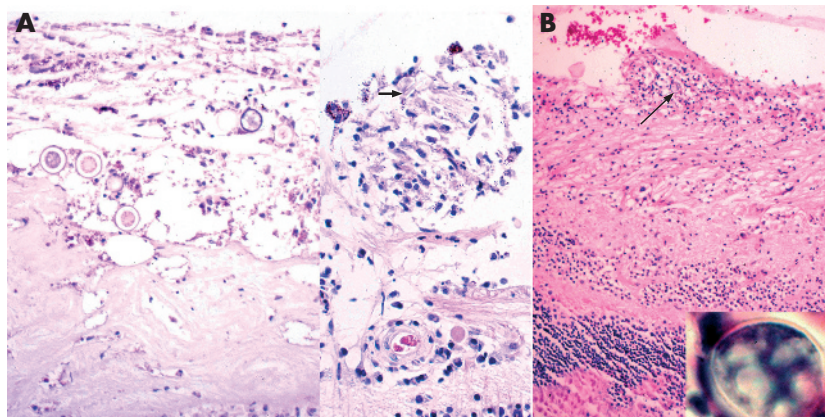


Figure 2 (A) Right, photomicrograph of a retinal surface granuloma with a collapsed spherule, arrow (haematoxylin and eosin, original magnification $\times 300$), left, numerous spherules lying on the extensive anterior fibrous tissue, proliferative vitreoretinopathy (haematoxylin and eosin, original magnification $\times 300$). (B) Photomicrograph from the case published by Stone *et al.*¹ The patient was a 26-year-old man with anterior segment coccidioidomycosis. After vitrectomy, there was evidence of posterior involvement, and the eye was subsequently enucleated. Illustrated is a granuloma on the surface of the retina (haematoxylin and eosin, original magnification $\times 120$). The inset in (B) shows a spherule of coccidioidomycosis (haematoxylin and eosin, original magnification $\times 400$).

from the vitreous. Vitrectomy may be a factor in the dissemination of *Coccidioides immitis* to the posterior segment from infection of anterior tissues. Corticosteroid treatment did not seem to be an important factor, as it was initiated in four of the cases without vitrectomy, of which no evidence of posterior segment involvement was noticed. We hypothesise that vitrectomy disrupts the anterior hyaloid, thereby permitting spherules accumulated between the lens and anterior hyaloid (Berger space) to seed the posterior segment. We are uncertain of the role of vitrectomy in producing disease in the two cases where posterior infection may have followed vitrectomy, but clearly there was no improvement after vitrectomy. Taken together, the findings suggest that the anterior hyaloid may present a barrier to the spread of organisms, and that vitrectomy should be avoided in infection of *C immitis* that is confined to the anterior segment.

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Optical coherence tomography can monitor reversible nerve-fibre layer changes in a patient with ethambutol-induced optic neuropathy

Ethambutol (EMB) has been used as an antimycobacterial agent against tuberculosis since 1961, and its principal side effect is toxic optic neuropathy, which can be seen in up to 6% of patients.^{1,2}

Through the use of optical coherence tomography (OCT), we can document evidence of reversible changes in nerve-fibre layer (NFL) secondary to EMB-induced optic neuropathy.

Case report

A 70-year-old man weighing 70 kg, who was being treated for *Mycobacterium avium intracellulare* complex pneumonia, initially presented with a 3-month history of gradual, painless loss of vision in both eyes. He had received EMB treatment for 7 months at 2 g/day (29 mg/kg/day). His visual complaints began 7 months after initiation of EMB treatment, and continued to worsen up to his presentation to our clinic. Before EMB treatment, his best-corrected vision was 20/30 OU (with mild nuclear sclerotic cataracts), but with normal subjective colour and contrast sensitivity.

Our patient underwent a full neuro-ophthalmological examination, which included an assessment of colour vision using the eight-plate Ishihara Color Vision Test, Humphrey Field Analyzer (HFA) 30-2 (SITA Fast test, Humphrey-Zeiss Medical Systems, Dublin, California, USA), and contrast sensitivity using the Vision Contrast Test System (Vistech, Dayton, Ohio, USA). In addition, OCT (OCT 3000, Humphrey-Zeiss) was performed on both eyes of the patient. All quantitative measurements were obtained by OCT using the retinal NFL (RNFL) analysis protocol (Stratus OCT 3). The basic principles and technical characteristics of the OCT have been described previously.^{3,4}

The results are presented categorised by the clinical tests performed. The patient visits are abbreviated as A for the initial visit (3 months after discontinuing a 7-month regimen of EMB), B for the second visit (5 months after discontinuing EMB) and C for the third visit (8 months after discontinuing EMB).

Humphrey visual field analysis

The patient presented with a new superior visual field (VF) defect in his right eye during

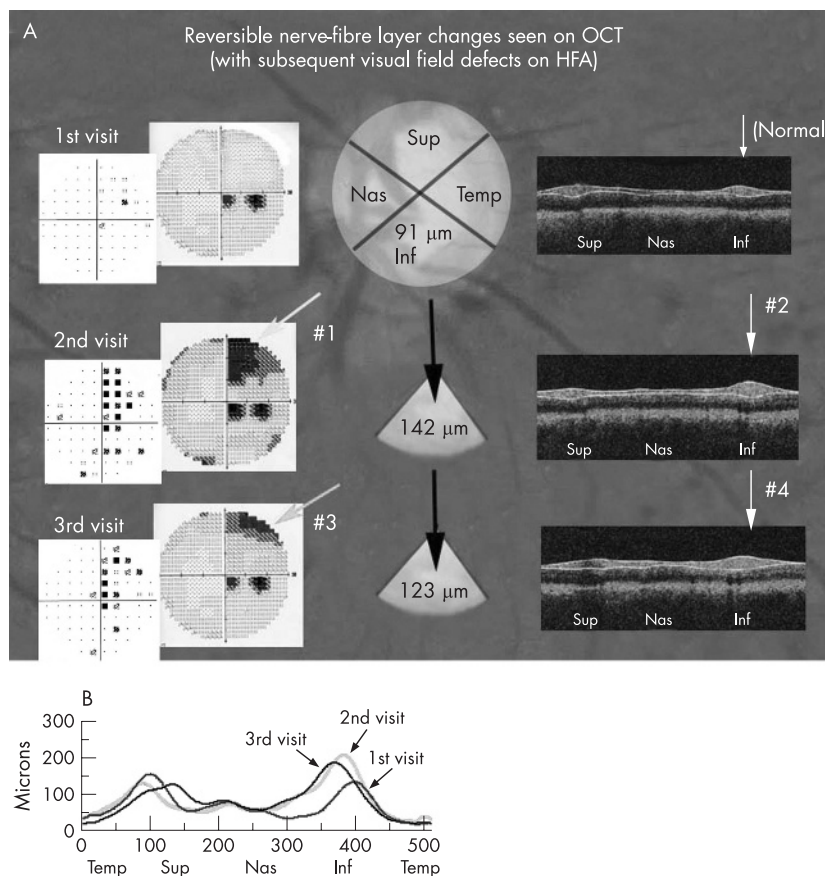


Figure 1 (A) There is a new onset superior–temporal visual field (VF) defect on Humphrey VF analysis (HFA) mean deviation (MD) and pattern standard deviation (PSD) plots observed on second visit, arrow #1. This corresponds well with increased nerve-fibre layer (NFL) thickness secondary to axonal swelling in the inferior layer on optical coherence tomography (OCT), arrow #2. Subsequently, there is a clinical improvement in the superior–temporal VF defect (MD and PSD) by the third visit, arrow #3, with reversible changes in the NFL thickness on OCT, arrow #4. (B) The arrows indicate the thickness (at the three separate visits) of the retinal NFL (RNFL) along the temporal–superior–nasal–inferior–temporal (temp–sup–nasal–inf–temp) plot provided by the OCT RNFL thickness analyser. Note the degree of thickening (axonal swelling) of the inferior quadrant RNFL by the second visit and the improvement (reversible changes) seen by the third visit.

visit B. By the third visit, the patient showed an improvement in his superior field VF defects when compared with his second visit. Figure 1 and table 1 give more detailed descriptions of the results.

Optical coherence tomography

OCT showed a significant increase in NFL thickness in the inferior quadrant of the right eye during visit B in comparison to visit A. This corresponded well with the HFA superior VF deficits. The average RNFL thickness of the inferior quadrant was 142 μm, ranging from a minimum 84 μm to a maximum 201 μm, or 156% thicker than the OCT data from the initial visit. We were unable to perform OCT of the left eye at this visit owing to patient non-compliance. Hence, we excluded the left eye from any further OCT or HFA analysis. By the third visit (C), OCT revealed a significant decrease in the inferior quadrant RNFL, down to an average 123 μm, or a 13.4% loss of NFL thickness when compared with the second visit, but still 135% thicker than that seen on the patient's initial presentation (fig 1).

Comment

OCT is a useful tool for examining the NFL thickness of certain optic neuropathies.^{5,6} In this study, we used OCT to monitor reversible axonal swelling in a patient with EMB-induced optic neuropathy. The marked thickening of the inferior quadrant nerve fibre on OCT corresponded well with the VF defects in the superior quadrant observed on HFA. Furthermore, as the thickness of the inferior quadrant NFL decreased, we saw a concurrent improvement in the patient's VF defects within the superior quadrant. We attribute these reversible NFL changes to retinal ganglion cell axonal swelling that resolved over time after cessation of EMB.

We believe that the heavier distribution of magnocellular axons (M cells) within the peripheral RNFL may play an important role in the reversible changes in NFL that we observed. Unlike parvocellular axons (P cells), M cells are larger, serve low spatial frequency of contrast sensitivity and motion stereopsis.^{6–8} The large-calibre M cell axons fire (neuronal activity/second) less often owing to their transient response characteristics and hold an anatomical advantage of having more mitochondria