

Figure 2A Large cell carcinoma with large nuclei. Note positive granular staining in the extensive cytoplasm of tumour cells for chromograffin A. Avidin-biotin method of immunostaining ($\times 200$).

fluorescein angiography patchy leakage at the level of the retinal pigment epithelium.

The electroretinogram (ERG) was abolished and the electro-oculogram (EOG) light rise was flat, with subnormal pattern and flash visual evoked responses. A chest x ray showed a right paratracheal mass, which was confirmed on thoracic computed tomography scanning. A biopsy of the mass was taken at mediastinoscopy which showed a large cell anaplastic carcinoma with large nuclei containing prominent nucleoli and large amounts of cytoplasm. Immunostaining for neuron specific enolase, chromograffin (Fig 2A), and synaptophysin was positive in the cytoplasm of tumour cells and transmission electron microscopy showed dense core granules (Fig 2B) indicating that the tumour was a large cell neuroendocrine bronchial carcinoma. Indirect immunofluorescence using the patient's sera (1:40 dilution) against cryostat sections of human retina revealed positive staining of ganglion cell nuclei, some cells of the inner nuclear layer, and around photoreceptor nuclei. The patient's serum (1:100) was immunoblotted against saline and detergent soluble extracts of human retina and showed a number of bands, all of which appeared in control sera from healthy subjects. The patient developed cerebral metastases soon after presentation and died. A postmortem examination was not performed.

COMMENT

This is the first reported case of paraneoplastic retinopathy found in association with large

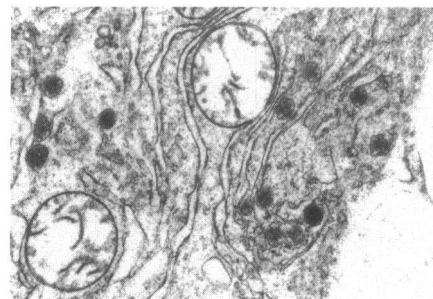


Figure 2B Tumour cell containing large dense core granules within the cytoplasm. Uranyl acetate and lead citrate staining ($\times 18\ 000$).

cell neuroendocrine carcinoma. Previous reports have demonstrated SCCL to be the commonest tumour association,¹⁻⁴ others being related to carcinoma of the breast,⁵ cervix,⁶ and uterus.⁷ There is one previous report of a large cell anaplastic lung tumour¹ but neuroendocrine features⁸ were not detected. The characteristic clinical picture of progressive nightblindness, ring scotomas, and eventual visual loss point to a process of photoreceptor degeneration which has been confirmed pathologically.^{3,7} The underlying pathogenesis for the association is thought to be due to the production of antibodies that cross react between tumour and retinal tissue. Grunwald *et al*⁴ have shown that such antibodies are only found in the sera of patients with both the relevant tumour and visual loss. The antibody is not found in those with visual loss and no tumour, nor in those with tumours but no visual loss. The retinal protein with which the sera of these patients react remains controversial. The immunofluorescent staining pattern in our patient is similar to that found by Kornguth² and Grunwald⁹ with antibody largely directed against the ganglion cell and inner nuclear layers, whereas Keltner found antibody predominantly staining photoreceptor inner segments.¹⁰ The 23 kDa protein, recently acknowledged to be the photoreceptor protein recoverin¹¹ and which has been postulated to be specific for the syndrome associated with SCCL¹ was not revealed by immunoblotting in our patient. This finding agrees with a recent study which found only one in 10 patients with cancer associated retinopathy demonstrating antibodies to this protein.¹² The most important clinical feature of this syndrome is to consider and then recognise the diagnosis and to realise that symptoms may precede detection of the underlying tumour for many months or years. Electrodiagnostic studies are important and immunological studies in future patients may clarify the relation between the retina and the tumour.

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Cryptococcus presenting as cloudy choroiditis in an AIDS patient

EDITOR.—*Cryptococcus neoformans* is a well known organism which causes opportunistic infection in patients with AIDS. Patients commonly present with meningitis and are referred to the ophthalmologist with extraocular muscle paresis and papilloedema.^{1,2} However, although rare, cryptococcal choroiditis has also been described: the clinical features are cells in the vitreous with focal choroidal lesions; the presence of the fungus in the choroid implies haematogenous spread and, consequently, is associated with a terrible prognosis.³ This paper describes a patient whose cryptococcal infection initially manifested with eye symptoms due to a hitherto unrecognised pattern of choroidal disease.

CASE REPORT

A 39-year-old white homosexual man with AIDS presented in May 1992 with a 1 week history of blurred vision in both eyes. He complained, in particular, that everything appeared wavy. He had been HIV positive since 1988 and had developed Kaposi's sarcoma in April 1992 when his CD4 count was $0.02 \times 10^6/\text{ml}$. Ophthalmic examination revealed visual acuities of 6/5 in each eye, full colour vision, and mild constriction to the I2e and I4e targets in both eyes on Goldmann perimetry. The pupillary reactions were normal. The eyes were white and slit-lamp examination was unremarkable with no

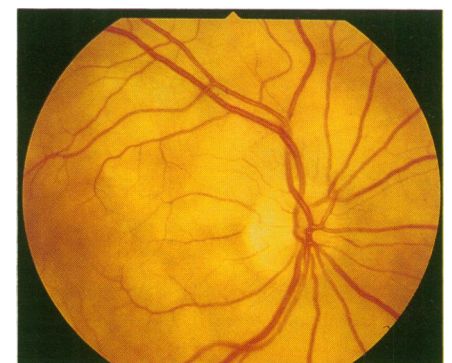


Fig 1A

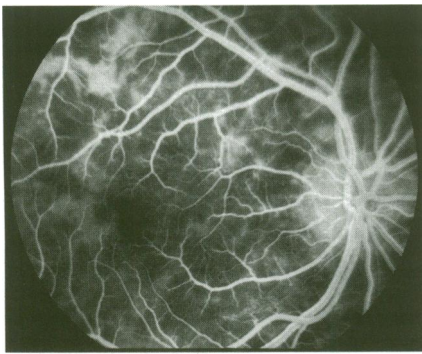


Fig 1B

Figure 1 (A) Right fundus showing diffusely abnormal pigment epithelium but normal retinal vessels. (B) Arteriovenous phase of fluorescein angiogram of same eye confirms the presence of abnormal pigment epithelium with patchy masking of the lesions.

anterior chamber or vitreous activity. Fundal examination revealed a striking blotchy appearance of the retinal pigment epithelium and choroid, which looked like clouds beneath the retina (Fig 1A). The optic discs and retinal vessels were normal. A fluorescein angiogram confirmed the presence of lesions which were underneath the neuroretina. These lesions masked fluorescence in an irregular pattern and there was no significant leakage in the late stages of the angiogram. The retinal component to the angiogram was normal (Fig 1B).

Although an opportunistic infection was suspected, this fundal picture was not recognised by us or by other specialists in HIV and so no treatment was given. During the next 2 weeks he became unwell with headaches and general lethargy. The differential diagnosis included cryptococcal meningitis, toxoplasma encephalitis, or cerebral lymphoma. Investigation showed a cryptococcal meningitis with an antigen level in both the CSF and serum of 1×10^6 /l. He was treated with intravenous amphotericin for 10 days followed by a maintenance oral dose of fluconazole (400 mg daily).⁴ This resulted in regression not only of his systemic symptoms but also of his visual symptoms and dramatic resolution of the fundal changes over a 1 month period (Fig 2). A repeat lumbar puncture, 3 weeks later, showed mild improvement with reduction of the cryptococcal antigen level of 1×10^3 /l.

COMMENT

This case report describes a patient with visual symptoms and a rare fundal picture which, on fluorescein angiography, was consistent with pathology of either the retinal

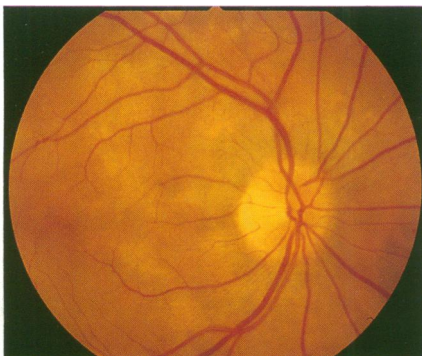


Figure 2 Right fundus 4 weeks later showing considerable resolution of the lesions.

pigment epithelium or the choroid. A diagnosis of cryptococcal meningitis was eventually made and both the visual symptoms and the fundal abnormality resolved quickly on systemic treatment.

This is strong circumstantial evidence that the visual symptoms were due to the observed fundal abnormality and that *Cryptococcus* was the offending agent even in the absence of pathological proof.

The ophthalmologist plays a valuable role in the management of patients with AIDS since 70% of these patients have ocular disease.^{5,6} Cytomegalovirus retinitis is the commonest ocular opportunistic infection and occurs in 30–40% of patients. The incidence of opportunistic infections which metastasise to the choroid is much lower and includes *Cryptococcus neoformans*, *Mycobacterium avium*, and *Pneumocystis carinii*.⁷ The prognosis for these patients is very poor by this stage but, nevertheless, the diagnosis may elude the physician until the choroidal involvement develops. It is, therefore, important for ophthalmologists to 'recognise' the pattern of choroidal involvement produced by opportunistic infections in AIDS as prompt treatment will prolong life.

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Diagnosis and management of an occult cyclodialysis cleft

EDITOR.—Non-intentional cyclodialysis may occur up to 6 months^{1,2} after anterior segment surgery or following trauma.^{3,4} The hypotony is due to aqueous outflow through the cleft to the uveoscleral pathway.^{5,6} In these patients, there is normal aqueous production dynamics,^{2,3,6} normal episcleral venous pressure,^{7,8} and an abnormal outflow facility.⁵ The cleft size is unrelated to the degree of the hypotony and maybe microscopic and hence occult.^{5,9}

CASE REPORT

Preoperatively Mrs AB, a 53-year-old white woman, had visual acuities of 6/18 in the left eye owing to cataract and perception of light in the right eye following retinal detachment. The left eye was otherwise normal and the IOP had varied from 11 to 15 mm Hg over

the preceding 5 years. A routine extracapsular cataract extraction with a limbal section and posterior chamber lens implantation was performed. The eye maintained an IOP of 11 mm Hg until she banged her head 1 month later and the vision worsened. Examination revealed an IOP of 2 mm Hg and a visual acuity of 6/9. Gonioscopy did not reveal any cyclodialysis cleft. Four months postoperatively, the IOP remained at 2 mm Hg but the refraction was dynamically unstable as a result of blinking and eye movements. An 8.0 mm diameter hard contact lens stabilised the corneal topography and the acuity at 6/9. At 12 months, the IOP had remained at 2 mm Hg but macular oedema reduced the acuity to 6/24. There was no evidence of uveitis, no cleft was visible on gonioscopy, and ultrasound showed no evidence of choroidal or ciliary body detachment.

Laser flare studies revealed an anterior chamber flare count of 11 photon counts/ms, which was within normal limits for her age. Topical timolol increases the anterior chamber protein concentration in normal eyes by reducing aqueous production. Two hours after administration of timolol drops, the aqueous protein concentration had risen by 35% and by 4 hours it had risen to 63%, compared with 75% in a normal eye. Following intravenous injection of fluorescein, an area of increased scleral fluorescence was demonstrated adjacent to the original cataract section. These observations suggested an occult cyclodialysis cleft at the site of the previous surgical wound.

Gonioscopy with viscoelastic and surgical exploration of the wound failed to reveal a cleft. The wound was closed and the viscoelastic was removed. The IOP rose to 46 mm Hg at 12 hours and this required acetazolamide, mannitol, and levobunolol drops. By 10 days the IOP was 14 mm Hg with the patient receiving levobunolol and dexamethasone, the choroidal folds had resolved, and the visual acuity was 6/9.

For the next 10 months the IOP was 10 mm Hg with no medication and the visual acuity was stable at 6/9. At 11 months, hypotony and macula oedema suddenly redeveloped. Argon laser trabeculoplasty to the wound region was unsuccessful on two occasions. Surgical gonioscopy and re-exploration of the original wound failed to find a cleft. The scleral flaps were closed and 12 hours later the IOP had risen to 55 mm Hg. The pressure fell slowly to 14 mm Hg over 14 days with medical treatment. One month later, the visual acuity was stable at 6/9 and the IOP has remained at 14 mm Hg on no treatment for 6 months.

COMMENT

The diagnosis of cyclodialysis requires an assessment of aqueous production and the facility of outflow but the latter is not possible because the eye is hypotonous. Therefore the cleft requires visualising with gonioscopy, sometimes with perioperative chamber deepening. With an occult cleft the diagnosis depends on proving both normal aqueous production and an abnormal outflow pathway.

Aqueous production must fall to less than 10% of normal to produce hypotony⁶ so that any test which shows approximately normal aqueous dynamics excludes ciliary body dysfunction as the cause of hypotony. Laser flare measurements can quantify the amount of protein in the anterior chamber aqueous.