cell neuroendocrine carcinoma. Previous reports have demonstrated SCCL to be the commonest tumour association,\(^1\)\(^-\)\(^4\) others being related to carcinoma of the breast,\(^2\) cervix,\(^6\) and uterus.\(^7\) There is one previous report of a large cell anaplastic lung tumour\(^1\) but neuroendocrine features\(^8\) 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\(^9\) have shown that such anti-bodies 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 Kornguth and Grunwald\(^5\) 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 recoverin\(^11\) and which has been postulated to be specific for the syndrome associated with SCCL,\(^1\) 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. Electrodagnostic studies are important and immunological studies in future patients may clarify the relation between the retina and the tumour.

We thank Ms Ann Dewar of the Electron Microscopy Department of National Heart and Lung Institute and Mrs D Paterson for preparing the manuscript.

M R STANFORD
C E EDELSTEN
I D HUGHES
M D SANDERS
Medical Eye Unit,
St Thomas’s Hospital,
London SE1

C I BROOKS
D MITCHELL
Department of Thoracic Medicine
M N SHEPPARD
Department of Histopathology,
Royal Brompton Hospital,
London SW3

Figure 2A Large cell carcinoma with large nuclei. Note positive granular staining in the extensive cytoplasm of tumour cells for chromogranin A. Avdin-biotin method of immunostaining (×200).

Fig 1A

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

The electoretinogram (ERG) was abolished and the electro-oculogram (EOG) light rise was flat, with subnormal pattern and flash visual evoked responses. A chest xray 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, chromogranin (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 core granules in the cytoplasm. Urynd acetate and lead citrate staining (×18 000).

Cryptococcus presenting as cloudy choroiditis in an AIDS patient

E Picard

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 papilloldea.\(^1\)\(^-\)\(^2\) However, the ophthalmologist may not suspect 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 haematoogenous 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 0-02×10⁹/ml. Ophthalmic examination revealed visual acuities of 6/5 in each eye, full colour vision, and mild constriction to the 12e and 14e targets in both eyes on Goldmann perimetry. The pupillary reactions were normal. The eyes were white and slit-lamp examination was unremarkable with no
pigment epithelium and 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.6 Cryptococcosis is the commonest 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 becomes obvious. 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.

SEEMA VERMA
ELIZABETH M GRAHAM
Department of Ophthalmology,
St Thomas's Hospital

Correspondence to: Seema Verma, Department of Ophthalmology, St Thomas's Hospital, Lambeth Palace Road, London SE1 7EH.

Accepted for publication 26 January 1995

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 pigment epithelium or vitreous activity. Fundus 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 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, toxoplasmosa encephalitis, or cerebral lymphoma. Investigation showed a cryptococcal meningitis with an antigen level in both the CSF and serum of 1×10³. He was treated with intravenous amphotericin for 10 days followed by a maintenance oral dose of flucanazole (400 mg daily). 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 1×10².

Diagnosis and management of an occult ciliary cleft

EDITOR.—Non-intentional ciliolysis may occur up to 6 months2 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,7,8 which is normal episcleral venous pressure,7,8 and an abnormal outflow facility.3 The cleft size is unrelated to the degree of the hypertony and maybe microscopic and hence occult.9

CASE REPORT
Preoperatively Mrs AB, a 53-year-old white woman, had visual acuity of 6/68 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 banded 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 corrected the refraction 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 1 photon counts, 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 content was increased 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 temporal 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, manitol, 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 14 mm Hg with no medication and the visual acuity was stable at 6/9. At 11 months, hypotony and macular oedema suddenly redeveloped. Argon laser trabeculoplasty to the wound region was unsuccessful on two occasions. Surgical 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 cleft requires an assessment of aqueous production and the facility of outflow but the latter is not possible because the eye is hypotonic. 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 hypotony8 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.