Cryptococcal chorioretinitis: a case report

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SUMMARY Chorioretinitis occurred in a young man whose long-standing cryptococcal meningitis had been identified and treated. In one eye spontaneous resolution had occurred. His case history and fluorescein angiograms are presented.

Cryptococcus neoformans (or *Torula histolytica*) is a yeast-like fungus producing systemic disease in man. Cryptococcosis (or torulosis) has a world-wide distribution. Infection is frequently by way of the respiratory tract. The organism is disseminated by the blood stream, particularly to the central nervous system, where a severe meningoencephalitis may develop. Before the introduction of amphotericin B in 1956 the disease was almost always fatal.

Many reports of cryptococcosis have appeared, but surprisingly few of ocular involvement. The eye may suffer the secondary effects of meningitis and raised intracranial pressure—papilloedema, optic atrophy, sixth nerve palsy, photophobia, and nystagmus (Khodadoust and Payne, 1969). The eye may be affected secondarily to orbital invasion, or the eye may be involved directly. Hiles and Font (1958) reviewed the literature to find just 9 cases of proved cryptococcosis of the eye. They added a case of their own. Khodadoust and Payne (1969) updated the count to 13 cases. Cameron and Harrison (1970) described 1 further case in which a mouse-virulent form of *C. neoformans* was identified in the patient's cerebrospinal fluid.

Case report

A 27-year-old white male was referred to his local general hospital in October 1969. He described a steadily increasing frontal headache, which developed over 2 weeks. Over several days before his admission he suffered from photophobia, was nauseated, and had vomited. He worked as a commercial artist, and over several years had worked in a tower inhabited by pigeons.

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On his first admission he was noted to be febrile (38.9°C) and to have neck stiffness. *Cryptococcus neoformans* was isolated from his lumbar cerebrospinal fluid and cultured on Sabourad's agar.

On 5 November 1969 the patient was transferred to Fairfield Hospital in Melbourne. Relevant laboratory findings are listed: Cerebrospinal fluid: 32 cmH₂O pressure; *C. neoformans* present in Indian ink preparation. Leucocytes: 11·500 thousand/mm³ (11·5 × 10⁹/l)—55% polymorphs, 32% lymphocytes, 0% eosinophils. Chest x-ray: a lesion present at the right lung base consistent with a toruloma. No bacteria or viruses were cultured from his throat, nasopharynx or blood-stream. No cryptococcus grown from pigeon faeces.

The patient began treatment on the day of his admission. Amphotericin B was administered as an intravenous infusion over 8 hours of each day. The dosage was 1 mg/kg per day, initially 5 days in 7, and later reducing to 3 days in 7.

The patient was transferred to St. Vincent's Hospital on 17 December 1969, where a right lobectomy was performed. The pathology report described a lesion surrounded by damaged lung parenchyma, in which both granulation and mucoid tissue were present. 'Innumerable cryptococci' were present within the mucoid material, and some cryptococci lay in alveoli adjacent to the main lesion. The lesion was diagnosed as toruloma of the right lung. The patient convalesced at Fairfield Hospital until 26 February 1970, when he was discharged clinically well. He was subsequently readmitted for several days each month for review of his general health and cerebrospinal fluid. Flucytosine tablets (8 g/day) were introduced to his treatment programme.

In March 1971 he had a generalised convulsion. He was prescribed phenytoin sodium tablets (100 mg) 3 times daily, which he still takes.

In November 1971 he was admitted to the Alfred Hospital. His symptoms of headache and vomiting had recurred, and he had lost weight. Although his electroencephalogram and brainscan appeared normal, the air encephalogram showed dilatation of both lateral ventricles, suggesting moderate cerebral atrophy.

In early October 1972 he was admitted as an emergency to Fairfield Hospital and transferred to the Alfred Hospital. His headaches and vomiting were severe, he was wasted and unable to walk. Mentally he was vague and disorientated. Both optic discs had blurred margins, and peripapillary haemorrhages were seen. A large haemorrhage partly obscured the right disc and inferonasal retina. *C. neoformans* was again isolated from the cerebrospinal fluid. An air encephalogram showed grossly dilated lateral ventricles. Surgery was performed. A right atrioventricular shunt was inserted and connected to a Rickham sub-aponeurotic reservoir, which permitted subsequent administration of intrathecal amphotericin. His level of consciousness improved rapidly. He was transferred back to Fairfield Hospital, where he was given a trial of clotrimazole to supplement his drug therapy. This ceased after 1 week following gastrointestinal upset and inadequate blood and cerebrospinal fluid levels of the drug.

In November 1972 and June 1973 further obstructions occurred, and additional shunts were installed. His drug treatment stopped in January 1974 as his renal function was disturbed.

He remained symptom free until June 1976, when he noticed blurring in his left eye. He attended the Royal Victorian Eye and Ear Hospital on 23 July 1976. Both eyes appeared white and uninflamed. His right eye saw 6/5, his left could count fingers at 0.5 m. An elevated greyish-yellow lesion was visible ophthalmoscopically above and involving the left macula (Fig. 1). The corresponding nerve fibre layer was disturbed. The right fundus contained two irregular, flat, pigmented scars along the upper temporal vessels (Fig. 2). The optic discs appeared healthy in both eyes. The vitreous was clear.

The fluorescein angiogram (Figs. 3 and 4) shows an elevated lesion at the left macula, with dilated and aneurysmal capillaries over its surface. The early retinal arterial phase shows leakage from these vessels and some subretinal staining. Extensive leakage of dye is apparent in the late picture. The lesions in the right fundus do not show any vessel leakage. The lesion in the left eye represents active chorioretinitis, those in the right eye old chorioretinitis. The blood picture was unremarkable, and serology was negative for syphilis, toxocara, toxoplasma, brucella, and leptospirosis.

Fig. 1 Fundus photograph showing active torulosis of the left eye

Fig. 2 Right fundus showing scarring from previous chorioretinitis

Argon laser was applied to the area of vessel leakage in the upper half of the macular lesions.

Discussion

Cryptococcus neoformans has been isolated from soil, fruit, and many animals. Its association with pigeons has been examined (Emmons, 1955) but 'no conclusive evidence exists that man has ever contracted

Figs. 3, 4 Arteriovenous (Fig. 3) and late (Fig. 4) fluorescein angiograms of the left fundus

the disease from infected birds' (Khodadoust and Payne, 1969).

In the cases reported so far chorioretinitis is the commonest form of direct eye involvement. Hiles and Font (1968) recorded that spontaneous resolution occurred in 1 eye of their patient. Uveitis, endophthalmitis, vitreous invasion by *C. neoformans*, and neuroretinitis have been reported (Khodadoust and Payne, 1969). The organism spreads to the eye either by the blood stream or in the meningeal sheaths surrounding the optic nerve.

A period of 6½ years elapsed between the onset of this patient's illness and the development of symptoms in his left eye. Hiles and Font (1969) noted a 2-year gap between meningitis and eye involvement in their reported case.

Treatment with amphotericin B has produced a 50% rate of cure in an American series (Okun and Butler, 1964). The risk of renal damage is considerable. Oral flucytosine has proved effective without significant adverse effects in some reports. Adequate cerebrospinal fluid levels can be achieved with oral administration (Stanton and Sanderson, 1974). Specific organism sensitivity to the drug should be demonstrated in the laboratory.

This patient, though relatively symptom-free, has regularly produced *C. neoformans* in his cerebrospinal fluid until his last examination in June 1975. His cerebrospinal fluid glucose remains low, protein high. Despite heroic treatment with amphotericin B, supplemented with flucytosine, the infection has not been eliminated. An uneasy truce exists between patient and pathogen.

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