Pulmonary and bilateral retinochoroidal cryptococcosis

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SUMMARY A case of right-sided pulmonary cryptococcosis with bilateral intraocular involvement is reported.

Cryptococcal infection of the lung and meninges is being diagnosed with increasing frequency. The lung is usually the primary site of infection, and the patient may present with cough associated with scanty sputum and infrequent haemoptysis, or the lesion may be detected as an asymptomatic abnormality on chest x-ray. *Cryptococcus neoformans* is the commonest cause of mycotic meningitis, the patient presenting most commonly with headache, mental changes, and visual disturbances.

Eye involvement is relatively uncommon. Chapman-Smith¹ found 14 reported cases and added one of his own. We report an additional case of bilateral intraocular cryptococcosis. The infection started with right lung involvement and blood stream dissemination.

Case report

A 19-year-old Zambian male was admitted on 25 October 1979 with a history of right-sided pleuritic pain, cough, occasional haemoptysis, malaise, and general body weakness and some loss of weight for about a year. There was no history of dyspnoea, headache, vomiting, photophobia, blurring of vision, or neck stiffness. The patient had looked after about 200 pigeons for a number of years.

On examination there was a mild fever (37.8°C) with pulse 72/min, blood pressure 120/70 mmHg, and respiratory rate 18/min. There were signs of consolidation of the right lung (upper and mid zones).

Laboratory investigations gave haemoglobin 9.0 g/dl; leucocytes $5 \times 10^9/l$; neutrophils 57%, lymphocytes 38%, eosinophils 4%, and monocytes 1%. Urine nothing abnormal. Blood urea 30 mg/dl (5 mmol/l). Serum electrolytes normal.

Chest x-ray showed a massive, dense, homogeneous

shadow occupying the right upper and mid zones, with a slight shift of the trachea and upper mediastinum to the left side; no calcification was seen (Fig. 1). A bloody fluid was obtained on chest aspiration. As bronchoscopy revealed no abnormality and sputum for acid-fast bacilli was negative, a thoracotomy was advised. The patient refused this and took his own discharge from hospital on 21 November 1979.

The patient was readmitted on 31 January 1980 with exacerbation of his previous symptoms. A thoracotomy revealed a large mass adherent to the

Fig. 1 Chest x-ray showing a well defined opacity involving the right upper and middle lobes, pushing the trachea and upper mediastinum to the left.

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Fig. 2 Section taken from surrounding lung tissue, showing presence of cryptococcal organism with granulomatous reaction and foreign body giant cell formation. (Haematoxylin and eosin, $\times 70$).

pleura and pericardium and almost filling the right side of the chest. The right lung was removed.

On pathological examination a specimen of lung tissue contained a cystic area with a necrotic wall surrounded by thick whitish fibrous material. It was filled with gelatinous polypoid material. On histological examination the gelatinous mass and wall contained large rounded bodies with dark central portions surrounded by a thick capsule. In the surrounding lung tissue multiple small collections of these organisms were seen with a granulomatous reaction and foreign body giant cell formation round them (Fig. 2). The organism was confirmed to be cryptococcus by special staining techniques (Fig. 3).

Treatment was started with 5-fluorocytosine orally at 120 mg/kg daily in 4 divided doses (6 g daily) and amphotericin B intravenously in 5% dextrose under steroid cover. Amphotericin B was given on alternate days in gradually increasing doses until 50 mg per dose was reached. Soon after the start of treatment with both drugs but before the optimum dose of amphotericin B was reached the patient complained of dizziness, headache, and fairly sudden diminution of vision in both eyes, and at the bedside he could barely count fingers at a distance of about a metre.

The anterior segment of both eyes showed no

Fig. 3 Section taken from the gelatinous polypoid mass showing presence of cryptococcal organisms. (Grocot staining, $\times 450$).

Fig. 4 Left: Right eye. Lesion shows well circumscribed 'healed' patch of retinochoroiditis with some pigmentary changes over macular area. Scattered along the inferior retinal vessels are numerous hard white exudates. Right: Left eye. Lesion same as in left eye, but the patch of central retinochoroiditis shows more pigmentary changes.

abnormality, but examination of the fundus revealed a roughly rounded, circumscribed, moderately elevated patch of active retinochoroiditis over the macular area of both eyes (Fig. 4). The vitreous showed fine cellular particles on biomicroscopic examination.

A lumbar puncture showed the cerebrospinal fluid to be under normal pressure and to contain one lymphocyte and 3 red blood cells per cubic mm. The protein concentration was 40 mg/100 ml (400 mg/l) and glucose 82 mg/100 ml (4.6 mmol/l). No organisms were seen or cultured, and no capsulated cells of cryptococcus were seen on 3 occasions in Indian ink preparations.

Surgical removal of the lung lesion plus chemotherapy with both drugs resulted in some improvement of the patient and the eye lesions over the next 6 to 10 weeks, and he was discharged on 13 May 1980 after having received approximately 1500 amphotericin B.

The patient was admitted to hospital on 3 subsequent occasions to February 1981 for follow-up of his eye lesions and received 5-fluorocytosine and

amphotericin B under steroid cover. There was no lesion in his left lung. Renal function was closely watched and remained normal throughout treatment. The blood count, serum electrolytes, and electrocardiogram were normal.

During follow-up examination the anterior uvea of both eyes was seen to be affected with fine keratic precipitates and moderate aqueous flare in both eyes. With application of topical atropine and steroid drops to both eyes, coupled with systemic steroids, 5-fluorocytosine and amphotericin B, the anterior uveitis cleared completely. The macular patches showed the onset of pigmentary changes. In addition there appeared numerous hard, dry exudates spreading along the vessels, especially the lower retinal arterial branches. The vessels near both discs showed some perivascular sheathing, and the temporal half of the disc showed slight pallor. The central vision was reduced to nil, but the peripheral vision improved, especially in the upper fields to finger counting at 2 m.

The patient took his own discharge and was lost to subsequent follow-up.

Discussion

Cryptococcosis (torulosis) is of world-wide distribution and is not an uncommon disease. Early cases in Africa were detailed by Friedlander and Gelfand,² who described some of their own cases. A case of eye involvement in Africa was described by Turner,³ when choroidal torulomata were seen in association with pulmonary cryptococcosis. Cases have been reported with increasing frequency from Africa south of the Sahara—for example, West Africa,⁴ East Africa,⁵ Central Africa,^{6,7} and South Africa.⁸ Cryptococcosis has also been reported in Zambia.⁹⁻¹¹ More cases, both pulmonary and of the central nervous system, are being diagnosed because of awareness of the condition and better diagnostic facilities, but in some cases the diagnosis is established only at post-mortem.

The disease is caused by a budding, yeast-like, non-mycelium-producing fungus *Cryptococcus neoformans* (*Torula histolytica*) which has a mucinous capsule and infects man and animals. Infection is usually by inhalation of the spores. It is detected by staining with Indian ink, which shows up the nonstaining capsule around the organism; otherwise cryptococci may be mistaken for lymphocytes or other mononuclear cells. The cryptococcus usually does not evoke an active inflammatory response for a long time, and a cellular reaction is slow to develop and is rarely intense. Sometimes biopsy of the affected tissue establishes the diagnosis. The organism may be isolated from sputum, urine, or blood culture.

The droppings of pigeons and to a less extent other birds are the main source of cryptococcal infection. Pigeon handlers have a much higher level of antibodies to cryptococci than nonhandlers.¹² The fungus has also been isolated from soil, fruit, and milk.

The disease usually starts as a primary infection of the respiratory tract with dissemination by the blood stream. It frequently infects the brain and meninges and less commonly bones, genitourinary tract, lymph glands, and viscera. The skin may also be a portal of entry. Surgical removal of isolated cryptococcal lesions in affected tissues may be curative, but concomitant antifungal chemotherapy is essential to eliminate dissemination, especially where there is a predisposing condition.¹³ Patients suffering from Hodgkin's disease, malignant lymphoma, tuberculosis, sarcoidosis, collagen disorders, diabetes mellitus, or taking long-term steroids or immunosuppressive drugs are prone to infection.

Pulmonary infections may be self-limiting, and diagnosis may be difficult, sometimes requiring biopsy of the affected tissue. Untreated infections of the central nervous system are invariably fatal and

may present as encephalitis, chronic basal meningitis, or a space occupying lesion with raised intracranial pressure and dementia.

Involvement of the eye with cryptococcus is the result of direct extension to the optic nerve from a basal meningitis along the meningeal sheath of the optic nerve or via the blood stream from a localised or disseminated cryptococcal infection. It is thought that in our patient the organism spread to the eyes via the blood stream. Rarely the infection may be localised in the eye.¹⁴ The ocular complications include photophobia, diplopia, nystagmus, ptosis, papilloedema, neuroretinitis, and optic atrophy,¹⁵ but uveitis, endophthalmitis, chorioretinitis, and vitreous invasion by *C. neoformans* have been reported.¹⁶

A combination of 5-fluorocytosine and amphotericin B has been found to be the most effective treatment, and the use of 5-fluorocytosine enables the dosage of amphotericin B to be reduced. However, since amphotericin B enhances the toxic effects of 5-fluorocytosine, the serum concentration of the latter drug should be kept below 100 mg/l.¹⁷ One case of failure of treatment of cerebral cryptococcoma and cryptococcal meningitis associated with pulmonary cryptococcosis ('coin lesion') with amphotericin B and 5-fluorocytosine was successfully treated with miconazole.¹⁸

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