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Papers

Neuro-ophthalmic Presentations of Sarcoidosis

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Jonathan Hutchinson gave the first illustrated description of the skin disease lupus pernio which is now recognized as but one manifestation of the multi-system disease sarcoidosis. At the turn of the century the disease was known as Mortimer's malady after one of Hutchinson's patients (Hutchinson 1898). Present-day concepts of sarcoidosis arose in the era of the second world war as a result of its clearer distinction from tuberculosis owing to the advent of chemotherapy, improved radiological techniques and the availability of the Kveim test.

In the absence of a proven etiological agent there is to date no satisfactory definition of sarcoidosis, the diagnosis of sarcoidosis being a statement of belief that noncaseating epithelioid cell granulomas are present in all of a number of affected tissues and organs (Scadding 1967).

Central nervous system disease occurs in about 5% of cases of sarcoidosis (Maycock *et al.* 1963, James & Sharma 1967, Herring & Urich 1969), and is clinically manifested as cranial neuropathies, meningeal infiltration or local granulomatous mass lesions. Pathologically the sarcoid granulomata are found in the leptomeninges and parenchyma of the brain. The granulomata penetrate the substance of the brain along the perivascular spaces of the perforating vessels and the process is therefore best considered as meningovascular sarcoidosis (Herring & Urich 1969).

Facial nerve involvement accounts for some 50% of cranial neuropathies in sarcoidosis, and usually occurs as a part of Heerfordt's syndrome of recurrent uveitis, parotitis and facial palsy. The complete syndrome is rarely seen (Crick *et al.* 1961, James & Sharma 1967, Scadding 1967). The optic nerve is the second most frequently involved and the ocular motor nerves are rarely affected (Collier 1930, Colover 1948).

The literature concerning optic nerve disease in sarcoidosis has been reviewed by Jampol *et al.* (1972) and includes reports of papillœdema, papillitis, optic atrophy and local disc granulomas. The following cases illustrate some of the diagnostic problems which may arise when the anterior visual pathways are affected in sarcoidosis.

Case 1 A 42-year-old English woman gave a six-month history of headaches. The visual acuity was normal but the right blind spot was enlarged and there was marked swelling of the right optic disc. There were no signs of ocular inflammation. The left disc was normal. Fluorescein angiography confirmed that the disc swelling was strictly unilateral.

The cerebrospinal fluid pressure was normal. Right carotid angiogram and pneumoencephalography showed no abnormalities. Chest X-ray showed bilateral hilar lymphadenopathy. The Mantoux test was negative at 1/100 dilution. The Kveim biopsy showed numerous non-caseating granulomas.

The disc swelling rapidly resolved after a short course of prednisolone therapy.

Papillœdema can undoubtedly occur in sarcoidosis when local granulomatous mass lesions are present within the cranial cavity (Jefferson 1957, Chumbley & Kearns 1971). The term 'papillœdema' should be rigidly reserved for those cases of optic disc swelling caused by raised intracranial pressure and the non-specific term 'disc swelling' be used to embrace all other causes of swelling of the optic nerve head. The use of such terminology would avoid diagnostic confusion and obviate the surprise of some authors that the cerebrospinal fluid pressure was normal despite the presence of disc swelling (James *et al.* 1967). Recognition of local disc œdema avoids resort to unpleasant, unnecessary, expensive, time-consuming neuroradiological investigations which have a definite morbidity.

Local disc swelling should be suspected when the swelling is unilateral, when visual loss or a field defect is present, when there are associated ocular signs of inflammation or evidence of orbital disease, and when fluorescein angiography shows the presence of a more widespread disorder.

The disc swelling in the present case was considered to be the result of infiltration of the optic nerve and disc by sarcoid tissue. There are reports in the literature of histologically proven sarcoid of the optic nerves (Statton *et al.* 1964, Anderson *et al.* 1966).

Case 2 A 37-year-old Scotsman gave a fourteen-year history of recurrent vitreous hæmorrhages which had

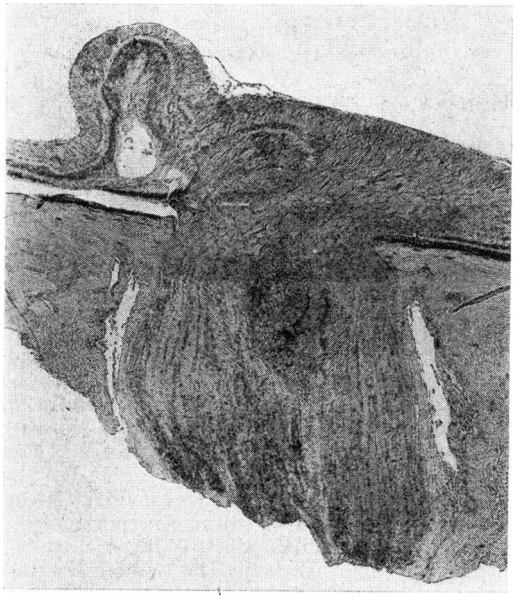

Fig 1 **Case 2** *Sarcoid infiltration of optic nerve. Note marked thickening of nerve.* × *20*

been diagnosed as Eales's disease. Neovascularization of both optic discs was present. The left eye was enucleated because of secondary glaucoma. During a study of Eales's disease, Professor Norman Ashton cut sections from this eye and discovered optic nerve sarcoidosis. Subsequently a Kveim biopsy was positive for sarcoidosis. No evidence of other systemic involvement was found.

The enormously thickened optic nerve is seen in Fig 1. Sarcoid granulomata are seen in relationship to the central retinal vessels. The nerve sheath is not thickened and the subarachnoid space is not distended. High magnification (Fig 2) shows typical epithelioid cell granulomatous lesions with multinucleated giant cells in relation to the central retinal vein.

It is now recognized that there are many conditions which may cause retinal vasculitis and vitreous hæmorrhages which in the past have been diagnosed as Eales's disease (Ashton 1966). The term Eales's disease should be restricted to that group of cases where no definitive cause can be found. The present case is interesting because of the long duration of the active disease process and the positive Kveim biopsy.

Case 3 A 59-year-old Negro woman complained of bilateral visual loss. Four years previously she had a left superior temporal retinal vein thrombosis followed a year later by a complete central vein occlusion and thrombotic glaucoma. One year ago she had a partial right venous occlusion and one week before admission a complete right central vein occlusion.

Visual acuity of the right eye was reduced to appreciation of hand movements and the left eye was blind. Bilateral optic atrophy was present and there were prominent collateral venous channels present on both optic discs. Perivenous sheathing was present bilaterally. No general physical abnormalities were found.

Radiological studies of the right optic foramen were normal but the left foramen was enlarged to 8 mm and the margins were not corticated. Bilateral carotid angiography showed no abnormality. Chest X-ray revealed bilateral hilar lymphadenopathy. The Kveim biopsy was positive.

Large retinociliary collateral vessels around the disc are often seen in central retinal vein occlusion at the level of the lamina cribrosa. A marked degree of optic atrophy following central retinal vein occlusion is extremely rare and should lead to consideration of infiltrative disease of the optic nerve.

The enlarged optic foramen in Case 3 raised the possibility of a chiasmal glioma with bilateral optic nerve involvement. The demonstration of systemic sarcoidosis led to recognition of bilateral optic nerve infiltration by sarcoid granulomas. Enlargement of the optic foramen in sarcoidosis was reported by Anderson *et al.* (1966) and craniotomy in their patient showed a thickened

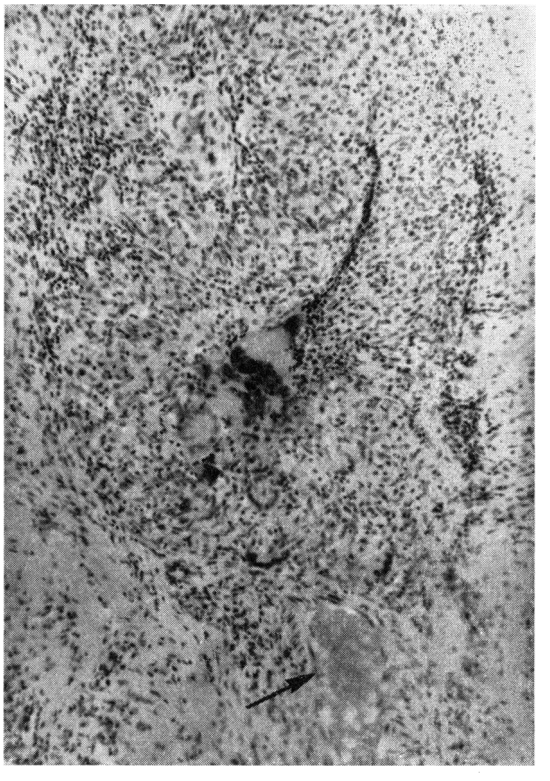

Fig 2 **Case 2** *Granulomatous lesion adjacent to central retinal vein (arrowed).* × *120*

optic nerve. Biopsy of the nerve showed non-caseating granulomas.

Case 4 A 30-year-old Portuguese man experienced sudden loss of left vision. The right acuity was 6/6 and the left was reduced to appreciation of hand movements. There was a dense bitemporal hemianopia in addition to the left central field loss.

Radiological studies showed a mass lesion obliterating the anterior part of the third ventricle extending into the interpeduncular cistern. At craniotomy a large white mass was found to involve both optic nerves, the chiasm and hypothalamic region. Biopsy showed the presence of a chronic granulomatous lesion. The Kveim test was positive. Following a course of systemic prednisolone the visual acuity and visual fields returned to normal after one year.

Bilateral optic nerve, chiasmal and hypothalamic involvement in this case raised the possible diagnosis of a glioma. The discovery of a granulomatous disease process by biopsy led to the performance of the Kveim test and the ultimate diagnosis of sarcoidosis.

There is a tendency in nervous system sarcoidosis for involvement of the hypothalamic region and other cases are on record with tumour-like masses producing filling defects in the third ventricle (Goodman & Margulies 1959, Walsh & Smith 1968).

Conclusion

Four patients with involvement of the anterior visual pathways by sarcoidosis have been described in whom recognition of the systemic disease was delayed owing to the mode of presentation. Infiltration of the optic discs, nerves and chiasm by sarcoid granulomata was the common underlying pathology.

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The Status of *Toxoplasma gondii* in the Etiology of Senile Human Cataract [*Abridged*]

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The presence of parasitic micro-organisms in the human lens, and in particular the protozoan *Toxoplasma gondii*, has not been seriously considered in the etiology of senile cataracts until recently, when Ourth (1971*a*, *b*) claimed to have demonstrated *T. gondii* in cataractous human lenses using a direct fluorescent antibody technique. The purpose of the work described in this paper was to re-examine this question and to see whether the claim of Ourth could be confirmed.

One hundred and three cataractous human lenses of the senile type together with 26 normal lenses were examined for evidence of the organism using a direct fluorescent antibody technique, 54% of these cataractous lenses being from patients with positive toxoplasma dye tests. Peritoneal fluid and brain homogenates from mice infected with *T. gondii* (RH strain), were used as positive controls. Evidence of the organism was not found in any lens.

Mouse inoculation was performed with 50 cataractous human lenses, 54% of which were from patients with positive dye tests. In no case was *T. gondii* isolated.

Although evidence of *T. gondii* was not found by means of the fluorescent antibody technique, fluorescent particles of irregular size and shape were seen but these were considered artifacts since they occurred with the same frequency in both normal and cataractous lenses and in lenses from patients with both positive and negative dye tests. Cryostat sections of human lenses, treated with the same fluorescent antitoxoplasma immune