PAPILLOEDEMA IN SARCOIDOSIS*†

BY

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POSTERIOR uveitis is not a frequent presentation of ocular sarcoidosis because it is usually obscured by overlying anterior uveitis (James, Anderson, Langley, and Ainslie, 1964), so that involvement of the optic disc is rarely recognized as a feature of sarcoidosis. Now that local and systemic corticosteroids are quickly resolving acute inflammation of the anterior segment of the eye, ophthalmoscopic examination is revealing hitherto unsuspected lesions of the posterior segment. In a personally studied series of 422 patients with histologically confirmed sarcoidosis, 112 (26 per cent.) had ocular and 31 (7 per cent.) neurological involvement. Amongst these patients were four with papilloedema (Table); two were intensively investigated at the onset for evidence of a cerebral space-occupying lesion rather than for neurological sarcoidosis. The third case illustrates that awareness of neurosarcoidosis can avoid needless and unfruitful neurological investigation.

TABLE
FEATURES OF 4 PATIENTS WITH PAPILLOEDEMA DUE TO SARCOIDOSIS

Case No.	Sex	Age at Onset (yrs)	Cerebrospinal Fluid			Clinical Accompaniments			Chest X-ray	Kveim Test	Mantoux Test	Other Histology
			Pressure (mm.)	Protein (mg.)	Cells	Facial Palsy	Iritis	Other				
1	F	27	130	70	8	+ left	+	Paraesthesiae of trunk Loss of taste, smell High tone deafness		+	—	Skin
2	M	49	90	60	10	+ left	No	Rash 6th nerve palsy Hypercalcaemia	Mottling	+	—	Liver Lymph node
3	F	26	100		0		+	Hypercalciuria Bilateral parotid gland enlargement	Bilateral hilar lymphadenopathy	+	—	Liver Parotid
4	F	40	No	No spinal tap performed			+	Abdominal pain Parotid gland enlargement Splenomegaly Lymphadenopathy	Bilateral hilar lymphadenopathy	+	—	—

Case Reports

Case 1, a woman aged 27 years, presented with a month's history of blurring of vision in both eyes. When it started in the left eye she was successfully treated with cortisone drops, but this was soon followed by blurring of vision in the right eye, loss of taste, anosmia, and stiffness of the left side

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of the mouth and tongue. Eating and drinking were accomplished with difficulty, she lost the smile on the left side of her face, and some letters like 'B' and 'P' were difficult to pronounce. 3 months previously she had noticed numbness of the left axilla and left breast.

Examination.—She had bilateral anosmia; visual acuity of 6/12 in the right eye and 6/9 in the left; and gross swelling of both optic discs. There was a left lower motor neurone facial weakness and she was unable to close the left eye. There was loss of taste sensation on the anterior two-thirds of the left side of the tongue. A provisional diagnosis of a space-occupying lesion, possibly a pontine glioma, was made. Spinal fluid contained 70 mg. protein and 8 white cells (6 lymphocytes, 2 polymorphs), and the pressure was 130 mm. Bilateral carotid arteriography and ventriculography revealed no abnormality.

Treatment.—Because of the presence of keratic precipitates and a left vitreous haze, oral corticosteroids were administered with a marked improvement in her eye condition, virtually complete resolution of the left facial paresis, and return of taste and smell within a month of treatment.

Mr. John Groves (Royal Free Hospital) found that the nerve excitability and the comparatively short duration of the facial palsy suggested that it was a neurapraxia and that the degenerative changes in the nerve had been minimal or absent. Audiometry showed very slight high tone loss at 4,000 c.p.s. in the right ear. Sarcoidosis was confirmed by a positive skin biopsy from a maculopapular rash of the legs and a positive Kveim test: and in keeping with the diagnosis was a negative Mantoux reaction.

Case 2, a man aged 49 years, presented with slowly progressive diplopia particularly on looking ahead and to the right; 12 years previously he had had attacks of vertigo which left him with residual left nerve deafness and 2 years previously he had sustained a fractured skull. He now complained of chest pain which he attributed to an insignificant chest injury.

Examination.—Ophthalmoscopy revealed left-sided papilloedema, two tiny haemorrhages at the proximal branching of the superior temporal vein, and venous congestion; the visual acuity in each eye was 6/5. He had a complete right sixth nerve palsy and a slight left facial weakness. Because of the history of trauma and the possibility of a subdural haematoma, an ultrasonogram and a left carotid arteriogram were done but were normal. At ventriculography, the dura was exposed (by Mr. A. E. Richardson) to reveal normal underlying brain. The lateral ventricle was tapped to 4.5 cm. and the fluid appeared to be under slightly increased pressure. 3 days later a lumbar puncture disclosed a pressure of 90 mm. and the fluid contained 60 mg. protein with 10 cells. Within a fortnight the sixth and seventh nerve palsies and papilloedema had cleared. A chest radiograph revealed bilateral pulmonary infiltration; scalene lymph node biopsy and aspiration liver biopsy revealed sarcoid tissue; repeated 24-hr urine calcium determinations showed hypercalciuria (339, 366, 397, 359, and 440 mg./24 hrs); electrophoresis of the serum proteins showed an increase in α_2 and γ globulins; the Mantoux reaction was negative.

Treatment.—He has responded to oral corticosteroids with regression of pulmonary infiltration and of the hypercalciuria.

Case 3, a woman aged 26 years, with a 13-year history of epilepsy developed pain and redness in both eyes. This started in the left eye 4 months earlier only to clear spontaneously and then recur in both eyes.

Examination.—She was found to have marked swelling of the eyelids and bilateral anterior uveitis, which was successfully treated with cortisone eyedrops. During the next 3 weeks she developed parotid swellings, initially left-sided and then bilateral, associated with mild bilateral anterior uveitis and bilateral papilloedema. No other neurological signs were found or became evident at any other time. Confirmatory evidence of sarcoidosis comprised bilateral hilar lymphadenopathy; hypercalciuria of 380 mg./24 hrs; histological evidence of sarcoid tissue in aspiration biopsies of the liver and left parotid gland, positive Kveim test; and negative Mantoux reaction. Spinal fluid at a pressure of 100 mm. contained a normal protein level and no cells.

Case 4, a woman aged 40 years, presented with an attack of abdominal pain at first sharp in nature which brought her under observation in hospital; but no abnormal physical signs were found and no diagnosis made; 2 weeks later she complained of blurring of vision.

Examination.—She was seen to have bilateral anterior uveitis and parotid swelling. The iridocyclitis settled in 2 days but fundoscopy showed bilateral papilloedema, exudates, and sub-hyaloid haemorrhages. No other lesions were found in the cranial or peripheral nerves. There was peripheral lymphadenopathy and splenomegaly and the chest radiograph revealed enlargement of the mediastinal glands. A Kveim test was positive, confirming the clinical diagnosis of sarcoidosis.

Treatment.—Although she showed some spontaneous improvement within 2 months, the papilloedema persisted and she was given systemic corticosteroids for 6 months. Since then she has remained well, except that 6 years after the original episode she has bilateral posterior synechiae and retinitis proliferans in the right eye but no papilloedema.

Discussion

Waldenström (1937) described five patients with bilateral parotid gland enlargement and bilateral uveitis due to sarcoidosis, four of them being women over 30 years of age. The disease was clearly multisystemic, for one or other of these patients had evidence of involvement of the neurological system, lungs, lymph nodes, or skin, as well as fever or hyperglobulinaemia. He drew particular attention to bizarre neurological manifestations, which included right facial or hypoglossal nerve palsy and bilateral optic neuritis; and at the same time indicated meningeal involvement with cerebrospinal fluid pleocytosis. In a review of the literature a decade later, Colover (1948) uncovered papilloedema in sixteen of 118 cases of neurological sarcoidosis.

The definition of neurological sarcoidosis has recently been clarified by an American report of eighteen patients (Silverstein, Feuer, and Siltzbach, 1965) and by a British series of nine patients (Matthews, 1965). These reports are complementary, since they emanate from entirely different backgrounds. The American material was chosen from patients attending a special sarcoidosis clinic at the Mount Sinai Hospital, New York, whereas the British series was drawn by one neurologist from a population of approximately 500,000 over a period of 10 years. The American series is predominantly Negro, and the British all white. But in both series there was a great predilection for women and a high incidence of facial palsy; and intrathoracic involvement was evident in 22 of the 27 patients. The appearance of neurological symptoms and signs during the course of known sarcoidosis was the principal reason for more detailed neuro-investigation in the American series. Without the knowledge of sarcoidosis in other systems, the pathogenesis of the neurological changes would have remained obscure. The usual diagnostic procedures used in neurology were unhelpful in the diagnosis of neurosarcoidosis, a fact which became obvious in two of our patients with papilloedema.

Matthews (1965) drew particular attention to pain and hypalgesia of a bizarre distribution on the trunk of his patients; in three instances this led to provisional diagnoses of pleurisy, appendicitis, or spinal arthritis. Three of our patients were so afflicted, and one of these endeavoured to claim compensation for a minor chest injury which he felt was the cause of his condition.

Colover (1948) found abnormal cerebrospinal fluid in only 23 of 118 patients. Siltzbach and his colleagues (1965) found the cerebrospinal fluid to be abnormal in only five of eleven patients studied and pleocytosis was evident in two of these.

Matthews (1965) likewise found spinal fluid examination to be unhelpful, particularly since it was normal in one of his patients at the height of the disease. Pleocytosis was found in two of our four patients and, despite papilloedema, the spinal fluid pressure was normal in all three patients.

In patients with papilloedema, the diagnosis of neurological sarcoidosis should be entertained when it develops rapidly in adults, particularly women, and also particularly if there is facial weakness or other cranial nerve palsies or unusual sensory symptoms over the trunk. Sarcoidosis is a multisystem disease, so suspicion is heightened by concomitant involvement of lungs, skin, lymph nodes, spleen, or iris. Clinical confirmation is most easily obtained by chest radiography and slit-lamp examination of the eyes. The Kveim test, right scalene node biopsy, or aspiration liver biopsy are worthwhile means of obtaining histological confirmation, and estimation of serum and urine calcium levels may disclose abnormal calcium metabolism.

Fine and Flocks (1953) have noted the rapid disappearance of papilloedema as a result of corticosteroid therapy, and we were also gratified by the early response of our patients, but the value of this treatment remains doubtful in a disease characterized by a high incidence of spontaneous resolution. The true worth of steroid therapy can be assessed only by carefully controlled trials, but in our present state of knowledge one cannot disagree with the authoritative conclusion of Siltzbach and others (1965) that the absence of any other effective agents makes a trial of oral corticosteroid therapy almost mandatory.

Summary

Four patients with sarcoidosis of the central nervous system were found to have papilloedema; in two it was the presenting feature and simulated a space-occupying lesion. Evidence of multisystem involvement, histological evidence of sarcoid tissue, the gratifying response to corticosteroids, and the subsequent benign course all serve to differentiate the diagnosis of neurological sarcoidosis from that of a cerebral tumour.

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