Neurosarcoidosis—demonstration of meningeal disease by gadolinium enhanced magnetic resonance imaging

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Abstract

Arriving at a firm diagnosis of neurosarcoidosis continues to pose serious problems, particularly when evidence of granulomatous disease outside the nervous system is lacking. The commonest mode of presentation of neurosarcoidosis is with cranial nerve palsies. Two cases of presumed neurosarcoidosis with cranial nerve palsies showed clear evidence of focal meningeal disease on gadolinium-DTPA enhanced MRI brain scans. Although not specific for sarcoidosis, this technique may be very useful in aiding the diagnosis in suspected cases.

Sarcoidosis is a disseminated disease of unknown aetiology characterised by non-caseating granulomatous infiltration. Neurological symptoms occur in about 5% of patients known to have the disease^{1,2} and in up to 14% of patients at necropsy.³ The commonest mode of presentation of neurosarcoidosis is with cranial nerve palsies.¹ Although facial nerve involvement, in particular, is frequently encountered, the pathophysiology of these lesions is poorly understood, probably because they are associated with a good prognosis.

Major diagnostic difficulties can arise, particularly in patients with no evidence of granulomatous disease outside the nervous system, because of problems in obtaining suitable tissue for histological examination. Diffuse meningeal infiltration particularly in the skull base region is frequently found at necropsy^{4,5} but is infrequently diagnosed positively during life, partly because until now imaging techniques have usually not shown up such meningeal involvement. This paper describes two patients with presumed neurosarcoidosis which presented with cranial nerve palsies, in whom evidence of focal meningeal disease was demonstrated on gadolinium-DTPA (Gd-DTPA) enhanced MRI.

Case 1

A 65 year old white woman presented at the age of 39 with right sided pleuritic chest pain and an abnormal chest radiograph showing an irregular mass in the right apex. Despite extensive investigations no firm diagnosis was made and her condition spontaneously improved. At the age of 43 she developed headaches, dysphagia and dysphonia. She was found to have bilateral conductive deafness

(attributed to bilateral mastoidectomies) and left sided ninth to twelfth lower cranial nerve palsies. Cerebrospinal fluid examination was unremarkable as was myelography and vertebral angiography. Biopsies taken of a possible mass in the left nasopharynx revealed no definite abnormality. Her erythrocyte sedimentation rate was 40 mm/hr. Her neurological condition again spontaneously improved. She remained well until the age of 61 when a 5 × 7 cm mass was removed from the left buttock which on histological examination was consistent with erythema nodosum. The patient then developed vaginal bleeding and other persistent gynaecological symptoms. These were treated surgically with hysterectomy and bilateral salpingo-oophorectomy at the age of 63 and colectomy at the age of 64. Histology from both these procedures revealed sterile non-caseating granulomatous tissue. The patient continued to have persistent vaginal ulceration and developed a urethro-vaginal fistula with granulomatous pathology.

At the age of 66 she had six episodes of dysarthria, blurred vision with scintillating teichopsia and numbness in her tongue lasting for about 30 minutes, without subsequent headache or vomiting. Neurological examination was unremarkable apart from severe bilateral deafness and a diminished left-sided gag reflex. The diagnosis was felt to be vertebrobasilar transient ischaemic attacks. Investigations revealed an ESR of 46 with

Figure 1 Case 1. Enhanced axial CT scan through posterior fossa showing enhancement of the tentorium cerebelli on the left.

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Received 3 April 1990
and in revised form
12 October 1990.

Accepted 7 November 1990

elevated serum calcium of 2.79 mmol/l. A chest radiograph showed a small calcified lesion in the left lower zone only. Serum angiotensin converting enzyme was normal. CT scan showed mild asymmetrical dilatation of the lateral ventricles and a possible mass in the left posterior fossa with contrast enhancement of the tentorium cerebelli on the left (fig 1). An MRI scan was obtained using a Siemens Magnetom 1.5 Tesla scanner. A T2 weighted sequence (TR 3.2 s TE 90 ms) showed no evidence of a mass lesion (fig 2a) but confirmed mild asymmetrical hydrocephalus and demonstrated a Chiari malformation. In addition abnormal bright enhancement of the meninges of the left cerebral hemisphere, tentorium cerebelli and left side of the posterior fossa was shown on Gd-DTPA enhanced T1 weighted sequences (TR 0.5 s TE 17 ms) carried out in the coronal and axial planes (fig 2b, c). Unenhanced T1 weighted images were not obtained as a bright sequence from the meninges would indicate a fairly acute bleed which was clinically highly unlikely.

At the age of 67 she developed epilepsy with eight attacks of right sided jerking followed by loss of consciousness for up to 20 minutes. These attacks stopped after treatment with phenytoin was started. The EEG was unremarkable. The Mantoux test was negative at 1:10,000 dilution, Kveim test was negative. No repeat CSF examination was carried out.

This woman had histologically proven non-caseating granulomatous disease of the female genital tract and of a subcutaneous buttock mass. Sarcoidosis affecting the uterus is well recognised but in fact few proven cases have been reported.¹ In addition she had evidence of neurological involvement, having had an episode of cranial nerve palsies and epilepsy, the latter being reported in up to 35% of cases of granulomatous meningitis.⁶

Case 2

A 53 year old businessman who had been born in India but had lived in England for twenty years developed double vision in 1985, which on examination was due to a partial pupil sparing right sided third nerve palsy. Extensive investigations were all unremarkable including erythrocyte sedimentation rate, chest radiograph and enhanced CT brain scan. Although no definite diagnosis was made at that time, the patient was treated with a short course of oral prednisolone (40 mg for two weeks) and all his symptoms and signs fully resolved.

He remained well till June 1989 when he again complained of double vision, which on this occasion was due to a complete right-sided lateral rectus palsy. Whilst he was being investigated for this isolated cranial nerve palsy, he gradually developed right facial numbness, increasing hoarseness of his voice and dysphagia over a six week period. Examination revealed multiple right-sided cranial nerve palsies involving the fifth, sixth, ninth and tenth nerves.

Investigations revealed an ESR of 55 mm/hr but normal serum calcium and angiotensin converting enzyme levels. Repeat chest radiograph and CT brain scans were again normal. Cerebrospinal fluid examination showed only mild abnormalities—six lymphocytes, protein 0.84 g/l and glucose 4.1 mmol/l. Acid-fast bacilli were not seen or cultured from the spinal fluid and cytological examination confirmed the absence of malignant cells. The Mantoux test was clearly positive at a dilution of 1:10,000. A Kveim test was not carried out. Gallium scanning showed marked bilateral lacrimal gland and bilateral hilar lymph node uptake, a pattern well recognised in sarcoidosis.⁷ MRI scan with Gd-DTPA enhancement showed clearcut abnormal enhancement affecting only the meninges

Figure 2 Case 1. a) T2 weighted (TR 3.2 s TE 90 ms) axial magnetic resonance images obtained at the level of the pons showing no mass lesion or area of abnormal signal. The CSF returns a normal high signal on this sequence. b) axial and c) coronal Gadolinium-DTPA enhanced T1 (TR 0.5 s TE 17 ms) weighted MRI scans showing bright meningeal enhancement over left hemisphere and tentorium cerebelli.

Figure 3 Case 2. a) Axial and b) and c) coronal Gd-DTPA enhanced T1 weighted MRI scans showing enhancement of the tentorium cerebelli on the right. d) and e) Axial T2 weighted MRI scans again showing no abnormality in the brain stem or CSF.

on the right side maximal in the region of the tentorium cerebelli (fig 3a, b, c). T2 weighted sequences using the same sequences as before showed no abnormality in the brain stem or adjacent CSF (figs 3d, e).

This patient presented with two episodes of cranial nerve palsies without any clinical evidence of systemic disease outside the central nervous system. The illness was felt to be due to sarcoidosis although tuberculosis was obviously an important differential diagnosis. The patient was again treated with oral steroids, initially dexamethasone (16 mg/day for three weeks) and subsequently put on to a reducing regime of prednisolone over a six month period. He was also treated with isoniazid (600 mg/day for six months) as a single agent as prophylaxis against activating any previous tuberculosis. There was a gradual but steady improvement over a three month period, during which all his cranial nerve palsies resolved.

Discussion

Both these cases presented with multiple lower cranial nerve palsies. In the first case, the patient was known to have non-caseating granulomatous tissue affecting other organs. In the second case, the evidence that the meningeal disease was due to sarcoidosis was based on the overall clinical picture and response to steroid treatment, combined with the gallium

scan, the lymphocytic CSF and the lack of any evidence over many years of follow up of other major causes of meningeal disease such as carcinoma and tuberculosis.

In sarcoidosis of the central nervous system, leptomeningeal disease is the commonest pattern of involvement seen, and may be localised or widespread, resulting in focal or disseminated meningeal nodules or plaques.² This may result in basal obstruction of ventricular outflow with hydrocephalus, and cranial nerve palsies. Less commonly, granulomatous masses can be found within the cerebral parenchyma, or there may be infiltration of the vascular structures.⁸⁻¹⁰

CT features of neurosarcoidosis are well documented,⁸⁻¹³ with hydrocephalus reported as the most common CT abnormality. Granulomatous masses within the cerebral parenchyma may be isodense or hypodense on CT and usually enhance with contrast. Meningeal nodules or plaques are shown by focal or diffuse thickening and contrast enhancement on CT; these appearances cannot be distinguished from bacterial or malignant infiltration.

The MRI appearances of neurosarcoidosis are less well documented. Intracerebral cortical or subependymal lesions may be shown on MRI as regions of high signal on T2 weighted images which enhance with Gd-DTPA.^{11 14 15} There are few reports of the demonstration of meningeal sarcoid infiltration with MRI. Greco

and Steiner in 1987¹⁶ reported high signal intensity of the basal meninges in one of four patients with neurosarcoidosis but Gd-DTPA was not given. Normal meninges may occasionally show faint enhancement on administration of Gd-DTPA, but abnormally brightly enhancing meninges usually indicate meningeal disease in conditions including inflammatory and malignant infiltration.¹⁷⁻¹⁹ As in CT scanning the appearances are non-specific and may be due to a wide range of pathology. In both these patients no significant meningeal abnormality was noted on unenhanced MRI scans, but the meningeal enhancement seen in both patients was of very high signal intensity, strictly unilateral and on the same side as the cranial nerve palsies.

Gadolinium-DTPA is a paramagnetic contrast agent used in MRI which functions by altering local magnetic environments to change signal intensity in tissues where it accumulates. Like radiographic contrast agents, it uniformly distributes throughout the extracellular space and does not cross intact cell membranes or the intact blood-brain barrier to any extent. Administration of Gd-DTPA therefore highlights damaged or altered tissue in a non-specific manner, similar to radiographic contrast administered in CT scanning.

In one of these patients CT scan and unenhanced MRI scan failed to demonstrate significant intracranial pathology. The sensitivity of MRI for detection of intracranial disease is superior to that of CT with a similar specificity. This is further increased by administration of Gd-DTPA. Gd-DTPA enhanced MRI should be performed in patients with suspected neurosarcoidosis as well as unsuspected cranial nerve palsies. Changes in the extent and pattern of enhance-

ment may well prove useful in monitoring the progress of the disease and in assessing the effects of treatment.

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