CNS Sarcoidosis: Evaluation with Contrast-Enhanced MR Imaging

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Reports of findings on unenhanced MR images and contrast-enhanced CT scans in patients with intracranial sarcoidosis have suggested that MR imaging without contrast enhancement may miss meningeal involvement, which is a frequent and prominent finding in neurosarcoidosis. We studied 14 patients with CNS sarcoidosis with T1- and T2-weighted pre- and postcontrast sequences and T1-weighted postcontrast sequences. Eight of 12 patients with intracranial sarcoidosis and one of two with spinal sarcoidosis had meningeal involvement that was not apparent on the unenhanced scans. Eight of 12 patients had intraaxial areas of high signal intensity on T2-weighted images, although only two of these lesions enhanced. Three patients had enhancing extraaxial masses mimicking meningiomas on postcontrast T1-weighted images. In two patients, the lesions decreased markedly in size after steroid treatment. In one patient with sarcoidosis of the optic nerve, the lesion decreased in size and the patient's vision returned to normal after Cytoxan therapy. In five of 14 patients, CNS findings were the initial clinical manifestation of the disease. In nine of 14 patients, the diagnosis of neurosarcoidosis was suggested only after administration of contrast agent.

Use of gadopentetate dimeglumine greatly enhances the sensitivity of MR imaging in the detection of CNS sarcoidosis.

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Symptomatic involvement of the CNS has been reported in 5% of patients with sarcoidosis, although autopsy results indicate that neurologic involvement is more common [1–3]. Neurosarcoidosis may be the presenting manifestation of this idiopathic granulomatous disease [1, 3], and CNS involvement may include meningeal disease, cranial neuropathy, hypothalamic and pituitary dysfunction, and both intra- and extraaxial masses [1, 3–6]. Although response to therapy is variable [1, 3, 5, 6] and few patients die from sarcoidosis, CNS involvement is one of the more common causes of sarcoid-related mortality [7]. Medical or surgical therapy can be palliative [1, 3, 5, 6, 8].

Reports of unenhanced MR imaging and contrast-enhanced CT [5, 8–11] have suggested that MR without contrast enhancement may miss meningeal involvement, which is a frequent and prominent finding in neurosarcoidosis. We report here the appearance of CNS sarcoidosis on contrast-enhanced MR images in 12 patients with intracranial involvement and two patients with spinal cord involvement. In our series, the addition of contrast material greatly enhanced the sensitivity of MR in the detection of CNS sarcoidosis and helped to evaluate patients' response to therapy.

Materials and Methods

Over the course of 1 year 14 patients, 18 to 57 years old, with a preexisting or subsequent diagnosis of CNS sarcoidosis, were studied on a 1.5-T GE superconductive magnet with both T1-weighted, 600/20 (TR/TE), and spin-density T2-weighted (2800/30,80) axial, sagittal,

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TABLE 1: MR Findings in 14 Patients with CNS Sarcoidosis[a]

Case No.	Age (yr)	Sex	Symptoms	Proof of Diagnosis	Hydrocephalus	Precontrast MR Imaging: Extraaxial Lesions T1-Weighted	Precontrast MR Imaging: Extraaxial Lesions T2-Weighted	Precontrast MR Imaging: Intraaxial Lesions T1-Weighted	Precontrast MR Imaging: Intraaxial Lesions T2-Weighted	Postcontrast MR Imaging: Meningeal Enhancement	Postcontrast MR Imaging: Extraaxial Enhancement	Postcontrast MR Imaging: Intraaxial Enhancement
1.	18	F	Amenorrhea	CXR	–	—	—	Slightly thickened infundibulum	Increased signal in chiasm, hypothalamus	—	—	Hypothalamus, chiasm
2.	34	F	Headaches	CXR	–	—	—	Thickened hypothalamus and infundibulum	Increased signal in chiasm, hypothalamus	Falx, frontal dura, plenum dura	—	Hypothalamus, infundibulum, pituitary
3.	42	F	Loss of balance; altered mental status	Brain biopsy	–	—	—	Superior sagittal sinus thrombosis	Increased signal in rt. posterior parietal and lt. cerebellar masses	Posterior fossa/tentorium, interhemispheric fissure	—	Rt. posterior parietal lesions
4.	29	M	Headache; suspected herpes encephalitis, not improved on acyclovir	Lacrimal gland biopsy, uveitis	–	—	—	—	Increased signal intensity at gray-white junction	Diffuse meningeal enhancement	—	—
5.	25	F	Loss of vision OS	Brain biopsy	–	Rt. temporal mass	Low signal intensity	—	—	—	Rt. temporal mass	Left optic nerve
6.	32	M	Ataxia; intermittent dementia	CXR	+	—	—	—	Increased signal in posterior internal capsule	Diffuse basilar meningeal enhancement	—	Hypothalamus
7.	41	M	Head and speech problems	Brain biopsy	–	Lt. parasellar mass	Low signal intensity	Mass effect	Vasogenic edema lt. temporal lobe	Lt. middle fossa	Left parasellar to middle cranial fossa mass	—
8.	32	F	Headache; increased intracranial pressure	Lung biopsy	–	—	—	—	—	Cerebellar meninges	—	Hypothalamus
9.	57	M	Hearing loss and tinnitus AD; decreased visual acuity	Lymph node biopsy	–	—	—	—	Increased signal in rt. middle cerebellar peduncle	—	—	Lt. temporal lobe mass; rt. middle cerebellar peduncle mass; ependyma
10.	38	F	Headache	CXR	–	—	—	—	Increased signal bilateral occipital regions	Interhemispheric fissure	—	—
11.	42	F	Headache	CXR	–	Interhemispheric mass	Low signal intensity	—	Frontal lobe edema	Interhemispheric fissure	Interhemispheric mass	—

12.	49	F	Headache; altered mental status	CXR	—	—	—	—	Increased signal intensity foci (masses) rt. parietal and subcortical	—	—	—
13.	47	F	Numbness in lower extremities	Mediastinal biopsy						Enhancement of the pia over the conus		
14.	56	F	Quadriparesis	Spinal cord biopsy				Intramedullary mass, cervical cord	Increased signal intensity			Intramedullary enhancement

[a] Patients 1–12 had intracranial sarcoidosis; patients 13 and 14 had spinal cord sarcoidosis.
Note.—CXR = chest X-ray film, OS = in left eye, AD = in right ear, rt. = right, lt. = left.

and, in some cases, coronal sections through the whole brain and/or spinal cord. T1-weighted images were also obtained after IV administration of gadopentetate dimeglumine (Berlex) (0.1 mmol/kg). Diagnosis was based on positive brain or spinal cord biopsy results in four cases, other tissue biopsy results in four cases, and on characteristic chest radiographic findings of pulmonary, hilar, and mediastinal sarcoidosis in six cases (see Table 1).

Results

Eight of 12 patients with intracranial sarcoidosis and one of two patients with spinal sarcoidosis had meningeal involvement, which was not apparent on the unenhanced scans (Fig. 1). Seven of 12 patients had intraaxial areas of high signal intensity in the cerebellum, internal capsule, and gray-white junction, on T2-weighted images, which did not enhance after contrast administration (Fig. 2). Eight patients had enhancing lesions that were not apparent, or were poorly seen on unenhanced scans; these included one patient with optic nerve enhancement (Fig. 3), two with parenchymal and one with ependymal lesions (Fig. 4), and three with enhancing hypothalamic lesions (Fig. 5). Three patients had enhancing extraaxial masses mimicking meningiomas on postcontrast T1-weighted images (Figs. 3 and 6). On unenhanced T2-weighted images, these lesions were of very low intensity. One patient presented with dementia and had hydrocephalus (Fig. 7). In addition, two patients had vasogenic edema (Fig. 6). Of the two patients with spinal sarcoidosis, one had enlargement of the cervical cord noted on the unenhanced scan with enhancement of the cord on postcontrast images (Fig. 8); the other had plaquelike enhancing thickening of the pia at the level of the conus, with no definite abnormality identified on the unenhanced study. Superior sagittal sinus thrombosis, a rare complication of sarcoidosis [5], was noted in one case (Fig. 2).

Discussion

Sarcoidosis is a systemic granulomatous disease of unknown origin that affects the CNS in 5% of cases [1–3]. Manifestations of the disease on unenhanced MR images have been reported [9, 10]. Recently, several reports have emphasized the sensitivity of MR imaging to the detection of meningeal disease (Ross MR et al., paper presented at the annual meeting of the Radiological Society of North America, Chicago, November 1989, and [12]). Since meningeal involvement in sarcoidosis is common, we hypothesized that the addition of gadopentetate dimeglumine would greatly enhance the sensitivity of MR in the detection of CNS sarcoidosis. Our study confirmed this hypothesis. Indeed, eight of our 12 patients with intracranial sarcoidosis and one of the two patients with spinal sarcoidosis had meningeal involvement that was not apparent on the unenhanced scans. The detection of meningeal enhancement immediately narrows the differential diagnosis to a few conditions, including bacterial, viral, lymphomatous, or carcinomatous meningitis, many of which may be diagnosed by lumbar puncture. The CSF findings in patients with sarcoidosis, even in the presence

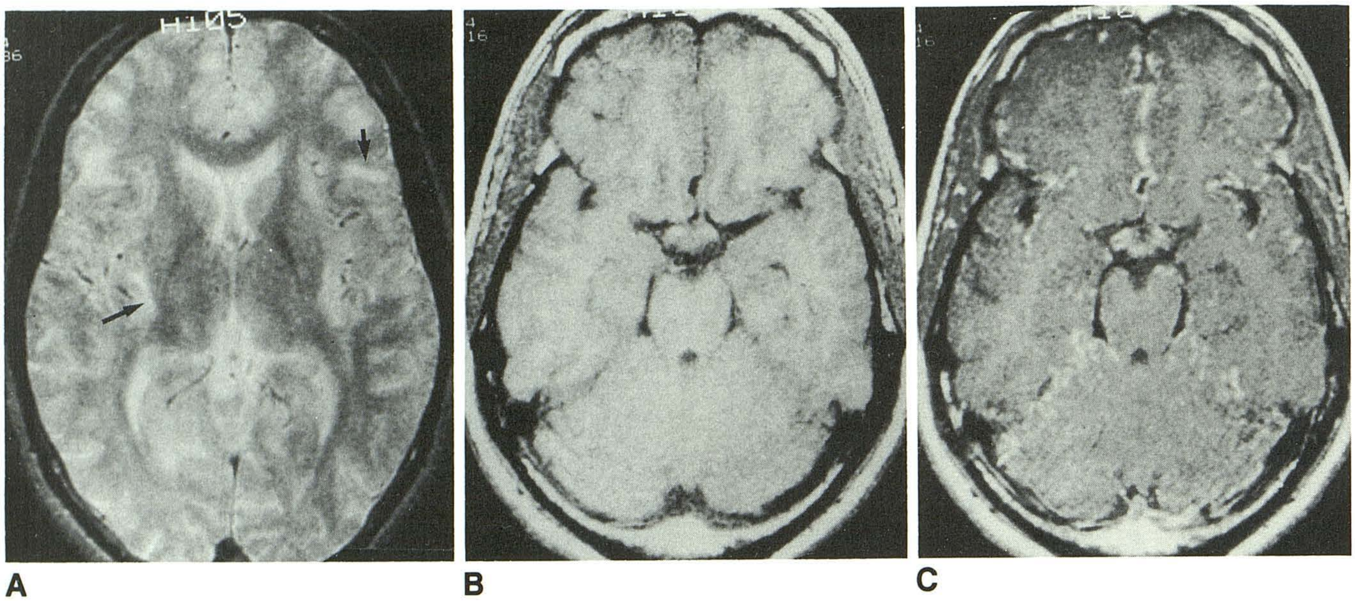


Fig. 1.—Case 4: 29-year-old man with suspected encephalitis.
A, Axial unenhanced T2-weighted image shows nonspecific foci of high signal intensity at gray-white junction (*arrows*).
B, Axial unenhanced T1-weighted image reveals prominent suprasellar soft tissue.
C, Axial postcontrast T1-weighted image shows diffuse marked enhancement of leptomeninges.

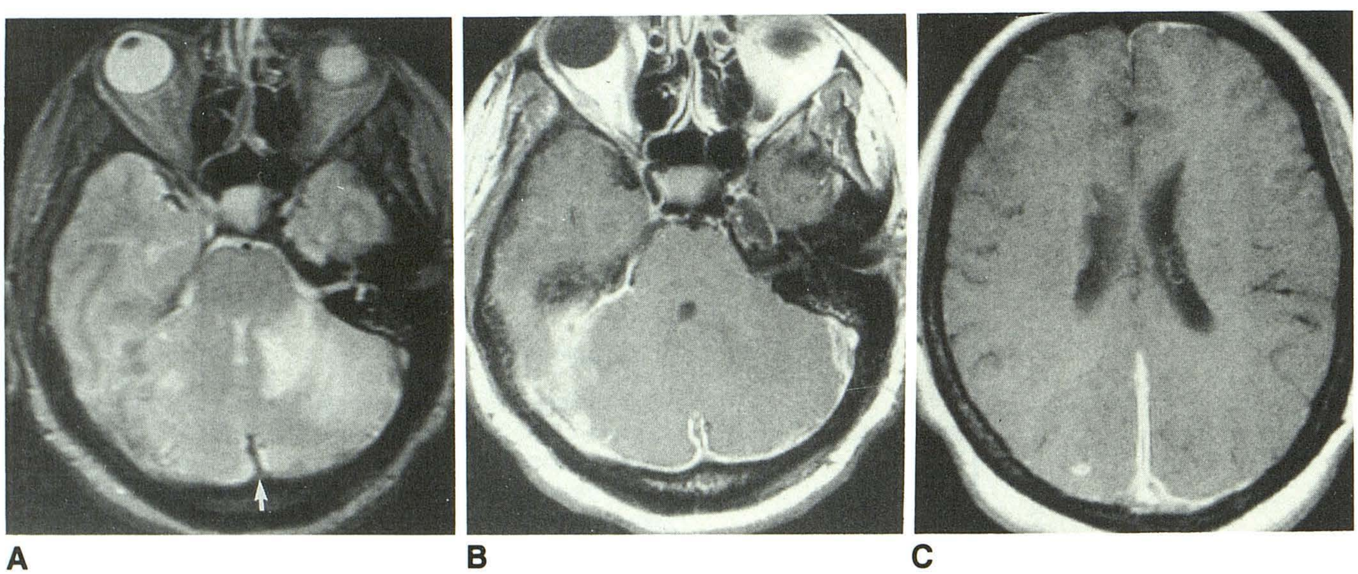
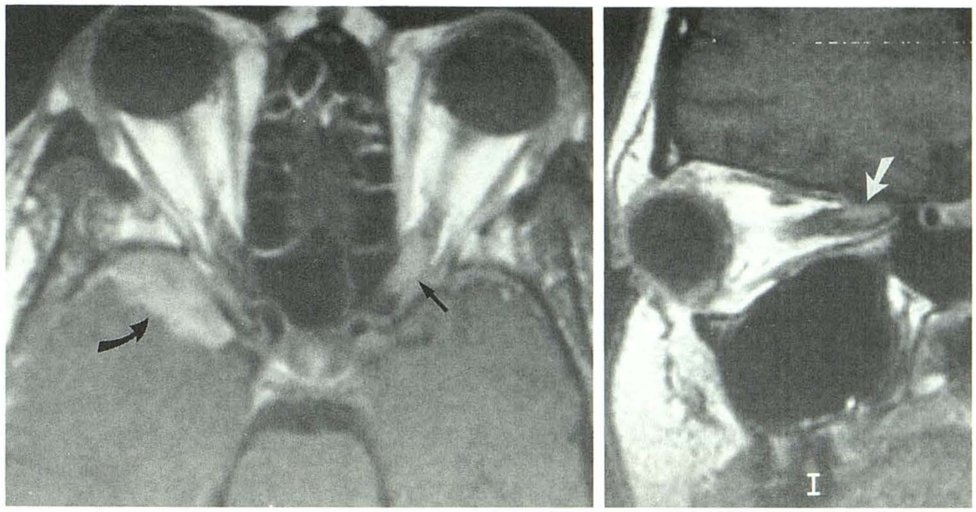


Fig. 2.—Case 3: 42-year-old woman with altered mental status.
A, Axial unenhanced T2-weighted image shows mass with increased signal intensity in left cerebellum. Note lack of flow void and flow artifact in superior sagittal sinus (*arrow*).
B, Axial postcontrast T1-weighted image shows marked enhancement of meninges. No flow in superior sagittal or transverse sinus. Note lack of enhancement of left cerebellar hemisphere.
C, Axial postcontrast T1-weighted image shows enhancing intraaxial lesion and meningeal enhancement in interhemispheric fissure. Repeat contrast-enhanced imaging showed resolution of the enhancing extraaxial lesion after a course of steroid therapy.

of meningeal enhancement, are nonspecific and tissue biopsy is necessary for definitive diagnosis. This can usually be obtained from sites such as the lacrimal gland, peripheral lymph nodes, or, rarely, the mediastinum or meninges.

Occasionally, meningeal enhancement may be due to hyperemia associated with dural sinus thrombosis (Ross MR et al., paper presented at RSNA, November 1988). We believe this to be the case in our patient with superior sagittal sinus thrombosis, since results of the biopsies of the meninges were negative while results of the cerebellar biopsy revealed noncaseating granulomata.

While the characteristic pathologic changes of sarcoidosis consist of noncaseating granulomata containing macrophages, epithelioid cells, and multinucleate giant cells, necro-



A B

Fig. 3.—Case 5: 25-year-old woman with loss of vision in left eye.

***A*, Axial postcontrast T1-weighted image shows enhancement and thickening of intracanalicular and proximal intraorbital optic nerve (*straight arrow*) and enhancing extraaxial mass along greater wing of right sphenoid (*curved arrow*).**

***B*, Oblique parasagittal postcontrast T1-weighted image confirms thickening and enhancement of left optic nerve (*arrow*).**

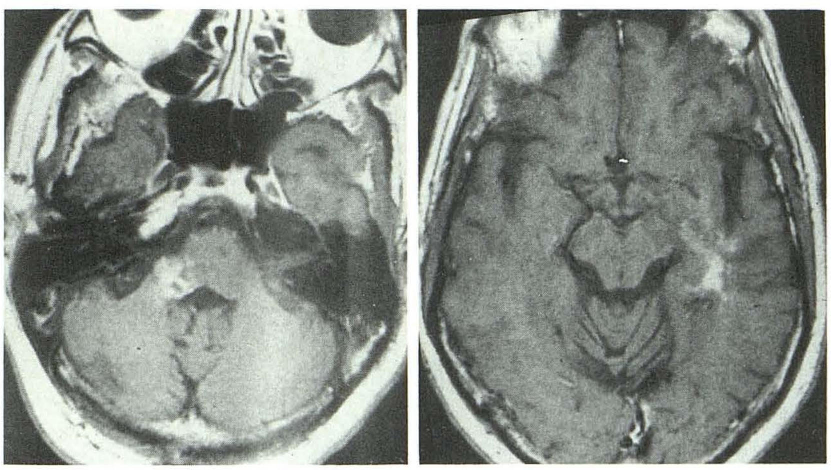


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Fig. 4.—Case 9: 57-year-old man with hearing loss and tinnitus in right ear.

***A*, Axial postcontrast T1-weighted image shows enhancing 1-cm lesion in right middle cerebellar peduncle bulging into right cerebellopontine angle at the emergence of cranial nerve VIII.**

***B*, Axial postcontrast T1-weighted image shows enhancement of ependyma of left temporal horn.**

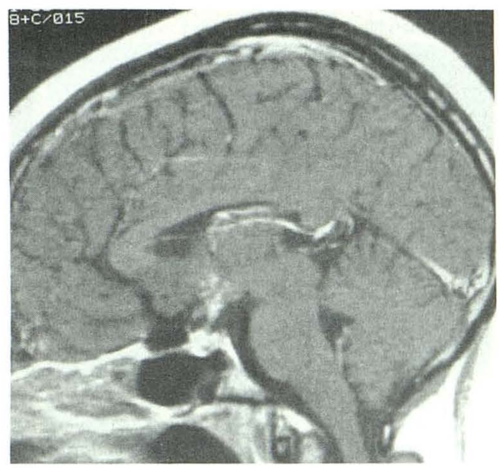

Fig. 5.—Case 1: 18-year-old woman with amenorrhea. Sagittal postcontrast T1-weighted image shows punctate enhancement of hypothalamus.

sis can mimic caseation, presenting problems in diagnosis. Such a problem was encountered in case 5, a patient in whom biopsy results of an extraaxial right temporal mass revealed necrotizing granulomas consistent with tuberculosis or sarcoidosis. All cultures and special stains were negative for acid-fast bacillus, and the patient improved on steroids.

The presence of abnormal areas of high signal intensity on T2-weighted images at the gray-white junction, as seen in seven of our patients, is a nonspecific finding that by itself is not characteristic of CNS sarcoidosis. The combination of such findings with meningeal enhancement or with lesions in the hypothalamus should suggest the diagnosis of sarcoidosis. In our series, enhancement of intraaxial lesions was uncommon (two of 12). In one patient in whom a biopsy of high-intensity nonenhancing lesion was done, noncaseating granulomata characteristic of sarcoidosis were encountered. Thus, while meningeal involvement with sarcoidosis often results in enhancement, the intraparenchymal lesions enhance more rarely.

Involvement of the hypothalamus and the pituitary stalk is characteristic of CNS sarcoidosis. Thickening of the hypothalamus may be apparent on the unenhanced study, but the lesion is more obvious on the postcontrast study when enhancement of the hypothalamus is seen.

Extraaxial masses in patients with CNS sarcoidosis may appear indistinguishable from other extraaxial lesions such as

A B C

Fig. 6.—Case 7: 41-year-old man with speech problems.

A, Axial postcontrast T1-weighted image shows enhancing mass in left cavernous sinus. Note previous left-sided craniotomy for biopsy.

B, Axial unenhanced T2-weighted image shows mass of low signal intensity in cavernous sinus. Note extensive vasogenic edema.

C, Axial postcontrast T1-weighted image obtained after steroid treatment. Note marked decrease in size of extraaxial lesion. The edema also showed a marked decrease on T2-weighted images (not shown).

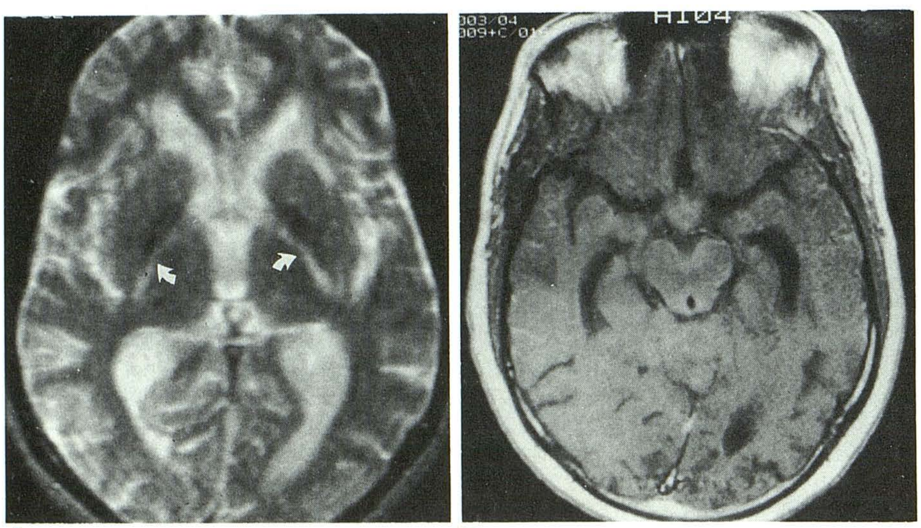

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Fig. 7.—Case 6: 32-year-old man with dementia.

A, Axial unenhanced T2-weighted image shows slight enlargement of ventricles and increased signal intensity of both internal capsules (*arrows*).

B, Axial postcontrast T1-weighted image confirms hydrocephalus. Note enhancement of hypothalamus and pia around brainstem. Sagittal postcontrast T1-weighted image (not shown) confirmed enhancement of hypothalamus and leptomeninges.

Fig. 8.—Case 14: 56-year-old woman with quadriparesis. Sagittal postcontrast T1-weighted image shows enhancing intramedullary mass mimicking a neoplasm.

meningiomas, lymphoma, metastasis, or syphilis. However, our study suggests that these lesions may have a characteristic, very low signal intensity on T2-weighted images, which may suggest the correct diagnosis. Heavily calcified meningiomas, of course, could have a similar appearance.

Even though it was retrospective, our study provides some information about the response of CNS sarcoidosis to treatment. Four patients in our series had repeat studies after steroid therapy. Corticosteroids constitute the most common treatment for sarcoidosis. The disease often responds initially to high doses but may recur as dosage is tapered. The extraaxial lesions as well as the adjacent edema can dramatically decrease in size following steroid treatment (Figs. 6C and 6D). Occasionally, the disease is resistant to high-dose steroids, or treatment needs to be interrupted owing to complications of the therapy. In such extreme cases, immunosuppressive drugs such as cyclophosphamide may be used. In one of our patients, with infiltration of the optic nerve and almost complete loss of vision despite high-dose steroid treatment, vision returned to normal following cyclophosphamide treatment. Simultaneously, infiltration of the optic nerve dramatically diminished and a contralateral extraaxial mass also almost completely resolved. Thus, MR imaging offered an objective measure of the patient's response to therapy.

Involvement of the cranial nerves is a rare complication of CNS sarcoidosis, with peripheral involvement of the 7th nerve the most common site. The optic nerve and the chiasm can also be involved. Cavernous sinus involvement may secondarily affect the cranial nerves coursing in the cavernous sinus. Contrast-enhanced MR imaging can provide, for the first time, evidence of sarcoid infiltration of the optic nerve (by demonstrating enhancement of the optic nerve) in the absence of morphologic changes. However, enhancement of the optic nerve is not specific for sarcoidosis and can be seen in optic neuritis with or without other findings of multiple sclerosis, syphilis, cryptococcosis, and radiation-induced optic neuritis [12]. Hearing loss in patients with CNS sarcoidosis can result from infiltration of the meninges in the internal auditory canal or from intraaxial lesions in the brainstem. MR imaging can easily differentiate between these two conditions (Mark AS et al., paper presented at the annual meeting of the Radiological Society of North America, Chicago, November 1990).

In this series, we found that the addition of contrast agent increased the sensitivity of MR imaging in the detection of CNS sarcoid lesions, permitting the detection of meningeal, parenchymal, optic nerve, and ependymal sarcoid lesions not seen on unenhanced MR scans. If the diagnosis of sarcoidosis can be made on the basis of clinical and imaging information, a CNS biopsy may be unnecessary. For cases in which a CNS biopsy cannot be avoided, contrast-enhanced MR imaging may indicate an optimal site for biopsy by identifying a region of active parenchymal or meningeal granulomata. MR imaging with and without contrast medium may also provide a noninvasive means of monitoring patients' response to therapy. We recommend that contrast agent be used routinely in patients in whom CNS sarcoidosis is suspected, especially if the unenhanced studies are normal or nonspecific.

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