Orbital and Optic Pathway Sarcoidosis: MR Findings

R. F. Carmody, M. F. Mafee, J. A. Goodwin, K. Small, and C. Haery

PURPOSE: To identify and characterize the MR findings of sarcoidosis when it involves the orbit and visual pathways. METHODS: The MR scans of 15 patients, 3 with presumed and 12 with proved orbital or optic pathway sarcoidosis were retrospectively reviewed. RESULTS: Eight patients had MR evidence of optic nerve involvement by sarcoid granuloma. Perineural enhancement was seen in four cases, optic atrophy in one. Three who had had unenhanced scans showed optic nerve enlargement. Nine patients had optic chiasmal involvement. One patient had increased T2 signal in the optic radiations. Three patients had orbital masses that had MR signal characteristics similar to pseudotumor. Five patients had periventricular white matter abnormalities closely resembling multiple sclerosis. CONCLUSIONS: Sarcoidosis should be considered in the differential diagnosis of optic nerve or nerve sheath enhancement on MR. Orbital sarcoidosis has MR characteristics very similar to pseudotumor.

Index terms: Sarcoidosis; Orbits, magnetic resonance; Orbits, disease; Optic tract

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Approximately 25% of patients with sarcoidosis have ophthalmic involvement, most frequently uveitis (1, 2). Visual system abnormalities are the most common extrathoracic manifestations of this disease (3). In addition to the globe, the conjunctiva, extraocular muscles, retrobulbar fatty reticulum, lacrimal gland, optic nerve, chiasm, and optic radiations (meningovascular infiltration) may be affected. These patients may present with confusing clinical and radiologic findings, especially if ophthalmic involvement precedes systemic symptoms. In one series, ocular disease was the first manifestation of sarcoidosis in 19% of cases (4).

Several investigators have characterized the magnetic resonance (MR) findings in neurosarcoidosis (5–13), and some of these reports include descriptions of visual pathway involvement. In this article we describe the MR findings in 15 patients with orbital or optic pathway sarcoidosis in order to show the spectrum of this disorder as it affects the visual apparatus. Three of these patients have presumed but not proved sarcoidosis; they are included because their cases are thought to have instructional value.

Materials and Methods

Fifteen patients, age range 17 to 52 years, with known or suspected orbital or optic pathway involvement by sarcoidosis were examined by MR. Thirteen were black and two were white; nine were female and six were male. The scans were performed from 1988 to 1992 and were reviewed retrospectively by two neuroradiologists. Most were done on a 1.5-T Signa unit (General Electric, Milwaukee, Wis), using the quadrature head coil and a variety of MR protocols. Orbits were examined in the axial plane with both T1- and T2-weighted spin-echo images, in the coronal plane with T1-weighted spin-echo images (3- to 5-mm sections), and in the sagittal plane with T1-weighted images (3-, 5-, or 7-mm section thickness). Twelve of the 15 patients had at least one gadopentetate dimeglumine-enhanced sequence (0.1 mm/kg intravenous administration) on their initial scan. T1-weighted postgadolinium fat-suppressed images were available in two cases. Eight of the patients were neuroophthalmologic referrals; the remaining seven came from a variety of other sources. The diagnosis of sarcoidosis was established by biopsy in eight cases, or by the presence of associated systemic disease (eg, pulmonary sarcoid) in four cases.

Three other patients had strong clinical and radiologic evidence indicative of neurosarcoidosis. The first of these
<table>
<thead>
<tr>
<th>Case</th>
<th>Age/Race/Sex</th>
<th>Symptoms</th>
<th>Basis of Diagnosis</th>
<th>Optic Nerves</th>
<th>Chiasm</th>
<th>Optic Tracts and Radiations</th>
<th>Other Intracranial</th>
<th>Lacrimal Glands</th>
<th>Extraocular Muscles/Orbital Apex</th>
<th>Basal Cisterns</th>
<th>Other</th>
<th>Gadopentetate Dimeglumine</th>
<th>Given?</th>
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<tbody>
<tr>
<td>1</td>
<td>17/B/F</td>
<td>Vision loss, OS ocular pain</td>
<td>(Presumed sarcoid)</td>
<td>Thickened, OS</td>
<td>Thickened</td>
<td>Two small periventricular T2 areas pituitary enlarged</td>
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<td>No</td>
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<tr>
<td>2</td>
<td>32/B/M</td>
<td>Vision loss, OU</td>
<td>Bronchial biopsy</td>
<td>Thickened, irregular margins, OU</td>
<td>Bilateral enlargement</td>
<td>Bilateral enlargement</td>
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<tr>
<td>3</td>
<td>30/B/F</td>
<td>Blurred vision narcolepsy</td>
<td>Bronchial biopsy</td>
<td>Thickening and enhancement</td>
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<tr>
<td>4</td>
<td>18/B/M (Presumed sarcoid)</td>
<td>Vision loss, OD</td>
<td>(Presumed sarcoid)</td>
<td>Thickening and enhancement</td>
<td>Periventricular lesions (T2) which enhanced</td>
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<td>5</td>
<td>26/B/F (Presumed sarcoid)</td>
<td>Vision loss, OD</td>
<td>(Presumed sarcoid)</td>
<td>Diffuse enhancement enlargement on right side</td>
<td>Enhancement on right side</td>
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<td>6</td>
<td>47/W/M</td>
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<td>Optic nerve biopsy</td>
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<td>7</td>
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<td>Tolosa-Hunt syndrome OS</td>
<td>Orbital mass biopsy</td>
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<td>8</td>
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<td>Vision loss OD</td>
<td>Biopsy (site not recorded)</td>
<td>Enlarged, OD</td>
<td>Enlarged</td>
<td>Extensive white matter disease (T1, T2)</td>
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<td>Left orbital apex mass</td>
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<td>9</td>
<td>26/B/M</td>
<td>Headache</td>
<td>Pulmonary biopsy</td>
<td>Bilateral intracranial ON sheath enhancement</td>
<td>Hydrocephalus</td>
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<td>10</td>
<td>51/W/F</td>
<td>Painful proptosis, chemosis OS</td>
<td>Lacrimal gland biopsy</td>
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<td>11</td>
<td>50/B/F</td>
<td>Left face and hand numbness; slowed speech</td>
<td>Systemic disease</td>
<td>Perineural enhancement, intracranial ONs</td>
<td>Enhancement</td>
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<tr>
<td>12</td>
<td>41/B/F</td>
<td>Blurred vision headache, facial pain, right ptosis</td>
<td>Intracranial mass biopsy</td>
<td>Slight compression on right by extraxial mass</td>
<td>Slight enlargement and enhancement</td>
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(case 1) was diagnosed as having sarcoïd optic neuropathy based on the MR findings, parotid and lacrimal gland uptake on gallium scan, clinical examination, and response to steroid therapy. The second patient (case 4), who also presented with unilateral optic neuropathy, had MR evidence of intracranial neurosarcoidosis, parotid uptake on gallium scan, and a negative workup for multiple sclerosis (negative visual evoked response, normal cerebrospinal fluid). The third patient (case 5) was presumed to have sarcoïd based on ophthalmoscopic findings, MR evidence of meningeal involvement, and characteristic response to steroids. Her workup for multiple sclerosis was also negative.

Results

Clinical symptoms and MR findings are summarized in Table 1.

Optic Nerve, Chiasm, and Optic Tract Involvement

Eight patients had abnormalities of the optic nerve by MR (Table 1). In four cases some combination of neural or perineural enhancement was seen after gadolinium administration. One of these four (case 5, presumed sarcoïd) also had uniform enhancement of the intraorbital portion of the optic nerve and nerve head (Fig 1). In this case follow-up MR after a course of steroid therapy revealed marked resolution of prior MR findings (Figs 1F and 1G). In another patient (case 6) the perineural enhancement pattern and clinical presentation suggested optic nerve sheath meningioma, and a biopsy was done (Fig 2). In cases 5 and 6, which had neural as well as perineural enhancement, both patients had profound visual loss. Conversely, in cases 9 and 11, in which only perineural enhancement was found, vision was normal.

Three patients were scanned before the availability of gadopentetate dimeglumine; all had optic nerve enlargement. One of these (case 1, presumed sarcoïd) had resolution of her left eye symptoms after steroid therapy but developed a recurrence on the right after tapering off her medication.

One woman with a long-standing history of bilateral sarcoïd optic neuropathy, now totally blind, showed advanced optic nerve, chiasm and optic tract atrophy (Fig 3). She also had an empty sella and diabetes insipidus, which has been described with sarcoïd infiltration of the pituitary-hypothalamic axis (11, 14).

Nine patients had chiasmal enlargement and/or enhancement, usually associated with pitui-
A and B, Axial gadolinium-enhanced T1-weighted (600/20/4 [repetition time/echo
time/excitations]) images show enhancement of the entire optic nerve (straight arrows),
of the optic papilla (open arrow), and along the anterior left sylvian fissure (curved
arrow). Note involvement of intracranial segment of the right optic nerve (straight black
arrow).

C and D, Coronal enhanced T1-weighted (650/20) images show neural (C) and
perineural enhancement (straight arrows) and left sylvian fissure enhancement (curved
arrow) (D). Note enhancement of the right chiasm (white arrow).

E, Enhanced study after 6 weeks of corticosteroid treatment. Note decreased right
optic nerve enhancement, and no enhancement of left sylvian fissure.

F and G, Enhanced T1-weighted (400/25) (F), and fat-suppressed enhanced (700/
15) images (G) done approximately 1 year later. No residual abnormal enhancement is
seen.

Lacrimal Gland and Posterior Orbital
Involvement

Three patients had MR evidence of lacrimal
gland sarcoidosis. One showed mild, bilateral
gland enlargement with diffuse, homogeneous
enhancement (case 15). Her lacrimal glands were
also enlarged on physical examination. The sec-
ond patient (case 10) had an infiltrating mass
involving the left lacrimal gland and adjacent
structures (Fig 5). The mass was isointense to
muscle on T1-weighted images, became progres-
sively more hypointense on intermediate and T2-
weighted images, and enhanced uniformly. The
third patient (case 2) had bilateral lacrimal gland
and extraocular muscle infiltration, which was
markedly hypointense on T2-weighted images
(gadolinium not available).

One patient (case 7) presented clinically with
Tolosa-Hunt syndrome (painful ophthalmoplegia
cased by cavernous sinus or superior orbital
fissure "inflammation" [15, 16]). MR showed an
infiltrating orbital apex mass which was isointense
to gray matter on T1- and T2-weighted images
and enhanced homogeneously (Fig 6). Biopsy
showed noncaseating granuloma. She also had
extensive white matter changes resembling multiple sclerosis.

**Basal Cisternal Involvement**

Seven of the 12 patients who received gadolinium had abnormal enhancement in the basal cisterns, most commonly in the parasellar region. In the most dramatic of those (case 12), an enhancing mass was seen in the right cavernous sinus region extending posteriorly onto the clivus (Fig 7). Although the preoperative diagnosis was en plaque meningioma, biopsy showed granulomatous inflammation compatible with sarcoidosis.

**Discussion**

Sarcoidosis, a granulomatous disease of unknown cause, involves the central nervous sys-
Fig. 4. Chiasmal sarcoidosis with hydrocephalus in a 26-year-old man (case 9).

A, Axial enhanced T1-weighted (400/11) image shows encasement of intracranial optic nerves (white arrows) and chiasm (black arrow) by enhancing sarcoid tissue.

B, Coronal enhanced T1-weighted (600/11) image shows perineural enhancement surrounding intracranial optic nerves (arrows) and mild ventricular enlargement. Note also basal cisternal enhancement.

tem clinically in 5% of cases (17, 18) but is found in 16% of autopsy cases (19). The optic nerves are occasionally affected; Beardsley et al, in a cooperative retrospective study from 1974 to 1982, found 11 cases of optic nerve sarcoidosis (20). According to this paper, the optic nerve may be affected by several mechanisms: 1) optic disk papillitis caused by intraocular inflammation; 2) papilledema secondary to increased intracranial pressure; 3) retrobulbar neuritis; 4) primary infiltration of the optic nerves and nerve sheaths; and 5) optic atrophy (20, 21).

*Retrobulbar neuritis* refers to a clinical picture of optic neuritis without objective evidence of granulomatous infiltration of the nerve. No granuloma of the optic nerve is seen at funduscopic examination, but definite infiltration of the nerve is seen at imaging. This classification, however, predates the use of gadolinium-enhanced MR, and there may be overlap between retrobulbar neuritis and primary infiltration of the optic nerve.

Four patients in our series had prominent gadolinium enhancement of the optic nerve or nerve sheath similar to that seen with leptomeningeal spread of tumor, nerve sheath meningioma, orbital pseudotumor, or optic neuritis from other causes. The first of those (case 5), a young woman with presumed sarcoid optic neuropathy, illustrates the difficulty in establishing the diagnosis of ocular or orbital sarcoidosis when it precedes systemic disease. Her MR study showed optic nerve, chiasm, and sylvian fissure enhancement. Workup for tuberculous, fungal and bacterial meningitis was negative. No systemic disease was found. In this type of situation the clinician has to choose between optic nerve biopsy, craniotomy with biopsy, or empirical treatment with corticosteroids. This patient received a course of prednisone and improved clinically and radiologically.

Moreover, an optic nerve biopsy that shows noncaseating granuloma does not unequivocally establish the diagnosis of sarcoidosis, which by definition is a multisystem disease (22). In the absence of systemic disease, some have referred to this isolated form of sarcoid as “granulomatous optic neuropathy” (23), or “sarcoid-like disorder” (24). Patient 6, who originally was thought to have had an optic nerve sheath meningioma, had optic nerve biopsy which showed noncaseating granuloma. Unfortunately, after the biopsy he had no light perception in the affected eye and did not recover vision despite intensive steroid treatment. Had sarcoid been considered in the initial differential diagnosis and had he received empirical steroid treatment with follow-up MRs, his outcome might have been better. Beardsley et al also described a patient who had an optic nerve biopsy for suspected meningioma which showed noncaseating granuloma (20). Their patient went from 20/30 vision before surgery to no light perception after surgery. These investigators suggest an empirical course of steroids as a noninvasive diagnostic test before biopsy of suspected nerve sheath meningioma. Gudeman et al also reported two cases of sarcoid optic neuropathy who were biopsied for suspected optic nerve sheath meningioma (25). Our experience, as well as that of several others (23, 25, 26), is that after steroid therapy granulomatous lesions of the optic nerve usually show a decrease in size and intensity of contrast enhancement, but meningiomas do not change.

Three patients, one with presumed and two with definite sarcoid optic neuropathy, had their MR studies before the availability of gadopente-
Fig. 5. Orbital sarcoidosis involving left lacrimal gland and retrobulbar space (case 10).

A, Axial T1-weighted (600/23) image. The mass infiltrates the lacrimal gland, lateral rectus muscle, and retrobulbar fat.

B, T2-weighted (1500/80) image. The mass becomes hypointense to fat, simulating pseudotumor.

C, Axial enhanced T1-weighted (616/23) image shows moderate, homogeneous enhancement of the mass.

tate dimeglumine. Although some thickening and irregularity of the optic nerve could be seen, the lesions were much harder to see than those seen on patients with enhanced scans. We agree with Seltzer et al that contrast enhancement greatly increases the sensitivity of MR for central nervous system sarcoidosis and should be used whenever this diagnosis is being considered (12).

Our three cases of orbital sarcoidosis presenting as retrobulbar infiltrating masses illustrate the difficulty in distinguishing this condition from idiopathic orbital inflammatory disease (pseudotumor), which has the same MR signal characteristics (27). One of these patients was originally thought to have lacrimal gland pseudotumor, but response to steroids was slow and incomplete. Biopsy was compatible with lacrimal gland sarcoidosis. We did not consider lymphoma or metastatic disease in this patient because these conditions are usually hyperintense on T2-weighted images.

Five of our patients also had periventricular white matter lesions of decreased T1 and increased T2 signal intensity. In most cases these lesions were indistinguishable from those seen with multiple sclerosis, and in the absence of other MR evidence of neurosarcoidosis this can be a diagnostic dilemma. For example, Smith et al (10) described five patients in whom the clinical and MR findings (ie, white matter lesions) made differentiation between these two diseases difficult or impossible. The presence of associated leptomeningeal enhancement, as was seen in three of our five patients with white matter lesions, supports a diagnosis of sarcoidosis rather than multiple sclerosis. One of our patients with periventricular lesions also had a peripheral seventh cranial nerve neuropathy—a common finding with neurosarcoidosis but not a feature of multiple sclerosis. Both multiple sclerosis and sarcoidosis may present with optic neuritis, but there are some clinical features that help in differentiating demyelinating optic neuritis from sarcoid optic neuropathy (28). Laboratory findings, such as cerebrospinal fluid values, may also overlap with neurosarcoidosis and multiple sclerosis (10). Moreover, it is certainly possible for the two diseases to coexist.

The sensitivity of MR for detecting optic neuritis (cause unspecified, but usually multiple sclerosis) seems to be about 50% (29, 30). The sensitivity of MR for demonstrating optic nerve sarcoidosis is, however, unknown. Patient 15 in this series was diagnosed clinically as having left optic neuritis caused by sarcoidosis, but this was not detected on her enhanced MR study. However, she had had 6 days of prednisone by the time she was imaged, which would tend to invalidate this case as a false negative. A prospective study to evaluate the sensitivity of MR for sarcoid
Fig. 6. Orbital apex sarcoidosis presenting as Tolosa-Hunt syndrome (case 7).

A, Axial T1-weighted (400/25) image shows a left orbital apex mass extending through the superior orbital fissure (white arrow).

B and C, Intermediate (3200/30) (B) and T2-weighted (3200/80) (C) images show the mass to be approximately isointense to gray matter.

D, T1-weighted (600/15) fat-suppressed enhanced image shows marked enhancement of the mass, which extends through superior orbital fissure into middle cranial fossa (arrow).

Fig. 7. Cavernous sinus and clival involvement.

A, T1-weighted (800/20) enhanced axial image shows an enhancing mass between right cavernous sinus and medial temporal lobe (large arrows). Also note compression of the right fifth nerve (small arrow) in the pontine cistern.

B, T2-weighted (2400/80) axial image shows the mass to be hypointense to brain.

C, T1-weighted (800/25) enhanced sagittal image shows an enhancing clival mass (arrows) resembling meningioma.

optic neuritis would be very helpful but difficult to accomplish because of the rarity of this condition.

In summary, the MR findings of orbital and optic pathway sarcoidosis may closely resemble several other diseases, both in anatomic location and signal characteristics. Isolated optic nerve sarcoidosis is virtually impossible to diagnose without biopsy in the absence of systemic involvement. However, in certain clinical settings,
a trial of steroid therapy may be helpful in distinguishing between optic nerve sheath meningioma and sarcoidosis. Leptomeningeal enhancement is strong supportive evidence of sarcoidosis providing that tuberculosis, fungal disease, syphilis, and neoplasm can be ruled out by appropriate clinical and laboratory tests. A gadopentetate dimeglumine–enhanced study should be performed whenever orbital or neurosarcoidosis is suspected.

References