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MR Findings in Acute and Chronic Coccidioidomycosis Meningitis

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Purpose: To characterize MR findings in acute and chronic coccidioidomycosis meningitis and relate the imaging features to the clinical course. **Methods:** We reviewed MR scans and clinical findings of 12 patients with coccidioid meningitis. **Results:** Patients with active or untreated disease were found to have hydrocephalus and intense enhancement of the cervical subarachnoid space, basilar, sylvian, and interhemispheric cisterns on postcontrast MR scans. Focal parenchymal signal abnormalities suggesting ischemia or infarction were common. Abnormal MR enhancement decreases during therapy, although patients develop cortical and/or brain stem atrophy. **Conclusions:** Widespread cisternal and cervical subarachnoid meningeal involvement is common in coccidioid meningitis. Serial contrast MR imaging reflects the effects of therapy in patients with coccidioid meningitis.

Index terms: Meningitis; Brain, magnetic resonance; Spine, magnetic resonance; Contrast media, paramagnetic

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Central nervous system (CNS) involvement is the most serious consequence of disseminated coccidioidomycosis. This is usually manifested as basilar meningitis with attendant cranial neuropathies, hydrocephalus, and vascular occlusions (1, 2). The CT findings are similar to those of other infectious meningitis, and are nonspecific (3-5). The magnetic resonance (MR) imaging appearance of infectious meningitis (6, 7) including coccidioid meningitis (8) has been reviewed, and MR appears to be the best imaging modality. This article describes MR imaging features of coccidioid meningitis at its presentation and during chronic therapy.

Subjects and Methods

Twelve cases of coccidioid meningitis were studied retrospectively from the records of our institutions. Patients ranged in age from 5 to 53 years; there was one female.

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Two patients were imaged serially over several years. Two patients had AIDS. CNS coccidioid infection was confirmed by cerebrospinal fluid (CSF) complement-fixing antibody titers, direct culture, or demonstration of the organism by meningeal biopsy.

MR imaging was performed on a 1.5-T GE Signa unit (GE, Milwaukee, WI) (10 patients) or a 0.5-T Picker unit (Picker International, Cleveland, OH) (two patients). All patients had precontrast T1-weighted images, 500-800/15-30/1-2 (TR/TE/excitations); intermediate (proton density) weighted images, 2200-3000/30/1; and T2-weighted images, 2200-3000/80-110/1-2. All except patient 9 were studied with T1-weighted images after intravenous injection of 0.1 mmol/kg Gd-DTPA (Magnevist, Berlex Imaging, Wayne, NJ). The images were reviewed by a neuroradiologist who was unaware of the patients' clinical status. Ventricular enlargement was graded none, mild, moderate, or severe. The presence or absence of MR signal abnormalities suggesting transependymal flow of CSF was also noted. Meningeal enhancement was graded 0, +, or ++, respectively, for normal or mildly or markedly abnormal intensity and distribution. T2-weighted images were reviewed for the presence and location (cerebral and/or cerebellar) of signal abnormalities consistent with cerebral ischemia/infarction.

Results

A summary of the MR results is given in Table 1. Four patients had MR studies at presentation or prior to intensive intrathecal or systemic antifungal therapy (patients 3, 6, 7, and 12). Cisternal

TABLE 1: Summary of MR and clinical features of 12 patients with coccidioidomycosis meningitis

Patient	Age, Sex	Prior Therapy	Degree of Meningeal Enhancement on Postcontrast T1 studies	Ventricular Enlargement	Abnormal High Signal on T2-Weighted Acquisition (ischemia/infarction)	Associated Findings
1	48, M	14 years IT amphotericin	0	Severe	Multiple cerebral/cerebellar	VP shunt
2	5, M	1 year IT miconazole	++	None	Absent	VP shunt
3	24, F	None	++	Moderate	Absent	VP shunt
4	40, M	7 years IT amphotericin	++	Mild	Multiple cerebral/cerebellar	VP shunt; pontine atrophy
		8 months later: IT amphotericin; oral fluconazole	+	Moderate	Multiple cerebral/cerebellar	CSF WBC 549
		18 months later: IT amphotericin; oral fluconazole	+	Moderate	Multiple cerebral/cerebellar	CSF WBC 485
5	28, M	14 years IT amphotericin	0	Moderate	Absent	None
6	53, M	None	++	Moderate	Multiple cerebral	None
7	36, M	None	++	Mild	Single cerebral	AIDS; VP shunt
		7 months IT amphotericin	+	Mild		Medial temporal abscess presumed coccidioidal
		11 months IT amphotericin	0	Mild	Single cerebral	Medial temporal lesion resolving
8	46, M	6 years IT amphotericin; fluconazole	++	None	Absent	VP shunt
9	29, M	None	Gd-DTPA not given	None	Absent	AIDS; midbrain abscess
10	30, F	3 years IT amphotericin; fluconazole	0	None	Absent	Disease quiescent by CSF parameters when MR performed
11	30, M	2 years IT amphotericin; fluconazole	0	None	Absent	Disease quiescent by CSF parameters when MR performed
12	20, M	7 months amphotericin 1 year prior to MR (non-compliant)	++	Moderate	Absent	None

Note.—IT, intrathecal; VP, ventriculoperitoneal; WBC, white blood cell.

obliteration and abnormal enhancement were prominent, involving all of the basilar cisterns, as well as the interhemispheric and sylvian cisterns (Figs. 1 and 2). Similar patterns of involvement were seen in patients receiving long-term intrathecal therapy who had CSF findings indicating active disease (patients 2, 4, and 8) (Fig. 3). During treatment, progressive diminution of enhancement paralleled improvement of CSF parameters in patients 4 and 7 (Fig. 4). Four other patients still receiving antifungal therapy had quiescent disease as evidenced by CSF findings (patients 1, 5, 10, and 11). In these patients, Gd-DTPA-enhanced MR scans did not disclose abnormal meninges, but pretreatment scans were not available for comparison.

Ventricular enlargement of varying degrees was identified in seven patients. MR signal abnormality consistent with transependymal flow of CSF (periventricular edema) was not prominent in any patient. Focal parenchymal signal abnormalities on MR suggesting ischemia/infarction

were seen in four patients, predominantly in the deep white matter. Cerebral volume loss was evident in patients 4 and 7 (Figs. 4 and 5). A solitary, autopsy-proved *Coccidioidomycosis immitans* parenchymal abscess occurred in patient 9 who also had AIDS. The MR finding was a discrete area of increased signal on T2 scan in the right midbrain with a low signal center suggesting necrosis. A presumed coccidioidal abscess was also identified in patient 7 (Fig. 5). Pathologic confirmation is lacking and the abnormality may represent meningeal enhancement within the choroidal fissure or a deep sulcus.

Striking abnormal enhancement of the dura and subarachnoid spaces dorsal and ventral to the cervical spinal cord was seen in three patients. Spinal cord flattening and compression by the thick inflammatory collections occurred in two of these cases (patients 3 and 6) (Fig. 1C). These individuals rapidly developed quadriplegia and sensory findings suggesting anterior spinal artery occlusion.

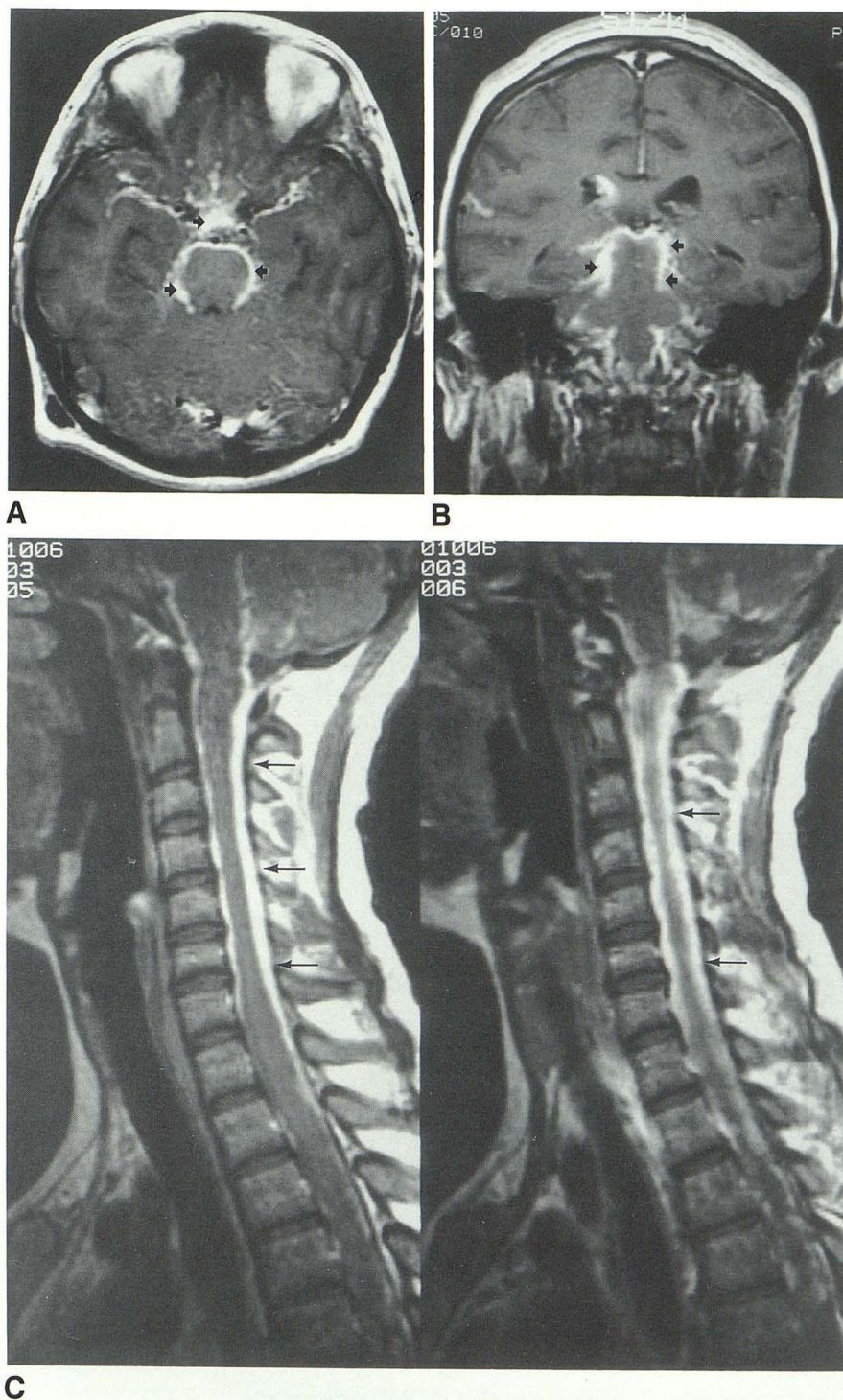


Fig. 1. Patient 3; 24-year-old woman presenting with quadriplegia and mental status changes.

A and B, Postcontrast T1-weighted (500/15) axial and coronal scans show widespread cisternal enhancement (arrows).

C, Postcontrast T1-weighted sagittal (500/20) scan demonstrating marked enhancement of thick meningeal granulation tissue coating entire cervical spinal cord (arrows).

Discussion

While human infection with *C. imitans* is usually subclinical, disseminated disease occasionally occurs. Meningitis is the most serious complication of disseminated coccidioidomycosis, and has been reported to have a predilection for the basilar cisterns and upper cervical subarachnoid

space (2). A particularly severe inflammatory response occurs, causing extensive arachnoidal scarring. Morbidity and mortality are related to uncontrollable hydrocephalus, progressive bulbar palsies, and spinal cord involvement (1, 2, 9). Although multiple infarcts secondary to inflammatory vasculitis are common in tuberculous and

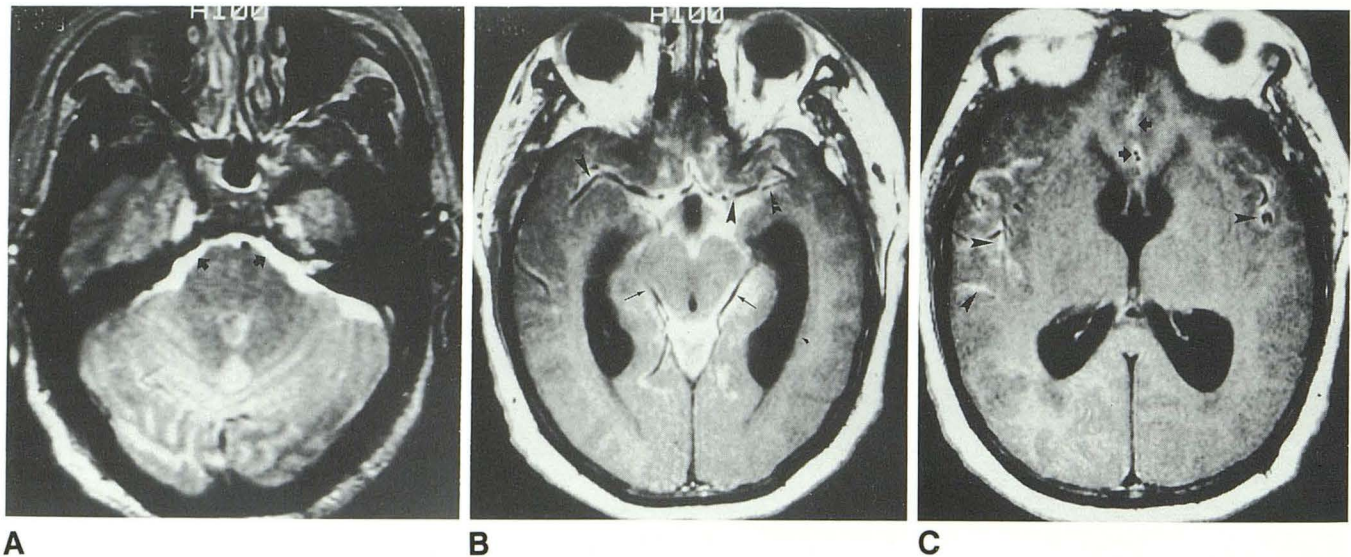


Fig. 2. Patient 6; 53-year-old man admitted for evaluation of dementia. Proton density (3000/30) axial images (A) show abnormal signal in the prepontine and cerebellopontine cisterns (arrows). B and C, Gd-DTPA-enhanced T1-weighted (600/20) images show sylvian (arrowheads), perimesencephalic (small arrows), and interhemispheric (large arrows) enhancement and acute hydrocephalus.

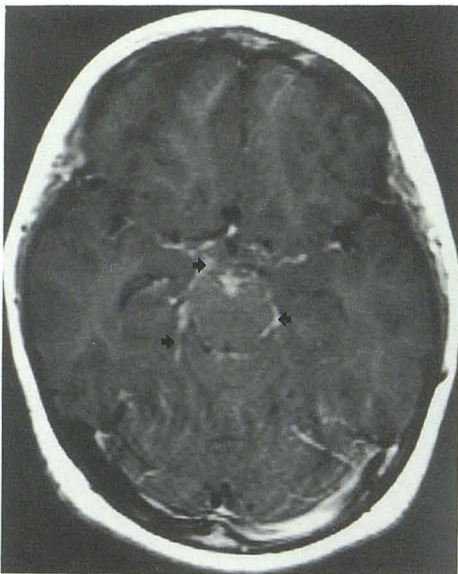


Fig. 3. Patient 2. Boy age 5 with meningeal enhancement after 1 year intrathecal therapy (arrows); T1-weighted (500/15) axial image. CSF cell counts indicated ongoing active disease.

other fungal meningitides, they are thought to be uncommon in coccidioidal meningitis (10).

In our cases, proton-density images demonstrated abnormal signal within the subarachnoid spaces of active cases. Devoid of any blood-brain barrier, these hypervascular areas enhanced intensely on T1-weighted images following intravenous Gd-DTPA. Involvement of the sylvian and interhemispheric cisterns was common. Persistent disease sequestered in these supratentorial locations may contribute to the difficulty in eradicating coccidioidal infections using amphotericin

B delivered by cisterna magna puncture (11, 12). Patients 4 and 7 exhibited sylvian foci of persistent contrast enhancement despite overall clinical, CSF, and MR scan improvement. Radiologic improvement during therapy has also been documented by CT for tuberculous meningitis (13).

Coccidioidal brain abscesses are uncommon lesions (5) and it is noteworthy that the two in this series occurred in AIDS patients. A high incidence of symptomatic coccidioidomycosis, including meningitis, has been reported among HIV-infected patients living in endemic areas (14). Impaired cell-mediated immunity and a diminished inflammatory response in these patients may be predisposed to the development of a coccidioidal brain abscess. Similarly, CNS involvement by the fungus *Cryptococcus neoformans* usually occurs as meningitis; parenchymal involvement is seen more commonly in the setting of HIV infection (15).

Symptomatic vascular occlusions in our series were limited to two patients suffering anterior spinal artery syndromes. Extensive cervical meningeal enhancement was seen in both cases; abnormal spinal cord MR signal, reported to occur in anterior spinal artery occlusion (16), was not documented.

In summary, Gd-DTPA-enhanced MR imaging reflects the initial extent of disease, and response to treatment, of coccidioidal meningitis. Widespread cisternal and cervical meningeal involvement is frequent. Ventricular enlargement without periventricular enlargement is common, as are

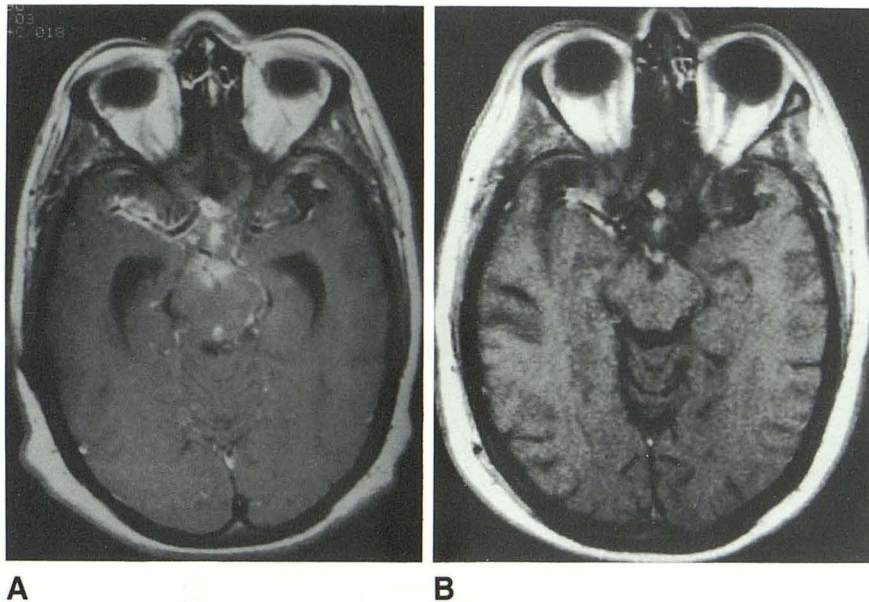


Fig. 4. A and B, Patient 4; 40-year-old man receiving intensive intrathecal therapy. Improvement in meningeal enhancement seen on Gd-DTPA-enhanced T1-weighted (600-700/20) axial images during 18 months therapy (A, baseline; B, 18 months later).

focal areas of high signal intensity in central white matter on T2-weighted images. AIDS patients living in areas endemic for coccidioidomycosis are particularly susceptible to brain abscess.

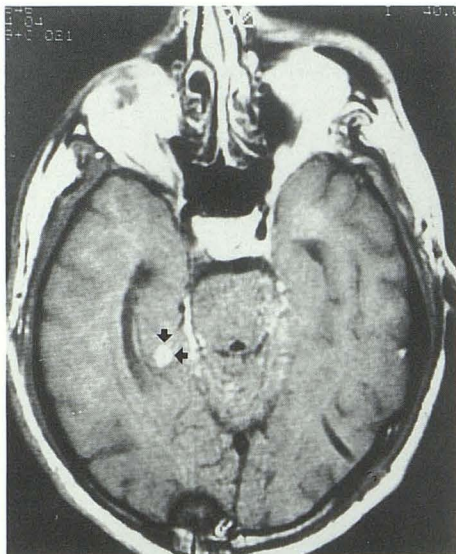


Fig. 5. Patient 7; 37-year-old man with AIDS and coccidioidal meningitis who has had a ventriculoperitoneal shunt. Gd-DTPA-enhanced T1-weighted (800/20) axial image showing coccidioidal abscess in the mesial right temporal lobe, or possibly abnormal meningeal enhancement in the choroidal fissure (arrows).

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