Efficacy of Gadolinium in MR Brain Imaging of HIV-Infected Patients

Michael Tuite,[1] Leena Ketonen,[1,4] Karl Kieburtz,[2] and Brigid Handy[3]

PURPOSE: To determine the value of gadolinium in routine head MR imaging of HIV-infected patients. **METHODS:** One hundred and three consecutive human immunodeficiency virus-infected patients referred for head MR imaging were scanned without and with intravenous gadopentetate dimeglumine (Gd-DTPA) contrast. **RESULTS:** The precontrast scans of 82 patients were either normal, or had atrophy or diffuse white matter changes only. Sixteen of these 82 demonstrated enhancing abnormalities: eight meningeal/ependymal enhancement and eight focal enhancing lesions. Twenty-one of the 103 scans had focal or mass lesions on the precontrast images; in eight of these scans, new information was obtained with Gd-DTPA. Of the 24 patients in both groups where new information was obtained with Gd-DTPA, the information contributed to a change in the clinical care of nine patients. **CONCLUSION:** Gadolinium-enhanced MR is useful in the management of selected patients with human immunodeficiency virus infection, for example those with symptoms suggesting meningeal involvement, focal brain lesions, or if the unenhanced MR does not explain all the patient's symptoms.

Index terms: Acquired immunodeficiency syndrome (AIDS); Contrast media, paramagnetic

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Almost 40% of patients infected with the human immunodeficiency virus (HIV) have central nervous system (CNS) complications, including the acquired immunodeficiency syndrome (AIDS) dementia complex, opportunistic infections, and tumors (1). Brain imaging, as well as the clinical examination and cerebrospinal fluid (CSF) analysis, is an important part of the evaluation of patients with these complications (2). The primary purpose of brain imaging is to detect potentially treatable opportunistic processes (3). Magnetic resonance (MR) imaging has recently been demonstrated to have greater sensitivity than computed tomography (CT) in detecting brain abnormalities in this patient population (3, 4). This increased ability to detect abnormalities has led to changes in the clinical management of some patients (3).

Recently, contrast-enhanced MR has been shown to further increase the sensitivity of MR in certain clinical situations: meningitis, meningeal carcinomatosis, and difficult-to-visualize masses (5–7). In addition, contrast enhancement can also help to distinguish a mass lesion from surrounding edema, thus aiding stereotactic biopsy (8). No reports have been published, however, comparing noncontrast and contrast-enhanced MR in a large group of HIV-infected patients. To examine this issue, we determined what additional MR imaging information was obtained with the use of intravenous gadolinium dimeglumine (Gd-DTPA) contrast in our HIV-infected population, and then determined whether this information influenced patient care.

Materials and Methods

The patient population for this study was composed of all patients seen in our infectious disease clinic or admitted to our hospital with a diagnosis of HIV infection, during the period January 1989 through January 1991. Because we had begun using Gd-DTPA enhancement in the head MR imaging of all HIV-infected patients at our institution, a radiology department list of patients who had received a Gd-DTPA-enhanced MR scan was matched with the above

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From the Departments of [1] Radiology, [2] Neurology, and [3] Preventive Medicine, University of Rochester Medical Center, Strong Memorial Hospital, 601 Elmwood Avenue, Rochester, NY 14642.

[4] Address reprint requests to Leena Ketonen, MD, Department of Radiology, Box 648, University of Rochester Medical Center, 601 Elmwood Ave, Rochester, New York 14642.

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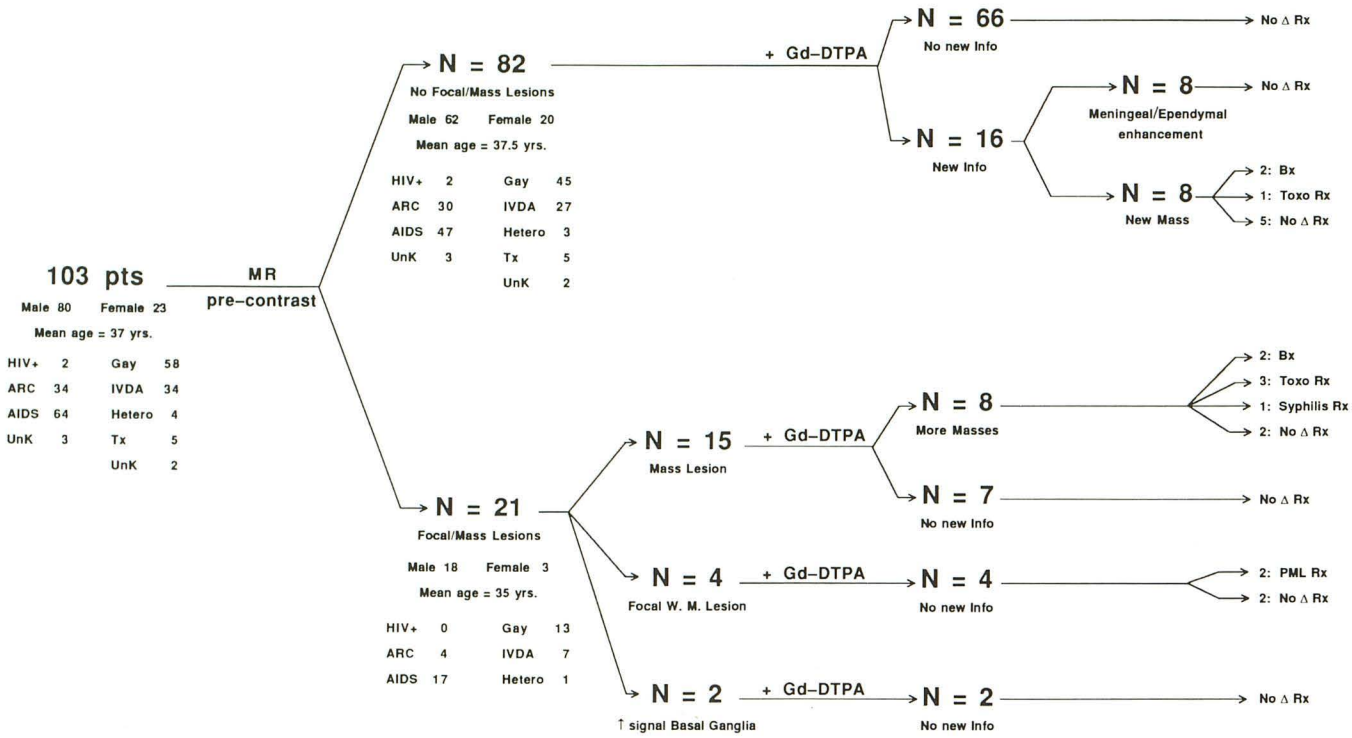
TABLE 1: Summary of clinical and MR findings



Legend: HIV+, asymptomatic human immunodeficiency virus infected; AIDS, acquired immunodeficiency syndrome; ARC, AIDS-related complex; UnK, unknown; IVDA, intravenous drug abuser; Hetero, heterosexual; Tx, transfusion, MR, magnetic resonance; Gd-DTPA, gadopentetate dimeglumine; W.M., white matter; Bx, biopsy; Toxo, toxoplasmosis; Rx, therapy; PML, progressive multifocal leukoencephalopathy.

list of HIV-infected patients to give our final study population. Hospital chart numbers were used to protect patient confidentiality.

Using this method, 103 patients were identified, with a mean age of 37 years. Eighty men and 23 women comprised the study population. The risk factors for HIV infection were: gay/bisexual, 58; intravenous drug use, 34; heterosexual transmission, four; transfusion, five; unknown, two. The stage of illness was: asymptomatic, two; AIDS-related complex (ARC), 34; AIDS, 64; unknown, three.

All the scans were obtained on a 1.5-T (Signa, GE, Milwaukee, WI) MR scanner. Each patient had T1-weighted (600/20) (TR/TE) sagittal and coronal, and intermediate (2000/20) and T2-weighted (2000/80) axial sequences performed before Gd-DTPA administration. After intravenous Gd-DTPA, each patient had T1-weighted (600/20) axial, and TR/TE 150/10, 60° flip angle coronal sequences performed.

Consensus readings of the scans were done by two radiologists blinded to the original readings and the clinical status of the patient. The precontrast images were reviewed and graded regarding atrophy, diffuse white matter changes, focal high signal lesions, and mass lesions. Patients were divided into two groups by whether or not they had focal or mass lesions. The group that did not have a focal or mass lesion either had a normal scan, or had atrophy or diffuse white matter changes only. These latter abnormalities could be seen in patients in the other group, but they in addition had focal or mass lesions. The postcontrast images were then analyzed and any new findings noted. If Gd-DTPA provided additional imaging information, the patient's chart was reviewed to determine if this information had any impact on patient care.

Eleven randomly selected scans were reviewed a second time to determine the reliability of the readings, and the grading was identical in all 11 cases.

Results

Of the 103 precontrast scans, 82 demonstrated no focal or mass lesions (Table 1). Twenty-one precontrast scans had focal lesions of the following types: mass lesions, 15; focal white matter lesions, four; basal ganglia high signal, two. This latter group tended to have later stages of HIV infection, but had a similar gender and risk factor distribution compared to the group with no focal or mass lesions.

Following the intravenous administration of Gd-DTPA, 16 of the 82 (19%) patients in the group with no focal or mass lesions demonstrated new findings: eight enhancing parenchymal le-

sions, and eight meningeal/ependymal enhancement. In no case was there enhancement of the diffuse white matter changes. The finding of a new enhancing lesion contributed to a change in clinical care for three patients: biopsy in two, and empiric toxoplasmosis therapy for the third, who had multiple lesions. There was no change in the clinical care of the patients with meningeal or ependymal enhancement (Fig. 1).

Of the 15 patients with mass lesions, Gd-DTPA enhancement revealed more masses in eight (38%) (Figs. 2 and 3). This additional information helped in guiding the care of six patients (29%): biopsy in two, empiric toxoplasmosis therapy in three (Fig. 4), and syphillis therapy in one (Fig. 5). No additional information was gained in the patients with basal ganglia high signal, or with focal white matter lesions. In the former, pathologic correlation with the MR finding is not available. Of the patients with focal white matter lesions, however, there were two in whom the absence of enhancement was supportive of a diagnosis of progressive multifocal leukoencephalopathy (9). It was felt that this diagnosis could

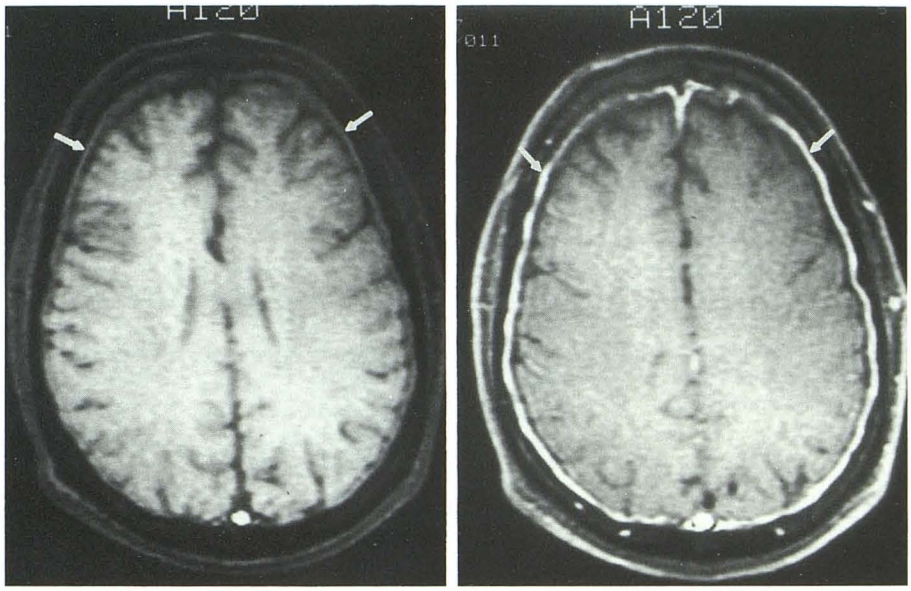


Fig. 1. Patient with increasing confusion and headache.

A, Axial T1-weighted (600/20) image shows thickened meninges (*arrows*).

B, Postcontrast T1-weighted (600/20) image demonstrates marked meningeal enhancement (*arrows*). Because CSF cultures were negative, the patient was felt to have an aseptic meningitis.

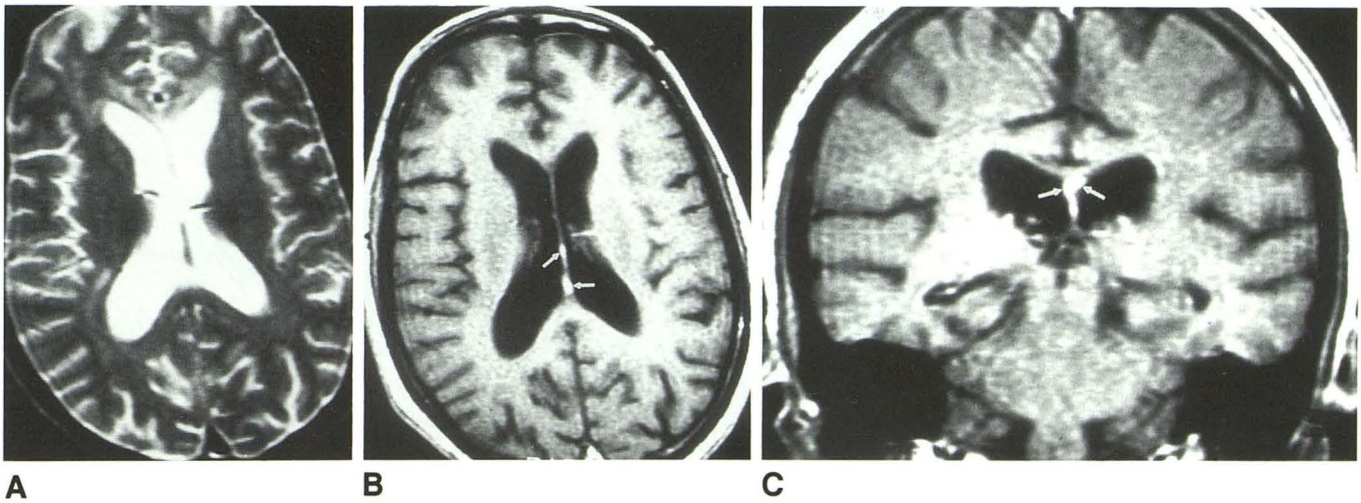


Fig. 2. Patient with rapidly worsening dementia. *A*, It is difficult to identify a mass or surrounding edema in the posterior fornix on the axial T2-weighted (2000/80) image due to the high signal CSF in the dilated lateral ventricles. On the postcontrast T1-weighted (600/20) axial (*B*) and coronal (*C*) images, an enhancing mass in the posterior fornix is identified (*arrows*). No mass was seen in this region on the unenhanced T1-weighted images (not shown). The patient did not improve on empiric antitoxoplasmosis therapy given to treat this and several other parenchymal lesions, and at autopsy was shown to have CNS lymphoma.

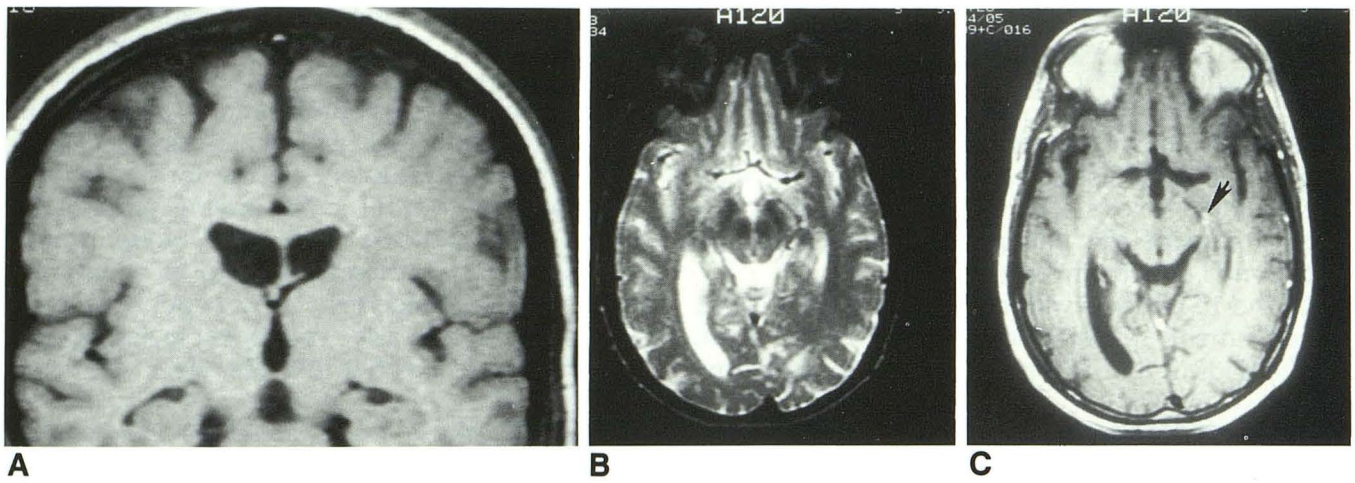


Fig. 3. Patient with one mass lesion on precontrast images. *A*, T1-weighted (600/20) coronal and *B*, T2-weighted (2000/80) axial images reveal no definite mass near the left temporal lobe. Postcontrast T1-weighted (600/20) axial image (*C*) reveals an enhancing mass just above the left temporal horn (*arrow*), seen better on the corresponding (*D*) coronal T1-weighted (600/20) postcontrast image (*arrows*). A T2-weighted coronal sequence was not performed. Because this was the patient's second mass, he was empirically started on antitoxoplasmosis therapy.

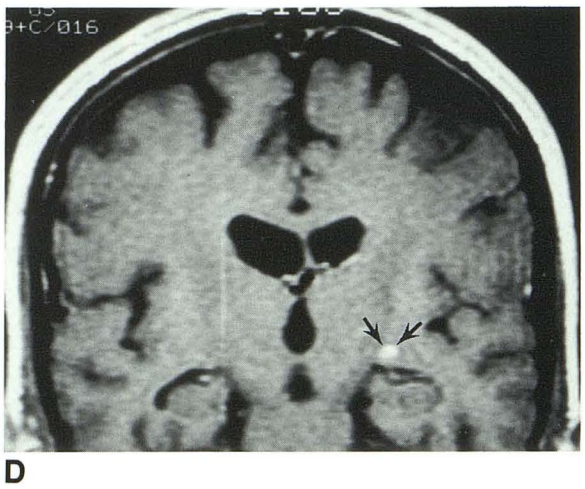
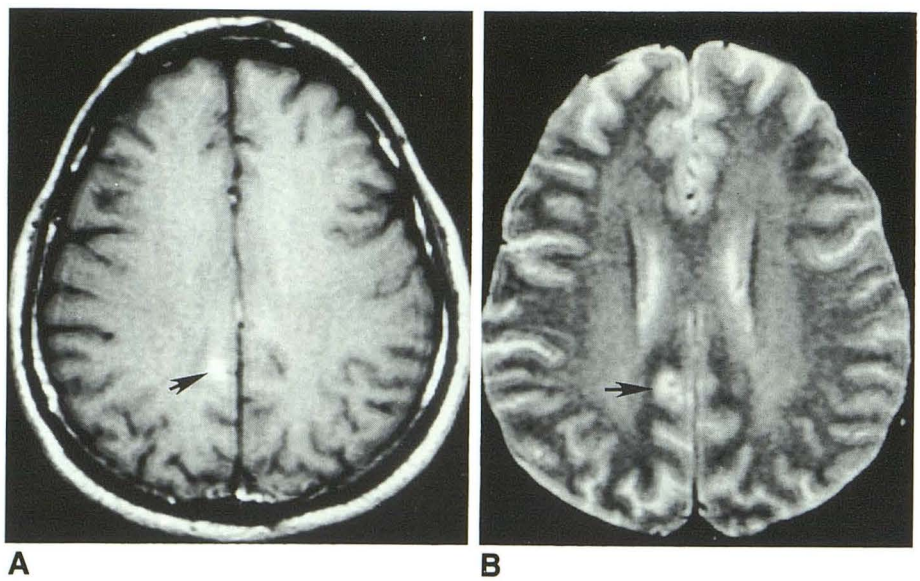
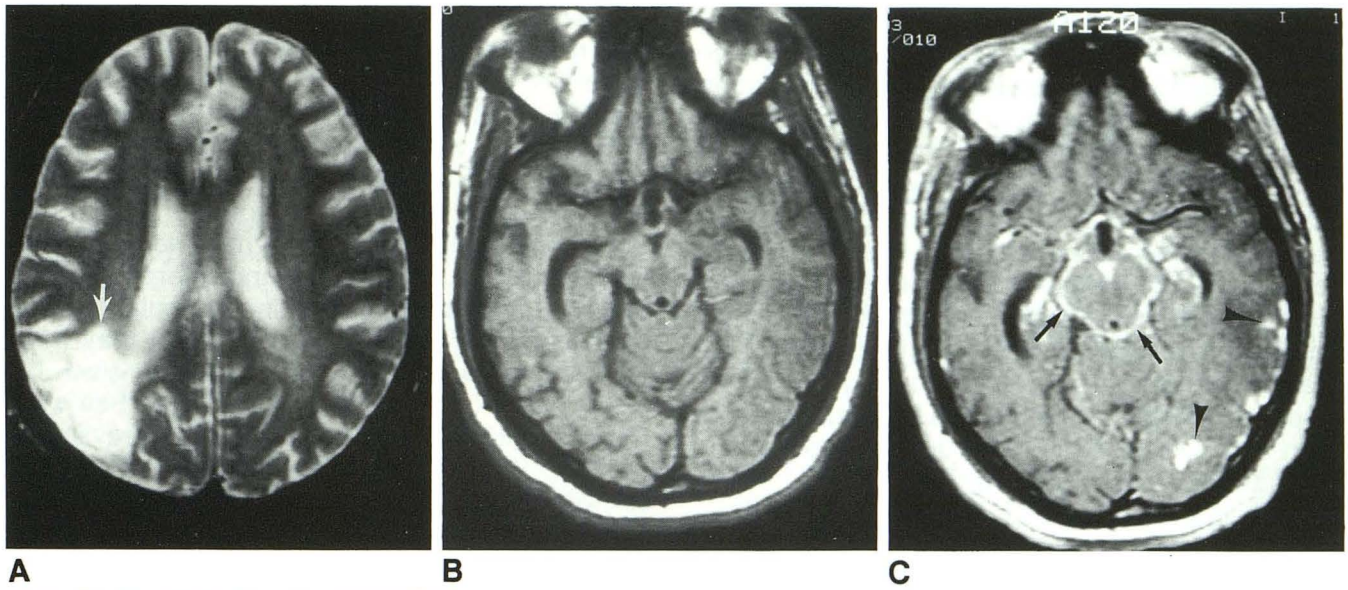


Fig. 4. Patient with several mass lesions that responded to antitoxoplasma therapy. One lesion in the right occipital lobe seen on *A*, the postcontrast T1-weighted (600/20) image (*arrow*) was missed on *B*, the T2-weighted image (*arrow*). In retrospect, what was felt to be a prominent sulcus is in fact edema around the enhancing lesion. The precontrast T1-weighted axial image (not shown) was unremarkable in this area.



not have been made confidently on the unenhanced images alone. One patient was begun on empiric treatment (interferon α), and the other had a confirmatory brain biopsy.

Combining both groups, new information was obtained in 24 of 103 postcontrast scans (23%). This information contributed to a change in the clinical care of nine patients (9%). The most



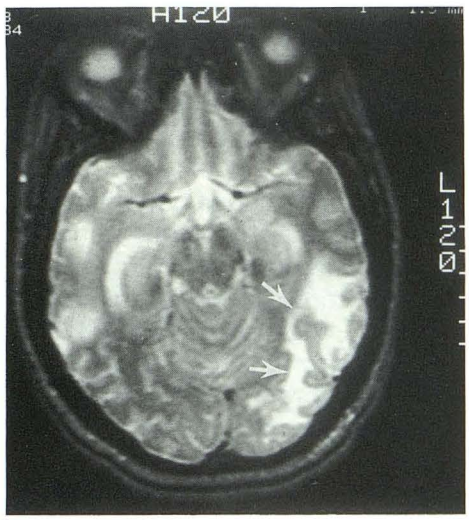


Fig. 5. Patient with progressive cognitive decline. *A*, Axial T2-weighted (2000/80) image reveals a wedge-shaped high signal region (*arrow*) consistent with infarction. *B*, Pre- and *C*, postcontrast T1-weighted (600/20) axial images demonstrate enhancing basilar meninges (*arrows*) and enhancing parenchymal lesions (*arrowheads*). The T2-weighted (2000/80) axial image (*D*) at this level shows the white matter edema (*arrows*) surrounding the parenchymal lesions. Because the patient also had a positive serum RPR (rapid plasma reagin) and a CSF lymphocytosis, the MR findings were felt to represent meningovascular neurosyphilis. He was treated successfully with intravenous penicillin, and is neurologically and cognitively asymptomatic 1 year later.

common interventions were brain biopsy and empiric toxoplasmosis therapy. In addition, the absence of contrast enhancement in the two patients with progressive multifocal leukoencephalopathy was useful in guiding their clinical care. Thus, the information obtained from the postcontrast scans contributed to the management of 11 patients.

Discussion

Recent research has focused on comparing MR and CT imaging of HIV-infected patients in an attempt to identify the optimum imaging strategy, with MR emerging as the more sensitive modality (3, 4). In certain settings, Gd-DTPA enhancement has been shown to increase further the sensitivity for lesions when compared with unenhanced MR (5–7). However, no large study has addressed the value of routinely giving Gd-DTPA to an unselected population of HIV-infected patients. In our study, we did not compare enhanced CT with enhanced MR, but only looked at unenhanced versus Gd-DTPA-enhanced MR. In addition, this was a retrospective study done by analyzing images obtained from a set of pulse sequences designed to maximize imaging information, and not specifically devised for this study.

Approximately 80% (82/103) of the MR scans done in our patient population were normal or revealed only atrophy or diffuse nonspecific white matter changes. These latter findings are commonly found in this patient population and are most likely due to HIV infection itself (10). With Gd-DTPA, enhancing focal lesions were found in eight (10%) of these 82 scans. While in three

patients this finding modified the clinical management, the newly seen lesions in the other five were either too small to biopsy, or of uncertain clinical significance. In each of these latter cases, the clinician elected to observe the patient clinically. In one patient, a follow-up MR scan was obtained during the study period and the previously detected lesion was no longer seen. In retrospect, the original enhancing lesion may have represented a prominent vessel. In another patient, an autopsy revealed multiple small cerebral hemorrhages, one of which may have corresponded with the small area of enhancement seen with Gd-DTPA (11). In the other three patients there was no follow-up.

Even in patients with known mass lesions on precontrast scans, additional masses were identified in eight of 15 patients (Figs. 2–4). These additional lesions were all less than a centimeter and were located in areas where edema is difficult to see on the T2-weighted images (Figs. 3 and 4). Identifying additional lesions is important because toxoplasmosis is reported to be more common than lymphoma in those HIV-infected patients who have multiple mass lesions (12), and at our institution these patients are treated empirically with antitoxoplasmosis therapy. Although differentiating toxoplasmosis from lymphoma by their MR appearance alone has proven unreliable in the past (1, 12, 13), a recent article by Dina has reported lesion characteristics that he feels help distinguish these two entities (14).

In three of our patients (3%), Gd-DTPA revealed multiple masses when only a single mass was visible on the unenhanced scans. Based on the articles by Ciricillo and Rosenblum (12) and Cohn et al (15), our neurologist (K.K.) usually recommends biopsy in any patient with a new solitary mass and a negative or stable toxoplasmosis titer. All three of these patients had an elevated toxoplasmosis titer (obtained for other reasons) for at least several months before the onset of CNS symptoms that led to their neuroimaging studies. Although our neurologist probably would have recommended biopsy if only a single lesion had been detected in these cases, it could not be determined from the patients' charts if a single lesion would have been treated empirically anyway. Because multiple enhancing lesions were seen, antitoxoplasmosis therapy was initiated. All three demonstrated clinical improvement, and in two of these patients, a follow-up MR scan was obtained that showed decreasing lesion size.

Gd-DTPA was also useful in the patient who was felt to have neurosyphilis (Fig. 5). Although the patient had a history of poorly treated syphilis, his CSF VDRL (Venereal Disease Research Laboratory) test was nonreactive. Bacterial, mycobacterial, and fungal cultures of CSF were also negative. The enhancement of the basilar meninges and multiple parenchymal masses, along with the areas of ischemia and infarction, were highly suggestive of meningovascular neurosyphilis (16, 17). Although the patient may have been treated with antisyphilitic therapy given his history alone, his clinicians stated that they were more confident in their diagnosis after reviewing the MR. With intravenous penicillin, the patient showed rapid improvement both clinically and by MR, and is asymptomatic on clinical examination 1 year later.

Ependymal enhancement was seen in four patients, but was of unknown clinical significance. This enhancement has been shown to correlate with active cytomegalovirus infection (18), but we did not obtain pathologic correlation in our subgroup of patients.

In summary, Gd-DTPA provided additional imaging information in over 20% of our patients, and in about 10% of patients this information helped modify clinical care. Based on this experience, we recommend the use of Gd-DTPA in patients who have symptoms suggesting meningeal involvement, focal brain lesions, or if the unenhanced MR does not explain all the patient's symptoms. It may also be useful if the lesions on the unenhanced scan need further characterization, or if surgery is planned. Due to the additional cost and time involved, the decision to use Gd-DTPA should be made individually for each patient.

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