

Persistent MR Contrast Enhancement of Calcified Neurocysticercosis Lesions

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PURPOSE: We sought to determine whether cysticercosis lesions in the brain continue to enhance after nodular involution and complete calcification, and to investigate the clinical significance of this finding with respect to seizure recurrence after cysticidal treatment.

METHODS: Serial contrast-enhanced MR images were obtained in all patients with neurocysticercosis seen at our hospital over a 6-year period (1991–1997). From this group, all patients with nodular calcified lesions were selected for study.

RESULTS: Sixteen of 29 patients with neurocysticercosis had nodular calcified lesions. Six of these 16 had rim enhancement of nodular calcified lesions for at least 1 year after imaging evidence of complete calcification. Three of these six patients with enhancing, calcified lesions continued to experience seizures. Three of the 10 patients without enhancement also continued to have seizures.

CONCLUSION: Contrary to the literature, which states that enhancement and disease activity cease with calcification, six (38%) of 16 patients had lesions that continued to enhance after complete calcification. This abnormality may be a risk factor for posttreatment seizures or may suggest eventual resorption of the calcified lesion.

The four stages in the evolution of cysticercosis lesions in the brain are vesicular, colloid vesicular, granular nodular, and nodular calcified. The fourth and final stage is characterized on computed tomographic (CT) scans as a calcified, nonenhancing nodule (1). Many cases of neurocysticercosis are now being followed up by magnetic resonance (MR) imaging rather than by CT. Although MR imaging is not as sensitive to the presence of calcium as is CT, it has greater sensitivity for contrast enhancement. This is particularly true in and around calcified lesions. On CT scans, the high attenuation of the calcium obscures the contrast agent. On MR images, contrast agent is more visible around calcified lesions because it increases signal intensity on T1-weighted images, opposite to the effect of calcium, which reduces signal intensity. In this manner, MR imaging is uniquely suited to the study of the brain adjacent to calcified lesions.

During the course of routine clinical work, we observed several cases of persistent contrast enhance-

ment of nodular calcified cysticercosis lesions. The objectives of this study, therefore, were to review cases of neurocysticercosis at our hospital to determine the frequency of persistent contrast enhancement of nodular calcified lesions and to investigate the clinical significance of this finding with respect to seizure recurrence after cysticidal treatment.

Methods

We retrospectively reviewed the MR and CT findings and clinical course of all patients ($n = 29$) with neurocysticercosis being cared for at the Tropical Disease Unit of our hospital between 1991 and 1997. Sixteen patients with calcified lesions (10 female and six male, 12 to 49 years old at the time of initial presentation) formed the basis of this study. All 16 patients had MR imaging, which was performed on a 1.5-T General Electric scanner. The typical MR imaging protocol consisted of unenhanced axial T1- and T2-weighted spin-echo images, contrast-enhanced T1-weighted spin-echo images, and T2*-weighted gradient-echo images. Six of the 16 patients also had CT, which was performed on GE (Milwaukee, Wis) 9800 scanners.

MR and CT studies were reviewed to characterize the stage of the cysticercosis lesions. All patients with lesions that had reached the nodular calcified stage were examined for enhancement. Lesions were considered to be calcified if they were isointense to hypointense on T1-weighted spin-echo images, hypointense on T2-weighted spin-echo images, and markedly hypointense on gradient-echo pulse sequences, or if they were nodular and calcified on CT scans. Evidence of calcification was provided by MR imaging alone in 10 cases and by MR imaging and CT in six cases. Enhancement was considered to be present if increased signal was noted on contrast-enhanced T1-weighted images that was not present on unenhanced T1-weighted images.

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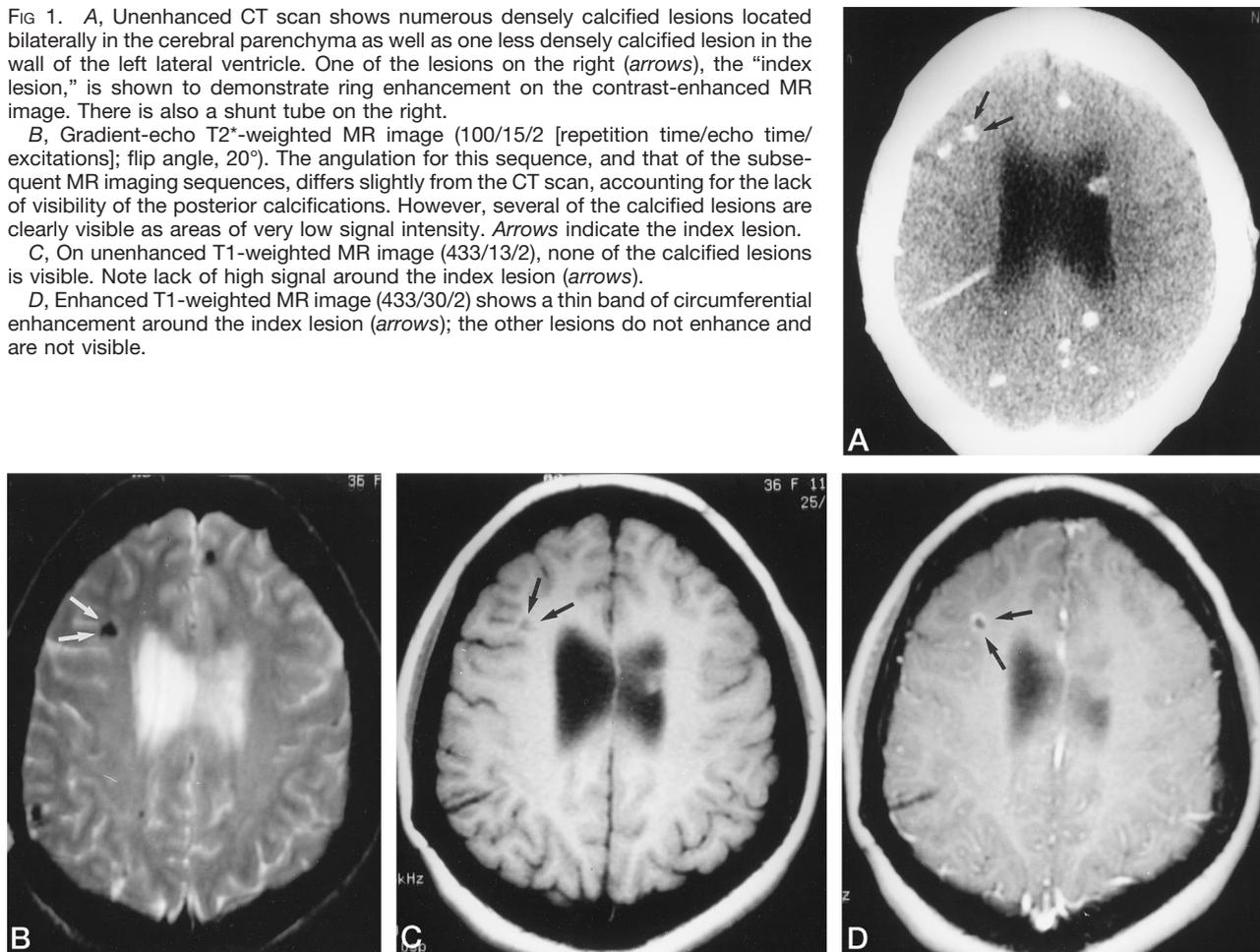
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FIG 1. A, Unenhanced CT scan shows numerous densely calcified lesions located bilaterally in the cerebral parenchyma as well as one less densely calcified lesion in the wall of the left lateral ventricle. One of the lesions on the right (arrows), the "index lesion," is shown to demonstrate ring enhancement on the contrast-enhanced MR image. There is also a shunt tube on the right.

B, Gradient-echo T2*-weighted MR image (100/15/2 [repetition time/echo time/excitations]; flip angle, 20°). The angulation for this sequence, and that of the subsequent MR imaging sequences, differs slightly from the CT scan, accounting for the lack of visibility of the posterior calcifications. However, several of the calcified lesions are clearly visible as areas of very low signal intensity. Arrows indicate the index lesion.

C, On unenhanced T1-weighted MR image (433/13/2), none of the calcified lesions is visible. Note lack of high signal around the index lesion (arrows).

D, Enhanced T1-weighted MR image (433/30/2) shows a thin band of circumferential enhancement around the index lesion (arrows); the other lesions do not enhance and are not visible.



MR imaging follow-up ranged from 1 year to 5 years after MR or CT evidence of calcification. The mean time from calcification to the most recent MR study was 2.5 years.

Results

Of the 16 patients, six had ring-shaped contrast enhancement of nodular calcified lesions. Nodular calcification in these six patients was proved by MR imaging alone in three cases and by MR imaging plus CT in three cases. Contrast enhancement on MR images persisted for at least 1 year after imaging evidence of lesion calcification was found. Figures 1 and 2 illustrate the imaging findings of densely calcified lesions with ring enhancement in two representative cases. These two cases also demonstrate that patients may have multiple lesions that are at different stages of evolution, such that nonenhancing and enhancing lesions may be present together.

The remaining 10 patients had multiple nodular calcified lesions, none of which enhanced. In nine of these patients, cystic lesions evolved to nodular calcification within the period of our study. One patient had nonenhancing nodular calcified lesions at presentation. In three of these 10 patients, the lesions eventually disappeared.

Clinically, 14 patients presented with seizures, including five of the six patients who later had enhanc-

ing calcified lesions and nine of the 10 patients who later did not. One patient presented with severe headaches and another with mental status change.

All patients except one received cysticidal treatment, consisting of a 30-day course of albendazole, a 14-day course of praziquantel, surgical extirpation, or a combination of these approaches; only two patients had surgery. In the one case in which imaging showed evidence of nonenhancing nodular calcified lesions at presentation, no cysticidal treatment was administered.

Of the six patients with persistent enhancement of nodular calcified lesions on MR images, three continued to have seizures requiring antiepileptic medication. Three were asymptomatic, including the patient who presented only with severe headaches. Of the 10 patients in whom, after treatment, no enhancement of nodular calcified lesions was present on MR images, five had persisting seizures and remained on antiepileptic medication. In two of these patients the seizures were attributed to a cause other than cysticercosis (postsurgical scar in one case and postpartum state in the other). Five patients, including the one who presented with mental status change and the three whose lesions completely resolved, were asymptomatic and able to discontinue all medications.

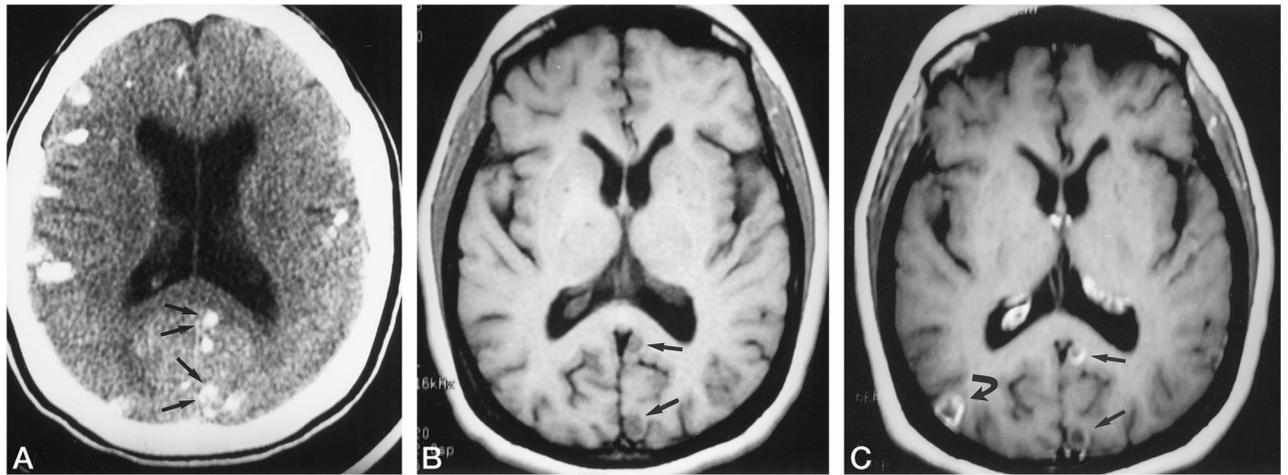


FIG 2. A, Unenhanced CT scan shows numerous densely calcified lesions located bilaterally in the cerebral parenchyma. Two of the lesions on the left (arrows), the "index lesions," are shown to demonstrate ring enhancement on the contrast-enhanced MR image.

B, Unenhanced T1-weighted MR image (500/11/2). The angulation for this sequence, and that of the subsequent enhanced MR imaging sequence, differs from that of the CT study. Note lack of high signal around the index lesions (arrows).

C, Enhanced T1-weighted MR image (566/16/2) shows a thin band of circumferential enhancement around the index lesions (straight arrows). The enhancement is most intense around the lesion directly posterior to the corpus callosum, and very faint around the lesion at the tip of the occipital pole. A third enhancing lesion, located on the right (curved arrow), was not calcified on the CT scan.

Discussion

Neurocysticercosis is common in Asia, Central and South America, Africa, and Mexico, and is being seen with increasing frequency in North America (2). Seizures are the most common clinical manifestation (3). Other clinical features may include intracranial hypertension, mental deterioration, neurologic deficits, and headache (4). Ingestion of the eggs of the adult pork tapeworm, *Taenia solium*, by humans is followed by larval release in the intestine and their subsequent migration hematogenously to the brain, eye, or subcutaneous tissue. In the brain, these larvae become the cystic lesions of neurocysticercosis (5).

The natural course of cerebral cysticercosis lesions may be divided into four stages: vesicular, colloid vesicular, granular nodular, and nodular calcified. MR findings vary according to stage (1, 5–7). When larvae are alive, in the vesicular stage, the cyst is antigenically inert. Consequently, little if any inflammation is seen at this stage (8). If left untreated, larvae die within 4 to 5 years and are destroyed by the host's immune system (9). If treated with cysticidal medication, sudden larval death leads to a more rapid evolution of the cyst to further stages.

As the larva dies, cyst degeneration is often accompanied by a marked inflammatory reaction to larval antigens, with surrounding edema. Lesions in this colloid vesicular stage have been frequently noted to enhance, presumably because of the inflammatory reaction and consequent disruption of the blood-brain barrier. Although less frequent, contrast enhancement of lesions has also been documented in the granular nodular stage as these isointense lesions retract and begin to mineralize, most likely as a result of some degree of persistent inflammation. In this context, contrast enhancement has been interpreted as representing active disease.

The final stage in the evolution of parenchymal

cysticercosis lesions is the nodular calcified stage, in which they appear as small areas of hypointensity on T2-weighted spin-echo images, especially on T2*-weighted gradient-echo images, and as small foci of calcification on CT scans. Current evidence suggests that lesions cease to enhance when they reach this stage (4–6). The results of this study, however, document a series of patients with persistent ring-shaped contrast enhancement of lesions in the nodular calcified stage.

Although a densely calcified lesion may have a band of high signal around its periphery on T1-weighted MR images as a consequence of the calcium itself (10), a review of the lesions on unenhanced T1-weighted studies allowed us to exclude calcification as a cause of the high signal. A potential shortcoming of this study was that CT evidence of calcification was not obtained in all 16 cases. It is possible that some of the lesions thought to be calcified solely on the basis of the MR findings were in fact mineralized and not calcified. However, the fact that the lesions were markedly hypointense on gradient-echo images and remained unchanged on serial follow-up studies makes this less likely.

We found no reports of pathologic examination of an enhancing nodular calcified lesion and surrounding tissue. Inflammation at earlier stages consists of an aggregation of mononuclear lymphocytes, plasma cells, and variable numbers of eosinophils at the lesion site (11, 12). The inflammatory reaction is predominantly of a granulomatous nature with epithelioid cells noted in most cases, although there is also a variable eosinophilic component. In the immediate vicinity of the lesion, the tissue reaction typically consists of astrocytic gliosis and a small rim of demyelination. Neurons are variably affected and tend to undergo degenerative changes. It seems reasonable to

assume that inflammation in the nodular calcified stage is of a similar nature.

The clinical significance of enhancement in the nodular calcified stage is not clear, particularly since the same patient usually has other calcified lesions that have ceased to enhance. There is evidence to suggest that the presence of calcified lesions after cysticidal treatment is a risk factor for posttreatment seizures (9). A large retrospective study noted that epileptic seizures are more frequent in patients in whom residual parenchymal calcified lesions are seen on CT scans (3). The presence of parenchymal brain calcifications on CT studies has also been identified as the only independent factor directly related to seizure recurrence after cysticidal therapy (13).

It is possible that the presence of persistent enhancement of these calcified lesions is an additional risk factor for posttreatment seizures. This hypothesis is supported by data from our study. Three (60%) of five patients who initially presented with seizures and later had enhancing calcified lesions continued to have seizures, whereas three (33%) of nine patients without enhancing calcified lesions continued to have seizures that were attributed to cysticercosis and not to other causes. It may be that persistent inflammation increases the likelihood that a patient with calcified lesions will continue to have seizures.

Another interesting hypothesis is that persistent enhancement may represent a calcified lesion that is in the process of completely resolving. With ongoing inflammation, there would be increased blood flow and cellular activity at the lesion site. This microenvironment may make it more likely for a lesion to resolve.

These hypotheses might be further investigated through longer term imaging and clinical follow-up of patients who have MR imaging evidence of persistent enhancement of nodular calcified lesions.

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