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# Cystlike White Matter Lesions in Tuberous Sclerosis

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**PURPOSE:** To investigate the presence of small cystlike structures in the cerebral hemispheric white matter on MR images of patients with tuberous sclerosis. **METHODS:** The MR images of 18 consecutive patients with tuberous sclerosis were reviewed retrospectively. **RESULTS:** Eight of the 18 patients were found to have cystlike structures in the cerebral white matter. The signal intensity of these lesions was isointense with cerebrospinal fluid on T1-, proton density–, and T2-weighted images. Four patients were imaged with a fluid-attenuated inversion recovery sequence, which in each case also showed fluid-type signal in these areas. Three of the patients had CT for correlation, and these scans supported the diagnosis of cystic lesions. Cysts ranged in number from one to 12 per patient and were usually smaller than 1 cm. The most common location was adjacent to the occipital horn or trigone of the lateral ventricle (six of eight patients). Less frequent sites were near the frontal horns, in the corpus callosum, and in the deep white matter near the body of the lateral ventricle. Cysts in five patients were either immediately adjacent to a cortical tuber or in the center of a white matter dysplastic lesion. A cyst in one patient had septa, and none of the cysts enhanced. **CONCLUSIONS:** Cystlike structures in the cerebral hemispheric white matter were seen on the MR images of 44% of 18 patients with tuberous sclerosis. Whether these findings represent cystic degeneration of dysplastic tissue or are unrelated to the disease process of tuberous sclerosis is unknown. More than one pathogenesis may exist.

**Index terms:** Brain, cysts; Brain, magnetic resonance; Sclerosis, tuberous

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Cerebral lesions of tuberous sclerosis have been long recognized and well described on computed tomographic (CT) and magnetic resonance (MR) imaging studies (1–10). The abnormalities include cortical tubers, subependymal nodules, white matter lesions, and subependymal giant cell astrocytomas, found in various combinations in patients with this neurocutaneous syndrome. We noted the presence of small cystlike structures in the cerebral white matter on MR images of several patients with tuberous sclerosis, and we describe our findings in this report.

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## Materials and Methods

Retrospective review was made of the cranial MR images of 18 consecutive patients seen during the past 5 years in whom a clinical diagnosis of tuberous sclerosis had been made. The studies were performed on 1.5-T imaging units. The imaging protocol in the older studies included a conventional T2-weighted spin-echo axial sequence (2000–3000/30–90/1–2 [repetition time/echo time/excitations]). More recent studies were done with a fast spin-echo T2-weighted sequence (3300–4300/18–102 effective/1), without obtaining conventional T2-weighted images. T1-weighted sagittal noncontrast and axial contrast-enhanced images (400–600/11–26/2) were also obtained in each patient. Gadopentetate dimeglumine was administered in a standard dose of 0.1 mmol/L per kilogram.

Eight of the 18 patients had cystlike lesions of the white matter and they are the focus of this report. Five of these patients were male and three were female; the mean age was 10 years. In addition to the above pulse sequences, four of the eight patients also had a fluid-attenuated inversion recovery (FLAIR) sequence (4000–8000/128–150/1; inversion time, 1500–1800) as part of the MR imaging examination. CT was available for correlation in three of the eight patients. Because of the pathognomonic

**Characteristics of white matter cysts**

| Patient | Age, y | No. of Cysts | Location | Size, mm | Relation of Cyst(s) to Tuber |
|---|---|---|---|---|---|
| 1 | 1.5 | 1 | Adjacent to L ventricular trigone | 3 × 4 | Not adjacent |
| 2 | 10 | 5 | Body of corpus callosum; adjacent to both occipital horns; R parietal deep white matter | Range, 2 × 5 to 4 × 20 | Three cysts at edge of a cortical tuber or white matter lesion |
| 3 | 39 | 11 | Genu and body of corpus callosum; adjacent to frontal and occipital horns; white matter of cingulate gyrus | Range, 2 × 2 to 4 × 10 | Not adjacent |
| 4 | 12 | 11 | Near frontal horns bilaterally; near R trigone | Range, 2 × 2 to 5 × 7 | Some cysts in central area of white matter lesions |
| 5 | 11 | 12 | Adjacent to frontal and occipital horns bilaterally; deep frontal white matter | Range, 2 × 2 to 12 × 12 | Large cyst at edge of cortical tuber; some small cysts in center of white matter lesion |
| 6 | 1.5 | 1 | Deep parietal white matter | 3 × 5 | Not adjacent |
| 7 | 2.5 | 1 | Deep frontal white matter | 8 × 8 | Not adjacent |
| 8 | 5 | 3 | Adjacent to ventricular trigone; subcortical parietal white matter | Range, 2 × 2 to 2 × 3 | One cyst at edge of white matter lesion |

clinical and imaging findings for tuberous sclerosis in these patients, no histologic correlation for the cystlike lesions was obtained.

## Results

MR imaging in eight (44%) of 18 patients revealed small white matter cysts in the cerebral hemispheres. These findings are summarized in the Table. The cysts ranged in number from one to 12 in each patient. Their configuration was typically round to oval, measuring 2 to 12 mm in greatest dimension. An unusual cyst in one patient was crescent-shaped, measuring 4 × 20 mm. Larger and more numerous cysts were seen in the older children and in the one adult in this series, as compared with the youngest children.

A periventricular location for the cysts was most common. Six of the eight patients had cysts adjacent to the occipital horn or ventricular trigone (Fig 1), three had cysts near the frontal horn (Fig 2), three in deep white matter near the lateral ventricular body, and two patients had cysts within the corpus callosum (Fig 3). In five patients, cysts were associated with dysplastic tissue, and these were best seen on the FLAIR images, when available (Figs 4 and 5). In three of these patients, cysts were noted at the periphery of a cortical tuber, and in two patients cysts were surrounded by abnormal noncystic white matter signal intensity. One of the larger cysts had septa (Fig 4). No enhancement of the cystic wall was seen in any patient. When both CT and MR studies were available, the cysts were more easily recognized on the MR images and were not mistaken for tubers.

Other intracranial lesions identified in these patients included subependymal tubers in six, cortical tubers in six, white matter lesions in three, and subependymal giant cell astrocytomas in two.

## Discussion

Tuberous sclerosis is an autosomal dominant neurocutaneous syndrome with frequent involvement of the central nervous system. The various brain lesions most likely result from abnormal cellular differentiation and disordered cell migration during development (11). The cortical tubers, subependymal nodules, and white matter lesions share a common histology of clusters of abnormally large cells. Some of these cells exhibit characteristics of astrocytes while others show neuronal differentiation or a form intermediate between the two (11). Cortical tubers and subependymal nodules are usually noted with nearly equal frequency at MR imaging, and each has been reported in 95% to 100% of patients with tuberous sclerosis in several series (1, 3, 9). White matter lesions have been identified less frequently on MR images (40% to 93% of patients) (1–3, 5). The least

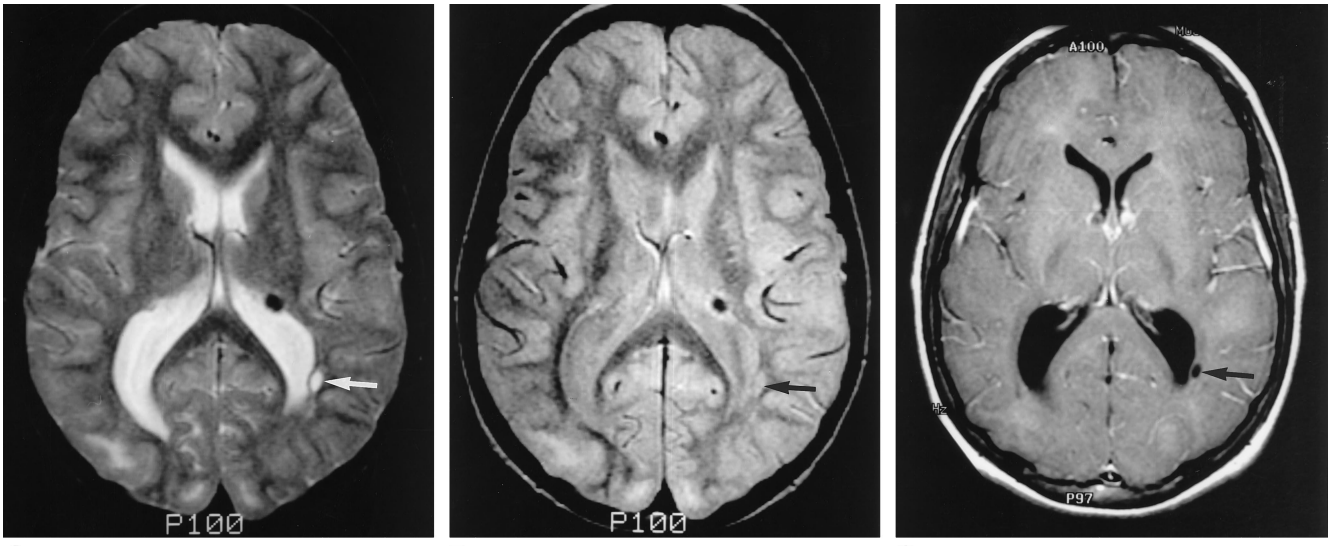


Fig 1. T2- (*A*) and proton density– (*B*) weighted spin-echo images show a cystlike lesion near the left occipital horn (*arrow*) that follows cerebrospinal fluid signal intensity. Bilateral cortical tubers are also seen. Contrast-enhanced T1-weighted image (*C*) with slightly different angulation shows isointense signal in the cyst and ventricle. Subependymal tubers at the foramina of Monro are also seen.

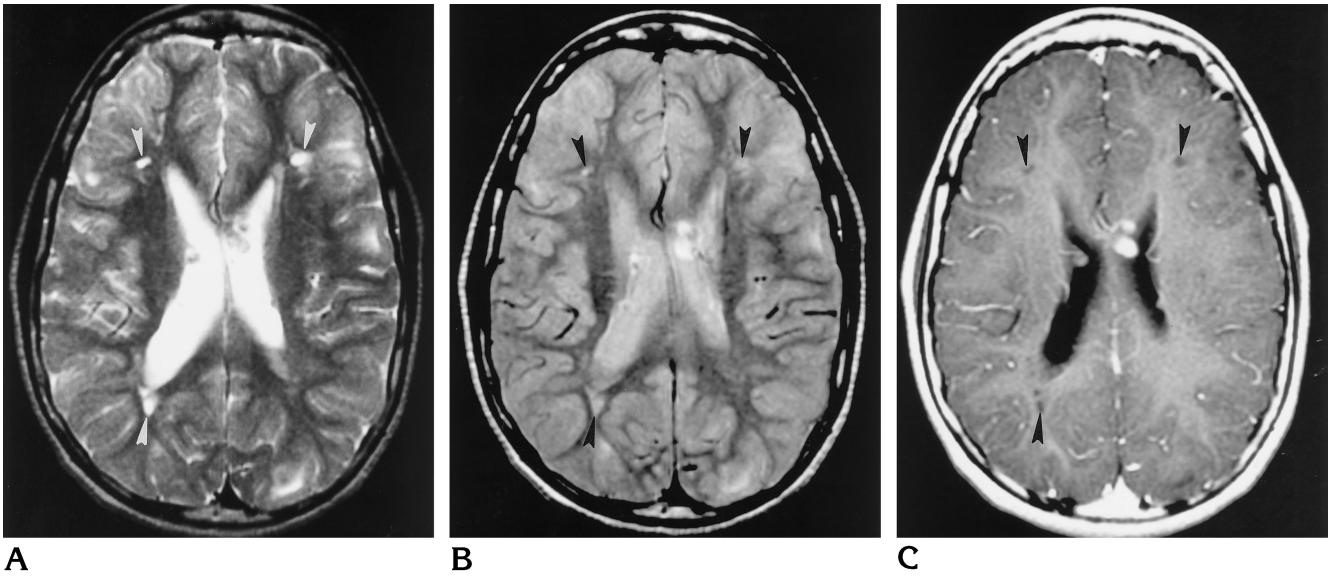


Fig 2. Fast spin-echo T2- (*A*) and proton density– (*B*) weighted and contrast-enhanced T1-weighted (*C*) images show several cystlike lesions near the corners of the lateral ventricles (*arrowheads*) and cortical and subependymal tubers. Signal intensity consistent with fluid is seen in the periventricular abnormalities on all pulse sequences. The left frontal cyst lies just deep to a cortical tuber and there is some surrounding noncystic signal abnormality.

common central nervous system finding is subependymal giant cell astrocytoma. It has a variably reported occurrence, but generally is seen in 15% to 20% of these patients (1, 2, 5).

We found little published information about white matter cystic abnormalities in tuberous sclerosis. One article mentioned but did not characterize brain cysts in a patient with tuberous sclerosis (12). It has also been stated that there are areas of cystic degeneration in the cerebrum and cerebellum of these patients that produce small cystic cavities, but again without further description (13). Several articles have included MR images showing white matter cystlike findings similar to our examples, but they were not discussed (2, 5, 6, 10). A reported

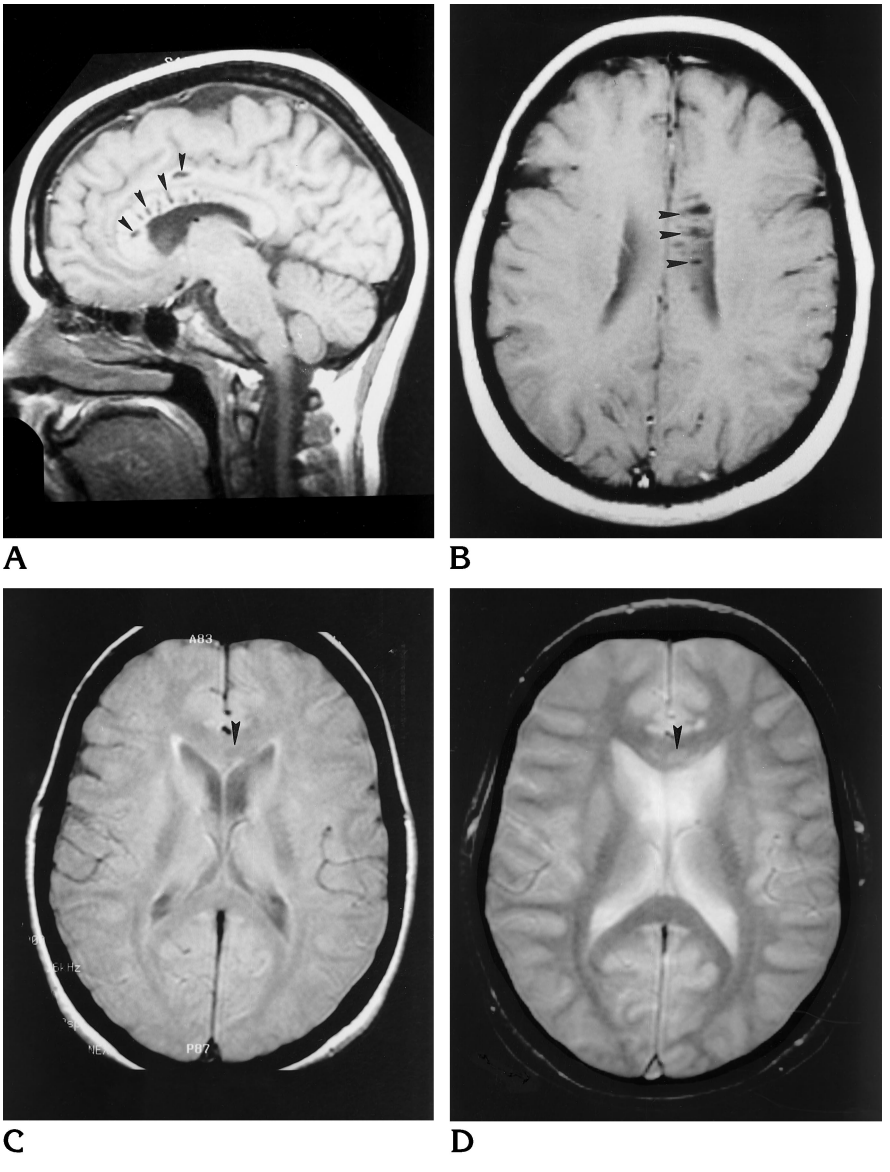


Fig 3. Sagittal (*A*) and axial (*B*) T1-weighted images show multiple cysts in the corpus callosum and one in the white matter of the cingulate gyrus (*arrowheads*). Axial proton density– (*C*) and T2*- (*D*) weighted images show that a representative cyst follows cerebrospinal fluid signal intensity (*arrowhead*).

case of hypomelanosis of Ito also exhibited small white matter cysts, which is interesting, as cerebral migration abnormalities and hypopigmented skin lesions are found both in this disease and in tuberous sclerosis (14).

Cortical tubers are known to undergo cellular degeneration, especially centrally, which may result in small calcific deposits, or, less commonly, small cysts (15, 16). Some cortical tubers have a depression or umbilication on the gyral surface, which, in one author's opinion, may represent cystic degeneration within the center of the tuber (15). In our series of patients, no cysts were seen in the center of cortical tubers. Instead, cysts were located in deeper white matter areas, typically near the lateral ventricles. Small periventricular cysts in two of our patients were surrounded by noncystic signal abnormality (Figs 2 and 5), perhaps analogous to the degeneration described above for cortical tubers. Cysts in three other patients were at the edge of cortical tubers (Fig 4) or in deeper white matter. The majority of cysts in our series were not associated with adjacent or surrounding noncystic signal abnormality.

If these cysts are unrelated to degeneration of dysplastic tissue and are not a result of the abnormal neuronal cell migration of tuberous sclerosis, the likely pathogenesis would be perivascular space enlargement, neuroepithelial cysts, or glial cysts. Enlarged perivascular spaces along the course of penetrating arteries

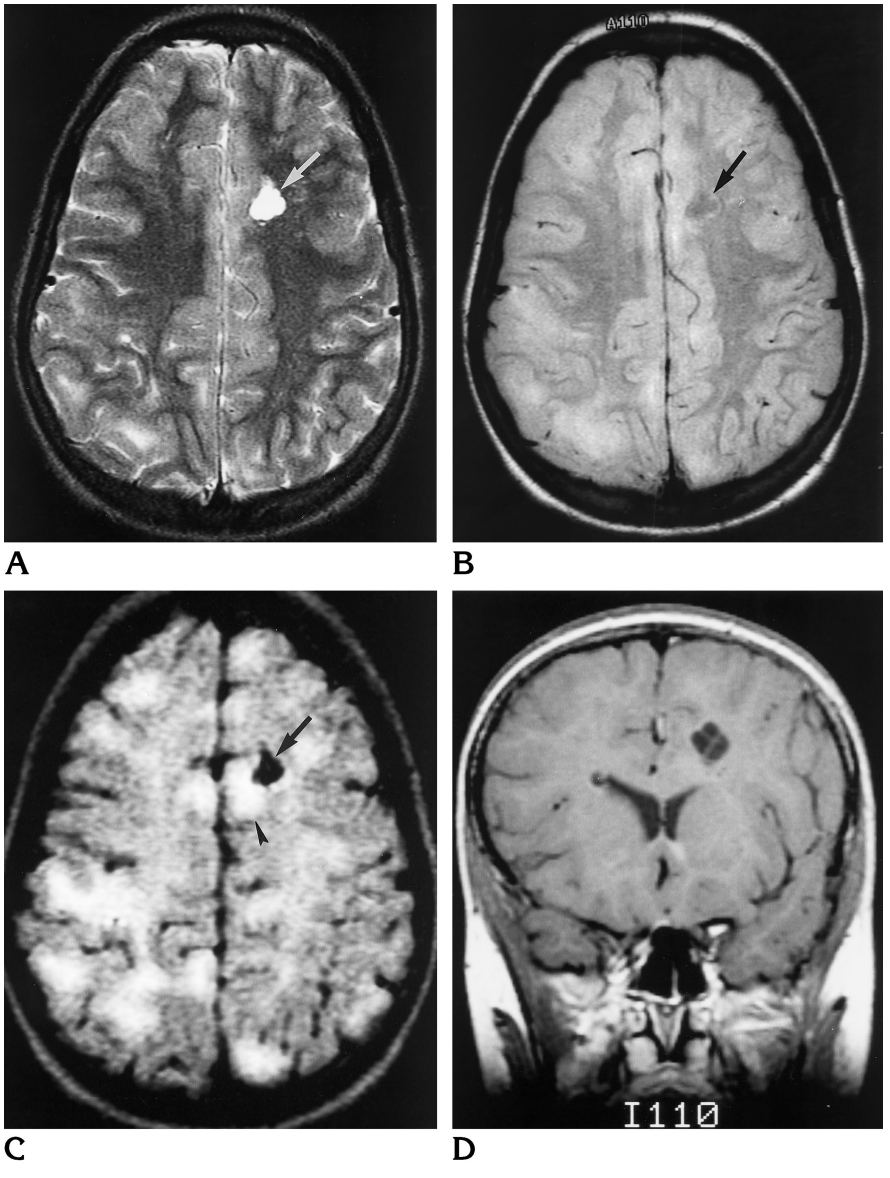


Fig 4. Fast spin-echo T2- (*A*) and proton density– (*B*) weighted axial images show a large cyst medially in the left frontal white matter (*arrow*). FLAIR image (*C*) confirms cystic nature of this structure and also shows a cortical tuber along the medial aspect of the cyst (*arrowhead*) as well as numerous other tubers poorly seen on the T2-weighted image. Contrast-enhanced coronal image (*D*) reveals septa within the cyst, a small cyst adjacent to the right frontal horn, and an enhancing tuber at the left foramen of Monro.

are seen on MR images as round, oval, or linear structures with signal intensity similar to cerebrospinal fluid. These are usually found in the lower basal ganglia near the anterior commissure, in the centrum semiovale and subcortical white matter, and in the midbrain; and they have a positive correlation with increasing age (17). There is a report of two patients with numerous, strikingly large perivascular spaces, some extending deep to the ventricular surface in a location similar to that of many of the cysts in our patients (18). Neuroepithelial cysts are typically found in the lateral ventricle near the trigone, and they infrequently occur in the brain parenchyma (19–21). These cysts also closely follow cerebrospinal fluid signal intensity. Ependymal streaks and ependyma-lined cavities are known to occur near the occipital horn owing to growth of cells into that area in development (22), which might explain the greater frequency of cystlike structures in this location in our patients. Nonepithelial (glial) cysts have also been reported in the brain parenchyma, often in the cerebellum, without obvious connection to the ventricles or subarachnoid spaces (23–25). These cysts often progressively enlarge and exert mass effect, requiring surgery, and the reported examples of these cysts are not similar to our cases.

An additional observation in our series was that cortical tubers were much more conspicuous on FLAIR sequences than on fast spin-echo

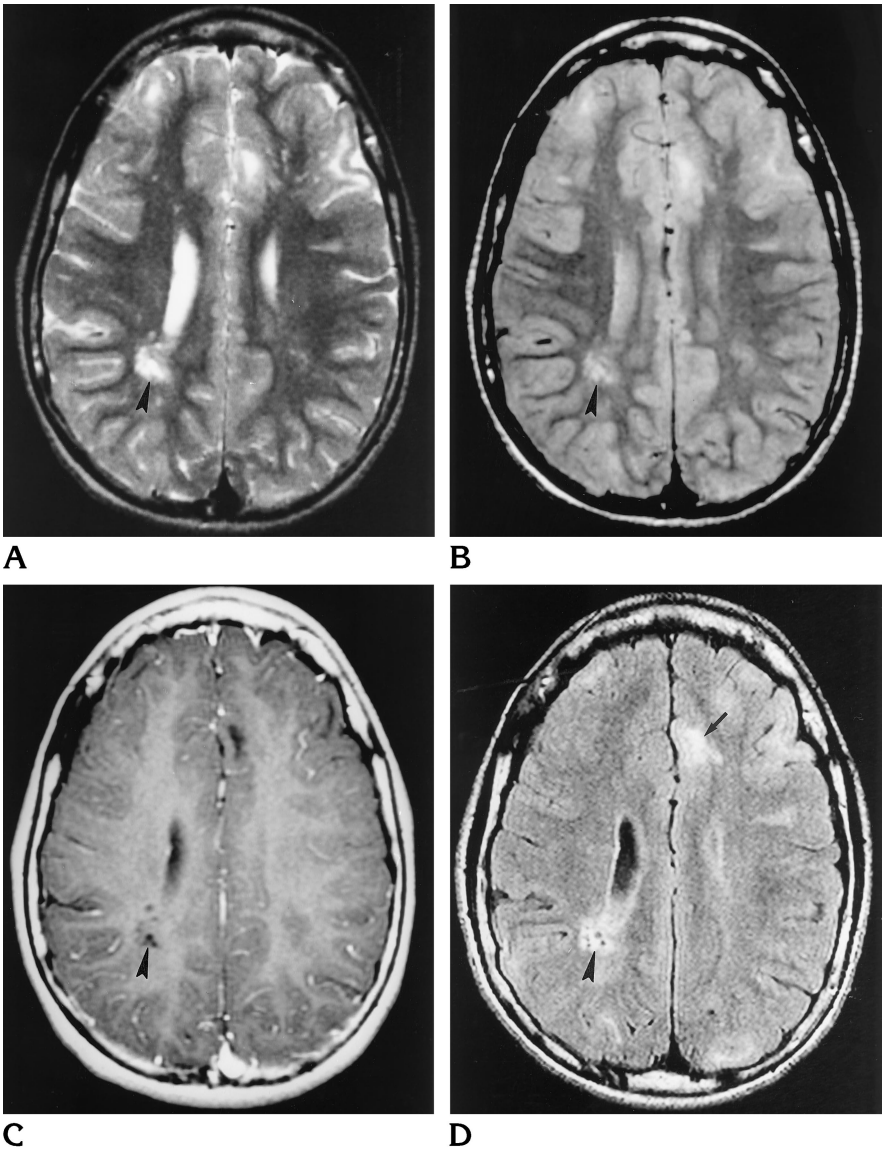


Fig 5. T2- (*A*), proton density– (*B*), and contrast-enhanced T1- (*C*) weighted axial images show a cluster of small cysts in the right parietal white matter near the lateral ventricle (*arrowhead*). FLAIR image (*D*) shows cerebrospinal fluid–like signal in the cysts and surrounding noncystic signal abnormality. This image also shows that the medial left frontal lesion is not cystic (*arrow*).

images in the four patients in whom both types of images were available (Fig 4). Similar results of a comparison of conventional spin-echo and FLAIR sequences in patients with tuberous sclerosis were published by Takanshi et al (26). The FLAIR technique has also been shown to be superior to T2-weighted spin-echo imaging for identifying numerous other intracranial abnormalities, especially those that lie adjacent to cerebrospinal fluid (27–31).

In conclusion, we have noted small cysts in the cerebral hemispheric white matter and corpus callosum on the MR images of eight (44%) of 18 patients with tuberous sclerosis. The origin of the cysts is not known, and they may not all have the same pathogenesis. They may reflect cystic degeneration of white matter dysplastic lesions of tuberous sclerosis or represent focal enlargement of perivascular spaces or parenchymal neuroepithelial cysts. Perhaps they are somehow related to the disordered neuronal migration that occurs in this syndrome. In addition to the well-known cortical tubers, subependymal nodules, white matter dysplasias, and subependymal giant cell astrocytoma, these benign-appearing cysts are another find-

ing that the neuroimager may encounter in brain examinations of patients with tuberous sclerosis.

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