MR Imaging of White Matter Disease in Children

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Twenty-three pediatric patients with white matter abnormalities on MR images were evaluated retrospectively to assess the contribution of MR compared with CT in diagnosing these conditions. In addition, the MR findings in major categories of white matter diseases were analyzed for sensitivity in detecting the presence of an abnormality. White matter disease categories included demyelinating disease (five cases), dysmyelinating disease (eight cases), developmental white matter abnormalities (four cases), and white matter abnormalities of unknown origin (idiopathic) (six cases), as seen on long TR images. We found that MR is not more sensitive than CT in detecting disease in the demyelinating or dysmyelinating categories, although it is more sensitive than CT in detecting the degree of disease present. In cases of developmental delay, MR is distinctly more useful than CT in demonstrating abnormalities of myelination. And in the idiopathic group, MR detected the presence of focal white matter abnormalities on long TR images in children with neurologic complaints and normal CT.

MR may serve to redefine and broaden the spectrum of reported imaging abnormalities in pediatric patients.

Although white matter diseases are uncommon in children, clinicians must be aware of their occurrence and able to recognize their MR appearances. Children can develop white matter disorders as a result of demyelination, dysmyelination, and developmental delay, as well as idiopathically. Using Poser's classification of white matter diseases, demyelinating lesions may be divided into primary disorders, such as multiple sclerosis (MS) and acute disseminated encephalomyelitis (ADEM), and secondary disorders whose origins include toxic or anoxic deficiency syndromes, viral disorders such as progressive multifocal leukoencephalopathy, and primary neuronal lesion Wallerian degeneration [1]. The more common primary dysmyelinating lesions include metachromatic leukodystrophy (MLD), Krabbe disease, Canavan disease, Alexander disease, and Pelizaeous-Merzbacher disease (PMD). The predominant secondary dysmyelinating disorders fall into the metabolic category. Poser [1] notes that adrenoleukodystrophy exhibits characteristics of both the demyelinating and dysmyelinating disorders.

We have also included in our study two other categories of disease that produce white matter abnormalities on MR: delayed myelination on a developmental basis and idiopathic pediatric white matter abnormalities. This report focuses on the MR diagnosis of pediatric white matter abnormalities.

Subjects and Methods

Twenty-three patients under 18 years old who were diagnosed as having abnormal white matter on MR were included in this study.

The study population included 11 girls and 12 boys ranging in age from 5 months to 13 years. Requirements for admission to the study were that the patient was under 18 and that a white matter abnormality was found on long TR MR images. The routine MR study performed on a GE 1.5-T Signa system included sagittal short spin-echo images 600/20/2

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(TR/TE/excitations) and axial and coronal long spin-echo images 2500/40, 80/2 and, if the patient was under 2 years old, 3500/40, 160/2 [2]. Eighteen patients had CT scans. One patient had both CT and cranial sonographic examinations. Two patients had no other studies, and information regarding outside examinations was unavailable in two other patients.

Results

The MR findings were categorized on the basis of clinical information. Of the 23 patients, five had demyelinating disease, eight had dysmyelinating disease, four were developmentally delayed, and six had white matter abnormalities with no known cause (Tables 1–4).

In 11 cases MR identified additional lesions not visualized on CT. These represented predominantly patchy, focal areas of increased white matter signal seen on long TR images in patients with demyelinating disease or in patients with white matter abnormalities with no known cause. In two cases the CT scans were unavailable for review. In the dysmyelinating diseases we observed that MR was equivalent to CT in identifying white matter abnormalities. Whether MR could be diagnostic early in the clinical course of the disease when CT is negative, as suggested by other authors, cannot be addressed in our group of patients because they were all studied in the subacute phases of their disease [3]. Our two cases of Alexander disease were radiologically atypical, with cerebellar and peritrigonal white matter disease as compared with frontal white matter disease, which is reported to be more common [3].

In two patients with metabolic diseases (carnitine deficiency and pyruvate dehydrogenase deficiency) CT scans with and without contrast were normal. In both cases abnormal periventricular white matter adjacent to the frontal and occipital horns was demonstrated by MR.

Only one of our four patients with perinatal asphyxia and/or developmental delay had a CT scan. This patient had a documented germinal matrix hemorrhage, and CT demonstrated periventricular low absorption in the white matter with minimal ventricular dilatation. MR also revealed a rind of hemosiderin (evidence of old hemorrhage) surrounding the lateral ventricles.

TABLE 1: Demyelinating Disorders

Clinical Diagnosis	Case No.[a]	CT	MR[b]
Acute disseminated encephalomyelitis	1	One lesion, centrum	Two white matter lesions, right and left centrum
	2	One lesion, centrum	Two centrum lesions, one medullary lesion
	3	Normal	Right parietal white matter lesion
Tick paralysis	1	One lesion, right temporal lobe	Right temporoparietal and left parietal lesions
Multiple sclerosis	1	Multiple lesions	Same number lesions

[a] Each number represents a different patient, e.g., case 1 of acute disseminated encephaloyelitis is a different patient from case 1 of tick paralysis or multiple sclerosis.

[b] All MR images are SE 2500–3500, 40/80–40/160.

TABLE 2: Dysmyelinating Disorders

Clinical Diagnosis	Case No.[a]	CT	MR[b]
Krabbe disease	1	Normal	Periventricular white matter high signal
Carnitine deficiency	1	Normal	Periventricular white matter high signal
Metachromatic leukodystrophy	1	No CT	Diffuse confluent white matter high signal
	2	No CT	Diffuse confluent white matter high signal
	3	Abnormal	Diffuse confluent white matter high signal
Alexander disease	1	Normal	Cerebellar high signal
	2	Normal	Periventricular white matter high signal
Pyruvate dehydrogenase deficiency	1	Normal	High signal in periatrial white matter

[a,b] See footnotes to Table 1.

TABLE 3: Developmental Delay

Case No.	Age	Gender	Clinical Diagnosis	CT	MR[a]
1	12 mo	M	Developmental delay, spasticity	Abnormal	Periventricular disease, ependymal hemosiderin
2	3 yr	F	Developmental delay, sensorineural hearing loss	No CT	Confluent white matter high signal
3	12 mo	F	Developmental delay, seizures, nonfocal exam	No CT	Relatively delayed myelination
4	9 yr	F	Developmental delay, esotropia	No CT	Periventricular disease

[a] All MR images are SE 2500–3500, 40/80–40/160.

TABLE 4: Unclassified White Matter Diseases

Case No.	Age	Gender	Clinical Diagnosis	CT	MR[a]
1	4 yr	M	Developmental delay, fine motor difficulties	No CT	Patchy periventricular white matter disease
2	19 mo	M	Seizures, nonfocal neurologic exam	Normal	Patchy lesions, centrum semiovale
3	6 yr	F	Hemifacial atrophy	Normal	Tiny focal lesions, ipsilateral parietal white matter
4	5 yr	M	Seizures, developmental delay, nonfocal neurologic exam	Normal	Tiny focal lesions, centrum semiovale
5	4 yr	M	Chediak-Higashi, spastic, developmental delay	Abnormal	Diffuse white matter high signal
6	5 yr	M	Ataxia, sensorineural hearing loss, developmental delay	Normal	Patchy periventricular white matter disease

[a] See footnote to Table 3.

Discussion

We have divided pediatric white matter diseases into four categories based on high-intensity abnormalities seen on long TR images and correlative clinical information: demyelinating disease, dysmyelinating disease, developmental delay (of myelination), and white matter abnormalities of unknown origin. Although there are certain trends from our data in the image patterns in these groups, MR generally lacked specificity with respect to diagnosis.

In this series CT was less sensitive to the extent of and/or number of patchy lesions in demyelinating disease. However, CT in combination with clinical history was diagnostic in all five cases. The diagnosis of a demyelinating disease in childhood is very dependent on correlation with viral titres, neurologic history, and examination. Two patients had an abnormal CT with nonenhancing hypodense focal lesions on CT, but in each case more lesions were demonstrated on MR (Fig. 1).

In one patient with ADEM, CT was normal. In one patient with tick paralysis a contrast-enhancing lesion was identified on CT, whereas two lesions were noted in the white matter on MR (Fig. 2). MR consistently depicted more lesions per patient than did CT in this category of patients. This sensitivity of long TR images is well described in the MR literature [4].

As expected, and as is also apparent from the CT and pathologic literature [1, 5–8], the dysmyelinating disorders demonstrated diffuse confluent high signal intensity in the white matter on long TR spin-echo images. We did not have any patients with a biochemically or biopsy-proved dysmyelinating disorder with patchy or focal white matter changes. We did, however, have two somewhat atypical cases of Alexander disease, both biopsy-proved (Fig. 3). One patient had diffuse cerebellar high signal intensity. The second patient had periventricular high signal, which was more prominent posteriorly. As noted in the literature [3, 9–11], Alexander disease usually manifests with abnormal white matter in the frontal region. Rarely, it involves the basal ganglia. The sensitivity of MR in these cases may result in widening the spectrum of radiologic manifestations of this disease. It is also possible that with further clinical follow-up our cases may demonstrate more typical findings and that presently we may

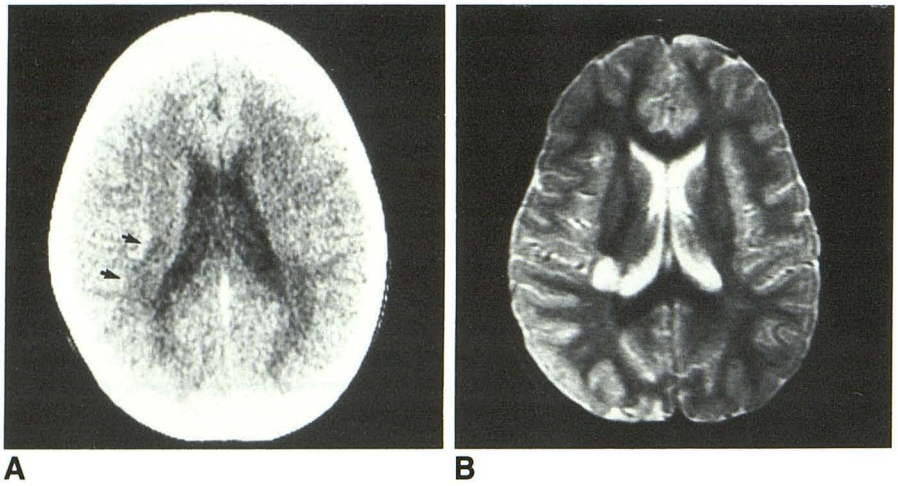


Fig. 1.—*A*, Contrast-enhanced CT scan suggests focal hypodensity in periatrial centrum semiovale on the right in 5-year-old boy who presented with a history consistent with acute disseminated encephalomyelitis (*arrows*).

***B*, Long spin-echo MR image 2500/80 at same level demonstrates unequivocal area of high signal intensity in same region as in CT scan. A second focus was seen on MR and not on CT (not shown).**

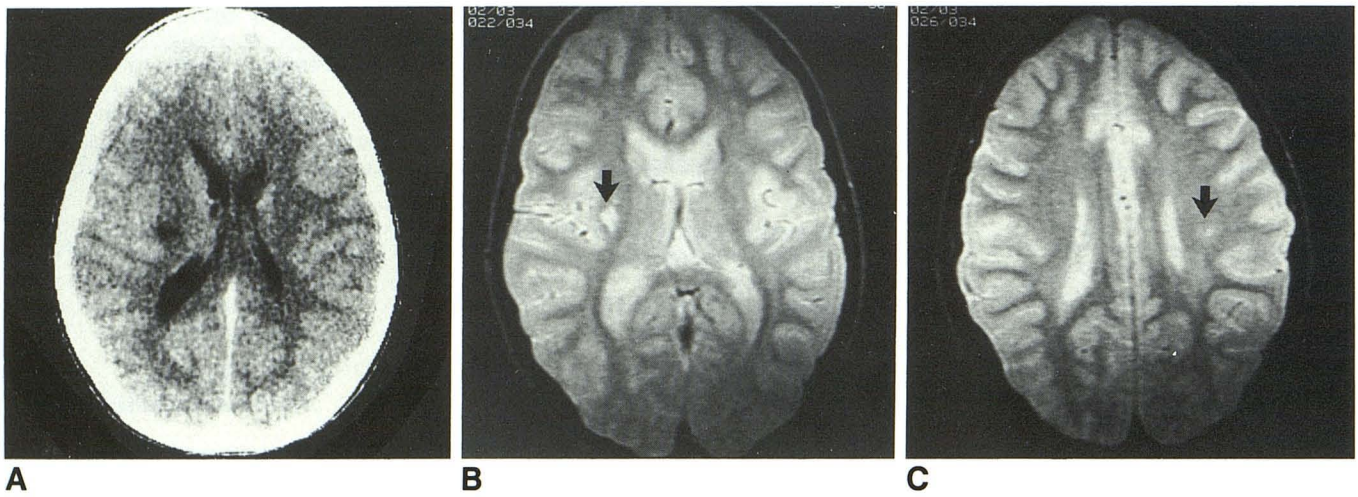


Fig. 2.—*A*, Focal hypodensity in right corona radiata on enhanced CT scan in 13-year-old boy who presented with tick paralysis is consistent with demyelination.

***B*, MR image 2500/50 shows lesion in right corona radiata (*arrow*).**

***C*, A second lesion superiorly is seen in corona radiata on left (*arrow*).**

just be imaging one point on the continuum of the disease.

In two cases with enzyme metabolic deficiencies (carnitine and pyruvate dehydrogenase), MR revealed white matter abnormalities when CT was normal (Fig. 4). One patient was scanned early in her clinical course and the second patient was scanned late in his clinical course.

Our patient with Krabbe disease (Fig. 5) demonstrated confluent periventricular high signal and the children with MLD (Fig. 6) had diffuse confluent high signal intensity in the white matter on long TR MR (long spin-echo imaging). The MLD patients were scanned several months after diagnosis. The MR findings did not appear to add any additional information to that provided by CT, which demonstrated diffuse periventricular white matter high signal in each case. The positive MR in Krabbe disease was performed early in the clinical course as was the CT, which was normal. In the literature [3, 12–14], five of eight reported cases had normal CT scans at diagnosis. If MR is performed early enough in the clinical course of the disease, the diagnosis of suspected white matter disease may be confirmed. The diagnosis of Krabbe disease is based on biochemical testing while the role of MR may be to suggest that such tests be performed at an earlier date [14].

In children with developmental delay, MR is more useful than CT, since the progression of myelination can be evaluated with greater sensitivity [15–18]. Associated findings such as old hemosiderin deposits in the germinal matrix are also made only by MR (Fig. 7). Clinical correlation and MR follow-up is necessary to fully evaluate the role of MR in this group of patients.

The last group of pediatric white matter diseases are those of unknown origin. It is in this group that perhaps MR had its

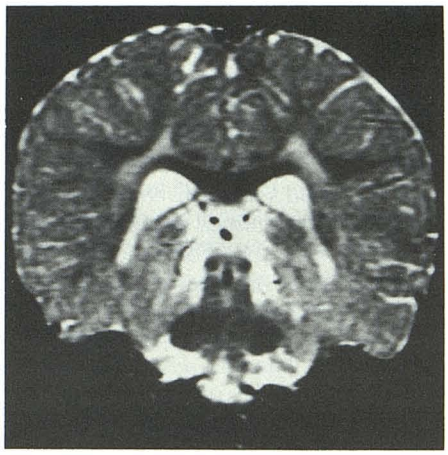


Fig. 3.—MR image 3500/16 shows patchy periventricular high signal in white matter of parietal lobes in 12-month-old boy with biopsy-proved Alexander disease. CT scan (not shown) was normal.

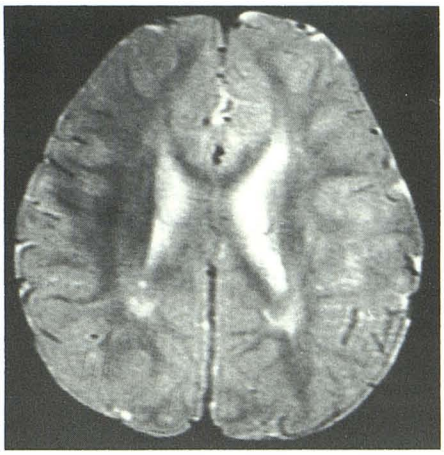


Fig. 4.—Minimal periventricular high signal is noted on long spin-echo MR image 2500/50 in patient with carnitine deficiency.

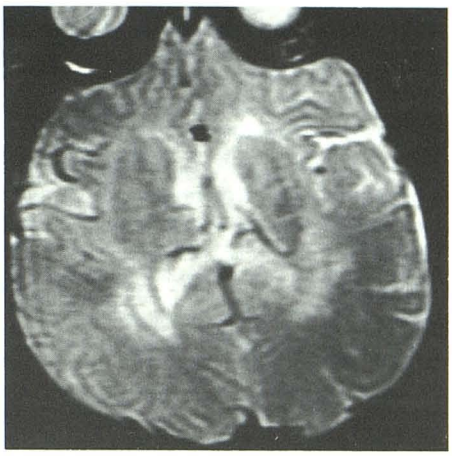


Fig. 5.—MR image 3500/20 shows confluent periventricular white matter disease in 5-month-old patient with Krabbe disease.

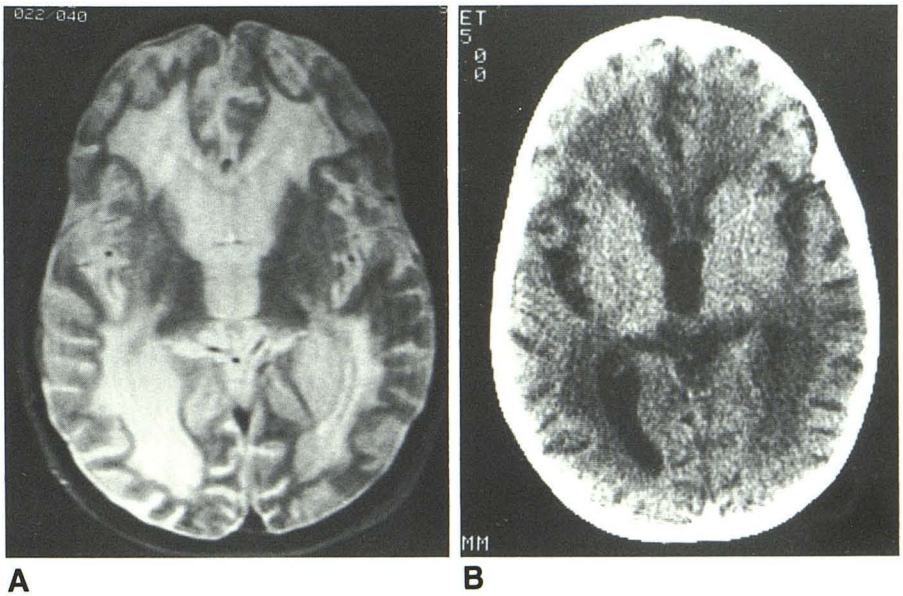


Fig. 6.—*A*, MR image 2500/80 shows diffuse confluent high signal throughout white matter in 4-year-old boy with metachromatic leukodystrophy diagnosed 3 years earlier. Moderate atrophy is present.

B, CT without contrast performed a few weeks before MR demonstrates diffuse white matter hypodensity, the extent of which is similar to that of the MR changes although somewhat less apparent.

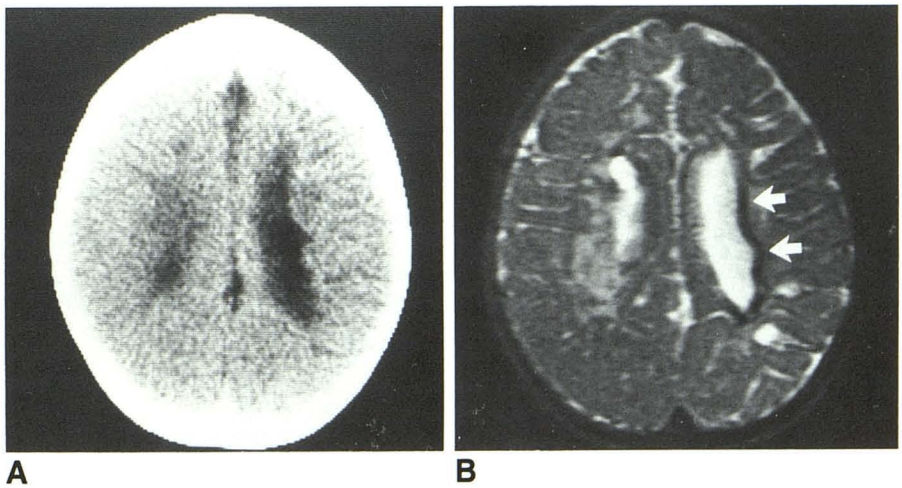


Fig. 7.—*A*, CT scan of 12-month-old infant who was premature and had a germinal matrix hemorrhage at birth shows mild ventricular dilatation and some periventricular low absorption.

B, MR image 3500/60 at same level demonstrates same degree of periventricular white matter change; in addition, some ependymal hemosiderin deposition can be seen (*arrows*).

greatest impact in lesion-detection capabilities. In our six patients there was a spectrum of clinical presentations responsible for the initial MR (Table 4). Four of these patients had normal CT, one patient had an abnormal CT, and one patient did not have CT. MR of a 3-year-old girl whose major complaint was sensorineural hearing loss and moderate developmental delay was grossly abnormal, demonstrating several patchy areas of high signal in the white matter. CT was normal. All metabolic screening tests were normal (Fig. 8). The one patient with diffuse confluent hypodensities in the white matter on CT had Chediak-Higashi disease. MR demonstrated an equivalent pattern of diffuse white matter high signal on long TR images. These images were obtained in the late stages of this patient's disease. The patient had not received prior chemotherapy or radiation, and the cause of the white matter abnormalities is unknown. There have not been prior reports in the literature of white matter disease in Chediak-Higashi disease [19] (Fig. 9). One patient with olivopontocerebellar degeneration had mild periventricular high intensity on long TR images. CT performed at the same time in his clinical course was unremarkable. To our knowledge, supratentorial white matter changes have not been described in olivopontocerebellar degeneration [20].

The remaining patients with idiopathic white matter abnor-

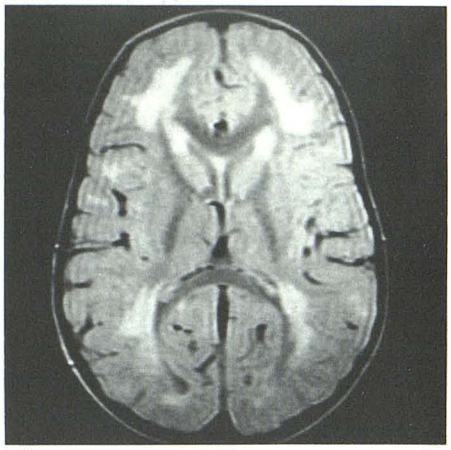
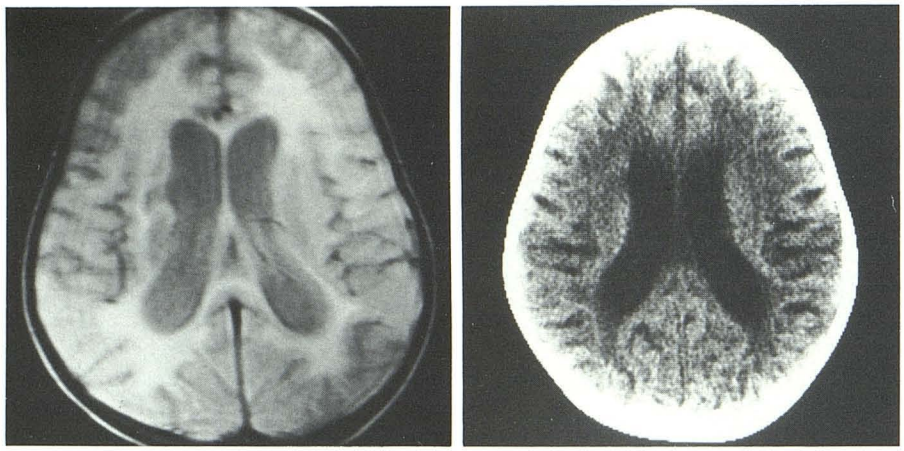
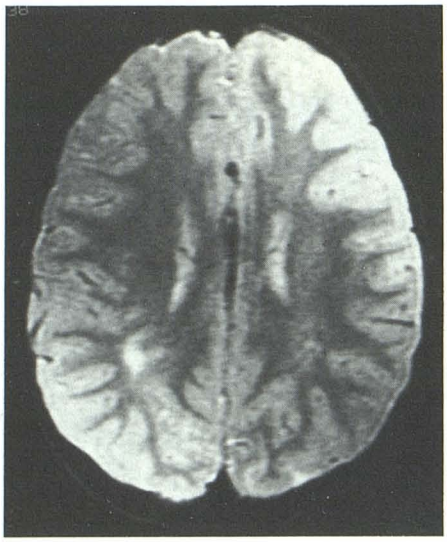


Fig. 8.—MR image 2500/40 of 3-year-old girl with developmental delay and sensorineural hearing loss demonstrates several areas of white matter high signal in periventricular regions. CT was normal.



A B

Fig. 9.—*A*, Confluent white matter hyperintensity is seen on long spin-echo MR image 2500/40 in 4-year-old boy with Chediak-Higashi disease.
B, CT scan shows white matter hypodensities in same distribution.



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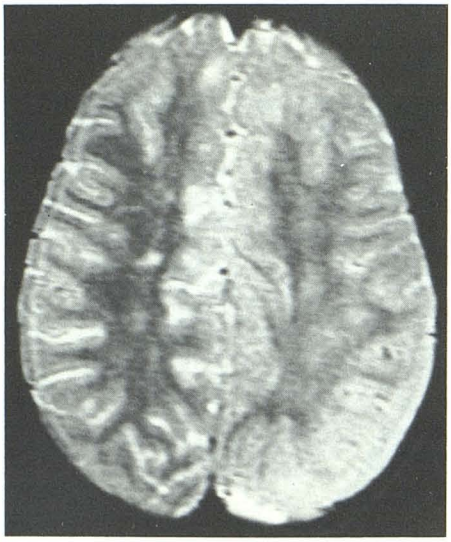

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Fig. 10.—A few focal regions of high signal intensity are seen in this MR image 2500/80 of 4-year-old boy with developmental delay and fine motor difficulties. CT scan was negative.

Fig. 11.—This 5-year-old boy presented with seizures and developmental delay with a nonfocal neurologic examination. Small focal areas of high signal intensity are seen on long spin-echo MR image 2500/40 in centrum semiovale. CT was negative.

malities had variably sized patchy focal areas of high signal intensity on long TR images in the white matter not causally related to the neurologic symptoms or examination (Figs. 10 and 11). None of these patients was premature or had a history of trauma, drug, or radiation exposure.

In summary, 23 pediatric patients with white matter disease were evaluated by MR. These patients were placed into four categories on the basis of long TR MR findings and clinical information: (1) demyelinating, (2) dysmyelinating, (3) developmental, and (4) idiopathic white matter abnormalities. MR was not more sensitive than CT or clinical evaluation in detecting white matter disease in demyelinating or dysmyelinating categories, although it certainly was more sensitive than CT in determining the extent of involvement. In the developmental group the pattern of myelination could be assessed and definitive evidence of old hemorrhage could be determined. In the idiopathic groups MR played a more useful role in identifying the existence of disease. In these cases subtle focal white matter abnormalities could be detected in children with neurologic complaints. In the latter patients a negative CT might preclude further imaging follow-up in certain clinical situations.

MR may serve to redefine and broaden the disease spectrum of reported white matter abnormalities in children.

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