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MR Imaging of the Brain in Patients with Mucopolysaccharidosis

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MR imaging of the brain was performed in eight patients with mucopolysaccharidosis (MPS). Two had MPS I S, one had MPS IIA, two had MPS IIB, two had MPS IIIB, and one had MPS VI. In the patients with MPS IIA and MPS VI, T1 and T2 were prolonged in various areas of the cerebral white matter. These findings seemed to correspond with the development of pathologic changes in MPS, such as perivascular pits in the white matter observed on slices of the fixed brain. In the patients with MPS IIA and MPS IIIB, the white matter did not show the proper signal intensity, which suggested that myelination was insufficient and that infiltration or deposition of glycosaminoglycan had occurred; this was consistent with the association of these two types with mental retardation. In the patients with MPS I S, no intracranial abnormalities were detected on MR images.

MR imaging of the brain may be used to obtain a differential diagnosis of the various types of MPS, to estimate the extent of mental retardation, and to monitor the progress of this disease.

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Mucopolysaccharidosis (MPS) is an inherited metabolic disorder involving a deficiency of specific lysosomal enzymes that take part in the degradation of acid mucopolysaccharides, or glycosaminoglycans (GAGs). MPS results in the intralysosomal accumulation of GAG in various tissues and organs. The clinical manifestations of MPS are multifarious, including a gargoylelike face, dwarfism, bone deformities, hepatosplenomegaly, corneal clouding, and mild to severe mental retardation [1]. Table 1 lists the various types of MPS, the products that accumulate, the mode of inheritance, the enzyme deficiency that determines the type, and the extent of mental retardation. CT has been used to detect abnormalities involving the CNS in MPS, and findings such as low density in the white matter and dilatation of ventricles have been described [2, 3]. However, these findings are not specific for MPS.

MR imaging is now important clinically in the diagnosis of degenerative or demyelinating changes and other diseases of the CNS [4, 5]. In this study, we performed MR imaging of the brain in patients with different types of MPS, and found changes corresponding with neuropathologic observations that have been reported elsewhere [6].

Subjects and Methods

Eight patients with MPS were studied. Two had MPS I S (Scheie), one had MPS IIA (severe type of Hunter), two had MPS IIB (mild type of Hunter), two had MPS IIIB (Sanfilippo B), and one had MPS VI (Maroteaux-Lamy). The diagnosis in each patient was confirmed biochemically. Clinical characteristics at the time of the examinations are summarized in Table 2.

MR examinations were performed on a 0.5-T unit* with the use of a standard head coil (diameter, 30 cm). Pulse sequences included spin echo (SE), SE 1800/120/1 (TR/TE/

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* Vista-MR, Picker International, Highland Heights, OH.

TABLE 1: Classification of Mucopolysaccharidoses (MPS)[a]

Type of MPS	Eponym	Urinary MPS	Mode of Inheritance	Enzyme Deficiency	Mental Retardation
I H	Hurler	DS, HS	Autosomal recessive	α-L-Iduronidase	Severe
I S	Scheie	DS, HS	Autosomal recessive	α-L-Iduronidase	Absent
I H/S	Hurler-Scheie	DS, HS	Autosomal recessive	α-L-Iduronidase	Mild
IIA	Hunter, severe	DS, HS	X-linked recessive	Iduronate sulfate	Severe
IIB	Hunter, mild	DS, HS	X-linked recessive	Iduronate sulfate	Absent
IIIA	Sanfilippo A	HS	Autosomal recessive	Sulfamidase	Severe
IIIB	Sanfilippo B	HS	Autosomal recessive	*N*-Acetyl-α-D-glucosaminidase	Severe
IIIC	Sanfilippo C	HS	Autosomal recessive	α-Glucosaminide-*N*-acetyltransferase	Severe
IIID	Sanfilippo D	HS	Autosomal recessive	*N*-Acetyl-α-D-glucosaminide-6-sulfatase	Severe
IVA	Morquio A	KS	Autosomal recessive	Galactosamine-6-sulfate sulfatase	Absent
IVB	Morquio B	KS	Autosomal recessive	β-Galactosidase	Absent
V	No longer used				
VIA	Maroteaux-Lamy (classic or severe)	DS	Autosomal recessive	*N*-Acetylgalactosamine-4-sulfatase	Absent
VIB	Maroteaux-Lamy (mild)	DS	Autosomal recessive	*N*-Acetylgalactosamine-4-sulfatase	Absent
VII	Sly	DS, HS	Autosomal recessive	β-Glucuronidase	Moderate

Note.—DS = dermatan sulfate; HS = heparan sulfate; KS = keratan sulfate.

[a] Modified from McKusick and Neufeld [1].

TABLE 2: Clinical Characteristics and CT and MR Findings in Patients with Mucopolysaccharidosis (MPS)

	Case No.							
	1	2	3	4	5	6	7	8
Age	5	21	5	8	10	10	5	11
Gender	F	M	M	M	M	M	M	M
Type of MPS	I S (Scheie)	I S (Scheie)	IIA (Hunter, severe)	IIB (Hunter, mild)	IIB (Hunter, mild)	IIIB (Sanfilippo B)	IIIB (Sanfilippo B)	VI (Maroteaux-Lamy)
Main clinical findings								
Gargoylism	+	+	+	+	+	+	+	+
Corneal clouding	−	−	−	−	−	−	−	+
Dysostosis multiplex	+	+	+	+	+	+	+	+
Cardiac involvement	+	+	+	+	+	−	−	+
Hepatosplenomegaly	+	+	+	+	+	+	+	+
Hearing loss	+	+	+	+	+	+	+	+
Mental retardation	−	−	+	−	−	+	+	−
MR findings								
Prolonged T1 and T2 of multiple foci in white matter	−	−	+	−	−	−	−	+
Reduced contrast of gray and white matter on T2-weighted images	−	−	+	−	−	+	+	−
Prolonged T2 of periventricular white matter	−	−	+	−	−	−	±	−
Atrophic changes	−	±	±	−	−	+	+	+
Prolonged T1 and T2 of left thalamus	−	−	−	−	−	+	−	−
CT findings								
Low density of white matter	−	−	±	−	−	−	−	−
Atrophic changes	−	±	±	−	−	+	+	±
Low density of left thalamus	−	−	−	−	−	+	−	−

Note.—+ = present; ± = borderline; − = absent.

excitations), producing T2-weighted images, and inversion recovery (IR), 2100/600/40/1 (TR/TI/TE/excitations), producing T1-weighted images. Eight multislices were obtained that were about 10 mm thick with 2 mm between adjoining slices. Images were acquired with the use of 256 phase-encoding steps and 256 frequency-encoding steps with each interpolated to 512 for the imaging display and one average. Spatial resolution was about 0.6 × 0.6 mm. With the Somatom 2 or DR 3 CT scanner, slice thickness was 8 mm.

Results

No intracranial abnormality was detected in case 1 (MPS I S) on either CT or MR imaging. In case 2 (MPS I S), thickening of the skull and mild ventricular dilatation were seen, but no intracranial abnormalities. In case 3 (MPS IIA; Fig. 1), T1 and T2 were prolonged in various areas of the white matter, and T2 was prolonged adjacent to the posterior horns of the lateral ventricles. T2-weighted SE images showed less contrast between the gray and white matter than in a healthy subject of the same age (Fig. 1F). However, this contrast abnormality was not demonstrated on IR images. In cases 4 and 5 (MPS IIB), there were no abnormal findings. Not only the clinical features but also the MR findings in MPS IIA were more severe than those in MPS IIB. In case 6 (MPS IIIB; Fig. 2), the contrast between the gray and white matter was reduced on the T2-weighted SE images, as it was in case 3. In addition, T1 and T2 were prolonged in the left thalamus. These findings indicated the possibility of porencephaly, as their signal intensity was equivalent to that of CSF; another possibility was the presence of an old infarction. Cerebral atrophy was recognized. In case 7 (MPS IIIB) also, contrast of the gray and white matter was decreased on the T2-weighted SE images. Ventricular dilatation and cerebral atrophy were seen on both CT and MR images. In case 8 (MPS VI, Fig. 3), the T1 and T2 in the white matter were even more prolonged than in case 3. Contrast between the gray and

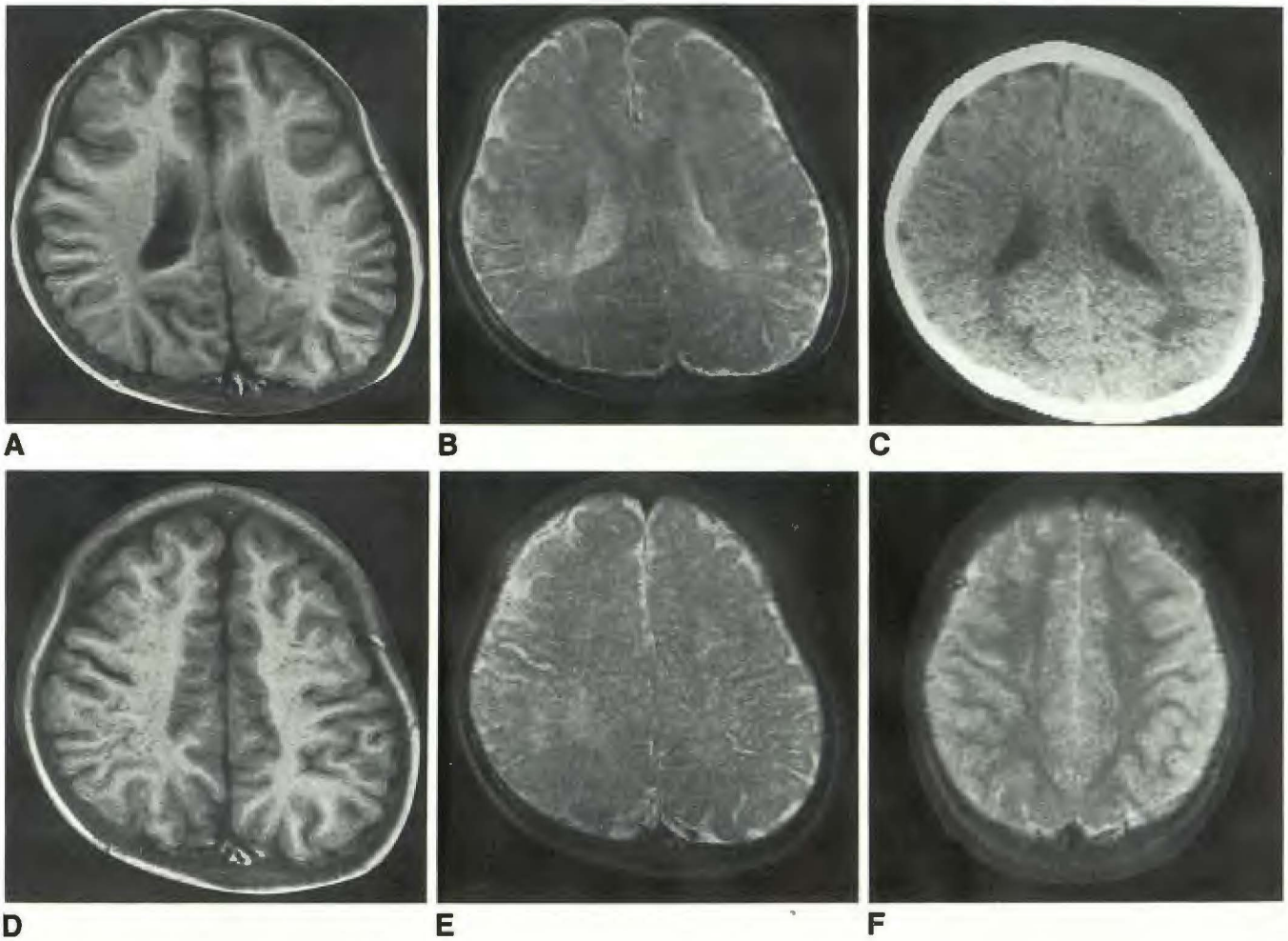

Fig. 1.—*A–E*, Case 3: Mucopolysaccharidosis IIA.
***A*, IR image, 2100/600/40, shows low signal intensity in various areas of white matter and mild dilatation of lateral ventricles.**
***B*, SE image, 1800/120, at same level shows high signal intensity in same areas of white matter, and also adjacent to posterior horns.**
***C*, Plain CT scan shows mild dilatation of lateral ventricles, but multiple foci seen in *A* and *B* are not seen as low density here.**
***D*, IR image, 2100/600/40, at another level also shows spots of low signal intensity in white matter.**
***E*, SE image, 1800/120, at same level shows little contrast between gray and white matter.**
***F*, Healthy boy of the same age as case 3. SE image, 1800/120, shows normal degree of contrast between gray and white matter.**

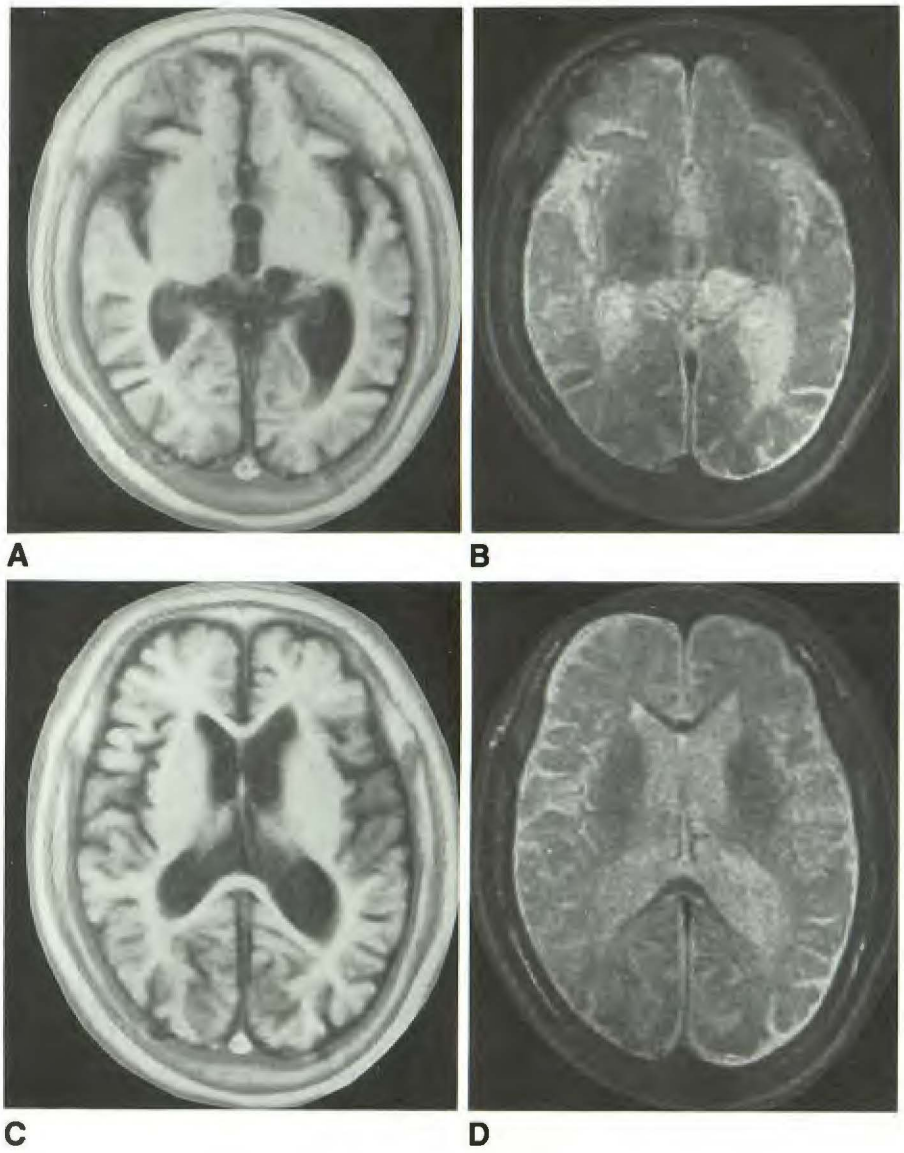

Fig. 2.—Case 6: Mucopolysaccharidosis IIIB.
***A*, IR image, 2100/600/40, shows low signal intensity (porencephaly or old infarction) in left thalamus.**
***B*, SE image, 1800/120, at same level shows high signal intensity in same area.**
***C* and *D*, IR, 2100/600/40 (*C*), and SE, 1800/120 (*D*), images at another level show cerebral atrophy and little contrast between gray and white matter.**

white matter on the T2-weighted SE images was normal. Mild to moderate ventricular dilatation was detected on both CT and the MR images shown in Figure 3.

The MR and CT findings are summarized in Table 2.

Discussion

Prolonged T1 and T2 values in the white matter, which were manifest as multiple small dispersed areas on MR images in MPS IIA and MPS VI, seem to account for the small pits or large lacunae observed in fixed brain specimens of MPS I H. These pits are caused by tissue rarefaction around blood vessels [6]. In the dilated perivascular spaces, vacuolar cells containing GAG are numerous. It follows, therefore, that the water content in the tissue of this region is increased, which seems to contribute to the prolongation of the T1 and T2. When the MR image shows dispersed spots in the white matter, the possibility that they reflect demyelination [7] or lacunar infarcts, which may occur as MPS progresses, should be considered. Dekaban et al. [8] examined the affected brain at autopsy and reported that dilatation of the perivascular space is a pathologic change found in MPS I, MPS II, and MPS IIIA. It is not clear whether this change is specific to MPS IIA and MPS VI only, as it seems to be from our results, or whether it may occur in other forms of MPS, perhaps appearing as the disease progresses.

The reduced gray/white-matter contrast observed in our cases of MPS IIA and MPS IIIB was identical to that found in Hurler syndrome, as reported by Johnson et al. [9]. They reported MR findings in a case of MPS I H before and after bone-marrow transplantation, and found that gray/white-matter contrast was improved and myelination enhanced after transplantation. Demyelination can be delineated as pro-

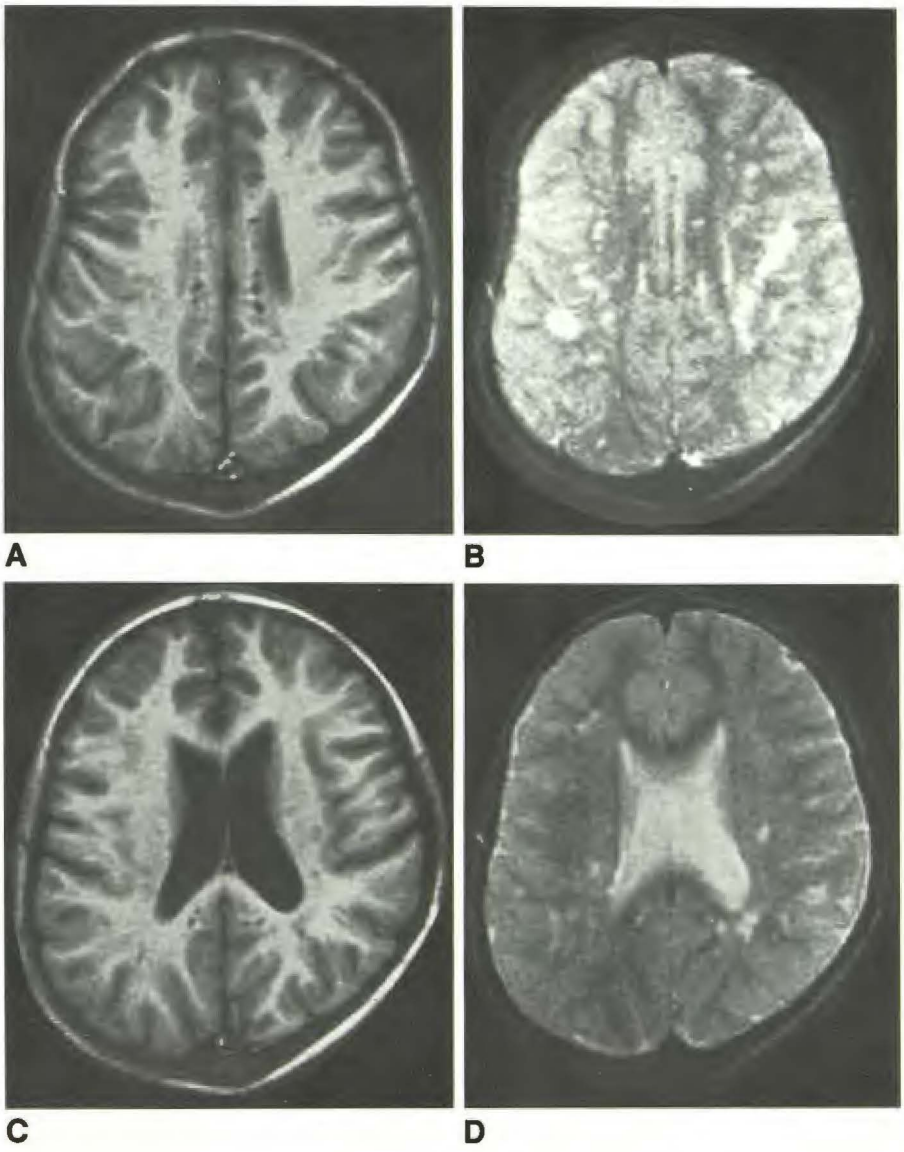

Fig. 3.—Case 8: Mucopolysaccharidosis VI.
***A*, IR image, 2100/600/40, shows low signal intensity in various areas of white matter. Mild to moderate ventricular dilatation is seen.**
***B*, SE image, 1800/120, at same level shows high signal intensity in same areas of white matter and little contrast between gray and white matter. Mild to moderate ventricular dilatation is seen.**
***C* and *D*, IR, 2100/600/40 (*C*), and SE, 1800/120 (*D*), images at another level show the same findings.**

longed T1 or T2 on MR images [10]. Diffusely reduced contrast between gray and white matter does not always represent demyelination. It is possible that such reduced contrast may indicate a process leading to general changes characterized by the accumulation of glycolipids and GAG in the lysosomes of neurons and in the astrocytes of the gray and white matter. Also, the absence of white-matter lesions in MPS I S (cases 1 and 2) seems to be a criterion for the differentiation of this type of MPS from Hurler syndrome, which is associated with white-matter abnormalities.

In our MR study, periventricular T2 prolongation as reported in Hurler syndrome was seen only in a patient with MPS IIA. In this patient, mild ventricular dilatation was evident on the CT scans, and the patient was suspected of having slight periventricular edema. Watts et al. [2] have reported that the low density in the white matter detected on CT covered too wide a range to be explained merely by periventricular edema caused by hydrocephalus, and ascribed the CT changes to other factors arising from the MPS. We postulate that the low density on CT may be caused not only by hydrocephalus but also by abnormalities in myelination. The increased signal in the periventricular white matter on MR images in one of our patients most likely reflected disordered myelination.

In our patients, mental retardation was associated with reduced gray/white-matter contrast, which was demonstrated on T2-weighted MR images (in MPS IIA and MPS IIIB), rather than with prolonged T1 and T2 multifocal small lesions in the white matter (in MPS IIA and MPS VI). This suggested that the extent of diffuse abnormality of the white matter is correlated with the severity of the disorder. Wolfe et al. [11] proposed that mental retardation may be associated with intraneural deposits of material; that is, with gray-matter abnormalities. Further, increased levels of sphingolipids may contribute to the brain damage that occurs in some forms of

MPS [12]. However, the relationship between the biochemical data and MR findings has not yet been studied.

In our study, we were able to distinguish among different types of MPS with MR; MR images were also useful in evaluating the extent of mental retardation and in monitoring the progress of the disease.

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