## 26. Inherited White Matter Disease

Recognizing the progression of myelination in normal brain development is critical for detecting white matter diseases of childhood. The MRI SI relationship between gray and white matter in neonates—in whom the latter is not yet myelinated—is reversed when compared to the adult. It is thought that the interaction of water with cholesterol, galactocerebrosides, and proteins of the myelin bilaminar membrane are responsible for the T1 shortening (and thus high signal intensity on T1-weighted scans) seen with normal myelination in the brain.

Myelination begins in the occipital lobe, centrum semiovale, internal capsule, and corpus callosum and is best assessed with T1WI in the first year of life. Myelination progresses from central to peripheral, posterior to anterior, and from sensory to motor tracts. By one year of age, T1WI demonstrate close to the adult pattern of gray and white matter SI. As the water content of newly-formed myelin progressively decreases, the SI of white matter on T2WI declines, with these changes seen on imaging mainly between one and two years of age (at which time the appearance is close to that of the adult pattern). Terminal areas of myelination—the white matter of the parietal lobes surrounding the ventricular trigones—may demonstrate high SI on T2WI up until 10 years after birth.

The leukodystrophies are inherited dysmyelinating conditions characterized by the improper laying down or subsequent breakdown of myelin. Adrenoleukodystrophy is a congenital peroxisomal abnormality in very long chain fatty acid metabolism presenting with adrenal insufficiency and rapid neurologic decline. Of the inherited leukodystrophies, its MRI appearance is the most characteristic. The T2WI of Figure 26.1 A demonstrates areas of high SI surrounding the atria of the lateral ventricles and extending across the slightly atrophic (due to disease involvement) splenium of the corpus callosum. Corresponding areas of low SI are seen on the sagittal T1WI of Figures 26.1 B, C. Involvement of the fornix and parieto-occipital white matter is also common. Contrast enhancement may occur along the leading edge of these lesions correlating with active demyelination. MRI appearances of other leukodystrophies are less specific. The mucopolysaccharidoses—including Hurler, Hunter, and Sanfilippo syndromes—are inherited conditions resulting from defects in the lysosomal enzymes that degrade glycosaminoglycans. The T2WI of Figure 26.1 D demonstrates a case of Hunter syndrome (caused by a defect in iduronate sulfatase) with nonspecific patchy periventricular hyperintensities. Gray-white matter differentiation may also be poor, while small cystic lesions (in reality dilated perivascular spaces), filled with glycosaminoglycans, are somewhat specific for the diagnosis of a mucopolysaccharidosis. Chronically, atrophic

changes and ventriculomegaly (Fig. 26.1 D) may be present.

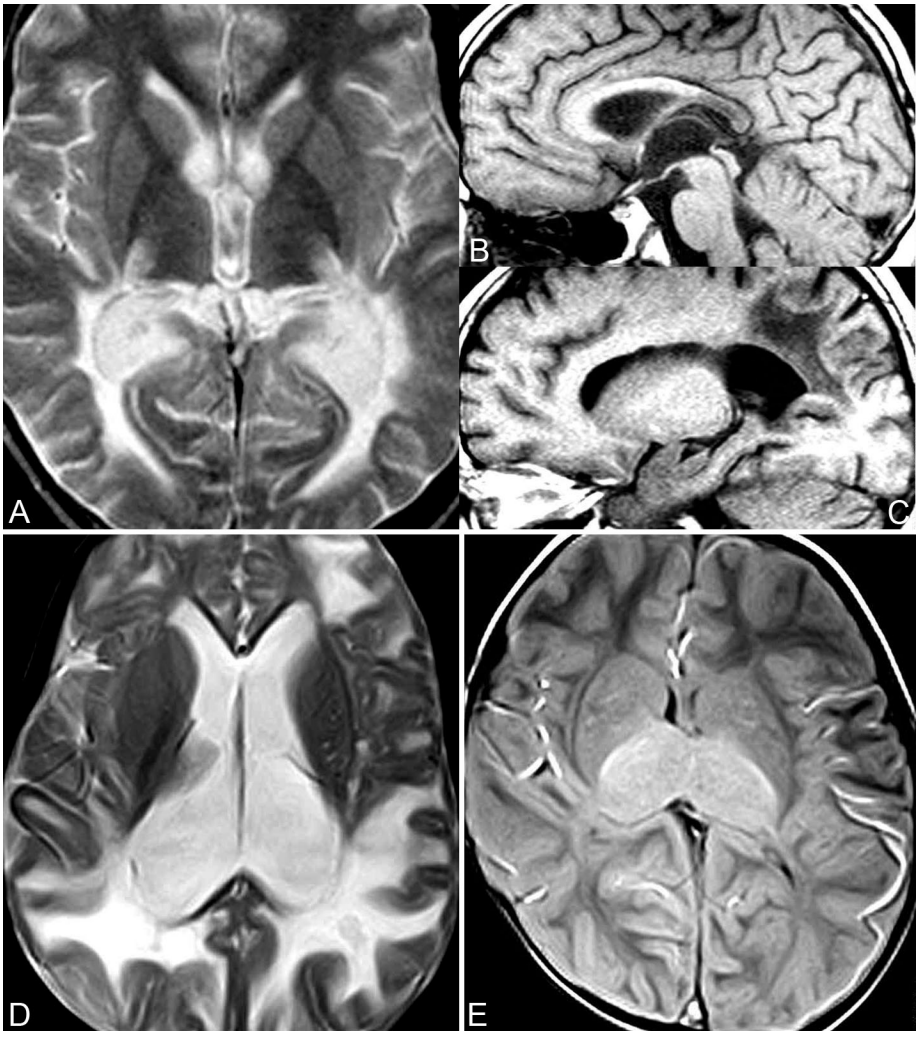


Fig. 26.1

The GM1 and GM2 (Tay-Sachs) gangliosidoses (lysosomal storage disorders) are leukodystrophies resulting from deficiencies in β-galactosidase and hexosaminidase, respectively. Figure 26.1 E demonstrates a case of GM1 that highlights the importance of recognizing the progression in normal brain MRI appearance with age. In this T1WI there is diffuse hypointensity throughout the parenchymal white matter except within the posterior limb of the internal capsule. In a neonate, this appearance would be typical of a normally developing brain with early myelination in the internal capsule posteriorly. However, this child is eleven months of age. The T1WI should thus appear similar to that of an adult, and so—by age criteria—the white matter in Figure 26.1 E is diffusely abnormal. Findings on T2WI (not illustrated) include areas of high SI corresponding in location with the abnormality seen on T1WI. Hyperintensity within the thalamus on T1WI is also

characteristic. Atrophic findings occur chronically.

Metachromatic leukodystrophy is the most common lysosomal storage disease and is due to a defective arylsulfatase A enzyme. On MR, diffuse, symmetric high SI is seen within the periventricular white matter on T2WI with characteristic sparing (early) of subcortical U-fibers and gray matter.

As discussed, MR findings seen early in a few of the leukodystrophies may suggest a specific diagnosis, however MR in late-stage disease is usually non-specific. For example, not previously discussed, enhancing lesions are more typical of adrenoleukodystrophy, Krabbe, or Alexander disease. Of clinical note, the latter along with Canavan disease characteristically present with macrocephaly.