MR imaging in rhizomelic chondrodysplasia punctata

Dysmorphic facial appearance, including a prominent forehead, hypoplasia of the midface, long philtrum, and thin upper vermillion border.

Bams-Mengerink et al. studied 11 patients with the peroxisomal disorder rhizomelic chondrodysplasia punctata (RCDP). Patients with a mild phenotype had no MRI abnormalities. Delayed myelination, ventricular enlargement and increased subarachnoidal spaces, supratentorial myelin abnormalities, and cerebellar atrophy were observed in patients with the severe phenotype of both RCDP type 1 and 3. The severity of both the MRI abnormalities and the clinical phenotype correlated with the plasmalogen level.

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Peroxisomal disorders, plasmalogens, and disturbances in myelination

Commentary by Michael J. Noetzel, MD

Rare neurologic diseases often offer an opportunity for greater understanding of pathophysiologic mechanisms of disease than might be expected based on their relative infrequency. Peroxisomal disorders are one such example. Currently, there are 17 disease states secondary either to a disorder of peroxisomal biogenesis or deficiencies of a single peroxisomal enzyme.¹ Peroxisomes play a key role in a variety of metabolic pathways, most notably beta oxidation of fatty acids and biosynthesis of ether-phospholipids, including plasmalogens, which compromise approximately 20% of the phospholipids found in CNS myelin. Peroxisomal disorders include neonatal and X-linked adrenoleukodystrophy, Zellweger syndrome, and Refsum's disease.

Bams-Mengerink et al. report their findings on 11 patients with RCDP, another peroxisomal disorder, and the correlation between biochemical disturbances and clinical and neuroradiologic imaging. In its most severe form, RCDP produces growth retardation, rhizomelia, and congenital cataracts, as well as profound mental retardation and spastic tetraplegia. RCDP has been subgrouped into

three types based upon the underlying genetic mutations. Type 1 is caused by a defect in the PEX 7 gene, which is responsible for encoding a cytosolic receptor necessary for correct targeting of enzymes to the peroxisome. RCDP types 2 and 3 are secondary to mutations in encoding of peroxisomal enzymes involved in plasmalogen biosynthesis. In all three types there is deficient plasmalogen biosynthesis; type 1 also has excessive levels of phytanic acid. The Bams-Mengerink et al. study suggests, in contrast to earlier hypotheses, that elevated phytanic acid is not responsible for the cerebellar atrophy noted in most cases of RCDP. In contrast, deficiencies in plasmalogen synthesis correlate with MRI findings indicative of disturbances in myelination, including T2 signal abnormalities in the cerebral hemispheres, delayed or incomplete myelination, and ventricular enlargement. A similar correlation between the levels of plasmalogens and clinical phenotype was also documented, indicating that in patients with RCDP (regardless of the genetic abnormality), the residual capacity to synthesize plasmalogen is a major factor

in the severity of clinical phenotype and disturbance in CNS myelination.

The findings of Bams-Mengerink et al. concerning the relationship between plasmalogen synthesis and the development of myelin also has broader implications for unclassified leukodystrophies. Despite advances in molecular genetics and MRI technology, unclassified white matter disorders remain a clinical problem in pediatric neurology.² In addition to the two peroxisomal enzymes deficient in RCDP, there is a third enzyme [acyl-DHAP: NAD(P)H oxidoreductase] which has a bimodal distribution in both the endoplasmic reticulum (ER) and peroxisome. Other enzymatic steps for the final production of plasmalogens take place in the ER. Testing for deficiencies in these plasmalogen biosynthetic enzymes may allow molecular identification of previously undiagnosed leukodystrophies.

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