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Visual Diagnosis

Girl With Progressive Head Enlargement and Gait Disturbance: Clinicoradiological Clues

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This four-year-old girl presented with progressive head enlargement and gait disturbance noted from late infancy. She had a mild delay in the achievement of motor milestones and was clumsy while walking. She had five episodes of generalized tonic-clonic seizures starting after age two years. She was born to a third-degree consanguineous couple after an uncomplicated perinatal period. Her cognitive and language milestones were age appropriate. There were no neurological illnesses among the family members. Examination revealed macrocephaly (53 cm, at ninety-ninth percentile of World Health Organization head circumference chart), bilateral spasticity, and cerebellar signs (gait ataxia, intention tremors, and dysmetria). Magnetic resonance imaging of the brain showed diffuse white matter changes with frontotemporal cysts (Fig). A possibility of megalencephalic leukoencephalopathy with subcortical cysts (MLC) was considered. Genetic analysis revealed a pathogenic homozygous variation in exon 2 of the MLC1 gene (c.135_136insC), confirming the diagnosis. She received oral levetiracetam (20 mg/kg/day), and parents were counseled about the nature and prognosis of the disease.

MLC is an autosomal recessively inherited leukodystrophy, characterized by macrocephaly, motor delay, and progressive spasticity with cerebellar ataxia.[1] Cognitive and language functions are usually preserved or mildly impaired. Seizures are infrequent, and a minority of patients may have extrapyramidal symptoms. Because of progressive spasticity and gait impairment, most of the children become wheelchair-bound by age 15 years.[2] Typical magnetic resonance imaging findings include diffuse cerebral white matter abnormalities, subcortical cysts in the temporal and frontal lobes, and partial involvement of the posterior limb of the internal capsule, cerebellar white matter, and brainstem. The corpus callosum and anterior limb of the internal capsule are usually spared.[1] The most common mutation reported in the Indian population is c.135_136insC, and it is frequently observed in the Agrawal community.[3] Subcortical cysts differentiate this condition from other inherited leukodystrophies and help in the early diagnosis and prognostication of the disease.

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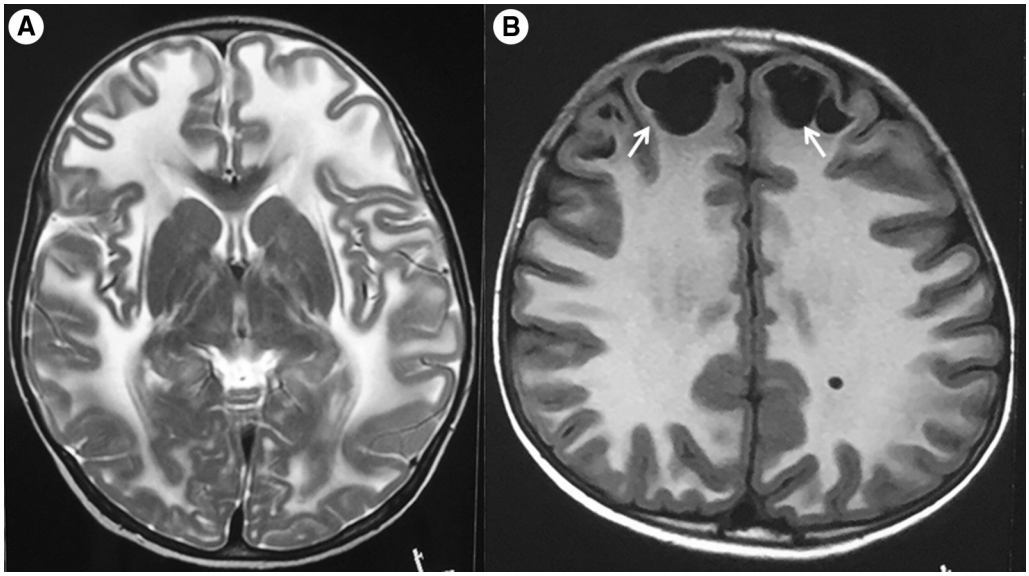

FIGURE. Magnetic resonance imaging of the brain. T2-weighted axial (A) section showing diffuse involvement of the subcortical and periventricular white matter bilaterally with relative sparing of occipital white matter and corpus callosum. The posterior limb of the internal capsule is also affected, as indicated by the presence of two hyperintense lines with a spared line in middle. Fluid-attenuated inversion recovery (B) sequence showed bilateral large anterior frontal cysts (arrows).

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