Case 12285

Van der Knaap disease, a megalencephalic leukoencephalopathy with subcortical cysts
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Section: Neuroradiology
Area of Interest: Neuroradiology brain
Procedure: Diagnostic procedure
Imaging Technique: MR
Special Focus: Congenital Case Type: Clinical Cases
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Patient: 4 years, male

Clinical History:

The patient had a history of delayed milestones, seizure and ataxia with enlarge head size.

Imaging Findings:

MRI brain revealed diffuse symmetrical hyperintensity in bilateral periventricular and subcortical white matter on T2 images. Relative sparing of corpus callosum was noted. Subcortical cysts were noted in bilateral high frontal and parietal region and bilateral anterior temporal region. Macrocephaly was noted. Brainstem and cerebellum did not reveal any abnormality.

Discussion:

Megalencephalic leukoencephalopathy (MLC) with subcortical cysts was first described by van der Knaap, et al. in 1995. MLC is a rare disease with a low carrier rate. The disease has a high incidence in populations in which consanguinity is common. MLC is an autosomal recessive disorder due to mutations in MLC1 gene which has its locus in chr22qter. The physiological function of the protein is at present unknown. It is probably an integral membrane protein. In India, the majority of the patients belong to the Agarwal community. [1, 2]

MLC is known for its mild neurological signs and symptoms in the setting of very abnormal MR findings. Macrocephaly is present at birth or, more commonly, develops within the first year of life in all patients. Early development is normal or mildly delayed.

Slow deterioration of motor functions with cerebellar ataxia and mild spasticity usually starts in early childhood. Some patients have extrapyramidal movement abnormalities with dystonia and athetosis, usually as a late finding. Mental decline occurs later and is much milder than motor decline. Most patients have epileptic seizures. [1, 3]

In typical cases, the MR findings are often diagnostic of MLC. MR shows 'swollen white matter' and diffuse supratentorial symmetrical white matter changes in the cerebral hemispheres with relative sparing of central white matter structures like the corpus callosum, internal capsule, and brain stem. Subcortical cysts are almost always present in the anterior temporal region and are also frequently noted in frontoparietal region. Grey matter is usually spared. Gradually the white matter swelling decreases and cerebral atrophy may ensue. The subcortical cysts may increase in size and number. Moderate decrease in NAA/ Cr and Choline/Cr ratios have been reported in patients with MLC on MR spectroscopy. [1, 3]

The differential diagnosis of MLC includes Canavan's disease, Alexander disease, infantile-onset GM2 and GM1
gangliosidosis. These conditions have relentlessly progressive infantile onset leukoencephalopathy that is frequently fatal within the first decade of life, however, MLC has a remarkably slow course of deterioration in neurologic function. MLC must be included in the differential diagnosis of macrocephaly with early onset leukoencephalopathy.

[1] **Differential Diagnosis List:** Van der Knaap disease, a megalencephalic leukoencephalopathy with subcortical cysts, Canavan’s disease, Alexander disease, Infantile-onset GM2 and GM1 gangliosidosis

**Final Diagnosis:** Van der Knaap disease, a megalencephalic leukoencephalopathy with subcortical cysts

**References:**


Description: MRI brain T2 axial image revealed diffuse symmetrical hyperintensity in bilateral cerebral hemisphere white matter. Origin: Sanya Diagnostics, Rajkot civil hospital, Rajkot, Gujarat, India
Description: MRI brain T2 axial image revealed subcortical cysts in bilateral anterior temporal region.
Origin: Sanya Diagnostics, Rajkot civil hospital, Rajkot, Gujarat, India
Description: MRI brain T2 coronal image revealed diffuse symmetrical hyperintensity in bilateral cerebral hemisphere white matter with subcortical cysts in bilateral anterior temporal region. Origin: Sanya Diagnostics, Rajkot civil hospital, Rajkot, Gujarat, India
Description: MRI brain T2 sagittal image revealed subcortical cysts in anterior temporal and parietal region with changes of macrocephaly. Origin: Sanya Diagnostics, Rajkot civil hospital, Rajkot, Gujarat, India
Description: MRI brain FLAIR axial image revealed subcortical cysts in bilateral high frontal and parietal region. Origin: Sanya Diagnostics, Rajkot civil hospital, Rajkot, Gujarat, India
Description: MRI brain FLAIR axial image revealed subcortical cysts in bilateral anterior temporal region. Origin: Sanya Diagnostics, Rajkot civil hospital, Rajkot, Gujarat, India
Description: MRI brain T1 axial image revealed diffuse symmetrical hypointensity in bilateral cerebral hemisphere white matter with relative sparing of corpus callosum. **Origin:** Sanya Diagnostics, Rajkot civil hospital, Rajkot, Gujarat, India.