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# A CASE REPORT OF MEGALENCEPHALIC LEUKOENCEPHALOPATHY WITH SUBCORTICAL CYST IN NON-AGARWAL HINDU PATIENT

Neurology

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## ABSTRACT

Megalencephalic leukoencephalopathy with subcortical cysts (MLC) is a rare genetic disorder, inherited as an autosomal recessive or autosomal dominant pattern. It predominantly involves white matter of the brain. Megalencephaly is the most common and earliest clinical finding during infancy, which is followed by progressive pyramidal signs, ataxia, cognitive impairment and seizures in some patients. Magnetic resonance imaging (MRI) brain shows predominant frontotemporal white matter involvement with subcortical cysts. Though the majority of the described cases of MLC in India belongs to the Agarwal community, our patient is non-Agarwal Hindu.

## KEYWORDS

Megalencephalic leukoencephalopathy, subcortical cyst, Van Der Knaap syndrome

## INTRODUCTION:

Megalencephalic leukoencephalopathy with subcortical cysts (MLC) is an infantile onset, benign disorder which presents with macrocephaly. Macrocephaly usually progresses during the initial 1-2 years, then head growth becomes normal. Other early onset manifestations are mildly delayed motor milestones, spasticity, ataxia, and seizure. Cognitive impairment can develop as the disease progresses.[1] Most characteristic findings on MRI is cerebral white matter swelling with subcortical cysts involving predominantly anterior temporal lobe and frontoparietal lobe.[2] This disorder was first described by Singhal et al, from India in 1991, mainly among Agarwal community.[3] The first description of the disease was published by Van Der Knaap in 1995.[4] Here we described a case of non-Agarwal Indian patient.

## CASE REPORT:

A 28-year old male, born out of nonconsanguineous marriage, having a history of macrocephaly at birth. He was presented with delayed motor milestones and difficulty in walking from 2 years of age. Over a period of time the patient had developed weakness of all four limbs with spasticity, progressive imbalance while walking and tremulousness while reaching the object in both upper limbs since last 15 years. Relatives also noticed the change in voice in the form of an inappropriate halt in between the words as well as straining while speaking. Patient becomes wheelchair-bound over a last 5 years period. The patient also had 4-5 episodes of generalized seizures, mild cognitive impairment and episodes of inappropriate laughing since last 5 years. Neither of the family members is affected by similar or any other major neurological disorder. No significant abnormality was detected on general examination.

On neurological examination mild cognitive impairment with predominant language involvement. He had spastic dysarthric speech with pseudobulbar affect, slow saccades, broken pursuits, brisk jaw jerk, spastic quadriparesis and pan-cerebellar dysfunction. His gait was ataxic and scissoring. No any sensory or sphincter abnormality was detected. Initial routine blood and serological work up and EEG were normal.

MRI showed diffuse bilateral symmetrical T2 and flair hyperintensity involving cerebral white matter with relative sparing of occipital region. There were extensive subcortical cystic changes in bilateral anterior temporal, frontal and parietal regions. On genetic evaluation, we found a homozygous mutation in intron 2 of the MLC1 gene.

## DISCUSSION:

MLC is an infantile onset cerebral white matter disorder with relatively slow progression. Mean age of symptom onset is 16 months, which ranges from birth to 25 years.[2] It can present with two different phenotypes: (1) MLC 1 and MLC 2A – Classical MLC, (2) MLC 2B – Remitting MLC. Classical form is inherited as an autosomal recessive pattern, while MLC 2B is inherited as an autosomal dominant pattern. The causative gene is located on chromosome 22q. MLC 1 and MLC 2A is caused by the mutation in MLC 1 and GLIALCAM gene respectively and MLC 2B is caused by mutation in GLIALCAM gene. MLC 1 protein is present on the membrane of astroglial cells in periventricular and subependymal regions. It helps in transport of ions and water across the blood-brain barrier and brain-CSF barrier. GlialCAM protein is a chaperone of MLC1, helps in MLC1 function.[6,7] Clinically patients present with macrocephaly in the first year of life, which is followed by delayed motor milestones, progressive spastic quadriparesis, and ataxia. Most patients with MLC1 and MLC2A becomes wheelchair bound within 15 years of symptom onset, while all patients with MLC2B remains ambulatory. Cognitive impairment and behavioral abnormality are common in MLC2B as compared to other variants. Around 50-60% of patients had seizures, less common in MLC2B and seizures were well controlled.[2]

MRI shows confluent T2 and flair abnormalities in cerebral white matter with relative sparing of the corpus callosum and occipital region. Subcortical cysts are seen predominantly in the anterior temporal and frontoparietal region. In the classical form (MLC1, MLC2A), patients had abnormal signal in the posterior limb of the internal capsule and cerebellar white matter, which is spared in MLC2B. Around 43% of MLC2B patients did not have true cysts.[2]

MLC should be differentiated from the patients who present with macrocephaly, motor disability, cognitive impairment with cerebral white matter changes on MRI. It mainly includes Alexander's disease, Canavan disease, and Glutaric aciduria. Major points that favour MLC are: (1) Presence of subcortical cysts, (2) No gray matter involvement, (3) Early onset and slowly progressive disorder.[1]

An infantile variant of Alexander's disease presents with megalencephaly with frontal white matter involvement with contrast enhancement.[9] Characteristic MRI findings of infantile Canavan disease are involvement of thalamus and Globus pallidus in addition to diffuse white matter involvement.[10] Glutaric aciduria type 1 presents with megalencephaly and variable clinical course. MRI shows less prominent involvement of cerebral white matter. Specifically, it shows hypoplastic temporal lobes, the involvement of dentate nuclei and atrophy of cerebellar vermis. [11]

## CONCLUSION:

MLC is an inherited disorder, but it can also present as a sporadic disorder. It should be suspected in an infantile patient with macrocephaly. MRI brain remains the most sensitive investigational modality to identify diffuse white matter changes with the temporal and fronto-parietal subcortical cyst. Genetic testing can help to identify the mutated gene as well as it can also help in prenatal diagnosis.

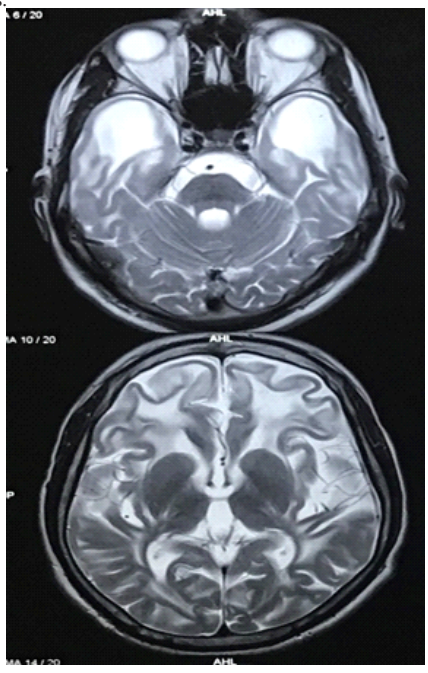

**Image I: Axial T2 image showing bilateral symmetrical white matter hyperintensity with multiple subcortical cysts.**

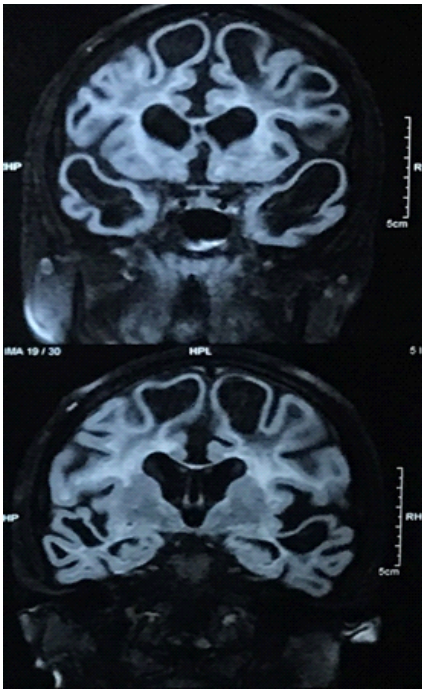

**Image II: Coronal image showing bilateral symmetrical multiple subcortical cysts.**

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