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***Case Report***

## **A case report of Megalencephalic leukoencephalopathy with subcortical cysts, a rare inherited autosomal recessive leukodystrophy, in a Nepalese child**

***Manoj Bhattarai<sup>1\*</sup> and Ashish Mohan Bhattarai<sup>2</sup>***

<sup>1</sup>Department of Radiodiagnosis and Imaging, B.P. Koirala Institute of Health Sciences, Dharan

<sup>2</sup>Department of Medicine, Nepal Police Hospital, Kathmandu

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**Abstract**

Megalencephalic leukoencephalopathy with subcortical cysts (MLC) is a rare inherited autosomal recessive leukodystrophy due to mutations in MLC1 or HEPACAM gene and have typical and characteristic neuroimaging findings. This article reports a case of 13 months old Nepalese male child with diagnosis of MLC.

**Key words**

*Macrocephaly, Megalencephalic leukoencephalopathy with subcortical cysts, Nepalese*

**Introduction:**

A rare inherited autosomal recessive leuko dystrophy, megalencephalic leuko encephalopathy with subcortical cysts (MLC) (Synonyms: Van der Knaap disease, Vacuolating Megalencephalic Leuko encephalopathy with Subcortical Cysts) was first reported by Singhal et al [1] and later described by Van der Knaap et al [2]. Of the clinical characteristics macrocephaly is the most consistent feature usually present at birth or developing during infancy with variable degree even up to 4 to 6 SD above mean. Other clinical manifestation of MLC includes mild motor developmental delay, seizures, pyramidal and cerebellar signs and mild delayed mental deterioration [3,4]. Wide age range from birth to 25 years for symptom onset with median age of 6 months is usually seen, however presentation even at fourth decade of life has been described in literature [4]. Mutations in MLC1 gene at chromosome 22q is found in about 75% of patients, whereas mutation in HEPACAM gene is responsible for remaining MLC

patients [5]. Typical clinical presentation and characteristic neuroimaging findings helps establishing diagnosis of MLC. This article reports a case of 13 months old Nepalese male child with diagnosis of MLC.

**Case presentation:**

A 13 months old male child presented with complaint of one episode of seizure one week back and progressive enlargement of head noticed for 7 months of age. He was a second child born from non-consanguineous marriage with uneventful pregnancy and uncomplicated vaginal delivery. Social smile was attained by 2.5 months; head control by 6 months, sit without support by 8 months and stand without support by 11 months. However, since then regression of milestones was seen with inability to stand or sit without support. Similar history of progressive enlargement of head and regression of milestones was present in his older male sibling who died at the age of 3.5 years. No investigations were carried out in his older sibling. On examination macrocephaly

was present with head circumference of 52.0 cm. Motor examination was normal. Computed tomography (CT) of brain was obtained which showed diffuse symmetrical white matter hypodensity in bilateral cerebral hemispheres with sparing of internal capsules and corpus callosum. Subcortical cysts of CSF density were present in bilateral anterior temporal lobes. Persistent cavum septum pellucidum was also noted. No change in appearance of lesions was seen in post contrast images. Basal ganglia, thalamus, brain stem and cerebellum were normal. (Figure: 1, 2, 3). Magnetic resonance imaging (MRI) of brain was suggested, but parents of child declined for further investigation. Considering clinical and CT scan findings diagnosis of MLC was made.



Figure 1

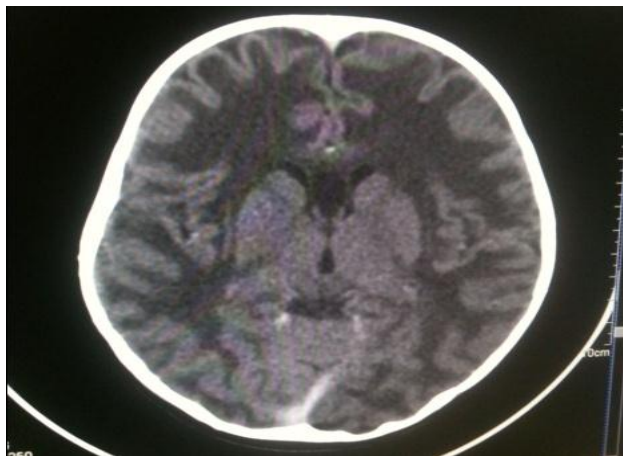


Figure 2



Figure 3

**Figure 1, 2 & 3:** Post contrast axial CT scan images of brain showing diffuse symmetrical white matter hypodensity in bilateral cerebral hemispheres with subcortical cysts in bilateral anterior temporal lobes. Persistent cavum septum pellucidum noted.

#### Discussion:

MLC is a rare inherited autosomal recessive leukodystrophy with mutations in MLC1 gene at chromosome 22q in about 75% cases and in HEPACAM gene in remaining cases [5]. It is more prevalent in certain ethnic groups like Aggrawal community in India, Libyan Jews and in Turks, and where consanguineous marriage is common [1,6-8]. In contrast a child in this case report was born from non-consanguineous marriage.

Typical clinical presentation and characteristic neuroimaging findings helps in establishing diagnosis of MLC. Macrocephaly is the characteristic and most consistent feature which is usually present at birth or develops during infancy with slow progression and delayed neurologic deterioration. Typical MRI findings are diagnostic for MLC. Diffuse symmetrical abnormal and swollen white matter of cerebral hemispheres showing confluent supratentorial white matter hyperintensity in T2 weighted and FLAIR images, and presence of subcortical cysts in bilateral anterior temporal lobes are typical. Cysts are also often found in frontoparietal region. These subcortical

cysts are completely suppressed in FLAIR images and may increase in size and number later on. No changes in appearances of white matter abnormalities and subcortical cysts are seen in post contrast images. Basal ganglia and gray matter are not involved. Internal capsule, corpus callosum and brain stem are relatively spared, whereas white matter of cerebellum may show mild abnormality or may be normal [5,9]. Even though diagnosis of MLC can be made by clinical and MRI findings, chromosomal analysis for detection of mutations in MLC1 or HEPACAM gene should be performed to identify genetic mutations in the family and for prenatal diagnosis [6,9].

In differential diagnosis of MLC other conditions like Canavan's disease, Alexander disease, infantile onset GM2 and GM1 gangliosidosis, glutaric aciduria and merosin deficient congenital muscular dystrophy which also presents with macrocephaly and early onset leukoencephalopathy should be considered [3,8,10,11]. However, in comparison with these conditions, MLC shows slow progression of neurological deterioration. In contrast to MLC, in Canavan's disease there is involvement of basal ganglia and thalamus and subcortical cysts as seen in MLC are absent. Frontal dominance of white matter abnormality showing post contrast enhancement is noted in Alexander disease, whereas in MLC there is diffuse leukoencephalopathy and no post contrast enhancement. Also involvement of basal ganglia may be seen in Alexander disease. Involvement of basal ganglia and thalamus is seen in infantile onset gangliosidosis unlike that of MLC. In glutaric aciduria, apart from macrocephaly and white matter abnormality there is widening of CSF spaces along frontal and temporal convexity with widened bilateral sylvian fissures and bilateral basal ganglia abnormalities. Whereas in patients of

merosin deficient congenital muscular dystrophy, subcortical cysts typically seen in MLC are lacking and patients have muscle weakness and hypotonia.

#### **Conclusion:**

MLC should be considered in differential diagnosis of a patient presenting with early onset macrocephaly with diffuse leukoencephalopathy. Even though MLC is more prevalent in certain ethnic groups and where consanguineous marriage is common, it can occur in child born from non-consanguineous marriage and found in Nepalese population. Typical neuroimaging findings are diagnostic for MLC which includes diffuse symmetrical abnormal and swollen supratentorial white matter with subcortical cysts in bilateral anterior temporal lobes. However further chromosomal analysis to be performed for detection of genetic mutation in the family and for prenatal diagnosis.

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