When the head is big, think this too: Megalencephalic leukoencephalopathy in a toddler with only a large head. A case report

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Abstract

We present a one-year old, developmentally normal toddler from a non Agarwal community, who presented to us with only a large head. The examination findings were unremarkable except a large head circumference. Neuroimaging confirmed the diagnosis of megalencephalic leukoencephalopathy (MLC). Although developmental delay and seizures are common manifestations in MLC, we want to highlight the fact that many children like ours may have no neurological manifestations at all which makes it necessary to do neuroimaging to establish the diagnosis and offer genetic testing for confirmation of the same.

Keywords: Cysts, demyelination, developmental disabilities, hereditary central nervous system demyelinating diseases, megalencephaly, Van der Knaap disease, white matter

Case Report

A one-year-old toddler came to our outpatient department with the complaint of progressively increasing head size since the age of six months. He was born at term by vaginal delivery to parents with third-degree consanguinity. The perinatal period was uneventful. The progressive increase in head size was noticed since about six months of age. There was no history of any seizures, behavioural problems, developmental delay or regression of milestones. There was no family history of similar illness. His general physical examination, weight, and height were normal, but his head circumference was 54.5 cm (>97th percentile for his age and sex [Figure 1a, 1b]. A central nervous system examination did not reveal any spasticity, hyperreflexia, or cerebellar signs with a normal developmental assessment. The fundus examination was also normal with no cherry-red spots or evidence of retinitis pigmentosa. The rest of the systemic examination was noncontributory.

The differential diagnosis that we had considered were MLC, Canavan disease, Glutaric aciduria type 1, Alexander’s disease and Infantile-onset GM2 gangliosidosis. Considering the large head, an a Magnetic Resonance Imaging (MRI) brain was done which showed bilateral symmetrical hypodensities on T1 images in the white matter and subcortical cysts in the anterior temporal lobes and frontal lobes [Figure 1c, 1d] and the T2 images showed hyperintensities in the same areas [Figure 1e] with a normal magnetic resonance spectroscopy (MRS) that was consistent with a diagnosis of MLC. We could not perform genetic testing in view of the financial constraints on part of the parents. Although mutation analysis is essential to confirm the diagnosis, a clinical diagnosis can be confidently made in the presence of a classical MRI feature as in our case.
MLC or Van der Knaap disease is an autosomal recessive disorder, commonly seen though not restricted to members of a particular Agarwal community. It was first described by Singhal et al. as early as 1991 but was published in 1995 by Van der Knaap et al. and subsequently the disease became recognized as Van der Knaap disease. Singhal et al. published their case series in 1996. It is characterized by macrocephaly that might be seen at birth or during the first year of life with other features like delayed attainment or regression of developmental milestones and seizures. The diagnosis is made based on the clinical presentation and classical brain MRI findings and confirmed by genetic study. MLC is a common cause of macrocephaly with leukodystrophy seen in children of consanguineous parents. The usual clinical presentation is of macrocephaly at birth or more commonly that develops during the first year of life along with near normal development. Later during childhood, they develop spasticity and seizures before 20 years of age with a majority becoming wheelchair bound by adolescence.

The diagnosis of MLC is based on typical MRI brain findings. With leukodystrophy, there is usually a diffuse white matter abnormality with the classical finding of subcortical cysts seen in the anterior temporal region with relative sparing of the central white matter as was seen in our case.

The differential diagnosis considered as mentioned in the case description above was ruled out with the following justifications.

Canavan disease presents similarly but has an N-acetyl aspartate peak in MRS. In Alexander’s disease, there is degeneration with cystic changes mostly involving the deep frontal white matter. The MRI of infantile GM2 gangliosidoses shows the central white matter of the child having a cherry-red spot on fundus examination and rarely organomegaly.

Hence, the clinical presentation, supported with the classic MRI findings led us to the conclusion of MLC. The prognosis in this condition is poor as is for other leukodystrophies and there is no specific treatment. The management is conservative with symptomatic treatment especially of seizures which is not very difficult and the prevention of injury or sequelae being important goals. The possibility of MLC should be considered in any child presenting with macrocephaly and neuroimaging should be advised even if asymptomatic at presentation. Our case draws the attention of the primary care physician to consider this particular condition even though the young child might be developmentally normal at presentation except for having only a large head. Considering this possibility and requesting for appropriate investigations would help arrive at a diagnosis earlier, rather than ignoring the parental concern or reassuring the parent which is what is usually done, causing a significant delay in establishing the diagnosis.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given their consent for their images and other clinical information to be reported in
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the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
On behalf of all the authors, the corresponding author states that there is no conflict of interest.

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