Van der knaap disease: A case report

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ABSTRACT

Van der Knaap disease or megalencephalic leukoencephalopathy with subcortical cysts (MLC) is a rare autosomal recessive degenerative disorder characterized by megalencephaly, cerebral leukoencephalopathy, and motor deterioration. Most cases reported with this disease in India belong to the Agarwal Community with Consanguinity. Here, we report the case of a 12-year-old boy belonging to this ethnic background presented with a history of delayed motor milestones, ataxia, poor scholastic performance, and seizures. MLC has a benign course and better outcome with life expectancy up to 3rd–4th decade of life. MLC should be included in differentials of macrocephaly and leukoencephalopathy with characteristic magnetic resonance imaging findings. A precise diagnosis helps for better management and to prognosticate its benign course.

Keywords: *Agarwal community, Megalencephalic leukoencephalopathy, Seizures, subcortical cysts, Van der Knaap's disease*

Van der Knaap disease or megalencephalic leukoencephalopathy with subcortical cysts (MLC) is a slowly progressive neurodegenerative disorder characterized by macrocephaly, cerebral leukoencephalopathy, and mild neurological symptoms [1]. The disease is inherited by an autosomal recessive pattern, and the gene is MLC1 on chromosome 22q [2]. It is commonly seen in the Agarwal Community of North India. It is clinically characterized by macrocephaly, motor developmental delay, seizures, spasticity, ataxia, and mild mental deterioration [3]. Magnetic resonance imaging (MRI) is the investigation of choice which will show extensive symmetrical white matter changes with subcortical cysts in the anterior temporal lobes and frontoparietal subcortical area [4]. This disease has a benign course with survival up to the 4th decade of life [5].

CASE REPORT

A 12-year-old boy born from a non-consanguineous marriage in the Agarwal Community by a normal vaginal delivery presented to our department with a history of delayed motor and social milestones with intellectual disability, resulting in poor scholastic performance with the presence of a large head, as noticed by the parents during infancy which was becoming less apparent as the child is growing. There is a history of insidious-onset, gradually progressive difficulty in maintaining balance while walking leading to recurrent falls without any history of sensory, bladder, or bowel involvement and there was no family history.

On examination, head circumference was 56 cm (>97th percentile), dysarthria and spastic paraparesis with positive Babinski sign with the presence of mild cerebellar signs and ataxia. The rest of the general physical and systemic examination was unremarkable.

Routine blood investigations along with serum creatine kinase, lactate levels were normal, and TORCH screen was negative. MRI brain done showed diffuse white matter hyperintensities and the presence of subcortical cysts in the bilateral anterior temporal region, features consistent with MLC (Fig. 1). MLC1 gene testing could not be done due to the refusal by the patient's caregivers.

The patient was symptomatically managed for seizures with antiepileptic drugs and was discharged after being clinically improved and good seizure control with oral antiepileptic (phenobarbitone at 5 mg/kg/day in two divided doses) and is under regular follow-up. MRI brain done after 3 months follow-up period did not show much difference compared to the initial imaging (Fig. 2). Informed consent was taken from his parents.

DISCUSSION

MLC is an extremely rare autosomal recessive which was first described by Singhal *et al*. in 1991 from India in the Agarwal community [5]. It was named in 1995 by Van der Knaap *et al.* [1]. MLC is the first known human genetic disease with a defect in brain ion and water homeostasis resulting in chronic cerebral white matter edema and vacuole formation [6]. The age of onset ranges from birth to 25 years, with a median of 6 months. Macrocephaly is the most consistent feature followed by ataxia and frequent falls [7,8]. Seizures are seen in 50% of the cases [9].

Diagnosis is by clinical and imaging findings. Genetic testing is not necessary. MRI is the investigation of choice, and

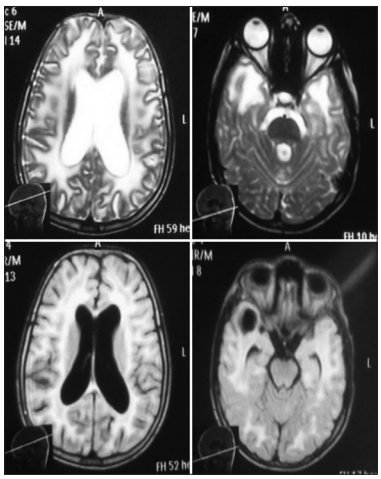

Figure 1: T2 and flair magnetic resonance imaging images showing diffuse white matter hyperintensities and the presence of subcortical cysts in the bilateral anterior temporal region which are hypointense in FLAIR images

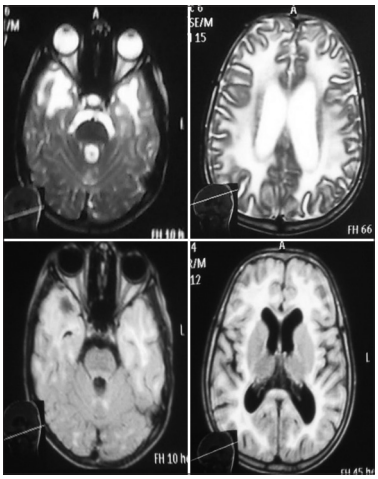

Figure 2: Follow-up T2 and flair magnetic resonance imaging (MRI) images after 3 months showing similar changes as first MRI

its characteristic features include extensive symmetrical white matter changes with subcortical cysts localized in the anterior temporal lobes and front parietal subcortical area with sparing of gray matter and central white matter structures. The characteristic feature of the disease is the relatively mild clinical course despite very abnormal findings on MRI study.

Differential diagnosis of MLC is limited, includes Canavan disease, Alexander disease, and infantile-onset GM2 gangliosidosis which can be differentiated by clinical and imaging findings [10]. All other leukoencephalopathies are fatal in early childhood or adolescence, but MLC has a benign course with a relatively better outcome with life expectancy up to 3–4th decade of life. At present, there is no definite treatment for MLC. Patients were treated with acetazolamide without any clinical or radiological improvement. Supportive therapy is suggested to control seizures which respond well to commonly used anticonvulsants and physical therapy to improve motor dysfunction [11].

CONCLUSION

MLC should be included in differentials of macrocephaly and early onset leukoencephalopathy with characteristic MRI findings. The precise diagnosis helps a clinician for better management of the child and to prognosticate its benign course to the parents. Genetic testing should be done whenever possible as families can be counseled regarding inheritance of the disease such that consanguinity can be discouraged.

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