

## Case Report

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# 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 megalcephaly, cerebral leukoencephalopathy, and motor deterioration. Most cases reported with this disease are from our country India, belong to Agarwal community, who have high rates of consanguinity. We report a 4 and 1/2 year old boy, with a history of delayed motor milestones, ataxia, increasing head circumference and abnormal body movements, who is belonging to the Bhat family of Handwara town of Kupwara district of Jammu and Kashmir, India.

**Keywords:** Child, Consanguinity, Macrocephaly, Subcortical cysts

## INTRODUCTION

Van der Knaap disease or megalencephalic leukoencephalopathy with subcortical cysts is a slowly progressive neurodegenerative disorder characterized by macrocephaly, cerebral leukoencephalopathy, and mild neurological symptoms.<sup>1</sup> The age at which manifestations ranges from birth to 25 years, with a median age of 6 months. The disease is inherited by an autosomal recessive pattern and the regulator gene is MLC1 on chromosome 22q.<sup>2</sup> It is commonly seen in Agarwal community of north India. It is clinically characterized by macrocephaly, motor development delay, seizures, spasticity, ataxia, mild mental deterioration.<sup>3</sup> Magnetic resonance imaging(MRI) is the investigation of choice in which extensive, symmetrical white matter changes with subcortical cysts in the anterior temporal lobes and fronto-parietal subcortical area are.<sup>4</sup> This disease has a benign course with a survival rate upto the 4<sup>th</sup> decade of life.<sup>5</sup>

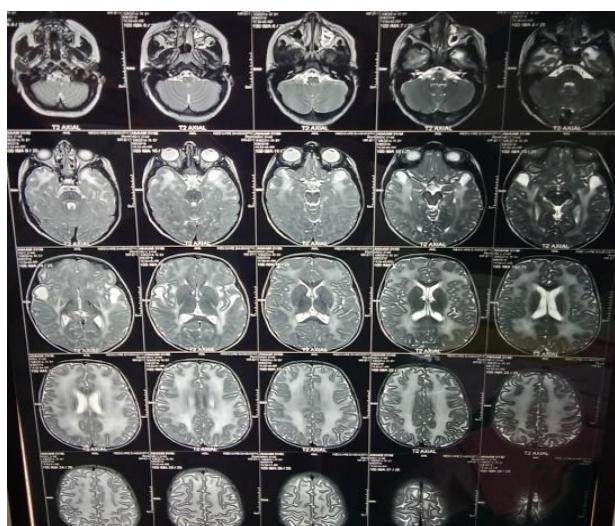
## CASE REPORT

A 4 and half year old boy born from 4<sup>th</sup> degree consanguineous marriage in the Muslim Bhat family from Handwara town of Kupwara district, J & K India, with normal prenatal and postnatal development, presented with first episode of abnormal body movements suggestive of tonic clonic seizures followed by loss of consciousness for ~ 1 hour. It was followed by unable to walk and stand, after regaining of consciousness. There is a history of delayed motor milestones replace intellectual disability resulting in poor scholastic performance with impaired cognition, in addition to presence of large head as noticed by parents during infancy which was becoming less with the age. There is history of similar complains in the third degree maternal cousin who expired after 32 years of age. On examination, a pulse of 82/min, respiratory rate 14 breaths/min, good peripheral pulses, blood pressure of 100/66 mm HG was recorded. Anthropometry revealed a head circumference was 58 cm (>97<sup>th</sup> percentile), with normal facies, weight 16 kg, height 104 cm, with mid

arm circumference of 16 cm. Central nervous examination revealed paraparesis with a positive Babinski sign bilaterally, with exaggerated knee and ankle reflexes all along. He was not able to stand and walk without support, however nystagmus was absent, with normal findings on rest of the general and systemic examination was unremarkable. Blood, CSF and urine investigation were unremarkable and serum creatinine kinase, lactate levels were also normal. EEG showed abnormal wave pattern during sleep while nerve conduction study did show axonal neuropathy of both peroneal nerves. On MRI brain diffuse white matter hyperintensities in the bilateral cerebral hemispheres predominantly in the frontotemporal parietal areas with cyst formation were noted suggestive of MLC (Van der Knaap disease) as is shown in (Figure 1 and 2). We could not process for MLC 1 gene testing due to financial constraints. The patient was symptomatically managed for seizures and was discharged on oral antiepileptic (valproic acid at the rate of 20 mg/kg/day in two divided dose), physiotherapy and regular follow up advised.



**Figure 1: Four and half year boy with MLC.**



**Figure 2: MRI brain depicting bilateral anterior temporal and frontal lobe sub cortical cysts.**

## DISCUSSION

MLC was first reported by Singhal et al in 1991 from India in the Agarwal community<sup>5</sup> and was named in 1995 by Knaap et al. In MLC the genetic defect lies in brain ion and water hemostasis resulting in chronic cerebral white matter edema and vacuole formation,<sup>6</sup> with age of presentation varying from birth to 25 years. Our patient presented at 4 and 1/12 years with abnormal body movement which forced the parents to seek medical attention. Parents of patient considered large head and motor delay as normal variant, and did not seek any medical consult. Although there was a history of maternal uncle death at 32 years who also had large head.

The megalcephaly is most consistent feature followed by ataxia and frequent falls, while as seizure are seen in 50% of cases.<sup>7-9</sup> 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 movement. All these clinical features were present in our patient at the age of 4 and 1/2 years representing a classic clinical course of Van der Knaap disease.

Diagnosis of this entity is by clinical and imaging findings. Differential diagnosis of MLC is limited, and includes Canavan disease, Alexander disease and infantile onset GM 2 gangliosides which can be differentiated by clinical and imaging findings.<sup>10</sup> All other leukoencephalopathies are fatal in early childhood or adolescence, but MLC has a benign course with a relatively better outcome with life expectancy upto 3-4th decade of life. At present, there is no definite treatment, and patients are managed symptomatically with anti-epileptics, acetazolamide and physiotherapy.<sup>1</sup>

## CONCLUSION

MLC should be included in differentials of macrocephaly and early onset leukoencephalopathy. The precise diagnosis helps to prognosticate its initial benign course, and genetic counselling should be offered to families to suit the required needs.

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