



# Megalencephalic leukoencephalopathy: van der Knaap disease

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Dear Sir,

Megalencephalic leukoencephalopathy with subcortical cysts (MLC) also known as van der Knaap's disease is a rare autosomal recessive degenerative disorder characterized by megalencephaly, early onset white matter degeneration, cerebral leukoencephalopathy, deterioration of motor function with ataxia, spasticity and a delayed onset of a slowly progressive neurological deterioration (1-5). A 5 year-old boy, born of non-consanguineous marriage in a Hindu community from Andhra Pradesh, with uneventful birth history, presented with progressively increasing head size noticed since he was 1 year of age. He attained social smile and head control normally as per his age but he was not able to sit or walk on himself. On examination, there increase in head circumference (61 cm). He was not able to comprehend or speak. Upper limbs were normal. Lower limbs examination revealed increased tone with spasticity. His sensory system examination was normal and there were no cerebellar signs. Cranial nerves were normal. Eye examination and abdominal examination were unremarkable. MRI brain revealed extensive bilateral symmetrical hyperintense white matter changes, on FLAIR images suggestive of extensive demyelination and in addition there were large well defined cortical cysts in anterior temporal, parietal and frontal lobes, which were hypointense on FLAIR sequences findings consistent with a diagnosis of megalencephalic leukoencephalopathy (**Figure 1** and **2**). The patient was treated symptomatically and with physiotherapy.

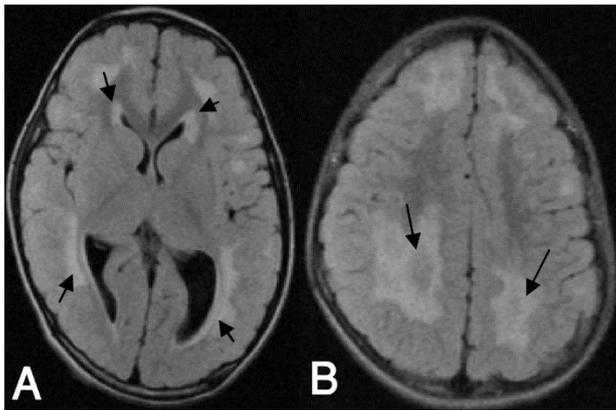
MLC is an autosomal recessive neurodegenerative disorder (3-4, 6) with a low carrier rate and has a high incidence in populations in which consanguinity is common (2, 7, 8) presenting with macrocephaly in the first year of life and delayed onset of motor deterioration and cognitive decline despite markedly abnormal initial MRI findings (5). MLC affect the white matter of the brain and on histopathology characterized by cavitating spongiform white matter changes caused by numerous vacuoles observed only in the outer lamella of the subcortical white matter (1, 5, 9, 10). Clinically van der Knaap's disease is characterized by an abnormally enlarged head appearing in infancy, mild motor developmental delay, seizures, spasticity, gradual onset of ataxia, and sometimes extrapyramidal findings; and usually late onset of mild mental deterioration (4, 11). CT may show white matter hypodensity, but it is much less sensitive than MRI. (5, 12-13) MRI is the investigation of choice and it will show characteristic features include extensive symmetrical white matter changes with subcortical cysts and typical cysts localized in the tips of the temporal lobes and in the frontoparietal subcortical area thus establishing the diagnosis of megalencephalic leukoencephalopathy (MLC) (4, 5, 11, 14). Central white matter structures, including the corpus callosum, internal capsule, and brainstem, are relatively spared. There is no gray matter involvement in early stages, however cortical atrophy with deepened sulci is observed in the late stages of the disease. The differential diagnoses of van der Knaap disease include Canavan's disease, Alexander's disease, glutaric aciduria type 1 and Tay-Sach's disease, however in presence of unique MRI finding and typical clinical presentation the diagnosis of MLC can be made with confidence (4, 5, 9, 11, 15). At present there is no definite treatment for MLC and the patients have been treated with acetazolamide without any clinical or radiological improvement. Supportive therapy is suggested to control seizures and physical therapy is to improve motor dysfunction (4).

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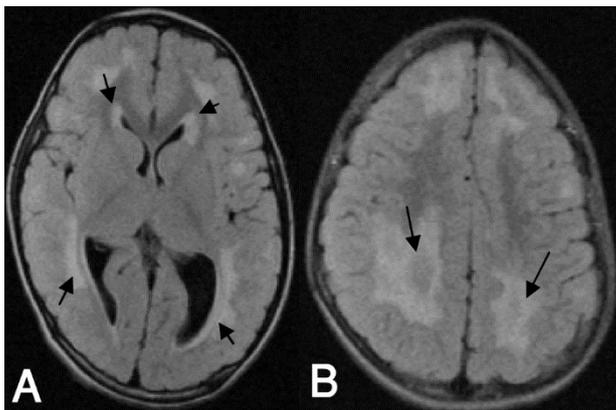
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**Figure 1:** MRI axial images FLAIR sequence showing bilateral symmetrical white matter hyperintensities (black arrows) suggestive of demyelination



**Figure 2:** MRI brain FLAIR axial images showing well defined hypointense cysts in left anterior temporal, right frontal and parietal lobes (black arrows)

## REFERENCES

1. Gorospe JR, Maletkovic J. Alexander disease and megalencephalic leukoencephalopathy with subcortical cysts: leukodystrophies arising from astrocyte dysfunction. *Mental retardation and developmental disabilities research reviews*. 2006;12(2):113-22.
2. Topcu M, Saatci I, Topcuoglu MA, Kose G, Kunak B. Megalencephaly and leukodystrophy with mild clinical course: a report on 12 new cases. *Brain Dev*. 1998 Apr;20(3):142-53.
3. Saijo H, Nakayama H, Ezoe T, Araki K, Sone S, Hamaguchi H, et al. A case of megalencephalic leukoencephalopathy with subcortical cysts (van der Knaap disease): molecular genetic study. *Brain Dev*. 2003 Aug;25(5):362-6.
4. Krishnan KH, Pauline CL, Kumaresan G, Mallika T. Megalencephalic leukoencephalopathy with subcortical cysts. *Indian Pediatr*. 2005;42(1):60-3.
5. van der Knaap MS, Barth PG, Stroink H, van Nieuwenhuizen O, Arts WF, Hoogenraad F, et al. Leukoencephalopathy with swelling and a discrepantly mild clinical course in eight children. *Ann Neurol*. 1995 Mar;37(3):324-34.
6. Leegwater PA, Boor PK, Yuan BQ, van der Steen J, Visser A, Konst AA, et al. Identification of novel mutations in MLC1 responsible for megalencephalic leukoencephalopathy with subcortical cysts. *Hum Genet*. 2002 Mar;110(3):279-83.
7. Ben-Zeev B, Gross V, Kushnir T, Shalev R, Hoffman C, Shinar Y, et al. Vacuolating megalencephalic leukoencephalopathy in 12 Israeli patients. *J Child Neurol*. 2001 Feb;16(2):93-9.
8. Singhal BS, Gursahani RD, Udani VP, Biniwale AA. Megalencephalic leukodystrophy in an Asian Indian ethnic group. *Pediatr Neurol*. 1996 May;14(4):291-6.
9. Ilja Boor P, Groot K, Mejaski-Bosnjak V, Brenner C, van der Knaap MS, Scheper GC, et al. Megalencephalic leukoencephalopathy with subcortical cysts: an update and extended mutation analysis of MLC1. *Human mutation*. 2006;27(6):505-12.
10. Tu YF, Chen CY, Huang CC, Lee CS. Vacuolating megalencephalic leukoencephalopathy with mild clinical course validated by diffusion tensor imaging and MR spectroscopy. *AJNR Am J Neuroradiol*. 2004 Jun-Jul;25(6):1041-5.

11. Aditya S, Gupta RD, Das D, Roy M, Dhibar T, Das T. Van der Knaap syndrome, a case from West Bengal, India. *Neurology Asia*. 2010;15(2):193-5.
12. van der Knaap MS, Breiter SN, Naidu S, Hart AA, Valk J. Defining and categorizing leukoencephalopathies of unknown origin: MR imaging approach. *Radiology*. 1999 Oct;213(1):121-33.
13. van der Voorn JP, Pouwels PJ, Hart AA, Serrarens J, Willemsen MA, Kremer HP, et al. Childhood white matter disorders: quantitative MR imaging and spectroscopy. *Radiology*. 2006 Nov;241(2):510-7.
14. Schiffmann R, van der Knaap MS. Invited article: an MRI-based approach to the diagnosis of white matter disorders. *Neurology*. 2009 Feb 24;72(8):750-9.
15. Sethi P, Sethi N. Megalencephalic leukoencephalopathy with subcortical cysts. *Indian journal of pediatrics*. 2004;71(5):473-5.



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