A rare cause of neonatal seizure - Van der Knaap disease: A case report

Panda K, Mishra N R

From Department of Pediatrics, Veer Surendra Sai Institute of Medical Sciences and Research, Burla, Sambalpur, Odisha, Bhubaneswar, India

Correspondence to: Mishra N R, Department of Pediatrics, Veer Surendra Sai Institute of Medical Sciences and Research, Burla, Sambalpur, Odisha, India. Phone: +91-9337797072. E-mail: drnihar.mishra@gmail.com

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ABSTRACT

Van der Knaap disease is a rare genetic autosomal recessive disorder characterized by megalencephaly and leukodystrophy with subcortical cysts. In India, most of the cases reported are from a particular ethnic background (Agarwal) with consanguinity. Here, we are reporting a case not belonging to this ethnic background and born out of non-consanguineous marriage and who presented with a primary complaint of recurrent neonatal seizures.

Key words: *Megalencephaly leukoencephalopathy, Seizures, Subcortical cysts*

Van der Knaap disease is a rare kind of leukoencephalopathy first reported in mid '90s [1] characterized by an increase in head size from infancy, white matter involvement, clinically manifested as mild neurological symptoms, and a slow progressive course. Broadly speaking it is a kind of neurodegenerative disease. They may present as ataxia, spasticity, movement disorders, or seizures for evaluation in childhood. Radiologically, subcortical cysts may also be found to be associated with it. The more specific scientific name for it is megalencephalic leukoencephalopathy with subcortical cysts. Here, we are reporting a case of a 1-month-old female infant who presented to us as recurrent unprovoked neonatal seizures for evaluation finally diagnosed as Van der Knaap disease.

CASE REPORT

A 1-month-old female, born out of non-consanguineous marriage in a Hindu farmer family hailing from Sonepur district of Odisha, presented with recurrent unprovoked seizures for evaluation. She was referred to us from a primary health center as a suspected case of neonatal meningitis. There was no previous history of birth asphyxia or perinatal insult and the birth was uneventful, and there were no previous sibling deaths and no family history of seizures.

On examination, the head circumference was 40 cm, i.e., >97th percentile for her age, anterior fontanelle was normal, sutures were not separated, scalp veins were not distended, and both the eyes were normal. Bedside fundoscopy was normal with no ocular signs of any central nervous system disease. A detailed neurological examination was done, and there were no long tract signs, no cerebellar signs, no evidence of dystonia, or any focal neurological deficits.

Routine blood examination reports were normal. A lumbar puncture for cerebrospinal fluid (CSF) analysis was done and sent for biochemical, cytological, and bacteriological analyses (including culture). No evidence of meningitis could be detected from CSF report or blood reports. TORCH screen was done and found to be negative. Arterial blood gas analyses were normal with normal serum lactate levels. Even CPK-BB was sent and found to be within normal limits for age. An inborn errors of metabolism panel for the screening of metabolic disorders was also sent, but no abnormality detected. After ruling out all possible causes of late neonatal seizures, we planned for neuroimaging. Transcranial ultrsonography (USG) revealed multiple anechoic cystic lesions.

Magnetic resonance imaging (MRI) brain revealed ill-defined areas of altered signal intensity involving subcortical white matter in bilateral parafalcine parietal lobes, temporal lobes (right> left), and anterior frontal lobes which appeared hypointense on T1 (Fig. 1a and b) and hyperintense on T2 images (Fig. 2a and b), along with few subcortical cysts in bilateral parafalcine parietal lobes. There was a loss of white matter with mild prominence of occipital horns of both lateral ventricles. These findings were suggestive of leukoencephalopathy. MR spectroscopy was advised to further explore the type of leukoencephalopathy. There were no peaks of NAA or myo-inositol or lactate excluding the two closest differential diagnoses, i.e., Canavan's disease and Alexander's disease, respectively. After a detailed discussion with the radiology team of our institute and other neurologists, a common consensus was achieved and all proposed it to be a case of Van der Knaap disease.

She 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 advised to follow-up after 14 days at the outpatient department for genetic assessment for MLC 1 gene, but she lost to follow-up.

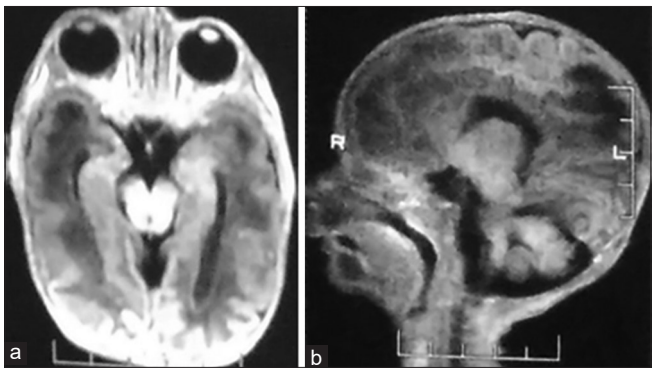

Figure 1: (a) T1 axial MRI brain revealing ill-defined areas of altered signal intensity involving subcortical white matter in bilateral parafalcine parietal lobes, temporal lobes. (b) T1 sagittal MRI brain showing ill-defined hypointense areas of altered signal intensity over anterior frontal lobes

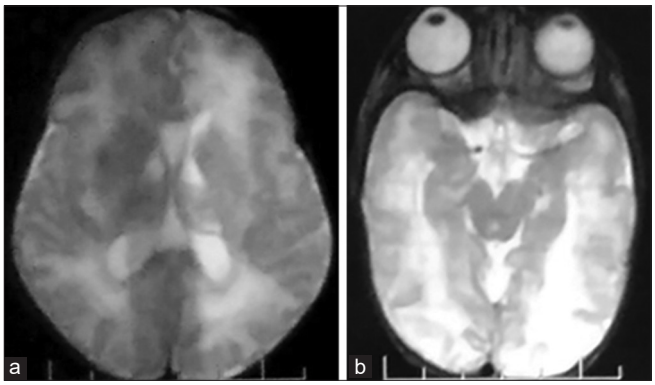

Figure 2: (a and b) T2 axial MRI brain showing hyperintense lesions with few subcortical cysts in bilateral parafalcine parietal lobes

DISCUSSION

This very case, not belonging to the particular ethnic group "Agrawal," is an inquisitive topic [2]. The typical MRI findings, megalencephaly, and associated seizures aided in the diagnosis of Van der Knaap disease which is an autosomal recessive genetic disease related to MLC1 gene [3]. Enlargement of the head may commence from birth but usually occurs in early infancy. It is usually associated with developmental delay. Patients may have ataxia, spasticity, and movement disorders. Mental involvement occurs later than motor involvement, and often, they have seizures. The characteristic MRI findings are the hallmark to clinch the diagnosis. Any symptomatic infant with increased head circumference and subcortical cysts in transcranial USG should be suspected of Van der Knaap as one of the differential diagnoses, and further evaluation should be done to confirm it, especially, genetic analysis.

The differential diagnosis of megalencephalic leukoencephalopathy includes other leukoencephalopathies such as Canavan's disease, Alexander disease, and even many mitochondriopathies. Most of these are fatal when compared to Van der Knaap disease. In this case, our limitation was that we were not able to do the genetic analysis of the patient as the baby was lost to follow-up.

CONCLUSION

Any symptomatic infant with increased head circumference and subcortical cysts in transcranial USG should be suspected of Van der Knaap as one of the differential diagnoses, and further evaluation should be done to confirm it, especially, genetic analysis.

REFERENCES

1. 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;37:324-34.
2. Singhal BS, Gursahani RD, Udani VP, Biniwale AA. Megalencephalic leukodystrophy in an asian indian ethnic group. Pediatr Neurol 1996;14:291-6.
3. Leegwater PA, Boor PK, Yuan BQ, van der Steen J, Visser A, Könst AA, *et al.* Identification of novel mutations in MLC1 responsible for megalencephalic leukoencephalopathy with subcortical cysts. Hum Genet 2002;110:279-83.

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