Megalencephalic Leucoencephalopathy with Subcortical Cysts (VAN DER Knaap Disease) – A Rare Case Presentation

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ABSTRACT

Introduction: Megalencephalic leucoencephalopathy with subcortical cysts (MLC) is a rare disease characterised by macrocephaly and early onset of white matter degeneration. This disease should be included in the differential diagnosis of macrocephaly with early onset leucoencephalopathy.

Case report: We report a case of 18 month old boy having diagnosed Megalencephalic Eucoencephalopathy with Subcortical Cyst (Van Der Knaap Disease). He had history of mild motor developmental delay seizures and also had megalencephaly during the first year of life. The diagnosis was made on the basis of characteristic finding in MRI.

Conclusion: So MLC should be included in the differentials of macrocephaly with early onset leucoencephalopathy.

Keywords: Vanderknaap disease, leucoencephalopathy.

INTRODUCTION

Megalencephalic leucoencephalopathy with subcortical cysts (MLC) also called as van der knaap disease is a relatively new entity of neurodegenerative disorder with autosomal recessive inheritance, in which the affected patient's presents typically presents with megalencephaly during the first year of life and extremely slow course of functional deterioration associated with mild motor developmental delay and seizures. It is very rare disease first described by Vander knaap et al, in 1995.[1,2] No definite or curative treatment is available and the affected patients dies in their second or third decade but some may leaves up to fourth decade.[3,4]

We report a case of 18 months old boy diagnosed to have this rare disease.

CASE REPORT

An 18 months old boy of non-consanguineous marriage from a Muslim community from Bihar presented with progressively increasing head size since last 6 months. The birth history was uneventful and the child was born full term with normal vaginal delivery. There was history of developmental delay and the child attained social smile at 4th month, neck holding at 7th month, sitting at 11th month. He was not able to stand or walk himself without support.

On examination the child was conscious and irritable. There was Macrocephaly and the head circumference measures 57 cm. He was not able to speak. Deep tendon reflexes were increased bilaterally. Chest, C.V.S. and abdominal examinations were within normal limits. Bladder and bowel habits were not affected.

Imaging findings

Non contrast and contrast enhanced computed tomography (CT) scan was formed using a 16 slice CT scanner (Somatoform) from GE health care and it revealed extensive bilaterally symmetrical white matter signal abnormalities which are hypodense and cystic lesions of C.S.F. densities affecting bilateral fronto-parietal and anterior temporal lobes. Both deep and subcortical u fibers were involved. There was no hydrocephalus seen. On post contrast study no abnormal enhancement seen.

A presumptive diagnosis of MLC was made and a non-contrast MRI of brain (T1W, T2W, FLAIR and MRS) was performed using 1.5 T MRI from SIEMENS. On T1W sequence- there is extensive white matter involvement as described in CT scan finding, which appears hypointense with multiple hypointense cysts in bilateral frontoparietal and anterior temporal lobes. (Figures 1-10).

{TE-59, TR-1920}- Echo time Repetition

On T2W sequence- the white matter and the cysts appears hyperintense as that of C.S.F. signal intensity. (Figures 11-14).

{TE-107, TR-3000}- Echo time Repetition

On FLAIR sequence- the white matter changes are still hyperintense suggestive of extensive demyelination but the cysts were suppressed and became hypointense confirming their cystic nature. (Figure 15-18).

{TE-102, TR-6000, TI-2500}- Echo time Repetition

On MRS- mild decrease in NAA/Ch and mild increase in ch/cr ratio is seen. The above MRI findings confirm the diagnosis of MLC. The child has an elder sister of 3 years old who was doing well and was asymptomatic for the disease. The child was discharged and put on physical therapy to improve the motor function.

DISCUSSION

Vanderknaap disease (MLC) is a very rare inherited (autosomal recessive) neurodegenerative disorder is named after Marjo van der knaap, a Dutch physician.[1] The affected gene locus has been mapped as MLC 1 at chromosome 22q.

In India majority of the reported cases till now were from northern part (Agarwal community of Gujarat). Our case is from a Muslim community of Bihar. The diagnosis of MLC is highly suspected in patients with typical clinical and radiological features. The characteristic feature of this disease is relatively mild clinical course despite very abnormal findings on cranial MRI study.[5,6]

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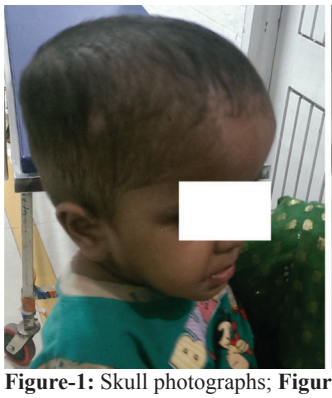
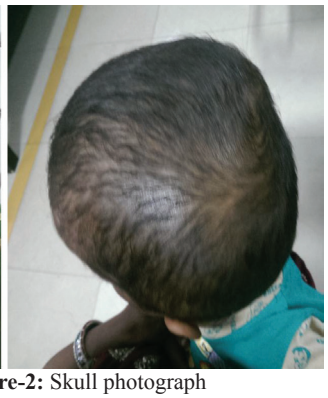

Figure-1: Skull photographs; **Figure-2:** Skull photograph

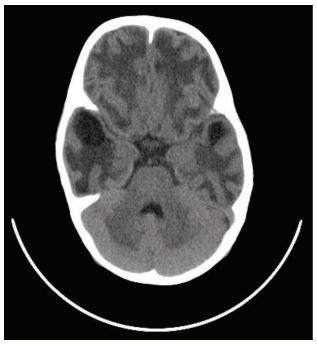
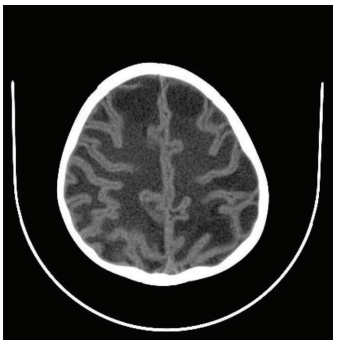

Figure-3: NCCT axial sections; **Figure-4:** NCCT axial sections

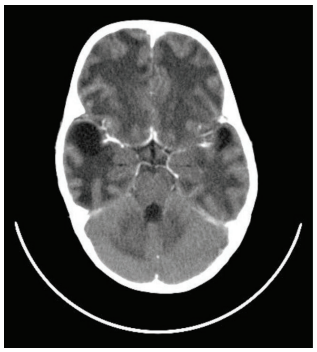
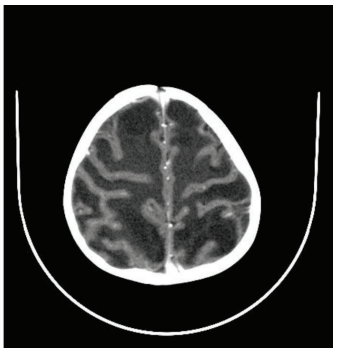

Figure-5: CECT axial sections; **Figure-6:** CECT axial sections

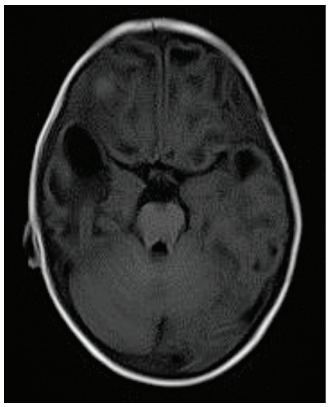
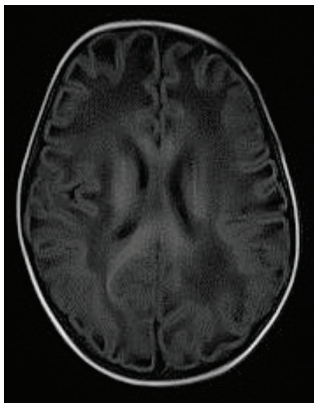

Figure-7: T1 W sequence; **Figure-8:** T1 W sequence

The typical clinical features are-

a) Megalencephaly during the first year of life.
b) Mild motor developmental delay.
c) Gradual onset of ataxia and spasticity in early childhood and is slowly progressive.
d) Most patients have seizures. Our patient had no history of

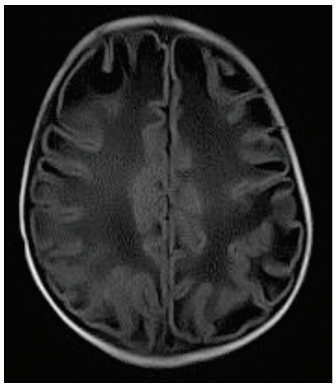
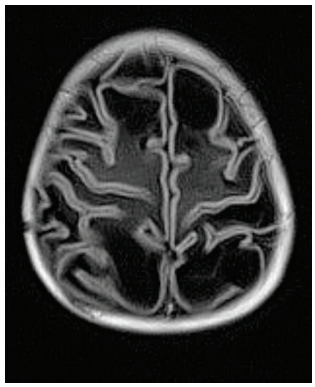

Figure-9: T1 W sequence; **Figure-10:** T1 W sequence

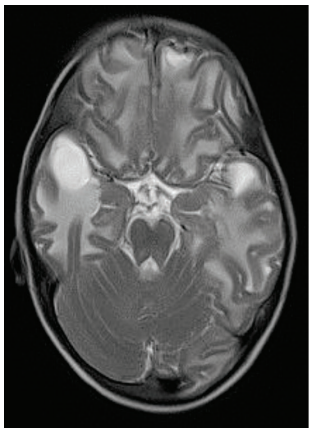
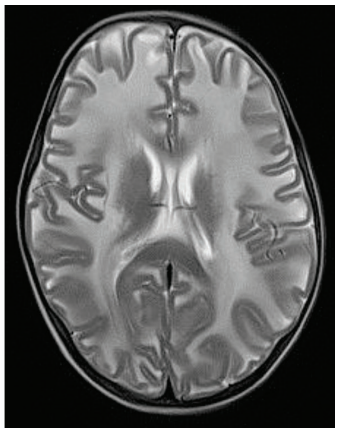

Figure-11: T2 W sequence; **Figure-12:** T2 W sequence

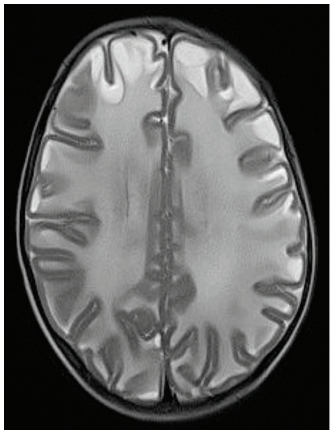
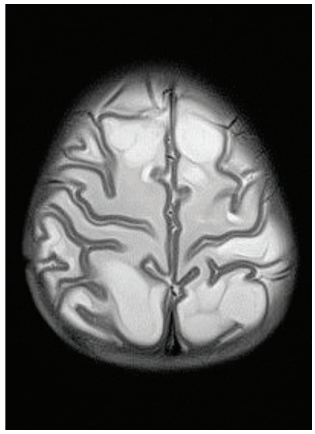

Figure-13: T2 W sequence; **Figure-14:** T2 W sequence

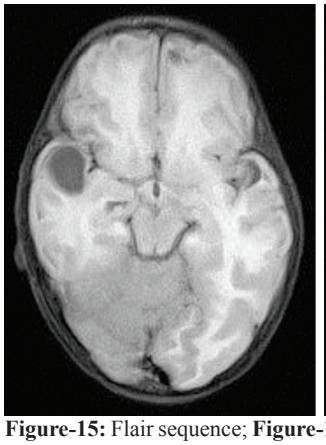
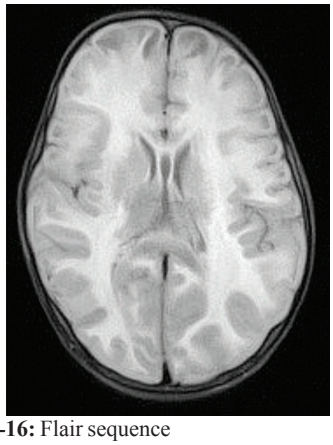

Figure-15: Flair sequence; **Figure-16:** Flair sequence

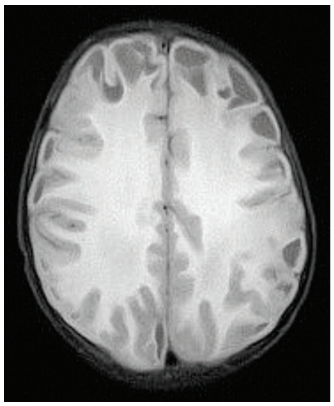
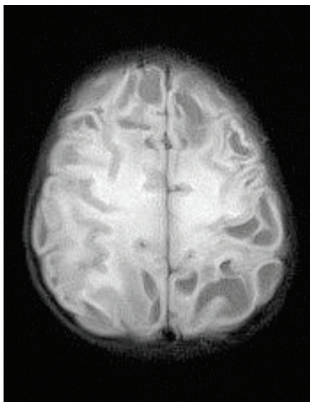

Figure-17: Flair sequence; **Figure-18:** Flair sequence

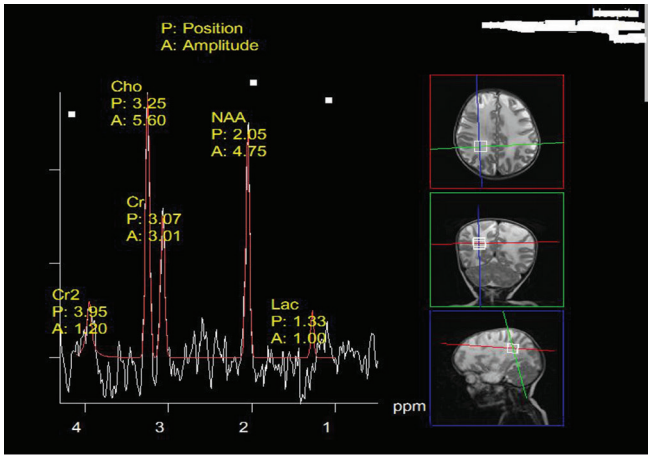

Figure-19: Magnetic resonance spectroscopy

seizure till now.

e) Mental status is relatively preserved till late stages and when decline occurs is much milder as compared to motor functions.

The characteristic radiological findings are-

a) On CT scan-bilaterally diffuse C.S.F. density hypodensities involving subcortical white matter and subcortical cysts.

b) Cranial MRI is the best diagnostic radiological test and is characterised by diffuse bilateral leucoencephalopathy associated with cystic degeneration of white matter. Cysts are predominantly seen in anterior temporal and frontoparietal lobes. Cysts may increase in number and size with age.

On MRS-moderate decrease in NAA/cr and ch/cr have been previously reported but in our case mild decrease in NAA/Ch and mild increase in ch/cr ratio is seen. On serology-increase glycine is seen in C.S.F.[2,7]

Other causes of megalencephaly with subcortical white matter involvement includes—

1. Canavans disease- characterised by spongiform degeneration of white matter. Subcortical cysts are not seen and shows NAA peak on MRS.
2. Alexander's disease- bilateral frontal and temporal lobes are predominantly involved.
3. Vanishing white matter disease- characterised by childhood ataxia and hypomyelination. White matter gradually looks the same as C.S.F.

None of the above mentioned disorders have subcortical cysts. All of them have some degree of deep grey matter involvement and are fatal in early childhood or in adolescence but MLC has relatively much better outcome as life expectancy up to third or fourth decade is expected.

Subcortical white matter involvement without macrocephaly includes galactosemia and Kearns sayre disease. Deep white matter disorders includes krabbe disease and infantile onset GM1 and GM2 gangliosidosis.

CONCLUSION

So MLC should be included in the differentials of macrocephaly with early onset leucoencephalopathy and the diagnosis should be made with confidence in patients with characteristic findings on cranial MRI and typical relatively mild clinical course.[6,7]

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