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Case Report

A Case Report of Megalencephalic Leukoencephalopathy with Subcortical Cysts

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Abstract

Megalencephalic leukoencephalopathy with subcortical cysts is a rare degenerative disease first described by Vander knap1.

Megalencephalic leukoencephalopathy with subcortical cysts is clinically characterized by macrocephaly, mild motor developmental delay, and seizures. Later, patients may develop gradual onset of ataxia and pyramidal features and mental deterioration. The combination of clinical findings and MRI features is essential for the diagnosis.The condition is inherited as an autosomal recessive pattern and the gene locus has been mapped to MLC 1 at chromosome 22q.

We report a case of young male with neuroregression and intractable seizures. On detailed workup and genetic analysis the patient is found to have a rare neurodegenerative condition the Vander knap disease.

Introduction

Megalencephalic leukoencephalopathy with subcortical cysts is a rare degenerative disease first described by Vander knap [1].

Megalencephalic leukoencephalopathy with subcortical cysts is clinically characterized by macrocephaly, mild motor developmental delay, and seizures. Later, patients may develop gradual onset of ataxia and pyramidal features and mental deterioration [2]. The combination of clinical findings and MRI features is essential for the diagnosis. The condition is inherited as an autosomal recessive pattern and the gene locus has been mapped to MLC 1 at chromosome 22q [3].

Case Details

24 years old male 1st born to consanguinous parentage from non agarwal community with normal perinatal history and normal development up to 13 years of age except macrocephaly . From 13 years of age neuroregression noted in the form of decreased attained scholastic performance, loss of communication skills, slowness of activities and development of seizures. Since 19 years age gradually progressive asymmetric spastic quadriparesis with spastic dysarthria. Significant family history with similar neruoregression was noted in younger sibling. On examination macrocephaly noted, conscious with decreased attention, left UMN facial palsy with spastic dysarthria & spastic quadriparesis with gross in coordination noted.

MRI Brain axial T2 w images showing multiple subcortical cysts in the bilateral tempero parietal regions and diffuse hyperintense white matter changes (Figure 1).

DNA sample analysis for mutation on MLC1 gene showed heterogeneous mutation in exon2 confirming the diagnosis of MLC.

Discussion

MLC is the most common leukodystrophy with megalencephaly observed in India in the agarwal community [4]. The disease has high incidence in populations in which consanguinity is common. MLC is an autosomal recessive disorder due to mutations in the MLC1 gene which has locus in chromosome 22q13 severity of pheno type does not correlate with the specific mutations found [5]. The diagnosis of MLC can be made with typical clinical features and characteristic abnormalities on cranial MRI [6].

Clinical findings of macrocephaly at birth or in 1st year of life with normal or mild developmental dealy and Slow deterioration of motor functions with cerebellar ataxia and mild spasticity usually starts in early childhood or later. The majority of affected children become wheelchair dependent in their teens. Speech can become increasingly dysarthric; dysphagia may develop. Most individuals have epileptic seizures that are usually easily controlled with medication.

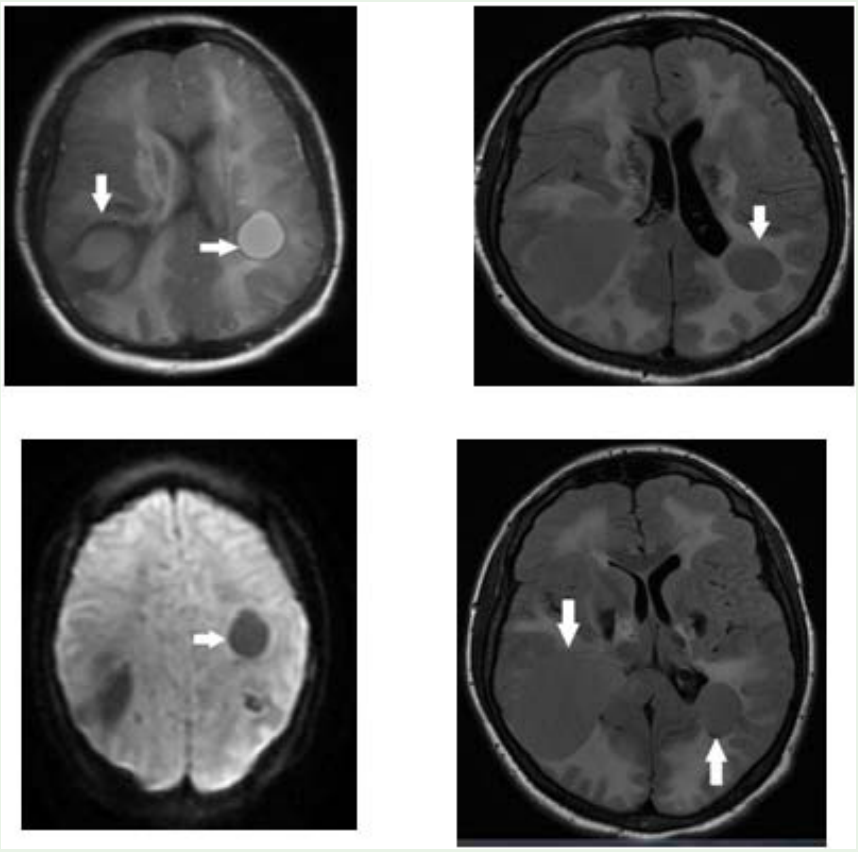

Figure 1: Axial T2 w images showing multiple subcortical cysts in the bilateral tempero parietal regions and diffuse hyperintense white matter changes.

MRI criteria

MRI of the brain is diagnostic. Cerebral hemispheric white matter is diffusely abnormal and mildly swollen. Subcortical cysts are almost invariable in the anterior temporal region and often in the frontoparietal region. Central white matter structures, including the corpus callosum, internal capsule, and brain stem, are better preserved. The combination of megalencephaly and leukoencephalopathy is seen in a limited number of disorders.

The magnetic resonance spectroscopy [MRS] findings in this disorder include mild to moderate decreases in the N acetyl aspartate [NAA] to choline and choline to creatine ratios [7].

The characteristic swollen white matter changes, as seen on MRI, have only been reported in MLC, Canavan disease, Alexander disease, infantile-onset GM2 gangliosidosis, glutaric aciduria type 1, and merosin-deficient congenital muscular dystrophy.

In Canavan disease, *N* acetyl aspartate is elevated in urine and blood and a deficiency of the enzyme aspartoacylase can be demonstrated in cultured fibroblasts [8].

Cystic degeneration may occur in Alexander disease but the location of the cysts is different: The deep frontal white matter is mainly affected [9].

MRI in infantile GM2 gangliosidosis is characterized by prominent involvement of the basal ganglia and thalami in addition to the white matter abnormalities [10].

In merosin deficient congenital muscular dystrophy, white matter involvement resembles that observed in MLC, but the typical subcortical cysts are generally lacking.

Individuals with merosin deficient congenital muscular dystrophy have prominent weakness and hypotonia, not shared by individuals with MLC [11].

Conclusion

MLC should be considered in the differential diagnosis of children with megalencephaly and leukoencephalopathy. One should suspect and carryout genetic tests to confirm the diagnosis because it has a remarkably slow course of deterioration in neurologic function and early rehabilitation may prolong ambulatory life.

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: 324-334.

2. Sethi PK, Sethi NK. Megalencephalic leukoencephalopathy with Annals of Indian Academy of Neurology, Kumar and Singh: Megalencephalic leukoencephalopathy with subcortical cysts in all three siblings in a non Aggarwal Indian family. 2012; 15.

3. Koussa S, Roukoz H, Rizk T, Megarbane A. Megalencephalic leucoencephalopathy with subcortical cysts: A study of a Lebanese family and a review of the literature. Rev Neurol (Paris). 2005; 161: 183-191.

4. Singhal BS, Gursahani RD, Udani VP, Biniwale AA. Megalencephalic leukodystrophy in an Asian Indian ethnic group. Pediatr Neurol. 1996; 14: 291-296.

5. Leegwater PA, Yuan BQ, van der Steen J, Mulders J, Könst AA, Boor PK, et al. Mutations of MLC1 (KIAA0027), encoding a putative membrane protein, cause megalencephalic leukoencephalopathy with subcortical cysts. Am J Hum Genet. 2001; 68: 831-838.

6. Topçu 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; 20: 142-153.

7. De Stefano N, Balestri P, Dotti MT, Grosso S, Mortilla M, Morgese G, et al. Severe metabolic abnormalities in the white matter of patients with vacuolating megalencephalic leukoencephalopathy with subcortical cysts. A proton MR spectroscopic imaging study. J Neurol. 2001; 248: 403-409.

8. Marks HG, Caro PA, Wang ZY, Detre JA, Bogdan AR, Gusnard DA, et al. Use of computed tomography, magnetic resonance imaging, and localized 1H magnetic resonance spectroscopy in Canavan's disease: A case report. Ann Neurol. 1991; 30: 106-110.

9. van der Knaap MS, Naidu S, Breiter SN, Blaser S, Stroink H, Springer S, et al. Alexander disease: Diagnosis with MR imaging. AJNR Am J Neuroradiol. 2001; 22: 541-552.

10. Chen CY, Zimmerman RA, Lee CC, Chen FH, Yuh YS, Hsiao HS. Neuroimaging findings in late infantile GM1 gangliosidosis. AJNR Am J Neuroradiol. 1998; 19: 1628-1630.

11. van der Knaap MS, Smit LM, Barth PG, Catsman-Berrevoets CE, Brouwer OF, Begeer JH, et al. Magnetic resonance imaging in classification of congenital muscular dystrophies with brain abnormalities. Ann Neurol. 1997; 42: 50-59.