Journal of Pediatric Sciences

Six Cases of Megalencephalic Leukoencephalopathy with Subcortical Cysts in a family

Shamrendra Narayan, Dipti Agarwal, Vandana Verma, Nirmal Chandra Prajapati

Journal of Pediatric Sciences 2014;6:e217

How to cite this article:

Narayan S, Agarwal D, Verma V, Prajapati NC. Six Cases of Megalencephalic Leukoencephalopathy with Subcortical Cysts in a family. Journal of Pediatric Sciences. 2014;6:e217

CASE REPORT

Six Cases of Megalencephalic Leukoencephalopathy with Subcortical Cysts in a family

Shamrendra Narayan[1], Dipti Agarwal[2] ,Vandana Verma[1], Nirmal Chandra Prajapati[2]

[1]Department of Radiodiagnostic, [2]Department of Paediatrics, SN Medical College, Agra, India

Abstract:
We present a case series of 6 children of Megalencephalic leukoencephalopathy with subcortical cysts. It is a very rare leukodystrophy that is characterized by macrocephaly, a slowly progressive clinical course and fatal outcome. Clinical presentation and MRI scans are the mainstay of diagnosis. 6 of 7 children from the same parents were affected suggesting variation from autosomal recessive pattern.

Keywords: *megalencephalic leukoencephalopathy, subcortical cysts*
Corresponding author: *Shamrendra Narayan, Department of Radiodiagnostic, S N Medical College, Agra – 282 002, India Mobile: 9411239593; Email: samarnarayan@yahoo.co.in*

Introduction

Megalencephalic leukoencephalopathy with subcortical cysts (MLC) is an extermely rare autosomal recessive neurological disorder in children [1]. There have been only few scattered case reports of this disorder globally. It is characterized by early-onset macrocephaly, in combination with developmental delay, seizures, ataxia, spasticity, sometimes extrapyramidal findings and late onset mental deterioration [2]. With early deaths only few have survived till forty years [3]. The diagnosis of MLC is established with typical clinical findings and characteristic findings on cranial MRI4. Here, we report clinical and radiological findings of this rare disorder in six patients clustered in a family.

Case report

The six children reported in this study are born to same parents with consanguineous marriage. The eldest sibling was spared and the rest were affected. Clinical profile of these children is presented in the table 1. Cranial MRI of all subjects showed nearly symmetrical multifocal areas of encephalomalacia involving bilateral antero-medial basitemporal convexities and peri-insular region. Involvement of fronto-temporal region and parafalcine high anterior frontal region was seen in children who were more than 5 years old. There were diffuse bilateral symmetrical areas of T2 white matter hyperintensity involving subcortical and subependymal deep white matter. There was sparing of the corpus callosum and internal capsule. No significant ventricular enlargement was seen and cortico-medullary junction was also normal. Prolongation involving supra-tentorial white matter predominantly appearing hypointense on T1 (Figüre 1) and hyperintense

Table I. Clinical presentation of the 6 patients with Megalencephalic leukoencephalopathy with subcortical cysts

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age	2.5yr	3yr	5yr	9yr	11yr	13yr
gender	male	female	male	male	male	male
Age of onset	6months	6months	7months	8months	6months	5months
Presenting complains						
Macrocephaly	yes	yes	yes	yes	yes	yes
Difficulty in walking	Not started walking	Not started walking	With Occasional fall since 4.5yrs	With Occasional fall since 4.8yrs	Bedridden since 9 yrs	Bedridden since 10yrs
Seizures (onset/year)	NO	GTCS at 2	GTCS at 3	GTCS at 2.5	GTCS at 3	GTCS at 2
Birth history	normal	normal	normal	normal	normal	normal
Head circumference (percentile)	52cm(97^{th})	53cm(98^{th})	55cm(98^{th})	57cm(98^{th})	56cm(98^{th})	57cm(98^{th})
Motor milestones						
Head control	7m	8m	7m	8m	8m	7m
Sitting without support	17m	15m	17m	18m	16m	15m
Standing without support	26m	24m	25m	24.5m	26m	25.5m
Walking without support	Not attained	Not attained	2.5yrs	3yrs	3yrs	2.5yrs
Neurological examination						
IQ/SQ	normal	normal	normal	borderline	borderline	borderline
Motor examination						
Tone	increased	increased	increased	increased	increased	increased
Power	Decreased	Decreased	Decreased	Decreased	Decreased	Decreased
Deep tendon reflexes	brisk	brisk	exaggerated	exaggerated	Clonus	Clonus
Planter response	extensor	extensor	extensor	extensor	extensor	extensor
Extrapyramidal signs	absent	absent	absent	absent	present	present
Cerebellar signs	absent	absent	present	present	present	present
Fundus	normal	normal	normal	normal	normal	normal

*****GTCS: Generalized tonic-clonic seizure

on T2W (Figure 2) images. The involvement of white matter was extending till subcortical arcuate fibres also involving external capsule. Smaller areas of cystic gliosis were also seen in parafalcine anterior frontal and postero-lateral parietal convexity.

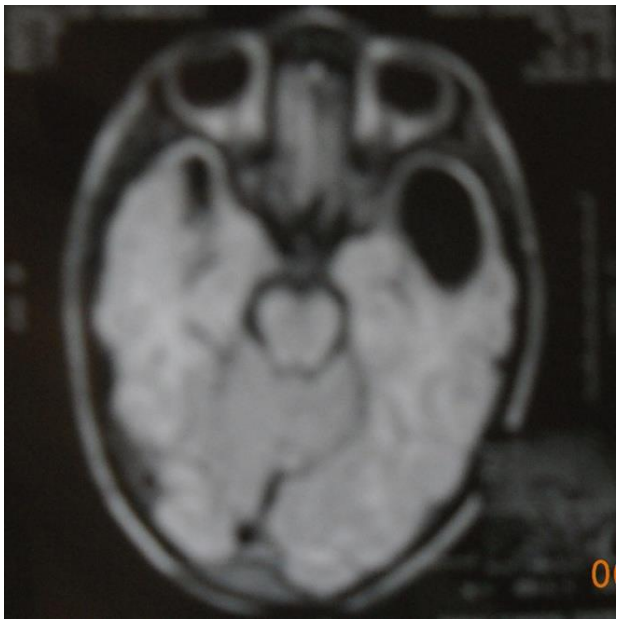

Figure 1. T1-weighted axial image showing subcortical cysts in the temporal lobes

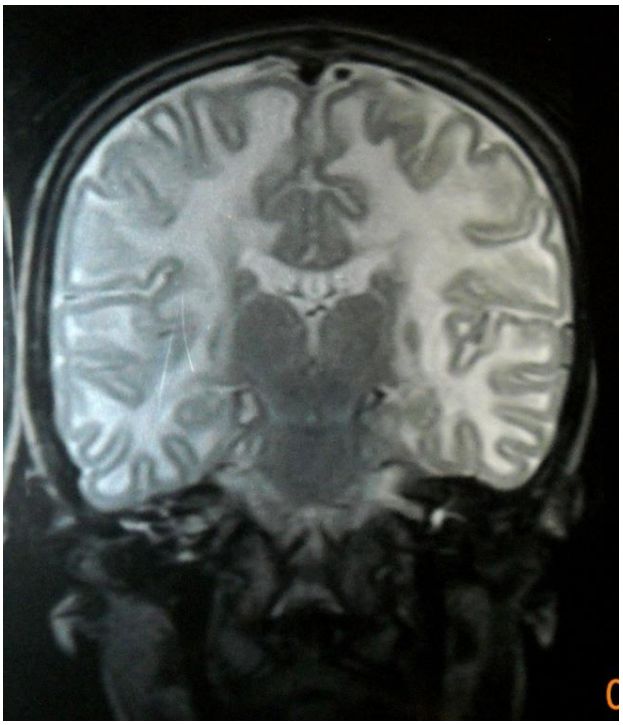

Figure 2. T2-weighted (TR/TE: 2200/90 msec) coronal image demonstrate high signal white matter Parietal and temporal lobes

Discussion

MLC is an extremely rare autosomal recessive disorder. There have been very few reports from the world. Singhal et al. described the disorder from India in 1991 for the first time [1]. In 1995, van der Knaap et al [2] named this disorder followed by few scattered reports. The disease has been found to occur in communities where consanguinity is common, such as in Turkey [4]. Almost all East-Indian individuals with MLC belong to the Agrawal community [5]. In our study all patients hailed from the same family in muslim community with presence of consanguity.

There can be varied clinical presentation of this disorder. The disease presents more frequently during the first year of life as seen in this case series. Macrocephaly has been observed in all individuals with MLC in various studies [1,2,4,6]. Head circumference is normal at birth and increases in infancy. After the first year of life, head growth follows a line parallel to the 98th percentile [4,6]. In our study similar pattern of increase in head circumference has been observed with all the subjects having head circumference more than 98th centile. Apart from progressive macrocephaly, the other common initial presentation is delay in gross motor milestones as also seen in our study in all study subjects [1,2]. Difficulty in walking, deterioration of motor function, ataxia of the trunk and extremities, pyramidal dysfunction, cerebellar signs has been observed in more severe forms of this disease as also seen in our study, however the severity increased with age of the affected child [2,4]. Children at the beginning of second decade (11 & 13 year of age) had become completely bed-ridden. Extrapyramidal movement abnormalities with dystonia and athetosis is also found in severe disease forms as seen in eldest two cases in our study who were more severely affected. Almost all children in our study have epilepsy from early age as reported by other studies too [7]. Mental deterioration is usually late and mild. Speech becomes increasingly dysarthric with increasing severity, has been seen in eldest two children [7]. Minor head trauma may induce temporary

deterioration in some individuals, although similar was not observed in this subjects [8]. Because the disease has been known for a relatively short time, little information is available about average life span of the disease.

MLC is inherited in an autosomal recessive manner [9]. Unavailability of the genetic studies is the limitation of this observation. In our study there has been variation from autosomal recessive inheritance as instead of 25% (<2 of 6)chances of affection, more than 85% (5 of 6) transmission was observed suggesting there may be other environmental factors which may modify the inheritance which need to studied further.

MRI imaging of the brain is an important diagnostic tool in MLC. A characteristic feature of the disease is the presence of subcortical cysts in the anterior temporal and frontoparietal regions [10]. These cysts are present early in the disease, and may increase in size or number over the disease course. Neuroimaging studies show signal abnormality of almost all cerebral hemispheric white matter.

Differential diagnosis of MLC is limited; it includes Canavan disease, Alexander disease and infantile-onset GM2 gangliosidosis. In Canavan disease the MRI typically shows involvement of the thalamus and globus pallidus which are not involved in MLC. White matter may be cystic in Canavan disease, but the typical subcortical cysts seen in MLC are lacking. Alexander disease has predilection for the anterior parts of the brain which is not shared by MLC [2]. Contrast enhancement of particular brain structures is almost invariably observed in Alexander disease, which is not a feature of MLC [2]. Moreover cysts are mainly located in the deep frontal white matter. MRI in infantile GM2 gangliosidosis is characterized by prominent involvement of the basal ganglia and thalami.

Conclusion

Patient with megalencephaly, clinical findings suggestive of MLC and characteristic MRI changes in communities with consanguineous marriages should raise suspicion for MLC. This clustering of cases also needs consideration and further studies for autosomal recessive mode of transmission as well.

References

1. Singhal BS, Gorospe JR, Naidu S. Megalencephalic leukoencephalopathy with subcortical cysts. J Child Neurol 2003; 18: 646-665.
2. Van der Knaap MS, Valk J, Barth PG. Leukoencephalopathy with swelling in children and adolescents: MRI patterns and differential diagnosis. Neuroradiology 1995; 37: 679-686.
3. Singhal BS, Gursahani RD, Biniwale AA, Udani VP. Megalencephalic leukoencephalopathy in India (abstract). In: Proceedings of the 8th Asian and Oceanian Congress of Neurology, Tokyo, Japan, 1991, 72.
4. Van der Knaap MS, Barth PG, Stroink H, et al. Leukoencephalopathy with swelling and a discrepantly mild clinical course in eight children. Ann Neurol 1995; 37: 324-334.
5. Topçu M, Saatçi I, Topçuoğlu MA, et al. Megalencephaly and leukodystrophy with mild clinical course: a report on 12 new cases. Brain Dev 1998; 20: 142-153.
6. Brockman K, Finsterbusch J, Terwey B, et al. Megalencephalic leukoencephalopathy with subcortical cysts in an adult: quantitative proton MR spectroscopy and diffusion tensor MRI. Neuroradiology 2003; 45: 137-142.
7. Yalcinkaya C, Yuksel A, Comu S, Kilic G, Cokar O, Dervent A. Epilepsy in vacuolating megalencephalic leukoencephalopathy with subcortical cysts. Seizure 2003; 12:388-396.
8. Shukla P, Gupta N, Ghosh M, Vasisht S, Gulati S, Balakrishnan P, Sharma R, Gupta AK, Kamate M, Kalra V, Kabra M. Molecular genetic studies in Indian patients with megalencephalic leukoencephalopathy . Pediatr Neurol 2011; 44:450-458.

9. Topcu M, Gartioux C, Ribierre F, Yalcinkaya C, Tokus E, Oztekin N, Beckmann JS, Ozgue M, Seboun E. Vacuoliting megalencephalic leukoencephalopathy with subcortical cysts, mapped to chromosome 22qtel. Am J Hum Genet. 2000; 66: 733-739.
10. Patrono C, Di Giacinto G, Eymard-Pierre E, et al. Genetic heterogeneity of megal-encephalic leukoencephalopathy with subcortical cysts. Neurology 2003; 61: 534-537.