The evolving spectrum of LAMA2 related congenital muscular dystrophy (MDC1)

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Introduction

•LAMA2 related MD has variable presentation

•Severe early onset congenital muscular dystrophy (MDC1) to mild variant of late onset muscular dystrophy (LAMA2-MD)

•MDC1-typically presents with hypotonia, respiratory and feeding issues.

•Epilepsy-33%; Independent ambulation-10%

•Cerebellar white matter and corpus callosum involvement is rare

•Increasing reports of milder phenotypes of MDC1

Objective

•To highlight the expanding clinico-radiological spectrum of MCD1

Methodology

•Data of five genetically proven CMD1 was collected

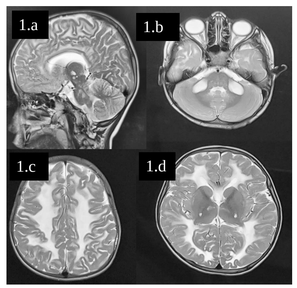
•Clinical features, serum CPK levels, neuroimaging details were collected

Results

Table 1. Characteristics of patients

	Case 1	Case 2	Case 3	Case 4	Case 5
Age/Gender	3.9y/ M	7y/F	6y/F	3y/M	1yr/F
Age of onset	Early infancy	Early infancy	Early infancy	Early infancy	Early infancy
Tone	Hypotonia	Hypotonia	Hypertonia (R>L)	Hypotonia	Hypotonia
Contractures	+	-	-	-	-
Cognition	N	Mild ID	Mild ID	N	N
Feeding/respiratory complaints	++	+	–	+	-
Seizures	-	++ (Eyelid myoclonia)	+ (GTCS)	-	-
Ambulation (A/NA)	NA	A	A	NA	NA
Motor	Sits without support	Independent ambulation	Independent ambulation	Sits without support	Sits with support
Neuropathy	No	Yes (axonal)	No	No	No
CPK (u/L)	1416	1918	501	325	120
MRI Brain	Symmetrical, confluent WM- SC, PV, Deep BS- MB, Pons Cerebellar peduncle	Symmetrical, confluent WM- PV, deep Cerebellar peduncle CC	Symmetrical, confluent WM- SC, PV (cystic), deep CC, thalamus BS- MB, Pons Cerebellar peduncle	Asymmetrical, patchy WM- SC, PV, Deep CC	Symmetrical, confluent WM- SC, PV (cystic), deep CC, thalamus BS- MB
Genetic (LAMA2)	Homozygous Nonsense mutation	Homozygous Missense Novel *Exon 14 c.2054T>G p.Leu685Arg*	Compound heterozygous Missense Novel *Exon 15 c.2131_2134dup p.Pro712LeufsTer*	Homozygous 5' splice site (intronic)	Homozygous nonsense mutation Exon 55 c.7732C>T

NA- Non Ambulatory; A- Ambulatory



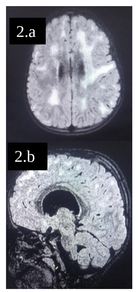


Figure 1. MRI Brain T2 weighted Sagittal (1.a) and axial (1.b-d) images of case 3 showing bilaterally symmetrical, confluent involvement of subcortical (SC), deep and periventricular (PV) white matter (WM), corpus callosum (CC), midbrain (MB), pons, thalamus, cerebellar peduncle.

Figure 2. MRI Brain Flair axial (2.a) and sagittal (2.b) images of case 4 showing asymmetrical, patchy involvement of SC, deep, and PV WM along with CC involvement

Conclusion

- MDC1 typically lies at the severe end of spectrum of LAMA2 related muscular dystrophy
- Normal IQ, peripheral neuropathy, borderline CPK values do not point against MDC1
- Neuroimaging findings aids in the diagnosis of MDC1
- Involvement of corpus callosum (CC) in MDC1 may mimic the pattern of CC involvement in mitochondrial disorders
- MDC1 is also a differential in cystic leukoencephalopathy
- Clinical as well as imaging findings can be variable and this data is ever evolving.

References

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