271

Pediatric Mitochondrial Disease: Clinical and Radiological profile, Experience from A Tertiary Care Hospital in Bangladesh

Kanij Fatema, Farah Naz Dola, Shaheen Akhter
Department of Pediatric Neurology,
Institute of Pediatric Neurodisorder and Autism, Bangabandhu Sheikh Mujib Medical University
Dhaka,Bangladesh

BSMMU

Bangladesh

Introduction

Mitochondrial diseases are rare group of heterogeneous, genetically determined disorders. These are caused due to defect in the electron transport chain within the mitochondria. Phenotypes vary from solely myopathy to multi organ involvement with variable age of onset, severity, and progression .
Common presentations are acute or chronic neuro regression, hypotonia, failure to thrive, seizures, cardiomyopathy, deafness, blindness, movement disorder, and lactic acidosis.
Most of them occur following febrile or infectious illness.

Objective

This study was aimed to describe the clinical, neuroimaging and genetic analysis of mitochondrial diseases.

Methodology

Study Design: Cross Sectional study
Number of Patients: 16 admitted patients
Place: Department of Pediatric Neurology and Institute of Pediatric Neurodisorder and Autism (IPNA), Bangabandhu Sheikh Mujib Medical University.
Study duration : January 2016 to December 2023
Detailed history regarding the demographic profile, antecedent illness, age of onset , age at presentation, presenting clinical features were taken.
Clinical examination including neurological examination was done in every patient . Basic metabolic screening , CSF study , EEG, MRI of brain with contrast and MRS were done in patients according to the indication . In every patient next generation sequencing including mitochondrial whole genome sequencing was advised .
Expert opinion from neuro-radiology and ophthalmology was taken.

Results

Table 1. Demographic characteristics of the studied subjects (n-16)

Age at onset	1month-6.5 years
Age at diagnosis	3 months -8 years
Sex	
Male	11 (69%)
Female	5(31%)
Consanguinity	
Present	6 (38%)
Absent	10(62%)

Table 2. Developmental status of the patients ,n=16

Developmental Impairment	
Developmental delay	13 (81%)
Hypotonia	11 (69%)
Developmental regression	9(56%)
Microcephaly	2(12.5%)
Hypertonia	2(12.5%)

Table 3. Movement disorder

Dystonia	8(50%)
Ataxia	6 (38%)
Tremor	3(19%)
Choreiform movement	3(19%)
Paroxysms of dyskinesia	1(6%)

Table 4. Seizures

Seizure 6 (38%)	
Myoclonic	3(19%)
GTCS	3(19%)

Table 5. Other features

Nystagmus	**6(38%)**
Cataract	1(6%)
Polydactyly	1(6%)
Hypertrichosis	1(6%)

Table 6. Biochemical status of the studied patients. (n-16)

INVESTIGATIONS PROFILE	
S. Lactate (increased)	9(56%)
Incraesed CPK	4(25%)
CSF lactate(increased)	3(19%)
Hypoglycemia	2(12.5%)
Urine ketone body(positive)	1(6%)
TMS	Carnitine deficiency=2 (12.5%)

Table 7. Neuroimaging profile

MRI OF BRAIN	
Basal ganglia hyperintensity	8(50%)
Dentate nuclei hyperintensity	6(38%)
Midbrain hyperintensity	5(31%)
Cortical atrophy	3(19%)
Corpus callosum thinning	2(12.5%)
Cortical hyperintensity	1(6%)
Normal	6(38%)
MRS	
Lactate peak	4(25%)

Table 8. Genetic profile of the patients, n=16

Cases	Location	Variance	Gene	Zygocity	Inheritance	Disease	Significance
Case 1 Araf, 18 months	Genetic study not done						
Case 2 Ariyan,3 years	Exone 1	c.164del, (p.Gly56AlafsTer35)	NDUFAF6(+)	Heterozygous	ARD	Mitochondrial complex 1 deficiency, nuclear type 17	US
Case 3 Sumiya ,19 months	Genetic study not done						

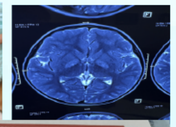
Genetic profile of the patients, n=16

Case 4 Leon, 2 years		c.24A>G(p.Thr9Ala)	MT-ND5+	Homoplasmic	Mitochondrial	Leber hereditary optic atrophy, Leigh syndrome, Mitochondrial Encephalopathy,lactic acidosis, stroke like episodes (MELAS) syndrome	US
		c.11111C>A(p.Leu371Met)	MT-CYB(+)	Homoplasmic	Mitochondrial	Leber hereditary optic atrophy, Leigh syndrome, Mitochondrial Encephalopathy,lactic acidosis, stroke like episodes (MELAS) syndrome	US
Case 5 Fardin,15 months			OPA 1 TARS 2 +ve.	Heterozygous	ARD	Mitochondrial DNA depletion Syndrome	P
Case 11 Israt, 2 years	MT-8701	A>G	MT-AP86		Germline mutation	Leigh syndrome, mitochondrial complex V deficiency	US
Case 12 Araf, 4 years	Genetic study not done						
Case 13 Samra Akhter, 2 years	Exone 8	c.6944A>G(p.Thr2332Pro)	NDUFv2(+)	Heterozygous	ARD	Mitochondrial complex 1 deficiency, nuclear type 7	US
	Exone 18	c.2891G>A(p.Arg964His)	POLG(-)	Heterozygous	ARD	Mitochondrial DNA depletion syndrome	US
Case 14 Sowad,8 years		c.1301A>G(p.Lys434Arg)	DNA2	Heterozygous	Autosomal dominant	Progressive external ophthalmoplegia, mitochondrial DNA deletions	US
Case 15 Hasan, 3 years	Exone 8	c.792_793delp.Arg264SerfsTer27)	SURF1(-)	Homozygous	ARD	Mitochondrial complex IV deficiency, nuclear type 1	P
Case 16 Hossen, 18 months	Genetic study not done						

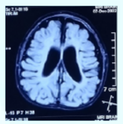
Genetic profile of the patients, n=16

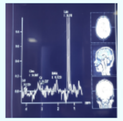
Case 6, Junayed ,3 years	Exone 2	c.176A>G(p.Asn59Ser)	ECHS1(-)	Likely compound heterozygous	ARD	mitochondrial short chain enoyl co-A hydratase deficiency	P
	Exone 5	c.518C>T(p.Ala173Val)					LP
Case 7 Oishi, 3 Years	Genetic study not done						
Case 8 Ankita ,2 years 7 months	Genetic study not done						
Case 9 Arpon , 6 years	Genetic study not done						
Case 10 Onim , 5 years	Genetic study not done						

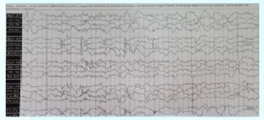
- A 3 years old boy
- Presented with periodic paroxysmal attacks of involuntary movement
- MRI showed Globus pallidus hyperintensity
- ECHs1(-) mutation
- mitochondrial short chain enoyl co-A hydratase deficiency



- 15 months old male child
- abnormal posturing for last 1year
- Jerky movement for 2 months
- developmental delay
- opisthotonic posturing ,hypotonia exaggerated in all 4 limbs with plantar extensor
- WES- OPA 1 & TARS 2 mutation
- Mitocondrial DNA depletion syndrome







Conclusion

Mitochondrial Disease are a genetically and phenotypically diverse group of inherited energy deficiency disorders.
Neuroregression ,Movement and tone abnormality and multisystem involvement are the key features.
MRI, MRS and some metabolic tests give clue for diagnosis.
Next-generation sequencing technologies have dramatically increased mitochondrial disease gene discovery .

18th INTERNATIONAL CHILD NEUROLOGY CONGRESS