USMF „NICOLAE TESTEMIȚANU"
CONFERINȚA ȘTIINȚIFICĂ ANUALĂ
CERCETAREA ÎN BIOMEDICINĂ ȘI SĂNĂTATE: CALITATE, EXCELENȚĂ ȘI PERFORMANȚĂ
20 22 octombrie 2021

LEIGH SYNDROME: A RARE CASE REPORT

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Introduction

Mitochondrial diseases are the most common group of inherited metabolic disorders characterized by defects in energy production, caused by mutation of genes encoded by nuclear or mitochondrial DNA. Leigh syndrome is a progressive neurological disorder, affecting 1:40,000 live births.

The purpose

To report a rare progressive neurodegenerative, mitochondrial disorder in a child with seizures, hypotonia, ataxia and psychomotor delay.

Material and methods

We report on a case of a 20 months old boy, born at term from non-consanguineous, healthy parents, with an uneventful perinatal history. He had no family history of any genetic or neurological disorder.

I. Clinical signs and symptoms, 1 point/symptom (max. 4 points)			II. Metabolic/ imaging studies (max. 4 points)	III. Morphology (max. 4 points)
A. Muscular presentation (max. 2 points)	B. CNS presentation (max. 2 points)	C. Multisystem disease (max. 3 points)		
Ophthalmoplegia†	Developmental delay	Hematology	Elevated lactate†	Ragged red/blue fibers‡
Facies myopathica	Loss of skills	GI tract	Elevated L/P ratio	COX-negative fibers‡
Exercise intolerance	Stroke-like episode	Endocrine/growth	Elevated alanine†	Reduced COX staining‡
Muscle weakness	Migraine	Heart	Elevated CSF lactate†	Reduced SDH staining
Rhabdomyolysis	Seizures	Kidney	Elevated CSF protein	SDH positive blood vessels†
Abnormal EMG	Myoclonus	Vision	Elevated CSF alanine†	Abnormal mitochondria/EM†
	Cortical blindness	Hearing	Urinary TA excretion†	
	Pyramidal signs	Neuropathy	Ethylmalonic aciduria	
	Extrapyramidal signs	Recurrent/familial	Stroke-like picture/MRI	
	Brainstem involvement		Leigh syndrome/MRI†	
			Elevated lactate/MRS	

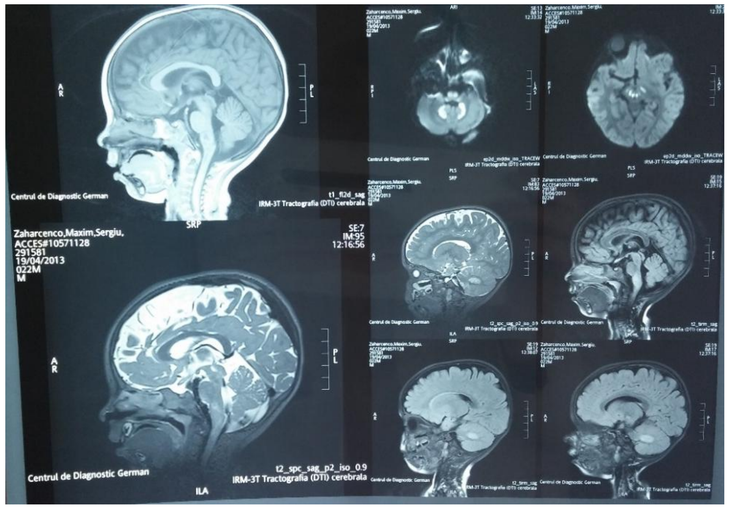
* Score 1: mitochondrial disorder unlikely; score 2 to 4: possible mitochondrial disorder; score 5 to 7: probable mitochondrial disorder; score 8 to 12: definite mitochondrial disorder.
† This specific symptom scores 2 points.
‡ This symptom in a higher percentage scores 4 points.

GI = gastrointestinal; L/P = lactate/pyruvate; COX = cytochrome c oxidase; SDH = succinate dehydrogenase; EM = electron microscopy; EMG = electromyography; TA = tricarbon acid.

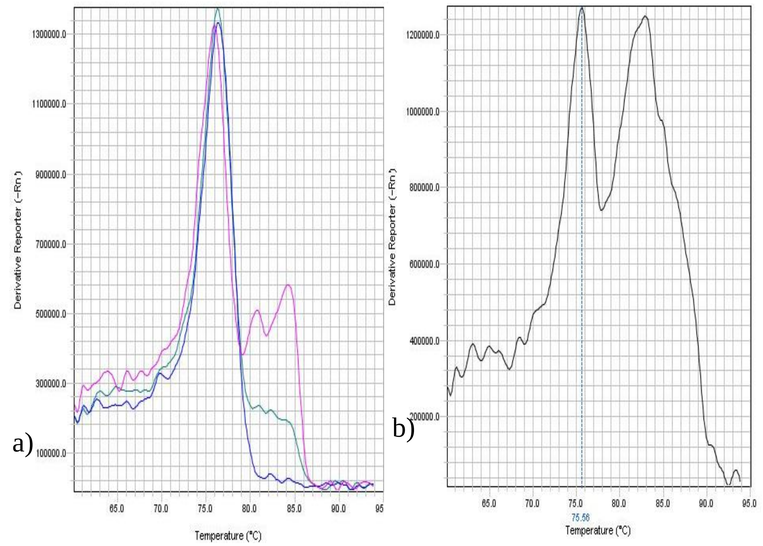
Nijmegen Mitochondrial Disease Criteria Scale: based on clinical signs and metabolic / imaging studies, the patient obtained 8 points, which suggests the presence of a mitochondrial disease

Results

According to the patient's clinical picture, an inborn error of metabolism was suspected. Blood lactate, LDH and CK-MB were markedly elevated. Amino acid analysis was performed in the blood and urine and a high level of Alanine and deviant Ala/Lys ratio was determined. The electroencephalography revealed dysfunction in cortical structures and low convulsive threshold. Magnetic resonance imaging revealed symmetrical hyperintensity in T2w images in thalamus, mesencephalon, brainstem, medullary tegmentum and cerebellar hemispheres (peri-ventricular), medulla oblongata. Genetic analysis revealed the m.3243A>G mutation in the TL1 gene of the mitochondrial genome.



MRI findings of Leigh syndrome – symmetrical hyperintensity in T2-weighted images in thalamus, mesencephalon, brainstem, medullary tegmentum and cerebellar hemispheres (periventricular) and medulla oblongata



a) Melting curve of amplicon-based controls for m.3243A>G mutation.
b) Melting curve of the patient's DNA for m.3243A>G mutation

Conclusions

The diagnosis of Leigh syndrome should be considered in a child with neurological symptoms whose MRI shows bilateral symmetric hyperintense T2w images of the brainstem and basal ganglia. Further investigations include evaluation of blood gas profile and genetic analysis.

Keywords

Leigh syndrome; mitochondrial DNA mutation; mitochondrial disease.