Mitochondrial Disease

How to Cite this Article: Ghofrani M. Mitochondrial Disease. Iran J Child Neurol Autumn 2012;7:4 (suppl.1):1-2.

Mohammad GHOFRANI MD [1,2]

1. Pediatric Neurology Research Center, Shahid Behesti University of Medical Sciences, Tehran, Iran
2. Department of Pediatric Neurology, Pediatric Neurology Center of Excellence, Mofid Children Hospital, Faculty of Medicine, Shahid Behesti University of Medical Sciences, Tehran, Iran

Corresponding Author:
Ghofrani M. MD
Mofid Children Hospital, Shariati Ave, Tehran, Iran
Tel: +98 21 22909559
Email: ijcn.journal@gmail.com

When we talk about mitochondrial diseases, we refer to the most ubiquitous of metabolic disorders, with pathogenic mitochondrial DNA mutation being found in at least 1 in 8000 individuals.

The following statement reveals very vividly, the true nature of mitochondrial disease; "Mitochondrial disease may cause any symptom in any tissue at any age by any inheritance (A. Munics)".

In view of the presence of mitochondria which are essential organelles of nearly all cells, with the exception of mature erythrocyte. Mitochondrial diseases may affect any organ system and for this reason are now called "Mitochondrial cytopathies".

Striated muscles, central nervous system and heart are the most frequently affected organs system. A series of studies described the ultra-structure characteristics of the mitochondrion. The four components of the organelle were characterized, including the outer and inner membranes, the intermembranous space and the inner matrix compartment. Two important observations were made in 1963. Each observation is central to the understanding of mitochondrial diseases. The first observation revealed the existence of intramitochondrial fibers with DNA characteristics. It is known that many human diseases are the result of mitochondrial DNA (mtDNA) mutation. The second observation was the description of ragged-red fibers in biopsy specimens of skeletal muscles. Because, mtDNA are inherited only from the mother, the term "Maternal Inheritance" is the same as "Mitochondrial Inheritance".

Clinical features of Mitochondrial cytopathies

In view of the presence in almost every cell, the wide variety of clinical manifestations of mitochondrial disease should not be sup rising. Classification of mitochondrial disorder may be based upon clinical features in accordance with the organ system most affected. In general, one important principle of mitochondrial disease is clinical involvement of multiple organ systems. The combined symptoms and signs referable to the central and/or periferal nervous system muscle is the most frequent clinical features of mitochondrial diseases are every different with recognized pathogenic point mutation and even among affected members of the same family.

Multiple genotypes of both mtDNA and nDNA defect may produce similar clinical and pathologic presentation. Some constant clinical features should raise the suspicion of the diagnosis of mitochondrial disorder, justifying investigation to confirm or refute the tentative diagnosis. Each of the mitochondrial syndromes may have similar clinical manifestation of multiple genetic defect, subsequently the phenotype-genotype correlation often are poor.

The most comment neurologic manifestation of mitochondrial diseases in infancy are seizures, visual deficit, hearing impairment, central dysphagia, apnea and respiratory failure, hypotonia and neurodevelopmental delay.

In older children and young adults neurological problems consist of: dystonia, cerebellar deficit, spastic diplegia, memory loss, cognitive deficit, progressive dementia, and autism.

Like any neurodegenerative disease, regression of previously acquired skills may occur.

Extra ocular muscles' have more mitochondria per unit volume of tissue than do most other muscles.

They often are involved and produce progressive external ophtalmoplegia of all six muscles.

Lactic acidosis is a frequent finding of many mitochondrial diseases but not all. It is universally present in MERRF and Kearn-Sayre syndromes, and most cases of Leigh encephalopathy.

Lactic acidosis is more likely in these cases with mtDNA. In some patient the serum lactate may be normal but cerebrospinal fluid (CSF) lactate is elevated. When drawing serum lactate, it is important to measure pyruvate. In mitochondrial cytopathies, if the lactate is elevated the pyruvate is normal or also high. The most common cause of high serum lactate is that the tourniquet has been placed on arm too long while looking for a good vein. The resulting acute anaerobic state causes pyruvate to be converted to lactate; hence the lactate is high but the pyruvate is very low.

Keywords: Mitochondrial disease; Cytopathy; Inheritance; Muscle cells; Metabolic