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Cardiac complications in inherited mitochondrial diseases

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Abstract

Maternally mitochondrial dysfunction includes a heterogeneous group of genetic disorders which leads to the impairment of the final common pathway of energy metabolism. Coronary heart disease and coronary venous disease are two important clinical manifestations of mitochondrial dysfunction due to abnormality in the setting of underlying pathways. Mitochondrial dysfunction can lead to cardiomyopathy, which is involved in the onset of acute cardiac and pulmonary failure. Mitochondrial diseases present other cardiac manifestations such as left ventricular noncompaction and cardiac conduction disease. Different clinical findings from mitochondrial dysfunction originate from different mtDNA mutations, and this variety of clinical symptoms poses a diagnostic challenge for cardiologists. Heart transplantation may be a good treatment, but it is not always possible, and other complications of the disease, such as mitochondrial encephalopathy, lactic acidosis, and stroke-like syndrome, should be considered. To diagnose and treat most mitochondrial disorders, careful cardiac, neurological, and molecular studies are needed. In this study, we looked at molecular genetics of MIDs and cardiac manifestations in patients with mitochondrial dysfunction.

Keywords Mitochondrial dysfunction · mtDNA · Cardiac · Atrioventricular

Abbreviations

ANT	Adenine nucleotide translocator
BSCL2	Berardinelli-Seip congenital lipodystrophy
CMP	Cardiomyopathy
COX	Cytochrome *c* oxidase
ECMP	Encephalocardiomyopathy
MELAS	Mitochondrial encephalopathy lactic acidosis and stroke-like episodes
MERRF	Myoclonus epilepsy red ragged fibers
MID	Mitochondrial dysfunction
MRP	Mitochondrial ribosomal protein
MTO	Mitochondrial tRNA translation optimization
ND1	NADH-ubiquinone oxidoreductase chain 1
NDUFAF1	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex assembly factor 1
OXPHOS	Oxidation-phosphorylation
ROS	Reactive oxygen species

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Introduction

Mitochondria are involved in various fundamental cellular processes like apoptosis, calcium signaling, and generation of reactive oxygen species (ROS), but the most principal action of mitochondria is the synthesis of adenosine triphosphate (ATP) through oxidative phosphorylation pathway. Electron transfer between respiratory chain enzymes occurs through an electrochemical slope in the inner mitochondrial membrane [1, 2].

Defects in the oxidative phosphorylation pathway cause a variety of diseases ranging from the involvement of one tissue to the involvement of multiple organs with high-energy demands such as the heart and brain. Mutations or gene variation can play a role in the onset and severity of the disease [3, 4]. Mitochondrial DNA in neonatal heart cells has a simple, amorphous and double-stranded structure. Branched forms appear in adults as mitochondrial DNA copy number increases in early childhood [5]. Adult human mitochondrial DNA has a complex organization with a large number of dimer molecules, four-way junction, and branching structures [6].