Cardiac Involvement of Mitochondrial Myopathy in Children

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Abstract

Mitochondrial disease is defined as hereditary or sporadic multi-systemic disorder to develop consequent to mutations in nuclear or mitochondrial DNA, with impaired mitochondrial energy metabolism.[1,2] Heart is one of the most frequent affected organs in mitochondrial disorders, and cardiac involvement is increasingly noticed, as the myocardium depends on a high level of oxygen metabolism to supply blood and energy substrate to all organs of the body.[1-3]

Mitochondrial disease can develop structural heart lesion, which may affect the myocardium, the coronary arteries, the pericardium, or the aortic root. Moreover, cardiac functional abnormalities can be accompanied, such as impulse generation, conduction abnormalities, systolic dysfunction, heart failure, pulmonary hypertension, or autonomic dysfunction.[1] Certainly, the most frequent cardiac manifestation is cardiomyopathy (CMP), which may present as hypertrophic CMP (HCMP), dilated CMP (DCMP), restrictive CMP (RCMP), or unclassified CMP like left ventricular hyper-trabeculation or noncompaction. Myocardial fibrosis and late enhancement can be recognized in various cardiomyopathies.[1-3]

Meanwhile, in children and infant with mitochondrial disorders, clinical presentation differs from adult onset, can be often correlated with genetic defects. The phenotypes are much more severe, often involving brain, frequently presenting as multi-systemic disorders and seldom as isolated myopathy. Mutations in DNA are more frequent in children rather than in adulthood.[4] The frequency of cardiac involvement may be different in children and adults. The variety with MD presentation may be a challenge to the cardiologist, especially in children.[5] As previously published, children in MD with oxidative phosphorylation defects, cardiac involvement was reported in 33%, the cardiomyopathy was approximately 5.6%.[1,6,7] HCMP is the most frequent CMP in MD.[1,8,9]

Cardiac hypertrophy is an adaptive response of the heart to increase work-load resulting from physiological or pathological stimuli, counteracting the increased wall tension and assisting to maintain cardiac output.[10] When the heart is extremely stressed with persistent overload, the hypertrophy might become maladaptive, cardiac function may progressively deteriorate to heart failure.[11] Primary mitochondrial cardiomyopathies lead to mitochondrial proliferation in cardiomyocytes.[12] The pathologic cardiac hypertrophy developed by an increased mitochondrial number resulting from enhanced mitochondrial biogenesis and protein synthesis.[13] At the hypertrophy phase in acquired cardiomyopathy, there is an increase in mitochondrial biogenesis, which is important to delay cardiac decompensation induced by pressure overload.[14] If the hypertrophic phase is bypassed, a severe and rapidly progressive dilated cardiomyopathy occurs.[15] Both cardiac systolic and diastolic functions are dependent on mitochondrial ATP, suggesting that mitochondrial energetic decline contributes to the progression of cardiomyopathy and further heart failure, which may lead to sudden cardiac death.

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