

New pathologic modality for diagnosis of mitochondrial cardiomyopathy

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Introduction: Definite diagnosis of mitochondrial cardiomyopathy has been challenging, because it requires respiratory chain (RC) enzymatic assay, and genetic testing. Now, we devised the new diagnostic approach of pathologic study including electron microscopic and immunohistopathologic study.

Methods: Ten patients with HCM were studied. Using results for respiratory chain enzymatic assay and genetic testing the patients were divided into MCM(4 patients) and non-MCM(6 patients) groups. Electron microscopy and light microscopy was performed using endomyocardial biopsy samples. In electron microscopy study, volume density within cardiac muscle cells (CM) of mitochondria [Vv(mit,CM)] were measured using a systematic random sampling design. Using stored Formalin-fixed paraffin-embedded tissue, quantitative immunohistopathologic study with monoclonal antibodies against mitochondrial electron transport chain complex (Complex I, II, and IV) was performed. Staining area of complex I and IV were divided by that of complex II, an internal control marker of mitochondrial RC. Thus, Area[Complex I/II] and Area[Complex IV/II] were measured.

Results: In the MCM group Vv(mit,CM) was significantly higher than the non-MCM group ($40.6\pm 2.8\%$, $21.9\pm 4.1\%$, $p<0.001$) and significantly reduced Area[Complex I/II] or Area[Complex IV/II] or both were found.

Discussion: Volume density of mitochondria using electron microscopy can differentiate between MCM and non-MCM cases. Furthermore, immunohistopathologic study also showed a new possibility for diagnosis of MCM, which maybe useful for first-line screening.

Conclusions: Immunohistopathologic study may be a good screening test for MCM.