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SCIENTIFIC LETTER

Leigh Syndrome with *MT-ND5* Mutation and Hypertrophic Cardiomyopathy

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To the Editor: Leigh syndrome (LS) is the most common mitochondrial disease occurring during childhood. The primary symptoms of LS are neurological, such as developmental regression, epilepsy, and gait disturbance. Among them, recent reports suggest significant associations between pathogenic variant in NADH dehydrogenase 5 (*MT-ND5*) and the presence of cardiomyopathy in LS [1, 2]. Here we report a case series that investigate the relationship between cardiac symptoms and *MT-ND5*-associated LS identified in infants at a single tertiary hospital in South Korea.

We used mitochondrial DNA whole genome sequencing to determine a genetic diagnosis in 31 patients with clinical LS. Four patients with the *MT-ND5* m.13513G>A variants were identified. The median mutant load was 66.7% (55.5–71.6%). All patients with pathogenic *MT-ND5* variants underwent electrocardiography (ECG) and echocardiography at the time of diagnosis. Hypertrophic cardiomyopathy was diagnosed by identifying features such as left ventricular hypertrophy and abnormal movement of the cardiac valves on M-mode imaging or two-dimensional echocardiography. ECG showed biventricular and left ventricular hypertrophy in three and one patients, respectively. In addition, hypertrophic cardiomyopathy in all four patients was revealed on echocardiography. Active respiratory support was required in two patients and three patients required respiratory support and oxygen dependency.

Cardiac involvement in *MT-ND5*-associated LS has been occasionally reported, including the presence of Wolff–Parkinson–White Syndrome and paroxysmal supraventricular tachycardia [3]. The purported mechanism underlying mitochondrial hypertrophic cardiomyopathy is a combination of elevated reactive oxygen species, limited antioxidant activity, impaired mitophagic clearance, and mitochondrial morphologic abnormalities of genetic origin. Thus, hypertrophic cardiomyopathy may be a characteristic phenotype of *MT-ND5*-associated LS. Studies of the mechanism of mitochondrial dysfunction in the myocardium should be the basis for the development of new LS treatments [4]. Here, our findings provide additional supportive data to strengthen the ongoing foundation of genotype–phenotype correlations in *MT-ND5*-associated LS.

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Declarations

Conflict of Interest None.

References

1. Sofou K, de Coo IFM, Ostergaard E, et al. Phenotype-genotype correlations in Leigh syndrome: new insights from a multicentre study of 96 patients. J Med Genet. 2018;55:21–7.
2. Na JH, Lee YM. Genotype-phenotype analysis of MT-ATP6-associated Leigh syndrome. Acta Neurol Scand. 2022;145:414–22.
3. Brecht M, Richardson M, Taranath A, Grist S, Thorburn D, Bratkovic D. Leigh syndrome caused by the MT-ND5 m.13513G > A mutation: a case presenting with WPW-like conduction defect, cardiomyopathy, hypertension and hyponatraemia. JIMD Rep. 2015;19:95–100.
4. Ranjbarvaziri S, Kooiker KB, Ellenberger M, et al. Altered cardiac energetics and mitochondrial dysfunction in hypertrophic cardiomyopathy. Circulation. 2021;144:1714–31.