

A case of Barth syndrome of early-onset and severe cardiomyopathy associated with triple compound heterozygosity

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Background

Barth syndrome is an X-linked recessive mitochondrial disorder characterized by cardiomyopathy, neutropenia, growth retardation, 3-methylglutaconic aciduria. It is caused by mutations in the TAZ gene, which is known to encode for the protein tafazin. We report a neonatal case of the Barth syndrome suffered from an early-onset and severe cardiomyopathy that may be associated with triple compound heterozygous mutations in TAZ, SDHA, and DTNA genes.

Case

A term male infant was born to a 33-year-old 5G4P mother. Acute heart failure from dilated cardiomyopathy with the left ventricular noncompaction developed to him immediately after birth. He was intubated and started on inotropic support. After stabilization of cardiac function, carvedilol was added under continuous infusion of dobutamine. Though he somehow discharged at 5 months old, he has suffered from acute aggravation of the chronic heart failure. The family history was reviewed and the second-born boy to the parents died suddenly several hours after birth and the maternal grandmother had spontaneous abortion twice. The whole exome sequencing of genes in the cardiomyopathy panel available at Laboratory for Molecular Pathogenesis at the Tokyo Medical and Dental University confirmed that the patient has novel mutations in TAZ, SDHA and DTNA genes. The novel mutations are identified in exon 6, c.469C>T (p.Leu157Phe) of the TAZ gene, exon 9, c.1351_1355delCGCCT, (p. Arg451fs) of the SDHA gene, and exon 19, c. 1763G>A, p.Ser588Asn) of the DTNA gene. In silico tools suggest these mutations might be disease causing. Further sequencing to the parents revealed his mother had the mutation in the TAZ gene with heterozygosity, and his father had mutations in the SDHA and DTNA genes with heterozygosity.

Discussion

This is the first case of Barth syndrome associated with triple compound heterozygous mutations. Hypertrophic cardiomyopathy with multiple mutations is known to be aggravated than that with single mutation. In this case, a similar mechanism might be involved in the early onset and severity of heart failure.