Phenotypic spectrum of SLC25A4 mutations.

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Abstract

There is no comprehensive overview concerning the phenotypic variability in patients carrying SLC25A4 mutations available. Therefore, the aim of the present review was to summarise and discuss recent findings concerning the clinical presentation and phenotypic heterogeneity of SLC25A4 mutations. The study was conducted by systematically reviewing the literature using the search terms 'mitochondrial', "myopathy', 'nuclear DNA', 'mitochondrial DNA', in combination with 'SLC25A4' or 'AAC1'. The results indicated that the phenotypic heterogeneity in patients carrying a SLC25A4 mutation is broader than so far anticipated. Patients carrying a SLC25A4 mutation not only manifest as encephalo-myo-cardiomyopathy but also with scoliosis, cataract, depression, headache, hydrocephalus or arterial hypertension. SLC25A4 mutations may result in mtDNA depletion or multiple mitochondrial (mt)DNA deletions. SLC25A4-associated mtDNA depletion presents with the more severe phenotype and the worse outcome than patients with multiple mtDNA deletions. Depletion syndrome due to SLC25A4 mutations is associated with congenital respiratory insufficiency requiring mechanical ventilation with poor prognosis in the majority of the cases. Mutations in the SLC25A4 gene manifest phenotypically with multiorgan abnormalities in addition to encephalo-myo-cardiomyopathy. SLC25A4 mutations, causing mtDNA depletion, present with a more severe phenotype, including respiratory insufficiency and more widespread cerebral disease than mutations causing multiple mtDNA deletions.

KEYWORDS: SLC25A4; cardiac involvement; central nervous system; mitochondrial; mtDNA; myopathy

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