MRPL44 mutations cause a slowly progressive multisystem disease with childhood-onset hypertrophic cardiomyopathy.

Defects in mitochondrial translation may lead to combined respiratory chain deficiency and typically cause childhood-onset multisystem disease. Only recently, a homozygous missense mutation (c.467T> G, p.Leu156Arg) in MRPL44, encoding a protein of the large subunit of the mitochondrial ribosome, has been identified in two siblings with hypertrophic cardiomyopathy. Using exome sequencing, we identified two further unrelated patients harboring the previously reported mutation c.467T> G, p.Leu156Arg in MRPL44 in the homozygous state and compound heterozygous with a novel missense mutation c.233G> A, p.Arg78Gln, respectively. Both patients presented with childhood-onset hypertrophic cardiomyopathy, which seems to be the core clinical feature associated with MRPL44 deficiency. However, we observed several additional clinical signs and symptoms including pigmentary retinopathy, hemiplegic migraine, Leigh-like lesions on brain MRI, renal insufficiency, and hepatopathy. Our findings expand the clinical spectrum associated with MRPL44 mutations and indicate that MRPL44-associated mitochondrial dysfunction can also manifest as a progressive multisystem disease with central nervous system involvement.
Of note, neurological and neuro-ophthalmological impairment seems to be a disease feature of the second and third decades of life, which should be taken into account in patient management and counseling.