Novel SCARB2 mutation in action myoclonus-renal failure syndrome and evaluation of SCARB2 mutations in isolated AMRF features.

ABSTRACT: Action myoclonus-renal failure syndrome is a hereditary form of progressive myoclonus epilepsy associated with renal failure. It is considered to be an autosomal-recessive disease related to loss-of-function mutations in SCARB2. We studied a German AMRF family, additionally showing signs of demyelinating polyneuropathy and dilated cardiomyopathy. To test the hypothesis whether isolated appearance of individual AMRF syndrome features could be related to heterozygote SCARB2 mutations, we screened for SCARB2 mutations in unrelated patients showing isolated AMRF features. In the AMRF family all exons of SCARB2 were analyzed by Sanger sequencing. The mutation screening of unrelated patients with isolated AMRF features affected by either epilepsy (n = 103, progressive myoclonus epilepsy or generalized epilepsy), demyelinating polyneuropathy (n = 103), renal failure (n = 192) or dilated cardiomyopathy (n = 85) was performed as high resolution melting curve analysis of the SCARB2 exons. A novel homozygous 1 bp deletion (c.111delC) in SCARB2 was found by sequencing three affected homozygous siblings of the affected family. A heterozygous
sister showed generalized seizures and reduction of nerve conduction velocity in her legs. No mutations were found in the epilepsy, renal failure or dilated cardiomyopathy samples. In the polyneuropathy sample two individuals with demyelinating disease were found to be carriers of a SCARB2 frameshift mutation (c.666delCCTTA). Our findings indicate that demyelinating polyneuropathy and dilated cardiomyopathy are part of the action myoclonus-renal failure syndrome. Moreover, they raise the possibility that in rare cases heterozygous SCARB2 mutations may be associated with PNP features.