POLG

Mutations in the mitochondrial DNA maintenance gene POLG (DNA Polymerase Gamma, Catalytic Subunit), encoding mitochondrial DNA polymerase gamma (pol γ), are associated with an extremely broad phenotypic spectrum. We identified homozygous POLG c.1879C>T; p.R627W mutations in two siblings from a consanguineous South Asian family following targeted resequencing of 75 nuclear-encoded mitochondrial genes. Both patients presented with encephalopathy, seizures and stroke-like episodes, and mitochondrial DNA depletion was confirmed in the proband's muscle tissue. Subsequent Sanger sequencing of POLG in a further 275 unrelated probands with genetically unconfirmed mitochondrial disease revealed a third unrelated proband with a similar phenotype harboring homozygous c.1879C>T; p.R627W mutations and a fourth patient, with a milder clinical disorder, harboring compound heterozygous POLG c.1879C>T; p.R627W and c.2341G>A; p.A781T mutations. Given endogamous practices in the Indian subcontinent, homozygous POLG c.1879C>T; p.R627W mutations should be excluded in South Asian patients presenting with encephalopathy, seizures and stroke-like episodes [1)].

1)
Paramasivam A, Venkatapathi C, Sandeep G, Meena AK, Uppin MS, Mohapatra S, Pitceathly RDS, Thangaraj K. Homozygous R627W mutations in POLG cause mitochondrial DNA depletion leading to encephalopathy, seizures and stroke-like episodes. Mitochondrion. 2019 Aug 16. pii: S1567-7249(18)30155-7. doi: 10.1016/j.mito.2019.08.003. [Epub ahead of print] PubMed PMID: 31425757.