

Parkinsonism, Ataxia, and Neuropathy due to a POLG2 Mutation

Josef Finsterer^{1*} and Sinda Zarrouk-Mahjoub²

¹Krankenanstalt Rudolfstiftung, Vienna, Austria

²University of Tunis El Manar and Genomics Platform, Pasteur Institute of Tunis, Tunisia

*Corresponding Author: Josef Finsterer, Krankenanstalt Rudolfstiftung, Vienna, Austria.

Received: March 12, 2018; Published: April 20, 2018

Keywords: Mitochondrial; mtDNA; Myopathy; Cerebral; Epilepsy; Parkinsonism

Recently, Maldergem, *et al.* reported about a family of which eight members (4 alive) carried a homozygote splice-acceptor mutation in the *POLG2* gene, clinically manifesting as cerebellar ataxia, tremor, parkinsonism, seizures, cognitive decline, hypoacusis, polyneuropathy, and ophthalmoparesis [1]. We have the following comments and concerns.

POLG2 mutations not only manifest with central nervous system (CNS) abnormalities, myopathy affecting extra-ocular muscles, and polyneuropathy but also with fulminant hepatic failure [2] and myopathy of limb muscles, manifesting as weakness, easy fatigability, exercise-intolerance, and hyper-CKemia [3]. Were there any indications for hepatopathy or limb myopathy in any of the mutation carriers?

POLG2 mutations may not only cause multiple mtDNA deletions [4] but also mtDNA depletion [2]. Was there any indication of mtDNA depletion in any of the mutation carriers?

Five of the mutation carriers had developed epilepsy with tonic clonic seizures, ultimately leading to status epilepticus and death in three of them [1]. Did the three patients with status epilepticus develop non-convulsive or convulsive status epilepticus? In case they developed convulsive status epilepticus, was it a focal or generalised status epilepticus? Concerning the antiepileptic treatment we should be informed which antiepileptic drugs (AEDs) were applied and if all five patients tolerated the AEDs without side effects? This is of particular importance since a number of AEDs are mitochondrion-toxic, in particular valproic acid, phenytoin, carbamazepine, and barbiturates [5].

Mitochondrial disorders (MIDs) frequently present as mitochondrial multiorgan disorder syndromes (MIMODSs), which generally affect all tissues, particularly the CNS, peripheral nervous system, endocrine organs, heart, gastrointestinal tract, and the kidneys. Did any of the mutation carriers develop cardiac, endocrine, gastrointestinal, or renal abnormalities during follow-up? Were mutation carriers prospectively investigated for MIMODS?

Patient II-10 is reported to have presented with dystonia [1]. Cerebral MRI of this patient is reported to have been normal [1]. How to explain dystonia in this affected female? Was it a side effect of a drug? How was dystonia treated?

Among the four mutation carriers who underwent muscle biopsy, in how many of them were biochemical investigations of the muscle homogenate carried out? Which respiratory chain complexes showed impaired function?

Overall, this interesting report would profit from a more detailed description of the phenotype, from more extensive clinical investigations, and from a detailed description of the applied therapeutic measures. MID patients should be extensively investigated to broaden the knowledge about the phenotypic and genotypic peculiarities of MIDs.

Conflicts of Interest

There are no conflicts of interest.

Funding

No funding was received.

Author Contribution

Both authors contributed equally. JF: design, literature search, discussion, first draft, SZ-M: literature search, discussion, critical comments.

Bibliography

1. Van Maldergem L., *et al.* "POLG2 deficiency causes adult-onset syndromic sensory neuropathy, ataxia and parkinsonism". *Annals of Clinical and Translational Neurology* 4.1 (2016): 4-14.
2. Varma H., *et al.* "Whole exome sequencing identifies a homozygous POLG2 missense variant in an infant with fulminant hepatic failure and mitochondrial DNA depletion". *European Journal of Medical Genetics* 59.10 (2016): 540-545.
3. Walter MC., *et al.* "Late-onset ptosis and myopathy in a patient with a heterozygous insertion in POLG2". *Journal of Neurology* 257.9 (2010): 1517-1523.
4. Craig K., *et al.* "A p.R369G POLG2 mutation associated with adPEO and multiple mtDNA deletions causes decreased affinity between polymerase γ subunits". *Mitochondrion* 12.2 (2012): 313-319.
5. Finsterer J. "Toxicity of Antiepileptic Drugs to Mitochondria". *Handbook of Experimental Pharmacology* 240 (2016): 473-488.

Volume 10 Issue 5 May 2018

©All rights reserved by Josef Finsterer and Sinda Zarrouk-Mahjoub.