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Letter to the Editor

Mitochondrial dysfunction in *ATP13A2* carriers

We read with interest the article by Suleiman et al. about a 10 years-old male with juvenile Parkinsonism being attributed to the compound heterozygote paternal variant c.1321A>T and the maternal variant c.3205G>A in the *ATP13A2 (PARK9)* gene [1]. We have the following comments and concerns.

We do not agree with the notion that dopaminergic neurons are reduced in the basal ganglia in patients with Parkinsonism [1]. It is predominantly the substantia nigra where loss of dopaminergic neurons occurs being made responsible for motor manifestations.

Patients carrying mutations in the *ATP13A2* gene may additionally manifest with impulse control disorder [2], paraspasticity, abnormal eye movements (saccades, supranuclear gaze palsy), or facial myokymias [3]. Were any of these features present in the index case or did any of them develop during follow-up?

In single carriers of *ATP13A2* variants accumulation of iron in the putamen and caudate nucleus leading to neurodegeneration with brain iron accumulation (NBIA) has been reported. Was the index case tested for iron accumulation in the basal ganglia?

Recent data suggest that heterozygous *ATP13A2* carriers may be at risk of developing Parkinsonism, similar to the association of mutations in the *GBA* gene with Parkinson's disease and Gaucher's disease [4]. Which were the abnormalities found on neurologic examination in the parents?

Reduced putaminal tracer uptake on the dopamine-transporter scintigraphy (DAT-scan) may support the diagnosis of Parkinsonism. Which were the results of the DAT-scan in the index case?

ATP13A2 mutations may cause mitochondrial dysfunction [5]. *ATP13A2* mutations particularly reduce autophagy resulting in increased reactive oxidative species (ROS) production. Were mitochondrial functions or ROS production ever tested and abnormal in the index case?

In conclusion, the phenotypic spectrum of *ATP13A2* mutations is broader than so far anticipated. Homo- and heterozygote *ATP13A2* carriers should be followed-up and thoroughly investigated for phenotypic features and mitochondrial dysfunction, which may not be present at onset but may develop during follow-up.

Author contribution

JF: design, literature search, discussion, first draft, Coauthors: literature search, critical review.

All authors contributed equally.

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