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Letter to the Editor

Reply to the Letter, "Leigh syndrome with spinal cord involvement due to a hemizygous NDUFA1 mutation"

Dear Josef Finsterer

Thank you for reading and giving us comments about our paper, "Leigh syndrome with spinal cord involvement due to a hemizygous NDUFA1 mutation".

1. Spinal cord affection is not infrequent in patients with mitochondrial disorders

As we noted in the text, we only cited genetically proven cases with Leigh syndrome, including your suggested case [1]. The number of these cases is small compared to the more than one thousand cases of Leigh syndrome reported with genetic defects. Spinal cord lesions may have been overlooked, since they are not included in the definition of Leigh syndrome [2].

2. Reason for the phenotypic heterogeneity in NDUFA1 mutations

We were unable to correlate the type of NDUFA1 mutations to the clinical phenotypes in the five reported patients, including our case. Even the same mutation, G32R in NDUFA1, resulted in considerable clinical heterogeneity among relatives.

3. Some antiepileptic are mitochondrion-toxic

Thank you for raising an important clinical point on epilepsy management for mitochondrial diseases [3]. Our patient was first treated with carbamazepine, and then levetiracetam was added. As he continues to be seizure-free, we plan to reduce his regimen to levetiracetam monotherapy.

4. Carrier status and symptoms of mother and twin sister; Parkinson's disease symptom; origin of ataxia

The mother and sister have not presented with any clinical symptoms. We have not examined their carrier status for the mutation, as they do not wish to undergo genetic testing. The patient has not manifested the Parkinson's disease symptoms of rigidity and resting tremor. His ataxia at the onset was accompanied by nystagmus and slurred speech. Therefore, the symptoms seem to have originated from the cerebellar tract, despite the lack of cerebellar atrophy. In the later stage, ataxia may be mixed with cerebellar and spinal origins.

References

[1] Tenney JR, Prada CE, Hopkin RJ, Hallinan BE. Early spinal cord and brainstem involvement in infantile Leigh syndrome possibly caused by a novel variant. J Child Neurol 2013;28:1681–5.
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[3] Finsterer J. Toxicity of antiepileptic drugs to mitochondria. Handb Exp Pharmacol 2017:473–88.

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