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Josef Finsterer, Sinda Zarrouk-Mahjoub

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Why does Leigh syndrome respond to immunotherapy?

Josef Finsterer MD, PhD [a,*,1], Sinda Zarrouk-Mahjoub PhD [b,1]

[a] Krankenanstalt Rudolfstiftung, Vienna
[b] Genomics Platform, Pasteur Institute of Tunis, Tunisia

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Letter to the Editor

With interest we read the article by Chuquilin et al. about a 20yo female with Leigh syndrome due to the m.9176T > C mutation in the ATP6 gene who responded favourably to plasmapheresis and immunoglobulins [1]. We have the following comments and concerns.

The main ambiguity of this report is the diagnosis. Except for the current case, Leigh syndrome has not been reported to respond to immunosuppressive treatment. Thus, the diagnosis of Leigh syndrome needs to be challenged. Which of the four variants in the ATP6, POLG1, DARS2, and LRPPRC respectively was the causative mutation? Was any of these mutations also detected in any of the parents or grandparents? Was there consanguinity between mother and father? Did the parents or other first degree relatives undergo neurologic work-up for mitochondrial disorder? Particularly the mother requires intensive work-up since she had a history of migraine, a frequent phenotypic manifestation of mitochondrial disorders [2]. Did the patient undergo muscle biopsy and a biochemical investigation? Were any deficiencies in the activity of the respiratory chain complexes detected? Did magnetic resonance spectroscopy (MRS) confirm elevated lactate in the cerebrum, particularly the basal ganglia [3]? Was glycogen storage disease 3A genetically confirmed in one of the half-brothers? Did the patient or her relatives ever experience a stroke-like episode, seizures, migraine, or a psychotic episode?

Second, POLG1 mutations may not only cause CPEO, Alpers-Huttenlocher, and SANDO, but also mitochondrial depletion syndrome, encephalomyopathy, mitochondrial epilepsy, mitochondrial neuropathy, a MNGIE-like phenotype, MELAS/SANDO overlap syndrome, POLG-related levodopa-related parkinsonism, and a number of complex non-syndromic mitochondrial disorders [4,5].

Third, we should be informed if plasmapheresis and immunoglobulins also had a beneficial effect on the cerebral lesions? Was follow-up MRI and MRS normal?

Overall, this interesting case merits confirmation of the genetic diagnosis and a plausible explanation why immunosuppression had such a beneficial effect.

Conflict of interest

There are no conflicts of interest.

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* Corresponding author at: Postfach 20, 1180, Vienna, Austria.
E-mail address: fipaps@yahoo.de (J. Finsterer).
[1] Both authors contributed equally.

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