

# Why does Leigh syndrome respond to immunotherapy?

Josef Finsterer, Sinda Zarrouk-Mahjoub

► **To cite this version:**

Josef Finsterer, Sinda Zarrouk-Mahjoub. Why does Leigh syndrome respond to immunotherapy?. *Molecular Genetics and Metabolism Reports*, Elsevier, 2016, 11, pp.90 - 91. <10.1016/j.ymgmr.2016.07.008>. <pasteur-01452699>

**HAL Id: pasteur-01452699**

**<https://hal-riip.archives-ouvertes.fr/pasteur-01452699>**

Submitted on 2 Feb 2017

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



## Why does Leigh syndrome respond to immunotherapy?

Josef Finsterer MD, PhD <sup>a,\*</sup>, Sinda Zarrouk-Mahjoub PhD <sup>b,1</sup>

<sup>a</sup> *Krankenanstalt Rudolfstiftung, Vienna*

<sup>b</sup> *Genomics Platform, Pasteur Institute of Tunis, Tunisia*



### ARTICLE INFO

#### Article history:

Received 22 July 2016

Accepted 23 July 2016

Available online 27 July 2016

#### Keywords:

Mitochondrial DNA  
Leigh syndrome  
Immunosuppression  
Plasmapheresis  
Respiratory chain

© 2016 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

### 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.

### Funding

No funding was received.

### References

- [1] M. Chuquilin, R. Govindarajan, D. Peck, E. Font-Montgomery, Response to immunotherapy in a patient with adult onset Leigh syndrome and T9176C mtDNA mutation, *Mol. Genet. Metab. Rep.* 8 (2016) 28–32.
- [2] B. Dermaut, S. Seneca, L. Dom, K. Smets, L. Ceulemans, J. Smet, B. De Paepe, S. Tousseyn, S. Weckhuysen, M. Gewillig, P. Pals, P. Parizel, J.L. De Blecker, P. Boon, L. De Meirleir, P. De Jonghe, R. Van Coster, W. Van Paesschen, P. Santens, Progressive myoclonic epilepsy as an adult-onset manifestation of Leigh syndrome due to m.14487T > C, *J. Neurol. Neurosurg. Psychiatry* 81 (2010) 90–93.
- [3] E. Jurkiewicz, S. Chełstowska, I. Pakuła-Kościeszka, K. Malczyk, K. Nowak, M. Bekiesińska-Figatowska, J. Sykut-Cegielska, D. Piekutowska-Abramczuk, E. Pronicka, P. MR, Spectroscopy in patients with Leigh syndrome, *Neuroradiol. J.* 24 (2011) 424–428.

\* Corresponding author at: Postfach 20, 1180, Vienna, Austria.

E-mail address: [fipaps@yahoo.de](mailto:fipaps@yahoo.de) (J. Finsterer).

<sup>1</sup> Both authors contributed equally.

- [4] B.H. Cohen, P.F. Chinnery, W.C. Copeland, POLG-Related disorders, in: P. RA, A. MP, A. HH, W. SE, A. Amemiya, B. LJH, B. TD, F. CT, M. HC, S. RJH, K. Stephens (Eds.), GeneReviews® [Internet], University of Washington, Seattle, Seattle (WA), Mar 16 2010 updated 2014 Dec 18. 1993–2016. Available from <http://www.ncbi.nlm.nih.gov/books/NBK26471/>.
- [5] J. Finsterer, Leigh and Leigh-like syndrome in children and adults, *Pediatr. Neurol.* 39 (2008) 223–235.