Int. j. adv. multidisc. res. stud. 2025; 5(6):1613-1614

Received: 07-12-2025
Accepted: 17-12-2025

International Journal of Advanced Multidisciplinary Research and Studies

ISSN: 2583-049X

Letter to the Editor

Stroke-Like Episodes in RNF213 Mutation Carriers should only be Diagnosed after Documentation of Stroke-Like Lesions in Multimodal MRI

[1] Carla A Scorza, [2] Fulvio A Scorza, [3] Josef Finsterer

[1, 2] Federal University of Sao Paulo (UNIFESP/EPM), São Paulo, Brazil

[3] Department of Neurology, Neurology & Neurophysiology Center, Vienna, Austria

DOI: https://doi.org/10.62225/2583049X.2025.5.6.5460

Corresponding Author: **Josef Finsterer**

Letter to the Editor

We read the article by Bovenzi *et al*. about two patients (father and son) with Leigh-like syndrome due to the heterozygous variant ENST00000319921.4:c.2157G>A; p.Trp719* in RNF213, which manifested as chorea (father), dementia (father), stroke-like episodes (SLE) (father, son), lesions of the brainstem and basal ganglia (father, son), and epilepsy (son) [1]. The study is noteworthy, but some ambiguities should be clarified.

The first point is that we do not believe that both patients had SLE [1]. SLEs are not defined by clinical manifestations alone, but also require documentation of a so-called stroke-like lesion (SLL) on magnetic resonance imaging (MRI) of the brain [2]. SLLs are characterized by a supratentorial lesion that is not confined to a vascular area and is characterized by hyperintensity on T2, fluid-attenuated inversion recovery (FLAIR), diffusion-weighted imaging (DWI), and perfusion-weighted imaging (PWI), as well as hypointensity on oxygen extraction fraction MRI [2]. In fluorodeoxyglucose positron emission tomography (FDG-PET), SLLs appear as hypometabolism [3]. In addition, magnetic resonance spectroscopy (MRS) can detect lactate within the lesion [4]. Furthermore, SLLs undergo dynamic development. After their onset, they increase in size until they reach a peak, then regress and either disappear completely from imaging or end up as a cyst, white matter lesion, toenail sign, laminar cortical necrosis, or atrophy [2]. The cerebral MRIs of father and son at the time of SLE should be shown.

The second point is that the son had an unremarkable cerebrospinal fluid (CSF) examination, but it is not reported whether the lactate level in the CSF was determined or not. The lactate level in the CSF may be elevated even if the MRS does not show a lactate peak [5]. Furthermore, no results of serum lactate levels for either patient were presented [1]. It is crucial to know whether lactic acidosis was present or not, as lactic acidosis is a common feature of Leigh syndrome and can greatly influence the course of the disease, including the triggering of seizures.

The third point is that the different ages of onset in the father and son were not adequately explained [1]. Were there any variants of unknown significance in the whole exome sequencing that could explain the widely varying ages of onset?

The fourth point is that the effect of the RNF213 variant on mitochondrial DNA (mtDNA) was not reported [1]. Several of the nuclear variants that cause mitochondrial disorders have a secondary effect on mtDNA, with single or multiple deletions, mtDNA depletion, or reduced mtDNA expression.

Finally, the therapeutic treatment of both patients was not reported [1]. We should know what the father received for chorea, how the SLEs were treated in the father and son, what antiepileptic drugs (ASMs) the son received, and whether these ASMs provided adequate seizure control.

In summary, before claiming that RNF213 variants are associated with SLE, concordant SLLs should be documented.

Declarations
Ethical Approval: Not applicable.

Consent to Participation: Not applicable.

Consent for Publication: Not applicable.

Funding: None received.

Availability of Data and Material: All data are available from the corresponding author.

Completing Interests: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contribution: JF was responsible for the design and conception, discussed available data with coauthors, wrote the first draft, and gave final approval. xx: contributed to literature search, discussion, correction, and final approval.

Acknowledgements: None.

Keywords: Leigh-Like Syndrome, RNF213, Stroke-Like Episode, Chorea, Dementia

References
1. Bovenzi R, Severino M, Nichols J, Shen F, Keller Sarmiento IJ, Bustos BI, *et al*. A STOP-Gain RNF213 Variant Causes Chorea, Stroke-Like Episodes, and Leigh Syndrome-Like Encephalopathy. Mov Disord, Sep 26, 2025. Doi: 10.1002/mds.70077
2. Finsterer J. Characteristics of stroke-like lesions on cerebral imaging. Ideggyogy Sz, Jan 30, 2023; 76(1-2):5-10. English. Doi: 10.18071/isz.76.0005
3. Liu F, Ruan W, Wang Y, Lan X. Simultaneous 18F-FDG PET/MRI Assists Diagnosis of a Rare Disease, MELAS. Clin Nucl Med, Jan 2019; 44(1):81-82. Doi: 10.1097/RLU.0000000000002344
4. Murakami K, Sakamoto K, Ishiguchi H, Ito H. Mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes diagnosed after metformin-triggered stroke-like episodes. J Stroke Cerebrovasc Dis, May 2023; 32(5):107080. Doi: 10.1016/j.jstrokecerebrovasdis.2023.107080. Epub Mar 16, 2023.
5. Shibao S, Otaduy MCG, Kok F, Leite CC. Does MRS Lactate Peak Correlate with Lactate in the CSF and Blood? J Pediatr Neuroradiol. 2015; 4:1-6.