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【 LETTERS TO THE EDITOR 】

Reply to the Letter "Reversible Vasoconstriction Syndrome is a Complication of SARS-CoV-2 Infection/Vaccination Rather Than That of Leigh Syndrome"

Key words: Leigh syndrome, Reversible vasoconstriction syndrome

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The Authors Reply We thank Drs. Josef Finsterer and Fulvio Scorza for the knowledgeable and constructive comments (1). We would like to respond to the questions and suggestions.

1. Heteroplasmic rates of the mitochondrial DNA variant

As documented in the Case Report section, we revealed the homoplasmic state of m.9176 T>C substitution in all samples. Furthermore, we agree that the status in the maternal line should be checked, since understanding the derivation of the homoplastic state is crucial. Unfortunately, we were unable to explore this point because consent to a genetic analysis with a detailed clinical investigation was not obtained from the family.

2. Radiological resolution findings

The initial lesion had clearly diminished in size, whereas the residual lesion showed a higher intensity than it had previously. Signal intensity does not have an absolute value, and brain lesions with tissue damage can remain on magnetic resonance imaging. The lesion did not match the vascular supply, so an RCVS mechanism was not considered a plausible explanation.

3. SARS-CoV-2 infection/vaccination status

At admission, polymerase chain reaction using a nasopharyngeal swab sample was negative. Furthermore, there were no symptoms compatible with SARS-CoV-2 infection and no sick contacts. In addition, considering the SARS-CoV-2 vaccination supply in Japan, the patient would not have been vaccinated yet, although this could not be confirmed clearly using a certificate of vaccination.

4. Lactate level in the cerebrospinal fluid (CSF)

As indicated, we agree that lactate elevation in the CSF would support the magnetic resonance spectroscopy findings. Unfortunately, we were unable to confirm this point afterwards because of insufficient amounts of CSF sample available. Furthermore, whether or not the lactate level in the CSF is a prognostic factor of disease severity in Leigh syndrome is controversial (2).

5. The differential diagnosis

We were able to exclude other diseases, such as hyperthyroidism, anemia, pulmonary disease, hypopigmentation, and acidosis. The data showed low T3 syndrome and a mildly elevated Troponin-I level (Troponin-I 0.13 [0-0.04] ng/mL). The D-dimer and hemoglobin levels were normal. There is no family history of cardiomyopathy in the mother's line.

6. Disease concept of Leigh syndrome

We completely agree that Leigh syndrome is no longer a pediatric disease (3, 4). However, Leigh syndrome has been described as a pediatric disease in the history of this disease entity (5). We hope that more cases including molecular genetic investigations will be accumulated to help clarify the disease concept of Leigh syndrome.

The authors state that they have no Conflict of Interest (COI).

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References

1. Ohyama-Tamagake A, Kaneko K, Itami R, et al. Adult-onset Leigh

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Syndrome with a m.9176 T>C Mutation Manifested as Reversible Cerebral Vasoconstriction Syndrome. Intern Med 2022.
2. Lim AZ, Ng YS, Blain A, et al. Natural History of Leigh Syndrome: A Study of Disease Burden and Progression. Ann Neurol **91**: 117-130, 2022.
3. Ogawa E, Fushimi T, Ogawa-Tominaga M, et al. Mortality of Japanese patients with Leigh syndrome: Effects of age at onset and genetic diagnosis. J Inherit Metab Dis **43**: 819-826, 2020.
4. Finsterer J. Leigh and Leigh-like syndrome in children and adults. Pediatr Neurol **39**: 223-235, 2008.
5. Leigh D. Subacute necrotizing encephalomyelopathy in an infant. J Neurol Neurosurg Psychiatry **14**: 216-221, 1951.