

Worsening of Leigh syndrome or Guillain-Barre syndrome after SARS-CoV-2 Vaccination

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Letter to the Editor

The article by Behzadi et al. presents a compelling case involving a 6-year-old girl diagnosed with diabetes. Subsequent evaluations identified multisystem Leigh syndrome, attributed to an mtDNA variant, characterized by diabetes, short stature, hypothyroidism, neuropathy, and psoriasis. Notably, the patient's clinical condition experienced an exacerbation following SARS-CoV-2 vaccination (SC2V) (1). The patient benefited from intravenous immunoglobulins (IVIG) and a mitochondrial cocktail (1). While the study provides valuable insights, certain aspects warrant further clarification to resolve existing ambiguities.

An initial point concerns the diagnostic classification of Leigh syndrome in this case. (1). Leigh syndrome is characterized by a multifunctional cerebral disorder and typical symmetric lesions in the basal ganglia, thalami, or brainstem, including the cerebellum (2). Since the cerebral lesions in the index case were described as being localized predominantly in the frontal white matter, Leigh syndrome cannot be diagnosed. Despite the mention of "Figure 1" in the case description, no magnetic resonance imaging (MRI) image was presented (1).

The second point concerns that the diagnosis of Guillain-Barré syndrome (GBS) is not sufficiently documented. GBS is most commonly diagnosed according to the Brighton or Ashbury criteria, requiring

cerebrospinal fluid (CSF) and nerve conduction velocity (NCS) studies (3). Clarification is required regarding the presence of cyto-albuminque dissociation in the CSF, as well as the findings of NCS, specifically concerning prolonged F-wave latencies or absent F-wave responses. Furthermore, it is essential to specify whether the diagnosis was AIDP or AMAN/AMSAN. Information regarding potential thickening of the lumbosacral nerve roots, or any enhancement observed following contrast administration, should also be provided (4). A strong argument against GBS arises because the NCS results were reported as normal (1). How could the authors exclude that paraparesis was a phenotypic manifestation of the mitochondrial disorder (MID) and not GBS?

Third, the effect of IVIG and the mitochondrial cocktail has not been reported, and no long-term follow-up has been conducted (1). Since MIDs typically progress over time, we should know whether the disease remained stable, progressed, or regressed. In particular, we should know whether IVIG resolved paraparesis or other symptoms of GBS.

The fourth issue concerns that the heteroplasmy rates of the mtDNA variant have not been reported (1). Knowledge of heteroplasmy rates is crucial for assessing the phenotype, its course, and the outcome of the disease. Since these variables also depend on mtDNA copy number, haplotype, and mutations in core genes, it would be useful to know these parameters and

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whether exome sequencing (WES) has detected a pathogenic variant in any of the core genes known to cause MID.

The fifth issue concerns first-degree relatives, specifically the mother, who have not been prospectively screened for the causative mtDNA variant or for subclinical involvement or mild clinical manifestations of MID (1). MtDNA variants are passed from mother to offspring in 75% of cases (5), suggesting that the mtDNA variant found in the index patient was most likely inherited from the mother and did not arise *de novo*. Healthy first-degree relatives should be prospectively screened for the mutation and for subclinical disease.

The sixth issue relates to the fact that the exact mutation was not reported (1). Knowledge of the mutation is crucial for assessing whether the variant was indeed causative and responsible for the phenotype. Knowledge of the exact mutation is also helpful for family screening for the mutation.

The seventh issue relates to the patient having a seizure; however, it was not reported whether she was also diagnosed with epilepsy. Knowledge of the seizure and epilepsy classification according to the ILAE is

crucial to assess whether antiseizure medication (ASM) is indicated and which type of ASM is most appropriate.

The last issue relates to the discrepancy between the patient's age stated in the case report (6 years) and the discussion (8 years) (1). This discrepancy should be resolved.

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None.

Authors' Contribution

Josef Finsterer was responsible for the design and conception, discussed available data with coauthors, wrote the first draft, and gave final approval. Sinda Zarrouk contributed to the literature search, discussion, correction, and final approval

Conflict of Interest

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.

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