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Letter to the Editor

Exclusive affection of the brain in m.4450G>A carriers rather suggests Leigh syndrome than MELAS

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Letter to the Editor

With interest we read the article by Kuwajima et al. about a 12yo female with MELAS due to the mtDNA variant m.4450G>A in the tRNA(Met) gene [1]. The study raises concerns.

We do not agree with the diagnosis of MELAS. MELAS is a multisystem disease not only involving the brain, but also the eyes, ears, endocrine organs, heart, gastrointestines, and potentially other organs [2]. Due to the mono-organ phenotype and the bilateral basal ganglia lesions on MRI at age 12y, the patient should be rather classified as late-onset Leigh-syndrome than MELAS. Presence of a stroke-like lesion (SLL) on MRI does not exclude Leigh-syndrome, as cases with Leigh-syndrome and SLLs have been reported [3].

Another shortcoming is that ADC and PWI sequences were not provided. SLLs on MRI, the morphological equivalent of a stroke-like episode (SLE) show up as hyperintensities on DWI and ADC, suggesting a vasogenic edema [4]. Additionally, there is hyperperfusion on PWI in the acute stage [4].

A further shortcoming is that the antiepileptic drugs (AEDs), which were presumably given from age 8y after the cluster of tonic-clonic seizures, was not mentioned [1]. From some AEDs it is well-known that they are mitochondrion-toxic (valproic acid, carbamazepine, phenytoin, phenobarbital) and that they potentially worsen the phenotype [5]. Is progression of the phenotype between ages 8-11y attributable to administration of mitochondrion-toxic AEDs?

Heteroplasmy rates of 20, 38, 59, 41, 27, and 35% respectively in blood, skin, urinary sediment, hair, saliva, and nail samples are low [1]. Are low heteroplasmy rates due to the fact that the investigated tissues were not affected or that the variant was not pathogenic? Pathogenicity should be confirmed by cybrid and single-fiber studies. Lastly, we should be informed if the mtDNA variant occurred spontaneously or was inherited from the mother.

Overall, this interesting case report could be more meaningful if the above mentioned concerns would be addressed.

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