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Letter to the Editor

Diagnose MELAS if its Diagnostic Criteria are Met and a Pathogenic Genetic Variant is Documented

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Letter to the Editor

We read with interest the article by Mutyala *et al*. on a 56-year-old male with hypoacusis since his 20s and arterial hypertension who developed visual field defects due to a stroke-like lesion (SLL) on MRI, lactic acidosis, increased pyruvate, increased alanine, and biochemical abnormalities [1]. He was diagnosed with mitochondrial encephalopathy lactic acidosis, and stroke-like episodes (MELAS) syndrome and received coenzyme-Q and B-vitamins [1]. The study is interesting, but some points should be discussed.

The first point is that the diagnosis MELAS was not genetically confirmed [1]. MELS is due ot the m.3243A>G variant in about 80% of cases, but other mtDNA mutation sand mutation sin POLG1 can also be responsible for the syndrome. According to which criteria was MELAS diagnosed in the index patient? Most commonly, MELAs is diagnosed according to the Hirano or Japanese criteria [2, 3]. According to the Japanese criteria MELAS is diagnosed when there are signs of encephalopathy associated with dementia or epilepsy, stroke-like episodes (SLEs) in early life, and biochemical evidence of mitochondrial dysfunction, such as acidosis and the presence of ragged-red fibres (RRF) on muscle biopsy [2]. According to the Hirano criteria MELAS is diagnosed when SLEs occur before age 40, and seizures or dementia, lactic acidosis or ragged-red fibres, normal early development, recurrent headache, or recurrent vomiting are present [3]. Based on these considerations, the index patient should not be diagnosed with MELAS syndrome.

The second point is that the SLL was documented only by T2/FLAIR and DWI modalities. SLLs are typically not only hyperintens on T2/FLAIR and DWI, but also on perfusion-weighted imaging (PWI), hypointens on oxygen-extraction fraction (OEF) MRI, and show hypometabolism on FDG-PET [4]. SLLs follow a dynamic course with an expansion in size unitl a nadir to regress thereafter and end up as either cyst, white matter lesion, atrophy, toenail song or laminar cortical necrosis or disappearance without a remaining lesion. Typically, SLLs are not confined to a vascular territory.

The third point is that the long-term outcome has not been reported [1]. Did the SLL resolve completely, or did it evolve into a permanent lesion? Did the patient benefit from coenzyme-Q and B-vitamins? We should know if he developed typical phenotypic features in addition to those reported.

Overall, MELAS should not be diagnosed if the Hirano or Japanese criteria are not met or if no pathogenic mutation associated with MELAS is documented. In addition, stroke-like episodes should be diagnosed only if corresponding SLLs on multimodal MRI are documented and if there is cerebral lactic acidosis.

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