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Letter to the Editor

Early manifestations of MELAS may be easily overlooked

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In a recent article Tetsuka et al. described a 58yo Japanese female with presumed late-onset mitochondrial disorder (MID) in whom stroke-like episodes (SLEs) were initially misinterpreted as ischemic stroke [1]. We have the following comments and concerns. Late onset or adult onset is not unusual and has been previously reported [2, 3, 4, 5]. Anyhow, the current patient is reported to have had short stature, which most likely was present already in infancy or childhood. Since short stature is a frequent endocrine manifestation of MIDs, clinical onset of MELAS was long before the first SLE**.** Furthermore, diabetes was detected at age 41y and was possibly present already before antidiabetic treatment was applied. Increased muscle tone, as described in the index case, can be due to a rigor or spasticity. Did the patient present with an extrapyramidal syndrome or did she have quadruspasticity? Parkinsonism is not unusual in MIDs and can occur in combination with spasticity or without. Did the patient present with both, rigor and spasticity? Was there cogwheel rigidity? MELAS was diagnosed upon the clinical presentation and the genetic investigations, revealing the common m.3243A>G transition [1]. Which tissue was investigated to establish the genetic diagnosis? Lymphocytes or muscle ? Which was the heteroplasmy rate of the mutation? Was it different between different tissues, such as hair follicles, buccal cells, skin fibroblasts, urinary epithelial cells, lymphocytes, or muscle? The family history is reported to have been positive for hearing loss (mother) and renal failure (sister) [1]. Were the son and the daughter of the index case also clinically or subclinically affected? Did any of the first-degree relative also carry the m.3243A>G variant? Nitric-oxide (NO) precursors are said to be beneficial in the acute stage of a SLE [6].

Did the patient receive L-arginine or L-citrulline during the occurrence of her SLEs? NO-precursors are given since it is assumed that SLEs are triggered by a shortage of NO [7]. It is reported that the patient developed tonic clonic seizures by age 68y for which phos-phenytoin was given in the acute stage [1]. Which was the long-term antiepileptic drug (AED) applied to prevent further seizure activity? Did the patient receive phenytoin also orally? From phenytoin it is well known that it can be mitochondrion-toxic [8]. Did seizure frequency resolve after establishing the AED treatment? Was the family history positive for epilepsy in any of the first-degree relatives? Which antibiotic was given for the urinary infection prior to the first tonic clonic seizure? Was it penicillin or a gyrase-inhibitor, or another agent known to trigger seizures? Which was the cause of the flexion contracture on the left upper limb? Was it due to a previous trauma? Was it due to spasticity or muscle weakness? Which was the reason that the patient received a percutaneous endoscopic gastrosotomy (PEG)? Overall, this interesting case could be more meaningful if more clinical, instrumental, and genetic data would be provided. Onset of MELAS remains early if all aspects of the phenotype are thoroughly considered. Mitochondrial epilepsy should not be treated by potentially mitochondrion-toxic AEDs.

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