

Stroke-Like Lesions Differ from Stroke in Terms of Etiology, Pathophysiology, and Clinical Presentation

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Letter to the Editor

In a retrospective study of ten patients with mitochondrial encephalopathy, lactic acidosis, and stroke-like episode (MELAS) syndrome, Naftali et al. aimed to establish a clinical score (Stroke-Like Episode (SLE) Early Clinical Score (SLEECS)) upon which MELAS patients can be identified before they ever develop SLE [1]. Twenty-three SLEs were analysed and the sensitivity and specificity of the SLEECS was 80 and 100% respectively [1]. The study is excellent but a number of considerations are in order.

A limitation of the study is the attempt to diagnose Mitochondrial Disorders (MIDs) solely on the basis of the phenotypic spectrum. It is well known that the diagnosis of MIDs with or without SLE must be established through a histological, immune-histological, biochemical and genetic approach. The approach of Naftali et al. is also not expedient because MIDs are phenotypically heterogeneous, especially MIDs due to variants in mitochondrial DNA (mtDNA). Accordingly, MELAS is most easily diagnosed using the Hirano criteria [2] or the Japanese criteria [3].

We also disagree with the statement that SLEs can easily be misdiagnosed as ischemic stroke [1]. Because SLEs have a typical imaging correlate, the Stroke-Like Lesion (SLL) [4], ischemic stroke should not be confused with SLE. Multimodal MRI, Magnetic Resonance Spectroscopy (MRS), Magnetic Resonance Angiography (MRA) and eventually Fluor-Deoxy Glucose-Positron Emission Tomography (FDG-PET) should be used to differentiate between the two entities. On multimodal MRI, SLLs typically present as hyperintensity on T2, FLAIR, DWI, and perfusion-weighted imaging (PWI) [4].

SLLs are hypointense on T1 and oxygen-extraction fraction (OEF)-MRI. MRS of a cerebral lesion typically shows a reduced N-acetyl aspartate (NAA) peak and a lactate peak. MRA often shows dilatation of the arteries supplying the area of the SLL [4]. In FDG-PET, SLL typically manifests with hypometabolism. In addition to these features, SLLs have a dynamic course with initial expansion of the lesion and regression after reaching a nadir. SLLs end as a white matter lesion, focal atro-

phy, cyst formation, laminar cortical necrosis, or toenail sign. In some cases, SLLs disappear without residual lesion.

Unless the SLE is the first phenotypic manifestation of a MID, MIDs potentially manifesting with SLE are usually evident long before onset of the first SLE. This is because MIDs usually present with a multisystem phenotype at the onset of the disease or become a multisystem disease as the disease progresses. Due to the multisystem character and the typical phenotypic pattern, MIDs can be easily recognised early on (syndromic MID). In the absence of a typical phenotypic pattern, it may be difficult to consider a MID prior to the onset of a SLE. The phenotypic spectrum of MELAS is broader than reported in the index study [1]. MELAS can manifest not only with seizures, hearing impairment, lactic acidosis, and SLEs, but also with short stature, facial and extra-facial dysmorphism, cognitive impairment, dementia, psychosis, migraine, ophthalmoparesis, ptosis, hypothyroidism, hepatopathy, vomiting, diarrhoea, constipation, hypogonadism, renal insufficiency, or anemia. There is also evidence that the frequency of neoplasms is increased in MELAS [5]. The organs most commonly affected in MELAS are the brain, eyes, ears, endocrine organs, heart, guts, kidneys, bone marrow, and skin. In general, however, all cell types can be affected.

In summary, the diagnosis of MELAS syndrome requires not only the presence of an appropriate phenotype, but also documentation of evidence from histological, immune-histological, biochemical, and genetic data. In addition to examining an index case, all of its first-degree relatives must be prospectively examined to ultimately document the heritability of the underlying genetic defect.

Declarations

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Consent for publication: was obtained from the patient

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Code availability: not applicable

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