LETTER TO THE EDITOR

Stroke-like episode of the optic nerve

Dear Editor:

We read with interest the article by Mack et al. about a 50-year-old male with MELAS syndrome attributable to the mtDNA variant m.3243A>G who developed transient optic disc edema being attributed to the underlying metabolic defect after exclusion of various differential diagnoses.[1] We have the following comments and concerns.

The mutation load of 13% in blood lymphocytes of the index case is fairly low[1] and hardly causative for the clinical manifestations. It thus would be interesting to know whether heteroplasmy rates were higher in hair follicles, muscle cells, buccal mucosa cells, skin fibroblasts, or urinary epithelial cells than in blood lymphocytes to confirm the pathogenicity of the described variant.

MELAS patients may manifest not only with ophthalmologic or neurologic abnormalities, but also with cardiac, renal, gastrointestinal, hematological, or dermatological disease. Thus, it would be interesting to know whether the index patient or his first-degree relatives were prospectively investigated for mitochondrial multisystem disease (MIMODS). Of particular interest in the index patient would be to know the results of the cardiac magnetic resonance imaging (MRI), magnetic resonance spectroscopy, electroencephalography (EEG), visual evoked potentials, and pituitary gland investigations.

Ocular involvement in mitochondrial disorders MIDs may include not only optic atrophy and retinal nerve fibre layer defects, but also ptosis, progressive external ophthalmoplegia, pigmentary retinopathy, cataract, or abnormalities of the cornea, ciliary body, intraocular pressure, or the choroidea.[2]

Because mitochondrial enecephalopathy, lactic acidosis, and stroke-like episodes MELAS may be also associated with vasoconstriction syndrome, it is conceivable that optic disc edema was caused by transient spasms of arterioles supplying the optic disc. Another pathomechanism not considered could be an increase in number or size of the mitochondria in epithelial cells resulting in swelling of endothelial cells, consecutively narrowing the vessel diameter, resulting in ischemia and breakdown of cell membrane functions and thus optic disc edema. A similar pathomechanism was suggested to explain the development of stroke-like lesions (SLLs), the morphological equivalent of a stroke-like episode (SLE) on MRI. This is why nitric oxide (NO) precursors have been proposed for the treatment of SLLs.

SLEs are frequently associated with seizures or EEG abnormalities.[3] Some experts even regard seizures, even in the absence of clinical manifestations, as a putative trigger for the development of an SLE.[3] We should be informed about the results of EEG recordings during the episode with optic nerve edema.

SLEs were repeatedly reported to respond not only to NO precursors but also to antioxidants or antiepileptic drugs (AEDs). Thus, it would be interesting to know whether any of these compounds was applied during the presence of the optic disc edema. Particularly and non−mitochondrion-toxic AEDs have been reported to exhibit a beneficial effect on SLLs.

Because the authors considered venous thrombosis as a differential diagnosis, it would be interesting to know whether the D-dimer was elevated at the onset of the disc edema and whether magnetic resonance venography was indicative of sinus venous thrombosis. We should also be informed whether the index patient carried the Leyden mutation in a homozygous or heterozygous form.

The patient is reported to have had headache 4 weeks before presentation.[1] However, findings of cerebrospinal fluid investigations were normal, the intracerebral pressure was not increased, and the intraocular pressure was within normal limits as well. Thus, it should be discussed whether headache was caused by status migrainosus, hypertension of the neck muscles, arterial hypertension, infection of the sinuses, or a sinus venous thrombosis. SLEs frequently go along with different types of headache.[4]

A shortcoming of the report is that the current medication of the index case was not provided and that no extensive family history was taken. Because the m.3243A>G variant is maternally inherited in 75% of the cases,[5] it should be reported whether the mother of the index case carried the tRNA(Leu) as well or whether the mutation had occurred sporadically. Clinical affection of the index patient's sister suggested that the mtDNA variant was rather inherited than sporadic.

In summary, this case could be more meaningful if the index case and first-degree relatives would have been systematically investigated for multisystem clinical manifestations of an MID, if first-degree relatives would have been investigated for the mtDNA variant, and if possible therapeutic interventions would have been more extensively discussed. To interpret the optic disc edema as SLE of the optic nerve is conceivable but requires further investigations.

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