Letter to Editor

Genetic background and phenotypic heterogeneity of MELAS and maternally inherited diabetes and deafness

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With interest we read the article by Li et al. about a family with mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS) syndrome [1]. We have the following comments and concerns.

The m.3243A>G mtDNA mutation may not only cause MELAS and maternally inherited deafness and diabetes (MIDD) but also MELAS/myoclonic epilepsy and ragged red fibers (MERRF) overlap syndrome, chronic progressive external ophthalmoplegia (CPEO), Kearns-Sayre syndrome (KSS), Leigh syndrome, floppy infant syndrome, non-syndromic enteromyopathy, or other non-syndromic mitochondrial disorders (MIDs) [2].

MIDD is not only characterised by insulin-deficient diabetes and hearing loss but may also include epilepsy, cerebellar ataxia, renal insufficiency not related to the diabetes, focal segmental glomerulosclerosis, hyporeninemic hypaldosteronism, maculopathy, retinopathy, cognitive impairment, cataract, hypothyroidism, renal insufficiency, stroke, intestinal pseudoobstruction, WPW-syndrome, myopathy, basal ganglia calcification, dilated cardiomyopathy, short stature, pancreatitis, hypoparathyroidism, Parkinson syndrome, Addison disease, and cerebral atrophy (Table 1).

Though MIDD is due to the m.3243A>G mtDNA mutation in 85% of the cases [3], it may be also due to the m.9276G>C mutation in the COXIII gene, the m.1555A>G in the 12S rRNA gene, the m.3308T>C mutation in the ND1 gene, the insertion m.14535_14536C or CC, the m.14709T>G mutation, the m.14709T>C mutation, the 8381 mtDNA mutation, or due to a mtDNA deletion (Table 1).

The index case is reported as having headache in addition to seizures, nausea, and vomiting [1]. Which type of headache did the authors diagnose? Did the patient report a history of migraine or cluster headache, headache types occasionally associated with MID [4, 5]. Was nausea and vomiting independent of headache or always associated with it?

It is reported that MELAS in the presented patient manifested with epilepsy [1]. Which type of seizures did the patient develop, which was the frequency of seizures, which type of antiepileptic treatment did the patient receive, and how effective was the seizure control? Since seizures can be associated with stroke-like episodes and respond to L-arginine, it would be interesting to know if seizures in the described patient were associated with stroke-like episodes each time and if she received L-arginine? Did the patient ever experience an epileptic state?

It would be also interesting to learn more about the treatment and course of diabetes. Which were the HbA1c values? Which secondary complications of diabetes did the patient develop?
Did the patient ever receive a biguanide and was ever lactacidosis diagnosed?

Overall, the didactic merit of this interesting case could be enhanced by providing and discussing essential lacking information. Patients with MIDD or MELAS are clinically and genetically more heterogeneous than anticipated.

Disclosure of conflict of interest

None.

References

Genetics of noncompaction


