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[LETTERS TO THE EDITOR]

Gastrointestinal Involvement in m.3243A>G-associated MELAS

Key words: gastro-intestinal, mtDNA, mitochondrial, encephalopathy, autonomic system, neuropathy

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To the Editor We read with interest the article by Suzuki et al. about three patients harbouring the m.3243A>G mutation manifesting as mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome and intestinal pseudo-obstruction (Table) (1). We have several comments and concerns.

Mitochondrial disorders (MIDs) may accompany neuropathy of the peripheral nerves, including affection of the autonomic fibers (2). As such, intestinal pseudo-obstruction can occur due to autonomic neuropathy. Were there indications for autonomic neuropathy in any of your cases, such as in-

creased sensitivity to light, dry mouth, dry eyes, orthostasis, abnormal heart rate variability, obstipation, urinary dysfunction, impotence, or dry skin? Were instrumental investigations carried out to search for autonomic neuropathy?

The hot cross bun sign is a non-specific morphological feature on magnetic resonance imaging (MRI) and has not only been described in multisystem atrophy-C, spinocerebellar ataxia-2 (SCA2) and SCA3 but also in Alzheimer's disease, natalizumab-induced, progressive multifocal leucoencephalopathy, neurosarcoidosis, late-onset SCA11, single large-scale mtDNA deletions, paraneoplastic syndromes, SCA34, leptomenigeal metastasis, SCA23, HIV-related multifocal leucoencephalopathy, brainstem stroke, familial amyotrophic lateral sclerosis, cerebrotendineous xanthomatosis, Parkinson syndrome, and Creutzfeldt-Jacob disease.

Atrophy of the cerebellum or brainstem is a frequent finding in MIDs and may even be the dominant feature of the phenotype (3). Cerebellar atrophy has been reported in Leigh syndrome, Kearns-Sayre syndrome, Myoclonus epilepsy associated with ragged-red fibers (MERRF) syndrome,

Table. A Comparison of the Three Described Patients.

	P1	P2	P3
Sex	f	f	f
Height (cm)	140	np	147.5
Weight (kg)	25.1	np	47.8
Age at onset (y)	10	12	39
First manifestation	SLE	SLE	Diabetes
Presentation	vomiting, headache, cerebral atrophy, multiple strokes	multiple strokes, headache, vomiting, seizures,	staggering gait, bradykinesia, rigidity, forced crying/laughing,
	blurring, seizures, abdominal pain, bloating	bloating	abdominal pain, vomiting, dystonia
	hypoaacusis, myopathy		muscle weakness, gait ataxia, neuropathy, increased reflexes, cerebral atrophy, hot cross bun sign, urinary retention
NOO involved	4	2	5
Creatin kinase (U/L)	105	np	16
Lactate (mg/dL)	14.7	np	19.4
Degree of progression	np	np	np
Age at death (y)	23	22	54
Cause of death	Aspiration pneumonia	Renal failure	Aspiration pneumonia
Genetic cause	m.3243A>G	m.3243A>G	m.3243A>G
Sampled tissue	blood	blood	blood
Heteroplasmy rate	np	np	np

NOO: number of organs, SLE: stroke-like episode, np: not provided

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external ophthalmoplegia, Neuropathy, Ataxia, and Retinitis Pigmentosa (NARP) syndrome, Leukoencephalopathy and Brainstem and Spinal cord involvement and Lactate elevation (LBSL), ponto-cerebellar hypoplasia-6, and non-specific mitochondrial multiorgan disorder syndrome (MIMODS). The causes of phenotypic heterogeneity within or between families are versatile and include a variable heteroplasmy rate in different individuals (4) as well as haplotype, mtDNA-polymorphisms, and nuclear mutations. Work-up for phenotypic heterogeneity should also include determination of the heteroplasmy rate in different affected and non-affected tissues, such as hair follicles, buccal mucosa, skin fibroblasts, muscle cells, and urine bladder cells.

Gastrointestinal compromise is a frequent manifestation in MIDs and may not only include pseudoobstruction but also poor appetite, gastroesophageal sphincter dysfunction, constipation, dysphagia, vomiting, gastroparesis, diarrhoea, pancreatitis, and hepatopathy (5). Rare gastrointestinal manifestations of MIDs include dry mouth, paradontosis, tracheoesophageal fistula, stenosis of the duodeno-jejunal junction, atresia or imperforate anus, liver cysts, pancreas lipomatosis, pancreatic cysts, congenital stenosis or obstruction of the gastrointestinal tract, recurrent bowel perforations with intra-abdominal abscesses, postprandial abdominal pain, diverticulosis, and pneumatosis coli (5). Were any of these manifestations present in any of the patients?

Overall, this interesting case study would profit from the determination of the heteroplasmy rates in different tissues,

prospective investigations for MIMODS, investigations for autonomic neuropathy, and from a more extensive family history. Gastrointestinal abnormalities should be regarded as typical manifestations of MIMODS.

The authors state that they have no Conflict of Interest (COI).

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References

1. Suzuki J, Iwata M, Moriyoshi H, Nishida S, Yasuda T, Ito Y. Familial pernicious chronic intestinal pseudo-obstruction with a mitochondrial DNA A3243G mutation. *Intern Med* **56**: 1089-1093, 2017.
2. Mancuso M, Orsucci D, Angelini C, et al. "Mitochondrial neuropathies": A survey from the large cohort of the Italian Network. *Neuromuscul Disord* **26**: 272-276, 2016.
3. Rankin J, Brown R, Dobyns WB, et al. Pontocerebellar hypoplasia type 6: A British case with PEHO-like features. *Am J Med Genet A* **152A**: 2079-2084, 2010.
4. Mancuso M, Orsucci D, Angelini C, et al. The m.3243A>G mitochondrial DNA mutation and related phenotypes. A matter of gender? *J Neurol* **261**: 504-510, 2014.
5. Finsterer J, Frank M. Gastrointestinal manifestations of mitochondrial disorders: a systematic review. *Therap Adv Gastroenterol* **10**: 142-154, 2017.

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