pISSN 1738-6586 / eISSN 2005-5013 / J Clin Neurol 2022;18(5):597-598 / https://doi.org/10.3988/jcn.2022.18.5.597

Comments on "A Case of MELAS With the m.3243A>G Variant of the MT-TL1 Gene Mimicking Acute Intermittent Porphyria"

Josef Finsterer

Neurology & Neurophysiology Center, Vienna, Austria

Dear Editor,

We read with interest the article by Cai et al.[1] about a 23-year-old male with mitochondrial encephalopathy, lactic acidosis, and stroke-like episode (MELAS) syndrome due to the m.3243A>G variant. The patient manifested phenotypically with epilepsy, quadriparesis, wasting, generalized hypotonia, bilateral facial palsy, dysarthria, dysphagia, anemia, lactic acidosis, polyneuropathy, and abdominal pain.[1] The patient was initially suspected as having acute intermittent porphyria (AIP), but the 4.5-h sunlight test produced normal findings.[1] The study is attractive, but it raises concerns that should be discussed.

Gastrointestinal abnormalities are a well-known phenotypic feature of MELAS.[2,3] The signs and symptoms of gastrointestinal compromise in MELAS can include poor appetite, gastroesophageal sphincter dysfunction, pseudo-obstruction, constipation, bloating, dysphagia, vomiting, gastroparesis, diarrhea, pancreatitis, hepatopathy, dry mouth, periodontitis, tracheoesophageal fistula, stenosis of the duodenojejunal 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.[3]

We disagree with the statement that "there is still little evidence of acute pseudo-obstruction symptoms in m.3243A>G-related mitochondrial disease."[1] Pseudo-obstruction has repeatedly been reported as a manifestation of MELAS[4] and in association with the m.3243A>G variant,[5] which is the most common cause of MELAS. Pseudo-obstruction is even suspected to trigger the development of stroke-like episodes (SLEs), which is the phenotypic hallmark of MELAS.[5]

According to Fig. 1,[1] the patient presented with bilateral ptosis and hypertelorism. Ptosis and hypertelorism have not been reported in AIP, whereas facial dysmorphism, including hypertelorism, is a frequent phenotypic feature of MELAS.[6,7]

Several critical pieces of information are missing. The first is the result of biochemical investigations of the muscle homogenate to assess which of the respiratory complexes had reduced activity. The second is the heteroplasmy rate of the m.3243A>G variant in various affected tissues. Since the heteroplasmy rate is one of the phenotype determinants, it is crucial to know their values in the most affected tissues, particularly muscles. The third is whether the polyneuropathy was of the axonal or demyelinating type. The fourth is an explanation of the multiple enhanced T1-weighted lesions, which were hypointense in susceptibility-weighted imaging. Do these lesions represent intracerebral bleeding, hemorrhagic stroke, or an abortive stroke-like lesion, which is the morphological equivalent of an SLE. The fifth piece of missing information is an explanation of dysarthria and dysphagia.

While the family history was unremarkable, it should be reported if the mother was clini-

Received July 21, 2022
Revised August 9, 2022
Accepted August 9, 2022

Correspondence
Josef Finsterer, MD, PhD
Neurology & Neurophysiology Center, Postfach 20, 1180 Vienna, Austria
Tel +43-1-5861075
Fax +43-1-5861075
E-mail fifigs@yahoo.de

cally and genetically investigated to assess if the variant was transmitted via the maternal line or occurred sporadically.

In summary, the interesting study of Cai et al.[1] has limitations and inconsistencies that call into question the obtained results and their interpretation. Addressing these limitations could further strengthen and reinforce the statements made based on the study. Abdominal manifestations are a common feature of MELAS, and in addition with the other features, suggest a mitochondrial rather than a lysosomal disorder.

Ethics Statement

Not applicable

Availability of Data and Material

Data sharing not applicable to this article as no datasets were generated or analyzed during the study.

ORCID iD

Josef Finsterer https://orcid.org/0000-0003-2839-7305

Conflicts of Interest

The author has no potential conflicts of interest to disclose.

Funding Statement

None

REFERENCES

1. Cai W, Yang S, Han X. A case of MELAS with the m.3243A>G variant of the MT-TL1 gene mimicking acute intermittent porphyria. *J Clin Neurol* 2022;18:361-363.
2. Suzuki J, Iwata M, Moriyoshi H, Nishida S, Yasuda T, Ito Y. Gastro-intestinal involvement in m.3243A>G-associated mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes. *Intern Med* 2018;57:771.
3. Finsterer J, Zarrouk-Mahjoub S. Gastrointestinal involvement in m.3243A>G-associated MELAS. *Intern Med* 2018;57:769-770.
4. Fernández Forcelledo JL, López Fernández E, Misiego Peral MM. Chronic intestinal pseudo-obstruction in MELAS. *Rev Esp Enferm Dig* 2021;113:152-153.
5. Gagliardi D, Mauri E, Magri F, Velardo D, Meneri M, Abati E, et al. Can intestinal pseudo-obstruction drive recurrent stroke-like episodes in late-onset MELAS syndrome? A case report and review of the literature. *Front Neurol* 2019;10:38.
6. Pronicki M, Sykut-Cegielska J, Mierzewska H, Tońska K, Karczmarewicz E, Iwanicka K, et al. Diversity of clinical symptoms in A3243G mitochondrial DNA mutation (MELAS syndrome mutation). *Med Sci Monit* 2002;8:CR767-773.
7. Dvorakova V, Kolarova H, Magner M, Tesarova M, Hansikova H, Zeman J, et al. The phenotypic spectrum of fifty Czech m.3243A>G carriers. *Mol Genet Metab* 2016;118:288-295.