Acta Diabetologica (2019) 56:1087–1088
https://doi.org/10.1007/s00592-019-01360-3

LETTER TO THE EDITOR

MELAS requires broad clinical and genetic work-up

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Received: 6 April 2019 / Accepted: 3 May 2019 / Published online: 5 June 2019

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With interest, we read the article by Cosentino et al. [1] about a 42-year-old female with MELAS syndrome due to the variant m.3243A>G, who was admitted for newly diagnosed diabetes treated with metformin. After diagnosing, MELAS metformin was replaced by insulin but recurrent hypoglycemia was noted why insulin was replaced by linagliptin [1]. We have the following comments and concerns.

A shortcoming of the study is that no heteroplasmy rates were provided. Since the phenotype can strongly depend on the mutation load of an mtDNA variant, we should be informed about the heteroplasmy rates not only in the blood lymphocytes, but also in hair follicles, buccal mucosa cells, skin fibroblasts, muscle cells, and urinary epithelial cells. Knowing heteroplasmy rates from different tissues is crucial as organs may be involved with varying severities.

It is unclear in which indication steroids were applied. From steroids, it is well known that they may cause severe side effects in some MID patients, whereas in others it may be well tolerated or even beneficial [2]. Thus, we should know in which indication steroids were administered and if diabetes deteriorated or if other side effects occurred.

Since the patient was initially treated with metformin and metformin potentially elevates serum lactate, we should be informed if serum lactate was elevated before starting metformin, after starting metformin, and after withdrawal of the compound.

Since aseptic pancreatitis can be a manifestation of a mitochondrial disorder (MID) [3], we should be informed if the index patient was investigated for pancreatitis, particularly if alpha-amylase and lipase values were elevated in the absence of elevated inflammatory parameters or clinical manifestations of pancreatitis. Imaging of the pancreas in MID patients may show fibrosis, pancreas lipomatosis, or cyst formation [3].

To discriminate the nature of a hyperintense lesion on DWI, it is definitively not necessary to perform a lumbar puncture. What is needed are the ADC maps, a perfusion study (PWI), and the oxygen extraction MRI [4]. If the lesion is also hyperintense on ADC, if there is hyperperfusion, if the oxygen extraction is reduced, if the lesion is not confined to a vascular territory, and if the lesion disappears, then the diagnosis of a stroke-like lesion (SLL) can be made. Furthermore, CSF lactate can be more elegantly determined by MRS [5].

Missing in this report is the family history. Since mtDNA variants are inherited from the mother in 75% of the cases, we should be informed if the mother of the index case exhibited any phenotypic features of MELAS or another mitochondrial syndrome and if she also carried the m.3243A>G variant.

Overall, this interesting case could be more meaningful by providing heteroplasmy rates of the causative variant, explanation why steroids were given, by providing lactate levels, results of imaging studies of the pancreas, by a more extensive description of the multimodal cerebral MRI, and by provision of an extensive family history.

Managed by Massimo Porta.

This comment refers to the article available at https://doi.org/10.1007/s00592-019-01302-z.

Reply to this comment is available at https://doi.org/10.1007/s00592-019-01361-2.

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Author contribution JF was involved in design, literature search, discussion, first draft, critical comments.

Compliance with ethical standards

Conflict of interest The author declares that he has no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from the patient included in the case report.

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