Int. j. adv. multidisc. res. stud. 2023; 3(4):762-763

Received: 24-07-2023
Accepted: 04-08-2023

International Journal of Advanced Multidisciplinary Research and Studies

ISSN: 2583-049X

Letter to the Editor

Steroids Can Be Harmful to Patients with a Mitochondrial Disorder

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We read with interest the article by Ohwada *et al*. on a 40 year-old male with a non-syndromic mitochondrial disorder (MID) due to the variant m.3243A>G [1]. The mtDNA variant manifested phenotypically with hypoacusis, diabetes, cardiomyopathy complicated by heart failure, presumably myopathy, renal insufficiency, and lactic acidosis [1]. After administration of steroids, the patient developed ketoacidosis and required continuous insulin infusion to manage ketoacidosis [1]. Insulin infusion, however was complicated by relapse of lactic acidosis, which resolved not earlier than after a few days [1]. The study is compelling but has limitations that should be discussed.

A limitation of the study is that heteroplasmy rates were not determined in any clinically affected or unaffected tissue. Knowing heteroplasmy rates in clinically affected tissues is critical not only to explain the phenotype, the phenotypic variability, to predict the course of the disease and thus the outcome of the condition, but also for genetic counselling.

A second limitation is that the patient was not clarified for involvement of the skeletal muscle. Knowing whether or not skeletal muscles were affected is crucial as they may be a major source of lactic acid. Therefore, we should know the results of the clinical neurologic exam, whether creatine kinase was elevated, if needle electromyography (EMG) was myogenic, if muscle biopsy was indicative of ragged fibers, ragged-blue fibers, and whether immune-histochemistry and biochemistry showed normal or reduced activity of respiratory chain complexes. Since the patient had muscle weakness and muscle wasting [1], it is quite likely that the skeletal muscles were affected.

A third limitation is that the current medication in addition to the anti-diabetic treatment was not provided. Knowing the current medication is crucial as it may contribute to lactic acidosis. From metformin and other biguanides it is known that they can cause lactic acidosis.

A fourth limitation is that cerebrospinal fluid (CSF) lactate was not reported. Lactate can be also produced in the brain, particular in case of a stroke-like episode (SLE). Therefore, it is essential that we know whether there was cerebral involvement in the disease, particularly if the patient had previous SLEs or epilepsy. In addition to SLE, seizures can be a strong trigger of lactate production due to temporary cerebral hypoxia.

Lactic acidosis can also be triggered by malignancy [2], why it is essential that malignancy is ruled out in the index patient. From steroids it is known that they can be harmful in certain patients with a MID [3]. Even fatalities have been reported after administration of steroids, particularly in patients with Kearns-Sayre syndrome.

In summary, the interesting study has limitations that put the results and their interpretation into perspective. Addressing these issues would strengthen the conclusions and could improve the status of the study. Steroids should be given with caution to patients with a MID, particularly if they have diabetes and require insulin. All causes of lactic acidosis should be considered.

Acknowledgements
Funding Sources and Conflict of Interest: None.

Financial Disclosures for the Previous 12 Months: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author contribution (1. Research project: A. Conception, B. Organization, C. Execution; 2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique; 3. Manuscript: A. Writing of the first draft, B. Review and Critique): author JF: 1A, 1b, 1C, 3A, 3B.

Data Access Statement: All data are available from the corresponding author.

Ethical Compliance Statement: The authors confirm that the approval of an institutional review board or patient consent was not required for this work. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Keywords: MTDNA, Stroke-Like Episode, m.3243A>G, MELAS, Epilepsy

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