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Letter to the Editor: Endocrine Compromise in Mitochondrial Disorders

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With interest we read the article by Al-Gadi *et al.* [1] about a retrospective study on endocrinological abnormalities in patients with a mitochondrial disorder (MID) registered in the North American Mitochondrial Disease Consortium Patient Registry. We have the following comments and concerns about the specificity of the information provided.

Because endocrinological abnormalities in MIDs may not only be primary but also secondary (*e.g.*, due to drugs, like ketoconazole, sulfnonamides, pentamidine, or infections), it would be of value to learn about the drugs that the included patients were taking regularly and about the prevalence of infectious diseases in the cohort.

Likewise, patients with MIDs have an increased risk for development of benign or malign neoplasms [2]. Pituitary adenoma, adenoma of the thyroid gland, and adenoma of the suprarenal gland have been reported in MIDs [2]. Adenoma may or may not go along with endocrinological abnormalities. It would be of great interest to learn how many of the 404 included patients the registry recorded as having a hormone-producing or nonhormone-producing neoplasm or hyperprolactinemia.

Another statistic the authors [1] present relates to polycystic ovary syndrome. This condition is usually associated with menses abnormalities (*e.g.*, amenorrhea, oligomenorrhea) [3], which the authors report separately. This raises the question of whether, in differentiating between PCOS and menses abnormalities, there is overlap of these classes.

In the article, Table 1 [1] mentions adrenal insufficiency in three patients, but Al-Gadi *et al.* did not specify whether it was hypoaldosteronism, hypocorticism, or catecholamine deficiency. All three different types of adrenal insufficiency have been reported in MIDs, and because treatment options are available for adrenal insufficiency, it would be of value to learn which type was found.

Al-Gadi *et al.* [1] provide statistics on the prevalence of hypothyroidism in MIDs. Because hypothyroidism in MIDs is frequently due to Hashimoto thyroiditis, it would be of value to learn how many of the patients with hypothyroidism were thyroperoxidase-antibody or TRAC-antibody positive.

In general, because most of the endocrine abnormalities in MIDs are accessible to treatment, it would have been helpful to learn how many received appropriate substitution and how often it was beneficial.

There are a number of MIDs associated with endocrinological disorders that are due to depletion of the mitochondrial DNA (mtDNA) [4]. It would be of value to learn how many of

Abbreviations: MID, mitochondrial disorder; mtDNA, mitochondrial DNA.

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the 404 included patients had a diagnosis of mitochondrial depletion syndrome, and how many had multiple mtDNA deletions in contrast to a single mtDNA deletion.

Most of the patients were younger than 18 years old [1]. Because pediatric MIDs are more frequently associated with mutations in nuclear DNA genes, it is surprising that only in 39.1% of the cases a nuclear DNA variant was found. Do the authors have an explanation for this discrepancy?

Because most of the MIDs are inherited, it would be of value to learn how often the family history was positive for an MID and, in particular, how often it was positive for endocrine abnormalities.

Specific and nonspecific MIDs are associated with endocrine abnormalities [5]. We wonder in how many of the included patients was the phenotype not attributable to a specific MID?

In summary, this interesting study has several limitations in terms of the details provided, which we hope the authors will be able to address in future publications.

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