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Involvement of the Endocrine System is Common in Mitochondrial Disorders and Requires Long-term Comprehensive Investigations

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Dear Editor,

We read with interest the article by Papatya Çakır et al. (1) on a cross-sectional study of 26 patients with syndromic and non-syndromic mitochondrial disorders (MID). The syndromic MIDs included Leigh syndrome (n = 4), LHON (n = 2), MELAS (n = 2) and KSS (n = 1) (1). In 15 patients, MID was due to a mutation in the nDNA and in 10 patients to a mtDNA mutation (1). Of the 26 patients, 6 had endocrine involvement (1). These included ovarian insufficiency, central adrenal insufficiency, central hypothyroidism, diabetes mellitus and critical illness-related adrenal insufficiency (1). It was concluded that there is a high risk of developing hormonal deficiencies in MID (1). The study is excellent, but some points should be discussed.

The first point is that evaluation for endocrine disease in general, and specifically for endocrine involvement in MIDs, should include cerebral imaging, including the pituitary gland. Since central nervous system involvement is a common feature of MIDs and often manifests with morphologic or functional abnormalities in the hypothalamus or pituitary gland (empty sella, adenoma, or pituitary apoplexy) (2), cerebral imaging with special attention to these structures is essential.

The second point is that MID is usually a progressive disease with multisystem involvement that is either present at the onset of the disease or develops over the course of the disease. Therefore, endocrine involvement is not necessarily detectable in cross-sectional studies, but can only be found in long-term studies, which are preferable to cross-sectional studies. For this reason, it is recommended that MID patients be followed up regularly and prospectively screened for subclinical or mildly manifesting multisystemic disease, including endocrine involvement.

The third point is that MIDs often manifest with lactic acidosis, so we should know how many of the included patients had metabolic acidosis due to lactate overproduction in the muscle, cerebrum, myocardium or endocrine organs. With regard to lactic acidosis, we should know how many patients had elevated lactate not only in the serum but also in the cerebrospinal fluid (CSF). Elevated CSF lactate can also be documented by magnetic resonance spectroscopy, which usually shows a lactate peak and a reduced NAA peak (3). CSF lactic acidosis may secondarily affect pituitary functions.

The fourth point is that polycystic ovary syndrome (PCOS) may be an endocrine involvement in MIDs (4). How many of the included patients were diagnosed with PCOS?

The fifth point is that the patient with critical illness-related adrenal insufficiency should not be included in the group with endocrine involvement. If the adrenal insufficiency is due to critical illness neuropathy, it is not due to the underlying MID.

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The sixth point is that no reference limits were given for most of the parameters analysed. Therefore, it is difficult to interpret whether a particular value is within or outside the normal range.

The seventh point is that patient 26 had a non-coding variant in MT-CR, suggesting that this nucleotide change was not pathogenic. How was the pathogenicity of the m.16519T > C variant confirmed?

In summary, this interesting study has limitations that put the results and their interpretation into perspective. Addressing these limitations could strengthen the conclusions and corroborate the message of the study. Endocrine system involvement is a common clinical manifestation of MID that can affect all endocrine organs and requires long-term follow-up, as it may not appear at the onset of the disease but may develop as the disease progresses. A comprehensive examination is required for early detection of endocrine disease in MID patients.

Footnotes

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References

1. Papatya Çakır ED, Ersıoy M, Çakır Biçer N, Gedikbaşı A. Endocrine Disorders in Children with Primary Mitochondrial Diseases: Single-Center Experience. J Clin Res Pediatr Endocrinol. 2024.
2. Ohkoshi N, Ishii A, Shiraiwa N, Shoji S, Yoshizawa K. Dysfunction of the hypothalamic-pituitary system in mitochondrial encephalomyopathies. J Med. 1998;29:13-29.
3. Maruyama S, Yamada T, Ishimoto Y, Hara H, Taniwaki T, Kira J. [A case of MELAS showing CSF pleocytosis associated with stroke-like episodes]. Rinsho Shinkeigaku. 1998;38:641-644.
4. Finsterer J. Mitochondrial Dysfunction in Polycystic Ovary Syndrome. Reprod Sci. 2023;30:1435-1442. Epub 2022 Oct 11