INTERNAL MEDICINE

□ LETTERS TO THE EDITOR □

Diabetes due to Mitochondrial Adipopathy

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To the Editor We read with interest the article by Ninomiya et al., about a 45-year-old woman with maternally inherited diabetes and muscle wasting due to the presence of a m.3243A>G mutation who developed insulin resistance despite possessing a normal amount of visceral fat (1). The patient's insulin resistance improved after the administration of pioglitazone (1). We have the following comments and concerns:

Insulin resistance may occur not only due to low adiponectin levels but also due to the reduced expression of insulin receptors or the synthesis of a dysfunctional receptor protein. Was the expression level assessed by measuring the insulin receptor mRNA levels? What were the expression levels of obestatin, ghrelin, the GPR39 receptor, PRDM16, visfatin, and insulin-like growth factor (factors that are known to be involved in glucose handling) (2)?

Is it conceivable that the patient's adiponectin level was low because her adipose tissue was affected by an underlying metabolic defect and that normalisation of adiponectin could be attributable to the antioxidative effect of pioglitazone? Were mitochondria in adipocytes abnormal on electron microscopy or was the function of the respiratory chain complexes reduced on immuno-histochemistry?

Is it conceivable that improvement in the patient's insulin resistance was not only due to the administration of pioglitazone but also due to stricter diet adherence? Did the patient change her dietary regimen during the three months of follow-up?

As mentioned, pioglitazone may not only exhibit beneficial effects but may also induce adverse reactions, such as an increase in blood volume and possibly the development of bladder, prostate, or pancreatic cancer (3). Did the patient's blood pressure values change over the three months of follow-up or did she develop heart failure?

Mitochondrial diabetes may not only occur in patients carrying the m.3243A>G mutation but also in patients carrying the m.8860A>G, m.3271T>C, m.16189T>C, or m.15326A>G mutations (4).

A 45-year-old woman who is 138 cm in height has to be diagnosed with short stature. Did the patient suffer from pituitary insufficiency? Were her somatotropic hormone levels reduced, or did the patient present pituitary adenoma, which is occasionally found in MID patients (5)? What were the results of cerebral examinations, including hypophysial MRI? Was there hypothyroidism, hypocorticism, or hypogonadism?

Overall, this interesting case confirms that mitochondrial diabetes may not only occur due to decreased insulin production but also due to insulin resistance. Although the cause of insulin resistance remains speculative, it is most likely also attributable to the underlying metabolic defect. Although pioglitazone seems to have a beneficial effect on insulin-resistance in mitochondrial diabetes, the potential side effects associated with pioglitazone need to be considered when it is administered to MID patients.

The authors state that they have no Conflict of Interest (COI).

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References

1. Ninomiya H, Hirata A, Kozawa J, et al. Treatment of mitochondrial diabetes with a peroxisome proliferator-activated receptor (PPAR)-gamma agonist. Intern Med **55**: 1143-1147, 2016.
2. Kolodziejski PA, Pruszynska-Oszmalek E, Sassek M, et al. Changes in obestatin gene and receptor-GPR39 expression in peripheral tissues of rat models of obesity, type 1 and type 2 diabetes. J Diabetes 2016 (Epub ahead of print).
3. Lewis JD, Habel LA, Quesenberry CP, et al. Pioglitazone use and risk of bladder cancer and other common cancers in persons with diabetes. JAMA **314**: 265-277, 2015.
4. Brisca G, Fiorillo C, Nesti C, et al. Early onset cardiomyopathy associated with the mitochondrial tRNALeu$^{(UUR)}$ 3271T>C MELAS mutation. Biochem Biophys Res Commun **458**: 601-604, 2015.
5. Mulliez E, Blanckaert M, Blanckaert J. Acute manifestation of LHON and coincidental finding of a pituitary adenoma: a case report. Bull Soc Belge Ophtalmol **277**: 35-42, 2000.

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