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LETER TO THE EDITOR

Renal involvement in mitochondrial disorders

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Letter to the Editor

We have read with interest the review by Gazdikova et al about renal involvement in mitochondrial disorders (MIDs) (1). Renal manifestations of MIDs reported were Fanconi syndrome, Bartter-like syndrome, renal insufficiency, nephrolithiasis, nephrotic syndrome, renal cysts, RTA, FSGS, tubulointerstitial nephritis (TIN), nephrocalcinosis, and benign or malign neoplasms (1). Syndromic MIDs with renal involvement include MELAS, MERRF, Leigh syndrome, LHON, MIDD, Pearson syndrome, and coenzyme-Q deficiency (1). The review is appealing but carries limitations that raise concerns and should be discussed.

A treatment option for end-stage renal disease (ESRD) in MIDs, namely the kidney transplantation (NTX) was not considered. Recently, five patients with MELAS due to the variant m.3243A>G have been reported, who required NTX for ESKD (2). Up to 2019, altogether, 13 patients carrying the m.3243A>G variant had been reported, who received NTX because of ESRD (2). The initial clinical manifestation of renal involvement was proteinuria which was found in 72 % of patients (2). Focal segmental glomerulosclerosis was detected in 69 % of patients (2). It was concluded that MID patients with ESRD should not be excluded from NTX (2).

MID patients having undergone NTX may particularly profit from mTOR inhibitors such as rapamycin (3). In four patients with MELAS/MIDD, the switching of the immunosuppressive treatment from calcineurin inhibitors to rapamycin resulted in inhibition of increased mTOR, which signalled the rescuing of mitochondrial morphology, mitochondrial membrane potential, and replicative capacity in fibroblasts in these patients (3). In addition to the immune-suppressive effect, rapamycin reduced the disease progression and improved mitochondrial functions in all four patients (3).

MIDs commonly manifest in the peripheral nerves including the autonomic fibers (mitochondrial neuropathy) (4). There may be also secondary neuropathy due to diabetes, renal insufficiency, or drug-toxicity. If autonomous fibers are affected, innervation of renal arteries may be impaired, leading to impaired artery contractility or hormonal dysregulation.

Missing is a discussion on primary manifestations of MIDs that incur secondary damage to the kidneys (5). The most common primary MID manifestation damaging the kidneys is that of mitochondrial diabetes, which usually causes diabetic nephropathy. Furthermore, if there is cardiac involvement manifesting in a MID such as heart failure or atrial fibrillation, the intra-cardiac thrombi may develop. If these thrombi embolise the renal arteries, renal infarcts may ensue. It is also conceivable that severe heart failure due to dilative cardiomyopathy may result in renal hypoperfusion and consecutively in renal insufficiency including anuria. If there is primary hyper-parathyroidism with elevated calcitonin levels, nephrocalcinosis may ensue.

An issue not addressed is the current medication that may affect kidney functions. MID patients commonly have to take drugs while some of them are nephrotoxic. Nephrotoxicity of antidiabetics (e.g., metformin), antiepileptics (e.g., valproic acid), antihypertensives, or analgesics (e.g., non-steroidal anti-inflammatory drugs) should be considered when writing about renal involvement in MIDs.

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