Only long-term follow-up data after liver transplantation in TYMP1 carriers allow assessing the outcome

Abstract:

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CORRESPONDENCE

With interest we read the article by Kripps et al., 2020 about four patients with mitochondrial neuro-gastro-intestinal encephalopathy (MNGIE) who all profited clinically and biochemically from liver transplantation (LTX) (Kripps, K. et al., 2020). The authors concluded that LTX stabilizes symptoms and nearly normalises thymidine levels in MNGIE-patients with a better safety profile than HSCT (Kripps, K. et al., 2020). We have the following comments.

The main shortcoming of the study is that the immunosuppressive therapy after LTX was not provided (Kripps, K. et al., 2020). Steroids may exhibit beneficial or detrimental effects in patients with a mitochondrial disorder (MID) (Finsterer, J., & Frank, M. 2015). Generally, long-term application of steroids, which is frequently necessary in transplanted patients, causes mitochondrial myopathy but in patients with Kearns-Sayre syndrome it may be even lethal (Finsterer, J., & Frank, M. 2015). Sirolimus can cause myopathy (Finsterer, J. et al., 2003). Cyclosporine can induce myopathy with subacute generalised muscle atrophy (Ding, H., Li, Z., & Zhang, J. 2019). Thus, we should know the detailed immunosuppressive medication of the 4 patients and the long-term outcome of myopathy. Particularly in patient 4 progressive muscle wasting despite LTX could be attributed to immunosuppression.

A second shortcoming is that the amount of depleted mtDNA was not determined. From TYMP1 mutations it is well-known that they secondarily cause mitochondrial depletion syndrome (MDS) (El-Hattab, A. W., & Scaglia, F. 2013). The amount of depleted mtDNA strongly determines the phenotype of MNGIE. Thus, it is crucial to know the mtDNA copy number in various tissues in the reported patients. It would be also interesting to know if the TYMP1 mutation induced mtDNA depletion in the donor liver. Was there ever a host-versus-graft reaction observed in any of the patients? Which was the copy number in the explanted livers?

A third shortcoming of the study is that no long-term follow-up data of patients 2, 3 and 4 were provided (follow-up duration 3-12 months). To assess the long-term outcome of these patients, longer follow-up periods are required.

Overall, this interesting study has some shortcomings, which do not allow conclusion as those mentioned above.

REFERENCES