Persistent Alpha-galactosidase A Deficiency After Simultaneous Liver-kidney Transplantation in a Patient With Fabry Disease

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Fabry disease (FD) is a rare X-linked disorder, resulting from alpha-galactosidase A (a-Gal A) enzyme deficiency and leads to globotriosylceramide (Gb3) accumulation in the vascular endothelial cells.1 Enzyme replacement therapy (ERT) can slow the disease progression and recurrence.2 The impact of liver transplant (LT) on FD expression or a-Gal A level is unknown. This study did not meet the definition of research involving human subjects, thus institutional review board approval was not required.

A 52-year-old African-American woman with alcoholic cirrhosis developed kidney failure secondary to FD based on low-serum a-Gal A level, GLA gene sequencing detected heterozygous p.W349S mutation, and kidney biopsy demonstrated intralysosomal concentric lamellar membranous inclusions in podocytes. At 4 weeks after simultaneous liver-kidney (SLK) transplant, serum a-Gal A level was unexpectedly normal at 37.4 nmol·h−1·mg−1 (28–80 nmol·h−1·mg−1) and subsequently decreased to 10.9 and 10.4 nmol·h−1·mg−1 at 3 months and 4 months after surgery. The Lyso-Gb3 levels were elevated to 1.9 and 2.4 nmol/L (≤1 nmol/L), consecutively.

A case with normalized serum a-Gal A level after kidney transplantation was once reported, but disease recurrence has been described.2 Liver transplant is the curative treatment forornithine transcarbamylase deficiency, where the deficient enzyme is expressed exclusively in the liver. In FD, most lysosomal enzymes are expressed throughout the body.3 Hepatic lysosomal enzyme in sinusoidal endothelial cells, Kupffer cells, have been studied in animal models, and high lysosomal enzyme activities have been observed in these cells.4 Touraine et al5 reported that an experience of fetal LTs in FD patients resulted in symptomatic improvement without significance in the a-Gal A level. It is unknown if LT from a donor without FD will have any impact on the disease expression or enzyme activity in a FD patient. Our hypothesis was that the transplanted liver could produce enough a-GAL A enzyme activity and affected the FD expression. We assumed the donor did not have FD, given the viable kidney received from a 44-year-old. We observed that the a-Gal A level was temporarily normal at 4 weeks after SLK transplantation, probably related to a short-term lysosomal enzyme released from the transplanted organ. However, LT did not have a positive long-term effect on a-Gal A level. The patient continues to receive ERT with excellent graft functions at 1-year post-SLK. The ERT is recommended in postkidney transplant recipients to protect the grafted kidney from Gb3 deposition.1,2 ERT costs approximately US $300 000 per year, also has risks of infusion reaction, and developing antibodies. An enhancement of a-GAL A enzyme release by using a pharmacological chaperone is being developed.1

In summary, FD is a lysosomal storage disease with substrate accumulations leading to multiorgan damages. We observed a transient normalization of serum a-Gal A enzyme post-SLK in our patient, unfortunately, the liver transplantation did not appear to have a positive long-term impact on FD expression. Studies are being undertaken for an alternative therapy. With the current advancement in the field of molecular genetics, we encourage to see the novel alternative treatment for FD in the future.