Report of liver transplantation in organic aciduria

M. Spada , A. Alluto , F. Gennari

Department of Pediatrics, University of Torino and Liver Transplantation Unit, Molinette Hospital, Torino, Italy.

The outcome for childrens suffering from severe and early-onset organic acidurias (OA), such as propionic acidemia (PA) and methylmalonic acidemia (MMA), due to the inherited propionyl-Coa carboxylase and methylmalonyl-CoA mutase deficieny, respectively, remains poor. Despite the conventional treatment with low-protein diet, carnitine and metronidazole supplementation, the course of severely affected patients who survived to the neonatal ketoacidotic coma is characterized by recurrent life-threatening episodes of metabolic acidosis, anorexia, vomiting, failure to thrive, developmental delay, stroke, extrapyramidal signs, pancreatitis, progressive renal disease and cardiomyopathy. Retrospective studies show a 80% mortality within the first 10 years of life . Alternative treatment such as liver transplantation (OLT) has been considered, but this option is not commonly adopted. The goal of OLT in OA is to provide normal enzyme activity at the liver in order to assure a sufficient clearance of toxic organic, deriving mainly from muscular aminoacid catabolism.

Here we report on a male patient with classical cobalamin non-responsive early-onset MMA due to methylmalonyl-CoA mutase deficieny. His urinary MMA excretion was between 6000 and 8000 mmol/mol C and mutase activity measurement in fibroblastes showed a very low enzyme level (< 1 % of normal). The diagnosis was finally confirmed also at the molecular level, as the patient was found to be compound heterozygous at the methylmalonyl-CoA mutase locus for the two already reported mutations, the G158V and R467X, respectively. Following the neonatal acute onset, he did not show major problems during the first year of life. However, since the age of 12 months frequent episodes of metabolic decompensations required several hospital admissions. Slight neuromotor retardation occured, but cognitive level was still normal. Because of poor quality of life and poor long-term prognosis under conventional therapy, parents opted for OLT as an alternative strategy. Patient entered the transplantion list at the age of 30 months and underwent the OLT at the age of 3 years. No complications were observed during the peri-operative period and the child was discharged after 8 days on tacrolimus monotherapy without corticosteroids. Currently, after 2 years post tranplantation, his methylmalonic acid concentrations continue to remain stable under only moderately restricted dietary protein intake (urinary methylmalonic acid concentrations now ranging from 500 to 1000 mmol/molC and serum AMM from 150 to 250 µmol/l). The child achieved full fasting and intercurrent catabolic illness tolerance and gastric drip feeding was no more employed. No more metabolic decompensation has been reported. He showed a marked neuromotor improvement, he started to frequent infant community and he had an important global improvement of quality of life.

In our experience, OLT was an effective treatment and we recommend it to be considered as a terapeutic option in early-onset MMA, so as to improve the prognosis quoad vitam and also to obtain a better quality of life.

Further follow-up is, however, required to study the long-term outcome and to value the effect of OLT on neurological manifestations.

References

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	Neonatal period At diagnosis	*before-OLT (age: 3 year)*	*A fter OLT (2 yrs follow-up)*
AMM plasma (µmol/L)	ND	716	185
AMM urina (µmol/mmol C)	11.000	3495	800