Domino Liver Transplantation for the Pre-emptive Therapy of Compound Heterozygous Familial Hypercholesterolemia: A Case of 3-Year-old Girl

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There is no conflict of interest

Background

Homozygous (compound heterozygous) familial hypercholesterolemia (FH) is a rare and life-threatening disease characterized by markedly elevated plasma low-density lipoprotein cholesterol (LDL-C) from birth, extensive xanthomas, and marked premature and progressive atherosclerotic cardiovascular disease (ACVD)(1-2). If untreated, patients develop cardiovascular atherosclerosis resulting in death before the second decade of life(3). Medication and apheresis are only partially effective in reducing LDL-C levels, and do not significantly improve the prognosis(4).

Liver transplantation (LT) can correct the lipid metabolism in the organ most active in the clearance of LDL, resulting in marked improvement of LDL-C levels(5). Although a possibly successful therapeutic strategy, there are obvious disadvantages, including the high risk of surgical complication and mortality, the paucity of donors, and the need for long-term treatment with immunosuppressive therapy(6).

We report a first case received living donor LT (LDLT) from the donor with maple syrup urine disease (MSUD) in early infancy as a preemptive, rather than preventive therapy for compound heterozygous FH.

Laboratory tests

<table>
<thead>
<tr>
<th>Blood test</th>
<th>[CBC+biochemistry]</th>
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</thead>
<tbody>
<tr>
<td>WN.L</td>
<td>no elevation of C/O lipoprotein T/BNP</td>
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</tbody>
</table>

- **[Blood test]**
  - [CBC+biochemistry]
    - WN.L: no elevation of C/O lipoprotein T/BNP

- **[Lymphocytic LDL activity]**
  - [CRX/EGG/UGG]
  - WN.L
  - [Lipid profile]
    - HDL-C: 49 mg/dL
    - LDL-C: 975 mg/dL
    - TG: 129 mg/dL
    - FFA: 881 μg/dL
    - apoA1: 114 mg/dL
    - apoB: 271 mg/dL
    - apoC2: 5.7 mg/dL
    - apoC3: 13.7 mg/dL
    - apoE: 121 mg/dL
    - sI-LDL: 9.5 μg/mL

- **[Genetic test] (LDLR)**
  - [c.418G>A; p.E139K]
  - [c.2212+2T>C]

Clinical course

- **Medication was only partially effective.**
- **Apheresis was not available because of her young age.**
- **LDLT from the donor with MSUD is perfectly effective without major complication.**

Discussion

**Classification of mutations of LDLR**

<table>
<thead>
<tr>
<th>Class</th>
<th>Phenotypic effects on the protein</th>
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<tbody>
<tr>
<td>1</td>
<td>No detectable LDLR synthesis</td>
</tr>
<tr>
<td>2</td>
<td>Defective LDLR transport</td>
</tr>
<tr>
<td>3</td>
<td>Impaired LDL to LDLR binding</td>
</tr>
<tr>
<td>4</td>
<td>No LDLR/LDL internalization due to defective clustering</td>
</tr>
<tr>
<td>5</td>
<td>No LDLR recycling</td>
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- Known for few expression of LDLR(7)
- In this case, c.418G>A; p.E139K) → class2
- c.2212+2T>C → class1

- Causes a severe clinical presentation and resistance to medication.

Liver using the liver from a patient with MSUD

MSUD is an autosomal recessive metabolic disorder that is characterized by impaired activity of the branched-chain a-keto acid dehydrogenase complex (BCKDH) (8). LT has been performed for some patients with MSUD who are difficult in medication management (9). The liver from a patient with MSUD is used for domino LT. The recipient maintained normal amino acid metabolism, because of normal extrahepatic BCKDH enzyme activity in the recipient without MSUD (10).

Conclusion

Liver transplantation for severe FH performed in early infancy before onset/progression of atherosclerosis is an effective pre-emptive treatment.

References


DOI: 10.3252/pso.eu.54espe.2015

Poster presented at: Ross Session Online