TRANSIENT NEONATAL DIABETES MELLITUS IN HANOI, VIETNAM: CLINICAL FEATURE AND OUTCOME

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Introduction

Transient neonatal diabetes mellitus type 1 (TNDM) is a rare with an incidence of between 1/400,000-1/500,000 but remarkable form of diabetes which presents in infancy, resolves in the first months of life, but then frequently recurs in later life. TNDM is mainly caused by anomalies in the imprinted region on chromosome 6q24; however, recently, mutations in the ABCC8 gene, which encodes sulfonylurea receptor 1 (SUR1), have also been implicated in TNDM.

Objectives:

To describe clinical features and laboratory manifestations of patient with TNDM and to evaluate outcome of management.

Methods:

Cases series study. Clinical features, biochemical finding, mutation analysis and management outcome of 5 cases from 5 unrelated families were studied. All exon of KCNJ11, ABCC8 and INS genes were amplified from genomic DNA and directly sequenced. If the mutation of KCNJ11, ABCC8 and INS has failed to detect, methylation – specific PCR would be done to detect the loss of methylated region on chromosome 6q24.

Results:

5 probands from 5 unrelated families were diagnosed TNDM and were identified mutation in Ch6q24 in 4 cases and ABCC8 genes in one case.

Demographics:

- Age of diagnosis was 19.5 ±11.8 days
- Gender: 3 males, 2 females
- Gestation age was 38.6±2.6 weeks
- BW: 2440 ± 512 gram (3 cases has BW < 3 percentile)

<table>
<thead>
<tr>
<th>Genotype-Phenotype</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
<th>Case 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype</td>
<td>Het of c.7450delT and c.7812C&gt;T on ZP57</td>
<td>material hypomethylation at TND (6q24), IGF2R (6q27), SNRPN (6q11) and GRB10 (7q12) loci</td>
<td>Het 398delT:133HtsX49, 499C&gt;CT:167R&gt;RC, 760C&gt;CT:254L&gt;LF</td>
<td>maternal hypomethylation at the GRB10 and PEG3 loci</td>
<td>Het mRNA mutation p.R1183W on ABCB8 gene</td>
</tr>
<tr>
<td>Clinical Phenotype</td>
<td>Polydipsia, polyuria, fever, cough, diarrhea, dehydration, shock, macroglossia, exumbilication</td>
<td>Polyuria, polydipsia, exumbilication</td>
<td>Polyuria, polydipsia, macroglossia, exumbilication</td>
<td>Macroangiopathy, exumbilication, Severe DKA</td>
<td>Polyuria, polydipsia, fever, lethargy</td>
</tr>
<tr>
<td>pH</td>
<td>7.32</td>
<td>7.3</td>
<td>6.8</td>
<td>6.7</td>
<td>7.08</td>
</tr>
<tr>
<td>HCO3^- (mmol/l)</td>
<td>21.7</td>
<td>20.7</td>
<td>3.3</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td>BE (mmol/l)</td>
<td>-4.2</td>
<td>-4.9</td>
<td>Very low</td>
<td>-26</td>
<td></td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>6.8</td>
<td>8.3</td>
<td>5.8</td>
<td>6.6</td>
<td>7.6</td>
</tr>
<tr>
<td>Glucose (mmol/l)</td>
<td>30</td>
<td>31.1</td>
<td>56</td>
<td>34.3</td>
<td>31.7</td>
</tr>
<tr>
<td>Ketourine</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age of resolve (months)</td>
<td>17</td>
<td>5.5</td>
<td>5</td>
<td>5.5</td>
<td>6</td>
</tr>
<tr>
<td>Current age (years)</td>
<td>7.4</td>
<td>6.0</td>
<td>4.2</td>
<td>2.7</td>
<td>2.25</td>
</tr>
</tbody>
</table>

Outcome:

- 4 out of 5 patients stopped insulin after 5-6 months of treatment. Among them, one case had been treated with insulin for a long time and recovered by 18 months of age.
- Currently, the patients are 51.6 ± 28.9 months old and are euglycemic and normal HbA1C without any insulin or oral hypoglycemic agents.
- Now 4 cases have normal development, one case has mild developmental delay.

Conclusions:

It is important to perform screening gene mutation for patients with diabetes diagnosed before 6 months of age to control blood glucose and follow up the patients.

References:


Conflicts of interest: None declared