INFLUENCE OF PANCREATIC AUTOIMMUNITY IN THE ONSET AND PROGRESSION OF DIABETES IN PEDIATRIC POPULATION

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Diabetes

Introduction:
Anti-islet autoantibodies are predictive and diagnostic markers for Type 1 Diabetes (T1D). The most frequently determined pancreatic autoantibodies in T1D are anti-glutamic acid decarboxylase (GAD), anti-tyrosine phosphatase (IA-2) and anti-insulin (IAA).

Objectives:
To study whether the pancreatic autoimmunity profile influences the initial presentation of diabetes, its metabolic behaviour and the presence of other autoimmune disorders in T1D.

Methods:
Retrospective study of 210 pediatric patients with T1D. We analyzed age, sex, age at diagnosis, type of clinical presentation: hyperglycemia, ketosis, ketoacidosis (KAD), HbA1c (HPLC-Menaquin, NV 5.31 0.31%), C-peptide levels and pancreatic autoimmunity (GAD, IA2, AAI). Additional autoimmune disorders were screened with an antibody array at diagnosis and at follow-up. The metabolic control (last year mean HbA1c and acute complications) were also analyzed.

Data are reported in percentages, median and interquartile ranges. Statistical analysis was performed with SPSS 22.0.

Results:
At diagnosis, mean age was 7 years (3.3-10.5), 53% female, HbA1c 10.7% (9.8-12.2), C-peptide 0.5 ng/mL (0.3-0.7). Initial presentation: hyperglycemia 23%, ketosis 40%, ketoacidosis 37%. In our cohort 88% of patients have pancreatic autoimmunity markers. Associated autoimmunity at follow-up: anti-thyroid antibodies 9%, celiac disease 10%, parietal cells antibodies 2%. Celiac disease was diagnosed in five patients before T1D. GAD+ patients showed more rapid progression to celiac disease. Other autoimmune markers: one patient had adrenal antibodies (GAD+/IA2+) with normal adrenal function, 4% of the patients presented positive ANA, one of them with olygoarthritis (IA2+) and another with associated autoimmune thyroiditis (GAD+/IA2+). Another patient was diagnosed with autoimmune hepatitis 3.7 years after T1D (GAD+). Within the last year follow-up no patient presented episodes of severe hypoglycemia or ketoacidosis. No significant differences were found between patient-groups with isolated, combined or absence of pancreatic autoantibodies. Eleven of children with negative autoimmunity had haplotype analysis and ten of them were HLA of risk of T1D.

<table>
<thead>
<tr>
<th>Table</th>
<th>GAD+</th>
<th>IA2+</th>
<th>GAD+ / IA2+</th>
<th>AAI+</th>
<th>GAD+/IA2+ / AAI+</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>45 (21%)</td>
<td>45 (21%)</td>
<td>92 (44%)</td>
<td>2 (1%)</td>
<td>26 (12%)</td>
</tr>
<tr>
<td>Years at DM1 onset</td>
<td>5.0 (2.1-10.5)</td>
<td>6.8 (3.6-9.6)</td>
<td>8.3 (4.7-10.9)</td>
<td>7.0 (3.8-10.3)</td>
<td>4.1 (2.7-8.2)</td>
</tr>
<tr>
<td>Sex (%)</td>
<td>44</td>
<td>62</td>
<td>52</td>
<td>50</td>
<td>54</td>
</tr>
<tr>
<td>DM1 debut (%)</td>
<td>29/36/33</td>
<td>20/32/48</td>
<td>29/36/33</td>
<td>50/0/50</td>
<td>19/50/23</td>
</tr>
<tr>
<td>HbA1c at DM1 debut (%)</td>
<td>10.6 (8.7-12.1)</td>
<td>10.7 (9.6-12.6)</td>
<td>10.7 (9.8-11.9)</td>
<td>9.9 (6.8-13.0)</td>
<td>11.0 (9.9-12.1)</td>
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<tr>
<td>Basal C-Peptide (ng/mL)</td>
<td>0.4 (0.3-0.5)</td>
<td>0.5 (0.3-0.6)</td>
<td>0.5 (0.3-0.7)</td>
<td>0.5 (0.4-0.7)</td>
<td>0.3 (0.1-0.6)</td>
</tr>
<tr>
<td>Follow up (years)</td>
<td>4.1 (2.6-8.3)</td>
<td>4.5 (2.2-7.8)</td>
<td>4.0 (2.1-6.6)</td>
<td>3.6 (2.6-4.6)</td>
<td>5.3 (3.0-9.2)</td>
</tr>
<tr>
<td>Mean HbA1c in the last year (%)</td>
<td>6.5 (6.2-7.2)</td>
<td>6.7 (6.2-7.1)</td>
<td>6.6 (6.3-7.0)</td>
<td>6.4 (6.3-6.5)</td>
<td>6.7 (6.3-7.1)</td>
</tr>
</tbody>
</table>

Graphic: Associated autoimmunity according to pancreatic antibody groups

Associated Autoimmunity

- Celiac antibodies
- Anti-thyroid antibodies
- Anti-parietal cells antibodies

Conclusions:
Pancreatic autoimmunity does not influence the type of disease onset nor evolution or frequency of associated autoimmune diseases.

References: