LATENT AUTOIMMUNE DIABETES IN ADULTS

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Background

Latent Autoimmune Diabetes in Adults may account for up to 10% of patients presenting as T2D. At diagnosis, patients with LADA are usually non-insulin requiring and clinically indistinguishable from patients with type 2 diabetes. We present two cases of diabetes to highlight the pitfalls and implications in diagnosis and management of LADA.

Case 1:

55yr old lady was first diagnosed with type 2 diabetes in November 2011 which was well controlled for 2 years with diet, Metformin and Gliclazide. She was also trying to lose weight at the time, however ended up losing two stone in weight. She also experienced significant osmolar symptoms. Her HbA1c jumped from 9% (75 mmol/mol) to 13% (118 mmol/mol), inspite of significant weight loss. Home blood sugar readings were consistently in between 17-30 mmol/L. She tested positive for GAD antibodies 1544 IU/ml. She was initiated on Insulin.

Case 2:

83yr old lady presented with 2 weeks history of polyuria, polydipsia, sweats, weight loss and being unwell. Preclinik fasting glucose was 17 – 19 mmol/l. Maternal family history of Type 2 diabetes was elicited. Past medical history included Pernicious Anemia and possible subclinical osmolar symptoms in preceding months. BMI was 24 Kg/m2. She was not acidic. Urine tested 2+ Ketones and 3+ Glucose. Late onset of Type 1 diabetes was suspected, and Insulin was commenced. GAD65 was >2000 IU/ml (0-10), with IA2 7222 IU/ml (0-10) and ICA (Islet cell antibodies) – borderline positive; in keeping with autoimmune diabetes.

Discussion

Given the risk of ketoacidosis, insulin should be started in such patients, regardless of whether they thought to have type 1 or type 2; especially those who are catabolic (weight loss or dehydration in the setting of hyperglycemia).

HBA1C

HBA1C must not be used as a diagnostic tool in these patients. Clinical situations where HbA1c must not be used as a sole test to diagnose diabetes.

- Pregnancy
- All symptomatic children and young people (< 18 years)
- Symptoms, suggestive of Type 1 diabetes (any age)
- Short duration of diabetes symptoms for less than 2 months.
- Medication use that may cause rapid glucose rise: e.g. corticosteroid, antipsychotics
- Acute pancreatic damage/pancreatic surgery

The table showing autoantibody profiles in T1DM, T2DM and LADA

<table>
<thead>
<tr>
<th>Markers</th>
<th>T1DM</th>
<th>LADA</th>
<th>T2DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Islet cell antibodies</td>
<td>+ve, even before onset</td>
<td>+ve, helps to differentiate from T2DM</td>
<td>Negative</td>
</tr>
<tr>
<td>Insulin antibody</td>
<td>Often found</td>
<td>Often found</td>
<td>Negative</td>
</tr>
<tr>
<td>Islet antigen 2</td>
<td>Often +ve</td>
<td>Often found</td>
<td>Negative</td>
</tr>
<tr>
<td>GAD antibody</td>
<td>Common in adults than children</td>
<td>More common than in T1DM</td>
<td>Rare, may suggest LADA</td>
</tr>
<tr>
<td>HLA link</td>
<td>High</td>
<td>Low</td>
<td>Negative</td>
</tr>
<tr>
<td>Insulin / C-peptide</td>
<td>Very low</td>
<td>Low</td>
<td>Normal to high</td>
</tr>
</tbody>
</table>

‘LADA clinical risk score’

1. Age of onset < 50 years
2. Acute symptoms (polydipsia / polyuria /unintentional, weight loss)
3. Body mass index (BMI) < 25 kg/m2
4. Personal or Family history of autoimmune disease (HLA DR3/DR4-related)

The presence of at least two of these distinguishing clinical features (LADA clinical risk score ≥ 2) had 90% sensitivity and 71% specificity for identifying LADA, and a negative predictive value for a LADA clinical risk score ≤ 1 of 99%.

Immunology of Diabetes society diagnostic criteria

<table>
<thead>
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<th>Minimal age of 30 yrs.</th>
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<tr>
<td>The presence of antibodies.</td>
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<td>Insulin independence for at least 6 months.</td>
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Conclusion-

These cases highlight the importance of considering a diagnosis of LADA even at an advanced age. It adds further fuel to the argument regarding routine use of screening strategies for early diagnosis of LADA.

References

2. Fourlanos S et al. Diabetes Care 2006