Updates on Two Interesting Cases: Case 2

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24y/o F with polyuria, blurred vision, and fatigue

- 24 y/o Filipino woman sent by PCP with c/o polyuria, blurred vision, and fatigue
- Last PCP visit, fasting BG 171, HbA1c 7.5%
- Had not started medication
Patient History

• PMHx
  – Seasonal allergies
  – GERD

• Meds
  – Loratadine 10mg PO daily
  – Nasonex two sprays each nostril daily
  – Prevacid 30mg PO BID

• Allergies
  – Lactose
  – NKDA

• FamHx
  – MGM: DM2 in 80’s
  – F: prediabetes, asthma, seasonal allergies
  – M: Sjogren’s disease, Rheumatoid arthritis, ASD
  – S: gestational diabetes
  – B: healthy

• SocHx
  – Single, no children
  – Graduate student in pediatric clinical neuropsychology
  – Denies tobacco, IVDU
  – Occasional EtOH
Physical Exam

- VS: BP 102/74 mm Hg, HR 68 bpm, Ht 61 in, Wt 57 kg, BMI 24, office fasting BG 146
- HEENT: oropharynx without crowding, thyroid normal
- Pulm: CTA bilaterally
- CV: RRR, nl S1, S2, no M/R, pedal pulses palpable, no edema
- Abd: soft, non-tender, non-distended, NABS
- MS: normal muscle strength 5/5 throughout
- Skin: no acanthosis nigricans, no skin tags
- Neuro: Sensation intact in b/l feet
### Laboratory Data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hgb A1c</td>
<td>7.5%</td>
</tr>
<tr>
<td>GAD65 Ab</td>
<td>0.00 nmol/L</td>
</tr>
<tr>
<td>IA2</td>
<td>negative</td>
</tr>
<tr>
<td>Insulin Ab</td>
<td>&lt;3% bound</td>
</tr>
<tr>
<td>Glucose</td>
<td>149 mg/dL</td>
</tr>
<tr>
<td>C-peptide</td>
<td>0.7 pmol/mL</td>
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<tr>
<td>Microalbumin</td>
<td>6.8 mcg/mg</td>
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<tr>
<td>TSH</td>
<td>2.2 mcU/ml</td>
</tr>
<tr>
<td>T4</td>
<td>7.9 mcg/dL</td>
</tr>
<tr>
<td>FTI</td>
<td>9.2</td>
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</tbody>
</table>
Plan

- Sample sent to test for MODY mutations
- Started pt on Januvia 100mg daily due to concern for beta cell dysfunction
- Added Metformin 500mg BID to improve fasting blood glucose
DNA Testing

• MODY3 mutation found
  – exon 8 E508K mutation in HNF1A gene
<table>
<thead>
<tr>
<th>MODY</th>
<th>Genetic Defect</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>MODY1</td>
<td>HNF-4α</td>
<td>Impairment of glucose-stimulated insulin secretion</td>
</tr>
<tr>
<td>MODY2</td>
<td>Glucokinase gene</td>
<td>Reduced activity of glucokinase, decreased insulin secretion</td>
</tr>
<tr>
<td>MODY3</td>
<td>HNF-1α</td>
<td>Weak transactivator of the insulin gene, decreased insulin secretion</td>
</tr>
<tr>
<td>MODY4</td>
<td>Insulin promotor factor-1</td>
<td>Abnl transcriptional regulation of beta cell development and function</td>
</tr>
<tr>
<td>MODY5</td>
<td>HNF-1β</td>
<td>Leads to early onset diabetes, kidney cysts</td>
</tr>
<tr>
<td>MODY6</td>
<td>NeuroD1</td>
<td>Regulatory switch for endocrine pancreatic development</td>
</tr>
</tbody>
</table>
Treatment

• No improvement in BG with Januvia and Metformin

• Patient started on Glyburide 5mg BID
  – Titrated to Glyburide 30mg BID, with improved BG control (HbA1c 6.8%)
Follow Up

- BG uncontrolled, Glyburide 40mg BID, started Lantus 8 units qhs
  - Titrated to Lantus 14 units qhs
- A1c 7.4%
  - Started Januvia 100mg daily, decreased Lantus to 8 units qhs
- A1c 7.6 - 8.0%
  - Continued to increase insulin dosing (Lantus 28 units BID)
  - Multiple dietary changes made to avoid mealtime insulin
- Increasing patient frustration as A1c not improving, BG uncontrolled
Follow Up

• Felt Januvia was not helping, glyburide only medication keeping BG relatively stable

• Changed regimen to:
  – Glyburide 40mg BID
  – Lantus 28 units BID
  – Victoza 0.6mg daily -> titrate to 1.2mg daily
  – Stop Januvia
Follow Up

• Patient emailed regarding hypoglycemia in the afternoon and evening

• Decreased glyburide to 40mg qPM, 30mg qAM

• Now with improvement in blood glucose without hypoglycemia

• Awaiting A1c at next visit