39 year old F with sickle cell anemia presenting with pain crisis

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11/8/12
HPI

• Knee and back pain typical of usual crises
• Nausea and vomiting 2 days prior to admission
• Had previously been on Lantus 15U daily that had been started in 2011
• Did not use Lantus for 2 days
• Not checking blood sugars at home
PMH
  Sickle cell anemia
  PE/DVT
  CVA x 2
  Asthma
  DM

PSH
  Cholecystectomy

FH
  SCT parents, daughter

SH
  No tobacco, etoh
  Lives with 18 yo daughter

MEDS
  Albuterol, T#4, Dilaudid,
  Lantus 15U qHS,
  Lisinopril 2.5 mg,
  Gabapentin 300mg qHS,
  Folic acid, Paxil 20mg qday, Coumadin, Oramorph
Physical Exam

Vitals: 36.4, 107/66, 90, 16, BMI 21, 95%RA
Gen: somnolent, appears in pain
CV: flow murmur
Pulm: clear bilaterally
GI: active emesis, soft, no rebounding or guaring
Neuro: unable to assess orientation
Skin: no rash
Initial Labs

- HbA1c 7.4%
- Lipase 220 (13-60)
- Ketones 8.17 (RR < 0.30)
- VBG pH 7.03
- UA: 1.025, Neg LE/Nit/bact, 3+ glu, 2+ ketones

PMN 87%
• Anti-GAD Ab 45 (RR < 0.02)
• C-peptide 0.04, Glucose 214
• Fructosamine 403 mcmol/L (RR 200-285)
HbA1c = 0.017 x Fructosamine + 1.61. In our patient, calculated HbA1c = 8.5
Clinical Questions

• Incidence of diabetes in SCD/SCT?
• Glucose metabolism/insulin secretion in SCD?
• Prevalence of diabetes-related autoantibodies in SCD?
• Assessing glycemic control in SCD/SCT?
Incidence of DM in SCD

- Concurrent sickle cell disease with diabetes is rare
- Type 1 Diabetes and sickle cell is even more rare
- Previous case reports were not associated with any diabetes complications
Reason for this uncommon association

• Previously patients with sickle cell anemia died younger so never manifested complications from diabetes

• Genetics?
  – No known association between inheritance patterns of diabetes and sickle cell hemoglobinopathies
  – Beta-globin and insulin genes are both on the short arm of chromosome 11
Prevalence of SCD + DM

• 185 total pregnant patients with hemoglobinopathy (123 SCT, 35 HbSS, 20 HbSC, 7 HbS-Thal)
• 2263 controls
  – 4% abnormal screening
• Screening at 28-30 weeks with 2h post-prandial glucose
• None of pregnant patients with sickle cell hemoglobinopathies demonstrated evidence of glucose intolerance
2h post-prandial plasma glucose

<table>
<thead>
<tr>
<th>Hemoglobin</th>
<th>Early gestation (8–20 weeks)</th>
<th>Late gestation (28–32 weeks)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>No. of patients</td>
<td>Range (mg/dl)</td>
</tr>
<tr>
<td>HbA-S</td>
<td>123</td>
<td>69–139</td>
</tr>
<tr>
<td>HbS-S</td>
<td>35</td>
<td>62–142</td>
</tr>
<tr>
<td>HbS-C</td>
<td>20</td>
<td>70–136</td>
</tr>
<tr>
<td>HbS-Thal</td>
<td>7</td>
<td>59–121</td>
</tr>
<tr>
<td>Controlº</td>
<td>2263</td>
<td>64–197</td>
</tr>
</tbody>
</table>

Controls: 14 had an abnormal early screening. 73 had an abnormal late screening.

Test group: no abnormal screenings early or late.
OGTT in SCD

- 12 kids with SCD, 9 controls

Mean fasting glucose was higher in SCD than in controls (81 vs 72).

Glucose remained higher among SCD. The difference between means at 30, 90, 120 minutes were significant.
C-peptide secretion in SCD

Organ damage from sickling in the pancreas?

Serum c-peptide levels at 0, 1, 3, 5, 10, 30, 60 minutes after glucose infusion

Acta Haemat 1989;82:81-84
Sickle Cell Trait and DM

• These conditions co-exist in >1 million worldwide
• In the US in 2008 the prevalence of diabetes and HbC or HbS trait was about 350,000.
• No evidence that SCT affects course of DM
Diabetes-related autoantibody Prevalence

- Prospective screening for hyperglycemia in pediatric ED
  - 30 hyperglycemic patients
  - 30 stress control subjects
  - 30 healthy controls
- 3.8% (35 of 926) ED patients were hyperglycemic. Mean glucose 192 mg/dL.
- Tested for ICA, IAA, GAD, HLA typing
- Results: After 30-36 months of follow-up no patients or controls developed diabetes. 4 of 8 patients with SCD had insulin autoantibodies compared with 0 of 52 ED patients without SCD.

Assessing glycemic control in SCD

- RBC life span is about 10-14 days
- HbA1c does not accurately represent glycemic control
- Fructosamine- avg blood glucose over a period of 2-3 weeks
- Both SCD and DM are associated with renal impairment and retinopathy
- Ketoacidosis and the associated dehydration can precipitate sickle cell crisis
Fructosamine study

- 150 patients with sickle cell disease
- 100 controls - non-diabetic
- 50 type 2 diabetics

- Mean glucose/fructosamine
  - SCD: 4.3 mmol/L (77 mg/dL) – 1.3 mmol/L
  - Controls: 4.6 mmol/L (83 mg/dL) – 3.2 mmol/L
  - T2DM: 18.2 mmol/L (328 mg/dL) – 1.4 mmol/L
Table 1: Serum fructosamine, fasting glucose, albumin and total bilirubin (Mean ± SEM and Range) in HbSS patients, Diabetics and Controls.

<table>
<thead>
<tr>
<th></th>
<th>HbSS Patients n = 150</th>
<th>Diabetics n = 50</th>
<th>Controls n = 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fructosamine (mmol/L)</td>
<td>1.3 ± 0.16 (0.7-1.9)</td>
<td>3.2* ± 0.16 (1.0-5.2)</td>
<td>1.4 ± 0.04 (0.6 - 2.2)</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>4.3 ± 0.07 (2.5-6.1)</td>
<td>18.2* ± 0.01 (4.0-32.4)</td>
<td>4.6 ± 0.07 (2.0-7.2)</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>40.0 ± 0.47 (28-52)</td>
<td>38 ± 0.58 (29-45)</td>
<td>38 ± 0.38 (30-45)</td>
</tr>
<tr>
<td>Total Bilirubin (μmol/L)</td>
<td>43* ± 1.7 (0-85)</td>
<td>14 ± 0.5 (0-17)</td>
<td>15 ± 0.9 (0-17)</td>
</tr>
</tbody>
</table>

* Significant difference (P < 0.05)
**Table ii:** Serum fructosamine (Mean ± SEM and Range) at different levels of serum total bilirubin concentrations in HbSS patients.

<table>
<thead>
<tr>
<th>Bilirubin (μmol/L)</th>
<th>No of (HbSS) patients</th>
<th>Fructosamine (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11-80</td>
<td>83</td>
<td>1.3* ± 0.11</td>
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<td>(0.62 – 1.98)</td>
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<tr>
<td>81 – 160</td>
<td>67</td>
<td>1.4* ± 0.12</td>
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<tr>
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<td>(1.22 – 1.98)</td>
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</tbody>
</table>

* No significant difference (P > 0.05)
Effect of SCT on HbA1c?

Am J Clin Pathol 2008;130:136-140
Effect of SCT on HbA1c?
Take home points

• Concurrent Sickle cell anemia and Diabetes is very rare
• Need more studies looking into insulin secretion, autoantibodies in SCD
• HbA1c is not reliable in sickle cell anemia but can be used in sickle cell trait
• Fructosamine is a better measure of glycemic control in sickle cell anemia
References