10 yo boy w/Chiari/pseudotumor seen for obesity

8/22/13
Jess Hwang
HPI

• Kids at school have been teasing him about his weight and the skin darkening around his neck
• 127lb was peak weight
• Quit desserts/soda and has lost 8lb in 12 months
• Exercise: Just Dance, planks, jumping jacks
HPI cont.

- No steroid since 2010 (had been on 2 month course of decadron for headaches)
- Headaches treated with excedrin, topamax
- No peripheral vision problems
- 6/2011 negative sleep study
- Used to see a therapist for his labile mood
More History

PMH
Chiari malformation (s/p decompression)
Pseudotumor (s/p LP shunt)
Distal ulnar fracture 2012

Meds
Topamax 75 mg BID

FHx
MGM: CAD, DM
PGM: DM
Sister: ?autoimmune disease

SHx
Negative
ROS

Constitutional: 8lb weight loss in 12 months but it has been very difficult losing weight
HEENT: wears glasses
CV: no chest pain
Resp: no shortness of breath
Neuro: +chronic headaches
GI: no nausea, vomiting, diarrhea
Skin: skin darkening
Physical Exam

Vitals: 110/65, 118, 135 cm (4’5”), 54 kg (119lb), BMI 29.4
Gen: no distress
HEENT: visual fields grossly normal, wears glasses
Neck: no thyromegaly, no nodules
CV: RRR
Pulm: CTA bilaterally
GI: soft, non-tender, obese abdomen, no striae
GU: prepubertal, testes 2.1 cm B, no axillary hair
Skin: acanthosis nigricans
Neuro: A+O, normal reflexes
2009 → 2013
Growth chart
Labs

<table>
<thead>
<tr>
<th>141</th>
<th>106</th>
<th>11</th>
<th>81</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5</td>
<td>20</td>
<td>0.7</td>
<td>9.5</td>
</tr>
</tbody>
</table>

A1c 5.0%
HDL 39
LDL 170
TG 69
IGF-1 361 (88-452)
TSH 1.64
FT4 1.24
Work-up

- Midnight Salivary Cortisol (RR <100)
  - 137, 105, 99
- Urine Free Cortisol 53 mcg/24h (2.6-37)
  - Vol 1.5L, UCr = 1410 mg
- Urine Free Cortisol 76 mcg/24h (2.6-37)
  - Vol 1.3L, UCr = 1000 mg
- 8AM ACTH 56.8 (RR <52)
- 8AM Cortisol 17.6 mcg/dL (6.8-26)
LDDST → CRH stim

LDDST: 0.5 mg dexamethasone q6h for 48h
Dexamethasone level 271 ng/dL (RR<20)

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>-15</th>
<th>0</th>
<th>15</th>
<th>30</th>
<th>45</th>
<th>60</th>
<th>90</th>
<th>120</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH</td>
<td>34.9</td>
<td>31.0</td>
<td>68.7</td>
<td>62.4</td>
<td>59.2</td>
<td>58.9</td>
<td>63.4</td>
<td>71.6</td>
</tr>
<tr>
<td>Cortisol mg/dL</td>
<td>3.4</td>
<td>3.2</td>
<td>9.6</td>
<td>15.5</td>
<td>14.3</td>
<td>15.2</td>
<td>17.2</td>
<td>18.3</td>
</tr>
</tbody>
</table>

IV CRH 1 ug/kg
Pituitary gland/stalk are normal without any evidence of abnormal enhancement.
## IPSS results

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>L/P ACTH ratio</th>
<th>R/P ACTH ratio</th>
<th>L/P PRL ratio</th>
<th>R/P PRL ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>-10</td>
<td>0.8</td>
<td>1.2</td>
<td>0.9</td>
<td>1.0</td>
</tr>
<tr>
<td>-5</td>
<td>1.1</td>
<td>1.1</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>0</td>
<td>0.9</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>2</td>
<td>1.1</td>
<td>1.1</td>
<td>0.9</td>
<td>1.0</td>
</tr>
<tr>
<td>5</td>
<td>1.1</td>
<td>0.9</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>10</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>15</td>
<td>1.0</td>
<td>0.9</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>30</td>
<td>1.0</td>
<td>0.9</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Actual Time (min)</th>
<th>sample</th>
<th>ACTH L</th>
<th>ACTH R</th>
<th>ACTH P</th>
<th>Cortisol L</th>
<th>Cortisol R</th>
<th>Cortisol P</th>
<th>Prolactin L</th>
<th>Prolactin R</th>
<th>Prolactin P</th>
</tr>
</thead>
<tbody>
<tr>
<td>-10</td>
<td>1</td>
<td>46</td>
<td>68</td>
<td>55</td>
<td>22</td>
<td>23</td>
<td>23</td>
<td>39</td>
<td>41</td>
<td>42</td>
</tr>
<tr>
<td>-5</td>
<td>2</td>
<td>74</td>
<td>71</td>
<td>68</td>
<td>23</td>
<td>23</td>
<td>23</td>
<td>40</td>
<td>41</td>
<td>39</td>
</tr>
<tr>
<td>0</td>
<td>3</td>
<td>64</td>
<td>67</td>
<td>70</td>
<td>23</td>
<td>23</td>
<td>23</td>
<td>40</td>
<td>40</td>
<td>39</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>71</td>
<td>71</td>
<td>67</td>
<td>22</td>
<td>23</td>
<td>23</td>
<td>36</td>
<td>38</td>
<td>39</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>112</td>
<td>98</td>
<td>105</td>
<td>23</td>
<td>24</td>
<td>23</td>
<td>37</td>
<td>38</td>
<td>38</td>
</tr>
<tr>
<td>10</td>
<td>6</td>
<td>121</td>
<td>122</td>
<td>121</td>
<td>27</td>
<td>26</td>
<td>26</td>
<td>38</td>
<td>38</td>
<td>38</td>
</tr>
<tr>
<td>15</td>
<td>7</td>
<td>126</td>
<td>115</td>
<td>132</td>
<td>30</td>
<td>31</td>
<td>29</td>
<td>37</td>
<td>37</td>
<td>38</td>
</tr>
<tr>
<td>30</td>
<td>8</td>
<td>123</td>
<td>113</td>
<td>124</td>
<td>34</td>
<td>35</td>
<td>33</td>
<td>33</td>
<td>34</td>
<td>34</td>
</tr>
</tbody>
</table>
Clinical questions?

• Pediatric Cushings- unique aspects
• Relationship between pseudotumor and Cushings Disease
• Management of pediatric CD w/neg MRI
Pediatric Cushings

- JCEM 2013, prospective observational
- 200 Cushing’s Disease patients
- Mean age sx = 10.6 ± 3.7 yrs
- Mean interval (sx to surg) = 3.3 ± 2.1 yrs
- Early remission rate 195 of 200 (98%)
- Factors affecting surgical outcomes in CD
  - Identifying adenoma in surgery
  - +immunohistochemistry for ACTH
  - Non-invasive adenoma

Pediatric Cushings

<table>
<thead>
<tr>
<th>Presenting Signs and Symptoms</th>
<th>Prepubertal Patients (n = 91)</th>
<th>Postpubertal Patients (n = 109)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid weight gain</td>
<td>88 (97)</td>
<td>98 (90)</td>
</tr>
<tr>
<td>Obesity&lt;sup&gt;a&lt;/sup&gt;</td>
<td>81 (89)</td>
<td>59 (54)</td>
</tr>
<tr>
<td>Dorsal cervical or supraclavicular fat pad</td>
<td>58 (64)</td>
<td>79 (72)</td>
</tr>
<tr>
<td>Moon facies</td>
<td>56 (62)</td>
<td>70 (64)</td>
</tr>
<tr>
<td><strong>Decreased linear growth</strong>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>77 (85)</td>
<td>48 (44)</td>
</tr>
<tr>
<td>Central obesity</td>
<td>57 (63)</td>
<td>66 (61)</td>
</tr>
<tr>
<td>Hirsutism</td>
<td>47 (52)</td>
<td>65 (60)</td>
</tr>
<tr>
<td><strong>Abdominal striae</strong>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>39 (43)</td>
<td>70 (64)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>43 (47)</td>
<td>52 (48)</td>
</tr>
<tr>
<td>Acne</td>
<td>44 (48)</td>
<td>50 (46)</td>
</tr>
<tr>
<td>Amenorrhea (primary or secondary)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>NA</td>
<td>49 (72)</td>
</tr>
<tr>
<td>Headaches</td>
<td>33 (36)</td>
<td>43 (39)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>27 (30)</td>
<td>44 (40)</td>
</tr>
<tr>
<td>Acanthosis nigricans</td>
<td>32 (35)</td>
<td>32 (29)</td>
</tr>
<tr>
<td>Depression, anxiety, mood swings</td>
<td>22 (24)</td>
<td>39 (36)</td>
</tr>
<tr>
<td><strong>Easy bruising</strong>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>14 (15)</td>
<td>35 (32)</td>
</tr>
<tr>
<td>Gynecomastia&lt;sup&gt;c&lt;/sup&gt;</td>
<td>8 (15)</td>
<td>9 (22)</td>
</tr>
<tr>
<td>Glucose intolerance or diabetes</td>
<td>2 (2)</td>
<td>11 (10)</td>
</tr>
<tr>
<td>Alopecia</td>
<td>3 (3)</td>
<td>8 (7)</td>
</tr>
<tr>
<td>Bone fractures</td>
<td>3 (3)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Nephrolithias</td>
<td>1 (1)</td>
<td>6 (6)</td>
</tr>
</tbody>
</table>

TSS in CD w/neg MRI

- Objective: Retrospective analysis of outcomes of TSS w/ biochemical CD and no visible adenoma on MRI
- 106 MRI+ and 18 MRI-
- Remission rate: 44% MRI- vs 94% MRI+
  - 0% in MRI- and IPSS-

TSS in CD w/neg MRI

Cushing’s disease

negative MRI (18 cases)

IPSS

inconclusive (one case)

positive (14 cases)

negative (3 cases)

CR adenoma(+) 7 cases

CR adenoma(−) one case

NR adenoma(−) 10 cases

Variables

• Neg MRI
  – Characteristics of tumor
  – Field strength
  – Technique
  – Method of analysis

Adenoma size vs. MRI results

Modifications to MRI

• Modifications to MRI
  – High-field strength: 1.5 or 3T MRI
  – Better methods: Dynamic or SPGR MRI
  • Acquires thin 1.0-2.0 mm cuts

# Pseudotumor and Cushings

<table>
<thead>
<tr>
<th>Reference</th>
<th>Case: age (yr) and sex</th>
<th>Treatment for hypercortisolism</th>
<th>Cortisol replacement</th>
<th>Time from treatment to PC onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newman et al (6)</td>
<td>18 M</td>
<td>Metrapone and aminoglutethimide</td>
<td>None</td>
<td>†</td>
</tr>
<tr>
<td>Martin et al (7)</td>
<td>29 F</td>
<td>Transsphenoidal surgery</td>
<td>HC, 30 mg/day</td>
<td>4 wk</td>
</tr>
<tr>
<td>Fischer &amp; Anast (8)</td>
<td>17 M</td>
<td>Transsphenoidal surgery</td>
<td>For 3 wk</td>
<td>7 wk</td>
</tr>
<tr>
<td>Weissman et al (9)</td>
<td>7 F</td>
<td>Transsphenoidal surgery</td>
<td>None</td>
<td>3 wk</td>
</tr>
<tr>
<td>Griffith et al (10)</td>
<td>55 F</td>
<td>Metrapone, 1,500 mg/day</td>
<td>HC, 30 mg/day</td>
<td>3 wk</td>
</tr>
<tr>
<td>Parfitt et al (11)</td>
<td>11 F</td>
<td>Transsphenoidal surgery</td>
<td>HC, 20 mg/day</td>
<td>14 wk</td>
</tr>
<tr>
<td>Current report</td>
<td>44 F</td>
<td>Total adrenalectomy</td>
<td>HC, 60 mg/day</td>
<td>2 wk</td>
</tr>
</tbody>
</table>

*HC = hydrocortisone; NA = not applicable; PC = pseudotumor cerebri.
†PC was present before treatment for hypercortisolism.
Steroid withdrawal is associated:

1. Reduction in CSF absorption
2. Increased resistance to CSF flow

Back to our patient

• Discussed case with his neurosurgeon Dr Frim and with Dr Stratakis (NIH) who recommended
  – CT chest (negative for ectopic source)
  – Chromogranin A (normal limits)
  – MRI abd/pelv

• Repeat MRI pituitary scheduled 8/26
Take Home Points

• Pediatric CD most common chief complaint: rapid weight gain and decreased linear growth
• Treatment in MRI neg, IPSS neg cases is controversial
• Pseudotumor cerebri can complicate the recovery of Cushing’s Disease patients post-treatment
References

• Rickels MR, Nichols CW. Pseudotumor Cerebri in Patients with Cushing’s Disease. Endo Prac 2004;10:492-496.