Cushing’s Disease in a 7-year-old due to corticotroph cell hyperplasia.

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Introduction

- Cushing's disease is the most common cause of endogenous Cushing's syndrome in children after the age of 5¹.
- It accounts for 70-85% of all paediatric Cushing's syndrome.
- In childhood it is male predominant, which equilibrates at puberty, and becomes female predominant as adults.
- The majority of Cushing's disease are caused by an ACTH-secreting pituitary corticotroph adenoma.
- Ectopic ACTH is extremely rare.
- Corticotroph cell hyperplasia has only been convincingly shown in two previous cases of paediatric Cushing's disease².

Clinical Presentation & Examination

- 7- year old presented with a ten-month history of obesity, hirsutism and growth retardation.
- He was a term baby and reached all appropriate developmental milestones.
- No specific drugs had been prescribed previously.

- Moon face
- Facial plethora
- Buffalo hump
- Central obesity
- Hirsutism
- Striae

Hgt: 2.5SD below age-mean
Wgt: 98th percentile

Diagnostic Imaging

- Noncontrast CT Adrenals.
- & MRI pituitary: unremarkable

Management

- Underwent Transphenoidal Surgery 3-months post IPSS confirmation of ACTH dependant Cushing’s syndrome.
- Abnormal tissue was resected from the left side of the pituitary.
- Histopathology revealed no adenoma but intense immunostaining for ACTH consistent with corticotroph hyperplasia.
- On the fourth day post-operation, am cortisol was 39nmol/L
- Three months post TSS, he remained hypocortisolaemic on hydrocortisone with significant clinical improvement.

Initial investigations

<table>
<thead>
<tr>
<th>Test</th>
<th>Basal (ng/ml)</th>
<th>Post CRH (1mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8am Cortisol</td>
<td>1159±64nmol/L</td>
<td>488.0±50pg/ml</td>
</tr>
<tr>
<td>8am ACTH</td>
<td>13±6nmol/L</td>
<td>69.2±14nmol/L</td>
</tr>
<tr>
<td>Midnight Salivary Cortisol</td>
<td>13±6nmol/L</td>
<td>69.2±14nmol/L</td>
</tr>
<tr>
<td>Midnight Salivary Cortisone</td>
<td>13±6nmol/L</td>
<td>69.2±14nmol/L</td>
</tr>
<tr>
<td>Urine Total Volume</td>
<td>1010±24hrs</td>
<td>232nmol/24hrs</td>
</tr>
<tr>
<td>Urinary Free Cortisol</td>
<td>1010±24hrs</td>
<td>232nmol/24hrs</td>
</tr>
</tbody>
</table>

Table 1 & 2 Endocrine testing at presentation

Inferior Petrosal Sinus Sampling

<table>
<thead>
<tr>
<th>Test</th>
<th>Basal (pg/ml)</th>
<th>Left IPS</th>
<th>Right IPS</th>
<th>Highest IPS : peripheral ratio</th>
<th>Lateralization ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH Sample</td>
<td>Peripheral</td>
<td>Left IPS</td>
<td>Right IPS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal</td>
<td>159</td>
<td>142</td>
<td>159</td>
<td>142</td>
<td>1.1</td>
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<tr>
<td>Post CRH</td>
<td>676</td>
<td>768</td>
<td>768</td>
<td>768</td>
<td>1.1</td>
</tr>
<tr>
<td>9min</td>
<td>676</td>
<td>768</td>
<td>768</td>
<td>768</td>
<td>1.1</td>
</tr>
<tr>
<td>10min</td>
<td>676</td>
<td>768</td>
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<td>768</td>
<td>1.1</td>
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<tr>
<td>15min</td>
<td>676</td>
<td>768</td>
<td>768</td>
<td>768</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Conclusion

- Early diagnosis of paediatric Cushing's disease remains a challenge.
- Definitive cure can be achieved by transphenoidal pituitary surgery but success rates vary from 45% to 78% in report series³.
- This case illustrates that pediatric Cushing's disease may be caused, albeit, rarely by corticotroph hyperplasia.
- The natural history of this entity is unknown, hence careful follow up is necessary.

References