An extremely rare cause of Cushing Syndrome in Childhood

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Case Vignette

- 3 year 4 month old female patient A.T.M.
- Referred from Stanger Regional Hospital
- Initially presented to base hospital with history of:
  - Body swelling for 1 month
  - Diarrhoea for 1 week
- Clinical examination at referral hospital revealed the following:
  - A body mass index that classified as overweight
  - Hypertension
  - Phenotypic features suggestive of Cushing Syndrome

Clinical examination at referral hospital revealed the following:

- Initially presented to base hospital with history of:  
  - Hypertension
  - Syndrome
  - Phenotypic Cushing
- No renal or other abdominal masses palpable.
- Abdominal distension with no visible veins.
- FSH (IU/L) 1,2
- Androstendione (nmol/L) 12,2 0,2-1,4
- CA 19-9(kU/L)
- Alpha Feto Protein (ug/L)
- Thyroid Function Tests Normal
- Renin (mIU/l) 23,4
- Vitals:
  - BP 159/118mmHg
  - Pulse 139 bpm
  - Height: 94 cm                (between 0 and -2SD)

Investigations at Stanger Regional Hospital

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Reference Range</th>
<th>Specimen 1</th>
<th>Specimen 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midnight Cortisol (nmol/L)</td>
<td>671</td>
<td>29-662</td>
<td></td>
</tr>
<tr>
<td>Midnight ACTH (pmol/L)</td>
<td>&lt;1.1</td>
<td>1,1-10,2</td>
<td></td>
</tr>
<tr>
<td>Morning cortisol (nmol/L)</td>
<td>1133</td>
<td>28-911</td>
<td></td>
</tr>
<tr>
<td>Morning ACTH (pmol/L)</td>
<td>45,1</td>
<td>1,1-10,2</td>
<td></td>
</tr>
<tr>
<td>24h UFC (nmol/L)</td>
<td>6280</td>
<td>85-807</td>
<td></td>
</tr>
<tr>
<td>Abdominal Ultrasound</td>
<td>Normal kidneys and adrenals. No masses identified</td>
<td></td>
<td></td>
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</tbody>
</table>

Laboratory

<table>
<thead>
<tr>
<th>Investigation</th>
<th>IALCH Normal Range</th>
<th>IALCH Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSH (IU/L)</td>
<td>1,2</td>
<td></td>
</tr>
<tr>
<td>LH (IU/L)</td>
<td>&lt;0,1</td>
<td></td>
</tr>
<tr>
<td>Radioactive (nmol/L)</td>
<td>1,6</td>
<td>0,1-0,3</td>
</tr>
<tr>
<td>STOHP (nmol/L)</td>
<td>5,1</td>
<td>0,5-3,1</td>
</tr>
<tr>
<td>SFEAS (ml/L)</td>
<td>3,5</td>
<td>0,1-0,6</td>
</tr>
<tr>
<td>Androstenedione (nmol/L)</td>
<td>12,2</td>
<td>0,2-1,4</td>
</tr>
<tr>
<td>Adrenosterone (nmol/L)</td>
<td>29,3</td>
<td>33-943</td>
</tr>
<tr>
<td>Nein (mU/L)</td>
<td>22,4</td>
<td></td>
</tr>
<tr>
<td>Urate Cholesterol</td>
<td></td>
<td>Negative</td>
</tr>
<tr>
<td>Thyroid Function Tests</td>
<td>Normal</td>
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</tbody>
</table>

Screening Tests for Cushing Syndrome

- Midnight Cortisol (nmol/L) 671
- Midnight ACTH (pmol/L) <1.1
- Morning cortisol (nmol/L) 1133
- Morning ACTH (pmol/L) 45,1
- 24h UFC (nmol/L) 6280

Abdominal Ultrasound

Solid, heterogeneous, well defined, 3.3 x 3.7 cm mass noted in the Left peri-renal space at the level of the mid pole of the left kidney.

Conclusion:

Left peri-re nal solid highly vascular mass noted. Highly suggestive of an adrenal mass however position and morphology is not typical of adrenal mass.

Investigations at Stanger Regional Hospital

- midnight cortisol = 907 nmol/L FAILED SUPPRESSION

Post-Operative Investigations

<table>
<thead>
<tr>
<th>Investigation</th>
<th>IALCH Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning cortisol(nmol/L)</td>
<td>58</td>
</tr>
<tr>
<td>Alpha Feto Protein(ug/L)</td>
<td>6,0</td>
</tr>
<tr>
<td>DHEAS (umol/L)</td>
<td>&lt;0,4</td>
</tr>
<tr>
<td>Testosterone (nmol/L)</td>
<td>0,5</td>
</tr>
<tr>
<td>Androstenedione (nmol/L)</td>
<td>&lt;1,1</td>
</tr>
</tbody>
</table>

Imaging

Abdominal Ultrasound

CT Abdomen Chest

There is heterogeneously enhancing well circumscribed exophytic mass lesion with foci of intra-tumoral necrosis noted in relation to the tail of the pancreas. The mass measures 4.6 x 3.9 x 4.5 cm.

Distal Pancreas:

Features are those of a solid pancreatic tumour with diffuse epithelial marker immunopositivity, patchy neuroendocrine immunopositivity, diffuse ACTH immunopositivity and focal Alpha-Fetoprotein immunopositivity.

The histomorphological features and patchy neuroendocrine immunopositivity favour a pancreatoblastoma.

Lymphovascular invasion is not identified.

Excision Biopsy

Final Assessment

Ectopic ACTH Dependent Cushing Syndrome secondary to AFP producing Pancreatoblastoma

Management and Progress

- Prior to surgery blood pressures were stabilized
- There was complete laparoscopic removal of the tumour (50g) (45 x 15 x 40mm)
- Hydrotoccosis was commenced immediately post surgery
- Chemotherapy deferred:
  - 1. Low trend AFP and low mitotic count on histology
  - 2. Complete excision of tumour
- Discharged home on oral hydrocortisone

References

- Available from: www.orpha.net

Acknowledgements: The Paediatric Endocrine team at IALCH

Cushing Syndrome in Children

- Rare in childhood
- Female predominance

- Classical clinical features include:
  - Weight gain
  - Growth failure
  - Hypertension
  - Compulsive overachieving behavior

- Causes include:
  - Exogenous administration of glucocorticoids and ACTH
  - Pituitary adenomas
  - Adrenal Tumours
  - Ectopic ACTH production

Ectopic ACTH producing Tumours

- Rare in children
- Accounts for less than 1% of Cushing Syndrome in adolescents
- Tumours that secrete ACTH include small cell carcinoma of the lung, carcinoid tumours of the bronchus, thymus and pancreas, phaeochromocytomas and neuroendocrine tumours particularly that of the gut and pancreas.

Pancreatoblastoma

- Pancreatic neuroendocrine tumour known to produce ACTH
- Very rare malignant, slow growing tumour
- One third present with metastases at presentation
- An incidental abdominal mass is the most common form of presentation
- The head and tail of the pancreas is the most common site while the liver is the most frequent site of metastatic disease
- Complete surgical resection of the tumour is the treatment of choice
- Chemotherapy maybe beneficial prior to surgery to reduce tumour size
- Even though these tumours are curable, long-term surveillance for recurrence is mandatory