Long Term Reversibility of Presumed ACTH Deficiency (ACTHd) in Children and Young People (CYP) with Intracranial Germ Cell Tumours (IGCT)

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Background

- ACTHd is life threatening and difficult to differentiate from ACTH suppression (ACTHs), especially in CYP receiving perioperative corticosteroids.
- In our experience, this is always the most robust anterior pituitary hormone whilst Ghd is the first and LH/FSHd and TSHd intermediate in hierarchy.
- We previously showed HPA axis recovery at 3.08 years after corticosteroid therapy in 13.6% of 44 CYP with craniopharyngioma and presumed ACTHd (1).
- Intact TSH and post-pubertal LH/FSH axis, as well as pre-dose ACTH>10ng/L were predictive of recovery (1).

Methods (figure)

- 46 CYP (24M) with IGCT treated at GOSH and UCLH were identified from local databases.
- Electronic case notes were reviewed.
- Patient auxology data, pituitary hormone dynamic evaluation and replacement therapy at first and last endocrine review in all CYP were recorded.
- Follow up was for 7.92 (0.75-24.18) years.
- Patients were examined in three groups; those never requiring cortisol replacement (Group A), those with presumed ACTHd who experienced ‘recovery’ from the suppression (Group B) and those with a persisting cortisol requirement at last endocrine review (Group C).
- Non-parametric statistical analysis (Mann Whitney, Chi squared and Kruskal Wallis) was used to analyse the differences between the groups.

Results (figure, tables 1,2)

- All but 14 patients had presumed ACTHd at diagnosis. Out of the 14: 8 purely pineal, 4 purely suprasellar, 2 bifocal IGCT
- 6/32 patients with presumed ACTHd discontinued hydrocortisone after 3.79 (0.02-6.16) years with median ACTH detectable at 23.05 (15.9-26.2)ng/L;
- 2 purely pineal, 3 purely suprasellar, 1 bifocal IGCT
- 26/32 patients remain ACTHd at latest follow up with median ACTH <0.7ng/L:
  - 3 purely pineal, 17 purely suprasellar, 6 bifocal IGCT
- Persisting cortisol requirement was associated with co-existing TSHd, LH/FSHd and ADHd (p=0.01) (Chi squared test Group A and B versus Group C).
- CYP remaining on hydrocortisone showed greater increment in BMISDS (p=0.039) (Kruskall Wallis between Groups A, B, C).

Conclusions

- Interval assessment of the HPA axis in CYP with IGCT shows recovery rate of 18.8% at 4 years follow up.
- Results are comparable with our previous craniopharyngioma cohort which showed HPA axis recovery at a rate of 13.6% (2).
- This data further supports that ACTHd overdiagnosis can aggravate secondary obesity.
- Purely pineal tumour position, detectable pre-dose ACTH and intact TSH, LH/FSH axis may predict the likelihood of ACTH recovery.
- We recommend interval re-testing of the HPA axis in all CYP after adolescence and inclusion of pre-dose 8am plasma ACTH in surveillance of CYP on hydrocortisone.

Aims

- To longitudinally assess the rates of HPA axis recovery in CYP with IGCT.
- To determine whether tumour position affects rates of HPA axis recovery in CYP with IGCT.

Table 1: Patient Characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>IGCT</th>
<th>ACTH Intact</th>
<th>ACTHs</th>
<th>Persistent ACTHd</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>14</td>
<td>13 (28.3%)</td>
<td>24 (52.1%)</td>
<td>9 (19.6%)</td>
</tr>
<tr>
<td>B</td>
<td>18</td>
<td>8 (57.1%)</td>
<td>4 (28.6%)</td>
<td>2 (14.3%)</td>
</tr>
<tr>
<td>C</td>
<td>20</td>
<td>2 (33.3%)</td>
<td>3 (50.0%)</td>
<td>1 (16.7%)</td>
</tr>
</tbody>
</table>

Table 2: ACTH recovery rates by tumour position

<table>
<thead>
<tr>
<th>Tumour Type</th>
<th>Pineal</th>
<th>Suprasellar</th>
<th>Bifocal</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>13 (28.3%)</td>
<td>24 (52.1%)</td>
<td>9 (19.6%)</td>
</tr>
<tr>
<td>ACTH intact</td>
<td>8 (57.1%)</td>
<td>4 (28.6%)</td>
<td>2 (14.3%)</td>
</tr>
<tr>
<td>ACTHs</td>
<td>2 (33.3%)</td>
<td>3 (50.0%)</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>Persistent ACTHd</td>
<td>3 (11.5%)</td>
<td>17 (65.4%)</td>
<td>6 (23.1%)</td>
</tr>
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References: