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% *(1).*
- 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.

Figure: ACTH Status with Time

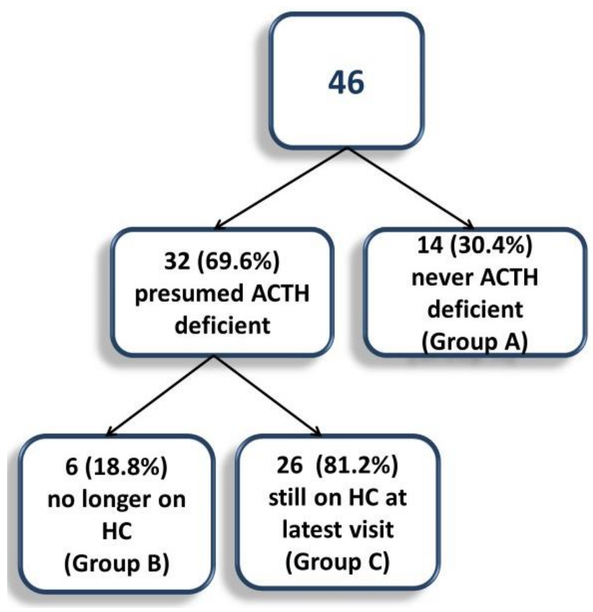

Table 1: Patient Characteristics

IGCT	ACTH intact	ACTHs	Persistent ACTHd
Age (years) at diagnosis	11.77(9.4-15.6)	10.6(9.79-12.23)	9.26(5.13-17.87)
Follow up (years)	9.10(3.82-15.33)	8.14(0.75-14.68)	7.59(1.33-24.18)
ACTH ng/L median (range)			
Primary visit	19.45(9.56-18.12)	16.0	<0.7(<0.7-12.0)
Latest Visit	8.3	23.05(15.9-26.2)	<0.7(<0.7-25.0)
Duration of HC Rx (years)	n/a	3.79(0.02-6.16)	9.46(0.54-34.24)
Pituitary hormone status at last follow up (N= patients with data)			
GHd	8/10(80%)	4/6(66.7%)	19/21(90.5%)
TSHd	3/10(30%)	2/6(33.3%)	19/21(90.5%)
LH/FSHd	0/10(0%)	1/6(16.7%)	16/21(76.2%)
ADHd	1/10(10%)	2/6(33.3%)	18/21(85.7%)
Latest auxology median (range)			
BMISDS	+0.16(-1.18 , +2.71)	+1.84(+0.04, +3.57)	+2.01(-1.11, +3.54)
BMISDS increment	+0.04(-1.61, +1.57)	+0.2(-1.27, +1.16)	+0.97(-0.28, +4.88)
HeightSDS	-0.07(-1.77, +2.83)	+0.35(-1.38, +1.73)	-0.58(-2.73, +1.58)

Table 2: ACTH recovery rates by tumour position

Tumour Type	Pineal	Suprasellar	Bifocal
All patients (N = 46)	13 (28.3%)	24 (52.1%)	9 (19.6%)
ACTH intact (N=14)	8 (57.1%)	4 (28.6%)	2 (14.3%)
ACTHs (N=6)	2 (33.3%)	3 (50.0%)	1 (16.7%)
Persistent ACTHd (N=26)	3 (11.5%)	17 (65.4%)	6 (23.1%)

References:

1) Pieri K, Michaelidou M, Dastamani A, Spoudeas HA. ACTH deficiency and potential for reversibility in children and young people (CYP) with craniopharyngioma.
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