Growth Outcomes in Childhood Craniopharyngioma: A Longitudinal Assessment of 20 Cases at a Single Centre

Michaelidou M[3], Losa L [1], Ederies A[2], Spoudeas HA[1]

[1]Paediatric Endocrinology, Great Ormond Street Hospital, London
[2]Paediatric Neuroradiology, Great Ormond Street Hospital, London
[3]School of Medicine, The University of Manchester

Great Ormond Street Hospital for Children NHS Foundation Trust

Background

Craniopharyngiomas are rare suprasellar tumours with good survival but high endocrine and hypothalamic morbidity. GH deficiency (GHD) is the commonest endocrinopathy and, like others, may precede diagnosis though often considered treatment-induced. Later obesity (BMI > +2SDS) may also be treatment or tumour related.

Aims and objectives

- To evaluate endocrinopathy, height, weight and BMI before and after conservative treatment aimed at avoiding hypothalamic morbidity.
- To assess pituitary integrity by dynamic testing before definitive therapy and by hypothalamic tumour invasion, with subsequent 6 monthly review for at least 6 months.

Methods and Population

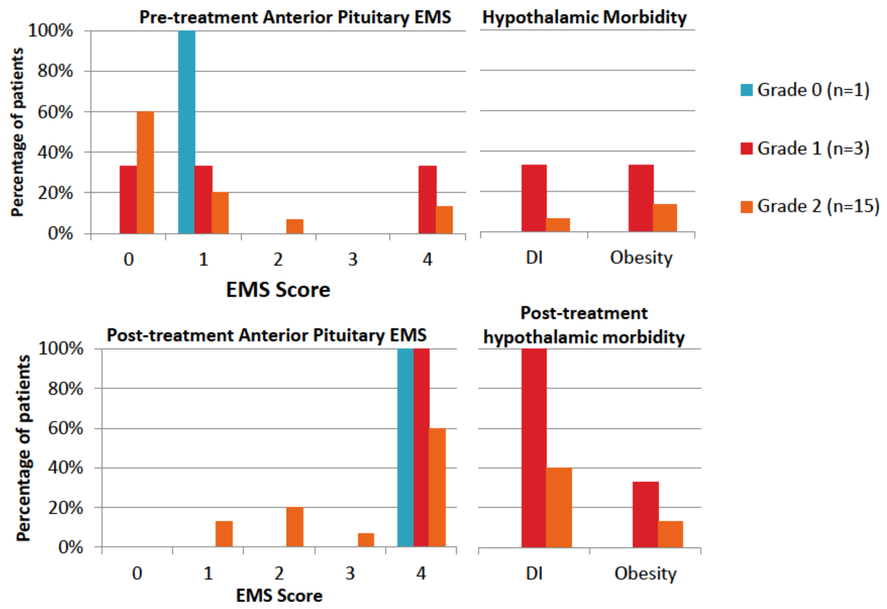
- Retrospective, longitudinal electronic case note review of patients diagnosed between 01/01/10 and 01/01/2015.
- Height, weight, BMI and Mid-parental height (MPH) SDS.
- Anterior pituitary endocrine morbidity score (EMS) at diagnosis and last follow up.
- Paris grade (0-2) of hypothalamic damage on presenting MRI.
- Paired data analysed by non-parametric statistics.

Table 1. Prevalence of Endocrinopathies- current cohort vs previous GOSH series

	Current Study 2010-2015 *(prospective hypothalamic sparing)* N=20, 13M, 7F		Prior GOSH 1998-2010 *(conservative treatment)* N = 40 [ref 1]	C De Vile et al 1996 *(radical surgery)* N=75 ref 2]
	Diagnosis	Last follow-up *Median 3.6 years*	Last follow up *Median 6 years*	Last follow-up *Median 7 years*
Hormone deficiency	N (%)	N (%)	N (%)	%
GH	7 (35)	20 (100)	39 (97.5)	96.0
TSH	3 (15)	15 (75)	35 (87.5)	93.3
GnD	2(10)	13(65)	27 (100)	94.5
ACTH	**3 (15)**	**14 (70)**	**29 (72.5)**	**85.3**
DI	**2 (10)**	**10 (50)**	**22 (55.0)**	**80.0**
Obesity	3 (15)	3 (15)	N/A	N/A

There may be less life-threatening ACTHd and DI with conservative regimens, but longer follow-up is required .

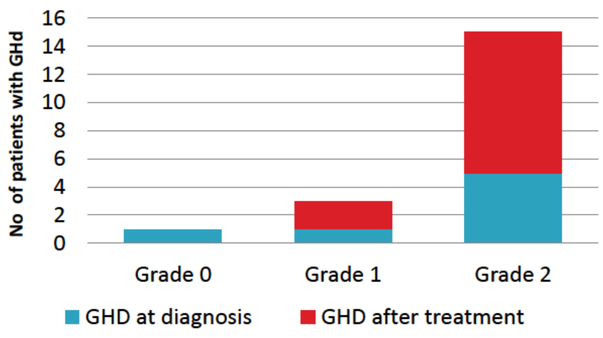
Figure 1: EMS at diagnosis and latest follow-up, by Paris Tumour Grade.



- Just 1 patient had G0 tumour and intact hypothalamus before and after treatment
- Definitive therapy increased EMS and hypothtlamic morbidity but tumour grade did not appear predictive (although small numbers prevented analysis)
- 1/3 G1 and 2/15 G2 were obese at diagnosis and this persisted after treatment.
- Even G1 patients had significant potential for hypothalamic morbidity

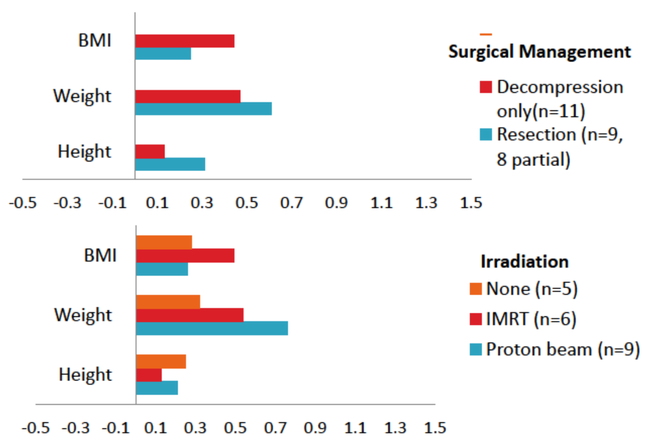
Results

Figure 2: Tumour grade does not appear to affect the timing of GHD deficiency.



- At presentation, 7/20 patients had pre-existing GHd even with Grade 0 or 1 tumours.
- The remaining 12 patients (57.1%) developed GHd at a median 0.15 [0.01-1.81] years after treatment.

Figure 3: Auxology increments do not appear related to treatment intervention



The type of surgical approach does not appear to influence auxology outcomes (p>0.05).

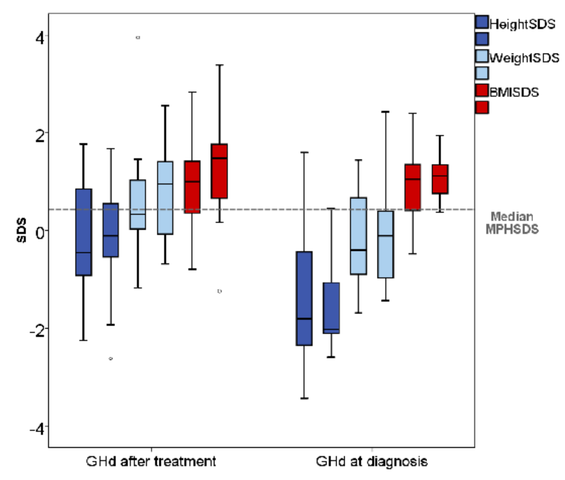
Patients not irradiated had comparable increase in BMI as those receiving irradation without a difference between IMRT and proton beam .

Table 2: Mean and 95% CI for baseline and incremental auxology by tumour grade

	HeightSDS		*WeightSDS*		*BMISDS*	
	Base	*Incr*	*Base*	*Incr*	*Base*	*Incr*
G 0	1.60	-1.89	1.44	-0.85	0.77	0.39
G 1	-0.64 [-22.8-21.54]	0.36	1.14 [-4.91-7.19]	1.10 [-5.12-7.32]	2.055 [-7.79-11.90]	-1.05 [-17.11-15.02]
G 2	-0.88 [-1.67-0.09]	0.25 [-0.63-0.57]	0.44 [-0.52-0.60]	0.72 [0.096-1.34]	0.94 [0.36-1.51]	0.34 [-0.11-0.79]
Total	-0.57 [-1.35-0.21]	0.05 [-0.36-0.45]	0.32 [-0.29-0.92]	0.58 [0.03-1.13]	0.95 [0.42-1.49]	0.14 [-0.32-0.61]

Patients were not significantly short at diagnosis (wide c.i.) but G2 patients were heavier (higher BMI SDS) than norms.
For the group overall, increments in height, weight and BMI SDS occurred with time and treatment.

Figure 4: Comparison of height, weight and BMI SDS by GHD status at presentation



Children with pre-existing GHd were significantly shorter at diagnosis than those without GHd (p=0.03); this difference persisted at follow-up (p=0.03).

Patients with pre-existing GHd are significantly shorter than their MPHSDS (p=0.04) even after GH replacement while those with post treatment GHd are not.

Children in both groups tend to be overweight before and after treatment, with comparable BMISDS scores. BMI does not significantly change after treatment for either group.

Summary

- Very few patients present with an intact hypothalamic floor (1/20) at diagnosis.
- Prospective dynamic pituitary assessment identifies a highly susceptible cohort for GHd, (35%) and obesity (15%). GH deficiency is an inevitable consequence within 2 years of presentation.
- Paris tumour grade at diagnosis does not appear to predict pre or post-treatment EMS and its effect on hypothalamic morbidity seems unrelated to the degree (grade 1 or 2) of disruption.
- Neither the application or type of irradiation or surgical intervention affect auxology outcomes, at least in the presence of timely replacement therapy.

Conclusion

- These data suggest a significant pre-treatment tumour-related aetiology for endocrine and hypothalamic morbidity, not always predictable by Paris grading and increased by treatment.
- A conservative treatment strategy avoiding hypothalamic morbidity together with timely GH replacement, may further preserve endocrine and auxology outcomes.

References 1. Ikazoboh EC et al. Endocrine, hypothalamic and neuro-developmental outcomes following treatment for craniopharyngiomas. Presented in BSPED Meeting 2010, Manchester UK. Endocrine Abstracts 24 P21.
2. DeVile et al. (1996b). Management of childhood cranio-pharyngioma: can the morbidity of radical surgery be predicted? J. Neu-rosurg.85, 73–81.

ESPE 2015 1131--P3
Puberty
Maria Michaelidou
DOI: 10.3252/pso.eu.54espe.2015
Poster presented at: 54th Annual Meeting 1-3 October ESPE 2015 BARCELONA European Society for Paediatric Endocrinology
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