Endocrine Outcomes in Hypothalamic Hamartoma – a single centre study

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Background

- Hypothalamic hamartoma (HH) are rare tumour-like formations of disorganised neuronal tissue
- Incidence: 1: 200 000 (children and adolescents) with slightly higher incidence in males (M:F ratio 1.3:1)
- Diverse presentation and severity of symptoms – most commonly central precocious puberty (CPP) and/or epilepsy (including gelastic seizures) and other neuro-behavioural changes
- Associated with Pallister-Hall Syndrome (mutations in *GLI3* but up to 25% show somatic mutations in *GLI3 i*n HH tissue even without features of Pallister Hall
- Neurology: Seizures can often have significant effect on quality if life for child (and their family) due to accompanying severe cognitive and behavioural problems
- Endocrinology: CPP is typically GnRH dependent. It results in a rapid increase in growth rate, advanced bone age and the development of early secondary sexual characteristics. It can compromise final height and lead to various other social consequences.
- At present the majority of reviews and case series are focused on evaluating the neurological outcomes following neurosurgery. The current literature on the endocrinological outcomes is scarce

Aim

To look at the endocrine outcomes of patients with hypothalamic hamartomas in a single centre

Methods

- A retrospective casenote review of all patients diagnosed with hypothalamic hamartoma over a twenty year period (1995-2015) was analysed in a single endocrine centre.

GnRHa therapy decelerated bone maturation over time

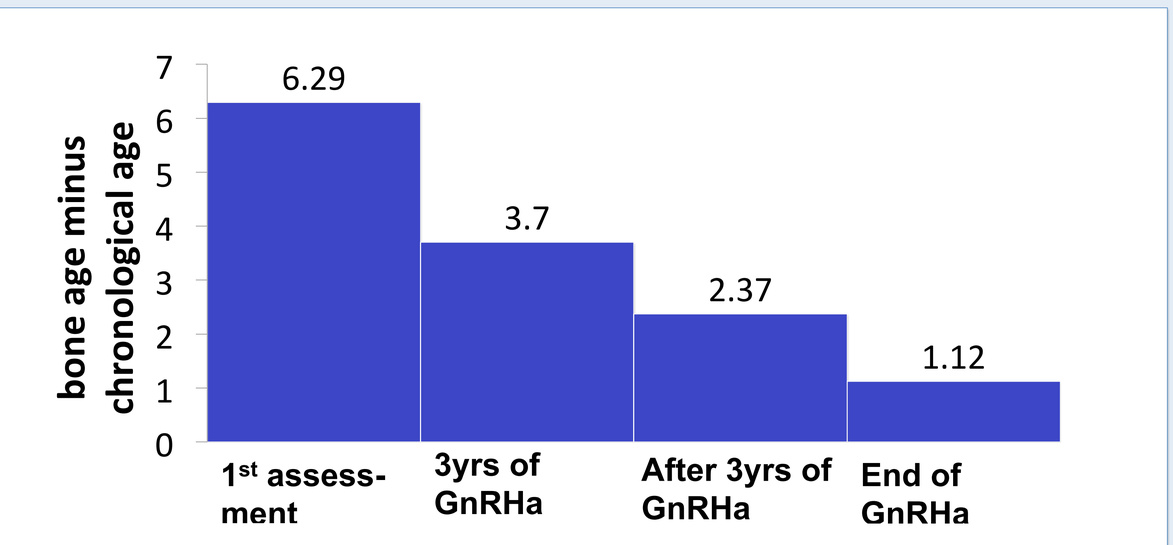

Chart 1: change in difference between bone age and chronogical over time with GnRHa therapy

Data was available for 10 children. Bone maturation decelerated with GnRHa therapy. Mean advancement in bone age at diagnosis was 6.29 (n=10) and near the end of therapy is 1.12 (n=9).

Conclusions

Most studies on HH have focussed on neurological/behavioural outcomes or endocrine presentations. Here we show that final height in the majority of patients is not adversely affected compared to the general population and that the main endocrine abnormalities at diagnosis are CPP and GHD with excessive weight gain being a long-term issue

Results

Demographics

- 17 patients (6M: 11F); 13 with CPP (4M: 9F)
- 1 patient had Pallister-Hall Syndrome
- Mean age at first assessment 3.39 (n=17)
- Mean age of diagnosis of CPP 3.83years (n=13; range 0.08-9.5)
- 4 had surgery for intractable seizures

Auxology

- Mean Final Height 0.02 (n=8; range -1.52-+2.06)
- Most patients (4/6) achieved height within the expected mid-parental target range

Metabolic Outcomes

- Mean BMI SDS +2.36 (1.39-3.33)
- For 8 who completed puberty, 2 were severely obese with BMI SDS >3SD, 5 were overweight with BMI SDS > 2 with only 1 with a normal BMI at final height
- Of the 4 patients who underwent surgery for epilepsy, 2 were severely obese with BMI SDS >3

Puberty

- 4/9 had vaginal bleeding at presentation - All menses ceased with GnRHa therapy.
- Average of 2.25yrs (n-4) for regular menstruation to return once GnRHa therapy stopped
- No data is available about fertility

Other Endocrinology

- 2 patients demonstrated growth hormone deficiency (GHD)
- 3 patients developed diabetes insipidus post surgery for intractable seizures

Table of diagnoses identified

Gelastic seizures	3	Isolated GH deficiency	1
Generalised tonic clonic	1	Juvenile xanthogranuloma	1
Epileptic encephalopathy	1	Haemangioma	1
Drop attacks	2	Histiocytosis non-langerhans cell cutaneous lesions	1
Complex partial	1	Autoimmune hepatitis	1
CPP	9	Visual defect	4
Learning difficulty and developmental delay	4	NF1	1
Autistic spectrum disorder	1	Café au lait	1
Hypothalamic obesity	3	Multiple hamartoma	1
hypopituitarism	1	Acanthosis nigricans	2
Pallister Hall Syndrome	1		2

Table 1: Diagnoses identified in our group of patients.

There was a total of 17 children, 9 of which had CPP. 3 children had gelastic seizures of which 1 progressed to epileptic encephalopathy.

References

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