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# Growth hormone-secreting pituitary adenoma with gigantism: A challenging case

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## Introduction:

Pituitary gigantism is a rare condition arising from excessive secretion of growth hormone (GH) during childhood, usually associated with a pituitary micro- or macro-adenoma and sometimes with specific gene mutations which predispose to these (1). Successful treatment goals include limiting final height attainment as well as normalisation of GH to prevent future development of acromegaly and co-morbidities, definitive tumour control, and replacement of any pituitary hormone deficiencies. We present a case requiring the full spectrum of therapeutic options.

## Case Report:

**History:** A 15 yr old boy presented with 3 yr history of intractable occipital headache and complaint of rapid, excessive growth during puberty. He was psychologically distressed by his height of 203cm, and how his tall stature had impact on social relationships and daily lifestyle. He had mild clinical features (facial) suggestive of GH excess. Pubertal development was age appropriate. Bone age not advanced. No visual deficit.

## Investigations:

***Serum IGF-I*** 103 nmol/L (RR 13-66)
***Testosterone*** 3.7 nmol/L (low for pubertal status)
***fT4*** 15pmol/L (normal)
***Cortisol response to Synacthen (250mcg IV) was impaired***:
- - - - (basal 72 nmol/L, 447 nmol/L at 30 min).
***Serum GH failed to suppress with oral glucose*** (75G)
- - - - (see table).

| Time min | GH ug/l | Glucose mmol/l |
|---|---|---|
| -30 | 28.4 | 4.5 |
| 0 | 24.2 | 4.1 |
| 30 | 24.4 | 5.8 |
| 60 | 19.2 | 7.3 |
| 90 | 14.9 | 6.3 |
| 120 | 11.1 | 5.4 |
| 150 | 23.0 | 4.7 |
| 180 | 34.4 | 4.1 |

**MRI pituitary** revealed a pituitary macroadenoma (18mm x 18mm x 22mm), impinging from below on the posterior aspect of the optic chiasm, with lateral invasion of left cavernous sinus (see images far right).

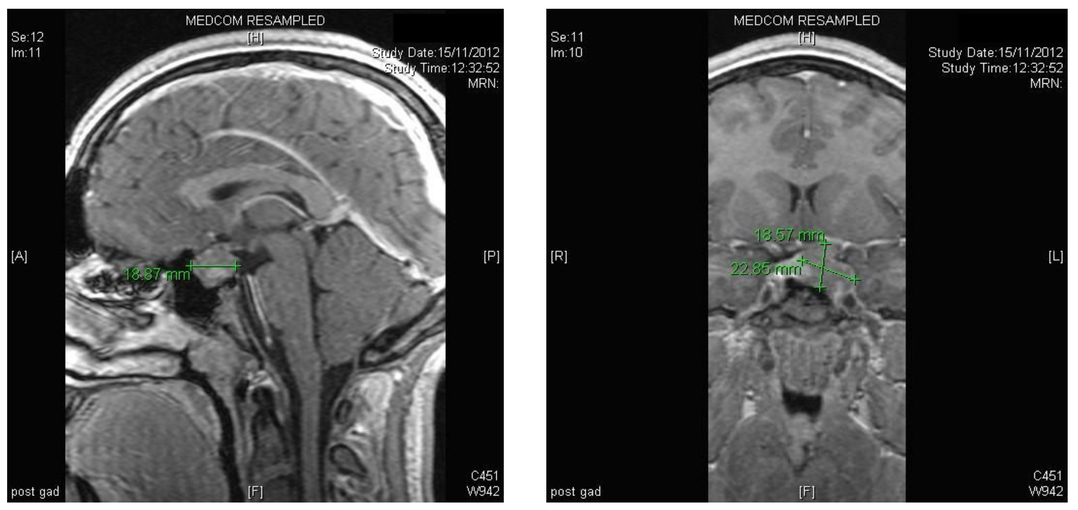



*Figure (above): Pituitary MRI at presentation*

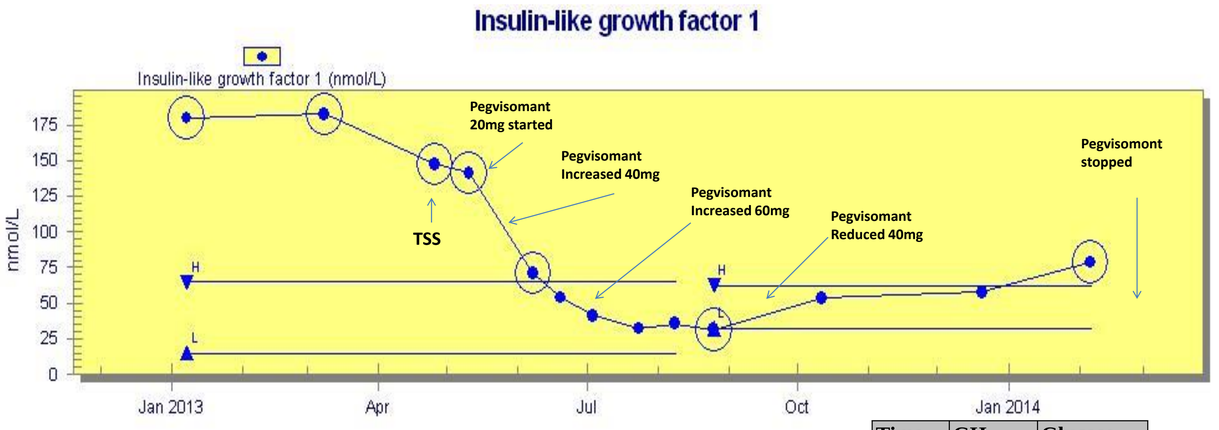
GH was partially suppressed by ***Octreotide*** (100mcg) from 50 to 25 mcg/L by 6 hrs, and possibly better suppression observed with ***Pasireotide*** (600 mcg) from 28 to 8 mcg/L by 6 hrs (see tables).

**Octreotide 100mcg sc**

| Time (hr) | GH (mcg/l) |
|---|---|
| 0 | 50.5 |
| 2 | 30.6 |
| 4 | 22.7 |
| 6 | 25.3 |

**Pasireotide 600mcg sc**

| Time (hr) | GH (mcg/l) |
|---|---|
| 0 | 27.6 |
| 2 | 7.9 |
| 4 | 7.6 |
| 6 | 8.4 |




## Treatment & Progress:

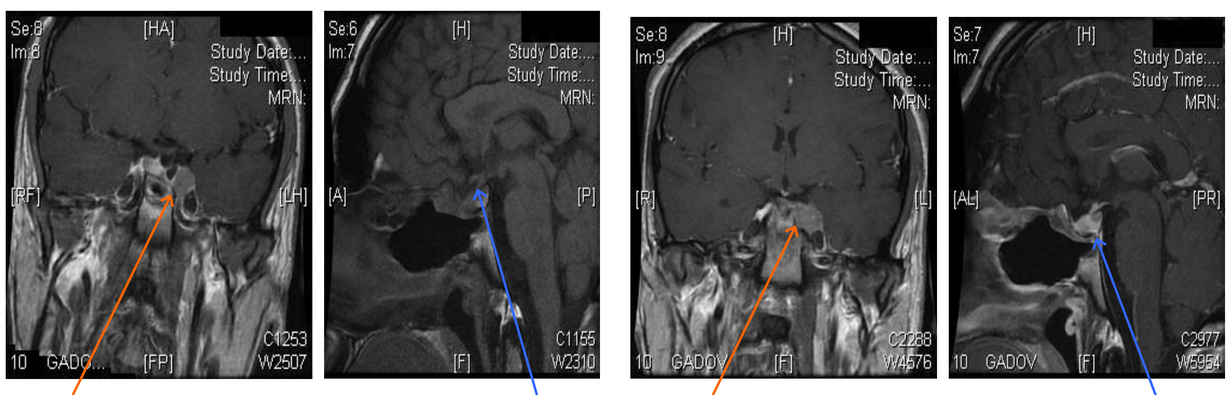
- ***Testosterone*** (Nebido 1000 mg IM 3-monthly ) was started to accelerate epiphyseal fusion.
- ***Hydrocortisone*** replacement started at standard dose.
- ***Depot Octreotide*** (Sandostatin Lar; 20 mg sc/month) was started.

Over 2 months the headaches failed to improve, tumour mass failed to show regression in volume and a slight unilateral upper quadrant visual field deficit was apparent – suggesting tumour expansion. Serum IGF-I levels were not significantly suppressed (see figure above right panel).

## Surgery:

Trans-sphenoidal debulking of tumour was performed, leaving residual left parasellar and posterior tumour mass (see MRI images below).

**Histology** - pituitary adenoma, strongly immuno-positive for GH, Ki67 3%.




*Post-operative (3-month) MRI appearances:*
Residual parasellar mass
Optic chiasm decompressed

*Post-operative (7-month) MRI appearances:*
Increased size left parasellar and posterior residual somatotroph adenoma

## Outcome:

- Headaches improved.
- Visual fields normalised.
- Post-op. Oral Glucose load showed basal GH 3 mcg/l without suppression – see table.

| Time min | GH mcg/l | Glucose mmol/l |
|---|---|---|
| -30 | 3.4 | 4.3 |
| 0 | 3.3 | 4.4 |
| 30 | 3.1 | 5.8 |
| 60 | 2.5 | 6.5 |
| 90 | 2.5 | 6.0 |
| 120 | 2.9 | 5.0 |
| 150 | 3.4 | 4.1 |
| 180 | 7.8 | 4.0 |

Serum IGF-I levels remained markedly elevated, and treatment with Pegvisomant to block peripheral effects of GH was started, the dose rising to 60 mg/day, which achieved normalisation of IGF-I after 2 months. Epiphyses on hand radiograph for "Bone age" were then effectively fused and height stabilised at 205 cm.

**Radiotherapy** to control residual tumour was offered, but the patient declined at that stage, wishing to focus on a return to his academic studies with a view to radiotherapy after current academic year, unless changed clinical circumstances led to reconsider that plan. However, interval MRI scan after 4 months (images to left) showed significant increase in residual adenoma and the patient has since undergone standard photon 47 Gy radiotherapy in 25# over 5 weeks, completed April 2014.

## Further Medical Treatment

- Patient profoundly disliked the taste of Hydrocortisone – this has been substituted with Prednisolone once daily.
- Compliance with Pegvisomant was increasingly poor (see rising IGF-I level in figure in adjacent column). This has now been discontinued.
- Consideration is being given to introduce Pasireotide treatment which will potentially be better tolerated than Pegvisomant as a monthly injection, and may prove to be more effective than Octreotide (see test dose responses and refs 2 and 3 – the latter suggesting that Pasireotide may be more effective in patients with gigantism who harbour mutations in the *AIP* gene).
- Genetic studies are underway.
- Psychological support is being provided to help the patient and his mother.
- Latest MRI shows possible reduction in pituitary size, though it was too soon after radiotherapy to appreciate full effects. Further MRI scan is booked for December 2014

**References**

1) Chahal HS, Stals K, Unterlander M, Balding DJ, Thomas MG *et al. AIP* mutation in pituitary adenomas in the 18th century and today. *New Engl J Med* 2011, 364:43-50.
2) Colao A, Bronstein MD, Freda P, Gu F, *Shen C-C et al.* Pasireotide versus Octreotide in acromegaly: a head-to-head superiority study. *J Clin Endocrinol Metab* 2014, 99(3):791-799.
3) Gadelha MR, Kasuki L & Korbonits M. Novel pathway for somatostatin analogs in patients with acromegaly. *Trends in Endocrinology & Metabolism* 2013, 24(5):238-246.