# Growth hormone (GH) secreting pituitary adenomas in Paediatric Practice: 5 cases over 20 years in a single tertiary Neuro-Endocrine Centre

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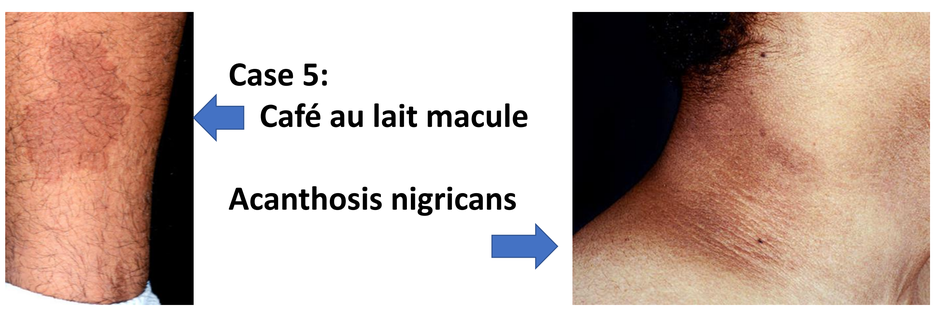
## Background

Growth hormone (GH) - secreting Pituitary adenomas rarely present in childhood and seem more likely to require multi-modal therapies than adults (1). We report the clinical features, management and outcome of the 5 cases presenting to a Regional Paediatric Endocrine/Neurosurgical service (population catchment ~3.5 million) over a 20-year period.

## Presenting Demographics and Clinical Features

| No | Sex | Date of presentation | Age (years) | Tanner Puberty | Symptoms | Clinical features of GH excess | Growth | Visual field defect | Cutaneous markers |
|---|---|---|---|---|---|---|---|---|---|
| 1 | M | 04/1997 | 15.5 | G5 TV20 | Ankle pains; **HA** 4 years, TS (noted by GP) MPH 172cm/ - 0.89 SDS | Broad hands, shoe #13, thick skin, Xs sweating, subtle facial features | Ht 196.5cm (+ 3.5 SDS) Wt +2.2 SDS | None | Small café-au-lait macules (2) on trunk |
| 2 | F | 07/2001 | 15.4 | B5 | **HA** 4 years, 2° amenorrhoea | Broad hands, thick skin | Ht 176.0cm (+2.2 SDS) Wt +5.6 SDS | None | None |
| 3 | M | 12/2012 | 15.1 | G5 TV20-25 | Occipital **HA**, TS, Rapid height gain in puberty | Tall stature, shoe #13, subtle facial features | Ht 202.7cm (+4.0 SDS) Wt + 2.6 SDS | None at Δ ? Evolving on Lanreotide | None |
| 4 | M | 10/2014 | 15.4 | G3 TV6 | **HA**, arrested puberty Blurred vision ~ 1 year | Clinically normal | Ht 167.0cm (-0.6 SDS) Wt – 0.3 SDS | BH – resolved post-surgery | None |
| 5 | M | 02/2018 | 15.9 | G5 TV20-25 | HA, rapid growth, blurred vision, polydipsia, AN | Excess sweating, large feet, acromegalic facial features | Ht 189.7cm (+2.1 SDS) Wt +3.2 SDS | BH – resolved post-surgery | Large café-au-lait macule on shin Bone scan -ve |

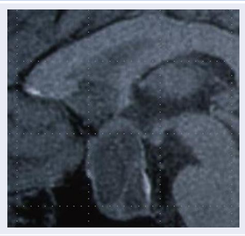
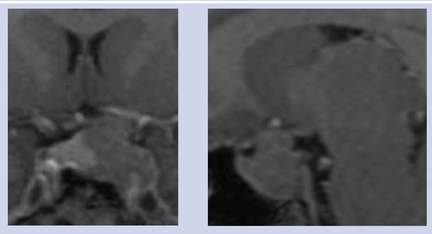
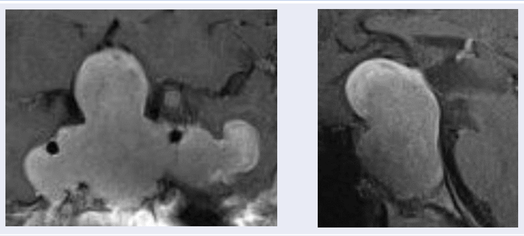
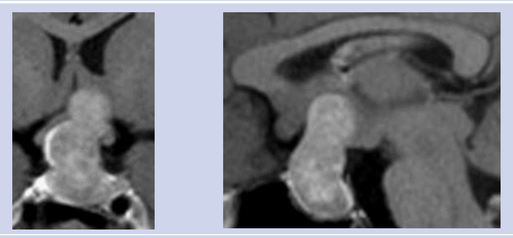
**Key: HA** – headache, **TS** – tall stature, **GP** – General practitioner, **AN** – acanthosis nigricans, **BH** – Bitemporal Hemianopia




## Biochemical Findings

| Number | Peak GH (mcg/L) | GH nadir on OGTT | Basal IGF (nmol/L) | Prolactin (mIU/L) |
|---|---|---|---|---|
| 1 | 26.6 | 14.3 | 149 (no ref. range) | 288 |
| 2 | 5.3 | 4.2 | 85 (no ref. range) | **1570** |
| 3 | 34 | 11.1 | 103 (13-66) | <40 |
| 4 | 9.7 (random) | Not performed | 66 (15-66) | **44675** |
| 5 | 115 (random pre-surgery) | Not performed | 172 (6-68) | 378 |

## Imaging and Histopathology

| Number | 1: Max diameter 20mm | 2: 25mm CC x 20mm AP | 3: 22mm CC x 18mm Trans x 19mm AP | 4: 58 mm coronal x 52 mm sagittal | 5: 34mm CC x 24mm Trans x 20mm AP |
|---|---|---|---|---|---|
| **Imaging:** Max dimensions CC: cranio-caudal Trans: Transverse AP: Anterior-Posterior | Largely intrasellar mass larger eccentrically on the Left – extends upwards slightly deviating hypophyseal stalk to Right and extends eccentrically posteriorly. |  |  |  |  |
| **Histopathology** | Pituitary adenoma – somatotroph; strong positivity GH and pan α. | Pituitary adenoma – somato-mammotroph | Pituitary adenoma; GH strongly positive, a few scattered positive cells with pan-α-subunit and prolactin (1+); **Ki67: 3% NB:** ***Genetics AIP +ve*** | Pituitary adenoma; focal GH positive, predominant prolactin positive **Ki67: 1%** | Pituitary adenoma, diffuse GH expression with focal prolactin expression. Sparsely granulated somatotroph adenoma **Ki 67: 8%** |

## Treatment and Follow-up

| No | Transsphenoidal cyto-reductive surgery | Endocrine deficits | Somatostatin analogue | Pegvisomant | Photon beam irradiation | Date of last follow-up | Status at last follow-up |
|---|---|---|---|---|---|---|---|
| 1 | 05/1998 (Δ + 13 months) | ACTH deficiency (pre-surgery); peak 485 on IST post-surgery | Octreotide => Lanreotide | Not available | 08/1999 | 09/2002 (Δ + 4yrs) | **Active GH excess**. *Final height 202cm* On: Lanreotide 90mg monthly. IGF normal. |
| 2 | 09/2001 (Δ + 2 months) | None | None | Not available | 10/2003 | 08/2008 (Δ + 7yrs) | Acromegaly ***in remission***. *Final height 176cm* No treatment. |
| 3 | 04/2013 (Δ + 4 months) | ACTH and prolactin deficiency (present pre-surgery) | Lanreotide / =>Pasireotide: *- non-compliant* | No | 04/2013 | 06/2017 (Δ + 4yrs) | Acromegaly ***in remission***. *F. Ht 205cm* On: Prednisolone OD (poor compliance Hydrocortisone); Thyroxine; Testosterone |
| 4 | 11/2014 (Δ + 1 month) | ACTH, TSH and GnRH deficiency (present pre-surgery) | Lanreotide: 02/2018 | No | Under consideration | 09/2018 (Δ + 4yrs) | **Active GH excess** – no acromegaly. *Height 180cm* On: Lanreotide 120mg/mo; *IGF 51 (16-67 nmol/L*); Cabergoline 0.5mg OD; *PRL 238 (<410 mIU/L).* |
| 5 | 02/2018 (Δ + 4 days) - for **PET scan** to guide surgical approach to residual tumour | ACTH, TSH and GnRH deficiency, diabetes insipidus, Type 2 DM (resolved on metformin and decrease of hydrocortisone) (all post-surgical) | Lanreotide 120mg/mo. (stopped 09/18 as ineffective) | 09/2018 | Under consideration | 09/2018 (Δ + 6mo.) | **Active GH excess** *Present Height 191.5 cm (+2.25SDS)* On: Hydrocortisone; Thyroxine; DDAVP; Metformin; Testosterone Pegvisomant 20 mg/d |

## Discussion

These patients, although rare, present significant management issues. All patients were 15 years old, presenting during adolescence. In itself this is a time of great change, physical, social and emotional. The complexities of their medical and surgical management plans were complicated by educational and psychological challenges. In the UK 15-year-olds are studying for and sitting their GCSE examinations, the results of which will help to shape their future educational and career plans. Patient 1 demonstrated variable compliance with his medication, and patient 3 was unable to tolerate the side effects of both the somatostatin analogue and Pegvisomant. As a Multidisciplinary Team, we need to be aware of these challenges and ensure that we offer adequate support to these young people.

**Reference:**

***1) Nagata Y, Inoshita N, Fukuhara et al.*** **Growth hormone-producing pituitary adenomas in childhood and young adulthood: clinical features and outcomes. Pituitary 2018, 21:1-9**