# ACTH-dependent Cushing's syndrome unmasked following transphenoidal surgery for Acromegaly – the rare coexistence of dual endocrinopathies

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## INTRODUCTION

- Coexistence of Acromegaly with Cushing's syndrome in the same individual is rare.
- We describe the case of a woman, whose hypercortisolism was unmasked following transphenoidal surgery for Acromegaly and discontinuation of her somatostatin analogue.

## INITIAL PRESENTATION: *Acromegaly*

- A 59 year old lady presented to the Endocrine Clinic with acromegalic appearances.
- ***Past Medical History:*** Hypertension, glaucoma, subtotal thyroidectomy for multicystic thyroid
- ***Drug History:*** levothyroxine, lisinopril, atenolol

### Course of events:

- MRI revealed a pituitary macroadenoma 20×18×18 mm.
- Repeat dynamic evaluation showed inadequate GH suppression (initially normal), in keeping with Acromegaly.

| Minutes | Glucose (mmol/L) | Growth Hormone (mU/L) |
|---|---|---|
| **0** | 4.4 | 8.8 |
| **30** | 7.7 | 5.5 |
| **60** | 9.0 | 4.1 |
| **90** | 6.8 | 3.2 |
| **120** | 4.9 | 3.9 |

**Table 1:** Oral Glucose Tolerance Test shows inadequate suppression of growth hormone to normal levels <3mU/L.

- She was started on Cabergoline 500mcg twice weekly; later increased to 1mg twice weekly.
- As IgF-1 remained elevated, Cabergoline later switched to Lanreotide with increasing doses.
- Due to evolving visual defects, she was referred to MDT and underwent transphenoidal surgery.
- Histology revealed a sparsely granulated somatotroph adenoma, ACTH-staining negative with Ki67<1%. Cytology showed monotonous neuroendocrine cells.
- ***Pre-operative*** 9am serum cortisol = 287nmol/l.
- P***ost-operative serum cortisol >1000 nmol/l on discharge***.

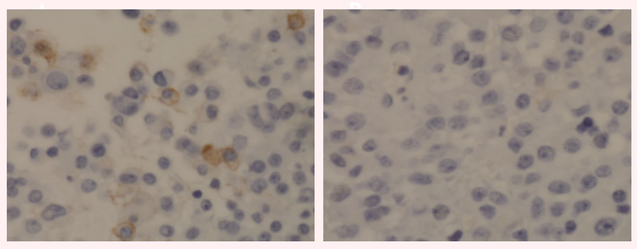

**Figure 1:** **[A]** Immunostaining confirms GH positivity in a proportion of cells (x60). **[B]** ACTH immunohistochemistry in high power indicates negative staining (x60). Prolactin, LH, FSH, TSH were also negative.

## POST-OPERATIVE PRESENTATION: *The unmasking of Cushing's syndrome*

### 1. One month post-operatively:

- Presented with typical Cushingoid facies, new onset diabetes mellitus, hypertension with severe hypokalaemic alkalosis and significant proximal myopathy.

### 2. Baseline investigations:

| | Pre-operative | 1 month Post-operative | Reference Range |
|---|---|---|---|
| **Sodium** | 138 mmol/L | 142 mmol/L | 137-145 mmol/L |
| **Potassium** | 4.6 mmol/L | 2.4 mmol/L | 3.6-5 mmol/L |
| **Urea** | 7.6 mmol/L | 4.9 mmol/L | 2.5-6.1 mmol/L |
| **Creatinine** | 80 mmol/L | 49 mmol/L | 46-92 mmol/L |
| **Cortisol** | 287 nmol/L | 2020 nmol/L | 119-618 nmol/L |
| **ACTH** | - | 186 ng/L | 0-46 ng/L |
| **TSH** | 0.82 mu/L | 0.8 mu/L | 0.35-5.5 mu/L |
| **fT4** | 18.0 pmol/L | 10.9 pmol/L | 9-22.7 pmol/L |
| **LH** | 38.1 U/L | < 0.1 U/L | - |
| **FSH** | 100.4 U/L | < 0.5 U/L | - |
| **GH** | 2.39 ug/L | 0.49 ug/L | - |
| **IGF-1** | 33.3 nmol/L | 17.9 nmol/L | 6-36 nmol/L |
| **Prolactin** | 521 mu/L | 112 mu/L | - |
| **24hrs Urinary Cortisol** | - | 7906 nmol/24hr | 119-618 nmol/24hr |

**Table 2:** Pre- and post-operative baseline bloods.

## FURTHER INVESTIGATIONS

- **Overnight, Low & High-dose dexamethasone suppression tests: -** failure to suppress
- **CT chest/abdomen/pelvis:** Bilateral pulmonary emboli, right lung nodule (unchanged from previous imaging), bilateral adrenal hyperplasia

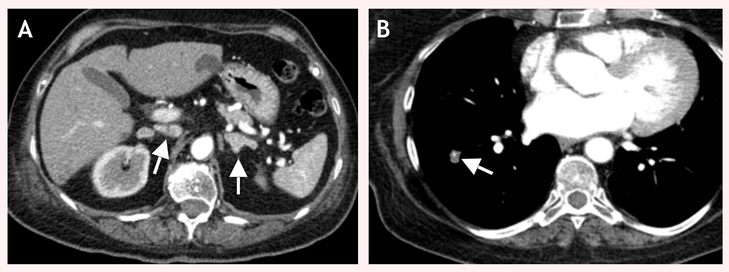


**Figure 2:** **[A]** CT scan confirming bilateral adrenal hyperplasia. **[B]** Right lung nodule remaining unchanged on

- **FDG-PET:** New bilateral avid adrenal hyperplasia (normal 6months earlier), with persistent incidental non FDG-avid lung and thyroid lesions
- **MRI pituitary**: significant residual pituitary tumour burden post-operatively

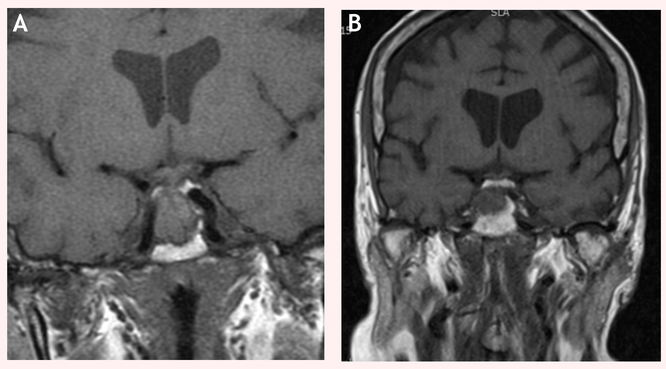


**Figure 3:** MR imaging of the sellar region demonstrated an enlarged pituitary gland – pre-operative image **[A].** Post-operative imaging showed significant residual tumour burden **[B]**.

## MANAGEMENT

- She was initiated on Metyrapone 250mg TDS and Octreotide 50mcg OD with clinical improvement a few days later.
- Discussion in Lung/Thyroid MDT advised FNA not required as lung and thyroid lesion unlikely to be ectopic ACTH source.
- Whilst awaiting transfer to the local tertiary centre, she unfortunately became septic and died from a stroke.

## DISCUSSION & LEARNING POINTS

1. Co-existence of Cushing's syndrome with Acromegaly in the same individual is rare.
2. The true source of excess ACTH causing hypercortisolism in this case remains a discussion point, as post-mortem findings were inconclusive. However, it is apparent her ACTH dependent Cushing's was unmasked following transphenoidal surgery and discontinuation of Lanreotide.
3. Multiple pituitary lesions are very rare, with an incidence evaluated at <1% in unselected autopsy series; most of which are clinically silent.
4. Co-occurrence of Acromegaly and hypercortisolaemia may also be a consequence of coexistence of the GH-secreting pituitary adenoma and adrenal tumour/nodular adrenal hyperplasia or ACTH-secreting bronchial carcinoid.
5. Further investigations ideally required include bilateral inferior petrosal sinus and peripheral vein sampling.
6. Close endocrine surveillance in postoperative pituitary patients in the acute, medium and long-term phases remains paramount.
7. Prompt early management of active Cushing's is imperative to minimize significant morbidity and mortality.

**References:**

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BES2016 10--CC

Neuroendocrinology and pituitary

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DOI: 10.3252/pso.eu.BES2016.2016

Poster presented at: SfE BES 2016 7-9 November BRIGHTON

PosterSessionOnline.com