A difficult case of Cushing's disease with unexplained hypertension and rapid metabolic decompensation

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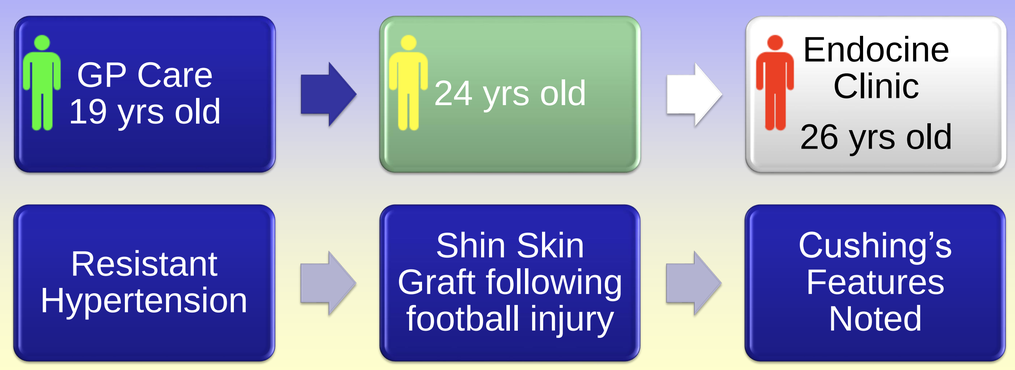
CASE HISTORY

<u>Endocrine Referral</u>: A 26 year old man of Angolan descent presented to the endocrine clinic with poorly controlled hypertension (systolic blood pressure >200 mmHg). He had been treated with Amlodipine for almost six years, and more recently the addition of Irbesatan and Indapamide had not led to adequate blood pressure control. His hypertension was diagnosed at age 19 and progressive features of Cushing's disease had remained unnoticed, with truncal striae, easy bruising, myopathy, puffiness around the face and lower leg swelling. In the previous year he had had a skin graft to his right leg following a football injury, which prompted his referral.

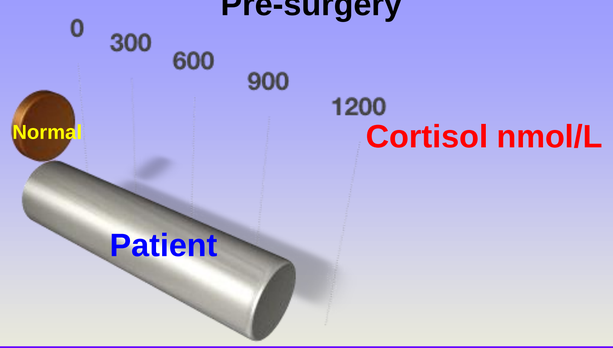
<u>Cushing's disease</u>:
Insidous- onset; typical late diagnosis pick-up



Investigations

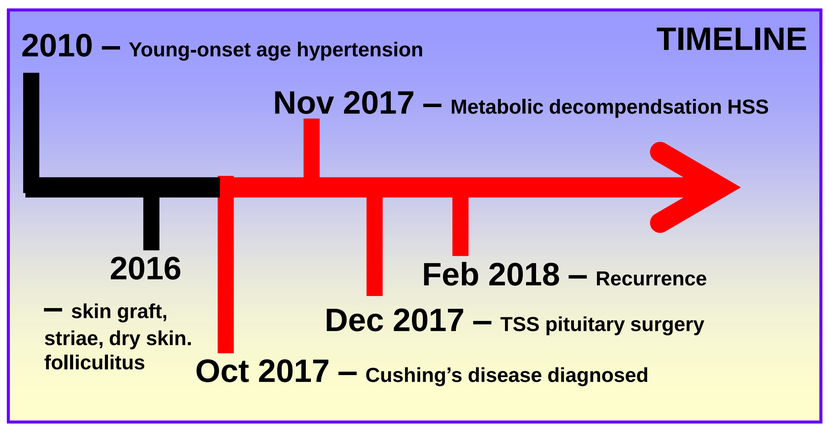
Investigations showed failure of cortisol suppression on a low dose dexamethasone suppression test (time=48 hours, cortisol 1107nmol/l) and magnetic resonance (MRI) imaging demonstrated a right-sided pituitary macroadenoma of 13x9.6 mm. Urgent petrosal venous sampling was scheduled, but he acutely decompensated in the interim after being admitted with newly diagnosed diabetes mellitus, a hyperosmolar hyperglycaemic state (HHS) and multiple cranial nerve dysfunction, including facial nerve palsy. Brainstem MRI imaging was unremarkable and the working diagnosis was imminent pontine myelinolysis secondary to osmotic change.

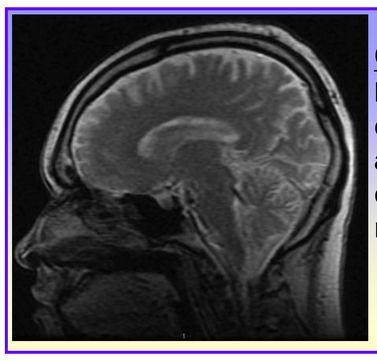
Overnight Dexamethasone Suppression Test Pre-surgery



Cushing's pre-operative investigations
1. Overnight dexamethasone suppression test; cortisol 692 mmol/L.
2. ACTH 66.4 ng/L, cortisol 590 mmol/L at 9.00 am.
3. Low dose dexamethasone suppression test, cortisol 332 mmol/L after 48 hours.
4. Urine cortisol output, 24 hours urine 321 (high).
5. Urinary Metanephrines - normal profile
6. Renin/Aldosterone Renin 3.4 [0.5-3.5] / Aldosterone < 60 pmol/L [90-700]

TIMELINE





<u>Oct 2017</u>
Right pituitary macroadenoma encroaching on internal carotid artery with no suprasellar extension. Clinically visual fields never impaired.

Sudden Metabolic decompensation

New Diabetes Mellitus	HbA1c 48>> 100 in 3 months

↓

Hyperosmolar Hyperglycaemic State (HSS)

Hypovolaemia Hyperglycaemia CBG > 30	Osmolality [2 Na + Glucose + Urea] > 320

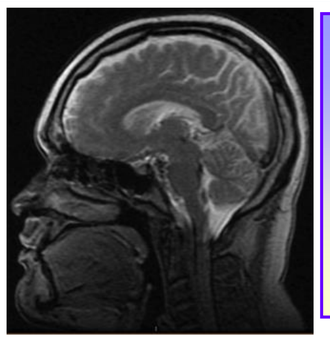
↓

Imminent Pontine demyelination

Cranial Nerve Palsies	Cranial nerve dysfunction - blurred vision in right eye, nystagmus, slurred speech, difficulty in swallowing

Management

He was treated appropriately for the HHS and recovered fully. Hypercortisolaemia was treated with Ketocanozole and he went on to have urgent transsphenoidal hypophysectomy. Histology confirmed tumour cells expressing ACTH with P-53 overexpressed at 2% and the Ki-67 index high at 5%. Cushing's post-operative work-up showed he was not biochemically cured and an interval MRI showed residual tissue extending into the right cavernous sinus. Further treatment options are being considered including a second trans-sphenoidal procedure and/or stereotactic radiotherapy. A referral to andrology for sperm cryopresevation bas requested prior to treatment.



March 2018

<u>Ketocanozole</u>
- **Inhibits side chain cleavage**
- **Inhibits 11-deoxycortisol >> cortisol**
- **Inhibits C17-20 desmolase**
- **Inhibits ACTH secretion in vitro**

(corticotroph adenylate cyclase activation)

<u>Medications post transsphenoidal surgery</u>
- **Ketoconazole 200 mg bd**
- **Metformin 1000 mg + 500 mg**
- **Amlodipine 5 mg od**
- **Atorvastatin 20 mg od**

Cushing's workup postoperatively
1.24 hour urine free cortisol 607 (708 ml) + 425 (537 ml) nmol/L
2.Low-dose Dexamethasone suppression test: 363 (0h) >> 160 (48h) nmol/L
3.3. Hydrocortisone day curve: Cortisol 528 (0h), 493 (2h), 360 (4h), 486 (6h) nmol/L.
4.4. IGF-1 24.2 nmol/L, testosterone 7.8 nmol/L, SHBG 13, prolactin 448 mIU/L, FT4 12.7 pmol/L, TSH 1.50 mU/L, HbA1c 44 mmol/mol

CONCLUSIONS

This rare case demonstrates two interesting presentations; firstly, a rapid decompensation of Cushing's disease resulting in HHS, and secondly a rising osmolality in HHS causing cranial nerve dysfunction.

REFERENCES

1. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. Lynnette K. Nieman Beverly M. K. Biller James W. FindlingM. Hassan Murad John Newell-Price Martin O. Savage Antoine Tabarin. *The Journal of Clinical Endocrinology & Metabolism*, Volume 100, Issue 8, 1 August 2015, Pages 2807–2831
2. Endocrinology Handbook, Imperial Centre for Endocrinology, Imperial College Healthcare NHS Trust, Charing Cross, Hammersmith and St. Mary's Hospitals, February 2018