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

CASE HISTORY

Endocrine Referral: 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 Irbesatran 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.

Cushing’s disease: Insidious onset; typical late diagnosis pick-up

Investigations

Investigations showed failure of cortisol suppression on a low dose dexamethasone suppression test (time=48 hours, cortisol 1107 nmol/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.

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 Urgent petrosa surgery.

Ketocanozole
- Inhibits side chain cleavage
- Inhibits 11-deoxycortisol >> cortisol
- Inhibits C17-20 desmolase
- Inhibits ACTH secretion in vitro (corticotroph adenylate cyclase activation)

Medications post transsphenoidal surgery
- Ketocanozole 300 mg bd
- Metformin 1000 mg + 500 mg
- Amlodipine 5 mg od
- Atravastatin 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. Hydrocortisone day curve: Cortisol 528 (0h), 493 (2h), 360 (4h), 486 (6h)
4. IGFB-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
2. Endocrinology Handbook, Imperial Centre for Endocrinology, Imperial College Healthcare NHS Trust, Charing Cross, Hammersmith and St. Mary’s Hospitals, February 2018