# Lump it or leave it: clinical insights from a case of bilateral adrenal macronodular hyperplasia

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**Identifier/ Topic:** *Clinical Case Reports – Pituitary/ Adrenal*

## CLINICAL CASE

### History

MG (57yo F) was referred for investigation of an adrenal incidentaloma. Relevant history included overweight, poorly controlled hypertension (2 agents), dyslipidaemia and previous minimal trauma fracture.

### Investigations

Baseline labs (including 24hr urine collection) and clinical examination (except hypertension) were unremarkable. Overnight cortisol failed to suppress on consecutive 1mg Dexamethasone testing (DST).

Dedicated CT adrenal study showed **bilateral adrenal hyperplasia** (left gland largest, **Figure 1**). Testing for aberrant receptors (TRH, GnRH, mixed meal and postural changes) and Short Synacthen with 17-OH-P levels all normal.

**Figure 1. CT Adrenal**

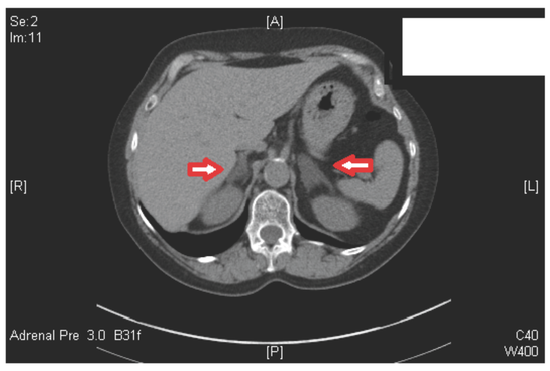



**Figure 2. Results of adrenal vein sampling**

| | Cortisol (nmol/L) |
|---|---|
| Left Adrenal | 1782 |
| Left renal distal to left adrenal | 350 |
| Left renal proximal to left adrenal | 337 |
| Right adrenal | 8084 |
| Right renal | 414 |
| IVC above renal vein | 403 |
| IVC below renal vein | 403 |
| Peripheral | 444 |

### Diagnosis & initial management

**Bilateral adrenal macronodular hyperplasia** (BAMH) **with subclinical Cushings' syndrome** (sCS) was confirmed by adrenal vein sampling (**Figure 2**). sCS manifested with the metabolic syndrome and osteoporosis. MG elected for medical management of co-morbidities and monitoring of sCS.

### Progress

Follow-up CT adrenal studies showed increasing size bilaterally (left largest).

Clinically there was worsening of H/T despite 3 agents, impaired fasting flucose, moderate weight gain and despite bisphosphonate treatment new minimal trauma vertebral fracture and higher grade osteoporosis. Eventually H/T and lipids were better controlled.

In 2014, four years after diagnosis, MG elected for surgical management.

She successfully underwent a laproscopic posterior extra-peritoneal left adrenalectomy. Histopath showed diffuse adrenal macronodular hyperplasia (**Figure 3**).

Post-operatively MG does not require glucocorticoid therapy, is on reduced doses of antihypertensive and statin medications and has normal BGLs. She is followed up by endocrinology for complications from sCS.

## DISCUSSION

### BAMH

ACTH independent primary bilateral macronodular adrenal gland hyperplasia, benign & without malignant potential.

Is approximately <1% of endogenous CS & typically presents in 5th and 6th decade (female preponderance) with sCS or CS.

### Diagnosis

Typically presents as sCS with absence of clinical signs but features of metabolic syndrome and/or osteoporosis. Investigations include normal 24hr UFC but subnormal suppression of fasting cortisol after 1mg overnight DST.

Variants include expression of ectopic GIP Rc (excess post-prandial cortisol) & LH/hCG Rc (manifests as CS during pregnancy or following menopause). Aberrant receptor testing warranted.

### Imaging

Typical size of non-pigmented nodules 10-55mm (avg 30mm).

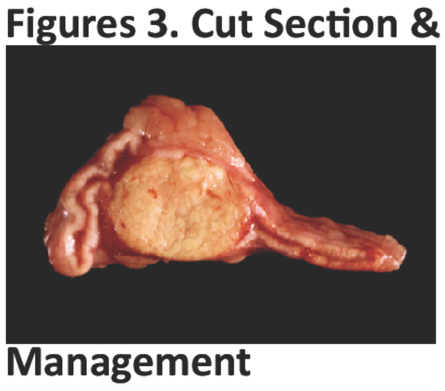
CT (see **Figure 1**) shows asymmetric bi-adrenal enlargement with numerous nodules **or** diffused bi-adrenal enlargement with minimal nodules. MRI shows T1 hypodense relative to liver, T2 hyperintense while on PET-FDG there is increased signal.

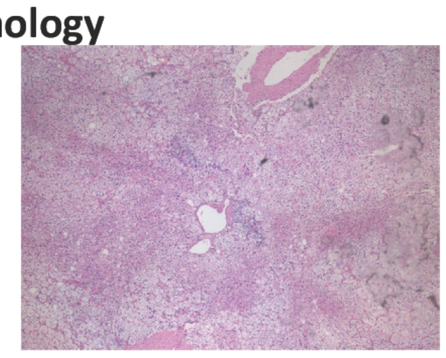
### Pathophysiology

Compared to normal adrenals, decreased expression of steroidogenic enzymes and inefficient hormone synthesis means despite massive sized adrenals, clinically presents as sCS.

The mean wgt per gland is up to >100gms with cut section showing yellow nodules with high lipid content (**Figure 4**). Microscopically there are both lipid rich and poor cell types but always diffuse internodular hyperplasia

**Figures 3. Cut Section & Histopathology**





### Management

Manage complications of sCS/ CS and monitor (biochem + image) every 6 to 12 months.

Consider **surgery** if evidence of increasing cortisol excess and or progressive complications

* Unilateral adrenalectomy if <2x UFC, but risk of future CS

* Bilateral adrenalectomy for severe CS or >2x UFC w/o aberrant hormone Rc or not amenable to Rx. While there is no risk of Nelson's Syndrome, this means life long glucocorticoid Rx.

There is evidence for improved outcomes for the posterior extra-peritoneal approach but no role for pre-op planning with AVS.

Also little role for long term pharmacoRx to suppress cortisol.

### Genetics

Most cases are sporadic but there are reports of familial/ inherited cases. The genetics is heterogeneous: MEN1, FAP (APC) & Armadillo Repeating 5 germline (ARMC5) mutation all noted. Expert recommendations are to screen all adult 1st degree relatives >30yrs and for FAP/APC +ve, to screen for other associated conditions.

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References available on request



DOI: 10.3252/pso.eu.17ece.2015

Poster presented at: ECE2015 16-20 May 2015 DUBLIN, IRELAND 17th EUROPEAN CONGRESS OF ENDOCRINOLOGY