Cushing's Disease and Primary Aldosteronism Confounded by a Non-Functioning Solitary Adrenal Incidentaloma

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Background

Adrenal incidentalomas are common, affecting ~2% of the general population. The presence of adrenal incidentaloma necessitates biochemical testing for hypersecretion, however hypercortisolism and/or hyperaldosteronism may not necessarily originate from the nodule that prompted the initial workup.

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Clinical Case

A 53-year-old man with a history of obesity and hypertension was referred for workup of a 2.4 x 1.4 cm R adrenal nodule that was incidentally discovered on an abdominal CT (Figure 1) to rule out pancreatitis. He was noted on examination to have some Cushingoid features. He was on three antihypertensives (amlodipine 10 mg, carvedilol 50 mg, and spironolactone 50 mg) with adequate blood pressure control and no hypokalemia. He denied spells nor exogenous steroid exposure.

Initial testing for hypersecretion showed an elevated cortisol 8.7 ug/dL (<1.8) after 1 mg dexamethasone with adequate dexamethasone level, aldosterone concentration (PAC) 9 ng/dL (3-16), plasma renin activity (PRA) 0.7 ng/mL/h (0.25-5.82), potassium of 3.8 mmol/L (3.5-5.1), and normal plasma metanephrines.

Further testing revealed elevated 24-hour urinary free cortisol 81.3 mcg/24h (4-50) and elevated late night salivary cortisol 0.10 and 0.13 mg/dL (<0.09). Baseline 8 AM ACTH was not suppressed 16.3 pg/mL (7.2-63.6).

Figures

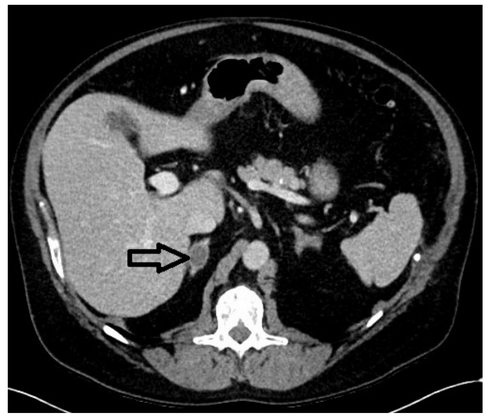

Figure 1: Incidentally discovered 2.4 x 1.4 cm R adrenal nodule (black arrow) on abdominal CT that prompted initial workup

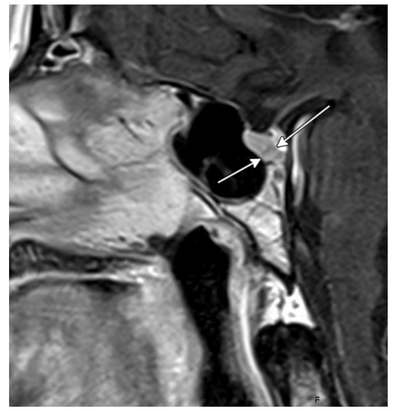

Figure 2: A 3.6 mm pituitary microadenoma (white arrows) on contrast-enhanced MRI

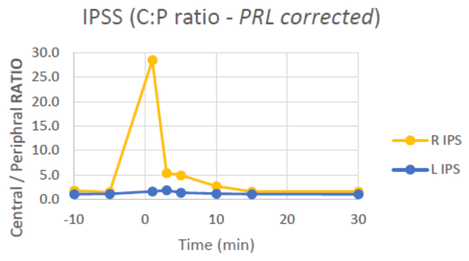

Figure 3: Inferior petrosal sinus sampling showing an elevated central: peripheral ACTH gradient (corrected for PRL level) at R inferior petrosal sinus consistent with pituitary source of hypercortisolism

	RAV	LAV	IVC	RAV/IVC	LAV/IVC
Cortisol	1376	391	33.5	41.1	11.7
Aldo	390	1100	26		
A:C	0.3	2.8	0.8		

Lateralization index: 9.3 (L Side)
Contralateral (R Side) Suppression Present at 0.4

Figure 4: Adrenal vein sampling demonstrating lateralization to L adrenal gland

Clinical Case, Continued

Pituitary MRI showed a 3.6 mm microadenoma (Figure 2). DDAVP stimulation resulted in an increase in cortisol and ACTH suggestive of Cushing's disease, which was confirmed by inferior petrosal sinus sampling (IPSS) (Figure 3). He underwent transsphenoidal resection with pathology consistent with an ACTH-staining pituitary adenoma. Immediate post-op cortisol nadir was 4.9 ug/dL.

A few months after surgery, he underwent retesting for primary aldosteronism (while off spironolactone) notable for PAC 14 ng/dL, PRA 0.58 ng/mL/h, and K 4.0 mmol/L. After oral salt loading, 24-hour urine aldosterone was 14.4 mcg/24h (<12) with urine sodium 247 mmol/24h (>200). He completed AVS which lateralized to the L adrenal gland despite a R adrenal nodule (Figure 4). He underwent L adrenalectomy with significant improvement in blood pressure which is now well-controlled on carvedilol monotherapy with normalization of PRA to 1.94 ng/ml/h. The R adrenal nodule remains stable in size and appearance on follow up imaging.

Conclusion

The presence of an adrenal adenoma with concomitant biochemical evidence of hormonal excess cannot inherently be attributed to nodular autonomous function without further workup. Other hormonal assessment including ACTH level and localization studies are necessary prior to any surgical procedure to avoid missed diagnoses of Cushing's disease and contralateral primary aldosteronism in the presence of a non-functioning adrenal nodule.