

Carbamazepine and Cushing's: a cautionary tale of assay interference mimicking disease

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Case studies

- Male, 44 years old
- Presented to nephrology with malignant hypertension.
- Routine investigation for secondary causes performed.
- Marked hyper-reninaemia, marked elevation in urinary free cortisol (UFC) and marked disparity of kidney size all present.
- Referred to endocrinology for investigation of Cushing's syndrome but clinically no convincing evidence of Cushing's.
- PMH: bipolar disorder
- DH: venlafaxine, carbamazepine, pericyazine, amlodipine 10mg daily, perindopril 4mg BD, bisoprolol 5mg daily, spironolactone 100mg daily and phenoxybenzamine 10mg BD.
- Female, 68 years old
- Initial presentation to nephrologist with hypertension and obesity.
- Routine investigation for secondary causes performed.
- Elevated urinary free cortisol and lack of suppression after 1mg overnight dexamethasone test.
- Referred to endocrinology for investigation of Cushing's but again unconvincing clinical assessment.
- PMH: mental health issues
- DH: venlafaxine, carbamazepine, amlodipine 10mg daily, ramipril 10mg daily, atenolol 50mg daily and atorvastatin 20mg at night.

Examination findings

- BP 150/110
- Slim (Height 184 cm, Weight 78.7 kg, BMI 23.2)
- Normal skin character, no bruising, striae, plethora or myopathy
- BP 170/84
- Obese (Height 158cm, Weight 78.1 kg, BMI 31.3)
- Normal skin character, few pale striae and one bruise, no myopathy

Investigations

		Case 1		Case 2	
		Before	After	Before	After
24h UFC (nmol/24h)	UFC 1	2036	Not performed by patient	501	321
	UFC 2	698	Not performed by patient	360	331
Low dose dexamethasone test (nmol/L)	Time 0h	708	214	-	166
	Time 48h	355	<22	-	37
Overnight dexamethasone test (nmol/L)		-	-	514	-
Renin level (5.4 – 60 mU/L in upright position)			241	-	
Aldosterone level (100 – 450 pmol/L in upright/random)			411	-	
Potassium level (3.6 – 5 mmol/L)			4.1	3.8	

- Case 1: Before & after carbamazepine withdrawal. (note: Case 1 had normal bone density and HbA1c)
- Case 2: Before & after changing serum cortisol assay from Roche Cobas assay to Abbott platform assay.(note: Case 2 remains on carbamazepine)

Conclusions

- Both cases presented with hypertension but no obvious clinical features of Cushing's.
- In both cases a non specialist performed screening test for Cushing's which were apparently positive.
- Detailed clinical assessment by an endocrinologist refuted the diagnosis in both cases and considered carbamazepine interference either through the enzyme induction effects leading to false positive dexamethasone suppression test results, or by direct interference in some cortisol assays.
- Drug withdrawal in one, and the use of an alternative platform in the other allowed the diagnosis to be excluded and prevented further unnecessary investigation and anxiety.