Hypertension in Familial Adenomatous Polyposis (FAP) – Think of Cushing's or Conn's

Tom Glass Hopkins M.B.B.S.¹

Victoria Salem M.R.C.P.¹

Heba El-Gayar M.R.C.P.¹

Fausto F Palazzo M.S., F.R.C.S.²

Karim Meeran M.D., F.R.C.P., F.R.C.Path¹

Tricia Tan M.R.C.P.¹

1. Endocrine Unit, Imperial College Healthcare NHS Trust, Hammersmith Hospital, Du Cane Road, London W12 0HS.

2. Department of Endocrine Surgery, Imperial College Healthcare NHS Trust, Hammersmith Hospital, London W12 0HS.

A 36-year-old man was found to be hypertensive by his GP: 210/110 mmHg. He had been diagnosed with familial adenomatous polyposis (FAP) in childhood, and had undergone a total colectomy at the age of 17. The patient had been under endoscopic surveillance since, with a recent polyp count of 50-60, and remained problem-free. The following month, as part of his routine FAP screening programme, the patient underwent an abdominal CT scan. This revealed bilateral macronodular adrenal hyperplasia. The largest of these nodules measured 4 by 2 cm on the right and 2.7 by 2.9 cm on the left (see Figure 1).

On assessment in our unit, the patient was found to be hypertensive at 150/100 mmHg on lisinopril and amlodipine. Examination revealed a well-healed midline laparotomy scar, and no clinical features suggestive of Cushing's syndrome. Serum potassium concentration was normal at 3.8 mmol/L. Other biochemical investigations excluded Cushing's syndrome and pheochromocytoma.

With confounding antihypertensive medications discontinued, plasma aldosterone measured 590 pmol/L, plasma renin activity (PRA) 0.2 pmol/ml-hr, giving an aldosterone:PRA ratio of 2950, where values >2000 are considered highly suggestive of primary hyperaldosteronism.¹ Saline infusion did not suppress aldosterone to <280 pmol/L, further supporting this diagnosis.

Selective adrenal vein sampling was undertaken in September 2009. The cortisol-corrected aldosterone ratio in the left adrenal vein (A/C_L) was 3.05 versus a ratio of 0.74 in the right adrenal vein (A/C_R), with a ratio of 0.80 in the low inferior vena cava (A/C_{IVC}). The dominant to non-dominant ratio ($A/C_L:A/C_R$) of 4.15 was above the

recommended cut-off of 4.0 for diagnosing unilateral aldosterone hypersecretion with 95% sensitivity and 100% specificity.¹ Furthermore, the non-dominant to peripheral ratio ($A/C_R:A/C_{IVC}$) of <1 confirmed that autonomous secretion of aldosterone was confined to the left.

There were no radiological features of the right adrenal mass suspicious of malignancy apart from its size. With the finding of dominant left-sided aldosterone secretion in this case, it was decided that the patient would benefit from laproscopic left adrenalectomy, and he is currently awaiting surgery.

FAP is associated with numerous extra-intestinal manifestations, with which the attending physician should be familiar.² Adrenal gland enlargement is commoner in patients with FAP above the expected ascertainment bias due to frequent abdominal imaging. In a series of 738 FAP patients, 14 (7.4%) were found to have adrenal enlargement, compared to 0.6–3.4% in the general population.³ Of these, two were hypertensive and required surgical removal of cortisol-secreting tumours. The histology revealed adrenal carcinoma in one, and nodular hyperplasia in the other. In another follow-up study of 30 FAP patients with adrenal adenomas, 3 required adrenalectomy: one for a pheochromocytoma, one for a non-functioning, malignant tumour, and one for an enlarging, non-functioning, benign adenoma.⁴ Thus, the majority of adrenal tumours associated with FAP are non-functioning and require no treatment unless they enlarge. However, it is important to diagnose those rare cases that are associated with hormone hypersecretion, as these are surgically treatable. All FAP patients with incidentally discovered adrenal masses should have regular blood pressure measurements and be screened for possible Cushing's syndrome

(using a 9 am ACTH level or dexamethasone suppression test), Conn's syndrome (using an aldosterone:PRA ratio), and phaeochromocytoma (with urine catecholamine or metanephrine excretions).⁴

This case report describes aldosterone-secreting adrenal enlargement in a hypertensive patient with FAP. Recently, an association between tumour-suppressor *APC* (*adenomatous polyposis coli*) gene mutations and hyperaldosteronism has been proposed. Mice heterozygous for a truncating *APC* mutation had higher aldosterone levels than controls, with corresponding increases in urinary potassium excretion, despite the presence of hypertension and plasma volume expansion. This suggests a potential pathophysiological link between the causative *APC* mutation and hyperaldosteronism in FAP.⁵

Legends

Figure 1. Coronal section of unenhanced abdominal CT of a patient with familial adenomatous polyposis (FAP) and noted to be hypertensive one month earlier. Bilateral adrenal enlargement highlighted.

Contributions

TGH, VS, HEG, FFP, KM and TT: diagnosis and patient management. Written consent to publish was obtained from the patient.

Conflicts of Interests

None declared.

References

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