Case Report

A Mother/Daughter Case of Familial Hyperaldosteronism

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Introduction

We describe a case of familial primary hyperaldosteronism in 2 family members, a mother and daughter. Two types of familial hyperaldosteronism have been described, type I and type II.^{1–3} It has recently come to light that the prevalence of familial primary hyperaldosteronism is higher than originally believed. It is likely that many more hypertensive patients, who have a family history of hypertension with no known etiology, have 1 of the 2 types of this genetic disease and may benefit from diagnosis and treatment. Indeed, 1 of our 2 patients has been cured of her hypertension, and has not required further treatment since her definitive therapy.

Case 1: Daughter

A 33-year-old woman with a medical history of labile hypertension, a heart murmur since childhood, severe perimenstrual cramping, and anemia, presented in December 2006 for evaluation and management of labile hypertension. She described a history dating back to age 14 of severe back spasms and muscle cramps that seemed to be associated with premenstrual syndrome. In 1997, in the process of undergoing an exploratory laparoscopy to rule out endometriosis (which was negative), she was noted to be markedly hypertensive. Since then she has had labile hypertension, periodically requiring alterations in her anti-hypertension regimen. Both her mother and grandmother have hypertension. In the course of her workup, a CT scan done at an outside institution, found a left adrenal tumor. Upon presentation, her blood pressure was 115/70, she was being treated with hydrochlorothiazide and spironolactone. Blood tests revealed a serum renin activity of 1.73 (ng/mL/hr), serum aldosterone was 30 ng/dL, plasma metanephrines of 94 (pg/mL), and serum potassium was 3.7 (mmol/L). This translated to a borderline elevated aldosterone and aldosterone/renin ratio (17.34). The patient then underwent an MRI of the abdomen, which revealed a 1.7 cm × 0.9 cm left adrenal mass. The patient was then referred for adrenal vein sampling, which was consistent with a hyperfunctioning left adrenal adenoma (Table 1). She underwent a laparoscopic adrenalectomy a short while later. After surgery, the patient was also referred to a clinical geneticist to undergo genetic testing for familial hyperaldosteronism type I (FH-I). Her blood tested negative for the FH-I gene. Upon further follow-up the patient's hypertension and hypokalemia had resolved with no significant sequelae.

Table 1. Case 1 (Daughter) — Adrenal Vein Sampling Results

	Aldosterone (ng/dL)	Cortisol (μg/dL)	Aldosterone/ Cortisol Ratio
Basal			
Right	5	6	0.83
Left	652	19	34.31
Peripheral	18	5	3.6
Post-stimulation (12 min)			
Right	39	17	2.29
Left	4216	487	8.66
Peripheral	34	14	2.42
Post-stimulation (36 min)			
Right	31	20	1.55
Left	6116	447	13.68
Peripheral	34	18	1.89

Case 2: Mother

A 62-year-old woman with a medical history significant for hypertension and hypokalemia, presented in June 2007 for evaluation and management of lower extremity edema, which had been present for 1 year, worsening over the past several months. At this point her daughter had been diagnosed with an adrenal tumor and scheduled for an adrenalectomy. Her family history included a mother with hypertension. The patient's blood pressure upon presentation was 170/80, which was being treated with atenolol, olmesartan/hydrochlorothiazide, and triamterene/hydrochlorothiazide. She was also taking potassium supplementation daily for hypokalemia, and furosemide as needed for lower extremity edema. Her blood tests revealed a serum aldosterone level of 12 ng/dL, a plasma renin activity of 0.2 (ng/mL/hr), aldosterone/renin ratio was 60, and serum potassium was 3.3 (mmol/L). She was found to have a 14 mm × 4 mm left adrenal tumor and an unremarkable right adrenal gland on CT scan. Her medications were altered and she was referred for adrenal vein sampling, which was consistent with bilateral adrenal hyperplasia (Table 2). Since then her blood pressure has been

Table 2. Case 2 (Mother) — Adrenal Vein Sampling Results

	Aldosterone (ng/dL)	Cortisol (μg/dL)	Aldosterone/ Cortisol Ratio
Basal			
Right	78	20	4
Left	677	28	24.2
Peripheral	16	14	1.14
Post-stimulation (12 min)			
Right	1279	1017	1.3
Left	2413	456	5.3
Peripheral	18	14	1.06
Post-stimulation (24 min)			
Right	2344	659	3.6
Left	5938	677	8.8
Peripheral	26	21	1.24

much better controlled on atenolol, telmisartan, and spironolactone, and her lower extremity edema has resolved. She was referred to a clinical geneticist to undergo genetic testing for FH-I. Her blood tested negative for the FH-I gene. She continues to be followed with controlled hypertension on a regimen that includes enalapril and spironolactone.

Discussion

Aldosterone, a mineralocorticoid, participates in the regulation of blood volume and potassium homeostasis. Aldosteronism, classically characterized by hypertension and hypokalemia, is due to increased aldosterone secretion from the zona glomerulosa in the adrenal glands. Primary hyperaldosteronism was first described by Conn in 1955,⁴ and was originally described as a syndrome caused by an aldosterone-secreting adenoma. Since then other causes have been described, including adrenal carcinoma, adrenal hyperplasia, and glucocorticoid-suppressible hyperaldosteronism. Primary aldosteronism has been shown to account for at least 8.5% and as many as 20% of hypertensive patients, a large number of which are surgically curable.^{5–8} Further studies described 2 familial forms of primary hyperaldosteronism. FH-I is an autosomal dominant disorder caused by a hybrid gene mutation formed by a crossover of genetic material between the adrenocorticotrophic hormone-responsive regulatory portion of the

11 β -hydroxylase gene (*CYP11B1*) and the coding region of the aldosterone synthase gene (*CYP11B2*).⁹ The precise genetic cause of familial hyperaldosteronism type II (FH-II) is yet unknown, however it may be linked to chromosome 7p22.¹⁰ Families with either FH-I or FH-II can present with adrenal adenomas, bilateral adrenal hyperplasia, or have both entities in 1 family pedigree.^{2,11}

Our mother-daughter patients underwent serum biomarker testing and adrenal vein sampling, the gold standard test for primary hyperaldosteronism. Once diagnosed, they underwent genetic testing for FH-I, which was negative. We conclude through our description of this mother-daughter case of FH-II, that physicians treating hypertension should maintain a lower threshold for considering primary hyperaldosteronism as the etiology of hypertension in their patients, and that once a patient is diagnosed with primary hyperaldosteronism, all family members with hypertension should be tested for primary hyperaldosteronism. Since diagnosing this mother and daughter, we have found primary hyperaldosteronism to be the etiology of several other patients' hypertension and have suggested a more aggressive workup for those family members with hypertension as well.

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