

IDIOPATHIC HYPERALDOSTERONISM PRESENTING AS RESISTANT HYPERTENSION

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INTRODUCTION

Secondary hypertension constitutes about 2-10% of all cases of hypertension. Uncontrolled hypertension or hypertension requiring control with two or more antihypertensive drugs require evaluation of secondary hypertension. Among the causes of secondary hypertension endocrinal abnormalities constitutes upto 1-2% of all cases and can be due to endogenous or exogenous hormonal imbalances.

Primary Aldosteronism (PA) is a group of endocrine disorders in which aldosterone production is inappropriately high, autonomous of the renin-angiotensin system and not suppressed by sodium loading¹. Bilateral idiopathic hyperaldosteronism (IHA) and aldosterone producing adenoma (APA) are the most common subtypes of PA. It is estimated that more than 10% of patients with secondary hypertension in both general and specialty settings are a result of PA^{2,3}.

We present two cases of idiopathic hyperaldosteronism presenting as resistant hypertension.

CASE 1

A 55 year old female, married for 32 years and a mother of three children had a history of recurrent admissions to emergency and inpatient wards with episodes of headache, palpitations associated with marked fluctuations in blood pressure rising upto 210/120 mmHg at times for the last 4-6 months. She was a known hypertensive for the last 5 years and was taking tab Enalapril 5 mg once, tab Amlodipine 10 mg once and Bisoprolol 5 mg once daily. In May 2011, she had a renal angiogram done in search of secondary cause of

hypertension because of similar though less frequent fluctuations in blood pressure which showed 50-60% stenosis of the right renal artery which was stented. Her resting ECG was normal. Echocardiography showed normal LV systolic function with diastolic dysfunction grade I. Despite strict compliance with medications and diet the patient kept on coming to the emergency department with acute rise in blood pressure. In June 2012, her renal angiogram was repeated which showed no stenosis in right and left renal arteries and a



Figure:- No stenosis in right and left renal arteries and a patent stent.

patent stent. (Fig)

Her biochemical profile was within normal limits with serum urea of 28 mg/dl, serum creatinine of 1.1 mg/dl, serum sodium level of 144 mmol/l and serum potassium level of 4.5 mmol/l.

Her thyroid profile was also within normal limits with serum TSH of 2.8 mIU/l and free T4 level of 1.4 ng/dl.

Considering frequent fluctuations in blood pressure despite compliance with three different antihypertensives, she was further evaluated for any secondary cause of hypertension. So her 24 hour urinary cortisol, serum renin and aldosterone after 96 hour abstinence from medications and 24 hour urinary Vannilylmendallic acid (VMA) levels were done. The following results were obtained:

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- 24 hrs urinary free cortisol 217 nmol/l (N : 55-248 nmol/l)
- Aldosterone: 208 sitting (Normal : 10-160 pg/ml sitting , 40-310 pg/ml standing)
- Renin 8.16 sitting (Normal < 4-23.7 pg/ml sitting, < 4-37.5 pg/ml standing)
- VMA 37 umol/24 hr (5-56 umol/24 hrs)

Her CT scan abdomen was done which revealed no mass in the adrenal region. Contrast enhanced MRI scan of abdomen was subsequently done which showed 2-3 benign cysts in left kidney with normal adrenal glands.

Considering her above mentioned results a diagnosis of idiopathic hyperaldosteronism (IHA) was considered and she was started on Tab Aldactone 50 mg twice daily. She dramatically responded to this aldosterone antagonist tablet with relief in symptoms and fluctuations of blood pressure.

CASE 2

A 30 year old soldier, a known hypertensive, had several admissions in last six months with episodes of accelerated hypertension and blood pressure at times touching 190/115 mmHg despite being on three types of anti-hypertensives i.e., Amlodipine (calcium antagonist), Atenolol (beta-blocker) and Lisinopril (ACE inhibitor). He was also a known case of retinitis pigmentosa. Her clinical examination including cardiovascular system was unremarkable. His ocular fundi revealed grade II hypertensive retinopathy. His resting ECG, 2D echo and renal Doppler scan did not reveal any abnormality. His biochemical profile revealed raised cholesterol (306 mg/dl), triglycerides (402 mg/dl), urea 62 mg/dl, creatinine 2.3 mg/dl with normal electrolytes. 24 hour urinary VMA and 5 hydroxyindole acetic acid (HAA) were within normal limits. His serum Aldosterone levels (seated) were 1260 pmol (reference range 28-438 pm/L) and serum Renin 1.73 pm/L (reference range < 0.11-0.65 pmol/L) with serum aldosterone to renin ratio around 728 (normal < 613). CT scan abdomen with intravenous contrast was non-revealing. In view of the above, possibility of IHA was considered and aldosterone antagonist spironolactone was added. Subsequently his

frequent fluctuations in blood pressure were lessened.

DISCUSSION

The presence of late onset hypertension, persistent hypokalaemia or difficult to control hypertension should raise the clinician's suspicion of primary aldosteronism as a cause of secondary hypertension.

The aldosterone renin ratio (ARR) is the recommended initial screening test for PA¹. The measurement of both aldosterone and renin is superior to measurement of aldosterone or renin in isolation^{1,4}. Serum potassium should not be used for screening as only 9-37% of patients would have low levels⁵. Antihypertensive medications that might interfere with ARR results should be discontinued. Diuretics, ACEIs, ARBs, β -blockers and clonidine are stopped two weeks prior to testing while aldosterone antagonists (spironolactone or eplerenone) should be discontinued at least four weeks prior to testing¹. Calcium channel blockers (preferably from the non-dihydropyridine group), hydralazine, and peripheral alpha-blockers are recommended for blood pressure control during this period. Primary aldosteronism is suspected if the morning ARR is > 20-40 (plasma renin expressed as ng/mL per hour) and the plasma aldosterone > 15 ng/dL¹. Attention to the plasma aldosterone concentration is important as an elevated ARR ratio can also be obtained in patients with low-renin hypertension. The initial studies in our patients met these criteria.

IHA caused by hyperfunctioning of the adrenal glands can be associated with normal appearing adrenal glands on CT or MRI scans as in our case⁵.

IHA should be treated medically⁶. In addition, aldosterone producing adenoma (APA) patients may be treated medically if the medical treatment includes mineralocorticoid receptor blockade. There have been no placebo-controlled randomized trials evaluating the relative efficacy of drugs in the treatment of primary aldosteronism⁷. Spironolactone has been the drug of choice to treat primary

aldosteronism for more than three decades. However, it is not selective for the aldosterone receptor⁸.

Conflict of Interest

This study has no conflict of interest to declare by any author.

REFERENCES

1. Funder JW, Carey RM, Fardella C, Gomez-Sanchez CE, Mantero F, Stowasser M et al. Case detection, diagnosis, and treatment of patients with primary aldosteronism: An endocrine society clinical practice guideline. *J Clin Endocrinol Metab* 2008; 93: 3266-81.
2. Fardella CE, Mosso L, Gomez-Sanchez C, Cortes P, Soto J, Gomez L et al. Primary hyperaldosteronism in essential hypertensives: Prevalence, biochemical profile, and molecular biology. *J ClinEndocrinolMetab* 2000; 85: 1863-7.
3. Gordon RD, Stowasser M, Tunny TJ, Klemm SA, Rutherford JC. High incidence of primary aldosteronism in 199 patients referred with hypertension. *ClinExpPharmacolPhysiol* 1994; 21: 315-8.
4. Sinclair AM, Isles CG, Brown I, Cameron H, Murray GD, Robertson JW 1987 Secondary hypertension in a blood pressure clinic. *Arch Intern Med* 147:1289-1293
5. Lau J, Balk E, Rothberg M, et al. Management of clinically inapparent adrenal mass. Rockville, MD: Agency for Healthcare Research and Quality; 2002. AHRQ Publication No. 02-E014. Evidence Report/Technology Assessment. No. 56.
6. Abdelhamid S, Muller-Lobeck H, Pahl S, Remberger K, Bonhof JA, Walb D, Rockel A 1996 Prevalence of adrenal and extra-adrenal Conn syndrome in hypertensive patients. *Arch Intern Med* 156:1190-1195
7. Young Jr WF. Primary aldosteronism: a common and curable form of hypertension. *Cardiol Rev* 7:207-214
8. Lim PO, Young WF, MacDonald TM. A review of the medical treatment of primary aldosteronism. *J Hypertens* 19:353-361.