AT THE FOREFRONT
UChicago Medicine

Pearls about Primary Hyperaldosteronism

Learning Objectives

- How to screen for and diagnose primary hyperaldosteronism
- Learn how to review and interpret results from Adrenal Venous Sampling
- Understand the cardiovascular outcomes and mortality in patients with primary hyperaldosteronism who are treated medically
- Predicting resolution of hypertension after adrenalectomy for aldosteronoma

History and Physical

Reason for Consultation/ Referral: Hypertension

HPI:

- 58 y/o AAF with a history of HTN (secondary to primary hyperaldosteronism), Obesity, Hypothyroidism and previous CVA - presented to Comprehensive Hypertension Center in 2020 for second opinion regarding HTN management
- Dx with HTN in 2000
- Incidental Right adrenal lesion - was evaluated and diagnosed with primary hyperaldosteronism in 2009
- Declined surgical intervention at that time
- Hypertensive crisis in 2017 (with SBP >210s mmHg) resulting in an SAH. Her medication regimen was adjusted to also include Eplerenone, Amlodipine and Clonidine

History and Physical

HPI - continued:

- SBP was in the 150-170s mmHg
- Transitioned care to The University of Chicago - and was seen by Dr. Angelos about pursuing potential surgical intervention
- Was to referred to Dr. Bakris for further w/u and management

History and Physical

PMH: HTN, Obesity, Hypothyroidism, SAH,, Seizures (2/2 SAH), HLD

PSH: Ventricular shunt

Social History: No Tobacco, EtOH or Illicits

Family History: Father - HTN, Prostate Cancer, CAD
Mother - HTN, CAD, CVA

History and Physical

Allergies:

PCN

Physical Exam:

Normal

physical exam

Home Meds:

Amlodipine 10mg
Atorvastatin 20mg
Clonidine 0.1mg BID
Eplerenone 25mg BID
Vimpat 150mg BID
Levothyroxine 88mcg

Labs and Imaging

Normal BMP (with sCr 0.8mg/dL and K 4mmol/L) and Normal CBC

TSH: 1.57

Aldosterone: 25 ng/dL

Renin: 0.7 ng/mL/hr

Plasma Metanephrines:

Normetanephine 0.90nmol/L (<0.9 nmol/L)

Metanephrine <0.20nmol/L (<0.5nmol/L)

Salivary Cortisol: 97ng/dL (100-750ng/dL AM)

CT Scan:

Right adrenal nodule 1.7 x 1.3 cm. This nodule measures (31 Hounsfield units)

What is the next step in work-up and management?

Further Evaluation

- Estimated that 4-19% of patients with HTN and 3-14% of patients with normotension have Primary Hyperaldosteronism (PA)
- PA should be suspected in patients with the triad of hypertension, hypokalemia and metabolic alkalosis
- Estimated that only 9-37% of patients with PA are hypokalemic
- Consider testing in patients with the following:
    - HTN and Hypokalemia
    - Resistant HTN
    - Adrenal incidentaloma and HTN
    - Onset of HTN at a young age (<30 y/o)
    - Severe HTN (>150 mmHg SBP or >100 mmHg DBP)
    - Whenever considering secondary HTN

Diagnosis - Primary Hyperaldosteronism

- Initial evaluation - identifying that plasma renin activity is suppressed (less than 1 ng/mL/hr) and the plasma aldosterone concentration is inappropriately high (≥ 15ng/dL)
- Plasma aldosterone-to-renin ratio most sensitive screening test for PA
- This ratio should be greater than 20
- A combination of PAC above 20 and PAC/PRA above 30 has a sensitivity and specificity of 90% for the diagnosis of PA
- In most patients, the diagnosis must be confirmed (24-hr urine aldosterone, sodium, creatinine on high Na diet OR Fludrocortisone suppression test OR Saline suppression test)

During Initial Hypertension Clinic Visit

1) Patient was referred for Adrenal Venous Sampling to be performed

   What medication should be held and for what duration?

Adrenal Venous Sampling Results

	Measured Values		Calculated Value		
Location	Aldosterone (ng/dL)	Cortisol (ug/dL)	Aldosterone (pmol/L)	Cortisol (nmol/L)	Aldo/ Cortisol Ratio
Right Adrenal Vein	7700	634	213290	17498	12.2
Left Adrenal Vein	67	78	831	891	0.9
Femoral Vein	19	26	526	720	
			Highest Aldo:Cortisol / Lowest Aldo:Cortisol = 13.5		

Interpretation:

1) Compare the Adrenal Cortisol : Femoral Cortisol ratio for each vein - to confirm catheter placement in adrenal veins. Ratio must be 3:1
2) Use the Highest side Aldo:Cortisol / Lowest Aldo:Cortisol ratio to confirm lateralization
   - -A ratio of >4:1 confirms and lateralizes the aldosteronoma
   - -Ratios between 3:1 and 4:1 are equivocal, interpret with caution
   - -Ratios <3:1 confirms bilateral adrenal cortical hyperplasia

During Initial Hypertension Clinic Visit

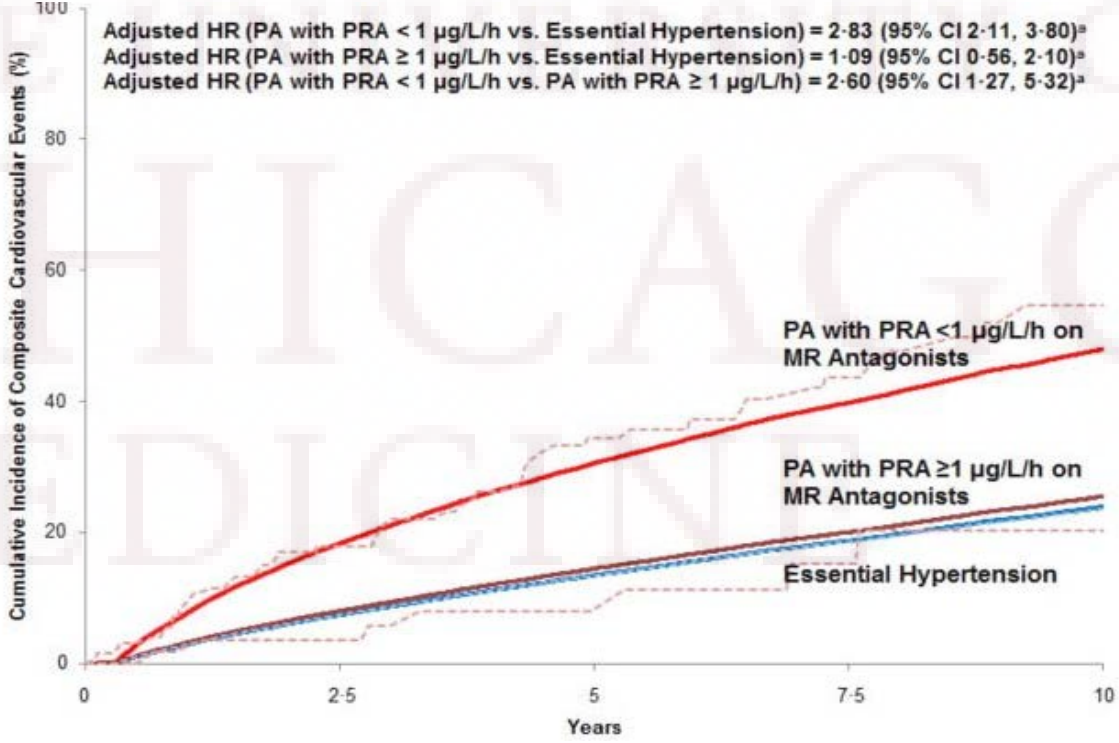
1) Patient was referred for Adrenal Venous Sampling to be performed

1) Medications were adjusted (after AVS was performed):
   - Amlodipine 10mg was continued
   - Clonidine was discontinued
   - Started on Azilsartan 80mg
   - Eplerenone was increased from 25mg BID → to 50mg BID (after completion of AVS, as medication was held for 4 weeks prior to procedure)

Cardiometabolic Outcomes and Mortality

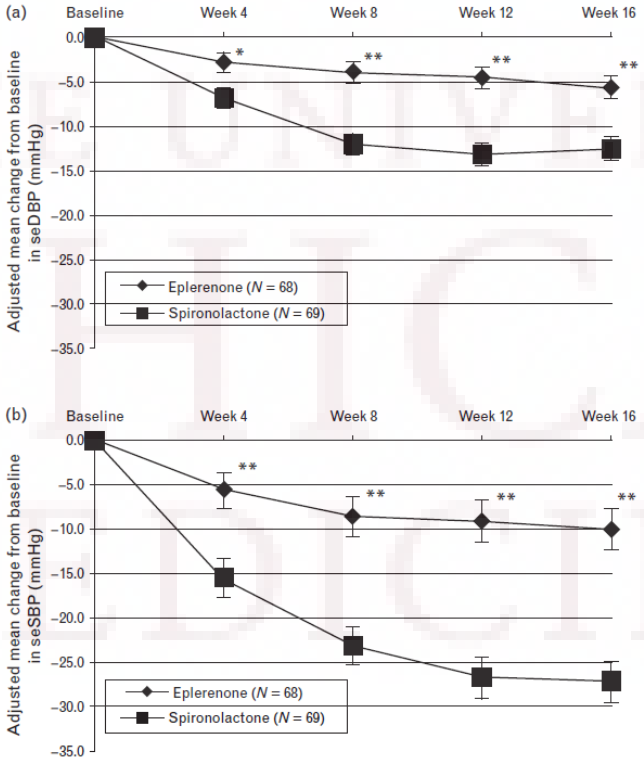
Cardiometabolic Outcomes and Mortality in Medically Treated Primary Aldosteronism: A Retrospective Cohort Study Lancet Diabetes Endocrinol. 2018 January; 6 (1) 51-59

- MRAs (mineralocortico
  PA
- Cohort study of 602 PA
  essential HTN
- The incidence rate of C
  Atrial fibrillation (HR =
- Increased risk of CV ev
  remained suppressed
- Patients treated with hi
  increased risk



AT THE FOREFRONT
UChicagoMedicine

Antihypertensive effect of MRAs



AT THE FOREFRONT
UChicagoMedicine

Parthasarathy HK, et al. A double-blind, randomized study comparing the antihypertensive effect of eplerenone and spironolactone in patients with hypertension and evidence of primary aldosteronism. Journal of Hypertension 2011; 29: 980-990

Surgical Intervention

- Patient was admitted for scheduled right laparoscopic adrenalectomy
- POD #1 - Hypertension Team was consulted for recommendations regarding BP medications
- Prior to procedure - patient was well controlled on Amlodipine, Azilsartan and Eplerenone
- BPs during hospitalization (after adrenalectomy) were consistently in the 100-110s/ 60s mmHg (off all her HTN medications)
- Patient was discharged home on **NO HTN medications** and scheduled for follow-up in 1 week

Results after Adrenalectomy

- Hypokalemia - resolved in 98% of patient
- Control of HTN improves in approximately 90% of patients, however ONLY 33-35% have complete resolution of HTN (not requiring antihypertensive medications)
- Multiple studies have assessed the likelihood of complete resolution of HTN - potential predictors included:
  - Taking less than 3 HTN medications
  - Duration of HTN
  - FH of HTN
  - Younger age
  - Female

Aldosteronoma Resolution Score

- Multivariate analysis indicated that 4 variables were independently associated with complete resolution of HTN
  - Taking ≤ 2 HTN medications
  - BMI ≤ 25
  - Duration of HTN ≤ 6 years
  - Female sex

Aldosterone Resolution Score: 4 Variable Model		
	Points	
Predictor	Present	Absent
No. HTN medications ≤ 2	2	0
Body Mass Index ≤ 25	1	0
Years of HTN ≤ 6	1	0
Female	1	0
Total*	5	0
**Possible score range from 0 to 5*		

- Using this scoring system helps identify patients with **LOW (≤ 1) and HIGH (≥ 4) likelihood of complete resolution of HTN** without needing lifelong antihypertensive medications

The Aldosteronoma Resolution Score - Predicting Complete Resolution of Hypertension After Adrenalectomy for Aldosteronoma. Annals of Surgery; March 2008; Volume 247, Number 3, 511-518

Follow-up

- Patient has continued to email her home BP readings following her surgery (she is now out 3 months from adrenalectomy)
- Her BP readings have been consistently 106-122/ 68-77 mmHg with HR 55-64 BPM
- She remains currently on no HTN medications and is doing well

References

1. Blumenfeld JD, et al. Diagnosis and treatment of primary hyperaldosteronism. Ann Intern Med. 1994; 121 (11): 877
2. Weinberger MH, et al. The diagnosis of primary aldosteronism and seperation of two major subtypes. Arch Intern Med. 1993; 153 (18): 2125
3. Young WF, et al. What are the keys to successful adrenal venous sampling (AVS) in patients with primary aldosteronism? Clin Endo 2009; 70: 14-17
4. Hundemer GL, et al/ Cardiometabolic outcomes and mortality in medically treated primary aldosteronism: a retrospective cohort study. Lancet Diabetes Endocrinol. 2018; 6 (1): 51-59
5. Zarnegar R, et al. The Aldosteronoma Resolution Score - Predicting Complete Resolution of Hypertension After Adrenalectomy for Aldosteronoma. Annals of Surgery 2008; 247 (3): 511-518
6. Parthasarathy HK, et al. A double-blind, randomized study comparing the antihypertensive effect of eplerenone and spironolactone in patients with hypertension and evidence of primary aldosteronism. Journal of Hypertension 2011; 29: 980-990

AT THE FOREFRONT
UChicago Medicine

Questions/ Comments