How to Recognize Adrenal Disease

CME Away
India & Sri Lanka
March 23 - April 7, 2018

Richard A. Bebb  MD, ABIM, FRCPC
Consultant Endocrinologist
Medical Subspecialty Institute
Cleveland Clinic Abu Dhabi
Barriers To Change
Disclosure of Commercial Support

• This program has not received financial support, or in-kind support, from any Pharmaceutical Company.

• Potential for conflict(s) of interest:
  – None to declare
Faculty/Presenter Disclosure

- Faculty: Richard Bebb
- Relationships with commercial interests: None to report
Learning Objectives:

- Understanding Endocrine Hypertension
- Recognition of “Common” Adrenal Disorders
Case 1: 42 female

- 6 months of worsening diarrhea
- 15 lb weight loss (7 kg)
- Malaise, amenorrhea
- O/E BP 105/70
- Creatinine 2.0 X normal
  - K 5.3 mmol/L
  - Na 132 mmol/L
  - mild anemia
  - benign urine sediment
Case 1: Your Next Step?

1) refer for renal biopsy
2) refer for GI work-up
3) am cortisol
4) ACTH level
# Adrenal failure: signs & symptoms

- Weakness & fatigue
- Anorexia & weight loss
- Nausea, vomiting & diarrhea
- Hyponatremia
- Hypotension
- Shock & death
- Hyperkalemia*
- Hyperpigmentation*

*Only in primary adrenal failure
Addison’s Disease
Adrenal failure: causes

• Primary (cortisol & aldosterone deficient)
  – AUTOIMMUNE
  – tuberculosis, fungal infections
  – adrenal hemorrhage

• Secondary (cortisol deficient)
  – pituitary lesions
Adrenal failure: evaluation

• Cortrosyn stimulation test:
  – Cortrosyn 250 mcg IV
  – Plasma cortisol @ 30 & 60 min
  – Normal: > 550 nmol/L (20mcg/dl)
  – Not sensitive for new onset secondary adrenal failure (after pituitary surgery, pituitary apoplexy)
Testing in Adrenal Insufficiency

<table>
<thead>
<tr>
<th>ACTH pg/ml @ 8 AM</th>
<th>Primary</th>
<th>Secondary</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td></td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td></td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td></td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td></td>
<td>○</td>
<td>○</td>
</tr>
</tbody>
</table>

Serum Cortisol

- Normal
- Recent Onset
- Long-Standing
- 1° Adrenal Insufficiency

0 30 60
Time minutes

= Normal Range
Obesity: Differential Diagnosis

• How to differentiate generic obesity from Cushing’s syndrome
Cushing’s Syndrome
Cushing’s Striae

1) Thin depth
2) Wide width
3) Violaceous
Screening for Cushing’s Syndrome

3 options:

• Over night 1 mg dexamethasone suppression testing (normal response is am cortisol < 50 mmol/L; <1.8 mg/dl)

• 24 hr. Urinary free cortisol

• Late Night Salivary Cortisol (LNSC)
  – Beware age, DM, BP, Stress, Shift workers
  Future: ? Salivary Cortisone??
Late Night Cortisol

![Cortisol Graph](image)

Cortisol (µg/dL) vs. CLOCK TIME (HOURS)
Late-night Salivary Cortisol

- Evening values discriminated between the groups
- Morning values were not helpful
Salivary Cortisol: Helpful with Pseudo Cushings

UFC and LNSC in 43 patients with surgically proven Cushing's disease

Salivary cortisol may be elevated when UFC is normal

Case 2: 24 year old female

- Routine physical BP 170/90
- No meds
- Asymptomatic other than new headaches
- PRA 5 times upper limit of normal
  aldosterone high normal
Case 2: Diagnosis

1) Conn’s Syndrome
2) Pheochromocytoma
3) Fibromuscular dysplasia of renal artery
4) Cocaine use
Secondary Hypertension

- The Big 3 are:

  Renal artery stenosis
  Hyperaldosteronism
  Pheochromocytoma
Hyperlaldosteronism
Hyperaldosteronism

- Adenoma
- Bilateral Hyperplasia
- Adrenal Carcinoma
- GRA (Glucocorticoid remedial aldosteronism)
Endocrine Society Guidelines: Hyperaldosteronism is often Missed; who to screen

1) Patients with hypertension (≥140/90 mm Hg) with hypokalemia.
2) Patients with hypertension and sleep apnea.
3) Patients with sustained blood pressure above 150/100 mm Hg.
4) Patients with resistant hypertension (uncontrolled with three conventional antihypertensive drugs).
5) Patients with hypertension controlled with four or more medications.
6) Patients with hypertension and an adrenal incidentaloma (mass in the adrenal gland).
7) Patients with an early onset of hypertension (<40 years of age) and those with a family history of early-onset hypertension or stroke.
8) Patients with first-degree relatives with hypertension and a diagnosis of primary aldosteronism.
Signs and Symptoms in Primary Hyperaldosteronism

- Hypertension
- Weakness
- Muscle Cramps
Hyper-aldosteronism
Screening tests

Serum Potassium

Random plasma Aldosterone / Renin Ratio
(potassium should be normalized)
(no interfering medications)

Adenoma (APA) vs Hyperplasia (IHA)

• Very High PAC/PRA → Adenoma

• More severe hypertension and lower potassium suggests an adenoma

• Adrenal Vein Sampling Often Indicated
Safe Anti-hypertensives to use while Investigating

- Verapamil
- Hydralazine
- Alpha Blockers

- Do NOT start spironolactone. It makes investigating hyperaldosteronism impossible and takes 6 weeks to wear off.

Endocrine Society Guidelines 2016
Case 3: 34 year female

- 10 months of anxiety, headaches and sweating
- Stock trader
- Hypertensive for 5 years. BP now up to 160/90
Hypertension In Pheochromocytoma

- Paroxysmal in 48%
- Persistent in 29%
- Normal in 13%
Pheochromocytoma
Pheochromocytoma
Symptoms (3 P)

- Attacks of Headaches (80%)
- Palpitations (64%)
- Diaphoresis (57%)

Symptomatic Triad Of Headache, Sweating, And Tachycardia In A Hypertensive Patient ➔ Sensitivity 90.9% And Specificity 93.8%
How To Screen...

- Urine Catecholamines or metabolites: metanephrines, normetanephrines, (VMA less helpful)

- Plasma Collection:
  Plasma-Free Metanephrines Are Recommended As The Test Of Choice For Excluding Or Confirming The Diagnosis Of Pheochromocytoma
Adrenal Conditions Not to Miss:

- Addison’s Disease
- Cushing’s Syndrome/Disease
- Conn’s Syndrome
- Pheochromocytoma
Endocrine Diseases

Often hard to detect

THINK about them
Order screening tests
Do not be afraid to refer early