Diagnosing and Managing Common Adrenal Disorders

Veronica Piziak MD, PhD
Emeritus Director of Endocrinology Scott & White
Fellowship Director Endocrinology Baylor S&W

vpiziak@sw.org
Disclosures: None
Objectives

Discuss the Management of Incidental Adrenal Masses
Discuss the management of common Adrenal Disorders
Incidental Adrenal Masses
What do you need to know?

Is it cancer?  What is the potential for morbidity or mortality?

Is it functional?  Does it produce hormones that can cause problems?

Is there a mass effect?  Is it growing?  What vital structures could be compromised?

About 80+ % of the time the nodules of the adrenal are just warts!
Adrenal Mass > 1.0 cm

Is it malignant?  
Very rarely

Is it functional?  
Rarely it can make hormones that cause hypertension, weight gain and diabetes

Is there a mass effect?  
Rarely adrenal tumors can destroy the normal tissue and cause the gland to fail
Adrenal Incidentalomas

Prevalence of incidentally discovered adrenal Masses: 4.4%- 10% of patients undergoing CT scan
Terzolo M et al Eur J Endo 2011;164:851

- nonfunctioning benign lesion 82.5%
- cortisol-secreting adenoma 5.3%
- pheochromocytoma 5.1%
- adrenocortical carcinoma 4.7%
- metastatic lesion 2.5%
- aldosteronomas 1%
- Malignant overall 8%

Musella et al. BMC Surgery 2013; 13:57
Goals:

Find adrenal carcinoma
Identify all adrenal non-functioning lesions suspicious for adrenocortical cancer (imaging)
Identify functional pheochromocytomas
Identify cortisol or aldosterone secreting lesion
Identify benign adenomas

You should perform biochemical testing
Obtain adequate imaging - CT or MRI adrenal protocol
Indications for Surgery

Functioning nodules:
- Unilateral aldosterone producing masses
- Hormonally active pheochromocytomas
- Overt Cushing’s Syndrome

Non functioning lesions larger than 4 cm

93% of the adrenal carcinomas were $\geq 4$ cm when found.

Musella et al. BMC Surgery 2013, 13:57
Biochemical Testing

Screening:
Cortisol secreting tumors --- 24 hour/ urinary cortisol
Pheochromocytoma --- urine and plasma metanephrine levels
Aldosteronoma --- Potassium, aldosterone, Aldosterone/Renin
How Accurate are Hormones?

282 incidental adrenal masses
39/39 cortisol secreting lesions,
18/18 aldosterone secreting lesions
19/24 (79.1%) pheochromocytomas
Were detected by biochemical testing

Adrenal carcinoma 2 < 4 cm nonfunctional - Missed

Remember 1 year follow up will help

Musella et al. BMC Surgery 2013, 13:57
 Imaging

Radiologist will report benign, suspicious, malignant

Help evaluate < 4 cm tumors

Adenomas have a high lipid content and a low attenuation (dark) on a non-enhanced CT hence the Hounsfield scale. Low suggests benign.

< 10 benign adenoma 100%

< 20 and < 4 cm benign adenoma

Contrast enhanced look at washout more than 50% at 10 minutes = adenoma
Case: Abdominal Pain

48 yo man complaining of lower abdominal pain was found to have an adrenal mass on CT. Hounsfield units = 8 (dark)
Case: Abdominal Pain

He had noted weight gain and some thin skin but was otherwise asymptomatic

Examination:

Blood pressure 140/88, BMI 32, upper abdominal obesity, thin skin, bruises

Lab: Urine cortisol 210 (nl to 45)
Adrenal Tumor

Low ACTH
ACTH independent tumor
Case 2 Weight Gain + IBS

22 yo lady complaining of weight gain and has a history of irritable bowel syndrome with increased cramping pain. She had a CT of the abdomen for follow up of IBS and was found to have bilateral adrenal hyperplasia.

Recently she reported some thinning of her skin and was found to have a blood pressure of 140/90.

Her fasting glucose was checked due to the weight gain and was 132mg%, A1c was 6.0%

Does she have diabetes?
Bilateral Adrenal Incidentalomas

10-15% Bilateral enlargement or masses = bothersome

Must screen for both hyper and hypofunction

**ACTH dependent Cushing’s - overactivity**

Congenital adrenal hyperplasia – enzyme deficiency – found in infancy

Metastatic disease, Infection TB, Fungus

May cause adrenal insufficiency

24 hour urine for cortisol

Angeli A et al Horm Res 1997;47:279
Test Results

Urinary free cortisol  200 normal  <45
ACTH  186 normal < 150
1 mg Dexamethasone ➔ cortisol  10
CT scan of abdomen
Bilateral adrenal enlargement
MR scan of the head --- Pituitary tumor
Bilateral adrenal hyperplasia

High ACTH

Pituitary tumor or ectopic ACTH production

ACTH dependent tumors
Case 3 Massive Polyuria

10 yo female who developed massive polyuria about 10 liters daily and was found to have diabetes and she had bruising on her extremities and muscle weakness and wasting in her extremities.

She developed excess body hair and lethargy

A urine cortisol was 580 and her potassium was low.

ACTH was 658 normal up to 150

CT of the abdomen showed bilateral adrenal hyperplasia

CT chest Tumor that was an ectopic ACTH producing tumor - benign

Surgery was curative
Hormone measurements
Cushing’s syndrome

Cortisol producing tumor:
24 hour urine for cortisol  3-4 x normal
Overnight 1 mg dexamethasone suppression test
> 1.8 mcg/dl

Salivary cortisol -- late night x 2 elevated
Usually symptomatic and have signs hypercortisolism
Adrenal carcinoma usually produces high levels of multiple hormones

Rapid progression, virilization

Musella et al. BMC Surgery 2013, 13:57

ACTH level key to finding cause of adrenal overactivity
Case 4  Well Women Exam? Or Common Adrenal Problem

36 yo lady comes with irregular menses, mild hirsutism and a BMI of 36
BP 150/80, upper abdominal obesity
Difficulty losing weight, despite exercise and a reasonable diet.

You think Cushing’s syndrome? Should I screen? Yes
Urinary cortisol was 90 -- normal 45
ACTH low
Overnight 1 mg Dexamethasone suppression test cortisol was 5.0
Normal < 1.8

some adrenal autonomy, not full adrenal Cushing’s syndrome
Subclinical Cushing’s
Most common functioning adrenal mass

24 hour urine cortisol < 3-4 x normal
1 mg dexamethasone does not cause suppression
preferred tests for incidental masses to identify sub clinical disease
May have obesity, abnormal A1c, osteopenia, hypertension
May be symptomatic with difficulty losing weight
Subclinical disease needs to be observed annually – for progression of obesity, A1c, bone disease, blood pressure,
It may remit

BUT always image - if it grows remove it!
Indications for Surgery at 1 year Follow up

Patients younger than 40 presenting with a subclinical Cushing syndrome of recent onset and worsening, hypertension, glucose intolerance and osteoporosis.

Non functioning lesions smaller than 4 cm but increasing in radiographic dimensions or becoming hormonally active within the first year from diagnosis.
Pheochromocytoma

Many are screened but few tumors are found.

Common symptoms:
- labile hypertension, anxiety, headaches

Imaging:
- CT scan HU > 20 --- frequently = brightest bulb in the box
Pheochromocytoma  the Brightest Bulb in the Box!
Pheochromocytoma, Biochemical Testing

24 hour urine for metanephrines and plasma metanephrines

Plasma metanephrines  3 x normal
Sensitive test---false positives   Normal no pheochromocytoma
24-hour urine total metanephrine level above 1,800 μg
Specific test --- false negatives   High pheochromocytoma

Some pheochromocytomas secrete poorly and cause subclinical disease or are nonfunctional
Malignant pheochromocytomas very rare.
Musella et al. BMC Surgery 2013, 13:57
Preoperative Preparation

Surgery
Dibenzylamine 10 mg / day (alpha blockade)
Hydration
Then beta blockers to control tachycardia or labetalol
Echocardiogram to check for cardiomyopathy

There are subclinical pheochromocytomas you can use the same meds for control of symptoms and monitor annually
Hormone measurements

Aldosteronoma

Serum potassium /normal, no hypertension  STOP
Either serum potassium low or hypertension  GO
Plasma aldosterone concentration/plasma renin activity
Positive : plasma aldosterone concentration/plasma renin activity ratio > 20
plasma aldosterone concentration greater than 16 ng/dL

Musella et al. BMC Surgery 2013, 13:57
I am changing color

32 yo lady developed hypothyroidism from thyroiditis here for routine follow up.
She mentions that her skin is becoming darker particularly her gums and that she has been feeling dizzy on standing, lost weight and has nausea.
She brings a picture form 1 year ago and last week
Blood pressure 102/70 sitting and 80/60 standing
Laboratory: potassium 5.5, sodium 132, CO2 20
Then and Now
Laboratory Abnormalities

CBC: anemia +/- neutropenia, relative lymphocytosis, and eosinophilia
Chemistry: hypoglycemia, hyponatremia, metabolic acidosis hyperkalemia*; rarely may have hypercalcemia

*seen in primary Adrenal Insufficiency

Our patient’s lab
ACTH 5000 -- normal up to 150,
Random cortisol AM 4.5 Normal 7-20 AM

You have made the diagnosis!
Primary adrenal insufficiency
Adrenal Insufficiency

Signs

- Weight loss 100%
- Hyperpigmentation 94%*
- Hypotension 88-94%
- Viteligo 10-20%

*Primary Only
Adrenal Insufficiency Signs

- Weight loss 100%
- Hyperpigmentation 94%*
- Hypotension 88-94%
- Viteligo 10-20%

*Primary Only
All of a Sudden I Don’t Feel Well

38 yo lady who came to the ED with nausea, dizziness on standing, weight loss and back pain for several days.

Blood pressure 130/70 no orthostatic change

Lab: e group normal
- Cortisol 0
- ACTH undetectable
For the past year she was receiving prednisone 40 mg daily for a connective tissue disease. She decided that it was not doing any good and so stopped it abruptly.
Anyone age 25-70 comes in to your office with complaints of nausea, dizziness on standing, weight loss and fatigue.

Just recovered from (meningitis, stroke, head injury, or is on Opioids). She was told that this is chronic fatigue, after her illness, but she thinks that it is her adrenal.

Lab: e group normal
AM Cortisol 6 Normal 7-25
ACTH low
Frequently remits after 2-3 months or if opioids are stopped
Hyperkalemia and RAAS system stimulate aldosterone production and androgens are low.
Circadian and Pulsatile Rhythm of Cortisol
A Random Cortisol doesn't make the diagnosis
Making the Diagnosis
Stimulation Testing

Can be done while dexamethasone is on board

Traditional dose ACTH “stim” test

  Draw baseline cortisol and ACTH
  Inject 250ug IM/IV
  Cortisol in 30 and 60 min

Can be done anytime of day

Normal response is a level greater than 18-20ug/dL
  (the “delta” does not matter)

You can add aldosterone levels
Stimulation Test Responses

Case 1

Case 2 and Case 3

Serum cortisol, μg/100 mL

Normal adrenal

2° Adrenal insufficiency

1° Adrenal insufficiency

TIME
Therapy

Glucocorticoid Replacement

Several regimens can be used
  Hydrocortisone 10-20mg q AM and 0-10mg qPM
  Prednisone 5-7.5mg daily

Divided doses are usually given
Give last dose in the afternoon to avoid insomnia
Can try a single AM dose to help with compliance
Development of any sign of Cushing’s indicates overreplacement

Be sure patient has Solucortef 100 mg for IM use in emergencies.
Double dose for illness: infections, day surgery
Mineralocorticoid Replacement

Only indicated in primary adrenal insufficiency as the zona glomerulosa is also affected

Only 1/3 of the aldosterone is controlled by ACTH

Hyperkalemia and the RAAS system 2/3 control of aldosterone

Fludro cortisone (Florinef) 0.05-0.1mg daily

Some patients may require much higher doses

Monitor with e group
Tapering Steroids

Glucocorticoids may be used in the treatment of autoimmune/inflammatory disorders

Any treatment duration greater than 3 weeks at doses more than 7.5mg of prednisone per day can cause HPA suppression and adrenal atrophy

When given for periods of time less than 3 weeks, dose can be stopped without a taper (use caution in frail or critically ill patients—a rapid taper may be beneficial)

Tapering in this setting is usually dictated by the underlying disease process and likelihood of a “flare”
Taper steroids

Patient dependent!
Prescription for low dose tablets (2.5 mg hydrocortisone)
  12 hour ½ life
5 half lives = about 3 days
Decrease the dose by the small tablet size every three days
Avoid symptoms if they occur go back to previous dose and then try again.
Keep the AM cortisol about 10 – 15

Cortrosyn stimulation test at the end of taper
Summary

Adrenal Insufficiency

Diagnosis: Cortrosyn stimulation test
ACTH gives the location

Therapy
- Primary: replace cortisol and aldosterone
- Secondary: replace cortisol only

Dosage is based on body surface area

For emergencies: Hydrocortisone IV 100mg q 8 hours,
D5 normal saline
Questions?