57-year-old man with anxiety, diaphoresis, fatigue and bilateral adrenal nodules

Celeste Thomas
November 1, 2012
History of Present Illness

- 8 months prior to presentation developed intermittent right flank pain
- 4 months prior to presentation pain worsened and was associated with voiding symptoms so he sought medical attention
- Lower urinary tract symptoms resolved with tamsulosin but pain persisted
- CT scan identified bilateral adrenal nodules, 5.2 cm on the right, 4.2 cm on the left
- His local endocrinologist performed some studies:
  - Plasma metanephrines 0.26 (normal <0.5)
  - Plasma normetanephrines 0.78 (normal <0.9)
  - 24h urine studies with metanephrine of 195 (normal 44-261), normetanephrines 689 (normal 44-261)
  - Low-dose dexamethasone suppression test with AM cortisol of 4.7

- He and his wife were referred to urology here who discussed options and referred to Dr. Weiss
Outside Images of Adrenal Nodules
History of Present Illness

- Symptoms included profuse sweating, anxiety attacks, extreme fatigue, headaches
- He would like to proceed to surgery
Bilateral Nodules

- **Questions to consider**
  - Are the nodules hormonally active?
  - Do they have radiologic characteristics suggestive of malignant lesions
  - Does the patient have a history of malignancy

- **Which endocrine disease processes are we concerned about?**
  - Hyperaldosteronism
  - Hypercortisolism
  - Pheochromocytoma

- **What’s most likely?***
  - approximately 80% of those incidentally found are nonfunctioning adenomas,
  - 5% of patients had subclinical Cushing syndrome (SCS)
  - 5% had a pheochromocytoma
  - 1% had an aldosteronoma
  - <5% had an adrenocortical carcinoma (ACC)
  - 2.5% had a metastatic lesion
  - The remaining incidentalomas were ganglioneuromas, myelolipomas, or benign cysts

**Hormonal findings in adrenal incidentalomas***

<table>
<thead>
<tr>
<th>Endocrine state</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonhypersecreting adenoma</td>
<td>65–90%</td>
</tr>
<tr>
<td>Hypercortisolism</td>
<td>5–14%</td>
</tr>
<tr>
<td>Hyperaldosteronism</td>
<td>1–3.3%</td>
</tr>
<tr>
<td>Hyperandrogenism</td>
<td>0–11%</td>
</tr>
<tr>
<td>Hyperestrogenism</td>
<td>Rare</td>
</tr>
<tr>
<td>Congenital adrenal hyperplasia</td>
<td>Rare</td>
</tr>
<tr>
<td>Pheochromocytoma</td>
<td>1.5–25%</td>
</tr>
</tbody>
</table>

*NIH State-of-the-Science Conference on Management of the Clinically Inapparent Adrenal Mass ("Incidentaloma")*
Past Medical and Surgical History

- Hypertension
- Diabetes Mellitus
- Hyperlipidemia
- Carotid Artery Stenosis s/p Endarterectomy
- Benign Prostatic Hypertrophy with LUTS
- Bladder Tumor s/p TURBT
- Anal Sphincterotomy
**Allergies and Medications**

- **Allergies**
  - Bee Venom causes shortness of breath

- **Medications**
  - Metformin 1000 mg PO BID
  - Sitagliptin 100 mg PO daily
  - Lantus 42 units daily
  - Clopidogrel 75 mg PO daily
  - Aspirin 325 mg PO daily
  - Rosuvastatin 20 mg PO QHS
  - Lisinopril 40 mg PO daily
  - Metoprolol succinate 50 mg PO daily
  - Gabapentin 1200 mg PO QHS
  - Tamsulosin 0.4 mg PO daily
Family History and Social History

- **Family History**
  - Mother: Type 2 DM, Stroke, Dementia
  - Father: Type 2 DM, CAD
  - 2 Brothers: Type 2 DM

- **Social History**
  - Lives with his wife
  - Superintendent of a school district
  - Current every day smoker, 1ppd x 40 years
  - No alcohol or illicit drug use
Physical Exam

- **BP:** 163/93  **Pulse:** 80  **Height:** 188 cm (6' 2'')  **Weight:** 118.253 kg (260 lb 11.2 oz)
- Constitutional: He is oriented to person, place, and time. He appears well-developed and well-nourished. **He is not Cushingoid appearing.**
- Head: Normocephalic and atraumatic.
  - Right Ear: External ear normal.
  - Left Ear: External ear normal.
- Nose: Nose normal.
- Mouth/Throat: Oropharynx is clear and moist.
- Eyes: Conjunctivae and EOM are normal. Pupils are equal, round, and reactive to light.
- Cardiovascular: Normal rate, regular rhythm, normal heart sounds and intact distal pulses.
  - No murmur heard.
- Pulmonary/Chest: Effort normal and breath sounds normal. **Marked bilateral gynecomastia.**
- Abdominal: Soft. Bowel sounds are normal. He exhibits no distension and no mass. There is no tenderness. There is no rebound and no guarding. **No violaceous striae**
- Genitourinary: Penis normal. Right testis shows no mass, no swelling and no tenderness. Right testis is descended. Left testis shows no mass, no swelling and no tenderness. Left testis is descended.
- Musculoskeletal: Normal range of motion. He exhibits no edema and no tenderness.
- Neurological: He is alert and oriented to person, place, and time. He has normal reflexes. No cranial nerve deficit.
- Skin: Skin is warm and dry. No rash noted. No erythema. **No ecchymosis**
- Psychiatric: He has a normal mood and affect. His behavior is normal. Thought content normal.
Laboratory Studies

Total Testosterone = 171 ng/dL (180-800)
Te Binding Globulin = 30 nmol/L (10-80)
Free Testosterone (calc) = 54 pg/dL
FSH = 42.4 mIU/mL    LH = 13.4 mIU/mL    Estradiol = 17 pg/mL
Laboratory Studies

- **Plasma Normetanephrine:**
  - 0.61 nmol/L ref range: <0.90

- **Plasma Metanephrine:**
  - 0.21 nmol/L (ref range: <0.50)

- **ACTH = <5 pg/mL**

- **Midnight salivary cortisol:**
  - 182 ng/dl (ref range <100)

- **Aldosterone <4.0 ng/dL**

- **Renin <0.6 ng/mL/h**
ACTH-Independent Cushing’s Syndrome

Several investigators have shown that elevated nighttime cortisol levels appear to be the earliest and most sensitive markers for Cushing syndrome with sensitivity and specificity approaching 90% to 95%.*

AACE/AAES Guidelines

Adrenal incidentaloma

<4 cm with benign characteristics (homogeneous, regular borders, HU <10 on noncontrast CT scan)

Hormonally active (PAC/PRA; plasma-free metanephrines and normetanephrines; and overnight 1-mg dexamethasone suppression test)

Yes, adrenalectomy

≥4 cm on CT scan, indeterminate or malignant

Adrenalectomy after hormonal evaluation

*No, follow patient with repeat CT scan and biochemical evaluation
Suggested evaluation of an incidentally found adrenal mass.

Evaluation of an adrenal incidentaloma

- **Size**
  - > 4 cm → Surgery after pheochromocytoma evaluation*
  - < 4 cm
    - **CT/MRI characteristics**
      - malignant
        - < -20 HU: myelolipoma
          - F/U if large
        - benign
          - Hormonal eval
      - If normal, follow-up @ 1 yr
        - Exclude pheochromocytoma
        - Exclude hypercortisolism
        - (no eval for aldosteronism)
        - Image for mass increase
          (obtain at 6 mo if worrisome)
        - Surgery if abnormal
          - If normal, 1 additional F/U only
      - Dex suppression
        - LN salivary cortisol
        - UFC
          (consider DHEAS, ACTH)
        - If clearly abnormal and symptomatic, surgery
    - Urine catecholamines
      - Plasma free metanephrine
      - If clearly abnormal, surgery
      - If hypertensive,
        - Renin:Aldo
        - If >20, confirm with other test then
          Surgery

*Evaluation of pheochromocytoma characteristics includes:
- Calcium
- Metabolic profile
- Renin
- Aldosterone
- BUN/Creat
- 24h urinary catecholamines
- 24h urinary metanephrines
- Catecholamine precursors
- Aldosterone precursors
- 17-hydroxyprogesterone
- 17-OH progesterone
- Kt/C

Nieman L K JCEM 2010;95:4106-4113

©2010 by Endocrine Society
Hormone-secreting or large (>6 cm) masses should be surgically removed.

Silent masses smaller than 3 cm should be imaged further. No further followup is needed if the mass is lipid-rich based on unenhanced and enhanced CT or chemical shift MR imaging. No further followup is needed if a concordant image with CT is obtained with NP-59 nuclear scan. If the mass is lipid-poor, it could still be an adenoma; in this case, followup CT scans should be performed to evaluate for change in size at 6, 12, and 18 months. A malignant tumor is likely to grow, whereas a benign tumor will remain stable.

Masses between 3 and 6 cm should be evaluated by radiographic and scintigraphic techniques to ascertain whether they are potentially benign or malignant. If the imaging features are consistent with a benign adenoma, the patient should be observed if 50 years of age or older. Surgical resection should be considered if the patient is younger than 50 years.
Similar Case

- 69 year-old woman who had a 10-15 year history of controlled hypertension, back pain associated with osteoporosis, easy bruising, and truncal obesity. Her medications included conjugated estrogens.
- Physical examination revealed classical features of CS. She had a raised blue lesion on her buccal mucosa. Plasma cortisol concentrations were elevated at 36 (a.m.) and 38 (p.m.) microg/dL.
- Urinary free cortisol was normal at baseline (65 microg/24 hours) but failed to suppress adequately in response to the low-dose dexamethasone suppression test (75 microg/24 hours).
- The plasma ACTH concentration was undetectable. Plasma cortisol concentrations failed to suppress (37 microg/dL) with an 8 mg overnight dexamethasone test.
- A CT scan of the abdomen revealed bilateral adrenal masses.
- Adrenal venous sampling showed cortisol secretion from both adrenals.
- The patient underwent bilateral adrenalectomy with pathology confirming bilateral adenomas.

Back to Our Patient

- Laparoscopic bilateral adrenalectomy
- Felt remarkably well after surgery
- Initially required little insulin but insulin requirements have increased postoperatively
- Post op stress dose steroids were titrated down discharged on 40 and 20 with plan for 20/10, now on 25 and 15
- Fludrocortisone 0.1 mg PO daily → 0.05
3.1 x 2.0 x 2.4 cm golden-yellow to orange nodule (right adrenal nodule)

moderately firm, 5.6 x 3.4 x 2.3 cm yellow-to-orange nodularity (left adrenal nodule)