Indications for Adrenal Surgery

Anand Vaidya, MD MMSc
Director, Center for Adrenal Disorders
Assistant Professor of Medicine
Division of Endocrinology, Diabetes, & Hypertension
Brigham and Women’s Hospital
Harvard Medical School
None
Sources

Management of adrenal incidentalomas: European Society of Endocrinology Clinical Practice Guideline in collaboration with the European Network for the Study of Adrenal Tumors

The Management of Primary Aldosteronism: Case Detection, Diagnosis, and Treatment: An Endocrine Society Clinical Practice Guideline

Pheochromocytoma and Paraganglioma: An Endocrine Society Clinical Practice Guideline

Adrenal Scientific Committee
Indications for Adrenal Surgery

1. Primary Adrenal Malignancy

2. Adrenal Tumor with Autonomous Adrenal Hormone Secretion with Clinical Consequences
46 year old pre-menopausal woman was in a car accident.

No known medical conditions

Brought to ER and complained of some abdominal pain. Had a rapid unenhanced Abdominal CT that revealed no hemorrhage or other injuries

Incidental discovery of a 2.2 cm R adrenal mass, with 5 HU unenhanced density

What, if anything, do you tell her about the incidental adrenal mass??
Incidentally Discovered Adrenal Masses

• Adrenal tumors are incidentally discovered in 1-10% of adults.

• A minority represent malignant entities (primary adrenal malignancy or extra-adrenal metastasis)

• The majority are determined to be benign and “nonfunctional” and therefore are considered to pose no health risk.

• In contrast, ~10-15% of adrenal tumors autonomously secrete adrenal hormones. These “functional” tumors are associated with an increased risk for cardiometabolic outcomes, such as CV disease, diabetes, and osteoporosis/fracture.

• Therefore, all incidentally discovered adrenal tumors should be carefully evaluated to determine whether they are: 1) **malignant** and/or 2) **functional**.
Differential Diagnosis of Adrenal Mass

<table>
<thead>
<tr>
<th></th>
<th>NON-FUNCTIONAL</th>
<th>FUNCTIONAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BENIGN</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MALIGNANT</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


## Differential Diagnosis of Adrenal Mass

<table>
<thead>
<tr>
<th>BENIGN (~90-95%)</th>
<th>NON-FUNCTIONAL (85-95%)</th>
<th>FUNCTIONAL (5-15%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenocortical Adenoma</td>
<td>Myelolipoma Neuroblastoma</td>
<td></td>
</tr>
<tr>
<td>Ganglioneuroma</td>
<td>Cyst Hemorrhage Infection (fungal, tuberculous) Hemangioma</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MALIGNANT (~5%)</th>
<th></th>
<th></th>
</tr>
</thead>
</table>
# Differential Diagnosis of Adrenal Mass

<table>
<thead>
<tr>
<th></th>
<th>NON-FUNCTIONAL (85-95%)</th>
<th>FUNCTIONAL (5-15%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BENIGN (~90-95%)</strong></td>
<td>Adrenocortical Adenoma</td>
<td>Adrenocortical Adenoma</td>
</tr>
<tr>
<td></td>
<td>Myelolipoma</td>
<td>Aldosterone producing</td>
</tr>
<tr>
<td></td>
<td>Neuroblastoma</td>
<td>Cortisol producing</td>
</tr>
<tr>
<td></td>
<td>Ganglioneuroma</td>
<td>Micro- or Macro-nodular Disease</td>
</tr>
<tr>
<td></td>
<td>Cyst</td>
<td>Aldosterone producing</td>
</tr>
<tr>
<td></td>
<td>Hemorrhage</td>
<td>Cortisol producing</td>
</tr>
<tr>
<td></td>
<td>Infection (fungal, tuberculous)</td>
<td>Pheochromocytoma</td>
</tr>
<tr>
<td></td>
<td>Hemangioma</td>
<td></td>
</tr>
<tr>
<td><strong>MALIGNANT (~5%)</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Differential Diagnosis of Adrenal Mass

<table>
<thead>
<tr>
<th></th>
<th><strong>NON-FUNCTIONAL</strong></th>
<th><strong>FUNCTIONAL</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(85-95%)</td>
<td>(5-15%)</td>
</tr>
<tr>
<td><strong>BENIGN</strong> (~90-95%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adrenocortical Adenoma</td>
<td><strong>Adrenocortical Adenoma</strong></td>
<td><strong>Adrenocortical Adenoma</strong></td>
</tr>
<tr>
<td>Myelolipoma</td>
<td></td>
<td><strong>Aldosterone producing</strong></td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td></td>
<td><strong>Cortisol producing</strong></td>
</tr>
<tr>
<td>Ganglioneuroma</td>
<td></td>
<td><strong>Micro- or Macro-nodular Disease</strong></td>
</tr>
<tr>
<td>Cyst</td>
<td></td>
<td><strong>Aldosterone producing</strong></td>
</tr>
<tr>
<td>Hemorrhage</td>
<td></td>
<td><strong>Cortisol producing</strong></td>
</tr>
<tr>
<td>Infection (fungal, tuberculous)</td>
<td></td>
<td><strong>Pheochromocytoma</strong></td>
</tr>
<tr>
<td>Hemangioma</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MALIGNANT</strong> (~5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adrenocortical carcinoma</td>
<td></td>
<td><strong>Adrenocortical carcinoma</strong></td>
</tr>
<tr>
<td>Metastatic cancer from a non-adrenal primary</td>
<td></td>
<td><strong>Pheochromocytoma</strong></td>
</tr>
</tbody>
</table>
General Diagnostic Approach

1. Is there evidence for malignancy?
2. Is there adrenal hormone excess?

Clinical Phenotype
- History and physical exam for evidence of hormone excess or malignancy

Biochemical Phenotype
- Laboratory evaluation for evidence of adrenal hormone excess

Radiographic Phenotype
- Radiographic evidence supportive of a benign or malignant mass
# Clinical Phenotype

<table>
<thead>
<tr>
<th>Overt Cortisol Excess</th>
<th>Overt Catecholamine Excess</th>
<th>Overt Aldosterone Excess</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity/weight gain</td>
<td>Episodic symptoms</td>
<td></td>
</tr>
<tr>
<td>Lipodystrophy</td>
<td>o Hypertension</td>
<td></td>
</tr>
<tr>
<td>o Central adiposity</td>
<td>o Palpitations</td>
<td></td>
</tr>
<tr>
<td>o Supraclavicular fat pads</td>
<td>o Anxiety/Panic</td>
<td></td>
</tr>
<tr>
<td>o Dorsocervical fat pad</td>
<td>o Sweats/Tremors</td>
<td></td>
</tr>
<tr>
<td>o Rounded face</td>
<td>o Headache</td>
<td></td>
</tr>
<tr>
<td>Hyperglycemia/Diabetes</td>
<td>o Arrhythmia</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mood disorder/Psychosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteoporosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunesuppression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelet dysfunction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypercoagulable state</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myopathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrophic skin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypokalemia</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Case 1 – Clinical Phenotype

• No symptoms
• No signs to suggest hypercortisolism, pheochromocytoma, hyperaldosteronism, or hirsutism.

• No evidence of weight loss, abdominal distention, or androgen excess, to suggest metastatic cancer or hyperfunctioning adrenocortical carcinoma

Unrevealing
Case 1 – Radiographic Phenotype

Normal comparison

Patient’s non-contrast CT

2.2cm right adrenal mass
5 Hounsfield units
Round, homogenous
## Case 1 – Radiographic Phenotype

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Likely Benign</th>
<th>Potentially Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attenuation on unenhanced CT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contrast washout on CT protocol at 15 minutes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI chemical shift suggestive of lipid-rich content</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FDG avidity on PET</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Irregular Borders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneous content</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Necrosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcifications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rate of Growth</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**BENIGN:** Suggestive of adrenocortical **adenoma**
### Suggested screening biochemical evaluation for adrenal masses:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Patients</th>
<th>Test</th>
<th>Abnormal Value</th>
</tr>
</thead>
</table>
| Autonomous cortisol secretion            | ALL      | 1 mg Dexamethasone Suppression Test          | Nonfunctional: ≤1.8 mcg/dL  
Possible: 1.9-5.0 mcg/dL  
Autonomous: 5.0 mcg/dL |
| Primary Aldosteronism                    | HTN and/or hypokalemia | Serum aldosterone to plasma renin activity ratio (ARR) | • Suppressed PRA  
• ARR>20-25 |
| Pheochromocytoma                         | ALL (almost) | Plasma (or urinary) fractionated metanephrines | >2-4x ULRR |
| Adrenal androgen excess                  | Hirsutism or virilization | DHEAS Total Testosterone | Higher than ULN |
Case 1 – Biochemical Phenotype

- 1mg DST #1 => cortisol: 8.0 µg/dL
- 1mg DST #2 => 7.8 µg/dL, ACTH<5 pg/mL
- 8mg DST => 8.1 µg/dL, ACTH<5 pg/mL

- 24h Urine Free Cortisol: 45 µg/24h (<45)

- Midnight Salivary Cortisol: 3.7, 3.9, 4.6, 4.3 nmol/L (<4.3)

- Random ACTH: 5 pg/mL
- Plasma metanephrines: normal
- Aldosterone/PRA: not suggestive
- DHEAS: normal
Case 1 – Clinical Diagnosis

Benign adrenocorticol adenoma

Autonomous cortisol secretion

No clinical signs of hypercortisolism

Should surgery be recommended?
Case 1 – Outcome

- BP = 122/75 mmHg
- Fasting Blood Glucose = 99 mg/dL
- HbA1c = 5.8%
- Bone Mineral Density:
  - Spine T= -3.2
  - Femoral Neck T= -2.2
  - Total Hip T= -2.0

**INDIVIDUALIZED DECISION:** Laparoscopic R adrenalectomy

- Peri-operative IV hydrocortisone considered, but not given
- Pathology revealed 2.5 cm adrenal cortical adenoma
- Post-op AM cortisol 4 mcg/dL, ACTH<10 pg/mL (asymptomatic)
- 1 week post-op, morning cortisol = 17 µg/dL
Suggested Diagnostic Algorithm for Incidentally Discovered Adrenal Mass

1. Adrenal Mass
   - Clinical Phenotype
     - (+)
       - Biochemical Phenotype
         - (+)
           - Confirm Overt Hormone Excess with Clinical Syndrome
             - Radiographic Phenotype and Localization
               - Consider surgery
                 - Growth >0.5 cm/year or +20%
                 - Suspicious radiographic features
                 - New or worsening hormonal excess
             - Suspicious
               - >4-6 cm, >10 HU, contrast avid, heterogeneous
               - ((Consider alternative imaging: CT with washout, MRI))
               - If Unilateral: Consider surgery
               - ?Metastases or infection: Biopsy
               - Unsure? => Surveillance: repeat imaging in 3-6 months
             - Benign Appearing
               - <10 HU, <4 cm, non-contrast avid, homogeneous
               - Surveillance Considerations:
                 - If initially “nonfunctional”:
                   - No strong evidence for repeated biochemical testing
                   - Repeat biochemical testing if worsening comorbidities (HTN, DM, low BMD)
                 - If autonomous cortisol secretion without clinical syndrome:
                   - Individualized consideration for surgery based on comorbidities and other factors.
                   - Repeat biochemical testing annually
                   - No firm evidence for radiographic surveillance
   - (-/+)
     - Radiographic Phenotype
       - Consider surgery
Adrenal Tumors with Autonomous Cortisol Secretion

&

Risk for CVD, Diabetes, Skeletal Disease
Comorbidities associated with adrenal tumors with autonomous and “subclinical” cortisol secretion

<table>
<thead>
<tr>
<th>Comorbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Glucose intolerance/type 2 diabetes</td>
</tr>
<tr>
<td>Obesity</td>
</tr>
<tr>
<td>Dyslipidemia</td>
</tr>
<tr>
<td>Osteoporosis/Vertebral Fracture</td>
</tr>
</tbody>
</table>
Autonomous Cortisol Secretion

- **Stable “nonfunctional”**
  - DST ≤ 1.8 mcg/dL

- **Worsening**
  - ≤ 1.8 => 1.8-5.0
  - or
  - 1.8-5.0 => >5.0

- **Stable, but Any Autonomous Cortisol**
  - DST 1.8-5.0 mcg/dL
  - DST > 5.0 mcg/dL

- **Proportion with Cardiovascular Disease (%)**

- **Proportion with Cardiovascular Mortality (%)**
Autonomous Cortisol Secretion

Most deaths due to cardiovascular or infectious causes
Autonomous Cortisol Secretion

Prediction of Vertebral Fractures in Patients With Monolateral Adrenal Incidentalomas

Valentina Morelli,* Cristina Eller-Vainicher,* Serena Palmieri, Elisa Cairoli, Antonio Stefano Salcuni, Alfredo Scillitani, Vincenzo Carnevale, Sabrina Corbeta, Maura Arosio, Silvia Della Casa, Giovanna Muscogiuri, Anna Spada, and Iacopo Chiodini

• Participants with adrenal incidentalomas who developed incident subclinical vertebral fractures detected on BMD and higher 1mg DST (2.7 vs 2.0 mcg/dL).
• Autonomus cortisol secretion associated with ~10-fold higher risk of incident (~3y follow-up) vertebral fracture.
"Non-Functional" Adrenal Tumors and the Risk for Incident Diabetes and Cardiovascular Outcomes

A Cohort Study

Diana Lopez, MD; Miguel Angel Luque-Fernandez, PhD, MPH, MSc; Amy Steele, BA; Gail K. Adler, MD, PhD; Alexander Turchin, MD, MS; and Anand Vaidya, MD, MMSc

Adjusted HR: 2.36 (1.45, 3.84)
Absolute Risk: 15.6 % (6.9, 24.3)
Incident Composite Diabetes (%)

Years of Follow-Up

Adjusted HR: 2.36 (1.45, 3.84)
Absolute Risk: 15.6 % (6.9, 24.3)

Adrenal Tumor with Subclinical Hypercortisolism
(1mg DST 1.9-5.0 mcg/dL)
32.0%
27.3%

“Non-Functional” Adrenal Tumor
(1mg DST ≤ 1.8 mcg/dL)
11.7%

No Adrenal Tumor
Adrenal Tumor
With Overt Cushing Syndrome

Adrenal tumor with Autonomous Cortisol Secretion but no Cushing syndrome

Insulin Resistance/Diabetes, VFx

“Nonfunctional” adrenal tumor

Morphologically Normal with no hormone excess

Continuum of Cardiometabolic Risk

Prevalence of Condition
Should Intervention be Performed?

Bancos et al. EJE 2016
Case 2

- 71 year old woman was found to have a NEW 3.8 x 2.9 x 1.9 cm Left adrenal mass on a non-contrast CT done to evaluate for appendicitis

- History of breast cancer 10 years prior (ER+, PR+, H2n-); treated with lumpectomy and chemotherapy and 7 years of aromatase inhibitor

- In complete remission on serial biannual restaging scans
  - Adrenals always normal on prior imaging

What, if anything, do you tell her about the incidental adrenal mass??
Case 2 – Radiographic Phenotype

- 3.8 x 2.9 x 1.9 cm NEW left adrenal mass
- Poorly circumscribed, not really a defined mass
- 20 HU on non-contrast CT
- On closer inspection, right adrenal gland is thickened/not normal
### Case 2 – Radiographic Phenotype

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Likely Benign</th>
<th>Potentially Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>&lt; 4 cm</td>
<td>&gt; 4-6 cm</td>
</tr>
<tr>
<td>Attenuation on unenhanced CT</td>
<td>&lt;10 HU</td>
<td>&gt; 10 HU</td>
</tr>
<tr>
<td>Contrast washout on CT protocol at 15 minutes</td>
<td>&gt;50-60%</td>
<td>&lt;50%</td>
</tr>
<tr>
<td>MRI chemical shift suggestive of lipid-rich content</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>FDG avidity on PET</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Irregular Borders</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Heterogeneous content</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Necrosis</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Calcifications</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Rate of Growth</td>
<td>&lt; 1cm/y</td>
<td>&gt;1cm/y</td>
</tr>
</tbody>
</table>
Case 2 – Clinical Phenotype

- No symptoms or signs to suggest hypercortisolism, pheochromocytoma, hyperaldosteronism, or hirsutism.

- No evidence of weight loss or abdominal distention, to suggest metastatic cancer or hyperfunctioning adrenocortical carcinoma.
Case 2 – Biochemical Phenotype

- Plasma metanephrines: normal
- 1mg DST => cortisol: 0.5 µg/dL

Should surgery be recommended?
Suggested Diagnostic Algorithm for Incidentally Discovered Adrenal Mass

**Adrenal Mass**

- **Clinical Phenotype**
  - (+)
  - Biochemical Phenotype
    - Confirm **Overt** Hormone Excess with Clinical Syndrome

**Radiographic Phenotype**

- Suspicious
  - >4-6cm, >10 HU, contrast avid, heterogeneous
  - Consider alternative imaging: CT with washout, MRI)
  - If Unilateral: **Consider surgery**
  - ?Metastases or infection: **Biopsy**
  - Unsure? => **Surveillance**: repeat imaging in 3-6 months

- Benign Appearing
  - <10HU, <4cm, non-contrast avid, homogeneous
  - Surveillance Considerations:
    - If initially "nonfunctional":
      - No evidence for repeat biochemical testing
      - Repeat biochemical testing if worsening comorbidities (HTN, DM, low BMD)
    - If autonomous cortisol secretion without clinical syndrome:
      - Individualized consideration for surgery based on comorbidities and other factors.
      - Repeat biochemical testing annually
      - No firm evidence for radiographic surveillance

- Radiographic Phenotype and Localization
  - Consider surgery
    - Growth>0.5cm/year or +20%
    - Suspicious radiographic features
    - New or worsening hormonal excess

**Surveillance Considerations:**

If initially "nonfunctional":
- No evidence for repeat biochemical testing
- Repeat biochemical testing if worsening comorbidities (HTN, DM, low BMD)

If autonomous cortisol secretion without clinical syndrome:
- Individualized consideration for surgery based on comorbidities and other factors.
- Repeat biochemical testing annually
- No firm evidence for radiographic surveillance
Case 2 Outcome

- CT guided L adrenal biopsy revealed:
  - NEGATIVE for: bacteria, mycobacterium, fungus
  - POSITIVE for: malignant breast cancer, ER\(^+\), PR\(^+\), H2n\(^-\)

- No other systemic evidence of metastases

- With resumption of aromatase inhibitor therapy for stage 4 recurrent breast cancer, adrenal masses decreased in size
Case 2 – Clinical Diagnosis

Recurrent, metastatic, breast cancer to bilateral adrenal glands

No surgery
Case 3

- 37yo healthy woman had an abdominal CT for RLQ pain
- No cause of pain found

- Incidental RIGHT 2.8cm Adrenal mass (<10HU), LEFT ~3cm adrenal mass (18HU)

- Was told that these are likely benign “adenomas” and to follow up in 1 year.
Case 3 – Radiographic Phenotype

R: 2.8 cm, <10 HU

L: 3.0 cm, 18 HU

Should surgery be recommended?
Suggested Diagnostic Algorithm for Incidentally Discovered Adrenal Mass

**Adrenal Mass**

- **Clinical Phenotype**
  - (+)
  - **Biochemical Phenotype**

**Confirm Overt Hormone Excess with Clinical Syndrome**

**Radiographic Phenotype and Localization**

- **Suspicious**
  - >4-6cm, >10 HU, contrast avid, heterogeneous

- **Benign Appearing**
  - <10HU, <4cm, non-contrast avid, homogeneous

**Surveillance Considerations:**
- If initially “nonfunctional”:
  - No evidence for repeat biochemical testing
  - Repeat biochemical testing if worsening comorbidities (HTN, DM, low BMD)
- If autonomous cortisol secretion without clinical syndrome:
  - Individualized consideration for surgery based on comorbidities and other factors.
  - Repeat biochemical testing annually
  - No firm evidence for radiographic surveillance

- Consider surgery

- Growth>0.5cm/year or +20%
- Suspicious radiographic features
- New or worsening hormonal excess

- ((Consider alternative imaging: CT with washout, MRI))
- If Unilateral: **Consider surgery**
- ?Metastases or infection: **Biopsy**
- Unsure? => **Surveillance:** repeat imaging in 3-6 months
Case 3

- She returned 1.5 years later
- Has new hirsutism on face and upper chest
- 1mg DST and plasma metanephrines were normal
- Androgens not measured

- Repeat imaging was performed
Case 3 – Radiographic Phenotype

R: Unchanged
2.8 cm, <10 HU

L: 4.3 cm, 30 HU
Larger
Heterogeneous
Nodular
Fat stranding
Case 3

• Underwent a radical L adrenalectomy

• Pathology revealed a high grade stage I Adrenocortical carcinoma…
Case 3 – Clinical Diagnosis

• STAGE I, HIGH GRADE, ADRENOCORTICAL CARCINOMA

• Adrenal carcinomas are rare, highly aggressive, fast growing, and can produce multiple adrenal hormones

• Only known cure is early recognition and radical surgery

• 50-70% are metastatic at time of presentation

• Median survival < 12 months from time of diagnosis; can be prolonged with cytoreduction (surgery/IR) or adjuvant mitotane/EDP therapy

• Morbidity and mortality associated with rapid tumor growth and spread, but also uncontrolled hormone excess states (i.e. Cushing’s syndrome, mineralocorticoid excess).
Case 4

- 47yo man with a history of hypertension
- Diagnosed with HTN 5 years earlier, well controlled on losartan and HCTZ
- Describes increasing anxiety and sweats, but no palpitations, worsening BP, headaches, visual changes
- Presented to ER with sudden onset L chest pain
- CT angiogram detected a pulmonary embolus and an incidental large R adrenal mass...
Case 4

RIGHT
5.7x5.2x4.6 cm mass  
T2 intense

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Possible Pheochromocytoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>&gt;1-2 cm</td>
</tr>
<tr>
<td>Attenuation on unenhanced CT</td>
<td>&gt;10 HU</td>
</tr>
<tr>
<td>MRI</td>
<td>T2 hyperintensity</td>
</tr>
<tr>
<td>FDG avidity on PET</td>
<td>Possibly</td>
</tr>
<tr>
<td>Rate of Growth</td>
<td>&lt; 1cm/y</td>
</tr>
</tbody>
</table>
Case 4

- Plasma metanephrine: <0.20 nmol/L (<0.49)
- Plasma normetanephrine: **19.0** nmol/L (<0.89)

- 24h urine metanephrine: 125 μg/24h (<400)
- 24h urine Normetanephrine: **8670** μg/24h (<900)
- 24h urine Epi: normal
- 24h urine NE: **1882** mcg/24h (<80)
- 24h urine dopamine: normal

**Should surgery be recommended?**
Suggested Diagnostic Algorithm for Incidentally Discovered Adrenal Mass

Adrenal Mass

→ Clinical Phenotype

(+)

Biochemical Phenotype

(-/+) (+-)

Radiographic Phenotype

Confirm **Overt** Hormone Excess with Clinical Syndrome

Radiographic Phenotype and Localization

Consider surgery

((Consider alternative imaging: CT with washout, MRI))

Suspicious

>4-6cm, >10 HU, contrast avid, heterogeneous

Benign Appearing

<10HU, <4cm, non-contrast avid, homogeneous

Surveillance Considerations:

If initially “nonfunctional”:
- No evidence for repeat biochemical testing
- Repeat biochemical testing if worsening comorbidities (HTN, DM, low BMD)

If autonomous cortisol secretion without clinical syndrome:
- Individualized consideration for surgery based on comorbidities and other factors.
- Repeat biochemical testing annually
- No firm evidence for radiographic surveillance

Unilateral:

Consider surgery

?Metastases or infection: **Biopsy**

Unsure? =>Surveillance: repeat imaging in 3-6 months

• Growth>0.5cm/year or +20%
• Suspicious radiographic features
• New or worsening hormonal excess
The goal of pre-operative medical therapy is to: block the peripheral effects of catecholamines (and rarely their synthesis) to minimize excessive intra-operative $\alpha$- and $\beta$-agonism that may result in end-organ damage, while simultaneously minimizing the risk for post-operative hypotension.

1) Identify experienced surgeon and anesthesia team
2) alpha-blockade (selective when possible)
3) Intra-vascular volume expansion (salt or saline)
4) beta-blockade (particularly in those with known heart disease)
5) calcium-channel blockade (if needed)
6) Metyrosine (if needed)
Case 4 Outcome

• Started on doxazosin – titrated to a dose of 8 mg PO BID over 3 weeks => BP ~105-110/60 with slight orthostasis

• High salt diet – admitted the day before for intravenous saline and low dose beta-blocker

• Laparoscopic R adrenalectomy without major intra- or post-operative hemodynamic complications
Take Home Points

• Surgery is indicated when a primary adrenal malignancy is suspected or overt biochemical secretion is confirmed. Other situations must be considered individually.

• Therefore, all incidentally discovered adrenal tumors should be carefully evaluated to determine whether they are: 1) **malignant** and/or 2) **functional**.

• Biopsy should be considered when suspecting extra-adrenal metastases or infection.
Indications for Adrenal Surgery

Anand Vaidya, MD MMSc
Director, Center for Adrenal Disorders
Assistant Professor of Medicine
Division of Endocrinology, Diabetes, & Hypertension
Brigham and Women’s Hospital
Harvard Medical School