Outline

• Epidemiology

• Differential Diagnosis

• Clinical Evaluation

• Management
Definition

- Clinically inapparent adrenal mass detected incidentally with imaging studies conducted for other reasons
Epidemiology

- Overall frequency 4-6%

- Prevalence increases with age
  - rare in patients <30yrs
  - ~3% of 50-year-olds
  - ~7% of 70-year-olds

- Incidence increasing
AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN ASSOCIATION OF ENDOCRINE SURGEONS MEDICAL GUIDELINES FOR THE MANAGEMENT OF ADRENAL INCIDENTALOMAS

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Which adrenal masses require workup?

- Any adrenal incidentaloma >1cm should be investigated.
Differential Diagnosis

• Benign or Malignant
  ▫ Adrenocortical carcinoma
  ▫ Metastatic disease

• Functioning or Non-functioning
  ▫ Cushing’s syndrome
  ▫ Conn’s syndrome
  ▫ Pheochromocytoma
  ▫ Virilizing/Feminizing tumors

• Other
  ▫ Cysts, myelolipomas, ganglioneuromas, hematoma
Differential Diagnosis

- Shen et al

  - 82% non-functioning, benign adenomas
  - 5% subclinical Cushing’s syndrome
  - 5% pheochromocytoma
  - 5% adrenocortical carcinoma
  - 2.5% metastatic disease
  - 1% aldosteronomia
Differential Diagnosis

• Depends on

1. Size

2. Patient’s history of malignancy
Adrenal Incidentaloma - Size Matters

- Mansmann et al
Adrenal Incidentaloma - Size Matters

- Adrenocortical carcinoma
  - 2% tumors $\leq 4$cm
  - 6% tumors 4.1-6cm
  - 25% tumors $> 6$cm
Adrenal Incidentaloma - History of Malignancy

- Choyke PL
  - 25-72% chance of mass being a metastasis
  - 10-15% bilateral
  - lung, melanoma, renal cell, breast, colon
Ask yourself 2 questions:

1. Is the tumor functioning?

2. Does the tumor have benign imaging characteristics?
History

- **Functioning?**
  - Hypertension, hypokalemia, muscle cramps, weakness
  - Flushing, diaphoresis, visual disturbance, headaches, tremor, anxiety attacks, palpitations, weight loss
  - Weight gain, easy bruising, glucose intolerance, fatigue, depression, proximal muscle weakness, osteoporosis, menstrual irregularities, poor wound healing

- **Malignant?**
  - Personal cancer history, constitutional symptoms, local symptoms
Physical Examination

• Functioning?
  ▫ Vital signs: hypertension, tachycardia
  ▫ General appearance: flushed, diaphoretic
  ▫ H & N: moon facies, facial plethora, dorsocervical fat pad, supraclavicular fullness, goiter, hirsutism
  ▫ Abdomen: truncal obesity, CVA or abdominal tenderness, purple striae, masses
  ▫ Extremities: thinned skin, peripheral edema, ecchymoses, proximal muscle weakness/wasting

• Malignant?
  ▫ General appearance: cachexia
  ▫ Abdomen: masses
Investigations

- All patients should be screened for Cushing’s and pheochromocytoma
- Only screen for Conn’s if hypertension
- All patients need dedicated adrenal imaging (adrenal protocol CT or MRI)
- Myelolipomas don’t need a functional workup
Cushing’s Syndrome

• Low dose dexamethasone suppression test
  ▫ Dexamethasone 1mg at 11pm
  ▫ Serum cortisol at 8am

• 24-hour urine free cortisol
  ▫ 4X the normal value diagnostic
  ▫ False positives from anxiety, obesity, smoking, alcoholism

• Late-night salivary cortisol
  ▫ earliest and most sensitive marker
Cushing’s Syndrome

- No screening tests has 100% sensitivity
- If clinical suspicion is high, use >1 test
- Once diagnosis made, a low serum ACTH confirms an adrenal source
Subclinical Cushing’s Syndrome

• A biochemical diagnosis of Cushing’s syndrome with no overt clinical features

• Progression to overt Cushing’s rare

• Young et al
  - operate on younger patients <40 years with recent onset or worsening of DM, HTN or osteoporosis
Pheochromocytoma

- 24-hour urine metanephrines and catecholamines
  - 4X normal diagnostic

- Plasma free metanephrines
  - High rate of false positives

- Ensure patient is not taking any interfering substances
Conn’s Syndrome

- Plasma aldosterone and renin levels
  - Collect at 10am and upright for 2 hours
  - Elevated ARR

- Do a confirmatory test
  - Saline suppression test

- Ensure patient is normokalemic and not on aldosterone antagonists
Conn’s Syndrome

- Consider adrenal venous sampling in every patient

- Kempers et al
  - systematic review of 950 patients
  - 38% patients had discordant imaging and AVS
    - only CT/MRI $\rightarrow$ inappropriate adrenalectomy in 14.6%
    - $\rightarrow$ inappropriate exclusion of adrenalectomy in 19.1%

- Some advocate for AVS only if $>40$yrs
Summary - Is the tumor functioning?

- Order
  - 24-hour urine for metanephrines, catecholamines and free cortisol
  - Low dose dexamethasone suppression test if UFC is elevated
  - Add aldosterone and renin if patient hypertensive
  - Routine screening for feminizing/virilizing tumors not necessary
Imaging

• Benign adenomas are lipid-rich
  ▫ imaging relies on density measurements

• CT Adrenal Protocol
  ▫ **Benign**: <10 HUs on unenhanced scan, ≥50% contrast washout on delayed scan, smooth borders, homogenous
  ▫ **Atypical** (cancer or pheo): >20 HUs on unenhanced scan, <50% washout on delayed scan, irregular borders, local invasion, central necrosis, size >6cm, heterogeneous

• MR Adrenal Protocol
  ▫ Loss of signal on out-of-phase imaging
Benign Adenoma

HU <-5, 82% washout
Atypical Imaging

HU 54.1, 29% washout
When to biopsy?

- Almost never!
- Always exclude pheo first
- FNA cannot diagnosis ACC
- May be helpful if considering a metastases and definitive diagnosis will alter oncologic treatment planning
When to operate?

- Functioning tumor

- Suspicion of malignancy
  - Atypical imaging characteristics
  - Size >4cm
  - Mass growing on serial imaging
How should I follow benign, non-functioning adenomas?

• Repeat imaging at 3-6 months and then annually for 1-2 years
  ▫ 5-25% of masses will enlarge in 5 years

• Repeat functional workup annually for up to 5 years
  ▫ Up to 20% will become functional, especially if >3cm
  ▫ usually Cushing’s
Surgical Approaches

- Minimally invasive is the gold standard unless suspicion of ACC
  - Laparoscopic transperitoneal
  - Retroperitoneoscopic
  - SILS

- Find an experienced surgeon
References

1. www.endocrinediseases.org