Disorders of the Adrenal Glands for the Primary Care Provider

JACQUELINE JORDAN SPIEGEL, MS, PA-C
ASSOCIATE PROFESSOR
DIRECTOR, CLINICAL SKILLS & SIMULATION

MIDWESTERN UNIVERSITY

ASAPA SPRING CME CONFERENCE 2015
Objectives

- Recognize the hormone products (& their actions) associated with the adrenal gland.
- Recognize the typical presentations and pathophysiology for:
  - Cushing’s syndrome
  - Addison’s disease
  - Pheochromocytoma
- Understand key diagnostic studies used in the evaluation of adrenal endocrinopathies.
- Review the main treatment and management strategies for adrenal gland disorders.
- Discuss evaluation and management of Adrenal Incidentaloma
Normal A&P Review

- Inner Medulla and outer cortex
- Cortex produces 3 major classes of hormone:
  - Zona Glomerulosa → Mineralocorticoids → aka Aldosterone
  - Zona Fasciculata → Glucocorticoids → aka Cortisol
  - Zona Reticularis → Adrenal Androgens → mostly Dihydroepiandrosterone (DHEA)
- Medulla secretes catecholamines
  - Epinephrine
  - Norepinephrine
  - Small quantities of Dopamine
General Functions of Glucocorticoids

- **Metabolic**
  - Increase blood glucose concentration by promoting gluconeogenesis in the liver
  - Inhibits insulin secretion which decreases glucose uptake into muscle and adipose tissue.
  - Stimulates protein catabolism

- **Growth suppressing**
  - Suppresses growth hormone release

- **Modulates effects of catecholamines**
  - Responds to long term stress and illness
General Functions of Glucocorticoids

- **Anti-inflammatory/Anti-immune properties**
  - Depresses proliferation of T lymphocytes
  - Decreases natural killer cell activity.
  - Reverses macrophage activity
  - Inhibits production of many mediators of inflammation & immunity such as prostaglandins & histamines

- **Awareness and sleep patterns**
Feedback Loop for Glucocorticoids

- Stress
  - Hypoxia
  - Hypoglycemia
  - Hyperthermia
  - Exercise
  - Cortisol insufficiency

- Corticotropin-releasing factor (CRF)

- Anterior pituitary
- Adrenocorticotropic hormone (ACTH)

- Adrenal cortex
- Glucocorticoids (especially cortisol)

- Hypothalamus
- Diurnal rhythms
- Somatostatin
- Hypothalamic lesions
The Cortisol Peak is a Response to ACTH Release
General Functions of Mineralcorticoids

- Acts on the kidney to increase the volume of fluid in the body by reabsorption of sodium, retention of water, and secretion of potassium
  - End result: Increased blood pressure
- Also indirectly acts on the posterior pituitary gland to release vasopressin (ADH)
  - End result: retention of water by kidneys and increased blood pressure.
General Functions of Sex Androgens (aka Dehydroepiandrosterone)

- Acts on the androgen receptor
- Converts to produce testosterone and estrogens (estrone and estradiol)
- Potent sigma-1 agonist (neurosteroid)
  - Increased mood and perceived energy levels
  - Early activation of pre-memory processing centers
- Limited but known protective effect on age-related disorders
Remember that these hormones are excreted thru the urine in a metabolite form:

- **Cortisol** is excreted in the urine as 17 hydroxysteroid (17OHS)

- **Androgens** are excreted in the urine as 17 ketosteroids (17-KS)
General Functions of Epinephrine and Norepinephrine

- **Metabolic**
  - Promotes hepatic glycogenolysis
  - Inhibits hepatic gluconeogenesis
  - Inhibits insulin release
  - Promotes free fatty acid release from adipose tissue

- **Cardiovascular Effects**
  - Positive inotrophic effect
  - Increases blood pressure
Adrenal Disorders

- Adrenal Insufficiency
- Cushing’s Syndrome
- Adrenal Incidentaloma
- Pheochromocytoma
Cushing’s Syndrome

- Definition:
  - The sign & symptom complex resulting from prolonged exposure to glucocorticoid hormones

- The syndrome was originally described by Harvey Cushing in 1932.

- Cushing’s Syndrome vs Cushing’s Disease
Cushing’s Syndrome

- **Etiology:** ACTH-dependent
  - Excessive ACTH production from the pituitary (ie: pituitary adenoma) = Most common cause
  - Ectopic ACTH producing tumor
    - Most common ectopic ACTH producing tumor is small cell lung cancer
    - Other cancers: thymus, pancreas, ovary
  - Excessive CRH production from hypothalamus
Cushing’s Syndrome

- **Etiology:** ACTH-independent
  - Adrenal tumor (nodular hyperplasia)
    - Benign or Malignant
  - Other hyperplasia associated with receptor/hormone excess
  - Neuroendocrine tumors (ie: MEN I, Zollinger Ellison Syndrome)
  - Pheochromocytoma
## Cushing’s Syndrome

### Epidemiology

<table>
<thead>
<tr>
<th>ACTH dependent (~70%)</th>
<th>ACTH independent (~18%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence 5-25 per million per year</td>
<td>Incidence &lt;2 per million per year</td>
</tr>
<tr>
<td>8-10 times more likely in females</td>
<td>Males and females equally affected</td>
</tr>
<tr>
<td>Age related incidence between 25-45 years. Unusual in children</td>
<td>Bimodal age distribution</td>
</tr>
<tr>
<td>Sources: pituitary, extrapituitary, hypothalamus, small cell lung ca,</td>
<td>Sources: Adrenal carcinoma, adrenal adenoma, neuroendocrine tumors, pheochromocytoma, other</td>
</tr>
</tbody>
</table>
Clinical Features of Cushing’s Syndrome

- Weight gain/Obesity (95%)
  - Facial plethora “moon face”
  - Truncal obesity with extremity wasting
  - Buffalo hump (only 20%)
- Fatigability and weakness (~80%)
  - Mostly proximal muscles
- Violaceous abdominal straie (~65%)
- Acne and Abnormal hair growth (~65-80%)
- Edema (80%)
Clinical Features of Cushing’s Syndrome

- HTN (~80%)
- Insulin Resistance (sometimes overt DM) (~65%)
- Osteoporosis/Ca++ disturbance (~20%)
  - Vertebral fractures, hypercalcuria, kidney stones
- Psychiatric disturbance (~45%)
  - Dysphoria, depression, paranoia
- Amenorrhea (~75%)
- Hypertrophy of the clitoris (~20%)
- Impotence (~20%)
Thinning of scalp hair
Acne
Increased facial hair
Cardiac hypertrophy and hypertension
Adrenal:
- hyperplasia
- tumor
Striae of skin
Easy brusing
Muscle wasting:
- Weakness
- Thin extremities

Emotional instability
Moon face
Buffalo hump
Osteoporosis
Truncal obesity
Differential Diagnosis In Hypercortisolism

- Alcoholism
- Depression
  - May be biochemically impossible to differentiate
- Obesity
  - Hypercortisolism without syndrome of Cushing’s
- Pregnancy
  - Supra-normal endogenous estrogen levels
- Polycystic Ovarian Syndrome
- Some drugs accelerate corticosteroid metabolism
  - Phenobarbitol, primadone, oral contraceptives
Diagnostic Work up

- **Plasma Cortisol level**
  Abnormal result:
  - >25 ug/dl at 8 AM
  - Less then the anticipated drop of 1/3 to 2/3 at the 4 PM reading

- **Serum ACTH level**
  Abnormal result:
  - >80 pg/ml at 8 AM, >50 pg/ml at 4 PM
  - < 20 pg/ml at any time
  - high or low depends on etiology

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Cortisol Level</th>
<th>ACTH Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenal hyperplasia or tumor (ACTH independent)</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>ACTH producing tumor – pituitary or ectopic (ACTH dependent)</td>
<td>High</td>
<td>High</td>
</tr>
</tbody>
</table>
Diagnostic Work up

- **Cortisol Precursors**
  - Pregnenolone
  - 17-hydroxypregnenolone
  - Preogesterone
  - 17-hydroxyprogesterone
  - 11-deoxycortisol

- Measured by radioimmunoassay

- **11-deoxycortisol**
  - Normal value → undetectable (<1mcg/dL) at 8AM
Diagnostic Work Up

- Dexamethasone suppression test (DST)
  - ~95% sensitive
  - GOLD STANDARD for screening

  Abnormal result:
  - Cortisol >5 ug/d is highly suspicious

- 24 hr. urine free cortisol
  - ~95% sensitive
  - Measuring 17-OCHS
  - MAIN STAY for diagnosis

  Abnormal result:
  - Cortisol >125 ug/d is indicative of Cushing’s
Diagnostic Work up

• **Salivary Sampling**
  - Free cortisol diffuses freely into saliva
  - Sample 2.5 mL saliva obtained after rinsing mouth but before brushing teeth at:
    ▸ 9:00am 3 mornings in a row when evaluating for Adrenal insufficiency
    ▸ 11:00pm 3 nights in a row when evaluating for Cushing’s syndrome
  - Normal =
    ▸ 5.6 ng/mL (15.4 nmol/L) at 8 to 9 AM
    ▸ 1 ng/mL (2.8 nmol/L) at 11 PM

Abnormal result:
- Morning salivary cortisol ↓ in adrenal insufficiency
- Late evening salivary cortisol ↑ in cushing’s disease
Management of Cushing’s Syndrome: The Diagnostic Dilemma

- Have you excluded exogenous cortisol use?

- Is Cushing’s due to pituitary tumor?
  - Consider MRI focused on sella

- Is it due to ectopic ACTH secreting tumor?
  - Clinical clues from history
  - Consider CXR to r/o lung mass, Pelvic U/S for ovarian mass

- Is it due to an adrenal tumor?
  - Palpable abdominal mass?
  - Consider CT abdomen
Management

- If exogenous corticosteroids in the picture →
  - Taper to the lowest therapeutic dose possible which treats the patient’s symptoms

- Other treatment aimed at underlying pathology
  - Pituitary adenoma → Transsphenoidal resection
  - Adrenal tumor → Adrenalectomy
  - Other adrenal hyperplasia, inoperable ectopic site, other malignancy → Medical
Medical Management of Cushing’s Syndrome

- **Adrenolytic Agents:**
  - **Mitotane**
    - Induces permanent destruction of the adrenocortical cells
    - AKA medical adrenalectomy
    - 0.5 mg p.o. at bedtime, increase to 1-12 mg in divided doses QID

- **Adrenal Enzyme Inhibitors:**
  - **Ketoconazole**
    - Antifungal with cortisol-reducing effects in higher doses
    - 200-1200 mg p.o. in divided doses BID - TID
    - Major SE is liver toxicity
  - **Metyrapone**
    - Inhibits cortisol synthesis
    - 500 – 750mg p.o. given Q6 hours (max 4g/day)
    - Frequently used in combination
Adrenal Insufficiency

- Definition: inadequate production of mineralocorticoids, glucocorticoids &/or sex androgens.

- Epidemiology
  - Difficult condition to diagnosis
  - Both primary and secondary adrenal insufficiency can occur at any age and both genders equally.
Etiology of Primary Adrenal Insufficiency

- Anatomic destruction (acute or chronic)
  - Autoimmune → Addison’s Disease → most common cause of primary AI
  - Surgical (s/p Adrenalectomy)
  - Infection (ie: histoplasmosis, TB, coccidiodomycosis)
  - Hemorrhage or Infarction
  - Metastatic or malignant
  - AIDS

- Metabolic failure in hormone production
  - Congenital adrenal hyperplasia
  - Adrenoleukodystrophy (ALD)
Etiology of Secondary Adrenal Insufficiency

- Etiology: Secondary
  - Suppression of HPA axis through abrupt cessation of exogenous steroid ➔ **Most common cause of secondary AI**
  - Pituitary disease (usually hypopituitarism)
  - Endogenous steroid producing tumor
  - Drugs which reduce corticosteroids:
    - Phenytoin, opiates, ketoconazole, rifampin
Clinical Features in Adrenal Insufficiency

- **Hallmark Tetrad:**
  - Weakness/Fatigue
  - Weight loss/anorexia
  - Hyperpigmentation
  - Hypotension

- **Symptoms:**
  - Weakness & fatigue (~99%)
    - Often sporadic & associated with stress
  - Anorexia (~95%)
    - May be seen with nausea, vomiting, abd pain
  - Hyperpigmentation (~98%)
    - Often marked & includes mucus membranes
    - Vitiligo may be evident (~10%)
More pictures of Adrenal Insufficiency
Clinical Features in Adrenal Insufficiency

- **Hypotension (orthostatic)**
  - May be asymptomatic or a presenting c/o
- **Salt craving (~25%)**
  - May be a late finding associated with hyponatremia
- **Syncope (~15%)**
  - May present as orthostatic syncope
- **Amenorrhea (~30% females)**
- **Hair loss (~20%)**
Specific presentation by hormone deficiency

<table>
<thead>
<tr>
<th>Hormone Deficiency</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glucocorticoid Deficiency</strong></td>
<td>Weakness, fatigue, hypoglycemia, wt loss, anorexia, nausea, vomiting, abdominal pain</td>
</tr>
<tr>
<td><strong>Mineralocorticoid Deficiency</strong></td>
<td>Na(^{+ +}) wasting (hyponatremia, salt craving), hypovolemia, orthostatic hypotension, hyperkalemia, mild metabolic acidosis</td>
</tr>
<tr>
<td><strong>Adrenal Androgen Deficiency</strong></td>
<td>Loss of axillary &amp; pubic hair in females; amenorrhea</td>
</tr>
<tr>
<td><strong>ACTH elevation in primary disease</strong></td>
<td>Hyperpigmentation (most apparent in Addison’s disease)</td>
</tr>
</tbody>
</table>
Diagnostic Work up

- **Plasma Cortisol level**
  - Low accuracy rate for AI
  - **Abnormal result:**
    - $< 5 \text{ ug/dl} \text{ in AM}$

- **Serum ACTH level**
  - **Abnormal result:**
    - $>80 \text{ pg/ml} \text{ at 8 AM, } >50 \text{ pg/ml} \text{ at 4 PM}$
    - $< 20 \text{ pg/ml} \text{ at any time}$
    - high or low depends on etiology

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Cortisol Level</th>
<th>ACTH Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addison’s Disease: Adrenal Gland Failure</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Hypopituitarism</td>
<td>Low</td>
<td>Low</td>
</tr>
</tbody>
</table>
Cosyntropin Stimulation Test

- Evaluates the ability of the adrenal gland to respond to ACTH administration
- Two forms: Standard high dose and low dose
- Have same full biologic potency of native ACTH
- Procedure:
  - Obtain baseline Cortisol level
  - Administer bolus of ACTH (Standard dose 250mcg via IV)
  - Then measure cortisol levels at 30 and 60 minutes
- Abnormal result:
  - Cortisol levels fail to increase to >18 mcg/dl
Diagnostic Work up

- **Metyrapone Stimulation Test**
  - Benefit → can be completed while on glucocorticoid supplementation
  - Three different forms → Overnight, 2 day, or 3 day
  - Procedure:
    - Obtain 24-hour urine baseline collection
    - Immediately following take 750 mg metyrapone p.o. Q4 hours x 6 doses (with food or milk)
    - Continue to collect 24-urine specimens day 2 and 3
    - Measure 17-OHCS and creatinine levels in urine
    - Measure serum cortisol, plasma ACTH, and 11-deoxycortisol 4 hours after last dose of metyrapone
## Metyrapone Stimulation Test

<table>
<thead>
<tr>
<th>Measure</th>
<th>NORMAL</th>
<th>ABNORMAL RESPONSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum cortisol</td>
<td>Decrease to &lt;5mcg/dL</td>
<td>Remain &gt;5mcg/dL</td>
</tr>
<tr>
<td>Plasma ACTH</td>
<td>&gt;75 pg/mL at 4 hrs post last dose</td>
<td>&lt;75 pg/mL</td>
</tr>
<tr>
<td>Serum 11-deoxycortisol</td>
<td>&gt;7-22 mcg/dL 4 hrs post last dose</td>
<td>&lt;7mcg/dL</td>
</tr>
</tbody>
</table>
Diagnostic Work up

• Salivary Sampling
  ○ Remember **morning** salivary samples are used for evaluation of Adrenal Insufficiency
  ○ 2.5mL saliva obtained at 9:00pm 3 mornings in a row

  Abnormal result:
  ▫ < 5.6 ng/mL in any of the three samples
Diagnostic Work up (other labs)

- **Comprehensive metabolic panel (CMP)**
  - Hyponatremia, Hyperkalemia, Hypercalcemia
- **Complete Blood Count (CBC)**
  - Normocytic anemia, moderate eosinophilia
- **Anti-adrenal Antibodies**
  - Found in ~70% because autoimmune Addison’s most common cause
- **Screen for other endocrine disorders as well**
  - TSH, Prolactin, FSH, LH
Diagnostic Work up

- These days, TB must be ruled-out
  - PPD for everyone with S&S of adrenal insufficiency
  - Less common infections include meningococcemia, histoplasmosis & coccidioidomycosis

- Lung, breast ca. or vascular disease may impair adrenocortical function
  - Think of screening with CXR and/or Mammogram if pt in high risk category for one of these conditions
Diagnostic Work up

- Radiographic evaluation of Adrenals
  - Not necessary in autoimmune adrenalitis
  - For other secondary causes, CT might be beneficial to identify infection, hemorrhage, malignancy.

- Other imaging:
  - MRI with coned down views of pituitary may be warranted if secondary adrenal insufficiency points toward hypothalamic or pituitary source.
Management

- **Glucocorticoid replacement**
  - Hydrocortisone 15-30 mg daily in single AM dose or divided doses (3/4 in AM, 1/4 in afternoon)
  - Prednisone 5-7.5 mg daily
  - Dexamethasone 0.75 – 1.25 mg daily

- **Mineralcorticoid replacement (for primary adrenal insufficiency)**
  - Fludrocortisone 0.05 – 0.2 mg daily

- **Adrenal Androgen replacement**
  - DHEA 25-50 mg daily
  - Cream vs Oral
Management

- Focus management on underlying cause if infectious or reversible (i.e. TB, cocci, etc.)

- Increase dosing of glucocorticoids in the face of highly stressful events to avoid adrenal crisis
  - Surgery, trauma, stressful diagnostic procedures, other stressors
Pheochromocytoma

- **Definition:**
  - Rare, Catecholamine-producing tumor of neurochromaffin cells.

- **Types:**
  - Sporadic Pheochromocytomas
  - Familial Pheochromocytomas (~20%)

- **Epidemiology**
  - Occurs from infancy to old age, Peak incidence 40-50 y/o
  - 10-15% are malignant
  - FATAL if undiagnosed and untreated
**Pheochromocytoma**

- **Etiology**
  - Majority arise from the adrenal medulla
  - Extra-adrenal pheochromocytomas are called “paragangliomas”.
  - Can also occur in autosomal dominant hereditary syndromes
    - IE: MEN2, von Hippel-Lindau syndrome, neurofibromatosis type 1
Extraadrenal locations for Pheo

- Within the sympathetic nerve chain along the spinal cord (orange spots)
- Overlying the distal aorta (the main artery from the heart) (green spots)
- Within the ureter (collecting system from the kidney) (yellow spot)
- Within the urinary bladder (blue spot)

Remember, 90% are in the adrenal glands (red spots on the kidneys)
Presentation

- Characterized by classic paroxysm attacks of:
  - Headache
  - Sweating
  - Palpitations
  - Profound acute hypertension at the time of the episode

- Pheochromocytoma “attacks”:
  - Usually last 30-40 minutes
  - May be precipitated by displacement of abdominal contents (eg lifting, bending, deep palpation)
  - Occur with varying frequency
  - Tend to increase in frequency and severity over time
Presentation: Other symptoms

- Other symptoms (<20%)
  - Pallor
  - Nausea
  - Tremor
  - Fatigue
  - Anxiety
  - Epigastric pain
  - Hypertensive retinopathy
  - Retinal angiomas (von Hippel-Lindau syndrome)
  - Café-au-lait spots (neurofibromatosis)
  - Mucosal neuromas/other neuromas (MEN2, neurofibromatosis)
When to suspect Pheo?

- Classic paroxysmal “attacks”
- Refractory HTN or onset <20 y/o
- Idiopathic dilated cardiomyopathy
- Abdominal mass
- Family history
- Incidentally discovered adrenal mass
- Other associated diagnoses (MEN2, Neurofibromatosis)
- Hyperthyroidism or thyroid storm – without thyroid pathology nor increased TFTs
Diagnostic Workup for Pheo

- **Initial work up:**
  - Thyroid Function tests
  - Plasma epinephrine and norepinephrine
  - Plasma metanephrines
  - 24 hour urine catecholamines, metanephrines, and vanillylmandelic acid (VMA)

- Catecholamines should be measured after a pt has been resting supine with venous access for 30 minutes

- 24 hour urine studies are generally **superior** to plasma studies but need all to compare**
### Causes of False Positive Catecholamine And Metanephrine results

<table>
<thead>
<tr>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricyclic Antidepressents</td>
</tr>
<tr>
<td>Antipsychotics</td>
</tr>
<tr>
<td>Beta blockers</td>
</tr>
<tr>
<td>Acetaminophen</td>
</tr>
<tr>
<td>Levodopa</td>
</tr>
<tr>
<td>ETOH</td>
</tr>
<tr>
<td>Withdrawal of clonidine (Catapres) or other anti-HTN drugs</td>
</tr>
<tr>
<td>Major physiologic stress (MI, Stroke, Sleep apnea)</td>
</tr>
</tbody>
</table>

Diagnostic Workup for Pheo

- **Clonidaine Suppression Test**
  - **Procedure:**
    - Stop hypotensive meds x 24 hours, fast overnight
    - Baseline BP and pulse taken, Baseline labs
    - Administer 0.3mg clonidine orally
    - Continue to monitor BP, pulse and draw labs at 3 hour intervals
  - **Results:**
    - Normal suppression range 3 hours after clonidine
      - Norepinephrine 0.2-0.8 ng/ml
      - Epinephrine 0.04-2 ng/ml
    - If does not suppress to this level, positive test.
Diagnostic Work up: Anatomic Localization

- Radiographic Evaluation should be initiated after biochemical dx is made

- Modalities can include:
  - CT
  - MRI
  - PET
  - 131 I-metaiodobenxylguanidine (MIBG) scan
  - 111 In-pentetrotide scan (OctreoScan)
Pheochromocytoma

CT Scan

MRI

Ectopic pheo
Management of Pheochromocytoma

- IV nitroprusside is reasonable initial treatment in a crisis

- “Chemical sympathectomy” will stabilize the patient until definitive therapy is accomplished
  - Utilize a pure alpha blocker (such as phenoxybenzamine) possibly followed by a beta blocker (such as propanalol)

- Surgical excision is definitive treatment

- Always refer to Endo and surgery
Rule of 10’s in Pheochromocytoma

**Rule of “10s”**
- 10% w/o HTN
- 10% extraadrenal
- 10% extraabdominal
- 10% children
- 10% familial
- 10% bilateral
- 10% metastatic disease at diagnosis
Adrenal Incidentaloma

- **Definition**
  - Mass lesion greater than 1 cm discovered incidentally by radiologic examination

- **Epidemiology**
  - Found in 4.4% of abdominal CT scans (10% in older patients)
  - Prevalence higher in obese, hypertensive, and diabetic patients
  - Rate of finding bilateral masses is 10-15%
  - 85-90% of incidentalomas are non-functional

- **Two questions?**
  - Is it malignant?
  - Is it functioning?
# Adrenal Incidentaloma: Work up

- **Evaluation for malignancy on imaging**

<table>
<thead>
<tr>
<th>Benign</th>
<th>Carcinoma</th>
<th>Metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homogenous</td>
<td>Inhomogenous with central necrosis</td>
<td>Inhomogenous, irregular shape</td>
</tr>
<tr>
<td>Unilateral</td>
<td>Unilateral</td>
<td>Bilateral</td>
</tr>
<tr>
<td>Diameter &lt;4</td>
<td>Diameter &gt; 4cm</td>
<td>Diameter variable</td>
</tr>
<tr>
<td>Lipid-rich (attenuation &lt;10 HU)</td>
<td>Calcifications</td>
<td>Low lipid content (attenuation &gt;20HU)</td>
</tr>
<tr>
<td>Rapid contrast wash out</td>
<td>Delayed wash out</td>
<td>Delayed wash out</td>
</tr>
<tr>
<td>Isointensity compared to liver on T1 and T2</td>
<td>Hypointensity on T1, High signal intensity on T2</td>
<td>Isointensity on T1, Intermediate signal intensity on T2</td>
</tr>
</tbody>
</table>
Adrenal Incidentaloma: Work up

- Evaluation of hormonal secretion?
  - Everyone gets plasma cortisol, serum ACTH, serum DHEA, plasma aldosterone
  - Sxs of Cushings?
    - YES = 24-hr urinary free cortisol
    - NO = 1-mg overnight dexamethasone suppression test
  - Sxs of Pheo?
    - 24-hr urine metanephrines, catecholamines
    - Serum metanephrines, catecholamines
Adrenal Incidentaloma: Work up

- **Fine needle aspiration/biopsy**
  - Relatively safe procedure, outpatient
  - **When to use it?**
    - Known primary malignancy elsewhere
  - **When NOT to use it?**
    - Biochemical evidence of pheochromocytoma
    - Known widespread metastatic disease
Adrenal Incidentaloma: Management

- Based on work up findings
  - Documented pheo or carcinoma $\rightarrow$ prompt surgical intervention
  - Pharmacologic interventions $\rightarrow$ as indicated for underlying disease
  - If benign appearance on imaging $\rightarrow$
    - $>3\text{cm}$ $\rightarrow$ most would consider resection
    - $<3\text{cm}$ $\rightarrow$ repeat imaging at 6 months (plus consider additional at 12 and 24 months)
  - Type of imaging dependent on initial imaging phenotype and clinical judgment (ie: CT vs MRI)
  - Repeat Dexamethasone suppression test annually for 4 years
Key Points to remember: Cushing’s Syndrome

• Most common cause is:
  o ACTH producing pituitary adenoma
• Most common cause for cushingoid symptoms:
  o Exogenous steroid use
• Findings suggestive of Cushing’s are:
  o Central obesity, straie, spontaneous ecchymosis, virilization, unexplained osteoporosis, HTN, new onset insulin resistance
Cushing’s Syndrome

- Dexamethasone suppression test is easiest, cheapest screening test BUT for definitive diagnosis use 24-hour urine cortisol

- Comparison of cortisol and ACTH levels helps distinguish b/w ACTH-dependent and ACTH-independent forms

- Surgical intervention is considered first line treatment for Cushing’s disease
Key Points to remember: Adrenal Insufficiency

- Signs and symptoms may be subtle

- Cosyntropin stimulation test is the gold standard for diagnosis

- Other diagnostic work up essential to pin-pointing etiology

- AI patients should be informed that while undergoing a physically stressful illness or procedure, they will need higher doses of glucocorticoid replacement.
Key Points: Pheochromocytoma

- Incidental discovery of adrenal tumor on CT
- Signs/symptoms of pheochromocytoma
- Screening of patients with familial syndromes (MEN-II, von Hippel-Lindau)

1. Biochemical testing (*i.e.*, 24-hour urine metanephrines and free catecholamines)
2. Localization studies (*i.e.*, CT, MRI, ± MIBG)
3. Preparation with alpha blocker
4. Surgical resection of pheochromocytoma
Questions?
References

References

  - Medical therapy of hypercortisolism (Cushing’s syndrome). LK Nieman, MD Metyrapone stimulation tests. A Lacroix, MD