Adrenal Incidentalomas

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Disclosures

• No financial, investment, or consulting relationship with any pharmaceutical or biotech firms
Guy’s Hospital

Thomas Addison describes adrenal failure in 1849
B. A. HOUSSAY and J. T. LEWIS
From the Institute of Physiology, Faculty of Medicine, Buenos Aires
Received for publication January 27, 1923

Loss of both adrenals provokes death in a few hours in nearly all species. In dogs within 1 to 3 days (average, 26 hours) according to our own experiments. In man alterations of these glands occasion death in a short time (Sergent-Bernard's syndrome) or else bring about Addison's disease, of longer duration but not less fatal. The suprarenals must therefore be considered as organs essential to life. But as they are formed by two different tissues, cortical and medullary, the question arises as to which of them plays a principal part.

Some authors maintain that the medulla is the vital tissue, others that it is the cortex. Pende believes that both are necessary to life. We will examine the evidence brought to support these different opinions and afterwards discuss them with the help of our own experiments on this subject.

*Predominance of medulla.* This tissue secretes a substance of powerful pharmacological activity, adrenalin; it is therefore natural to presume that it is of great importance, especially if we consider that the functions of the cortex have not yet been clearly established.

A. and H. Cristiani (1) observed that extirpation of both adrenals provokes death in rats, and that these animals survive if extirpation is incomplete, provided that in the part left behind, medullary tissue is found in good condition. They also observed that suprarenal grafts are unable to maintain life in adrenalectomized rats, although only the medullary tissue degenerates, the cortex being found in excellent condition. This evidence led them to believe that the medulla is essential to life.

Vassale and Zanfrognini (2) removed all the medullary tissue leaving only the cortex in cats and rabbits and found that this operation was fatal as double adrenalectomy. Vassale (3) claims that extirpation of one adrenal and the abdominal paraganglia is always followed...
Adrenal Tumor
Don’t panic;  
Bring a towel
Cushing’s Syndrome

- 9 year old golden retriever
- shedding hair
- bald spots
- gaining weight, particularly belly
- difficulty rising from lying
Dog owner

- Symptoms similar to pet
- Difficulty sleeping
- Abdominal weight gain
- Upper extremity weakness
- Read about “adrenal fatigue” on the internet.
Dog owner con’t

• 47 year old female
• One year hx of generalized fatigue
• Menses less regular
• Hair falling out
• Notices new stretch marks
• New heartburn
• No spells
Dog owner physical exam

- BP 130/85, p 74, afebrile
- No skin changes
  - palmar creases normal, no purple striae
  - No excess hair growth
- Normal eye exam
  - no disc swelling, normal visual fields to confrontation, no color perception changes
- Neck exam normal
  - no buffalo hump, no supraclavicular fat pads
  - thyroid normal
Exam continued

• CV exam normal
• Resp normal
• Abd exam reveals mild tenderness over stomach, otherwise unremarkable
• Back exam normal, no tenderness over kidneys
• GU exam normal (no internal performed)
• EOMI, no stare or lid lag, normal upper body strength, can rise from squatting by holding on for balance
Routine labs

- Na 138, K 3.6, glucose 98
- Nl CBC, no eos
- LFTs nl
- 11:00 AM cortisol 10.4
Adrenal Tumor
Differential Dx

- Adrenal Cortical Tumors
  - Adrenal adenoma
  - Glucocorticoid producing
  - Aldosteronoma
- Metastasis
- Adrenal cortical carcinoma
- TB
<table>
<thead>
<tr>
<th>Adrenal Cortex</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenoma</td>
<td>36-94%</td>
</tr>
<tr>
<td>Non-oncologic and non-selected series</td>
<td></td>
</tr>
<tr>
<td>Oncology patients</td>
<td>7-68%</td>
</tr>
<tr>
<td>Pigmented nodules (“black adenomas”)</td>
<td></td>
</tr>
<tr>
<td>Nodular hyperplasia</td>
<td>7-17%</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>0-25%</td>
</tr>
<tr>
<td>Ganglioneuroma</td>
<td>0-6%</td>
</tr>
<tr>
<td>Ganglioneuroblastoma</td>
<td></td>
</tr>
<tr>
<td>Pheochromocytoma</td>
<td>0-11%</td>
</tr>
<tr>
<td>Neuroblastoma (rare outside of early childhood)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other Adrenal Masses</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiomyolipoma</td>
<td>0-11%</td>
</tr>
<tr>
<td>Abcess</td>
<td></td>
</tr>
<tr>
<td>Amyloidosis</td>
<td></td>
</tr>
<tr>
<td>Cysts</td>
<td>4-22%</td>
</tr>
<tr>
<td>Parasitic (echinococcal most common): 6% of cysts</td>
<td>0-1%</td>
</tr>
<tr>
<td>Retention: 2% of cysts</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Endothelial (lymphatic or angiomatosus): 44% of cysts</td>
<td>2-10%</td>
</tr>
<tr>
<td>Degenerative adenomas: 7% of cysts</td>
<td>0-2%</td>
</tr>
<tr>
<td>Pseudocyst (most likely due to hemorrhage into normal tissue or adrenal neoplasm): 39% of cysts</td>
<td>2-9%</td>
</tr>
<tr>
<td>Other (e.g. dermoid): 2% of cysts</td>
<td>≤1%</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td></td>
</tr>
<tr>
<td>Fibroma</td>
<td></td>
</tr>
<tr>
<td>Granulomatosis (histoplasmosis, coccidiomycosis, blastomycosis, tuberculosis, sarcoidosis)</td>
<td></td>
</tr>
<tr>
<td>Hamartoma</td>
<td></td>
</tr>
<tr>
<td>Hematoma/hemorrhage</td>
<td>0-4%</td>
</tr>
<tr>
<td>Hemangio/lymphangiomas</td>
<td></td>
</tr>
<tr>
<td>Lipoma</td>
<td>0-11%</td>
</tr>
<tr>
<td>Liposarcoma</td>
<td></td>
</tr>
<tr>
<td>Myelolipoma [0.2% autopsy incidence (6.62)]</td>
<td>7-15%</td>
</tr>
<tr>
<td>Myoma</td>
<td></td>
</tr>
<tr>
<td>Neurofibroma</td>
<td></td>
</tr>
<tr>
<td>Teratoma</td>
<td></td>
</tr>
<tr>
<td>Xanthomatosis</td>
<td></td>
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</tbody>
</table>
Adrenal gland is frequent site of metastases

<table>
<thead>
<tr>
<th>Metastases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-oncology and non-selected series</td>
<td>0-21%</td>
</tr>
<tr>
<td>Oncology patients</td>
<td>32-73%</td>
</tr>
<tr>
<td>Breast carcinoma</td>
<td>&quot;</td>
</tr>
<tr>
<td>Kidney</td>
<td>&quot;</td>
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<tr>
<td>Leukemia</td>
<td>&quot;</td>
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<tr>
<td>Lung cancer</td>
<td>&quot;</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>&quot;</td>
</tr>
<tr>
<td>Melanoma</td>
<td>&quot;</td>
</tr>
<tr>
<td>Ovarian</td>
<td>&quot;</td>
</tr>
<tr>
<td>Other</td>
<td>&quot;</td>
</tr>
</tbody>
</table>
## Non-adrenal mimicry

<table>
<thead>
<tr>
<th>Pseudoadrenal Masses</th>
<th>0-10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diaphragmatic crura</td>
<td></td>
</tr>
<tr>
<td>Dilated inferior vena cava</td>
<td></td>
</tr>
<tr>
<td>Gallbladder</td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td></td>
</tr>
<tr>
<td>Lymph nodes (para-aortic, para-caval, retro-pancreatic, retro-crural)</td>
<td></td>
</tr>
<tr>
<td>Omentum</td>
<td></td>
</tr>
<tr>
<td>Pancreas</td>
<td></td>
</tr>
<tr>
<td>Primary retroperitoneal neoplasms, hematomas, and cysts</td>
<td></td>
</tr>
<tr>
<td>Small and large bowel</td>
<td></td>
</tr>
<tr>
<td>Spleen/accessory spleen</td>
<td></td>
</tr>
<tr>
<td>Stomach/gastric diverticulum</td>
<td></td>
</tr>
<tr>
<td>Other vessels (especially aneurysms, varices, tortuosity, renal veins)</td>
<td></td>
</tr>
</tbody>
</table>
Thoughts

- Cushing’s syndrome
- Aldosteronoma
- Metastasis
- Myelolipoma
- Pheochromocytoma
- Other less likely tumors
Clues from presentation and data

• Non-specific symptoms and signs
• Mass is largish
• K is borderline low
• BP is normal
• Glucose is normal
Evaluation

• 24 hour urine for cortisol
• Serum renin/aldosterone ratio
• Urinary metanephrine
• Repeat physical exam for cancer, especially breast
Size matters:
>3cm are more likely malignant

Adrenal Mass Characteristics & Malignant Potential

- Qualitative
  - Irregular margin
  - Inhomogeneous
  - Contrast Enhancement
  - Intermediate T2 Intensity
  - Lymph Nodes enlarged
  - Soft tissue density CT
Figure 5 - Size of adrenocortical tumors by Weiss’s score ≤ 3 and > 3. Each (*) represents one tumor.
Cost efficient evaluation

• Mild symptoms and signs; lowish K
• Suspect Cushings or Aldosteronoma
• BP is not good indicator unless elevated
• Obtain 24 urine for cortisol
• Serum renin/aldosterone assay
Cost efficient evaluation

- Elevated BP or presence of spells
- Suspect pheochromocytoma
- Obtain 24 urine for catecholamines, metanephrines and creatinine
- Chromagranin A may be helpful, although not routinely ordered
Very large tumors

- Myelolipomas can be extremely large, involve the kidney and have back pain as presenting symptom
- Benign
- Leave alone
Results

• 24 hour urine for cortisol reveals >3-4X upper limit of normal
• Dx - Cushings syndrome
• No need for dex suppression tests
Results

• 3 days of an unrestricted sodium diet
• 1 hour of full recumbency
• Aldosterone levels of less than 15 ng/dL
• Serum aldosterone is elevated above 22 ng/dL
• Renin is suppressed
• Dx - Aldosterone secreting tumor
Pheochromocytoma

- NI cortisol and aldo tests
- Suspect pheochromocytoma
- 24 urine for catecholamines, metanephrine and creatinine
- Dx - elevated: Pheochromocytoma
Treatment

- Surgery
- Except Myelolipomas
- Except metastatic adrenal cortical carcinoma
Adrenal Cortical Carcinoma

- Bad outcomes
- Surgery is almost always too late
- Tumors can be quite primitive
  - Secrete large amounts of precursors
  - So cortisol can be low
Things you should know

- Contralateral adrenal will be suppressed in:
  - Cortisol producing adenomas
  - Aldosterone producing adenomas often co-secrete cortisol or precursor
  - Adrenal cortical-carcinomas
Other things you should know

- Pheochromocytomas can produce peptide hormones such as CRH and ACTH
- Looks like Cushings Syndrome
- Patients with aldosteronomas may not return to normal BP
- Histologically benign large tumors may have very poor outcomes
- Biochemical markers are more sensitive
What did she have?
What did she have?

- Benign adrenal mass
- Biochemical studies were normal
- Repeat MRI in 3 months and 6 months showed no change