Medical Evaluation of VHL-Related Adrenal Tumors

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Outline

• How does VHL manifest in the adrenal glands?

• How are adrenal gland tumors diagnosed?

• How do endocrinologists detect and manage these tumors?
VHL: A Multisystemic Cancer Syndrome

Retina
Endolymphatic Sac

Brainstem
Cerebellum
Spinal Cord

Adrenal Gland
Pancreas
Kidney
Broad Ligament (Female)

Epididymis (Male)
Adrenal Gland

![Diagram of the adrenal gland with labels for adrenaline, aldosterone, cortisol, androgens, catecholamines, glomerulosa, fasciculata, reticularis, medulla.]
Pheochromocytoma

- Adrenaline producing tumor in the adrenal gland
- Benign or malignant

- Type 1 VHL
  - Lower risk of developing a pheochromocytoma

- Type 2 VHL
  - High risk of developing a pheochromocytoma
Paraganglioma

- An adrenaline-producing tumor that is outside of the adrenal gland
- Arise near ganglia (bundles of nerves) along blood vessels:
  - Parasympathetic paraganglioma:
    - Along nerves in the neck and base of the head
    - Most **do not** produce adrenaline
  - Sympathetic paraganglioma:
    - Along nerves in the chest, abdomen, and pelvis
    - Most **do produce** adrenaline
    - Rare: Dopamine → low blood pressure
Paraganglioma
Do All Pheochromocytomas or Paragangliomas Produce Excess Adrenaline?

No

- If they are detected early, less likely to produce adrenaline
- Paragangliomas in the head and neck *rarely* produce adrenaline
- Paragangliomas in the chest and abdomen *often* produce adrenaline
- About two-thirds of pheochromocytomas/paragangliomas produce excess adrenaline in patients with VHL
Symptoms of Pheochromocytoma and Paraganglioma

- “Feels like a panic attack”
  - Headache
  - Sweating
  - Fast heart rate, palpitations
  - High blood pressure
- May have no symptoms

Adrenaline

- Fast heart rate
- Sweating
- Headaches
- High blood pressure
Diagnosis

• Blood and urine tests:
  • Check adrenaline levels
    • Epinephrine, Norepinephrine
    • Metanephrine, Normetanephrine
  • Stop medicines that increase adrenaline levels:

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Common Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>Tylenol</td>
</tr>
<tr>
<td>Tricyclic antidepressant</td>
<td>Amitryptyline, Nortriptyline</td>
</tr>
<tr>
<td>MAO-I inhibitors</td>
<td>Phenelzine</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>Adderall</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>Labetalol</td>
</tr>
<tr>
<td>Clonidine</td>
<td></td>
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<tr>
<td>Alcohol</td>
<td></td>
</tr>
<tr>
<td>Cocaine</td>
<td></td>
</tr>
<tr>
<td>Decongestant</td>
<td>Sudafed</td>
</tr>
</tbody>
</table>

• Results of the blood and urine tests:
  • Real result: often very high (3 times normal)
  • Stress can increase adrenaline levels
Diagnosis

- **CT scan**: initial imaging choice

- **MRI**: paraganglioma in the head and neck area
Diagnosis

- **PET/CT scan:**
  - Whole body image
  - Looks for metastatic disease
  - May detect tumors not seen on CT or MRI

- **MIBG scan:**
  - Whole body image
  - Looks for metastatic disease
Treatment

1. **Alpha-blocker:** Block the effects of the high adrenaline level
   - Start 1-2 weeks before surgery

2. **Beta-blocker:** control heart rate
   - Start *after* taking alpha-blocker

3. Calcium channel blockers: lower blood pressure
4. Metyrosine: decreases adrenaline production
5. High sodium diet and water intake
   - Prevent dehydration
6. Surgery
**Alpha-blockers**

- **Phenoxybenzamine**
  - Non-specific alpha-blocker
  - 10 mg daily or twice daily, increase by 10-20 mg every 2-3 days
  - Final dose: 20 mg – 100 mg daily
  - Orthostasis, fatigue, nasal congestion

- **Selective alpha 1-adrenergic blockers:**
  - **Doxazosin, Prazosin, Terazosin**
  - Less side effects
  - Final dose: 2 mg – 32 mg daily
  - Lower cost $
What If Both Adrenal Glands are Removed?

- Cortisol replacement: Hydrocortisone
- Aldosterone replacement: Fludrocortisone
What if surgery cannot be done?

• Treat high adrenaline level:
  • Alpha blockers: block the effects of adrenaline
  • Beta blockers: slow down the heart rate
  • Calcium channel blockers: lower blood pressure

• Treatments to shrink or slow the growth of the tumors:
  • $^{131}$-I MIBG: effective in 60% of tumors
  • Chemotherapy: used if rapid progression of disease, bone disease
  • Radiation therapy
How often do patients with VHL get adrenal disease?

- 10-20% of patients with VHL will develop a pheochromocytoma
  - 20%: paraganglioma
- Age at diagnosis: 4 – 58 years
- Most common age at diagnosis: 12 – 25 years

**Screening for pheochromocytoma/paraganglioma:**

<table>
<thead>
<tr>
<th>Age</th>
<th>Evaluation</th>
<th>How often</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – 4</td>
<td>Blood pressure</td>
<td>Annually</td>
</tr>
<tr>
<td>5 – 15</td>
<td>Blood pressure sitting and standing, Blood or 24 hour urine test for metanephrines</td>
<td>Annually, Annually</td>
</tr>
<tr>
<td>16 and beyond</td>
<td>Blood pressure sitting and standing, Blood or 24 hour urine test for metanephrines, MRI Abdomen</td>
<td>Annually, Annually, Every other year</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Blood or 24 hour urine test for metanephrines</td>
<td>Once per trimester</td>
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<tr>
<td>Any surgery</td>
<td>Blood or 24 hour urine test for metanephrines</td>
<td>Before surgery</td>
</tr>
</tbody>
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Follow up

• Lifelong follow-up: detect recurrent or metastatic disease
  • Annual blood and/or urine test
  • Imaging based on results of blood/urine test and if surgery was successful
Summary

• 10-20% of patients with VHL will develop a pheochromocytoma or paraganglioma
• The typical symptoms are episodes of fast heart rate, sweating, headache and elevated blood pressure
• The diagnosis is made with blood and urine tests, and many medicines can interfere with the results
• If blood/urine tests are elevated, then imaging will help locate the tumor
• Surgery is recommended after medicines are given to block the effects of the elevated adrenaline levels
• Life-long followup to detect recurrence