Clinical and Surgical Management of VHL-Related Cysts and Cystic RCC

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Outline
- Prevalence of renal cysts and cystic RCC in VHL
- Biology of cystic VHL-related lesions
- Differentiating cysts from cystic RCC
- Surgical management

VHL Renal Manifestations

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Simple cyst
Complex cyst
Solid renal tumor
VHL Renal Manifestations

Cyst vs Cystic RCC

Benign Cyst
One layer of clear cells

Atypical Cysts
Multiple layers and/or focal papillary tufting

Cystic RCC
Cluster of clear cells associated with cyst

Chen et al. 2012 Arch Pathol Lab Med

How prevalent are renal cysts in VHL?

<table>
<thead>
<tr>
<th></th>
<th>CNS HB</th>
<th>RA</th>
<th>ELST</th>
<th>Kid Solids</th>
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<th>PS</th>
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<td>439 (57.3)</td>
<td>547 (71.7)</td>
<td>195 (25.6)</td>
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Missense, n (%): n=375

- 21 (5.6) 31 (8.2) 30 (8.1) 3 (0.8)
- 13 (3.5) 87 (23.4) 22 (6.2) 22 (6.2)
- 7 (1.9) 1 (0.3) 0 3 (0.8)
- 1 (0.3) 0 0 0

Range of Phenotypes

- Limited published data on behavior of cystic VHL tumors
- Must extrapolate from:
  - Sporadic cystic RCC
  - Solid VHL tumors
  - Institutional experience
Cyst Biology: CAIX staining

Normal Kidney (-)  Tumor (+)  Cyst lining (+)

Mandriota et al, Cancer Cell, 2002

Are any cysts truly benign?

Evolution of a complex cystic lesion

2014  2016  2017  2018

How do sporadic cystic lesions behave?

- 133 patients with resected complex renal cysts
- 76% low grade, low stage
- 1 local recurrence

336 patients with complex renal cysts
Only 60 patients had surgery
Mean cyst size 3.5 cm
1 cancer-specific death

Growth Kinetics in VHL-Associated Solid Renal Tumors

240 tumors in 152 patients, comprising 1301 tumor measurements

Median GR: 3.7 mm/yr (IQR: 2.6-5.7)

Ball et al Under Review
Solid tumors: No patients developed metastatic disease when managed by the 3 cm guideline.

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<tr>
<td>≤ 3 cm</td>
<td>0/178 (0%)</td>
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<tr>
<td>3-4 cm</td>
<td>4/109 (3.7%)</td>
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<tr>
<td>4-5 cm</td>
<td>8/62 (12.9%)</td>
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<tr>
<td>5-6 cm</td>
<td>7/27 (25.9%)</td>
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<tr>
<td>6-7 cm</td>
<td>6/12 (50%)</td>
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<tr>
<td>&gt; 7 cm</td>
<td>17/28 (60%)</td>
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Institutional Experience

- The vast majority of lesions that appear to be simple cysts on imaging are benign cysts on final path.
- Complex cystic lesions are often low grade (Fuhrman 1-2) ccRCC on final path.
- Patients who have developed metastatic disease have had large (> 3 cm) solid tumors.

Cyst behavior

Surveillance and Treatment

- MRI: workhorse
- Ultrasound: adjunct
MRI

- Both T2 and T1 contrast enhanced phases are useful

Clinic-Based Ultrasound

Ultrasound Adjunct

When to intervene

- Most interventions are based on solid tumors (i.e. when solid tumor reaches 3 cm)
- For mixed cystic lesions with a discrete nodule, the solid portion can be used as a trigger.
- For mixed honeycomb-like lesions, the proportion of solid tumor can be estimated.
Operative Consideration

- Cyst decortication: not recommended
- Enucleation
- Less parenchymal compression
- Intraoperative ultrasound is critical
Enucleation

Operative Approach

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- **Clinical Team:**
  - W. Marston Linehan, MD
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  - Debbie Nielsen, RN
  - Lindsay Middleton, RN
  - Clinical Fellow
  - George Washington U Residents
  - Georgetown U Residents
  - Walter Reed Residents

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  - Cathy Vocke, PhD
  - Chris Ricketts, PhD
  - Caitlin Drew, RN
  - Debbie Nielsen, RN
  - Lindsay Middleton, RN

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  - Kailash Daryanani

- **Data Management:**
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