Renal Angiomyolipoma

A Comparison of Sporadic and Genetic Cases

Emir S. Sandhu
Harvard Medical School, Year III

Gillian Lieberman, MD
Mini-Seminar Outline

1. Renal Angiomyolipoma (AML): Facts
2. Angiomyolipoma: Associated Syndromes
3. Clinical presentation of AMLs
4. Epidemiology
5. Overview of Renal Anatomy
6. Meet Our Patient: Clinical Presentation
7. Our Patient: Diagnostic Workup
8. AMLs: Role of Angiography
9. Our Patient: Therapeutic Management of AMLs
10. Companion Patient: Tuberous Sclerosis
11. Tuberous Sclerosis: Facts and Role of Imaging
Renal Angiomyolipoma: Facts

- Benign renal tumor
- 3 major histologic components, consisting of mature fat cells, smooth muscle, blood vessels.
- Characteristic features including adipose tissue shown below:

Image: http://path.upmc.edu/cases/case165.html
Associated Syndromes:

Tuberous Sclerosis

- Neurocutaneous syndrome
- 10% of angiomyolipomas are associated with Tuberous Sclerosis
- Rare multi-system genetic disease that causes non-malignant tumor formation, typically manifesting in brain, skin, kidney, heart, eyes, lungs.
- Associated symptoms include seizures, developmental delay, lung and kidney disease.

More to come on Tuberous Sclerosis.
Associated Syndromes:
Sporadic Lymphangioleiomyomatosis

- Smooth muscle infiltration into alveoli.
- Female predominance.
- Often occurs concurrently with TS.
- Rarely can occur sporadically. 60% of sporadic cases also develop AMLs.
- AMLs histopathologically identical to those seen in TS.

Images: (Left) High-resolution axial CT revealing cystic parenchymal changes of LAM. (Right) Renal CT showing multiple lesions (-15 to -100 HU) characteristic of fat.

Angiomyolipoma: Clinical Presentation

• Most common symptoms are the following:
  – Flank pain
  – Hematuria: may lead to hypotension (parenchymal, subcapsular, and/or perirenal hemorrhage)

• Underlying Pathology:
  – Arteries within AMLs lack an internal elastic membrane.
  – AMLs have disorganized adventitial smooth muscle.
  – Progresses to bleeding and aneurysms.
Shown above is an artery in AML (left) compared with a normal artery (right). The AML artery characteristically lacks an internal elastic membrane, surrounded by a collar of myomatous cells.

Image: Meilstrup et al, 1995
Angiomyolipoma: Epidemiology

Based on a study performed by Fujii et al in 1995:

- Renal ultrasonography performed on 17,900 healthy adult patients in Japan.
- Patients had no signs of urinary tract malignancies.
- Hyperechoic renal masses suggestive of angiomyolipoma found in 41 (0.23%).
- Upon further diagnostic confirmation, renal angiomyolipoma identified in 24 patients (0.13%).
- Stratification by gender reveals approximately 0.1% in males and 0.22% in females.
- Separate study of 8501 autopsies demonstrated similar incidence.
Mini-Seminar Outline

1. Renal Angiomyolipoma: Facts
2. Angiomyolipoma: Associated Syndromes
3. Clinical presentation of AMLs
4. Epidemiology
5. **Overview of Renal Anatomy**
6. Meet Our Patient: Clinical Presentation
7. Our Patient: Diagnostic Workup
8. AMLs: Role of Angiography
9. Our Patient: Therapeutic Management of AMLs
10. Companion Patient: Tuberous Sclerosis
11. Tuberous Sclerosis: Facts and Role of Imaging
Renal Anatomy: An Overview

Meet Our Patient: Clinical Presentation

- 38 year-old female who recently emigrated from China, initially presents to nephrology clinic.
- When in China, patient had an MRI suggesting she had a benign tumor on her right kidney.
- She was referred following renal ultrasound ordered by her primary care physician, which revealed a cortical-based echogenic mass in the right kidney, measuring approximately 3.9 x 3.5 cm, that was causing moderate hydronephrosis.
- On later visit, Urology felt the mass had been stable for the past year, and wanted to repeat MRI in 6 months.
Our Patient: Past Diagnostic Workup

- 10/2008 MRI: 4.8 x 4.2 cm
- 10/2010 MRI: 6.8 x 4.4 cm
- 1/2011 Presented to the BIDMC ED with dull right flank pain. No hematuria, dysuria, or urinary frequency.
- 5/2011: Seen by Urology, no plan for procedure. Follow up in 6 months.
- 10/2011: MRI: 8.9 x 5.7 cm
Shown on sagittal ultrasound of the right kidney is a cortical-based, echogenic mass measuring 3.9 x 3.5 cm. There is moderate hydronephrosis with no evidence of stones.

Image: BIDMC PACS
Our Patient: Right Kidney Doppler

Shown is a sagittal ultrasound of the right kidney. Note the poor Doppler flow evident within the renal mass.

Image: BIDMC PACS
Companion Patient: AML on CT

- Presence of fat in kidney highly suggestive of AML.
- Fat is -20 to -80 Hounsfield Units (prior to contrast)
- Contrast may be given to reveal aneurysms

Image above: Small AML shown in upper pole of right kidney (arrow), measuring -46 HU on axial CT scan.

Image: Meilstrup et al. (1995)
Our Patient: AML on Axial Vibe MRI

On axial MRI: Large 8.9 x 5.7 cm mass centered in lower pole of the R kidney, extending into the R hilum inferiorly. Diffuse low-grade enhancement seen, consistent with AML. There is also a 4-mm lesion in the lower pole of the R kidney, also an AML.

Image: BIDMC PACS
Shown on the left is our patient’s T1 axial, in phase MRI. Note the effect of fat suppression compared with the axial vibe image shown on the right.
On axial out-of-phase MRI, the **India Ink Artifact** is shown, which represents signal drop-out in voxels that contain both fat and non-fat components. It is seen surrounding interfaces, as if someone had outlined the interfaces with ink. A **renal AML** is also shown.

**Image:** BIDMC PACS
Mini-Seminar Outline

1. Renal Angiomyolipoma: Facts
2. Angiomyolipoma: Associated Syndromes
3. Clinical presentation of AMLs
4. Epidemiology
5. Overview of Renal Anatomy
6. Meet Our Patient: Clinical Presentation
7. Our Patient: Diagnostic Workup
8. AMLs: Role of Angiography
9. Our Patient: Therapeutic Management of AMLs
10. Companion Patient: Tuberous Sclerosis
11. Tuberous Sclerosis: Facts and Role of Imaging
AML: Role of Renal Angiography

- Not often used to diagnosis AML
- Often used for management of bleeding
- AMLs have circumferential peripheral vessels with whorled appearance during nephrographic phase
- Multiple aneurysms are also characteristic.
- In study by Becker, et al: aneurysms found on 16 of 34 AML cases

Image above: Angiography of R kidney revealing AML of the upper pole with aneurysms.

Image: Meilstrup et al. (1995)
AML: Treatment Recommendations

Steiner Study: 35 patients with AML evaluated.

**Recommendations:**

- Lesions <4cm should be followed with yearly CT/US.
- Asymptomatic patient with lesion >4cm should have semi-annual US.
- Symptomatic patient with lesion >4cm should undergo renal-sparing surgery or arterial embolization.
- Prophylactic intervention for patient with Tuberous Sclerosis and lesion >4cm, irrespective of symptoms.
- Two established treatment options include renal-sparing surgery or embolization.

Our Patient: AML Embolization

Based on these treatment recommendations, our patient underwent embolization of her AML.

- Particle embolization was performed to reduce flow rate through AML, closely monitored under fluoroscopic visualization.
- Post-embolotherapy R renal arteriogram demonstrated an avascular tumor with no detectable venous or arterial flow from an inferior polar branch of the R renal artery.

Images: BIDMC PACS
Companion Patient #2: Tuberous Sclerosis

Image: T1-weighted coronal MRI.

Shown to the left in our companion patient are two lesions with increasing signal intensity (arrows) similar to subcutaneous fat (asterisk).

These are compatible with large angiomyolipoma.

Mini-Seminar Outline

1. Renal Angiomyolipoma: Facts
2. Angiomyolipoma: Associated Syndromes
3. Clinical presentation of AMLs
4. Epidemiology
5. Overview of Renal Anatomy
6. Meet Our Patient: Clinical Presentation
7. Our Patient: Diagnostic Workup
8. AMLs: Role of Angiography
9. Our Patient: Therapeutic Management of AMLs
10. Companion Patient: Tuberous Sclerosis
11. Tuberous Sclerosis: Facts and Role of Imaging
Tuberous Sclerosis: Facts

- Bilateral renal involvement typical.
- 1/3 of cases are familial, remaining sporadic.
- Transmitted in an autosomal dominant trait.
- Characteristic formation of tubers in the skin, brain, kidneys, and other organs.
- Incidence is estimated to be approximately 1 in 6,000 live births.
- Two genes identified, TSC1 and TSC2, located on chromosomes 9 and 16 respectively.

# Tuberous Sclerosis: Diagnostic Criteria

Definitive diagnosis:
2 major features OR 1 major + 2 minor features required.

<table>
<thead>
<tr>
<th>Major Features</th>
<th>Minor features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial angiofibromas/forehead plaque</td>
<td>Multiple pits in dental enamel</td>
</tr>
<tr>
<td>Non-traumatic ungual fibroma</td>
<td>Hamartomatous rectal polyps</td>
</tr>
<tr>
<td>Hypomelanotic macules</td>
<td>Bone cysts</td>
</tr>
<tr>
<td>Shagreen patch (connective tissue nevus)</td>
<td>Cerebral white matter radial migration lines</td>
</tr>
<tr>
<td>Multiple retinal nodular hamartomas</td>
<td>Gingival fibromas</td>
</tr>
<tr>
<td>Cortical tuber</td>
<td>Nonrenal hamartomas</td>
</tr>
<tr>
<td>Subependymal nodule</td>
<td>Retinal achromic patch</td>
</tr>
<tr>
<td>Subependymal giant cell astrocytoma</td>
<td>“Confetti” skin lesions</td>
</tr>
<tr>
<td>Cardiac rhabdomyoma</td>
<td>Multiple renal cysts</td>
</tr>
<tr>
<td>Lymphangiomyomatosis</td>
<td></td>
</tr>
<tr>
<td>Renal angiomyolipoma</td>
<td></td>
</tr>
</tbody>
</table>

Tuberous Sclerosis: Renal Manifestation

- Most common TS manifestation is the formation of angiomyolipomas.
- Benign cysts and (less often) lymphangiomomas can also occur in patients with TS.
- Both cysts and angiomyolipomas tend to present bilaterally.
- Many patients, however, have no symptoms referable to the kidney.

From: Casper KA, et al. (2002).
Tuberous Sclerosis: Role of Imaging

- **Renal US** should be performed at time of diagnosis to define extent of angiomyolipomas and/or presence of polycystic disease.

- **US recommended every 1-3 years** to monitor growth of lesions and possible signs of malignancy.
  - Ex: of concern would be a non-cystic mass lacking low density (-10 to -100 HU) to suggest benign AML.

- If **malignant transformation** suspected or **large angiomyolipoma(s)** present:
  - CT or MR recommended to evaluate abnormality.
  - Avoid gadolinium based imaging in those with GFR < 30 mL/min given risk of nephrogenic systemic fibrosis.

Tuberous Sclerosis: Renal Complications

- Angiomyolipomas can become quite large, leading to abdominal or flank pain, bleeding into lesion (typically when > 4 cm diameter)
- Renin-dependent hypertension, due to focal areas of ischemia around lesions. Chronic renal failure also can occur.
- RCC also is a known complication. Occurs in 1-2% of patients, substantially lower than VHL syndrome. 
  - Histology is usually consistent with clear cell carcinoma.

Summary of Learning Objectives

In this mini-seminar, we have covered the following topics:

- **Renal Angiomyolipoma:**
  - Clinical presentation
  - Associated genetic syndromes
  - Diagnostic evaluation
  - Relevant imaging findings
  - Therapeutic management

- **Tuberous Sclerosis:**
  - Clinical presentation
  - Renal manifestations and complications
  - Role of imaging and diagnostic criteria
References

Acknowledgements

I would like to extend a warm thank you to the following people for their help with my presentation:

Dr. Gillian Lieberman
Dr. Samir Shah
Claire Odom
My fellow medical students