Radiologic Evaluation of Renal Cell Carcinoma

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Objectives

- Our patient: Initial presentation
- Differential diagnosis: Solid renal mass
- Background: Renal cell carcinoma (RCC)
- Imaging RCC: Menu of tests, key findings
- Our patient: Follow-up
- Summary
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Our Patient: Initial Presentation

- **CC**: Ms. K. is a 60yo woman w/ new back pain, unresponsive to conservative therapy → now w/ pain radiating down both legs + LE weakness.

- **Next step**: MRI of L-spine w/ unexpected finding!
Our Patient: Initial MRI L-spine

Sagittal pre-contrast T1W MRI:

L1 vertebral body w/ moderate-severe compression fracture

Retropulsion of osseous fragments into spinal canal, impinging on spinal cord

Sagittal T2W MRI:

Images courtesy of Dr. Jason Handwerker, BIDMC
Our Patient: Initial MRI L-spine

Scout MRI:

Intact thoracic vertebral body, superior to L1 lesion

Axial T2W MRI at L1:

Collapsed L1

Soft tissue mass w/ epidural, L paraspinal extension

Spinal canal stenosis

Large soft tissue mass in L renal fossa

Images courtesy of Dr. Jason Handwerker, BIDMC
Our Patient: Initial Presentation

2 Problems:

1. Large renal mass
2. Vertebral body compression fracture
Our Patient: Initial Presentation

2 Problems:

1. Large renal mass → Next step?
2. Vertebral body compression fracture
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Approach to a Renal Mass

Before reviewing the differential diagnosis of a solid renal mass, let’s take a look at the normal anatomy of the kidney:
Normal Anatomy: Coronal View

- **Kidney:**
  - Capsule
  - Cortex
  - Medulla
  - Collecting system
  - Hilum: renal artery + vein, ureter

Normal Anatomy: Axial View

- **Retroperitoneum:**
  - Kidneys in perinephric space surrounded by renal/Gerota’s fascia
  - Anterior paranephric space
  - Posterior paranephric space

On to the Differential Diagnosis:

- Now that we have reviewed the normal kidney anatomy, let’s review the differential diagnosis of our patient’s solid renal mass.

- For clarity, we will also review some companion images of benign renal conditions, which our patient does NOT have.
# DDx of a Solid Renal Mass

## Benign

<table>
<thead>
<tr>
<th>Angiomyolipoma (AML)</th>
</tr>
</thead>
</table>
DDx: Closer Look at AML

- **AML**: Benign renal mass containing blood vessel, fat, and muscle components.

- **CT features**:
  - *Fat* inside the mass (hypodense; not specific b/c RCC may contain fat too)
  - May be hyperdense on unenhanced CT
  - *Homogeneous* enhancement, hypodense compared to normal parenchyma

Atkins MB, *UpToDate*, http://up2date.com/utd/content/topic.do?topicKey=gucancer/4484&type=A&selectedTitle=2~51.
# DDx of a Solid Renal Mass

<table>
<thead>
<tr>
<th><strong>Benign</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiomyolipoma (AML)</td>
<td></td>
</tr>
<tr>
<td>Oncocytoma</td>
<td></td>
</tr>
</tbody>
</table>

DDx: Closer Look at Oncocytoma

- **Oncocytoma**: Benign neoplasm of cells derived from collecting duct.

- **CT features**:
  - Homogeneous, solid mass
  - With contrast, appears as a *homogeneous hypodensity* compared to normal parenchyma

# DDx of a Solid Renal Mass

<table>
<thead>
<tr>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiomyolipoma (AML)</td>
<td>Renal cell carcinoma</td>
</tr>
<tr>
<td>Oncocytoma</td>
<td>Transitional cell carcinoma</td>
</tr>
<tr>
<td>Mesenchymal tumors (rare) (reninoma, fibroma, lipoma, myoma, hemangiopericytoma)</td>
<td>Lymphoma (large cell, Burkitt)</td>
</tr>
<tr>
<td>Infection (chronic obstruction → xanthogranulomatous pyelonephritis)</td>
<td>Metastases (lung, breast)</td>
</tr>
<tr>
<td></td>
<td>Renal sarcoma</td>
</tr>
<tr>
<td></td>
<td>Bellini (collecting) duct tumor</td>
</tr>
</tbody>
</table>

DDx: Our Patient’s Considerations:

- Large differential for solid renal mass

- Given invasion of spine, metastatic disease is likely → ? Primary renal tumor vs. Metastasis from a different primary (e.g., lymphoma)

- Need dedicated imaging of kidney for diagnosis → Best test = Abdominal CT
Our Patient: Abdominal CT

Abnormal perfusion pattern in liver suggesting venous obstruction

Axial CT of abdomen, w/ contrast, early phase

Bulky mass almost replacing L kidney; soft tissue density; ill-defined borders; heterogeneous enhancement

Central low attenuation suggesting necrosis

Tumor thrombus distending renal vein, IVC

Paraspinal extension into lumbar spine

Chest wall invasion through capsule + fascia

Images courtesy of Dr. Jason Handwerker, BIDMC
Hallmark Features of RCC on CT:

- **Without contrast**
  - Renal mass, usually soft tissue density (>20 HU)
  - Exophytic w/ irregular borders
  - 30% w/ calcifications

- **With contrast**
  - *Heterogeneous enhancement* (hypervascular w/ areas of hemorrhage, necrosis)
Working Diagnosis: RCC

- CT images suggest the diagnosis of renal cell carcinoma (RCC).

- Let’s learn a little more about RCC …
Objectives

- Our patient: Initial presentation
- Differential diagnosis: Solid renal mass
- **Background: Renal cell carcinoma (RCC)**
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Background on RCC

- Epidemiology
- RCC Pathology
- Natural history of disease
- Clinical presentation
- Need for imaging
Epidemiology of RCC: Prevalence

- 3% of adult malignancies
- 80-90% of primary renal malignancies
Epidemiology of RCC: Risk Factors

- Most RCC sporadic, cause unknown
- Men >> Women
- Age > 50y
- Cigarette smoking (2x risk)
- Occupational exposure (cadmium, asbestos, petroleum)
- Obesity
- Chronic dialysis (acquired cystic disease of kidney)
- Genetics, e.g. VHL, tuberous sclerosis, familial RCC
Gross Pathology of RCC

RCC can be cystic or solid, often with hemorrhage.


Microscopic Pathology of RCC

RCC is most often conventional/clear cell type (from cells of proximal convoluted tubule).

Klatt EC, [http://www-medlib.med.utah.edu/WebPath/RENAHTML/RENAL055.html](http://www-medlib.med.utah.edu/WebPath/RENAHTML/RENAL055.html)
Natural Progression of RCC

- Natural history:
  - Slow-growing → often does not present until advanced

- Common sites of metastasis:
  - Lung, Lymph nodes, Bone, Liver, Brain
Clinical Presentation of RCC

- ~1/2 with varied symptoms due to:
  - Tumor — “classic” triad of hematuria, flank pain, abdominal mass (only 9% pts)
  - Renal vein/IVC spread (LE edema, ascites, etc.)
  - Metastases (bone pain, etc.)
  - Paraneoplastic syndromes (anemia, fever, etc.)

- ~1/2 present incidentally on imaging
Role of Imaging in Evaluating RCC

- Varied presentation → Need **imaging** for further evaluation:
  - Diagnosis
  - Staging
  - Treatment decisions
  - Prognosis
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Imaging RCC: Purpose

- Why image?
  - **What**: Benign vs. malignant mass
  - **Where**: Tumor size, localization, organ confinement
  - **Extent**: Visceral metastases, LN involvement, tumor thrombus in IVC
Imaging RCC: Context

- Surgery = only cure currently available
- Goals:
  - Identify patients w/ resectable disease
  - Determine extent of disease for accurate treatment planning (surgery vs. medical therapy)
Imaging RCC: Menu of Tests

- Computed tomography (CT)
- Ultrasound (US)
- Magnetic resonance imaging (MRI)
- Further imaging (bone scan, CXR/chest CT, brain MRI)
Imaging RCC: Menu of Tests

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CT Imaging of RCC: Technique (1)

- C-, C+ w/ 3 phases of enhancement:
  - **Corticomedullary** (25-70 sec post-contrast)
    - Contrast in renal cortex > medulla, corresponds to other organs’ arterial phase of enhancement
  - **Nephrographic** (80-180 sec post-contrast)
    - Contrast into medulla, renal parenchyma homogeneously enhancing, best phase for detecting renal mass
  - **Excretory** (> 3 min post-contrast)
    - Contrast excreted into pelvicalyceal collecting system, decreased enhancement of renal parenchyma

CT Imaging of RCC: Technique (2)

- Multidetector CT (MDCT) \(\rightarrow\) can image entire kidney during each enhancement phase
- Coronal, sagittal reconstructions \(\rightarrow\) map tumor extent
- 3D reconstruction \(\rightarrow\) surgical planning
Using CT to Stage RCC

- CT → 91% accuracy in staging RCC
- Anatomical staging related to renal fascia
- Why stage? → Determines treatment + prognosis

Sheth et al., 2001, Radiographics.
Two Staging Systems for RCC

- **TNM** (tumor, node, metastasis) (by American Joint Committee on Cancer, AJCC, 2002)

- **Robson** (older, simpler system) (by Flocks and Kadesky, modified by Robson et al.)
TNM Staging System of RCC

- TNM system (preferred)
  - T (0-4): Tumor size, extent of local invasion
  - N (0-2): Lymph node involvement
  - M (0-1): Distant metastasis
Conceptual Stages of RCC: Combining TNM + Robson Systems

1. Confined to renal capsule

2. Spread to perinephric fat

3. Venous extension

4. Regional lymph node metastases

5. Local organ invasion (past renal fascia), distant metastases

<table>
<thead>
<tr>
<th>Tumor Position</th>
<th>Robson Stage</th>
<th>TNM Class</th>
<th>CT Findings</th>
<th>CT Pitfalls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confined within renal capsule</td>
<td>I</td>
<td>I</td>
<td>Soft-tissue mass enhances less than normal renal parenchyma; central necrosis in large renal cell carcinoma</td>
<td></td>
</tr>
<tr>
<td>Small (&lt;7 cm diameter)</td>
<td>...</td>
<td>T1</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Large (≥7 cm diameter)</td>
<td>...</td>
<td>T2</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Spread to perinephric fat</td>
<td>II</td>
<td>T3a</td>
<td>Perinephric stranding; perinephric collateral vessels</td>
<td>Not reliable or specific; found in 50% of T1 and T2 tumors; false-negative if spread is microscopic</td>
</tr>
<tr>
<td>Venous thrombus</td>
<td>IIIA</td>
<td>...</td>
<td>Self-tissue mass in perinephric space Filling defect within a distended vein; direct continuity of thrombus with primary mass; IV contrast enhancement indicates tumor thrombus; collateral veins</td>
<td>Specific, not sensitive in 45%-50% of cases False-negative: right renal vein and IVC obscured by large renal cell carcinoma; false-negative: enhancing thrombus obscured; false-positive: venous enlargement due to increased flow; false-positive: streaming of unopacified blood in IVC (perform delayed scanning)</td>
</tr>
<tr>
<td>Renal vein only</td>
<td>...</td>
<td>T3b</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>IVC infradiaphragmatic</td>
<td>...</td>
<td>T3c</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>IVC supradiaphragmatic</td>
<td>...</td>
<td>T4b</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Regional lymph node metastases</td>
<td>IIIB</td>
<td>N1-N3</td>
<td>Lymph nodes 1 cm in diameter or larger</td>
<td>False-negative rate: 4%; false-positive: enlarged inflammatory nodes</td>
</tr>
<tr>
<td>Direct invasion of adjacent organs</td>
<td>IVA</td>
<td>T4a</td>
<td>Obliteration of normal soft-tissue planes between tumor and adjacent organs</td>
<td>False-positive: partial volume averaging; false-positive: tumor adherent but not directly invading</td>
</tr>
<tr>
<td>Distant metastases</td>
<td>IVB</td>
<td>M1a-d</td>
<td>Metastases enhance with IV contrast material; hepatic metastases best in arterial phase</td>
<td>Hypervascular metastases may be obscured in portal venous phase</td>
</tr>
</tbody>
</table>

Sheth et al., 2001, Radiographics.
Stage Correlates With CT Findings

- How do each of these stages appear on CT?

- Let’s take a look at CT images of 5 different companion patients, who each have RCC at a different stage of the disease.

- Then we will examine CT images of our patient, Ms. K.
Companion Patient #1: CT Findings

**Stage:** T1-2, Robson I
Confined to renal capsule

**On CT:** Soft tissue mass, enhancing < nl parenchyma; central necrosis in large RCCs; 30% w/ calcifications

Axial CT w/ contrast

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Companion Patient #2: CT Findings

Stage: T3a, Robson II
Spread to perinephric fat

On CT: Perinephric soft tissue mass (specific but 46% sens.); fat stranding, collateral vessels (nonspecific)

Axial CT w/ contrast

Sheth et al., 2001, Radiographics.
Companion Patient #3: CT Findings

Stage: T3b-c, Robson IIIA
Venous extension

On CT: Filling defect in distended vein; thrombus cont. w/ tumor; heterogeneous enhancement (FN = vein/thrombus obscured; FP = incr. flow distending vein, unopacified blood into IVC)

Axial CT w/ contrast

Sheth et al., 2001, Radiographics.
Companion Patient #4: CT Findings

Stage: N1-3, Robson IIIb
Retroperitoneal lymph node (LN) metastases

On CT: LNs > 1cm, enhancing similar to tumor (FP = reactive LN hyperplasia; FN = micromets)

Lymph nodes metastases

Axial CT w/ contrast

Sheth et al., 2001, Radiographics.
Companion Patient #5: CT Findings

Stage: T4, M1, Robson IV: Local organ invasion (past renal fascia), distant metastases

On CT: Obliterated soft tissue planes (FP = partial volume averaging, tumor adjacent, not invading)

On CT: Metastases enhance, best in arterial phase

Pelvic axial CT w/ contrast

Abdominal axial CT w/ contrast


Sheth et al., 2001, Radiographics.
## RCC Stage → Prognosis, Treatment

<table>
<thead>
<tr>
<th>Stage</th>
<th>5-year survival</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confined to renal capsule</td>
<td>&gt;90%</td>
<td>Surgical resection</td>
</tr>
<tr>
<td>Spread to perinephric fat</td>
<td>75-95%</td>
<td>Surgical resection</td>
</tr>
<tr>
<td>Venous extension</td>
<td>59-70%</td>
<td>Surgical resection</td>
</tr>
<tr>
<td>Retroperitoneal LN metastases</td>
<td>5-30%</td>
<td>Palliative medical therapy +/- surgical debulking</td>
</tr>
<tr>
<td>Local organ invasion (past renal fascia), distant metastasis</td>
<td>&lt;10% (if distant mets)</td>
<td>Palliative medical therapy +/- surgical debulking</td>
</tr>
</tbody>
</table>

Back to Our Patient: Staging

- What about our patient, Ms. K.?

- Abdominal CT showed a large, locally invasive renal mass suspicious for RCC.

- Additional CT imaging of the chest, abdomen, pelvis was performed to stage disease…
**Our Patient: Coronal CT**

Lobulated mass in RML, likely metastasis

Tumor thrombus extending into R atrium

IVC expanded, obstructed by tumor thrombus, heterogeneously enhancing

L renal mass: 18 x 9 x 10cm, soft tissue, heterogeneous enhancement, irregular borders

Bulky retroperitoneal lymph nodes along aorta

Image courtesy of Dr. Jason Handwerker, BIDMC
Our Patient: Sagittal CT

- Sagittal reconstruction of CT w/ contrast

- Tumor thrombus into IVC → R atrium
- Metastasis to L1 vertebral body → pathological compression fracture
- Bulky paraaortic lymph nodes

Sheth et al., 2001, Radiographics.

Image courtesy of Dr. Jason Handwerker, BIDMC
Imaging RCC: Menu of Tests

- Computed tomography (CT)
- Ultrasound (US)
- Magnetic resonance imaging (MRI)
- Further imaging (bone scan, CXR/chest CT, brain MRI)
US of RCC: Companion Images

- US w/ Doppler imaging
- Used to assess: atypical cystic lesions, hypovascular tumors, AMLs w/ minimal fat, R upper pole renal masses near liver
- Extent of venous tumor thrombus (better than CT)
- Limitations: operator-dependent, less detail of tumor spread
Imaging RCC: Menu of Tests

- Computed tomography (CT)
- Ultrasound (US)
- Magnetic resonance imaging (MRI)
- Further imaging (bone scan, CXR/chest CT, brain MRI)
MRI of RCC: Companion Image

- MRI w/ gadolinium contrast
- Used to assess venous involvement:
  - Cranial extent of tumor thrombus
  - Tumor vs. benign thrombus
  - IVC wall invasion
- Better detection of lymph node involvement
- Useful if CT contrast or radiation contraindicated

Hyperintense lesion on lower pole of L kidney = RCC.

T1W coronal MRI post-gadolinium enhancement

Image courtesy of Dr. Jason Handwerker, BIDMC
Imaging RCC: Menu of Tests

- Computed tomography (CT)
- Ultrasound (US)
- Magnetic resonance imaging (MRI)
- Further imaging (bone scan, CXR/chest CT, brain MRI)
Examples of Further RCC Imaging:

- If clinical picture warrants additional staging:
  - CXR, Chest CT (if CXR equivocal)
  - Bone scintigraphy, supplemented w/ plain films, CT (if bone pain, or elevated alk phos)
  - Cerebral CT, MRI

- 3D CT if planning partial nephrectomy:

  - Arterial 3D reconstruction
  - 3-dimensional reconstruction of R renal RCC in lower pole
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Our Patient: Imaging Diagnosis

- **Presumptive diagnosis**: Metastatic RCC

- **Stage**: IV = T4 N2 M1
  - Through Gerota’s fascia
  - Direct invasion into IVC, heart, spine
  - Metastases to multiple LNs, distant organs (lungs)
Our Patient: Tissue Diagnosis

- **Biopsy:** Percutaneous FNA + core needle biopsy of L renal mass under CT guidance

  Stereotactic grid on skin

  Axial CT w/o contrast

  Site of biopsy

- **Renal bx pathology:** RCC, conventional/ clear cell type

  Comparable pathology from a different patient.

Image courtesy of Dr. Jason Handwerker, BIDMC

Klatt EC, [http://www-medlib.med.utah.edu/WebPath/RENAHTML/RENA055.html](http://www-medlib.med.utah.edu/WebPath/RENAHTML/RENA055.html)
Treatment Options for Our Patient

- What treatments are available, given her widespread disease?
Treatment Options for Our Patient...

...If her cancer had been less invasive →
Treatment For Stage I-III RCC

**Surgery:**
- Radical nephrectomy vs. renal-sparing resections (can be curative)
- Adjuvant immunotherapy (survival benefit)
- If surgery contraindicated → Non-surgical procedures (RFA, cryoablation) vs. conservative management w/ close surveillance
Treatment Options for Our Patient

- Unfortunately, her cancer was extremely advanced →
Treatment For Stage IV RCC

- **Non-resectable RCC:**
  - Immunotherapy (IL-2)
  - Molecular targeted therapy
    - VEGF inhibitors: sunitinib, sorafenib, bevacizumab
    - mTOR inhibitors: temsirolimus
  - Palliative surgery, radiation therapy (for symptomatic metastases, e.g., painful bone mets)
Our Patient Received Palliative Spine Surgery:

Pre-op lumbar embolization (minimize bleeding from hypervascular metastasis)

L1 vertebrectomy + tumor resection, with T10-L3 thoracolumbar fusion and instrumentation

Pathology: Metastatic carcinoma most consistent w/ renal primary

CT scout, post-op

Spinal angiogram, T12

Images courtesy of Dr. Jason Handwerker, BIDMC
Objectives

- Patient DK: Initial presentation
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Summary (1)

- RCC is a slow-growing cancer, usually detected late → Varied clinical presentation, limited treatment options, poor prognosis

- Increasing cross-sectional imaging → Increasing incidental Dx of RCC → less advanced disease, better prognosis
  - Therefore it is important to recognize RCC on CT!
Summary (2)

- Imaging is essential for diagnosis, staging, treatment, surveillance of RCC
- Best imaging for Dx = Abdominal CT
- Hallmarks of RCC on CT = renal mass w/ heterogeneous enhancement, propensity to spread to renal vein + IVC
Summary (3)

- Staging is related to anatomy (Gerota’s fascia)
- Multiple imaging tests available for staging (CXR, chest CT, bone scan, MRI) → choose based on clinical picture
- Stage determines treatment + prognosis:
  - Stage I-III → Surgery, may be curative
  - Stage IV (invasive, metastatic) → Immunotherapy, molecular targeted therapy; poor prognosis currently
References

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