Papillary Renal Cell Carcinoma Presenting with Hemoptysis

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Our patient

• 57 y.o. man with a previous smoking history, and an 8 month history of COPD presenting with worsening dyspnea on exertion, cough, and wheezing

• A chest X-ray was performed to look for lung processes that could be acutely exacerbating his condition
  – Pneumonia
  – Obstruction/collapse
  – Pneumothorax
  – Pleural effusion
Our patient’s initial evaluation by chest X-ray is shown below

Frontal Upright Chest X-Ray

Left Lateral Upright Chest X-Ray

BIDMC PACS
ABCs of CXR: quality control

Is this our patient? Do we have the standard views?
Is the entire region of interest covered? Exposure?
ABCs of CXR: aberrant air

Frontal Upright Chest X-Ray

Left Lateral Upright Chest X-Ray

ABCs of CXR: bones
ABCs of CXR: cardiac silhouette

Frontal Upright Chest X-Ray

Left Lateral Upright Chest X-Ray

ABCs of CXR: diaphragm
ABCs of CXR: cardiac silhouette

Frontal Upright Chest X-Ray

Left Lateral Upright Chest X-Ray

BIDMC PACS

depressed diaphragm
ABCs of CXR: cardiac silhouette

Frontal Upright Chest X-Ray

Left Lateral Upright Chest X-Ray

small effusion
ABCs of CXR: extras

Frontal Upright Chest X-Ray

Left Lateral Upright Chest X-Ray

outside the patient
ABCs of CXR: fields

Frontal Upright Chest X-Ray

Left Lateral Upright Chest X-Ray

ABCs of CXR: gastric bubble and hila

Increased markings
Our patient’s course: worsening COPD

• Our patient was released with a diagnosis of worsening COPD
  – no acute lung problem

• 2 months later, he returned with a new COPD exacerbation, this time complicated by hemoptysis
Because of his acutely worsening condition, a CT scan was ordered.
Chest CT for to evaluate hemoptysis

axial chest CT: lung window

**yellow oval:** airspace filling

**DDx:** water, blood, cells, protein

**orange oval:** focal density

Could this be malignant?
Right bronchial mass on CT

coronal reconstruction CT of the chest: soft tissue window

Yellow circle: density in the right bronchus

malignancy? mucus plug?
Incidental finding in the abdominal portion of the CT

Axial CT through the abdomen: soft tissue window

Yellow circle: exophytic posterior left kidney cyst
Overview of normal renal anatomy

Exophytic kidney cyst

DDx
Benign Cyst (common)
Renal Tumor (RCC, TCC, other)
Abscess
Vascular Abnormality
Metastasis
Cystic Kidney Syndrome

follow-up is determined by specific radiographic features

Bosniak Classification System

• Bosniak I: hairline thin wall; no septa, calcification, or solid components. Water density, no enhancement.

• Bosniak II: a few hairline thin septa, fine calcification in wall or septa.

• Bosniak IIF: more hairline septa. Minimal septa or wall enhancement, minimal wall thickening. Nodular or thick calcifications. No soft tissue enhancement.

• Bosniak III: cystic masses with thickened irregular walls, or septa with enhancement

• Bosniak IV: Cystic lesions with enhancing soft-tissue elements
Generally Benign Cysts (I, II)

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Potentially Malignant (IIF – IV)

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Follow-up Required
Evidence that Bosniak criteria are clinically meaningful

<table>
<thead>
<tr>
<th>Bosniak Classification</th>
<th>% Malignant</th>
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</thead>
<tbody>
<tr>
<td>I</td>
<td>1.8% (2/114)</td>
</tr>
<tr>
<td>II</td>
<td>18.5% (20/108)</td>
</tr>
<tr>
<td>III</td>
<td>33% (218/660)</td>
</tr>
<tr>
<td>IV</td>
<td>92.5% (148/160)</td>
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</table>
Analyzing our patient’s cyst using the Bosniak criteria

axial CT through the abdomen: soft tissue window

yellow circles: exophytic cyst, soft tissue density, some regions of inhomogeneity, question of rim enhancement, calcified rim, accessory nodule.
How should we classify our patient’s cyst?

- Bosniak IIF: follow-up recommended
  - MRI can provide greater soft tissue detail
Further diagnostic steps for our patient

- Multiple pulmonary/bronchial nodules identified
  - Concern for primary pulmonary malignancy
  - Bronchial nodule was resected and sent to pathology

- Follow-up MRI of the kidneys was performed to further characterize the mass
Follow-up MRI was ordered

- Sagittal abdominal MRI: T1 pre-contrast fat suppressed
- Sagittal abdominal MRI: T1 post-contrast fat suppressed

**yellow circle:** posterior exophytic left kidney mass
high signal regions suggest focal hemorrhage

**orange circle:** hyper-intensity in the posterior renal fat
malignant invasion? inflammation?

**pink arrows:** enhancing papillary nodules
Coronal MRI of the kidney

pre-contrast images can be mathematically subtracted from post-contrast images to confirm regions of enhancement, outlining areas of blood flow
Further analysis of blood flow by MRI

coronal abdominal MRI: post-contrast subtraction view

pink arrows: enhancing papillary nodules
MRI aided diagnosis

- MRI imaging findings are characteristic of papillary RCC
  - Cystic mass
  - Well encapsulated
  - Relatively low/homogenous enhancement with gadolinium
  - Enhancing, papillary projections into lumen

- Diagnosis was confirmed by bronchoscopy
  - The mass in his bronchus was confirmed to be papillary RCC
Renal cell carcinoma

- Most common tumor of the kidney

- Subtypes of RCC
  - Clear Cell (75% – 85%)
  - Chromophilic/papillary (10% – 15%)
  - Chromophobic (5% – 10%)
  - Oncocytic (rare)
  - Collecting Duct (rare)
RCC staging and prognosis

- Staging
  - Stage I: < 7 cm
  - Stage II: > 7 cm but limited to kidney
  - Stage III: invasion into veins, adrenal, perirenal space
  - Stage IV: invasion beyond perirenal fascia, including distant metastases

<table>
<thead>
<tr>
<th>Stage</th>
<th>Prognosis (5 year survival)</th>
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<tbody>
<tr>
<td>I</td>
<td>91% - 100%</td>
</tr>
<tr>
<td>II</td>
<td>74% - 96%</td>
</tr>
<tr>
<td>III</td>
<td>59% - 70%</td>
</tr>
<tr>
<td>IV</td>
<td>16% - 32%</td>
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</tbody>
</table>
Use of CT for staging RCC

- Detect invasion of perirenal structures (Stage III disease)
  - Veins (renal, IVC)
  - Adrenal Gland
  - Perirenal fasica

- Identify distant metastases (Stage IV disease)
  - e.g. the pulmonary masses in our patient?

- Other modalities include:
  - MRI, metabolic bone scan, PET
• Clear cell RCC is more common than the papillary variant, and has a more typical, malignant presentation by CT using the Bosniak criteria as demonstrated by companion patient 1
Companion patient 1: typical presentation of clear cell RCC

Post contrast axial CT through the abdomen: soft tissue window

Yellow circle: complex cystic mass (Bosniak IV)
Orange rectangle: area of detail (next slide)
Magnification view

Post contrast axial CT through the abdomen centered on IVC:
soft tissue window

Yellow oval: tumor thrombus in the IVC (stage III disease)
Renal cell carcinoma treatment

- Surgical Resection (Stage I – III only)
- Standard chemotherapy has not been found to be effective
- Immune Therapy
  - IL-2, Interferon alpha, bevacizumab
- Targeted Therapy (Stage III, IV)
  - mTOR (temsirolimus), VEGF Receptor (sunitinib, sorafenib)
- Clinical Trials
  - response rates to current therapeutic regimens are poor
Immune therapy for RCC

• Tumors often express proteins that can be recognized as foreign by the immune system
  – Mutated proteins, developmental/tissue restricted proteins, etc.

• Spontaneous anti-tumor immune responses do occur, but are rare and often insufficient to clear tumors

• Immune therapy is used to augment nascent anti-tumor immune responses
  – cytokines, monoclonal antibodies
Cytokine therapy mechanism of action

• Both IL-2 and interferon alpha are important factors in promoting immune responses

• IL-2: potent T cell growth factor

• Interferon alpha: critical in for anti-viral responses, makes infected cells (or tumors) more susceptible killing by cytotoxic cells (CD8 T cells, and NK cells)
Cytokine therapy efficacy and side effects

- Objective response rates are currently low (~10%), and durable responses are rare

- Adverse effects are significant, and resemble those of influenza infection
  - Malaise, fever, night sweats, joint pain, nausea
Monoclonal antibody therapy for RCC

- Vascular Endothelial Growth Factor (VEGF) is an important growth factor in RCC
  - important in renal tumors associated with VHL disease

- VEGF can be directly targeted by monoclonal antibody therapy (bevacizumab)
  - Also targeted by new small molecule inhibitors (currently the treatment of choice for many patients due to improved tolerability)
Follow up on our patient

- Diagnosed with Stage IV papillary RCC with intra-bronchial metastases

- Poor prognosis, limited response to current therapies

- Entered into a clinical trial investigating a novel small molecule inhibitor
Conclusion

• Incidental renal cysts are a common finding

• Renal cysts are classified radiographically using the Bosniak system to separate benign findings from probable malignancies

• MRI can play an important role in correctly diagnosing cysts with indeterminate features on CT

• RCC is the most common tumor of the kidney, and, in early stage disease (stage I and II), can be treated by surgery alone

• Advanced RCC has a poor prognosis, and is managed using immune therapy or using targeted molecular therapy
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References

References