Kidney FNA – Pitfalls and Clues

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Objectives

• Kidney FNA – how good are we?
• Why it is challenging in the real life and why we don’t do more FNAs?
• How to approach kidney FNA?
• How far can we go?
• How far do we have to go in real life and why?

Kidney FNA – how good are we?

• Malignant vs. benign  73% - 94%
• Subclassification of RCC by morphology  74% - 90%
• IHC, cores  99%

• Exception – Oncocytic lesions

Loyola ~ 90.3% concordance between FNA (morphology only) and final histo dx
Loyola experience

- 2001 – 2016 – 195 kidney FNAs
- 2001 – 2016 – 1751 nephrectomies (total, simple and partial)
- Ratio of FNAs to nephrectomies – 11%

Why it is challenging in the real life and why we don’t do more kidney FNAs?

Radiographically

- Solid renal mass and known extrarenal primary malignancy
- Unresectable solid renal mass
- Solid renal mass and significant comorbidities
- Renal mass presumed secondary to infection

Loyola experience – 2001 - 2016

Total Number of Kidney FNAs - 195

- Benign 67
  - Negative 18
  - Cyst 35
  - AML 3
  - Infectious* 11
- Atypical 17
  - Oncocytic neoplasm ** 9
  - Not specified 8
- Malignant 80
  - RCC, Clear 18
  - RCC, Papillary 11
  - Not classified 27
  - Mets 5
  - Others *** 28

* Lymphoma, Granulomas, EMP, XGP
** Lymphoma, Sarcoma, PDCa, Urothelial ca, Wilms tumor, Mucinous tubular and spindle cell RCC
How to approach kidney FNA

CT US EUS

?Core Biopsy

Preserving medium

Diff-Quik

Papanicolaou

Cell-block

Cytospin or liquid based preparation

Cytogenetics, flow, cultures

Are we in the lesion?

• Normal kidney tissue – pitfall #1!

Glomeruli

• Cellular globular structures
• Spindled and round cells
• Prominent capillary loops
• DDx: Papillary RCC
Papillary RCC vs. Glomeruli

Glomerulus vs. AML

Proximal Tubules
- Granular cytoplasm with granules spilling
- Not well-differentiated cell borders
- Ddx. Oncocytic neoplasms (oncocytoma, chromophobe RCC)
**Distal Tubules**

- Clear-granular cytoplasm
- Small cell
- Well-defined cell borders

**Proximal tubules vs. RCC, clear cell type**

**RCC, clear cell type - Clues**

- Capillaries
- Low N/C, indistinct, "wispy" cell borders
- Magenta basement membrane-like material
Distal tubules vs. RCC chromophobe type

Distal tubules vs. papillary RCC

A 64 year old man, with a large, partially cystic right kidney mass, CT-guided FNA

Clinical impression: RCC vs. abscess

FNA Dx: cavitated RCC with necrotic center
Nephrectomy - Xanthogranulomatous pyelonephritis

<table>
<thead>
<tr>
<th></th>
<th>XGP</th>
<th>RCC</th>
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<tbody>
<tr>
<td>Lysosomes</td>
<td></td>
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</table>

| CD 10    | Positive | Positive |
| CD 68    | Positive | Negative |

CD 10 – RCC vs. XGP

<table>
<thead>
<tr>
<th></th>
<th>RCC</th>
<th>XGP</th>
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<tbody>
<tr>
<td>Is lesion neoplastic or inflammatory of...</td>
<td></td>
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<tr>
<td>Extramedullary hematopoiesis</td>
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Benign vs. Malignant

- Benign Neoplasms
  - Angiomyolipoma
  - Metanephric adenoma
  - Oncocytoma (oncocytic neoplasm)

Angiomyolipoma (AML)

- Rare in real life (3/195 FNAs).
- Classic three components:
  - spindle cell, epithelioid cells, adipocytic cells
  - and thick walled blood vessels

AML – Pitfalls and Clues

- Clinical
  - Young, middle-aged women
  - Incidental finding
- Radiographic
  - Fat – diagnostic
  - “Low-fat” or “fat-free”
  - FNA
- IHC (for any spindle cell proliferation)
  - HMB-45
  - MART1 (Melan A)
AML – Pitfalls and clues

Cystic Lesions

- Cysts (2001 – 2016)
  - 39 out of all 195 FNAs (20%)
  - 35 out of 68 benign FNAs (51%)
  - Size range: 1cm – 19.2cm; Mean: 5.3cm
- 19/39 (5%) surg F/U
  - 6/19 (33%) – 3 CCaC, 1 PapRCC, 1 Hybrid RCC and 1 Oncocytoma
  - 13/19 (69%) - Benign
- Common (~50% of >50 year old)
- <5% malignant (Clear cell, Papillary)

Cystic Lesions – Pitfalls and Clues
Oncocytic (eosinophilic) neoplasms

- Cells with pink/eosinophilic neoplasm
  - Oncocytoma
  - Hybrid oncocytic/chromophobe tumors (HOCTs)
  - Chromophobe RCC (eosinophilic variant)
  - Clear cell RCC with predominantly eosinophilic neoplasm

- And many others: follicular thyroid-like RCC, hereditary leiomyomatosis–associated RCC, acquired cystic disease–associated RCC, rhabdoid RCC, microphthalmia transcription factor translocation RCC, epithelioid angiomylipoma, and unclassified RCC.

Oncocytic neoplasms - Oncocytoma

- Cellular
- Cohesive fragments and single cells
- Abundant, granular cytoplasm
- Cell block, Core biopsy – Circumscribed cell nests

Oncocytic neoplasms – Chromophobe RCC

- Koilocytoid cells
  - Large, polygonal
  - Well-defined borders
  - Basoceleation, halo (CB)
  - Resinoid nuclei
  - Nuclear size variation
Oncocytic neoplasms – Pitfall - Hepatocytes

Oncocytic neoplasms

Chromophobe RCC
Oncocytoma
Chromophobe RCC
Clear cell RCC
Clear cell RCC
Chromophobe RCC

Oncocytic neoplasms – Diagnostic Conundrum - Management

• Oncocytoma → HOCT → Chromophobe RCC → Clear cell RCC
• Active surveillance → Enucleation → Partial nephrectomy → Thermal ablation → Nephrectomy

"It is controversial whether a definitive diagnosis of oncocytoma can be rendered on needle biopsy. Although some experts make a definitive diagnosis on biopsy, for needle core biopsy specimens that have morphologic and immunophenotypic findings of oncocytoma, we interpret them as oncocytoic renal cell neoplasm. We add the following comment: “If this biopsy is representative of the entire lesion, it would be consistent with an oncocytoma. However, renal cell carcinoma (RCC) and hybrid tumor may uncommonly show focal areas with oncocytic features.” Kurokawa ON, et al; Diagnostic Approach to Eosinophilic Neoplasms. Arch Pathol Lab Med. 2014; 138(11): 1530-1542."
Malignant Renal Neoplasms – 89 FNAs

How specific can we be? How specific do we need to be?

RCC, Clear cell type - Clues

• Cellular smears, bloody background
• Loose cell clusters with capillary network

RCC, Clear cell type - Clues

• Metachromatic basement membrane-like material
RCC, Clear cell type - Clues

- Abundant cytoplasm, pale, vacuolated, wispy
- Ill-defined cell borders

RCC, Clear cell type - Clues

- Nuclei centrally or eccentrically located
- Nucleoli vary in size from inconspicuous to large prominent
- Fuhrman grading possible

RCC, Papillary type - Clues

- Richly cellular aspirates
- Papillary structures
- Fibrovascular cores
RCC, Papillary type - Clues

- Large cell balls, spherules
- Tubules
- Psammoma bodies

RCC, Papillary type - Clues

- Foamy histiocytes
- Hemosiderin pigmentation of the cytoplasm

RCC, Papillary type - Clues

Type 1
- Small to medium size cuboidal cells
- Uniform nuclei
- Grooves, intranuclear invaginations
RCC, Papillary type - Clues

Type 2
- Large cells
- Prominent nucleoli
- Granular or vacuolated cytoplasm

Case
- 82-year-old man with diabetes, and severe congestive heart failure presents with hematuria
- 6.0 X 6.1 X 5.3 cm right renal mass
- US-guided FNA

Dx. 7 Papillary RCC but, CK 7 negative

Papillary architecture and clear cells
**Xp11.2 Translocation Carcinoma**

- Several different translocations involving chr. Xp11.2 resulting in gene fusions involving the TFE3 gene
- TFE3, PAX8, CD10, RCC, AMACR, E-cadherin (+); CK, EMA, vimentin (+);
  Melanocytic markers + (in TFEB carcinomas - t(6,11))
- Children and young adults (in general)
- Present at advance stage, clinical course more aggressive in adults

**A few months ago...**

- A 55 year old man with history of Papillary RCC, T1
- ?Recurrent ca at the scar site
- FNA of left chest wall

**Wilms Tumor**

- 22 year old male
- Acute onset of abdominal/flank pain
- CT – 17 cm R renal mass with invasion to IVC
- Multiple pulmonary masses
- Kidney FNA
Mucinous Tubular and Spindle Cell Renal Carcinoma

- Rare, low-grade, >females
- Histologically packed tubules, separated by pale mucinous stroma, with spindle cell component
- FNA – cellular, looks like pleomorphic adenoma – biphase pattern of epithelial and spindle cells in the metachromatic matrix
- IHC – EMA, CK 7, AMACR - positive

Collecting Duct Carcinoma

- Rare 1%
- Arises in renal medulla (unlike RCC arises from proximal tubule CD Ca arises from collecting duct epithelium)
- Cytology: Cellular, papillary/tubular structures, cells – like breast Ca
- DDX: Papillary RCC, TCC, metastasis

<table>
<thead>
<tr>
<th>CD10</th>
<th>PRCC</th>
<th>CD117</th>
<th>CCA</th>
<th>CDC</th>
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<tr>
<td>85–100%</td>
<td>+ (100%)</td>
<td>+ (100%)</td>
<td>± (100%)</td>
<td>-</td>
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<tr>
<td>RCC Ma</td>
<td>10–40%</td>
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<td>-</td>
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<tr>
<td>VM</td>
<td>+</td>
<td>+</td>
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<td>EMA</td>
<td>+</td>
<td>+</td>
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<td>CK7</td>
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<td>+ (100%) (diffuse)</td>
<td>+ (100%) (invasive)</td>
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<td>CK20</td>
<td>+ (type 2)</td>
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<td>CD10</td>
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<td>± (100%)</td>
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<td>+</td>
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<tr>
<td>MUC1</td>
<td>± (type 1)</td>
<td>± (100%)</td>
<td>± (type 1)</td>
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<td>10% (invasive)</td>
<td>10% (invasive)</td>
<td>10% (invasive)</td>
<td>10% (invasive)</td>
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<tr>
<td>LMWCK</td>
<td>-</td>
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<tr>
<td>HMWCK</td>
<td>± (focal)</td>
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<td>E-cad</td>
<td>± (type 1)</td>
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FNA of renal mass – proper management

- 56 y/o female presents with a large, left renal mass and para-aortic LAD
- Thyroid diffusely enlarged with small, rubbery nodule in lateral left lobe
- Large, 4-5 cm, cystic palpable mass in left upper lobe – FNA (?metastatic RCC)

Cell block
- CD30
- CD3
- Pankeratin
- S-100
- RPMI for flow

Urologist informed about preliminary impression

- Please, please do not operate yet, schedule FNA of the kidney
A couple days later – kidney FNA, patient scheduled for nephrectomy, “urologist is thinking it is RCC”

After Flow Cytometry and numerous “brown stains”, final diagnosis: Diffuse Large B-cell Lymphoma, Activated B-cell like phenotype with high proliferation fraction

- A 22 year old African American female presents with complaints of abdominal pain and hematuria
- Her physical exam demonstrates generalized lymphadenopathy
- A fine needle aspirate is requested from the enlarged left supraclavicular lymph node

What to do next?
- More clinical history
- Imaging studies
- Lab results

More clinical history
- Patient was transferred to Loyola with a diagnosis of a large renal mass, per imaging at the outside hospital
- She had a history of multiple ED visits complaining of intermittent hematuria and abdominal pain for about couple of years
  - The urinalyses were suggestive of urinary tract infections for which she was managed appropriately
What tests to request?

- After review of the cytologic material and learning about renal mass, we requested urine for cytologic evaluation and questioned the clinicians about her sickle cell status. At our request, a hemoglobin electrophoresis was performed.
- Urine cytology was positive for malignancy and Hb electrophoresis indicated sickle cell trait.
- ↓ HEMOGLOBIN A 87.4
- ↑ HEMOGLOBIN S 10.7

Diagnosis???

RENAL MEDULLARY CARCINOMA (RMC)

- Rare (about 150 cases reported) malignancy arising from the calyceal epithelium or distal portion of the collecting duct epithelium – centrally located.
- First described in 1995 as a distinct entity by Davis et al as:
  - "...a rare tumor of the kidney that tended to occur in young black patients with sickle cell trait or disease and hemoglobin SC."
  - All of these patients (n = 33) at diagnosis had tumor extension beyond the renal capsule and most had lymph node mets, with a mean survival of only 15 weeks after diagnosis.
- Referred to as the "seventh sickle cell nephropathy."
- 6 nephropathies seen in patients with sickle cell disease described by Berman in 1974: hematuria, papillary necrosis, nephritic syndrome, renal infarction, inability to concentrate urine, and pyelonephritis

Loosely cohesive groups of cells with cytoplasmic vacuoles that often indent the nuclei
Obviously malignant
Inflammatory cells, mostly neutrophils

Irregular nuclear contours with coarse chromatin and prominent nucleoli
Drepanocytes (sickled red blood cells) may be present

19 years old male with h/o ASD s/p surgical repair at 9 months
Presented with severe abdominal pain
Admitted with cardiogenic shock
Paroxysmal atrial fibrillation
Acalculous cholecystitis (CT)
Thrombocytopenia
10cm exophytic right renal mass "unusual in appearance". "Surgical intervention is not indicated nor would it be safe at this point". Ddx: lymphoma, leukemia, EMH, plasma cell neoplasm, retroperitoneal sarcoma

The relationship between Rosai–Dorfman disease (especially extranodal Rosai–Dorfman disease) and IgG4-related fibroclerotic disease is currently controversial, some authors suggesting a relationship, while others refute it. The number and percentage of IgG4 staining cells seen in the current case fall short of the consensus criteria for IgG4-related disease, but are still increased.

Objectives

- Kidney FNA – how good are we?
- Why it is challenging in the real life and why we don’t do more FNAs?
- How to approach kidney FNA?
- How far can we go?
- How far do we have to go in real life and why?
- We are really good
- Most tumors have to be removed anyway, FNAs for only “unusual” masses
- Systematically
- Far, really far...
- To make sure that patient will get the most appropriate management

FNA Diagnosis: Rosai-Dorfman Disease

CB Diagnosis: Rosai-Dorfman Disease with sclerosis and plasma cell infiltration

About 20% of plasma cells are positive for IgG4.

S100 CD68 CD68

5/15/2018
And whatever you do, use.....

[Image of common sense]

And keep your....

[Image of cells]