Management of Kidney Cancer in Young Patients

Brian Shuch, MD
Assistant Professor of Urology and Radiology
Yale School of Medicine
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Organization

• Incidence of Early Onset RCC

• Diagnostic Tools

• Management Strategies

• Several Non-Hereditary Entities
Incidence of Early Onset RCC
Epidemiologic Assessment- Standardized Incidence Ratio (incidence/100k)

SEER US Distribution of Renal Cell Carcinoma
1990-2008

• Age 45 or less represents the bottom decile of renal cell carcinoma in the United States
• These outliers may represent the “Zebras”
• Special diagnostic and management considerations for this population

Management Strategies
Management Considerations: Role of Renal Biopsy

- Not used often in the general patient population, but increasing utilization
- Considered safe, low risk of complications, low risk of seeding
  - when used in conjunction with IHC and molecular diagnostics, can determine histology
- May influence treatment strategy in a young patient with a renal mass
  - absolutely with metastatic disease (choice of surgery vs upfront systemic therapy)
  - strongly consider in localized disease (consideration for LND and partial nephrectomy)
Management Considerations: Lymph Node Dissection

- Randomized trial showing limited benefit in cN0 patients
  - However, may be less relevant to young RCC patients (median age ~60 in both arms)
- Omitted by most urologists in the community (less so at academic centers)
- For young patients- many tumor types with lymph node propensity
- Understanding histology could influence operative approach including RPLND
- Uncertainty exists in optimal method of RPLND
Management Considerations: Partial Nephrectomy

• Risk of CKD may be increased after RN (vs. PN)
• Respective data w/ improvement in survival but influenced by selection bias
• EORTC Randomized trial shows no survival advantage of elective PN vs RN
  • Median age ~62 in both arms
• Risk of CKD may be a subtle, time-dependent variable
  -Benefit may take many years to manifest, perhaps most evident in young patients

SEER Analysis of 10-Year Cancer Specific and Overall Survival for RCC Patients with <4 cm tumors Age 20-44

Harm in Parenchymal Loss In Young Patients: Extrapolation from Kidney Donors

- Prior comparisons compare donors to general population (many high-risk individuals)

- NHANES III participants with no identified contraindication to donation and were matched 1:1 to 96,000 kidney donors

- Median Age of Donors 40.2

- Significantly higher risk of ESRD in donors

• 38 male with left renal mass, biopsy showing chromophobe RCC
• Open PN performed showing T2b renal tumor with negative margins
Diagnostic Tools
Diagnostic Tools: Cytogenetics from Biopsy

24 Male with concern for translocation tumor, biopsy path consistent with an “oncocytic neoplasm.” Karyotype made diagnosis preoperatively. Influenced choice of surgery.

38,X,-Y,-1,-2,-6,-10,add(12)(q24),-17,-21,-22
Diagnostic Tools: FISH Testing for Translocations

ESW Break Apart FISH Probes at (22q12)
Diagnostic Testing: RT-PCR Based Testing for Translocations

a. EWS/FLI1, type 1
100 bp amplicon

b. SYT/SSX 1 or 2
77 bp amplicon

c. PAX3/FOXO1A
171 bp amplicon

Several Non-Hereditary Entities
29 year old African American male with right flank pain and hematuria

Renal/liver biopsy performed, demonstrating high grade lesion suspicious for Medullary vs collecting duct. No history of Sickle Trait
Diagnostic Testing: Hb HPLC and Electrophoresis

Many patients with sickle trait may not know about this diagnosis. HPLC and Hb electrophoresis necessary to determine distinct Genotype.
Medullary Renal Cell Carcinoma

- Median age ~21 years old
- African Americans (generally with sickle trait)
- Median size of ~6 cm
- >80% present with Nodal or Metastatic disease
- Histology: poorly differentiated cells that can have a cystic morphology. Neutrophil infiltrates common.
- Management:
  - Rare M0 case → surgery
  - M1- upfront chemo +/- surgery
- Several cytotoxic chemo regimens have been described (use of MVAC common)

22 year old with right flank pain

Large heterogenous perinephric collection, hemorrhage/enhancing elements
18 year old with left flank pain

Large heterogenous perinephric collection, hemorrhage/enhancing elements
Ewing’s Sarcoma/Primitive Neuroectodermal Tumor (PNET) of Kidney

- Median age ~25 years old
- Median size of ~12 cm, ~35% present with mets
- 90% with translocation- t(11;22), EWS-FLI-1
- Histology
  - Small, primitive round/ovoid/blue cells
  - minimal cytoplasm
- Management:
  - M0- surgery + adjuvant
  - M1- upfront chemo +/- surgery
- Multiple cytotoxic chemo regimens

“Homer–Wright rosettes”
http://www.webpathology.com

18 year old with left flank pain.

12 cm cystic solid renal mass.

Biopsy showed suspicion for clear cell tumor with papillary features.
TFE3/TFEB Renal Tumors

• Translocation RCC is the most common type of RCC in children (~30%)
• May account for up to 15% of tumors in patients 45 or less
• Median age 12-24 (depending on translocation)
• Median size of ~7 cm, ~30-70% with nodal involvement
• Female > Male
• Histology
  - Various histologic patterns and often misdiagnosed
  - Nested pattern with large clear/eosinophilic cells with voluminous cytoplasm
TFE3/TFEB Renal Tumors

- Multiple translocations have been described
- TFEB tumors rare (~30 cases in literature)
- Good prognosis even with node involvement (after resected)
- Management:
  - N0/1 M0 - Surgery and RPLND
  - M1 - +/- Surgery and systemic therapy
- Early experience with targeted agents poor

<table>
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<th>Translocation</th>
<th>Gene Fusion</th>
<th>Chromosomal Rearrangement</th>
<th>Recurrent in Other Tumor Types</th>
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<td>PRCC-TFE3</td>
<td>t(X;1)(p11.2;q21)</td>
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<td>ASPL-TFE3</td>
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<td>TFEB</td>
<td>Alpha-TFEB</td>
<td>t(6;11)(p21.1;q13)</td>
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Multiple Other Renal Entities in Young Adults

- Mixed Epithelial Stromal Tumors (MEST) - Females > Males
- Metanephric Tumors (Adenomas most common) - Females > Males
- Nephroblastic Tumors
  - Adult onset Wilms tumor (2-3% of Wilms Cases)
- Mesenchymal Tumors
  - Many rare and aggressive malignancies
  - Renal Leiomyoma occurs in woman in 30’s-40’s and arises from capsule
- Juxtaglomerular tumor - presents in 2nd and 3rd decade of life.
Conclusions

• Early onset kidney cancer is rare, but when faced with it, consider “zebras”
• Besides hereditary RCC syndromes, consider somatic and translocation alterations
• Molecular diagnostic testing (PCR, FISH, Karyotype) essential to make diagnosis
• Unique entities in this population
• Management strategies may slightly differ than general RCC population
Questions?

Brian.shuch@yale.edu