Disclosure of Relevant Financial Relationships

USCAP requires that all faculty in a position to influence or control the content of CME disclose any relevant financial relationship WITH COMMERCIAL INTERESTS which they or their spouse/partner have, or have had, within the past 12 months, which relates to the content of this educational activity and creates a conflict of interest.

Dr. Maria M. Picken declares she has no conflict(s) of interest to disclose.

Case history:

27 yo, air conditioning technician
1 day intermittent painless gross hematuria
PMH: herniated disk (L-S spine) with radiculopathy
SH: current smoker, 6 pack/yr, occasional EtOH, single, no children
Family History: (+) genitourinary malignancies

PE: BMI 23, BP 120/86
No meds, no drugs
Labs: Hgb 14.6, Plt 234, cr 1.2

Axial contrast enhanced CT: centrally located lobulated mass invading the renal vein and extending into the lumen of the inferior vena cava (IVC)

Axial contrast enhanced MR image: a lobulated hypo-enhancing mass occupying the majority of the IVC lumen at the level of the renal vein ostia

Oblique sagittal contrast enhanced MR image: a lobulated hypo-enhancing mass occupying the majority of the IVC lumen at the level of the renal vein ostia

Axial contrast enhanced MR image at approximately the tumor level: a lobulated hypo-enhancing mass in the renal hilum, with a lobulated filling defect in the lumen of the IVC, representing tumor extension

CT angiography chest: no obvious PE. Bone scan (-)
Right radical nephrectomy, partial adrenalectomy, inferior vena cava tumor thrombectomy (infra-hepatic), extended retroperitoneal lymphadenectomy, flexible cystoscopy - bulbar urethral stricture (not clinically significant), otherwise normal bladder. All gross disease resected
Category of renal tumors | Cystic - biphasic
--- | ---
Renal cell tumors | RCCc with smooth muscle stroma
metanephric | Metanephric adenofibroma
nephroblastic | Cystic partially differentiated nephroblastoma
Mesenchymal tumors | MEST
AMLEC
SMART
Primary renal synovial sarcoma
Congenital mesoblastic nephroma

Category of renal tumors | Cystic - biphasic
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Primary renal synovial sarcoma
Congenital mesoblastic nephroma
**[158] Low-grade spindle cell proliferation in clear cell renal cell carcinoma is unlikely an initial step in sarcomatoid differentiation**

Srinivasan, Tani; Huang, Yi; Men-de la Cruz, Rana; Kamel, Sharad; Palanisamy, Henry; Huiying; Ong, K. Henry; Palanisamy, Ozlem; Grossmann, Petr; Povovarcikova, Michal; Ondrej; Iowa, Henry; Hungary; Mexico City, Mexico; Ankara, Turkey; Beijing, China; Prague, Czech Republic; Zagreb, Croatia

**Background**: Low-grade spindle cell proliferation (LSCP) within clear cell renal cell carcinoma (CRCC) is usually considered as a sarcomatoid differentiation. Common (50-70%) in CRCC, it is an ominous phenomenon which can pose diagnostic challenges. The aim of this study was to describe morphologic, immunohistochemical and molecular characteristics of CRCC with LSCP.

**Design**: Using the Hematoxylin and Eosin-stained sections from 6800 CRCCs, we identified 10 cases of typical (50%) and focal (50%) LSCP. We performed EMA, CD99 and CD10 immunostaining and FISH analysis.

**Results**: All cases of typical LSCP showed a focal distribution and were composed of cells with round to oval nuclei, eosinophilic cytoplasm, prominent nucleoli, and bland cytoplasmic and nuclear ultrastructure.

**Conclusions**: Focal LSCP is a rare, low-grade spindle cell proliferation within CRCCs and likely represents a minor genetic and cytopathic entity.

**Category**: Genitourinary Pathology (including Renal tumors)

**Session**: Proffered Papers - SECTION A, Monday Afternoon

**Date/Time**: Monday, March 6, 2017 - 2:00 pm Room: CC SB 3&4 C

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**[81] Monosomy 8 as a surrogate for TCEB1 mutation in renal tumors with prominent stroma**

Earl R Williamson, Nathaomi Palanisamy, Henry Ford Health System, Detroit, MI

**Background**: Recent evidence suggests that many, or perhaps all, TCEB1 mutant renal cell carcinomas (RCCs) also exhibit monosomy 8. The objective of our study was to use monosomy 8 as a surrogate for TCEB1 mutation in renal cell tumors with unusual features emphasizing those with prominent stroma, using bacterial artificial chromosome (BAC) probes against the TCEB1 locus.

**Design**: We studied a cohort of renal cell tumors with unusual features, emphasizing those with prominent stroma, using bacterial artificial chromosome (BAC) probes against the TCEB1 locus (47). The cohort included 7 RCCs with prominent fibrous bands or increased CK7 positivity, and 7 tumors with borderline but imperfect features of clear cell papillary RCC.

**Results**: Of the entire cohort (n=14), only a single tumor with borderline but imperfect features of clear cell papillary RCC (including positive EMA staining and incomplete positivity for CK7) was found to have monosomy 8 by FISH. The remainder (n=12) demonstrated two signal pairs per nucleus.

**Conclusions**: Monosomy 8 as a surrogate for TCEB1 mutation in renal cell tumors with prominent stroma may represent two distinct entities.

**Category**: Genitourinary Pathology (including Renal tumors)

**Session**: Proffered Papers - SECTION A, Monday Afternoon

**Date/Time**: Monday, March 6, 2017 - 2:00 pm Room: CC SB 3&4 C

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**Categories of renal tumors**

<table>
<thead>
<tr>
<th>Category of renal tumors</th>
<th>Cystic - biphasic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal cell tumors</td>
<td>RCC with smooth muscle stroma</td>
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<tr>
<td></td>
<td>RAT: renal angiomyoanatomatous tumor</td>
</tr>
<tr>
<td>Metanephric nephroblastic</td>
<td>Cystic partially differentiated nephroblastoma</td>
</tr>
<tr>
<td>Mesenchymal tumors</td>
<td>MEST</td>
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<tr>
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<td>AMLEC</td>
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<tr>
<td></td>
<td>SMART</td>
</tr>
<tr>
<td>Primary renal synovial sarcoma</td>
<td>Congenital mesoblastic nephroma</td>
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</tbody>
</table>

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**Proffered Papers - SECTION A, Monday Afternoon**

**Date/Time**: Monday, March 6, 2017 - 2:00 pm Room: CC SB 3&4 C
This tumor

SMA (+), desmin (+), CD34 (+)

This tumor

SMA (+), desmin (+), CD34 (+)

Category of renal tumors | Cystic - biphasic
--- | ---
Renal cell tumors | RCC with smooth muscle stroma
metanephric | Metanephric adenofibroma
nephroblastic | Cystic partially differentiated nephroblastoma

Mesenchymal tumors | Primary renal synovial sarcoma
| Congenital mesoblastic nephroma

CPDN - cystic partially differentiated nephroblastoma

RARE VARIATION OF NPHRBlastoma (Wilms tumor):
- cystic, ~ biphasic
- islands of nephroblastomatous tissue in the septae WT1 (+)
- stroma CD34 (+)
- Majority of patients are <2 years old
3 cases in adults: 26 and 45 yo

Courtesy Dr. GM Vujanic

Category of renal tumors

| Renal cell tumors | RCC with smooth muscle stroma
| Metanephric | Metanephric adenofibroma
| Renal angiomyo/adenomatous tumor
| Cystic partially differentiated nephroblastoma

Mesenchymal tumors

| MEST | mixed epithelial and stromal tumor
| AMLEC | angiomylipoma with epithelial cysts
| SMART | smooth muscle & adenoma-like renal tumor

Primary renal synovial sarcoma

Congenital mesoblastic nephroma

Courtesy Dr. E. Perlman
RENAL MASS WITH IVC

**MEST - mixed epithelial and stromal tumor**

- rare, distinctive, adult, biphasic

1998 - Michal & Syrucek
2004 - WHO classification of renal tumors
2015 - WHO: “mixed epithelial and stromal tumor family”
- spectrum, predominantly cystic (adult cystic nephroma, CN) to variably solid (MEST)
- biphasic, epithelial & stromal components with epitheloid stroma, glands, and cysts
- adult CN & MEST:
  - overlapping morphology
  - very similar expression profiles, distinct from other renal tumors

Lesions similar to MEST in other organs:
pancreas, liver, stomach, duodenum, middle ear, seminal vesicles

**2016 WHO congenital mesoblastic nephroma (CMN)**

“mesenchymal tumors occurring mainly in children”

**“adult mesoblastic nephroma”**

exclusively infantile/congenital tumor.
Cellular CMN v infantile Nephroma
(t12;15)(p13;q25) — fusion of the ETV6 and NTRK3 genes, not detected in MEST

**pediatric cystic nephroma (PCN)**

“mesenchymal & cystic tumors occurring mainly in children”
multilocular, exclusively cystic, very young children,
DCCRT mutations in PCN, not detected in MEST/adult CN, not related to WT (Wilms tumor)

**MEST - microscopic**

- biphasic
- stroma: fibrous-appearing, leiomyoma-like,
  - ovarian-like, in variable proportions
- corpora albicantia-like females only?
- epithelium: monolayer, simple
- hobnail to cuboidal to flattened
- rare other, mucinous

<table>
<thead>
<tr>
<th>Component</th>
<th>MEST</th>
<th>Other Tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>stroma</td>
<td>SMA (+), desmin (+)</td>
<td>CD10 (+), ovarian-like</td>
</tr>
<tr>
<td>epithelium</td>
<td>Cytokeratins (+), CK7/distal nephron (+)</td>
<td>Cytokeratins (+), CD10/distal nephron (+)</td>
</tr>
</tbody>
</table>

**MEST - IHC**

- Cytokeratins (+), CD10/distal nephron (+)
- SMA (+), desmin (+)
- ER/PR (+)

**MEST - gross:**
- renal pelvis, most typical
- cystic with stromal nodules grossly apparent
- well-circumscribed, 2 - 24 cm
- no gross invasion of adjacent tissue
- variable proportion of solid and cystic components
- rare predominantly-solid MEST

**Renal epithelial stromal tumor**

Adult CN & MEST:
- overlapping morphology
- very similar expression profiles, distinct from other renal tumors

Lesions similar to MEST in other organs:
pancreas, liver, stomach, duodenum, middle ear, seminal vesicles

**MEST FAMILY - IHC**

- Cytokeratins (+), CD10/distal nephron (+)
- SMA (+), desmin (+)
- ER/PR (+)

(RENAL MASS WITH IVC)
RENAL MASS WITH IVC

<table>
<thead>
<tr>
<th>Clinical Feature</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
</tr>
<tr>
<td>Age</td>
<td>26 yo</td>
</tr>
<tr>
<td>Hormonal exposure</td>
<td>history of long term estrogen/hormonal treatment</td>
</tr>
<tr>
<td>Dietary exposure</td>
<td>meat of animals on hormones</td>
</tr>
</tbody>
</table>

Cystic RCC, other cystic tumors: differential diagnosis
- cystic RCC, other cystic tumors

Painless hematuria: presentation
- incidental, hematuria, abdominal pain

Involvement of the IVC, concerns for malignancy?
- most MEST = benign
- rare MEST with malignant transformation

Primary Renal Synovial Sarcoma

- very rare
- most = monophasic, v rare biphasic (epithelial differentiation)
- entrapment of native renal tubules, some cystically dilated
- aggressive tumor, similarities to malignant MEST with sarcomatous transformation of the stroma

IHC:
- (+) TLE1 (transducer-like enhancer split 1), vimentin, Bcl2, CD99
- (-) desmin, MSA and CD34
- Cytokeratins/EMA focally tumor cells (+), entrapped epithelium (+)
- most SS18-SSX2 gene fusion, not detected in MEST

Age: 13 to 78 years

Courtesy Dr. JM Hicks

Hemorrhagic and necrotic debris adjacent to the papillary mass
- milder atypia to frank dysplasia in more elaborate papillary proliferation

CD10

Primary Renal Synovial Sarcoma

Malignant MEST – sarcomatous stroma

Primary Renal Synovial Sarcoma

Malignant MEST with focal papillary RCC

IHC
- (+) TLE1 (transducer-like enhancer split 1), vimentin, Bcl2, CD99
- (-) desmin, MSA and CD34
- Cytokeratins/EMA focally tumor cells (+), entrapped epithelium (+)
- most SS18-SSX2 gene fusion, not detected in MEST

Age: 13 to 78 years

Surgical tumor

<table>
<thead>
<tr>
<th>Sex</th>
<th>Perimenopausal women</th>
<th>Rare male patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean age: 52 years</td>
<td>Exceptionally rare older children</td>
</tr>
<tr>
<td>Hormonal exposure</td>
<td>History of long term estrogen/hormonal treatment, including males prepubertal children (52 yo) sexual surge during puberty</td>
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<tr>
<td>Dietary exposure</td>
<td>Meat of animals on hormones</td>
<td>Environmental exposure to plastics</td>
</tr>
<tr>
<td>Cystic RCC, other cystic tumors</td>
<td>Differential diagnosis</td>
<td>Cystic RCC, other cystic tumors</td>
</tr>
</tbody>
</table>
RENAL MASS WITH IVC

Hemorrhagic and necrotic debris adjacent to the papillary mass; milder atypia to frank dysplasia in more elaborate papillary proliferation. CK7 (+); inset: PR (+)

SMART with focal papillary RCC

Tubulopapillary nodules/islands
Benign epithelium

CD34

Intravascular tumor - no features of malignancy: no epithelioid features in the smooth muscle stroma no necrosis no features of sarcoma
Hemorrhage, old & recent

This tumor

RCC

Smooth surface, no invasion into vascular wall
Irregular/rough surface, invasion into vascular wall

Diagnosis: benign mixed epithelial and stromal tumor of the kidney with extension into IVC

Follow-up: 2 years post surgery with no evidence of tumor
Angiomyolipoma
- renal vein involvement = growth pattern?
- fat pulmonary emboli rather than metastases
- nodal involvement = multifocal growth?

Intravenous leiomyomatosis - multiple worm-like plugs of tumor dislodging vascular spaces outside of leiomyoma, white and bulging cut surface

Intravenous leiomyomatosis: E. Olivia Rodriguez-Montalvo

Intravenous leiomyomatosis: multiple worm-like plugs of tumor dislodging vascular spaces outside of leiomyoma, white and bulging cut surface

Intravenous leiomyomatosis: E. Olivia Rodriguez-Montalvo

RENNAL MASS WITH IVC

RENAL MASS WITH IVC

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Angiomyolipoma

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Caution:
- MEST recurrence after incomplete excision
- peritoneal seeding with separate paracolic MEST
- inadequate tumor sampling (biopsy)

32 yo M with a complex cystic mass, treated with robotic decortication
recurrence 2 years later

38 yo C.F., flank pain, gross hematuria, urinary tract infections
PMH: HTN, polycystic ovarian syndrome on metformin
Nonsmoker, family history of GU diseases, hormonal therapy

CT abdomen: 9 cm cystic mass, cyst marsupialization via transperitoneal approach
Pathology: MEST 6 cm, focally (+) cauterized edge

3 years later CT scan:
11 cm right renal cystic lesion + multiple cystic lesions near the ascending colon, all MEST pathology

CONCLUSIONS
1. renal vein involvement not always malignant - careful gross & microscopic examination, follow-up warranted
2. caution in the management of MEST:
   • incomplete resection can lead to recurrence
   • rare cases of malignant transformation with a grim prognosis
3. caution with limited tumor sampling (core biopsy or cytology)

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Michael R. Pins, Advocate Lutheran General Hospital, Chicago
Gordan M. Vujanić, Cardiff University, UK

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