2017 Annual Meeting | September 14-17 | Deerhurst Skyline Resort | Huntsville, Ontario

# DIAGNOSTIC SLIDE SEMINAR: PART 1 RENAL TUMOUR BIOPSY CASES

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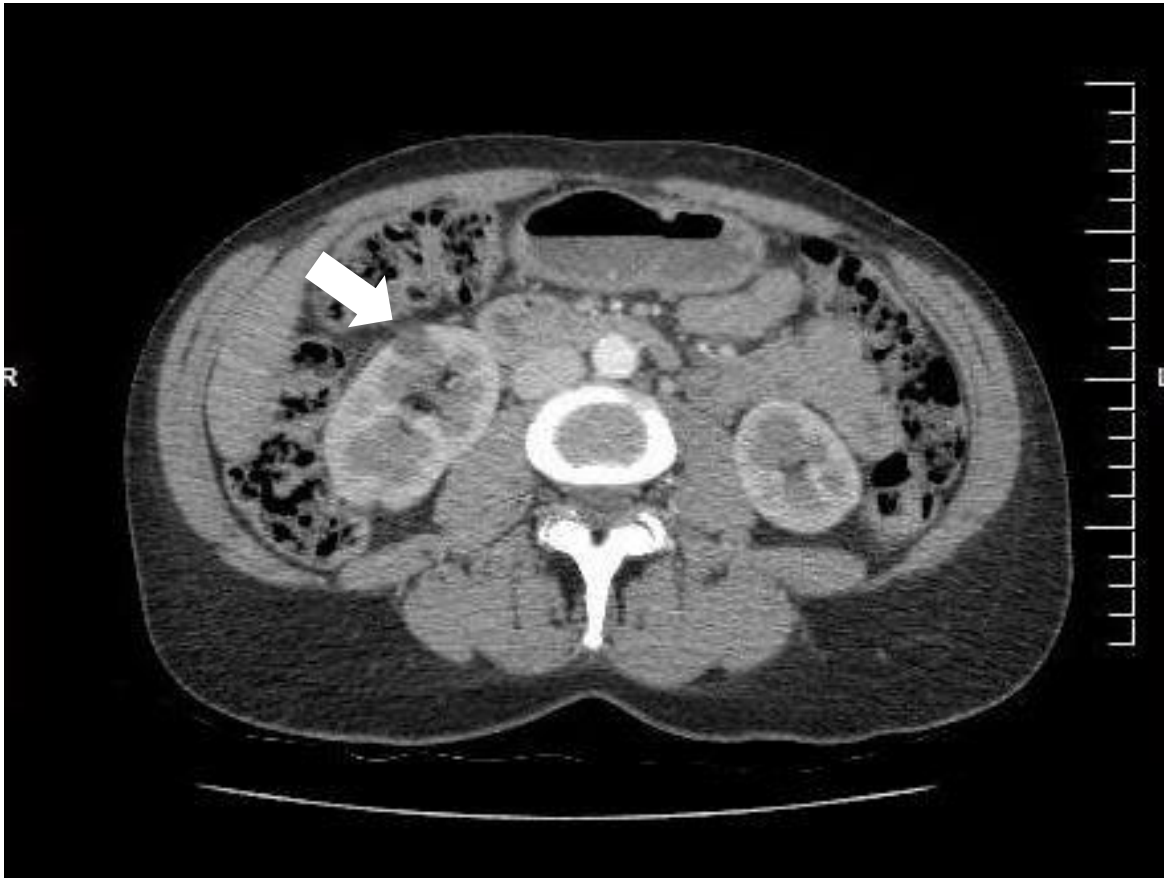
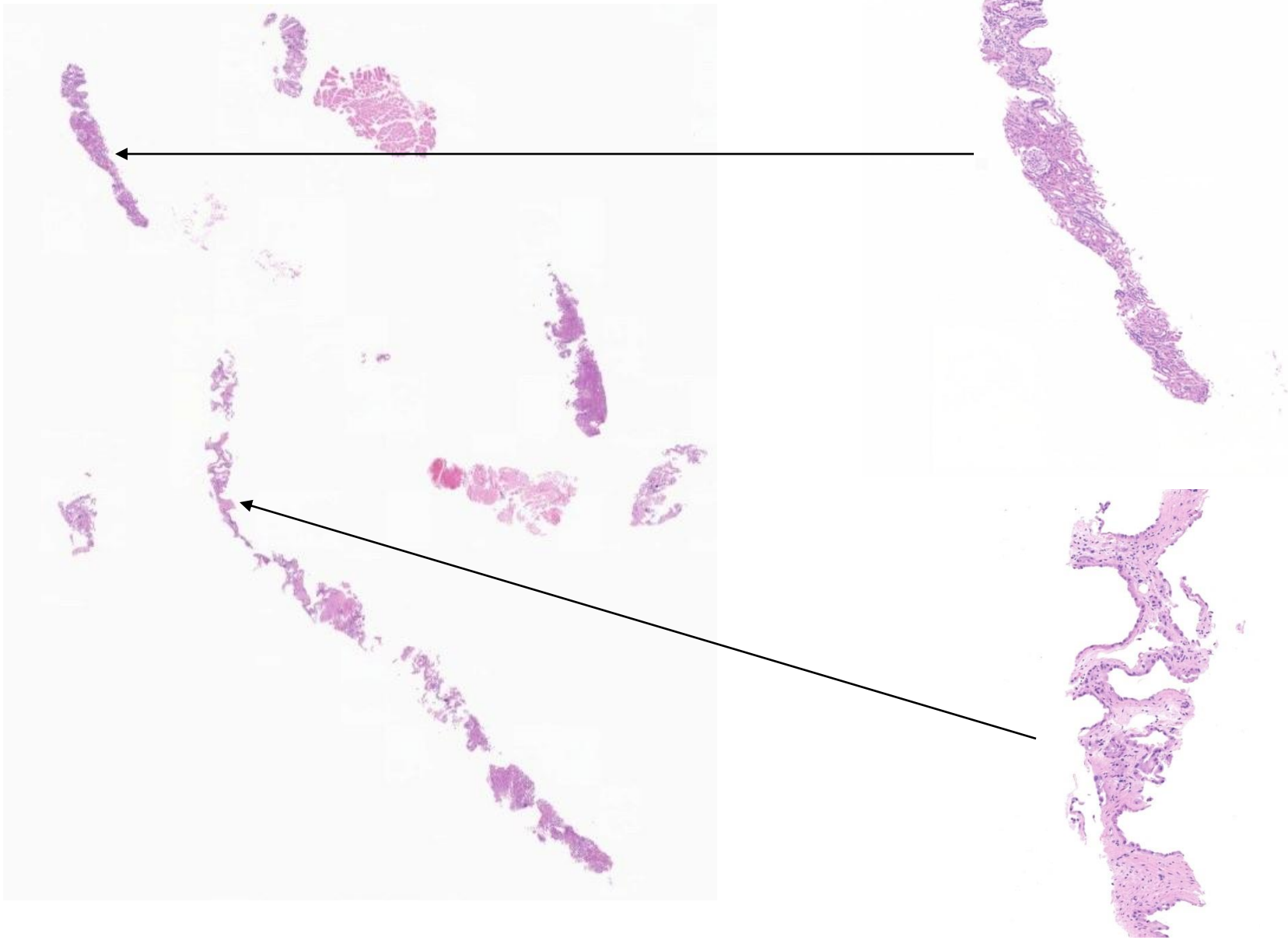
**Consultant in Genitourinary Pathology**
**University Health Network, Toronto, ON**

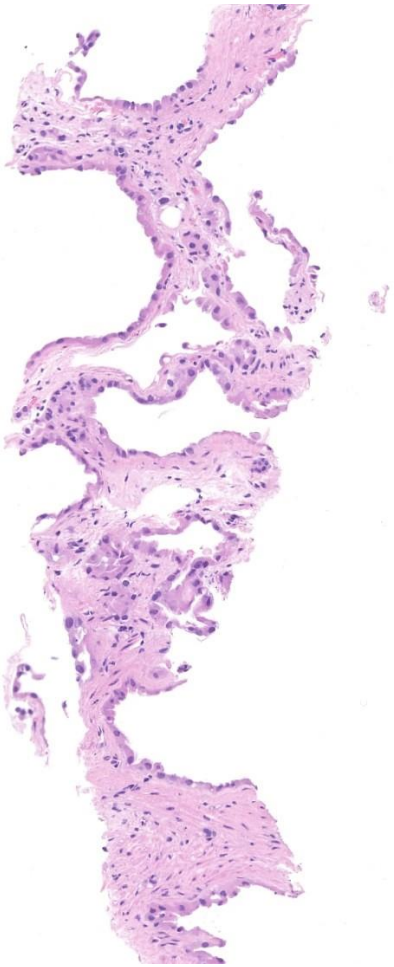
# Case 1

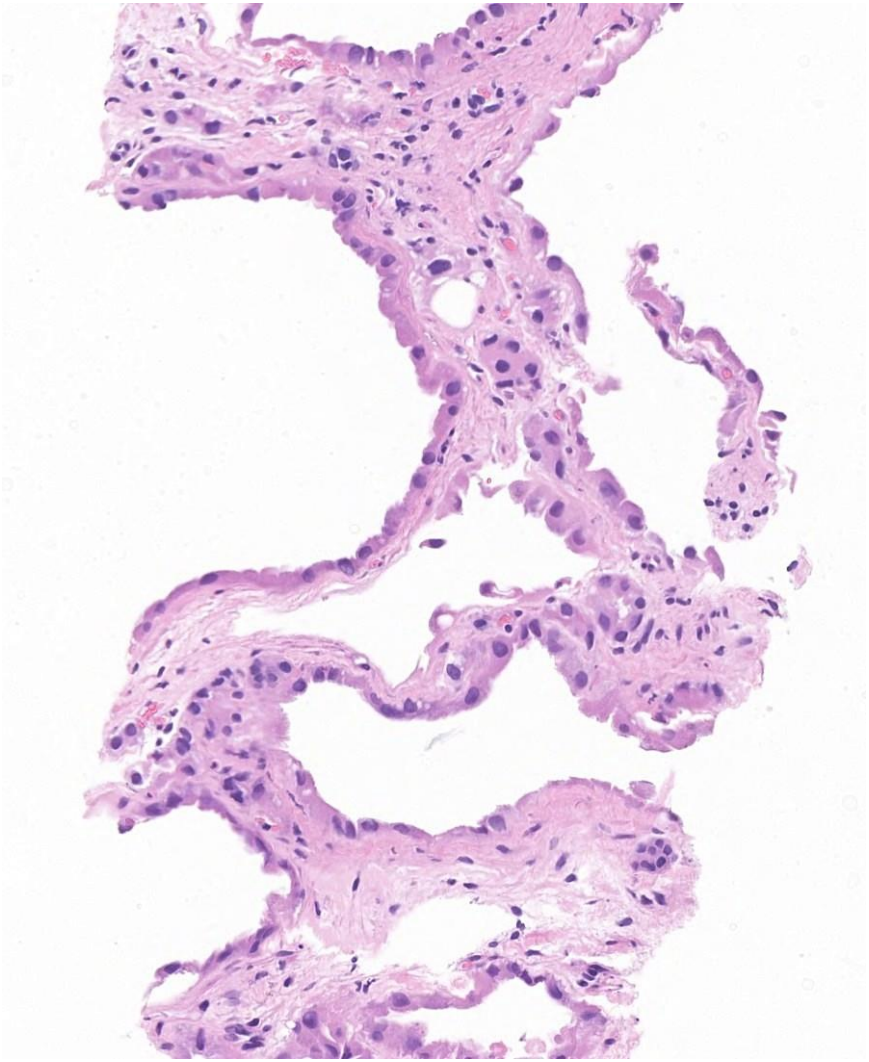
43 year-old female, incidentally found 1.5 cm right cystic renal mass

# CT Scan: Cystic Right Renal Mass



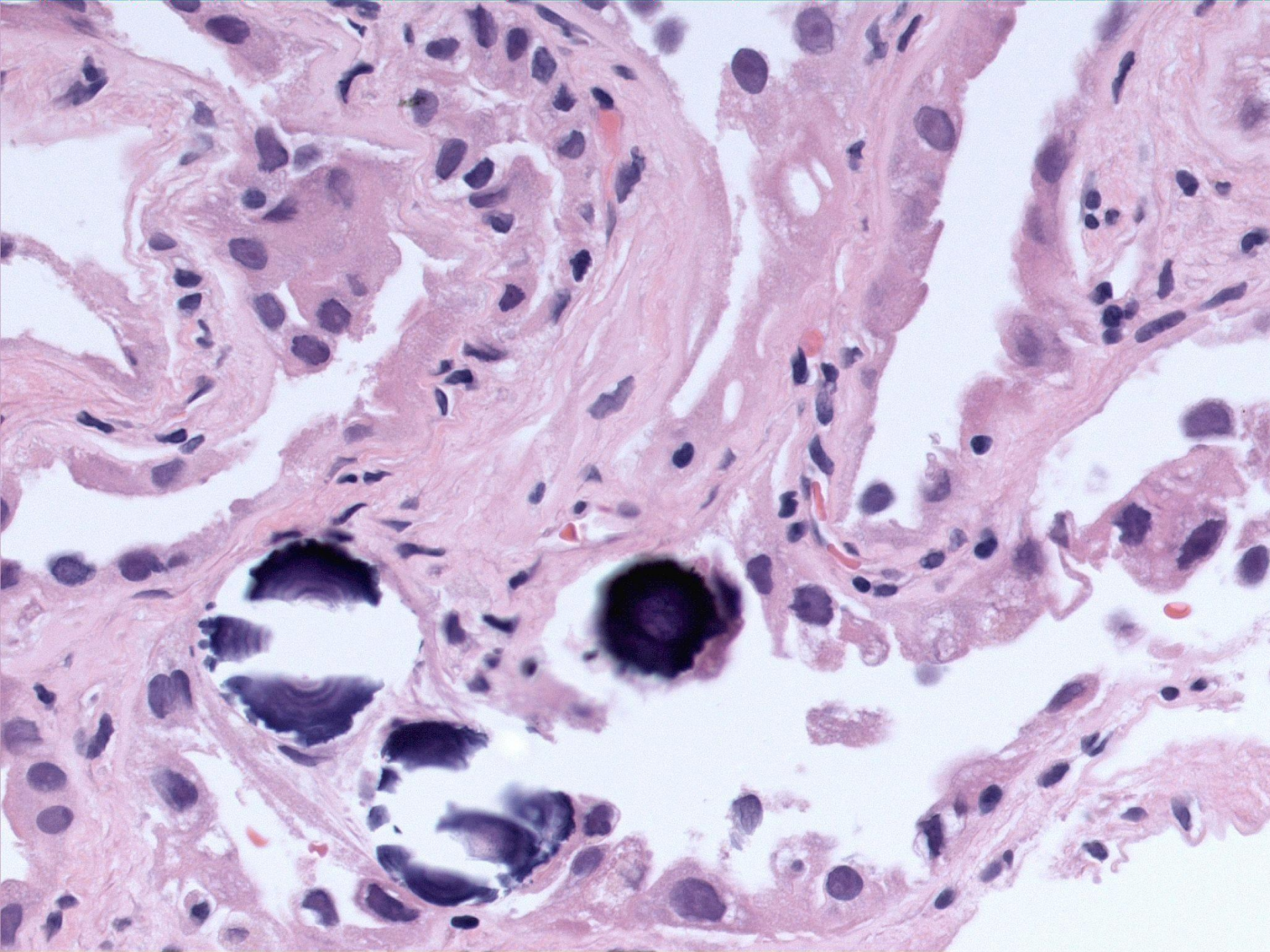






AMACR +’ve

CK 7 –’ve



# Histologic Differential

- Cystic nephroma
- MEST/REST
- Oncocytoma with cystic elements
- Tubulocystic carcinoma

## Diagnosis

Kidney: Right needle core biopsy:
- Cystic neoplasm with features suggestive of tubulocystic carcinoma. See comment.

**Comment**

The biopsy consists of fragmented cores of renal parenchyma, paucicellular fibrous stroma and a fragment of skeletal muscle. The background kidney is within normal limits. The fragments of fibrous stroma are consistent in appearance with a cystic lesion as per the supplied clinical history. The cystic spaces are lined by a single layer of plump cuboidal cells with slightly irregular nuclei and visible nucleoli, deeply eosinophilic cytoplasm and focal "hobnail" morphology. Psammomatous calcification is focally identified. No ovarian-type stroma is noted in the sampled tissue. No papillary structures or aggregates of clear cells are identified. Immunohistochemical staining shows the cuboidal lining cells to be positive for AMACR and negative for CK7.

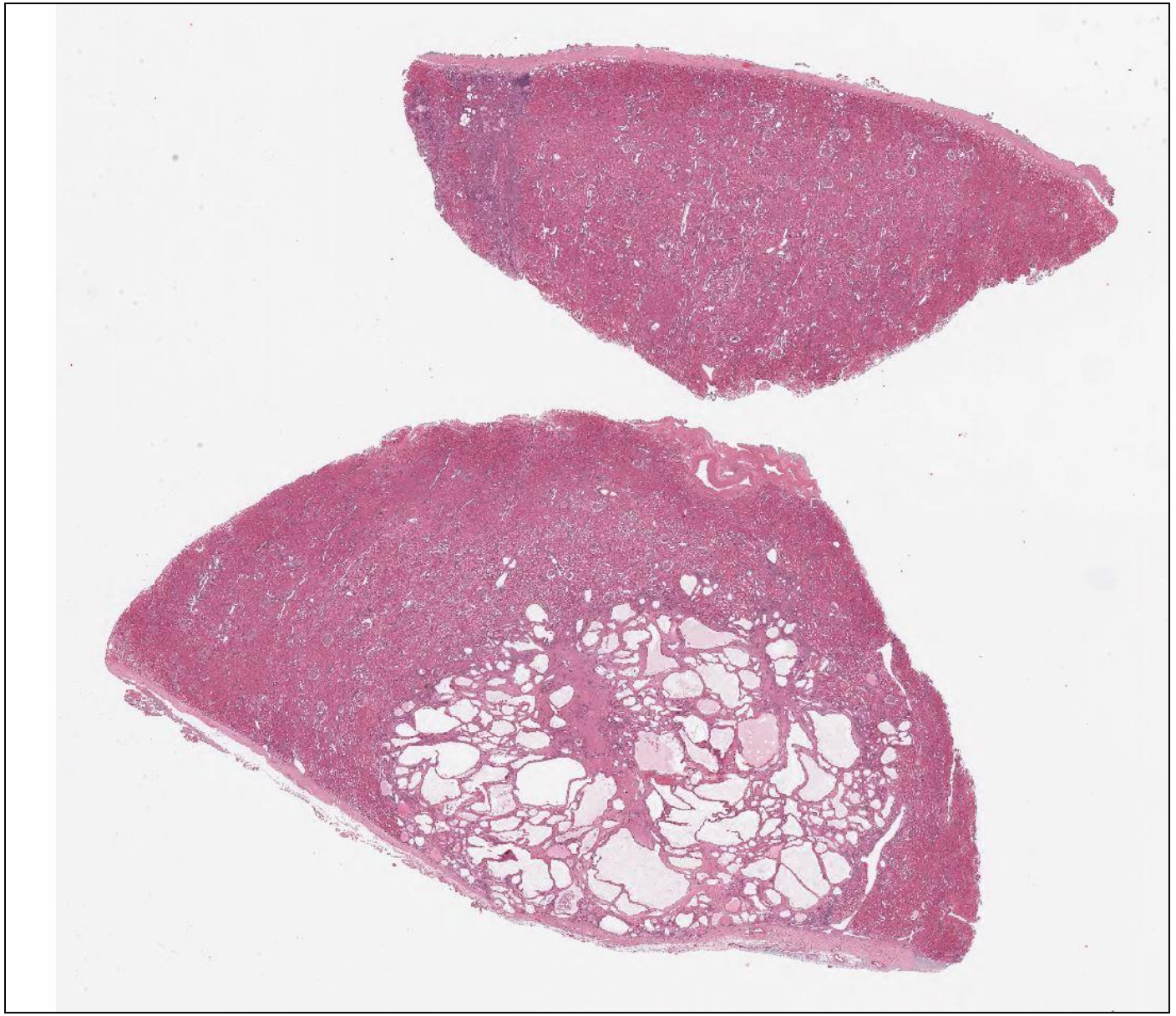
Taken together, the features are consistent with the biopsy having sampled a cystic neoplasm. The differential diagnosis lies between tubulocystic carcinoma, cystic nephroma, mixed epithelial stromal tumour (MEST) and papillary renal cell carcinoma. While the amount of lesional tissue that has been sampled is quite limited, the H&E morphology and immunohistochemical profile described above are in keeping with a diagnosis of tubulocystic carcinoma. It should be recognized that there are inherent limitations associated with biopsy findings in the setting of cystic lesions. As such, histologic examination of the completely excised lesion would be required to confirm the above interpretation.

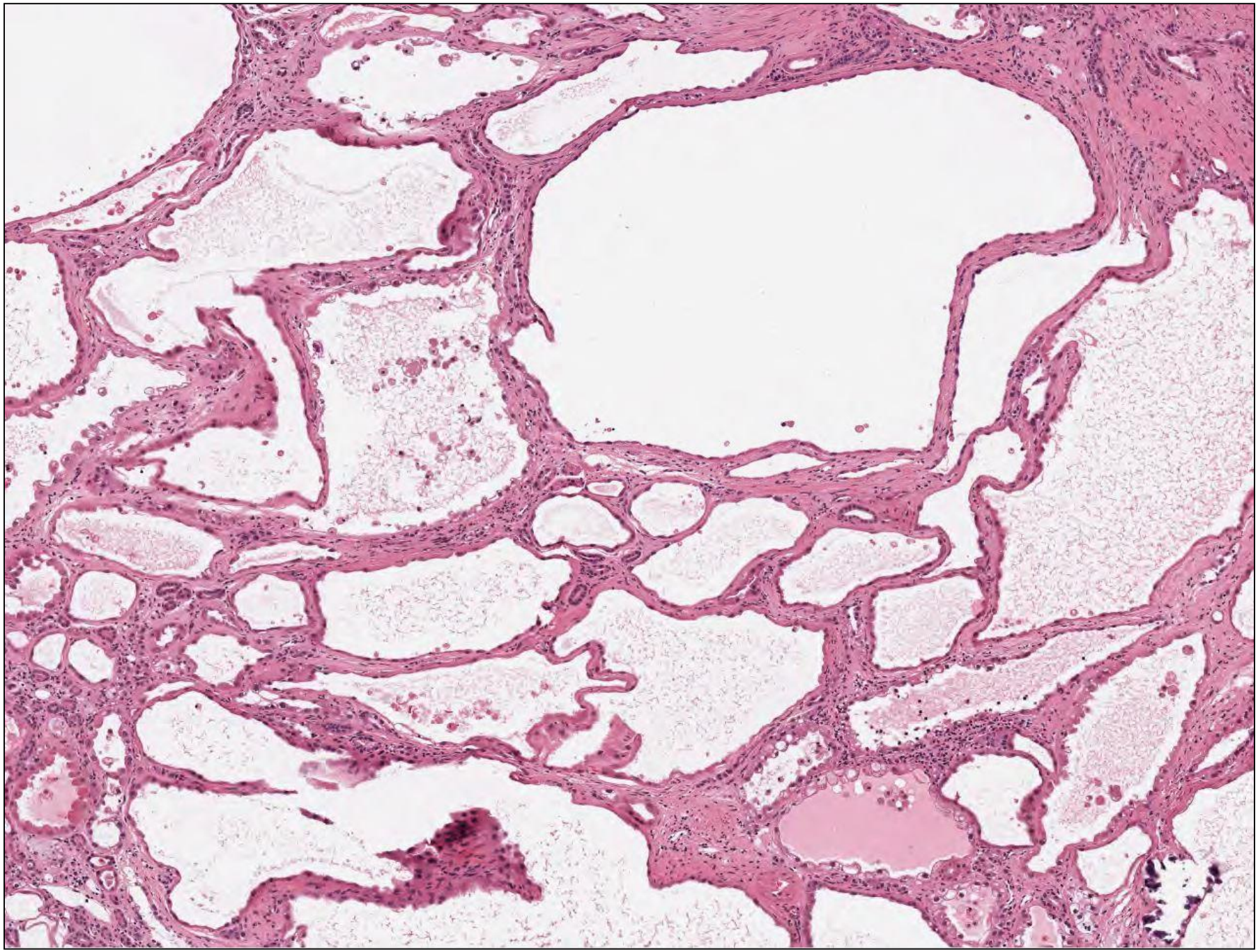
Tubulocystic carcinoma is regarded as low-grade malignant renal tumour. See the reference below for details on the clinicopathologic and molecular characteristics of this entity.

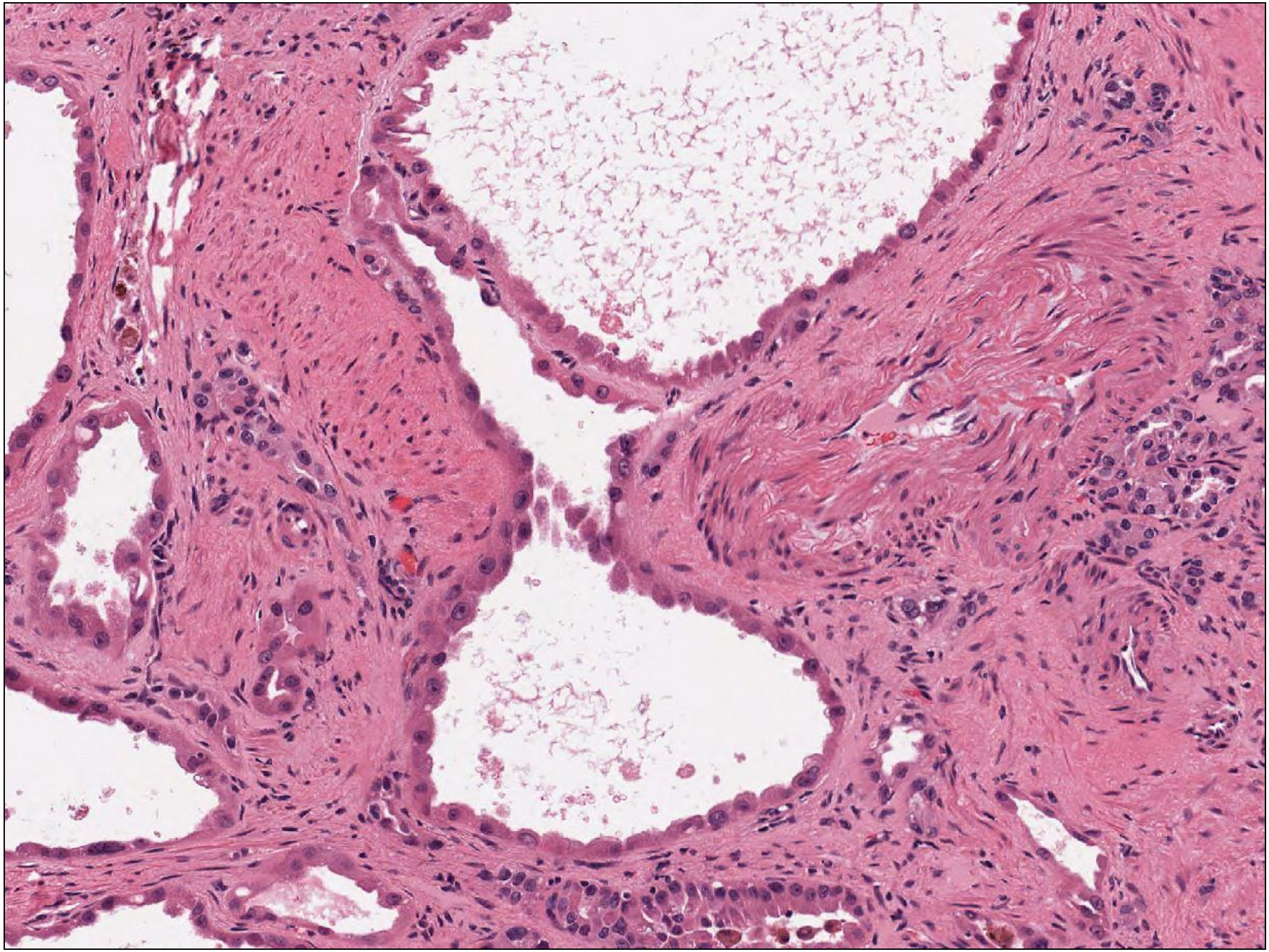
Reference:

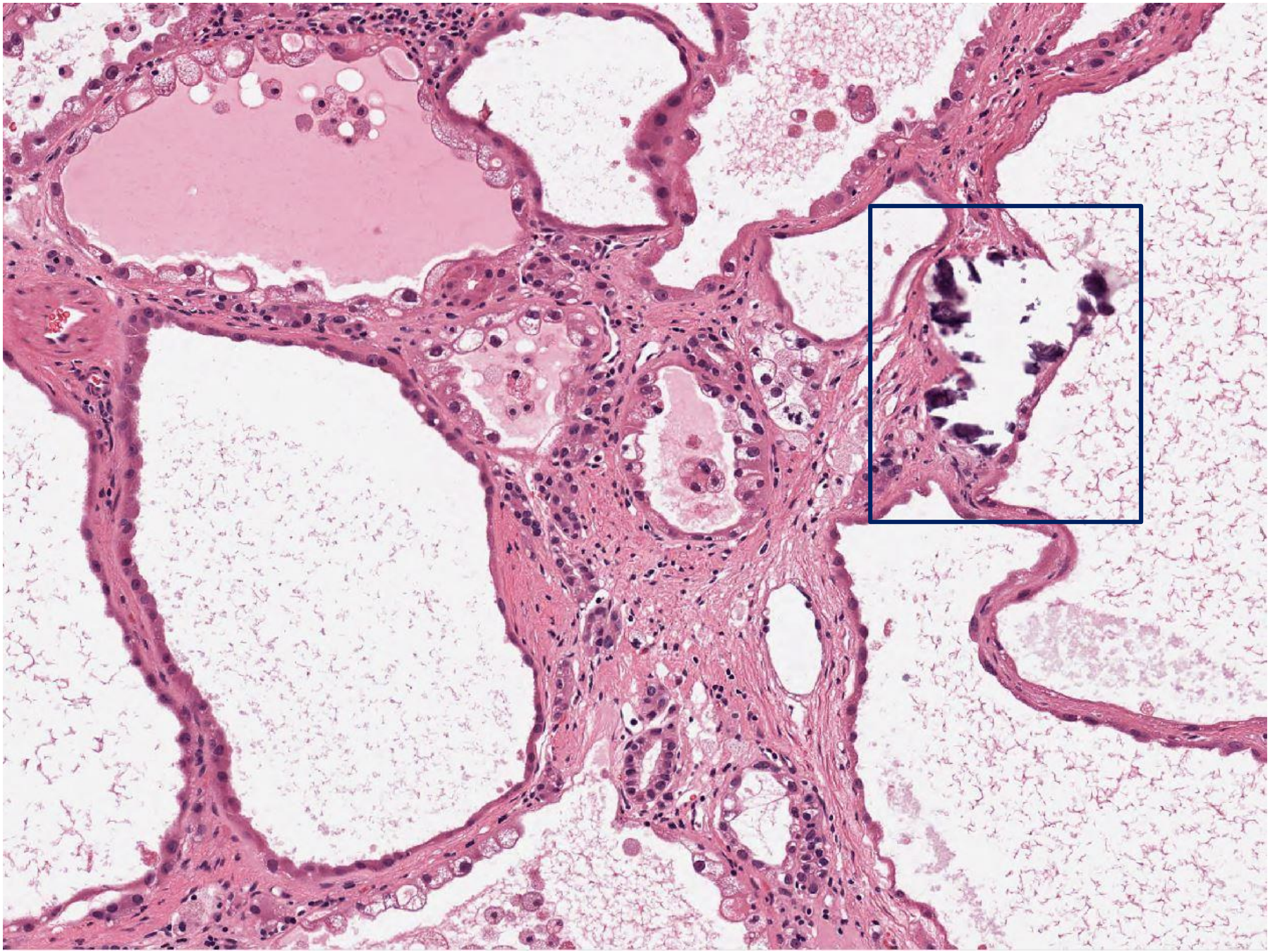
Tubulocystic carcinoma of the kidney: clinicopathologic analysis of 31 cases of a distinctive rare subtype of renal cell carcinoma. Amin MB, MacLennan GT, Gupta R, Grignon D, Paraf F, Vieillefond A, Paner GP, Stovsky M, Young AN, Srigley JR, Cheville JC. Am J Surg Pathol 2009; 33(3): 384-92.

# Partial Nephrectomy







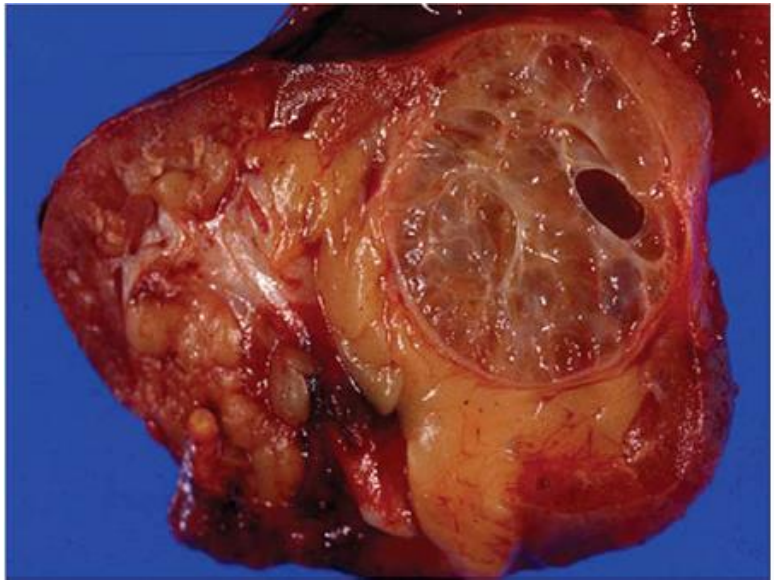


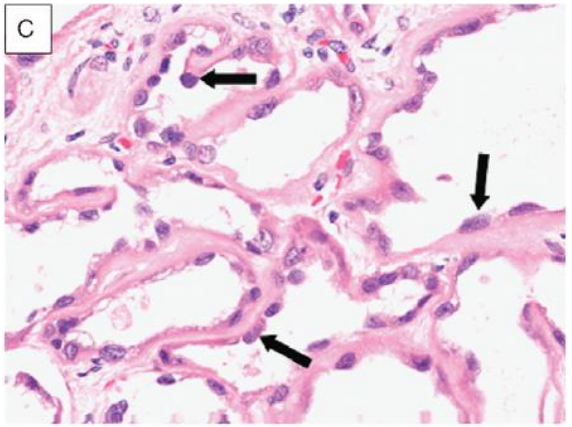
# Tubulocystic Carcinoma of the Kidney

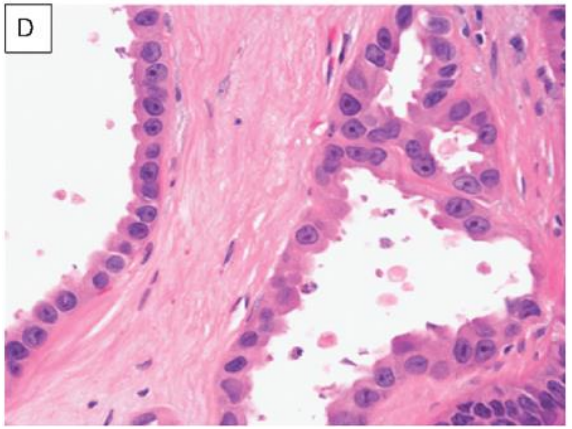
## *Clinicopathologic Analysis of 31 Cases of a Distinctive Rare Subtype of Renal Cell Carcinoma*

*Mahul B. Amin, MD,* Gregory T. MacLennan, MD,† Ruta Gupta, MD,* David Grignon, MD,‡ Francois Paraf, MD, PhD,§ Annick Vieillefond, MD,‖ Gladell P. Paner, MD,* Mark Stovsky, MD, MBA, FACS,† Andrew N. Young, MD, PhD,¶ John R. Srigley, MD,# and John C. Cheville, MD***

(*Am J Surg Pathol* 2009;33:384–392)





# Tubulocystic Carcinoma of the Kidney

## *Clinicopathologic and Molecular Characterization*

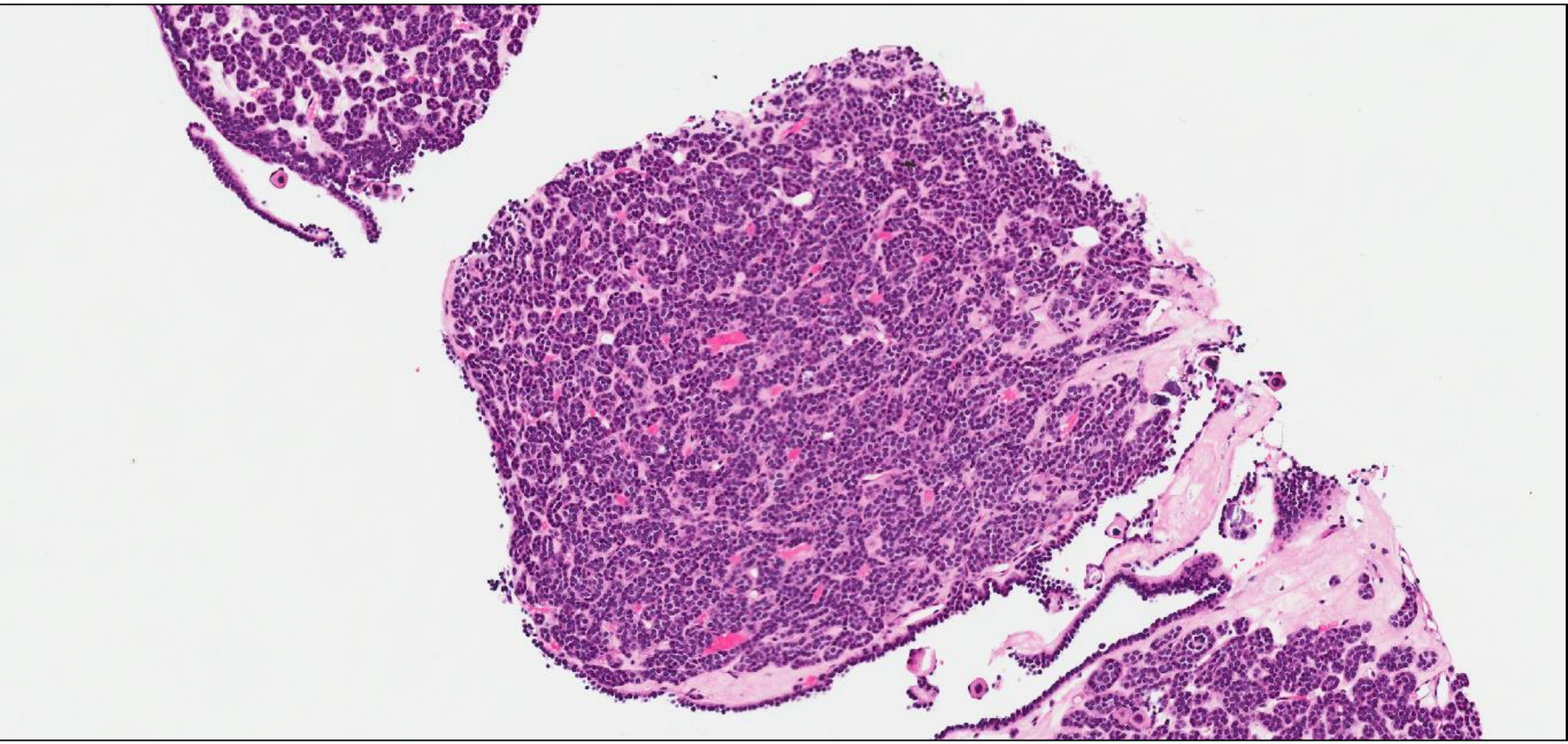
*Ximing J. Yang, MD, PhD,*† Ming Zhou, MD, PhD,‡ Ondrej Hes, MD, PhD,§ Steven Shen, MD, PhD,‖ Rongshan Li, MD, PhD,¶ Jose Lopez, MD,# Rajal B. Shah, MD,** Yu Yang, MD, PhD,†† Shang-Tian Chuang, DO,† Fan Lin, MD, PhD,‡‡ Maria M. Tretiakova, MD, PhD,§§ Eric J. Kort, MD,‖‖ and Bin Tean Teh, MD, PhD‖‖*

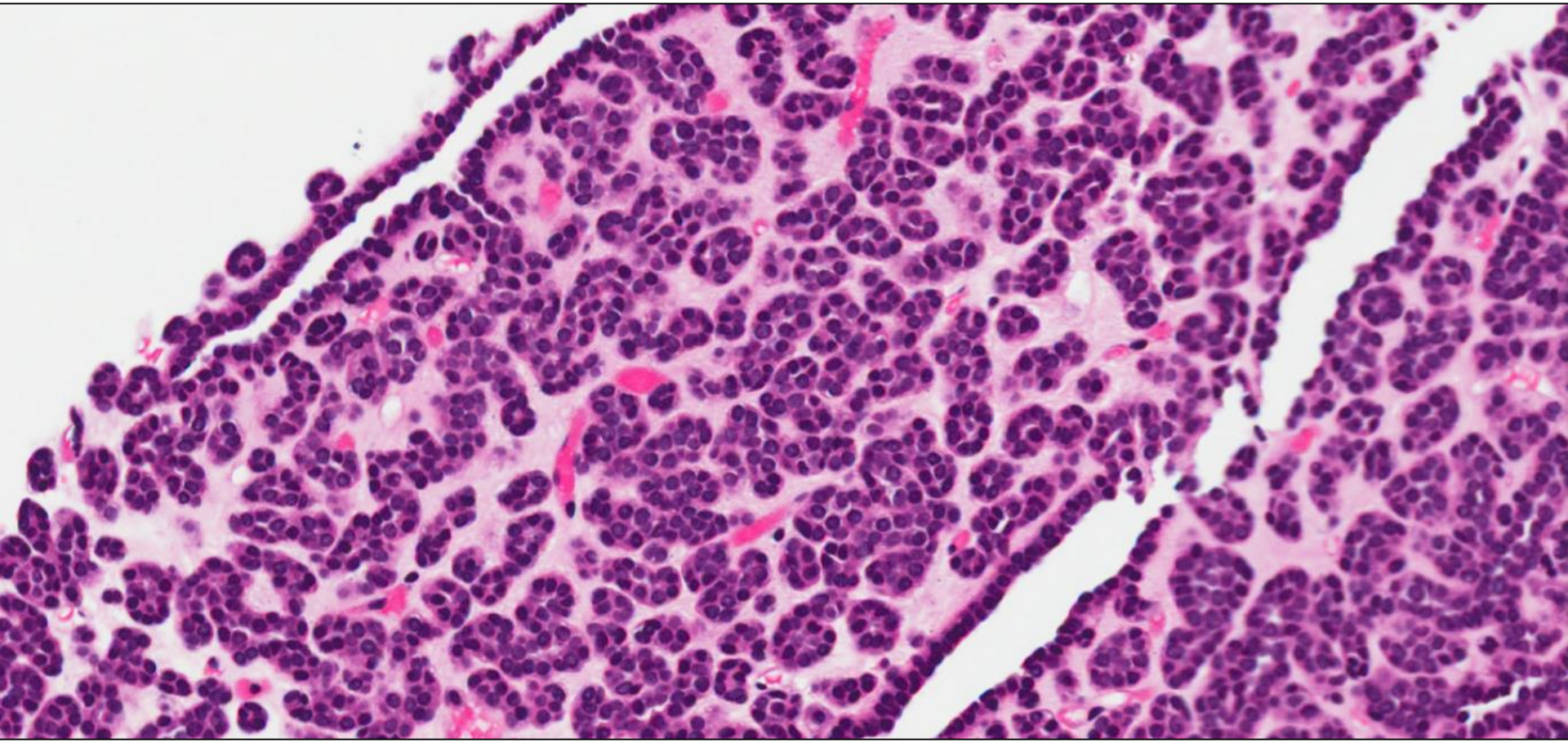
(*Am J Surg Pathol* 2008;32:177–187)

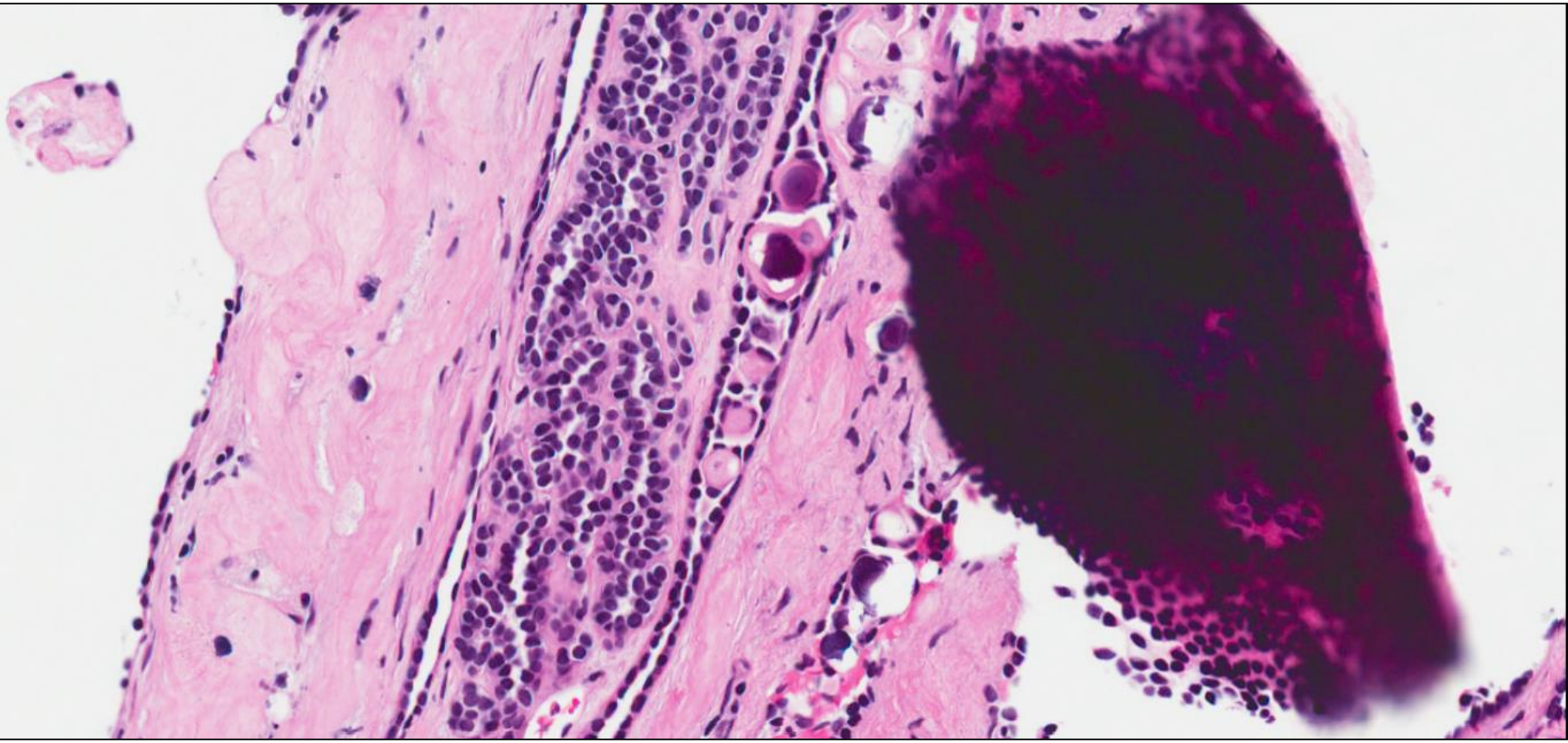
- 13 cases
  - age range 36-94 years
  - M:F = 3.3:1
  - 10/13 pT1a (< 4 cm, kidney confined)
  - indolent course
  - 1/13 with lymph node metastases
- 5/13 associated with separate papillary RCC or papillary adenoma(s)
  - lack of trisomy 7 or 17

# Case 2

46 year-old female, 2.0 cm
incidentally found solid renal mass







# Differential Diagnosis

- Papillary renal cell carcinoma, Type 1
- Epithelial-predominant adult Wilm's tumour
- Metanephric adenoma
- *Metanephric adenofibroma*

# Immunohistochemistry

**TABLE 4.** Solid PRCC Versus Metanephric Adenoma Versus Wilms Tumor

| | CK7 | AMACR | WT-1 | CD57 |
|---|---|---|---|---|
| Solid papillary | Positive | Positive | Negative | Negative |
| Metanephric adenoma | Negative or isolated cells | Negative | Positive, nuclear | Positive |
| Wilms | Negative or isolated cells | Negative | Positive, nuclear | Negative |

Best Practices Recommendations in the Application of Immunohistochemistry in the Kidney Tumors

*Report From the International Society of Urologic Pathology Consensus Conference*

# Metanephric Adenoma

- Benign neoplasm
- Female predominance (2:1)
- Young children to elderly (median age 50 years)
- 10% present with polycythemia
- Typically 3-6 cm
- Calcification can be extensive
- Highly cellular, tightly packed small uniform acini (± elongated branching tubules)
- 50% with papillary structures
- Mitotic figures rare/absent

# Metanephric adenoma: the utility of immunohistochemical and cytogenetic analyses in differential diagnosis, including solid variant papillary renal cell carcinoma and epithelial-predominant nephroblastoma

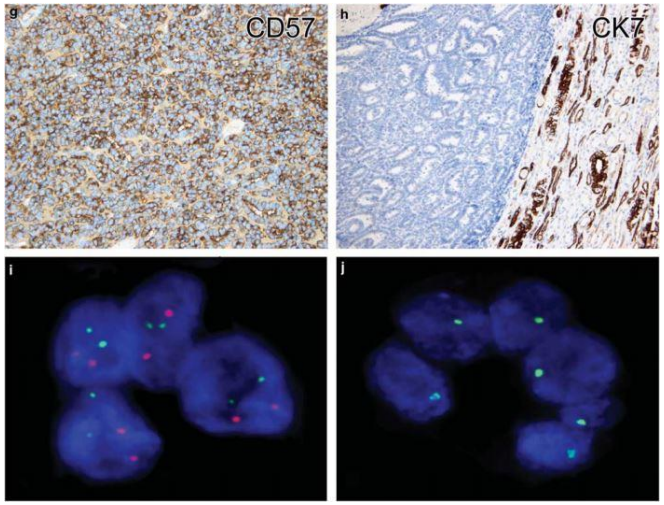
Stephanie N Kinney[1], John N Eble[1], Ondrej Hes[2], Sean R Williamson[3], David J Grignon[1], Mingsheng Wang[1], Shaobo Zhang[1], Lee Ann Baldrige[1], Guido Martignoni[4], Matteo Brunelli[4], Lisha Wang[5], Eva Comperat[6], Rong Fan[1], Rodolfo Montironi[7], Gregory T MacLennan[8] and Liang Cheng[1]

*Modern Pathology* (2015) **28,** 1236–1248;

**Table 3** Summary of immunohistochemical staining properties in metanephric adenoma, papillary renal cell carcinoma, and epithelial-predominant nephroblastoma

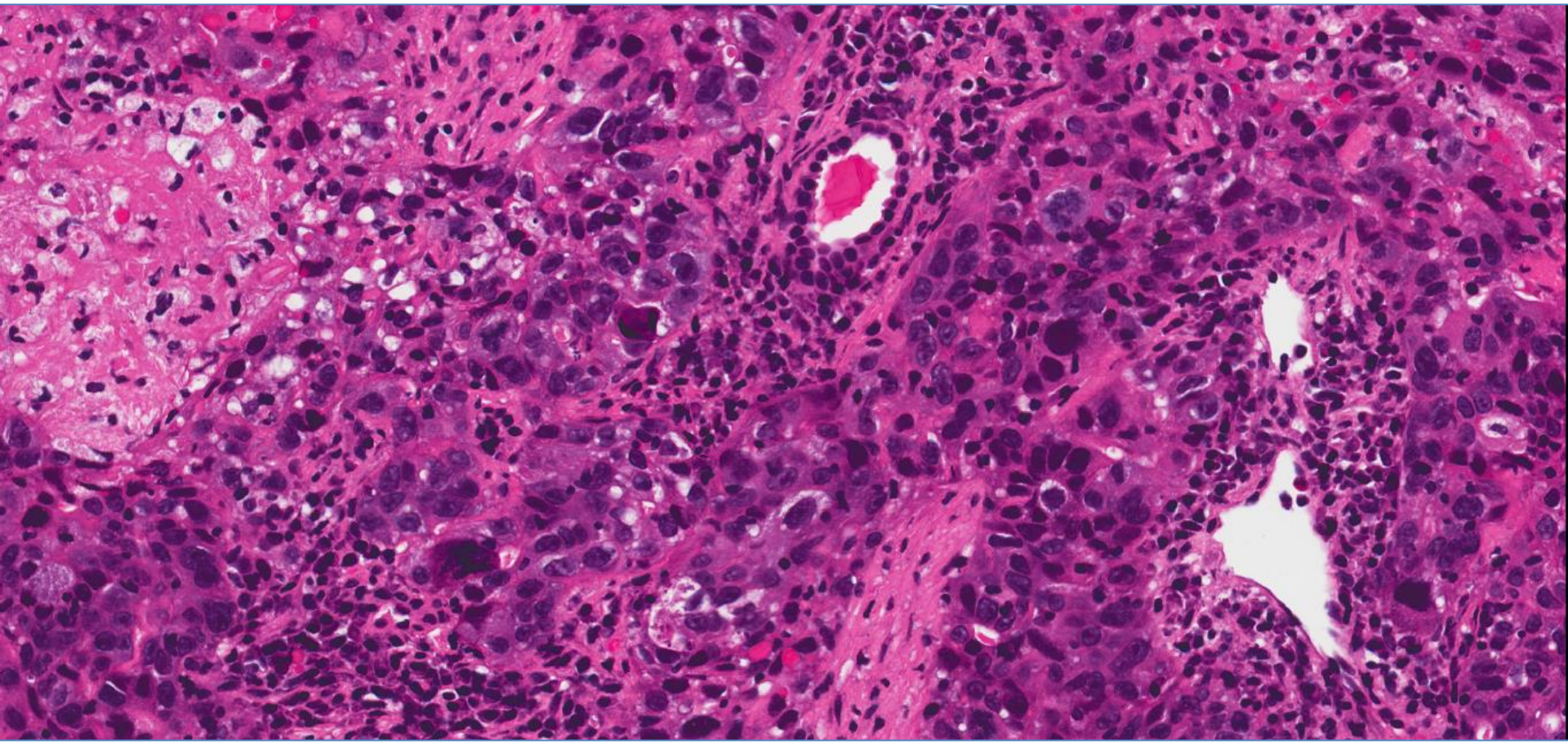
| *Antibody* | *Staining characteristics*[a] | *Metanephric adenoma, n = 35*[b] *(%)* | *Papillary renal cell carcinoma, n = 15*[c] *(%)* | *Epithelial-predominant nephroblastoma, n = 20 (%)* |
|---|---|---|---|---|
| WT1 | Negative | 0 | 15 (100) | 0 |
| | Focal | 0 | 0 | 0 |
| | Intermediate | 3 (9) | 0 | 2 (10) |
| | Diffuse | 32 (91) | 0 | 18 (90) |
| AMACR | Negative | 34 (97) | 0 | 20 (100) |
| | Focal | 1 (3) | 0 | 0 |
| | Intermediate | 0 | 0 | 0 |
| | Diffuse | 0 | 15 (100) | 0 |
| CK7 | Negative | 35 (100) | 1 (7) | 19 (95) |
| | Focal | 0 | 0 | 0 |
| | Intermediate | 0 | 0 | 1 (5) |
| | Diffuse | 0 | 14 (93) | 0 |
| CD57 | Negative | 0 | 14 (93) | 4 (20) |
| | Focal | 0 | 1 (7) | 10 (50) |
| | Intermediate | 0 | 0 | 2 (10) |
| | Diffuse | 35 (100) | 0 | 4 (20) |

[a]Scoring: Diffuse >50%, intermediate 26–50%, focal 1–25%, negative <1%. [b]Two tumors were reclassified as papillary renal cell carcinoma and were excluded from analysis with metanephric adenomas. [c]The two reclassified tumors were analyzed in the papillary renal cell carcinoma category.



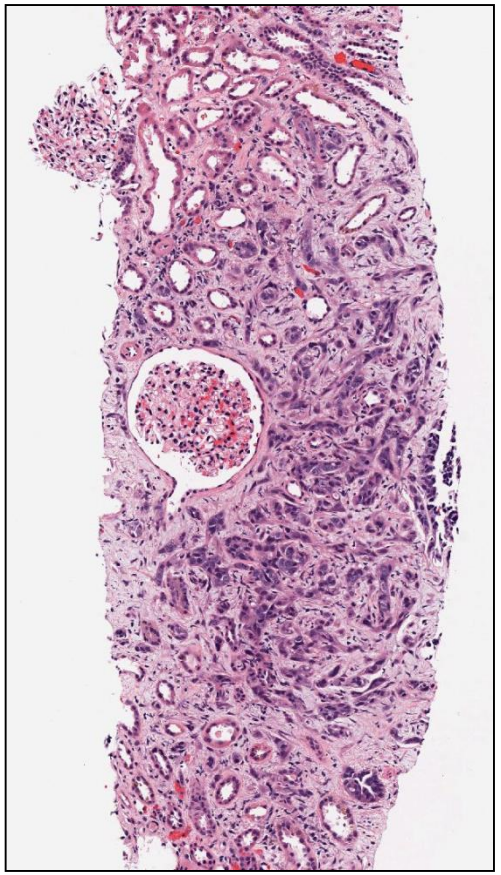
# Case 3

74 year-old female, gross hematuria and 5.4 cm renal mass



# Tumours That Infiltrate Renal Parenchyma

- Collecting duct/medullary carcinoma
- Urothelial carcinoma
- Lymphoma
- Metastatic carcinoma
  - lung
  - breast
  - gyne - PAX-8
  - head and neck



# Infiltrative Tumours: Diagnostic Approach

- History - other known cancer
- Radiology - tumour location in the kidney
- Immunohistochemistry
  - PAX-8
  - GATA-3
  - p63
  - 34βE12
  - CK19
  - others as appropriate based on history, morphology, etc

# Case 3: Immunohistochemistry

**Positive**

- CK7
- p63
- GATA3
- HMWK (34βE12)

**Negative**

- PAX8
- CK20
- GCDFP-15
- ER
- Mammoglobin

# Case 3: Diagnosis

**Diagnosis**

Needle biopsy of kidney (left renal mass):

- Invasive high-grade urothelial carcinoma. See comment.

**Comment**

Sections show cores of renal parenchyma that are extensively infiltrated by high-grade poorly differentiated carcinoma. Fragments of necrotic tissue are also present. The tumour cells have pleomorphic, hyperchromatic nuclei with some cells having prominent nucleoli. The cells are arranged in solid sheets as well as nests and cords within desmoplastic stroma. The tumour shows marked infiltration in between glomeruli and benign renal tubules. On immunohistochemical staining, the tumour cells are positive for CK7, GATA 3 and p63 and show weak patchy positivity with high molecular weight cytokeratin. They are negative for PAX-8, CK20, ER, GCDFP-15 and mammoglobin. The history of breast cancer supplied with the biopsy is acknowledged. Metastatic carcinoma was considered in the histologic differential diagnosis for this biopsy, however the H&E morphology and immunophenotype of the tumour is most consistent with high-grade urothelial carcinoma.

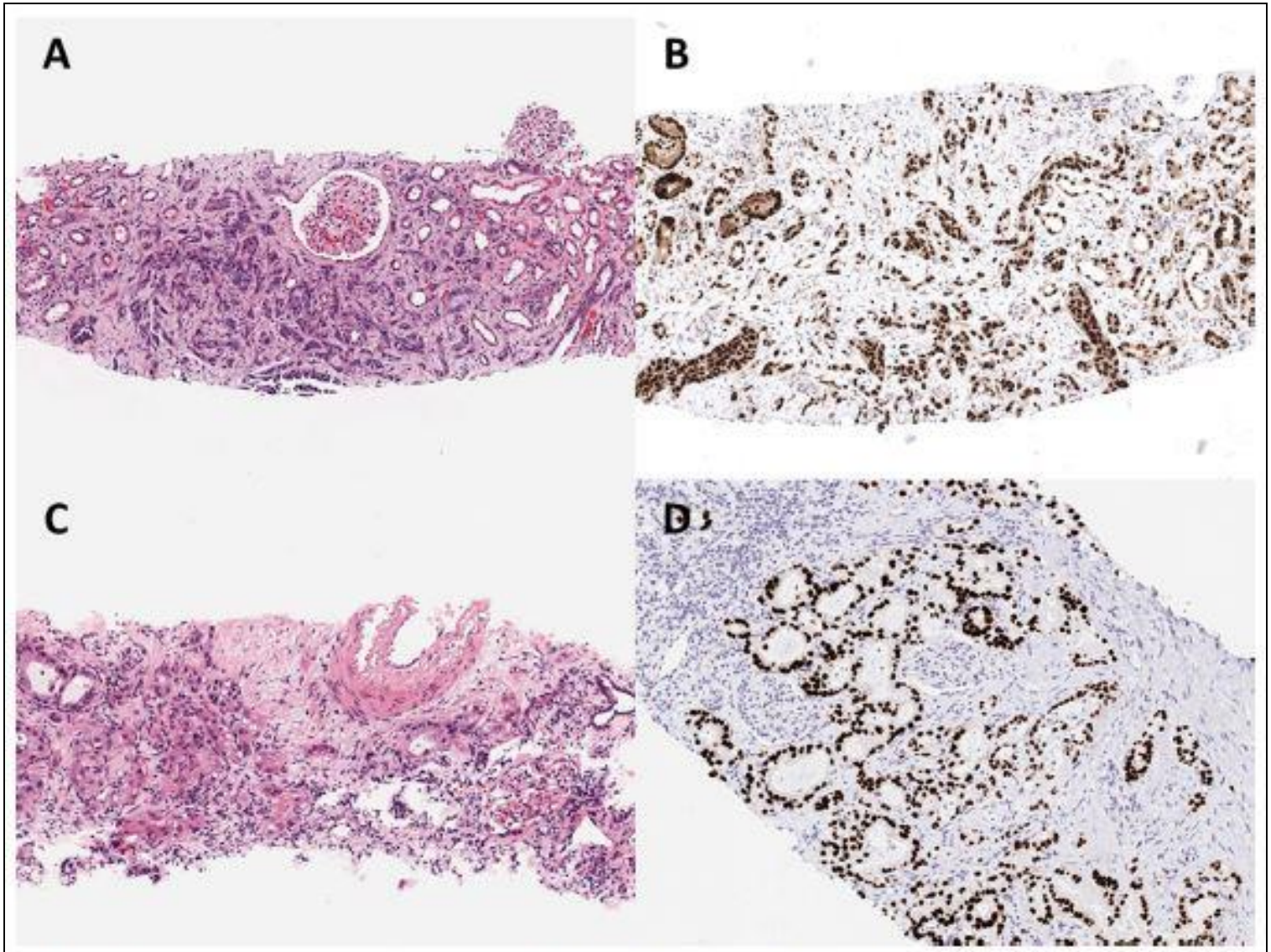



Fig. 7 – Renal tumour biopsies containing carcinoma with an infiltrative growth pattern. (A) Carcinoma infiltrating in between renal tubules and glomeruli in a patient with a solitary small renal mass and no history of a prior malignancy. (B) This tumour was positive for PAX-8. A biopsy diagnosis of *renal cell carcinoma consistent with collecting carcinoma* was given. (C) Another example of carcinoma infiltrating in between renal tubules and glomeruli in a patient with a solitary small renal mass and previous history adenocarcinoma of lung. (D) This tumour was positive for TTF-1 and the biopsy was reported as *metastatic adenocarcinoma consistent with lung primary.*

Collecting Duct Carcinoma

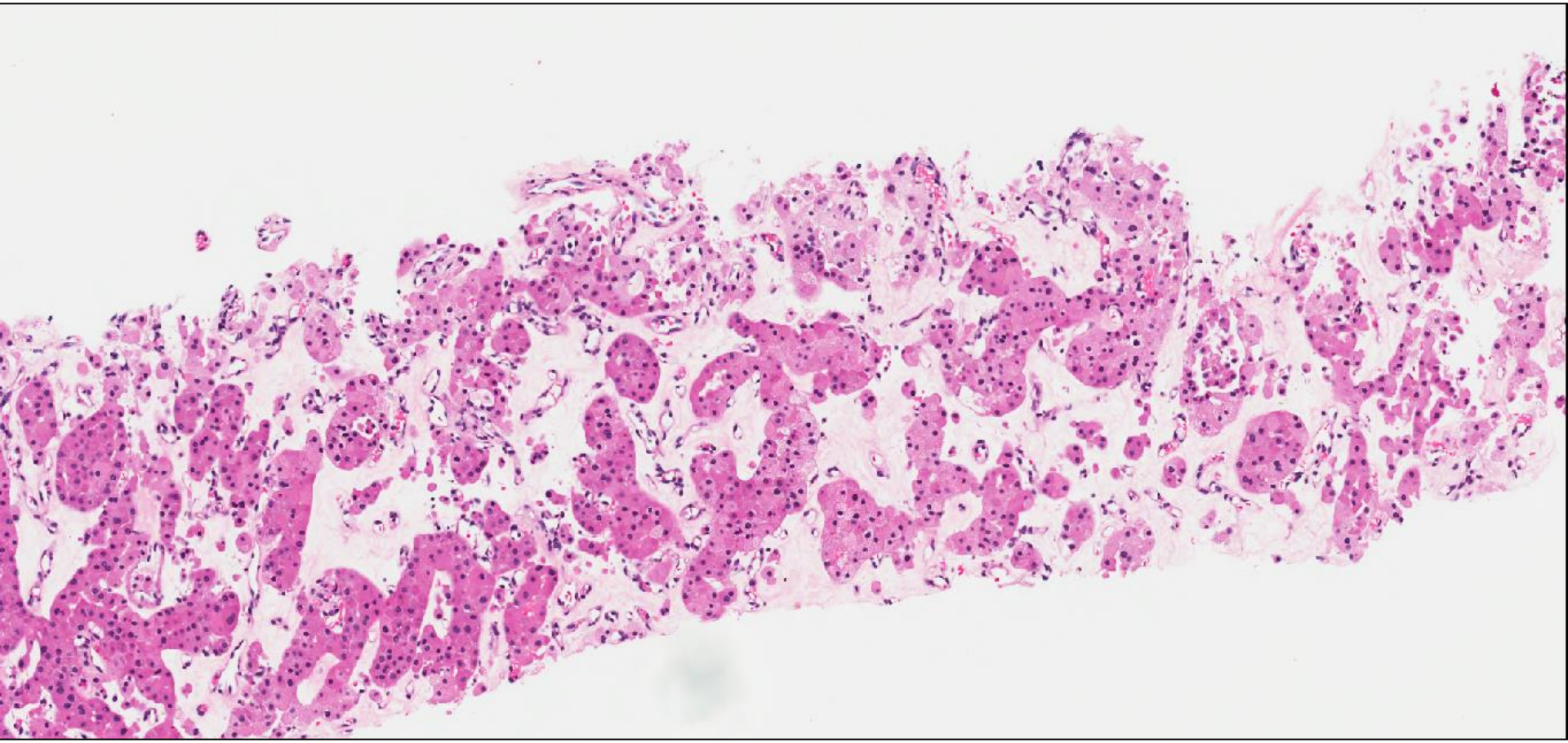
Metastatic NSC Lung Carcinoma

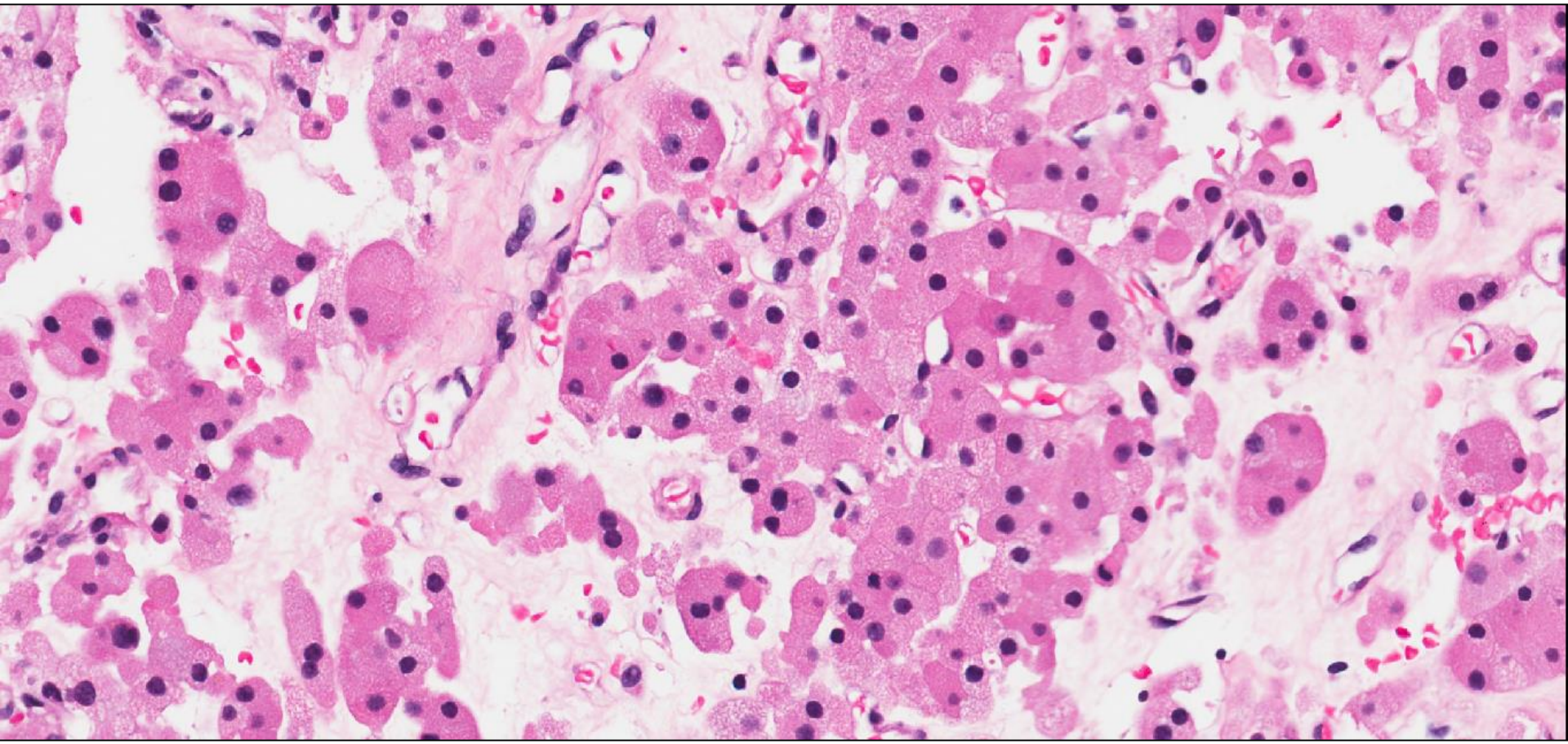
# Collecting Duct Carcinoma

- A difficult definitive diagnosis on biopsy
- Nephrectomy criteria:
    1. Medullary tumour
    2. Mostly tubular morphology
    3. Infiltrative growth
    4. High-grade cytological features
    5. Desmoplastic stroma
    6. Absence of other RCC subtypes or urothelial carcinoma

# Case 4

68 year-old male, 2.5 cm incidentally found left renal mass





# Renal Tumours with Oncocytic/Eosinophilic Cytoplasm

**Table 2 – Tumours characterized by cells with oncocytic or eosinophilic cytoplasm.**

| |
|---|
| Oncocytoma |
| Chromophobe renal cell carcinoma, eosinophilc variant |
| Hybrid oncocytic-chromophobe tumours |
| Clear cell renal cell carcinoma with eosinophilic cytoplasm (usually high grade) |
| Papillary renal cell carcinoma with oncocytic features |
| Papillary renal cell carcinoma, Type 2 |
| Tubulocystic renal cell carcinoma |
| Follicular thyroid-like carcinoma |
| Acquired cystic kidney disease associated renal cell carcinoma |
| Renal tumours associated with SDH-B mutations |
| Epithelioid angiomyolipoma |
| MiTF family translocation renal cell carcinoma |
| Renal cell carcinoma of any histologic type with rhabdoid features |

Usual Issue

Expanded Differential

Seminars in Diagnostic Pathology 32 (2015) 184–195

# Categorizing renal oncocytic neoplasms on core needle biopsy: a morphologic and immunophenotypic study of 144 cases with clinical follow-up☆

Megan A. Alderman MD[a], Stephanie Daignault MS[a], J. Stuart Wolf Jr. MD[b], Ganesh S. Palapattu MD[b], Alon Z. Weizer MD[b], Khaled S. Hafez MB, BCh[b], Lakshmi P. Kunju MD[a,*,1], Angela J. Wu MD[a,1]

[a]*Department of Pathology, University of Michigan Medical Center, Ann Arbor, MI 48109, USA*
[b]*Department of Urology, University of Michigan Medical Center, Ann Arbor, MI 48109, USA*

Human Pathology (2016) **55**, 1–10

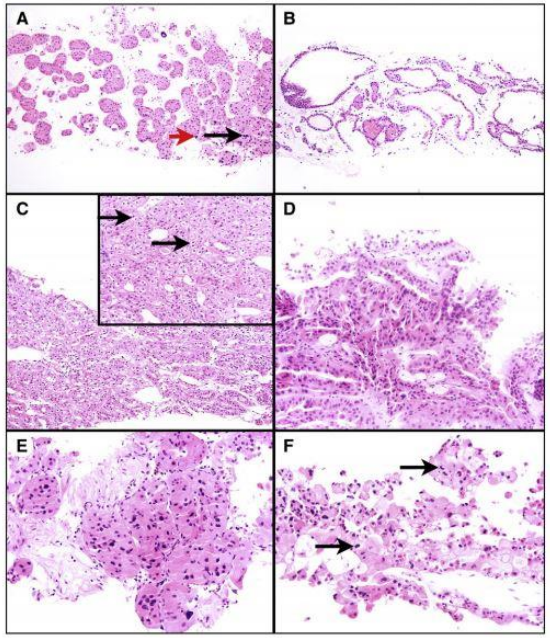



**Fig. 1** Morphologic features included A, nested architecture, edematous stroma, binucleation (red arrow), and degenerative type atypia (black arrow) and B, tubular architecture; these features were present in many of the favor oncocytoma biopsies. Features which would support a diagnosis of favor RCC included C, extensive sheet-like architecture and cells with flocculent to clear cytoplasm (inset, arrows); D, extensive papillary architecture with associated foamy macrophages; E, nuclear pleomorphism and enlarged hyperchromatic nuclei; and F, extensive flocculent cytoplasm, prominent cell borders, and raisinoid nuclei (arrows) (hematoxylin and eosin; original magnification A-C: ×4, C inset: ×20, D-F: ×10).



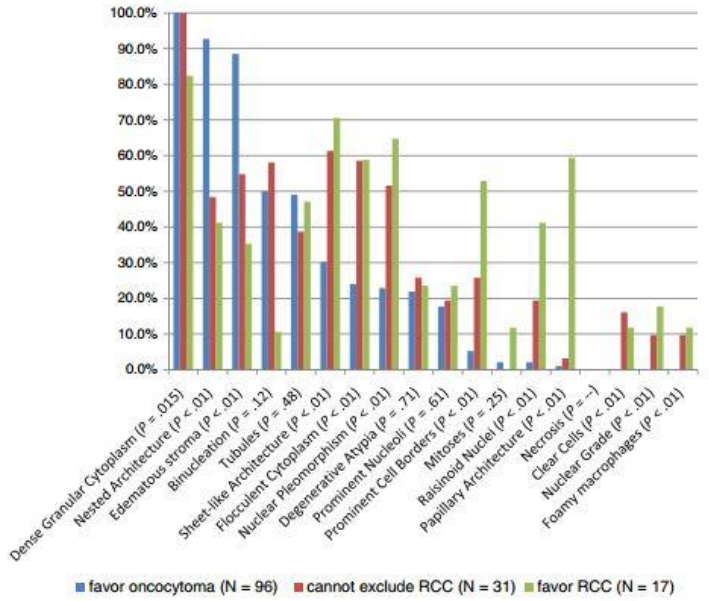
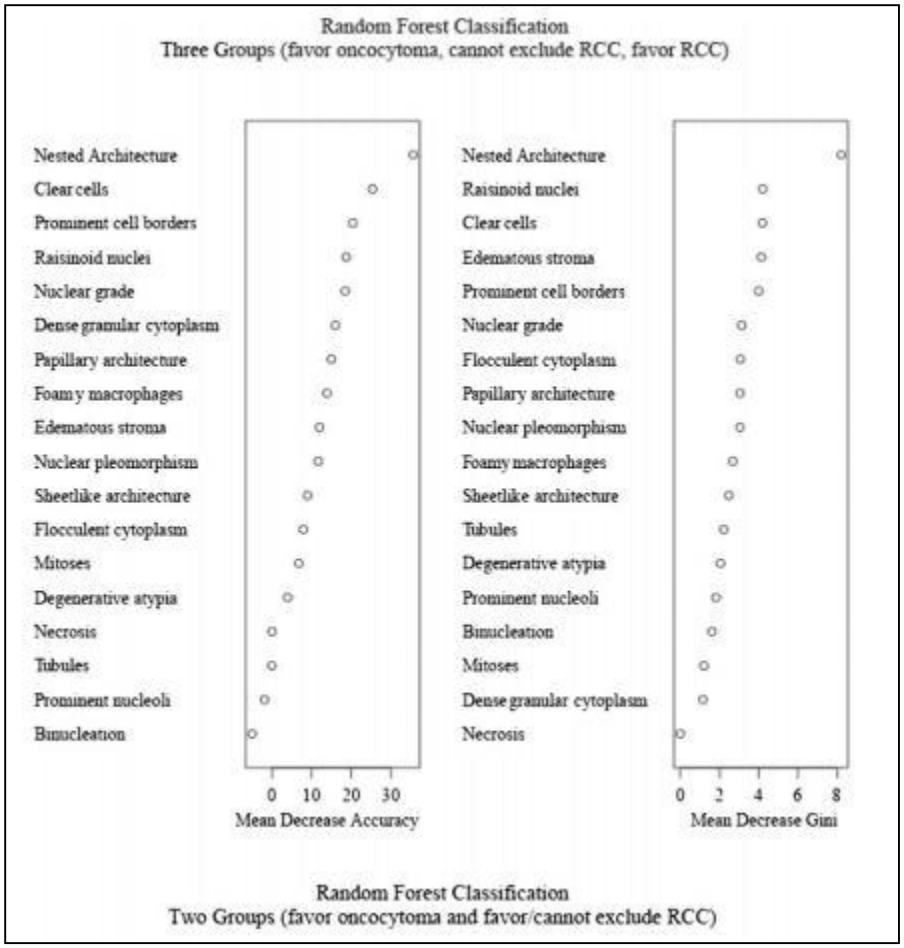



**Fig. 2** Depicted are the percentages of cases with the listed morphologic features in each diagnostic category.

# U of M Diagnostic Terminology

- Oncocytic/eosinophilic renal neoplasm -
  1. favour oncocytoma
  2. cannot exclude renal cell carcinoma
  3. favour renal cell carcinoma

# H&E Features Classifier




**Favour RCC**

- solid/sheet-like growth
- papillary architecture
- prominent cell borders
- nuclear pleomorphism
- high nucleolar grade
- necrosis
- frequent mitoses

**Favour Oncocytoma**

- dense granular cytoplasm
- nested architecture
- tubular architecture
- edematous stroma
- binucleation
- *degenerative-type atypia*

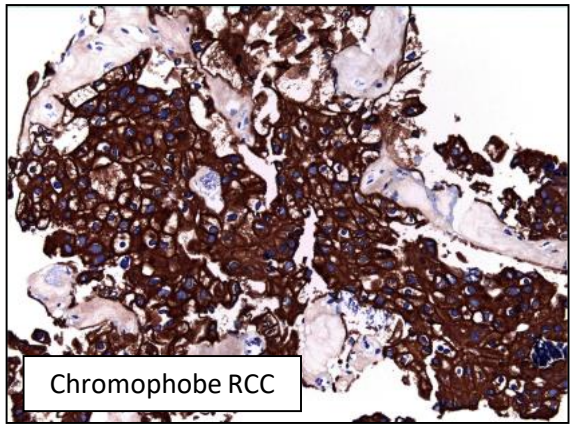
# ISUP Panel: Tumours With Oncocytic Features

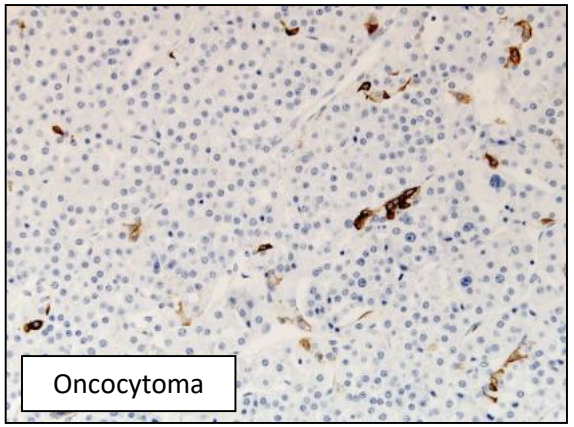
**TABLE 5.** Tumors With Oncocytic Features*

| | CD117 | CK7 | Ksp-cadherin | HMB-45 | Cathepsin-K |
|---|---|---|---|---|---|
| Oncocytoma | Positive, membranous | Negative | Positive | Negative | Negative |
| Chromophobe RCC, eosinophilic | Positive, membranous | Positive but variable | +/−Positive | Negative | Negative |
| Oncocytic PRCC | Negative | Positive but focal | Not known | Negative | Unknown |
| Oncocytic AML | Negative | Negative | Negative | Positive, focal | Negative |

Other Abs said to be differentially expressed on oncocytomas and chromophobe RCC.
Positive in oncocytoma, negative in chromophobe: S100A1.
*Hale colloidal iron: Although a histochemical rather than an IHC stain, it can be useful in differentiating chromophobe carcinoma (cytoplasmic granular staining) from oncocytoma (negative or luminal staining). However, this is a technically demanding stain and reliability is laboratory-dependent.

**CK 7**



*Arch Pathol Lab Med April 2012*

# Selected Common Diagnostic Problems in Urologic Pathology

## Perspectives From a Large Consult Service in Genitourinary Pathology

*Fadi Brimo, MD; Jonathan I. Epstein, MD*

### ONCOCYTOMA VERSUS CHROMOPHOBE RENAL CELL CARCINOMA

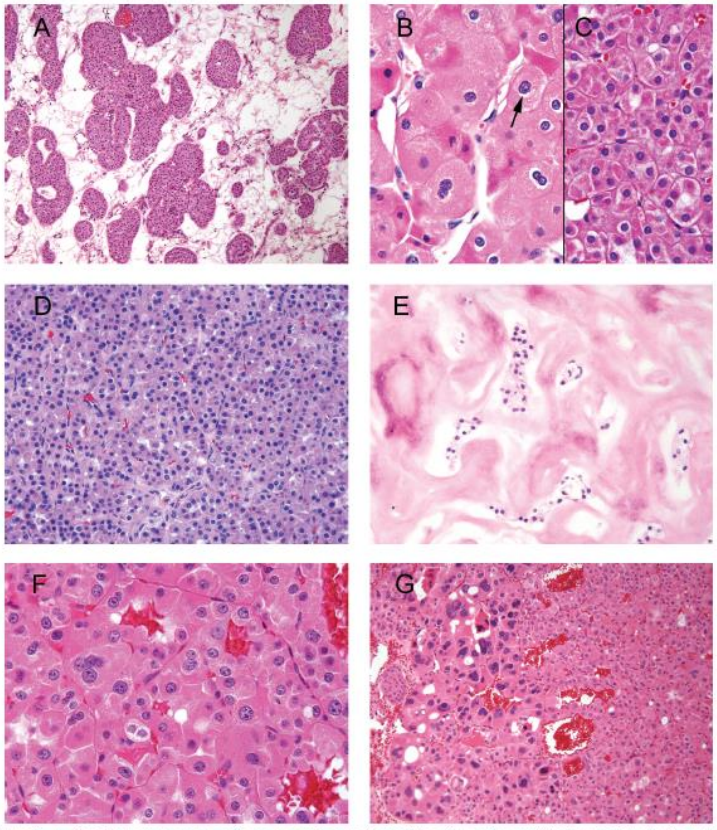
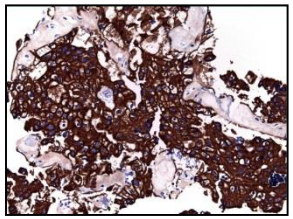
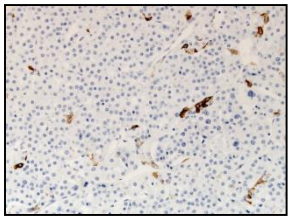
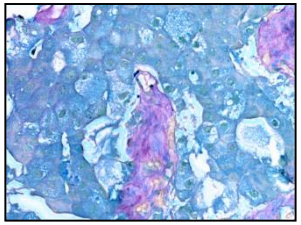


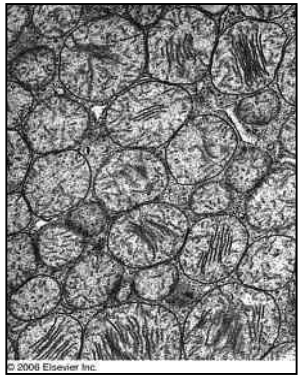

**Figure 3.** *A, Classic low-power appearance of oncocytoma with nests of eosinophilic cells in a fibromyxoid background. B, Nuclear features in chromophobe renal cell carcinoma (ChRCC) with irregular notches (arrow) and some nuclei with binucleation and perinuclear halos. C, Solid pattern of oncocytoma. Note the uniform, round nuclei of oncocytoma compared with the nuclei in ChRCC. D, Oncocytoma composed of numerous oncoblasts. E, Central scar of oncocytoma with degenerative cells having clear cytoplasm. F, Oncocytoma with uniform, round nuclei. Enlarged nuclei and prominent nucleoli are acceptable as long as the nuclei lack the irregular nuclei of ChRCC. G, Oncocytoma with a cluster of cells with degenerative nuclear atypia (left) (hematoxylin-eosin, original magnifications ×10 [A], ×60 [B and F], ×40 [C], and ×20 [D, E, and G]).*



CK 7








**The distinction ultimately comes down H&E morphology**

# Active Surveillance for Renal Neoplasms with Oncocytic Features is Safe

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Andrew J. Evans,† Narhari Timilsina* and Antonio Finelli*,‡

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THE JOURNAL OF UROLOGY® Vol. 195, 581-587, March 2016

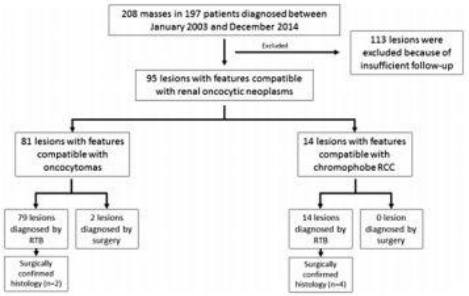



**Figure 1.** Study flow chart

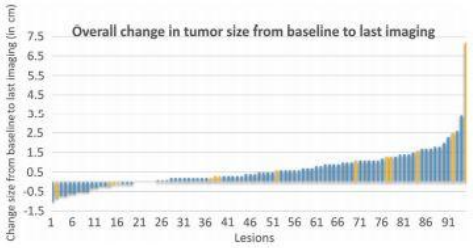



**Figure 2.** Waterfall plot demonstrating overall change in size (cm) from baseline to last imaging for oncocytoma (blue) and chromophobe RCC (orange).

**Biopsy Cohort (2003-2014):**

- 79 oncocytic renal neoplasms (2/2 surgically confirmed oncocytoma)
- 14 chromophobe RCC (6/6 surgically confirmed)
- no metastases or tumour-related death in either group

# Renal Tumour Biopsy: Barriers to Adoption

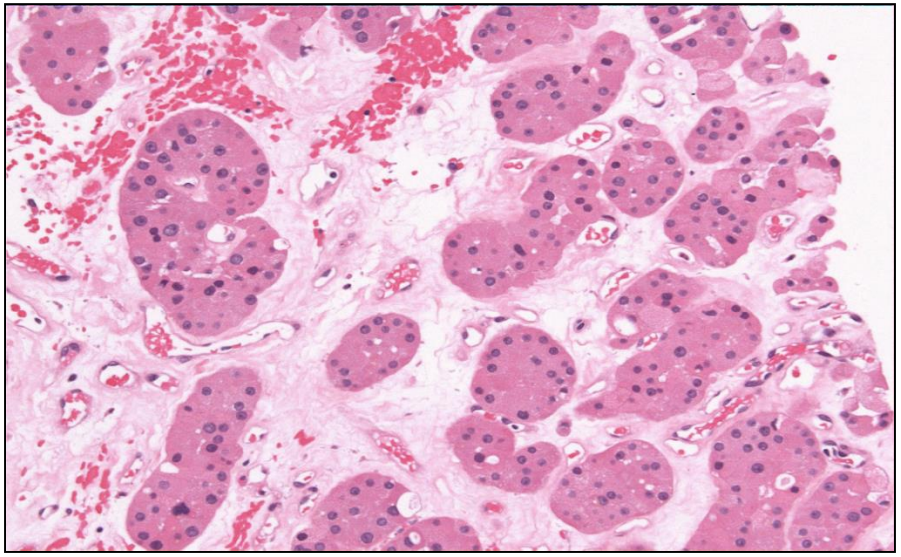
Survey of Canadian urologists (Richard 2017):

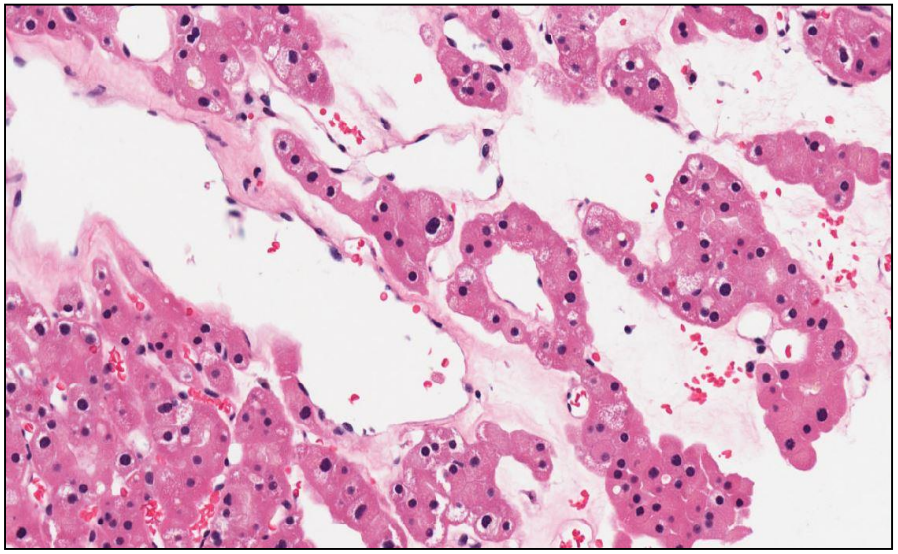
- Results do not change management (53%)
- Risk of false-negative or non-diagnostic biopsy (64%)

- "Neoplasm consistent with oncocytoma"
  - a frequently stated reason to avoid biopsies

# How to Address the Problem

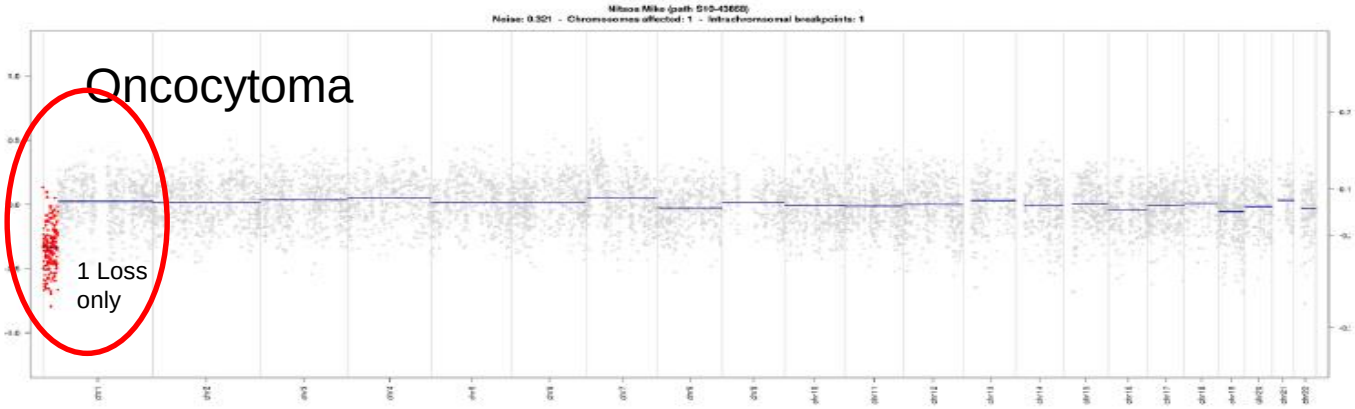
- Establish an ancillary test to help confirm a biopsy diagnosis of oncocytoma - a benign tumour



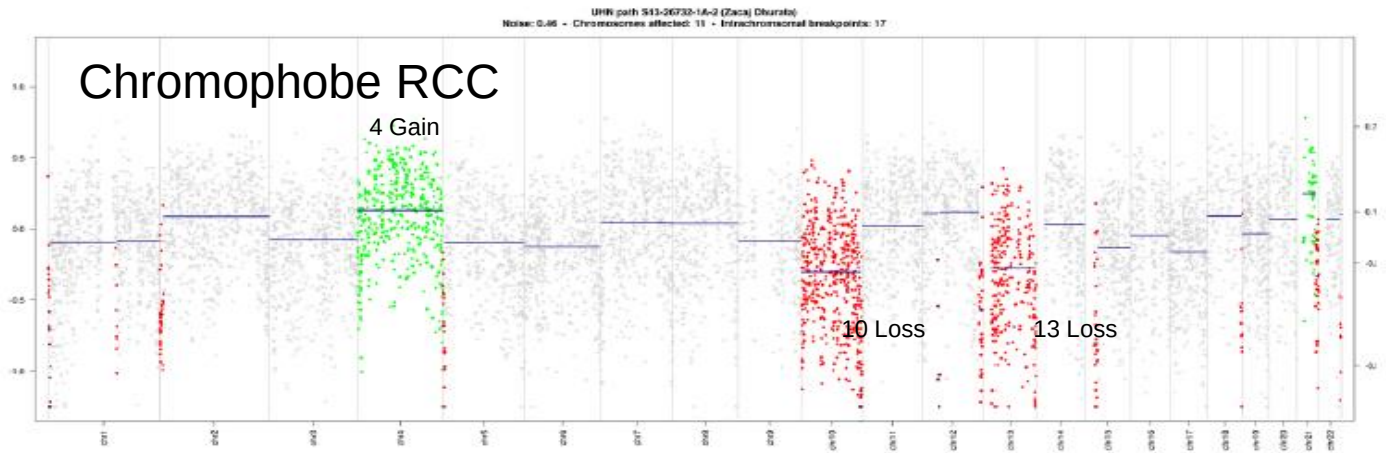


# Copy Number Variation Assay

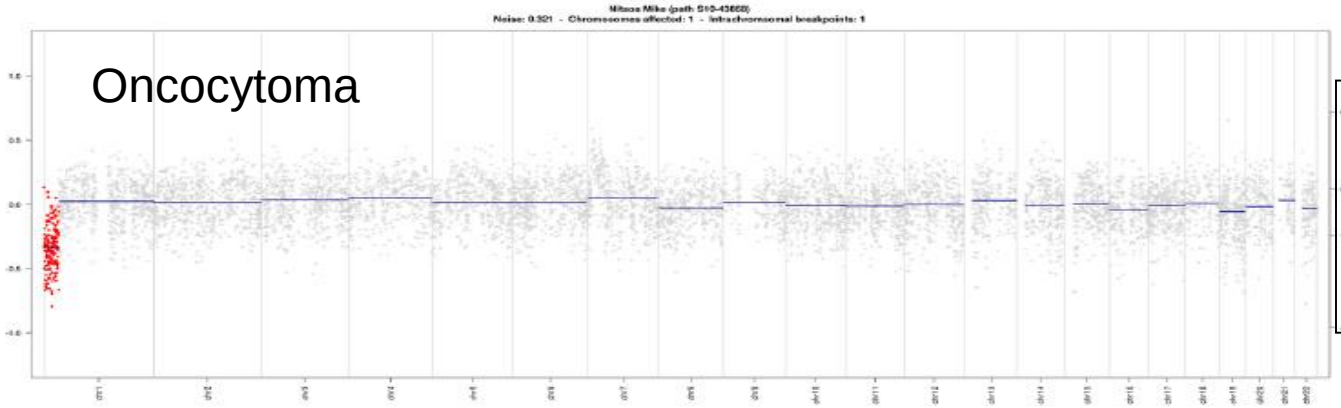
CNV-Plot:




CNV-Plot:



CNV-Plot:




Isolated Chromosome 1/1p loss is the key

**The purpose of the CNV/methylation assay is to confirm the biopsy diagnosis of a benign tumour!**

CNV-Plot:

Not an Oncocytoma

*Any other CNV plot interpreted as evidence the tumour is <u>not</u> an oncocytoma*

# Justification for CNV Approach

*The American Journal of Pathology, Vol. 180, No. 6, June 2012*

*http://dx.doi.org/10.1016/j.ajpath.2012.01.044*

*Tumorigenesis and Neoplastic Progression*

## Renal Cell Neoplasms Contain Shared Tumor Type–Specific Copy Number Variations

John M. Krill-Burger,* Maureen A. Lyons,*†
Lori A. Kelly,*† Christin M. Sciulli,*†
Patricia Petrosko,*† Uma R. Chandran,†‡
Michael D. Kubal,§ Sheldon I. Bastacky,*†
Anil V. Parwani,*†‡ Rajiv Dhir,*†‡ and
William A. LaFramboise*†‡

*From the Departments of Pathology* and Biomedical Informatics,‡ University of Pittsburgh, Pittsburgh, Pennsylvania; the University of Pittsburgh Cancer Institute,† Pittsburgh, Pennsylvania; and Life Technologies,§ Carlsbad, California*

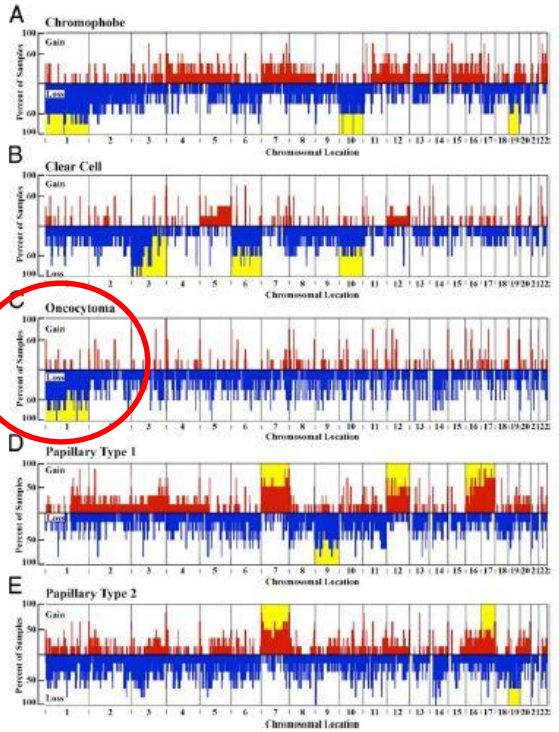



**Figure 3.** The location and frequency of CNVs in samples chromophobe (**A**), clear cell (**B**), oncocytoma (**C**), papillary type 1 (**D**), and papillary type 2 (**E**). The abscissa is divided into chromosomes delineated horizontally in line with the p arm of the chromosome to the left and the q arm to the right. Copy number gains (amplifications; red) are indicated by positive values. Copy number losses (deletions; blue) are indicated by negative values, which correspond to the percentage of samples containing the CNV. Chromosomes are highlighted yellow if the average values within each subclassification contain significant CNVs comprising at least 30% of the chromosome.

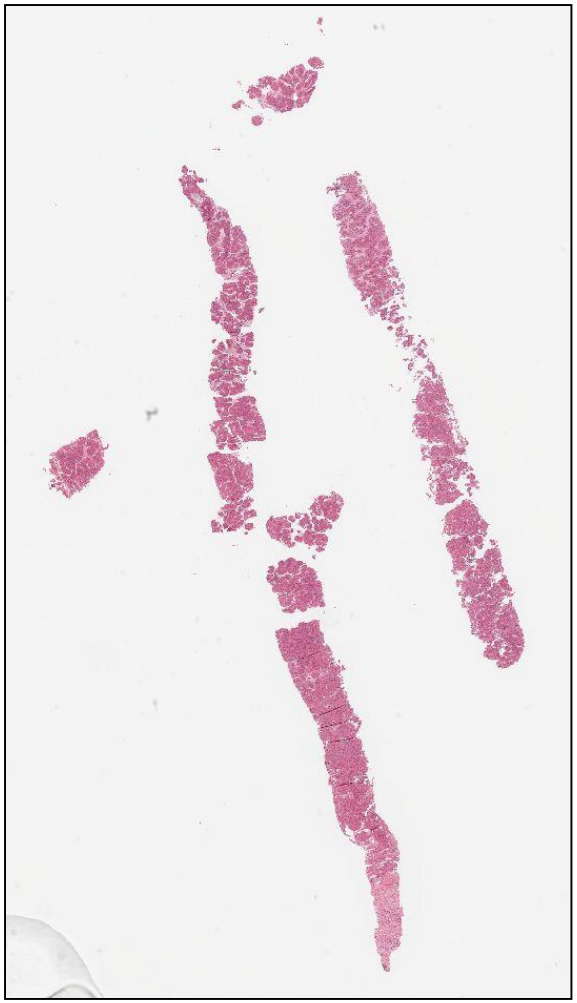
**Affymatrix Genome-Wide Human SNP Array 6.0**

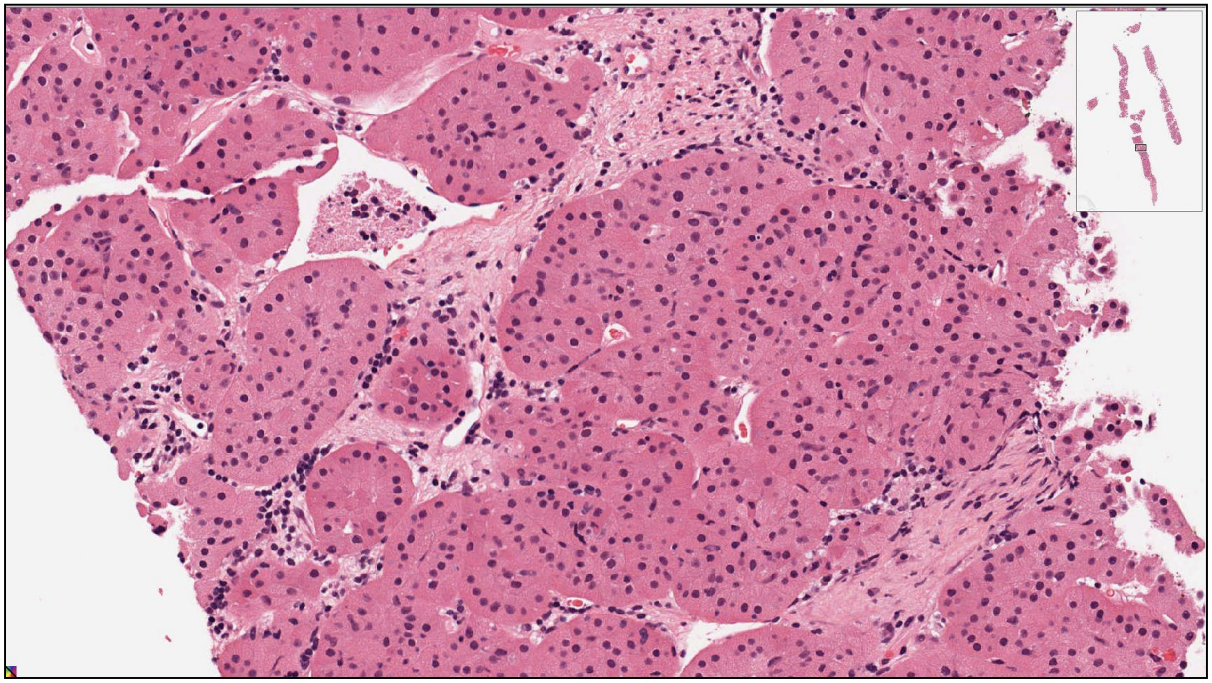
- 906.600 SNP's
- 946,000 non-polymorphic probes

# Illustrative Case

- 68 year-old female
- Poor renal function
- 5.1 cm left renal mass on U/S November 2012
- Left renal mass biopsy January 2013
  - consistent with oncocytoma
- Surveillance with serial imaging
- Liver mass biopsy November 2014
  - metastatic carcinoma consistent with renal primary
- Autopsy December 1, 2014
  - post-mortem interval 7 days (expired 25/11/2014)

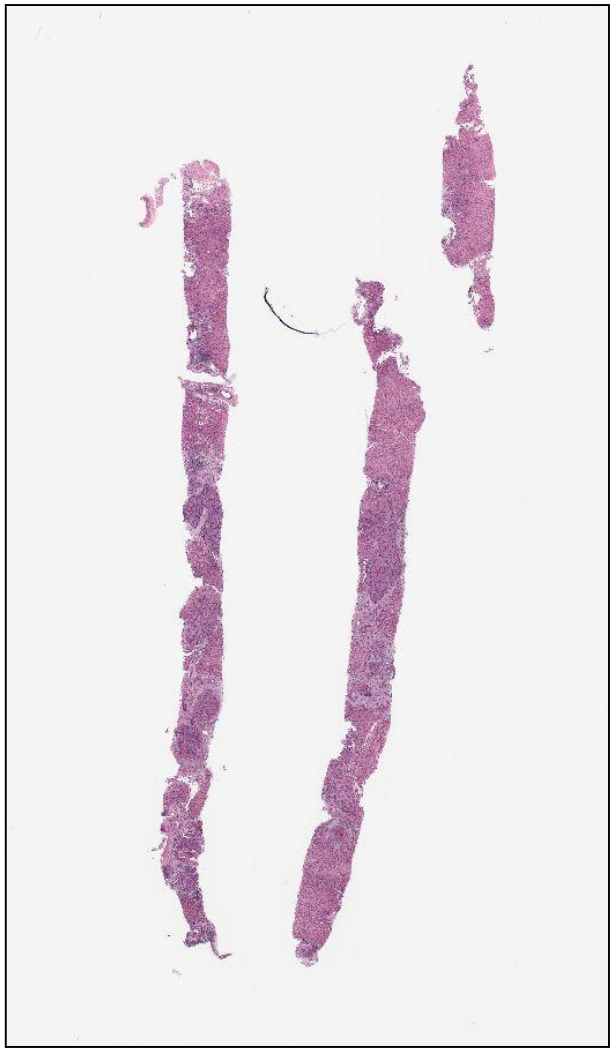
# Left Renal Mass Biopsy

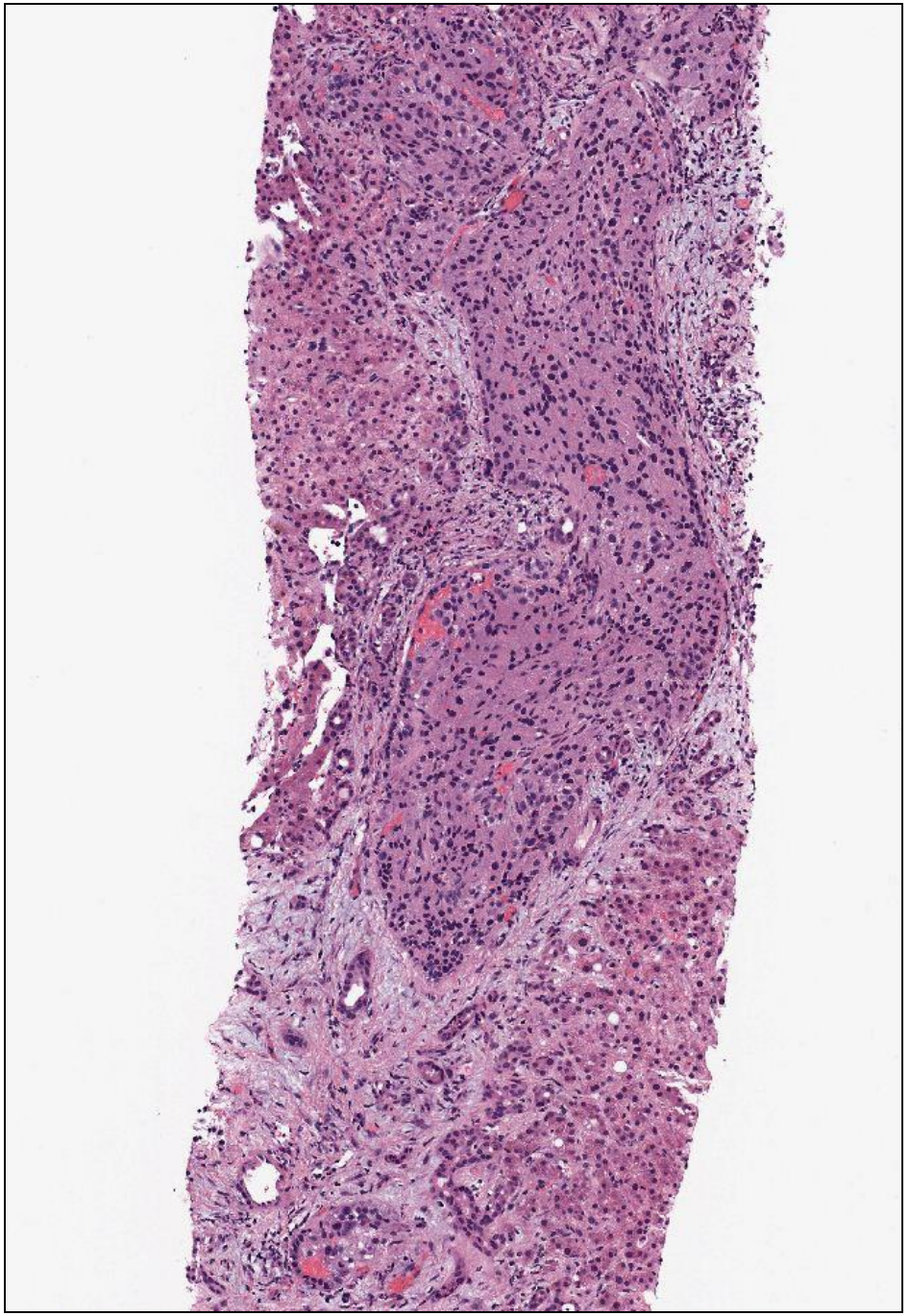


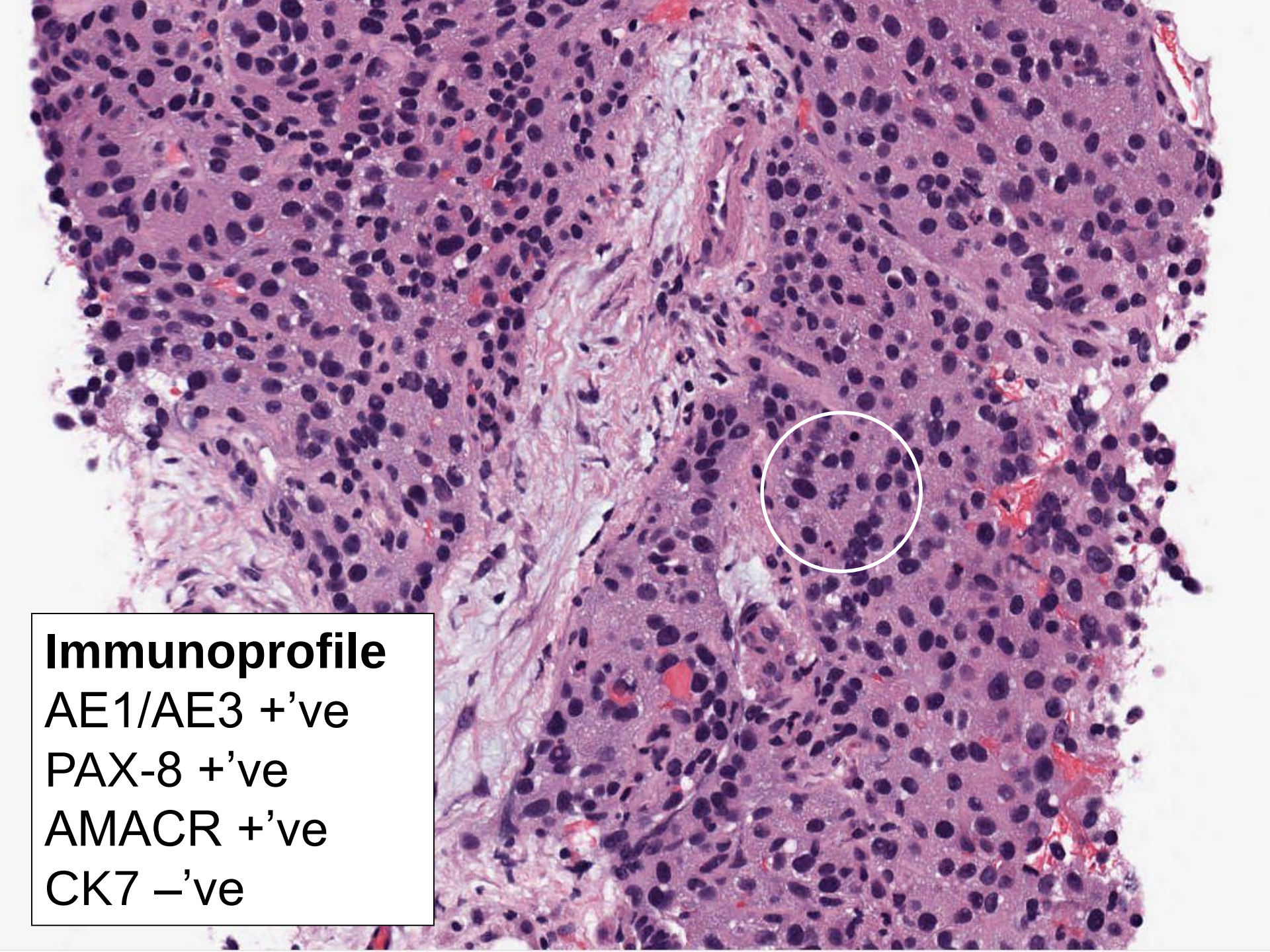


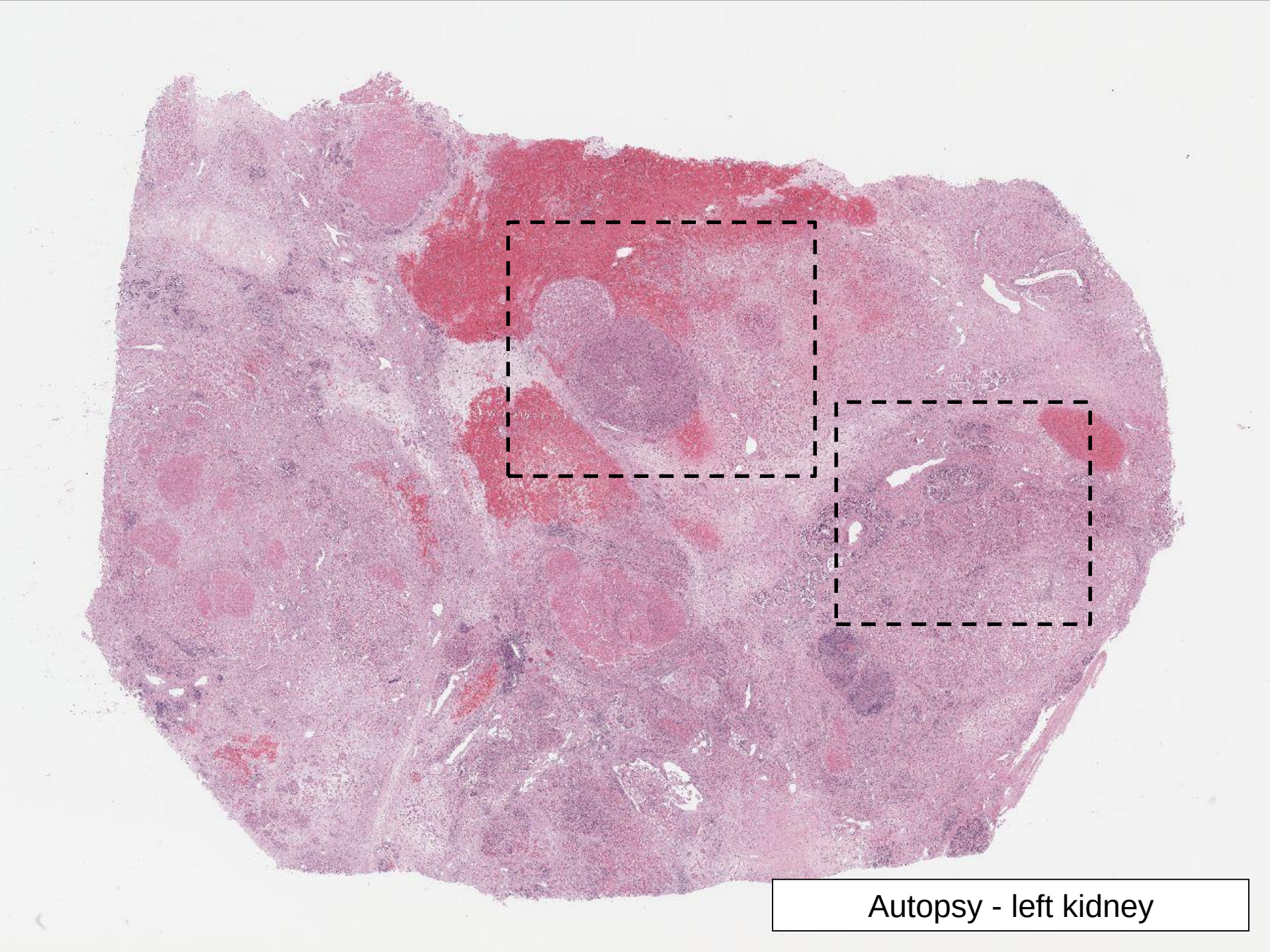
Oncocytic renal neoplasm consistent with oncocytoma

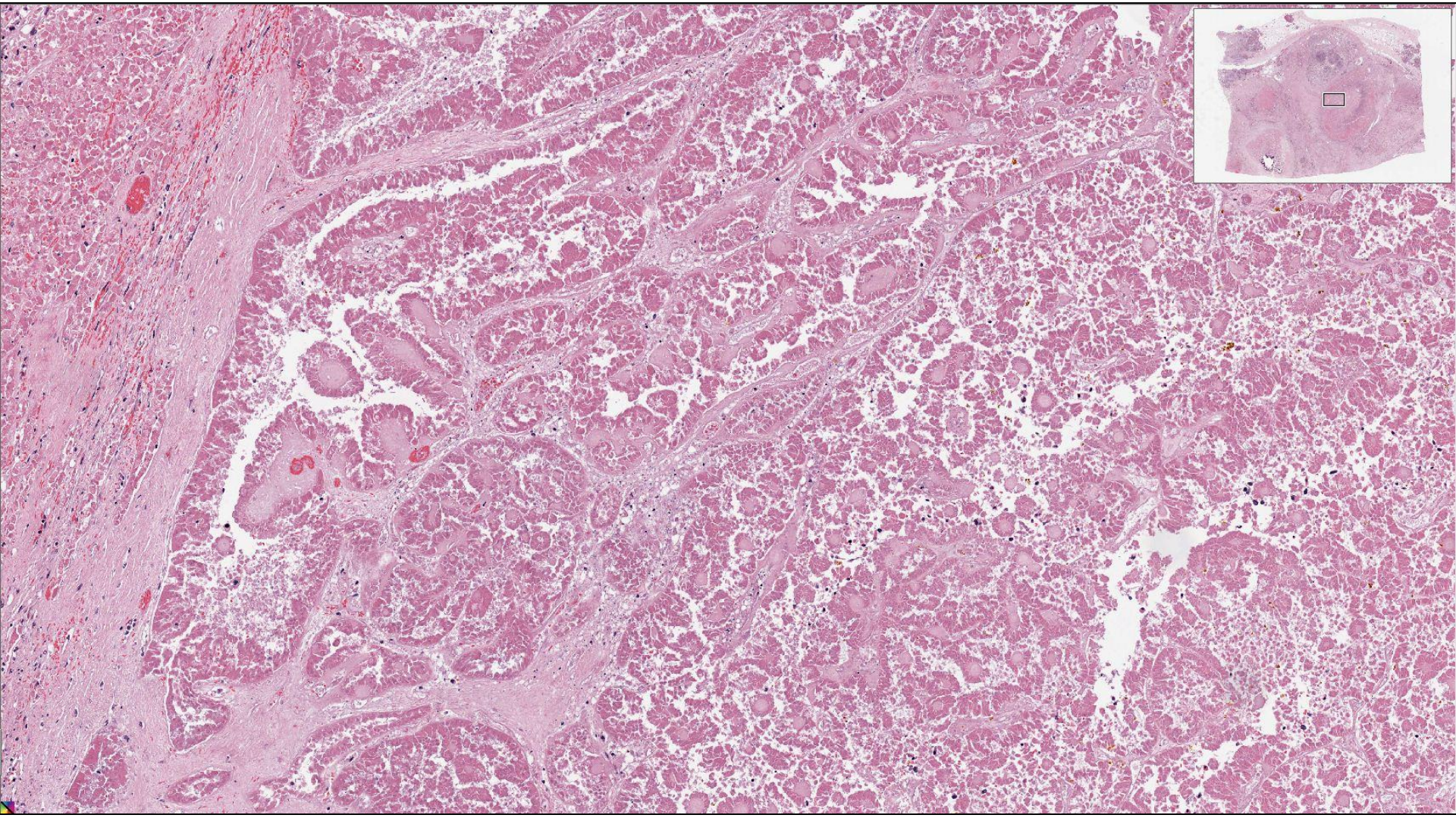
# Biopsy of Liver Mass

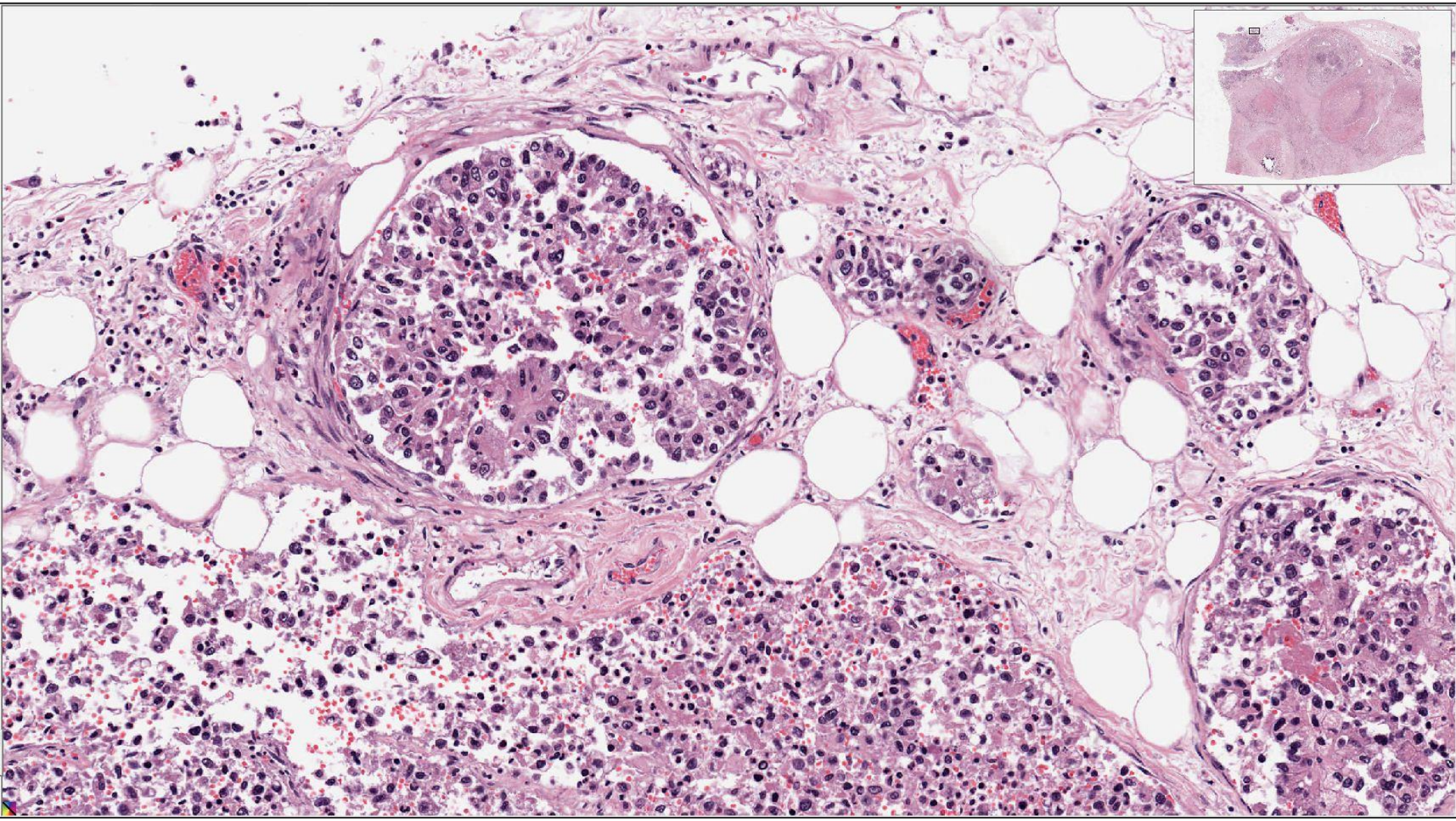


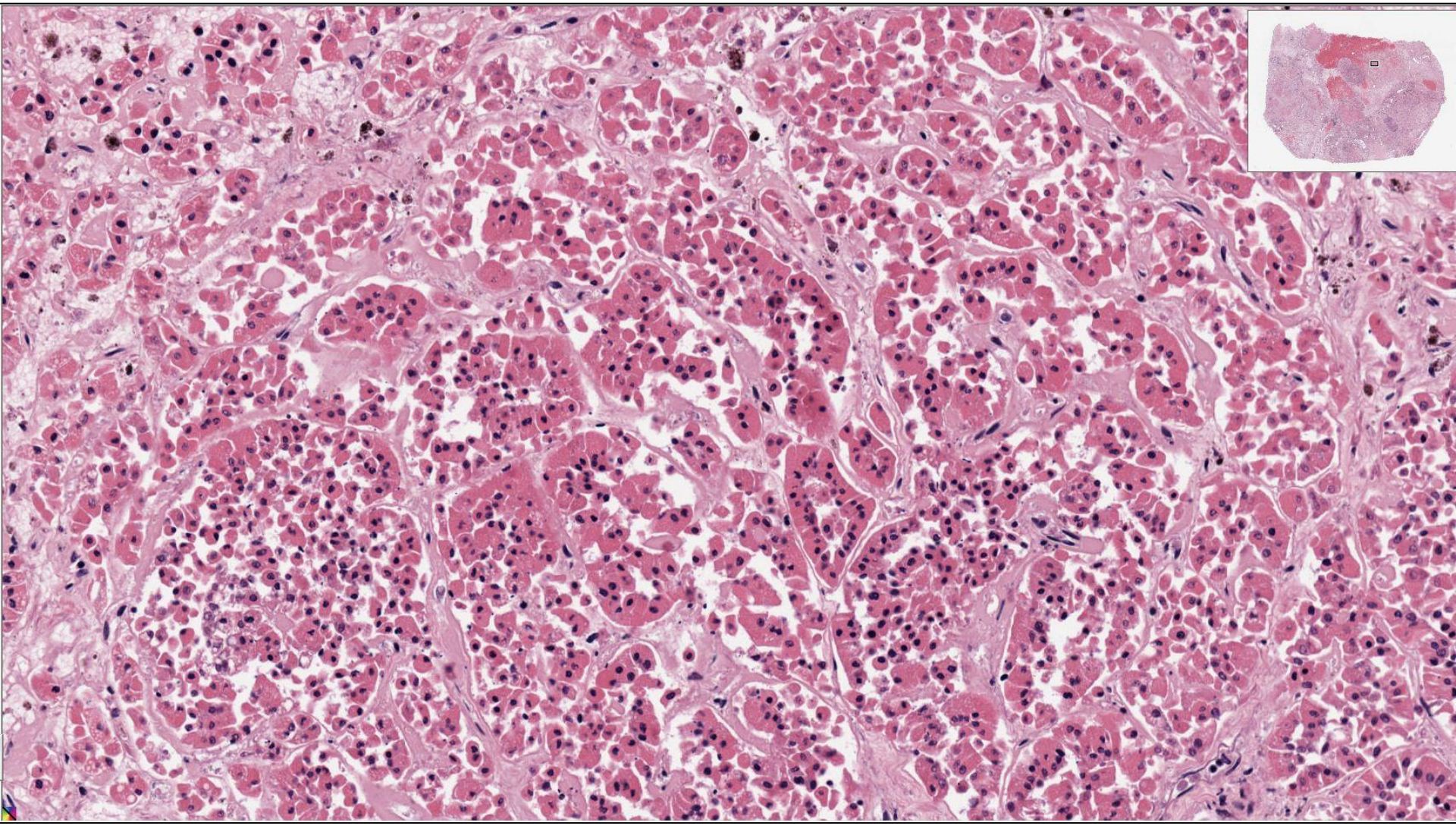



**Immunoprofile**
AE1/AE3 +'ve
PAX-8 +'ve
AMACR +'ve
CK7 –'ve


Autopsy - left kidney







**Final Diagnosis** – papillary renal cell carcinoma, NOS (most likely Type 2) with oncocytoma-like, glandular, solid and papillary areas

OPEN

# Oncocytoma-Like Renal Tumor With Transformation Toward High-Grade Oncocytic Carcinoma

## *A Unique Case With Morphologic, Immunohistochemical, and Genomic Characterization*

*Sahussapont J. Sirintrapun, MD, Kim R. Geisinger, MD, Adela Cimic, MD, Anthony Snow, MD, Jill Hagenkord, MD, Federico Monzon, MD, Benjamin L. Legendre Jr, PhD, Anatole Ghazalpour, PhD, Ryan P. Bender, PhD, and Zoran Gatalica, MD, DSc*

*Medicine* • Volume 93, Number 15, October 2014

- 74 year-old man
- 11 cm right renal mass
- Enlarged aortocaval lymph nodes
- Lung nodules
- "Oncocytic carcinoma"
  - 30% bland oncocytoma-like
  - No genomic changes in the bland area
  - 17p loss in carcinoma area (FLN –BHD)

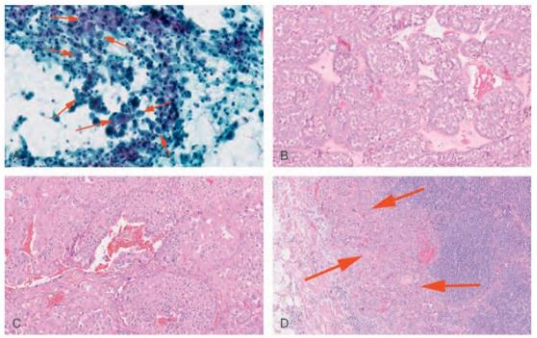



FIGURE 1. (A) FNA of the aortocaval lymph node (20× objective). (B) Benign oncocytoma-like region of the renal tumor (20× objective). (C) High-grade oncocytic carcinoma region of the renal tumor (20× objective). (D) Aortocaval lymph node with metastatic tumor (10× objective). FNA = fine needle aspirate.

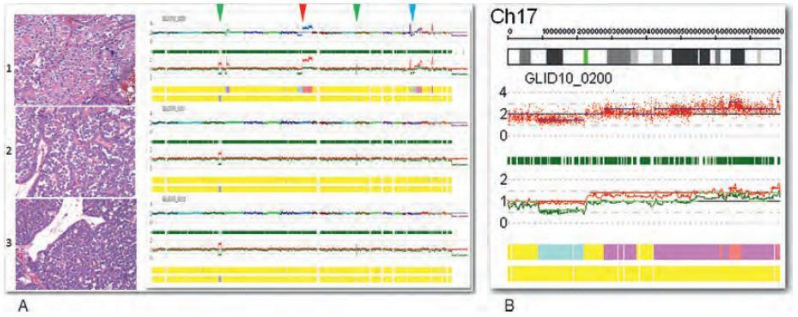



FIGURE 2. (A) Virtual karyotype using SNP-based array analysis. (B) Magnification of the heterozygous deletion in 17p that houses FLCN at 17p11.2. FLCN = folliculin (Birt–Hogg–Dubé protein).

# Case 5

55 year-old male, 2.8 cm incidentally found left renal mass

“Clear cell” renal cell carcinoma……

not so clear anymore

# Renal Tumours With Clear Cytoplasm

- Conventional clear cell RCC
- Papillary RCC with “clear cell” areas
- Clear cell papillary RCC
- Chromophobe RCC
- Epithelioid angiomyolipoma
- MiTF-associated RCC (Xp11/TFE3, TFEB)

# ISUP Panel: Tumours With Clear Cells/Papillary Components

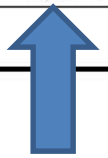
**TABLE 2.** Tumors Composed Predominantly of "Clear" Cells

| Tumor Type | CA IX | CK7 | CD117 | Cathepsin-K | HMB-45 |
|---|---|---|---|---|---|
| Clear cell RCC | Positive, diffuse membranous | Negative | Negative | Negative | Negative |
| Clear cell PRCC | Positive, cup-like | Positive | Negative | Negative | Negative |
| Chromophobe RCC, classic | Negative | Positive, cytoplasmic | Positive, membranous | Negative | Negative |
| Epithelioid-AML | Negative | Negative | Negative | Positive, cytoplasmic | Positive, cytoplasmic |
| MiTF-TFE tumors | | | | | |
| Xp11 family | Variable but focal | Negative | Variable | Positive (50%), cytoplasmic | Negative |
| t(6;11) | Variable but focal | Negative | Negative | Positive, cytoplasmic | Positive (always focal) |

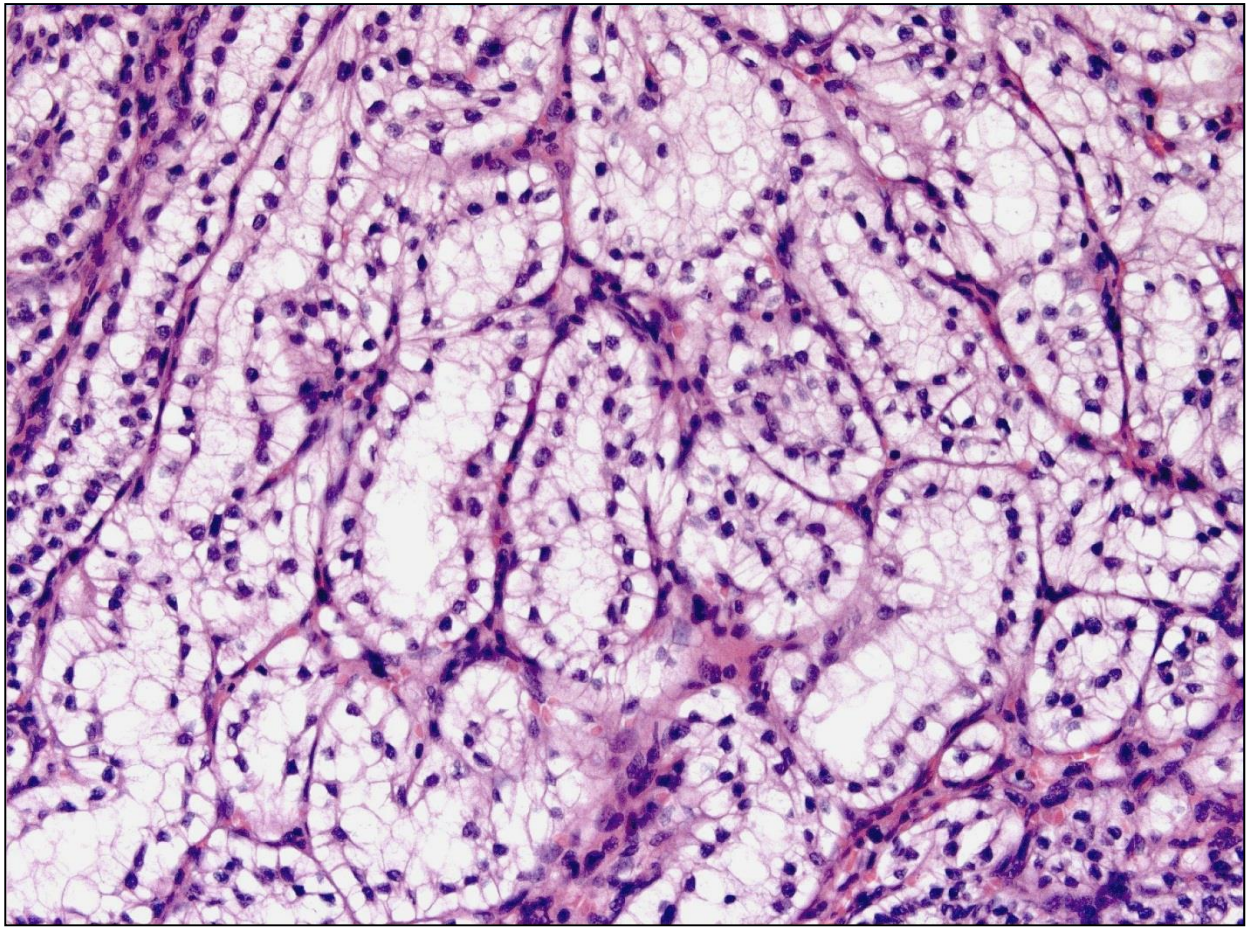
**TABLE 3.** Tumors With a Significant Papillary Component

| | CAIX | CK7 | AMACR | Cathepsin-K | 34βE12 | TFE3/TFEB |
|---|---|---|---|---|---|---|
| ccRCC with papillary growth | Positive, membranous | Negative | Negative | Negative | Negative | Negative |
| PRCC "type I" | Negative | Positive | Positive | Negative | Negative | Negative |
| PRCC "type II" | Negative | ± Positive | Positive | Negative | Negative | Negative |
| Clear cell PRCC | Positive, cup-like | Positive, diffuse | Negative | Negative | Negative | Negative |
| MiTF-TFE trans-assoc | Variable but focal | Negative | Positive | Positive (50%) | Negative | Positive* |

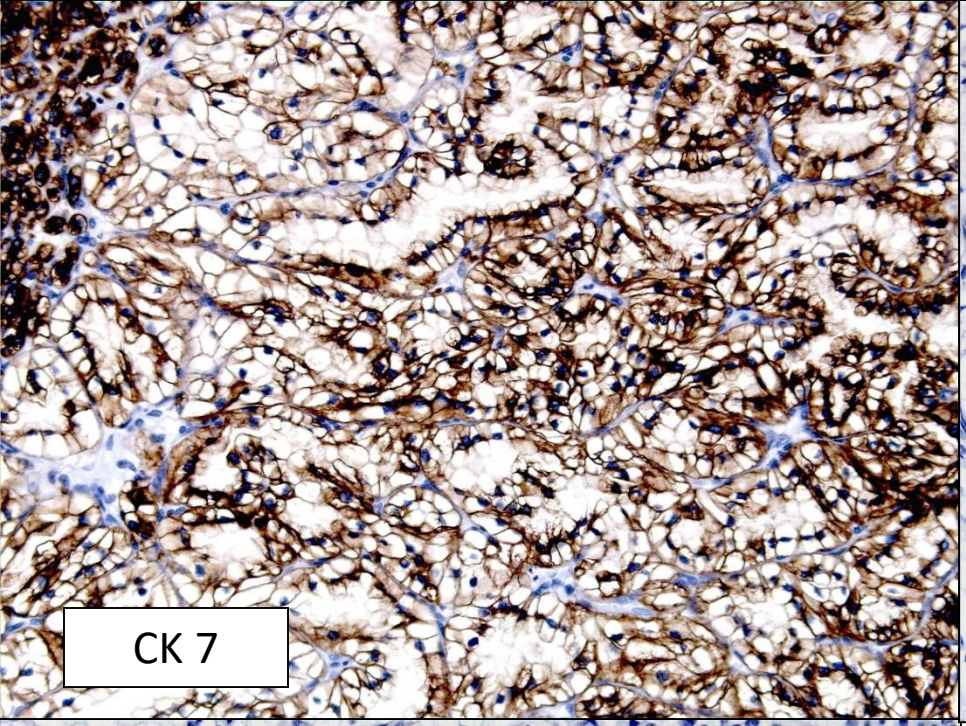
*Antibodies are difficult to standardize on automated platforms. FISH assays are more reliable.

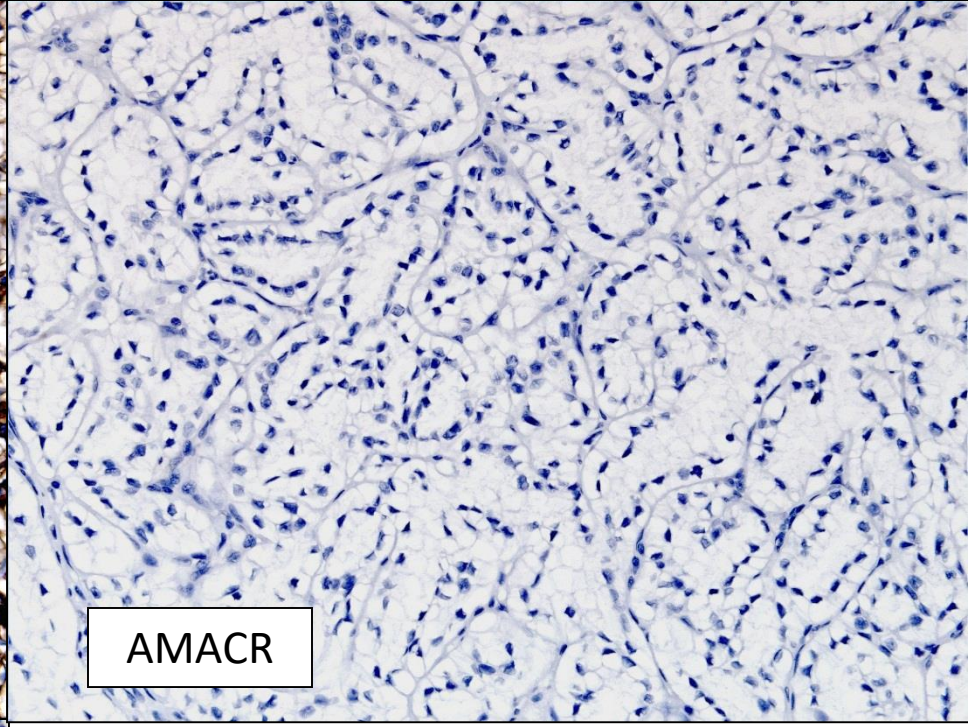


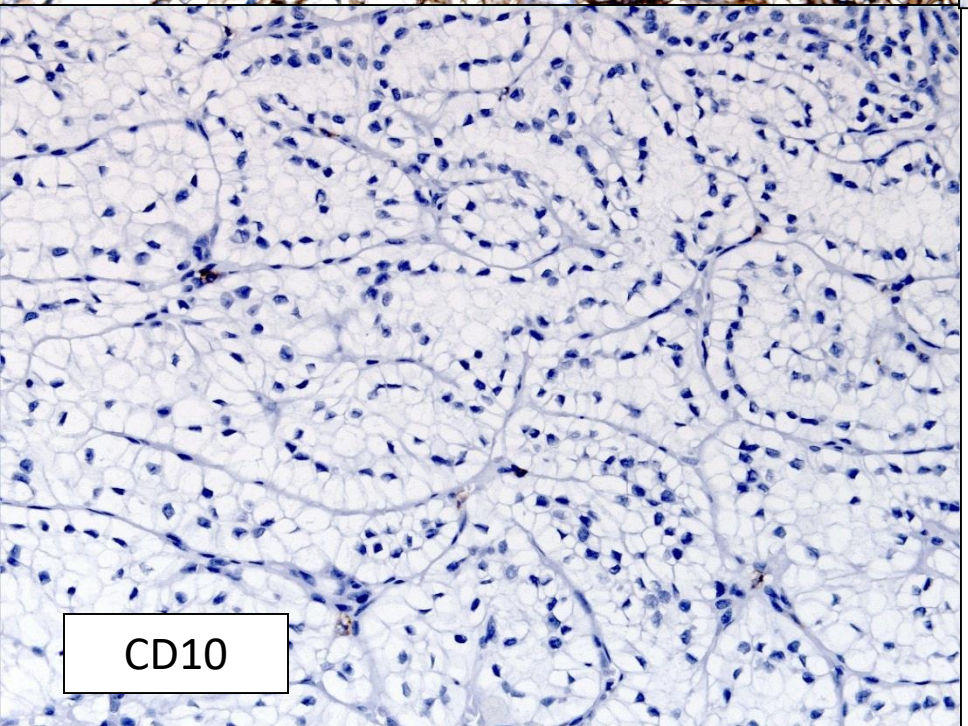
# Clear Cell Papillary RCC



- Tubulopapillary
- Clear cytoplasm
- **Apically oriented nuclei**

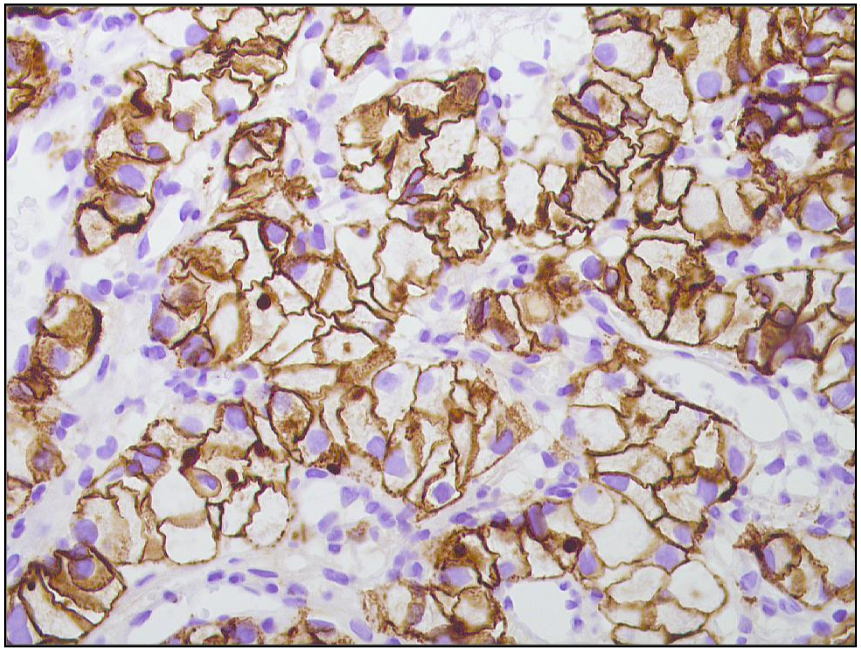


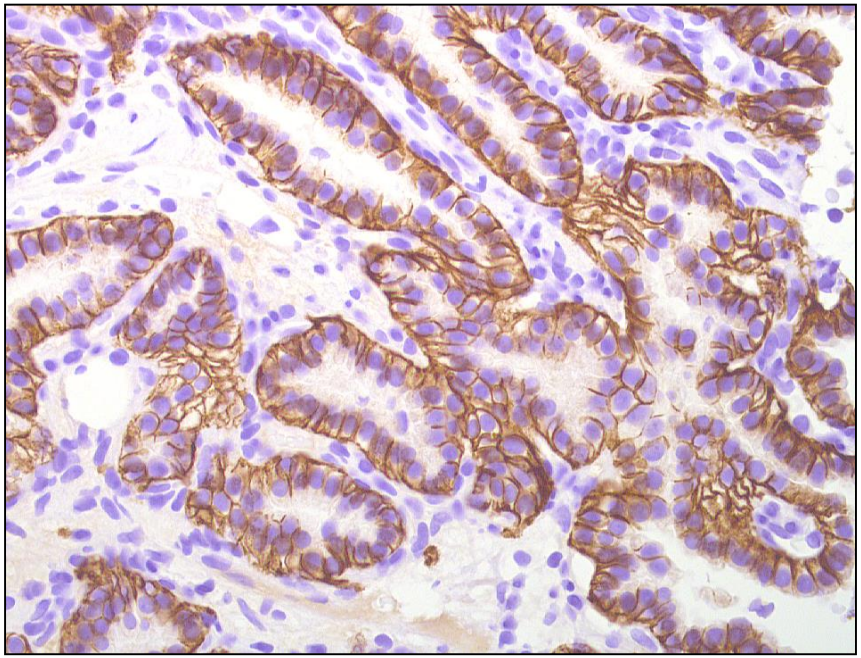

# Clear Cell Papillary RCC

# CAIX



**Complete Membranous**
Conventional clear cell RCC

*Beware of false positive staining adjacent to necrosis*



**“Cup-like” Membranous**
Clear cell papillary RCC

- CK7 +’ve
- HMWK (34βE12) +’ve
- AMACR –’ve

# Clear Cell Papillary Renal Cell Carcinoma

## *A Distinct Histopathologic and Molecular Genetic Entity*

*Stefano Gobbo, MD,*† John N. Eble, MD,* David J. Grignon, MD,* Guido Martignoni, MD,† Gregory T. MacLennan, MD,‡ Rajal B. Shah, MD,§ Shaobo Zhang, MD,* Matteo Brunelli, MD,† and Liang Cheng, MD**

*Am J Surg Pathol* • Volume 32, Number 8, August 2008

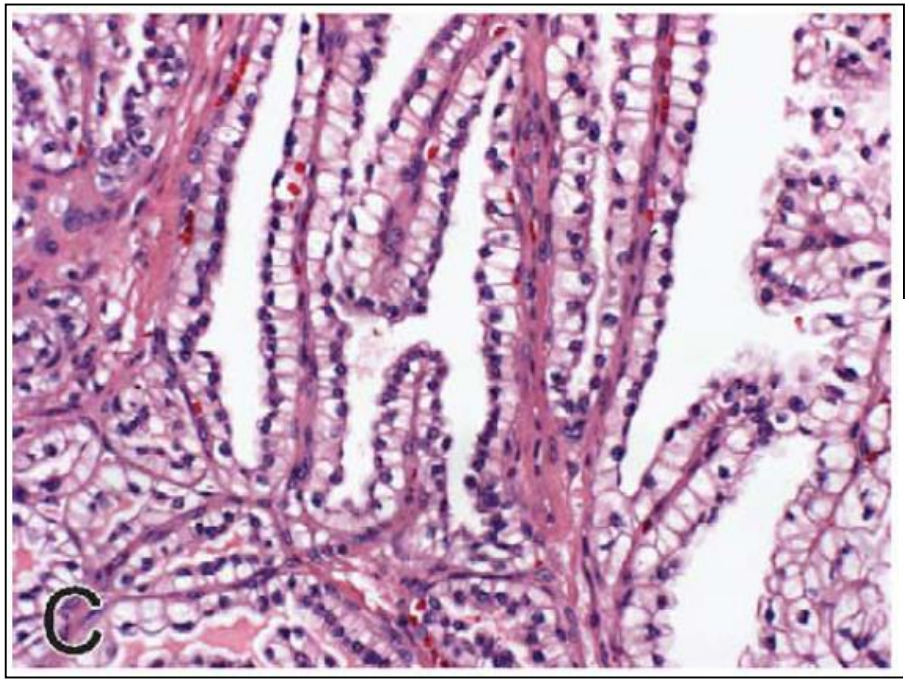



**TABLE 2.** Immunohistochemical Findings

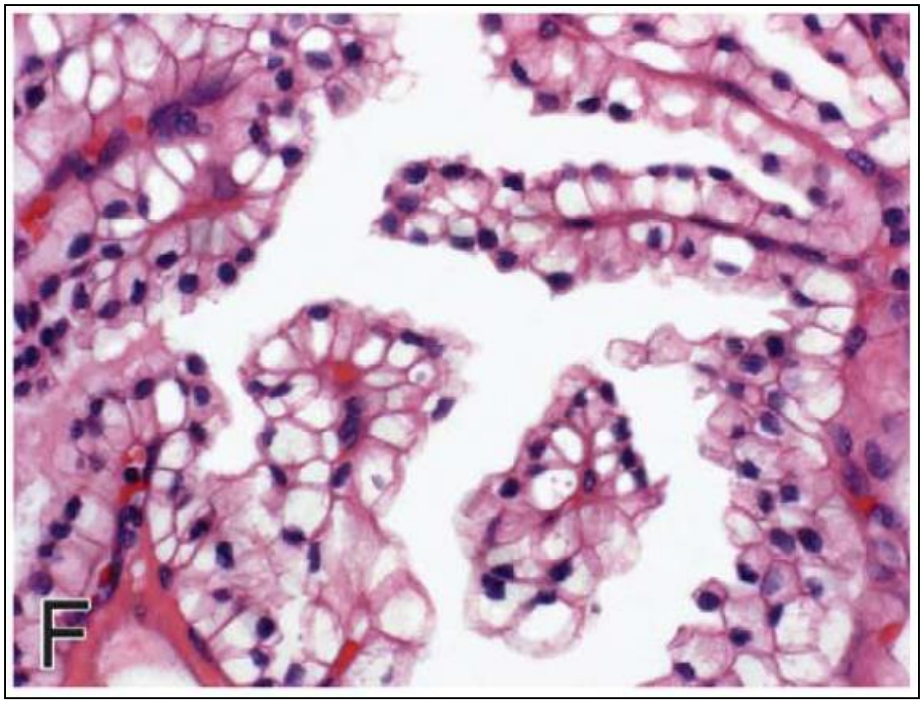
| | Antibodies | | | | |
|---|---|---|---|---|---|
| Case No. | AMACR | CA IX | CD10 | CK 7 | TFE3 |
| 1 | Neg | + + + | Neg | + + + | Neg |
| 2 | Neg | + + + | Neg | + + + | Neg |
| 3 | Neg | + + + | Neg | + + + | Neg |
| 4 | Neg | + + + | – / + | + + + | Neg |
| 5a | Neg | + + + | Neg | + + + | Neg |
| 5b | Neg | + + + | Neg | + + + | Neg |
| 5c | Neg | + + + | Neg | + + + | Neg |

Neg indicates negative; – / +, 1% to 25% positive; +, 26% to 50% positive;

**TABLE 1.** Clinicopathologic Findings

| Case No. | Age | Sex | Size (cm) | Fuhrman Grade | Stage | ESRD | Follow-up (mo) |
|---|---|---|---|---|---|---|---|
| 1 | 64 | W | 1.6 | G1 | pT1 | No | NED (24) |
| 2 | 63 | M | 2.9 | G1 | pT1 | No | NED (26)* |
| 3 | 64 | M | 4.2 | G2 | pT1 | No | NED (1) |
| 4 | 55 | M | 5 | G1 | pT1 | No | NED (48) |
| 5 | 53 | W | 0.4; 1; 1.2 | G2; G2; G2 | pT1 | Yes | NED (22) |

# Clear Cell Papillary RCC



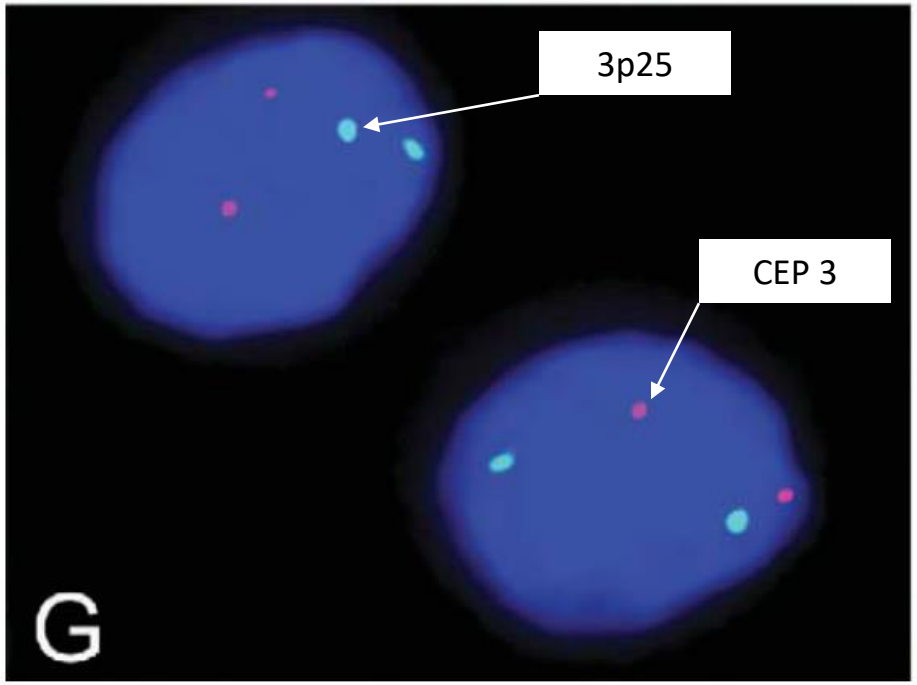




**TABLE 3.** Percentages of Nuclei With Different Numbers of Signals From Neoplastic Cells and Results for Chromosome 7, 17, and Y

| | CEP 7 | | | | CEP 17 | | | | CEP Y | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Case No. | 1 Signal (%) | 2 Signals (%) | ≥ 3 Signals (%) | Result | 1 Signal (%) | 2 Signals (%) | ≥ 3 Signals (%) | Result | 0 Signal (%) | 1 Signal (%) | Result |
| 1 | 35 | 53 | 12 | Disomic | 40 | 55 | 5 | Disomic | | | |
| 2 | 33 | 65 | 2 | Disomic | 6 | 34 | 60 | Trisomic | 10 | 90 | No loss |
| 3 | 33 | 65 | 2 | Disomic | 38 | 56 | 6 | Disomic | 22 | 78 | No loss |
| 4 | 32 | 63 | 5 | Disomic | 26 | 71 | 3 | Disomic | 18 | 82 | No loss |
| 5a | 27 | 66 | 7 | Disomic | 26 | 68 | 6 | Disomic | | | |
| 5b | 28 | 67 | 5 | Disomic | 38 | 51 | 11 | Disomic | | | |
| 5c | 38 | 59 | 3 | Disomic | 29 | 63 | 8 | Disomic | | | |