Carcinomas renales híbridos

La próxima frontera

Dr. José I. López

Servicio de Anatomía Patológica
Hospital de Cruces-Osakidetza
Universidad del País Vasco (UPV/EHU)

Conferencia pronunciada en el Hospital Marina Alta, Denia, Alicante, el 23 de Abril de 2010

CA Cancer J Clin 59: 225-249, 2009

Estimated New Cases*

Males			Females		
Prostate	192,280	25%	Breast	192,370	27%
Lung & bronchus	116,090	15%	Lung & bronchus	103,350	14%
Colon & rectum	75,590	10%	Colon & rectum	71,380	10%
Urinary bladder	52,810	7%	Uterine corpus	42,160	6%
Melanoma of the skin	39,080	5%	Non-Hodgkin lymphoma	29,990	4%
Non-Hodgkin lymphoma	35,990	5%	Melanoma of the skin	29,640	4%
Kidney & renal pelvis	35,430	5%	Thyroid	27,200	4%
Leukemia	25,630	3%	Kidney & renal pelvis	22,330	3%
Oral cavity & pharynx	25,240	3%	Ovary	21,550	3%
Pancreas	21,050	3%	Pancreas	21,420	3%
All Sites	**766,130**	**100%**	**All Sites**	**713,220**	**100%**

Estimated Deaths

Males			Females		
Lung & bronchus	88,900	30%	Lung & bronchus	70,490	26%
Prostate	27,360	9%	Breast	40,170	15%
Colon & rectum	25,240	9%	Colon & rectum	24,680	9%
Pancreas	18,030	6%	Pancreas	17,210	6%
Leukemia	12,590	4%	Ovary	14,600	5%
Liver & intrahepatic bile duct	12,090	4%	Non-Hodgkin lymphoma	9,670	4%
Esophagus	11,490	4%	Leukemia	9,280	3%
Urinary bladder	10,180	3%	Uterine Corpus	7,780	3%
Non-Hodgkin lymphoma	9,830	3%	Liver & intrahepatic bile duct	6,070	2%
Kidney & renal pelvis	8,160	3%	Brain & other nervous system	5,590	2%
All Sites	**292,540**	**100%**	**All Sites**	**269,800**	**100%**

EUROPEAN UROLOGY 49 (2006) 798–805

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Review - Kidney Cancer

2004 WHO Classification of the Renal Tumors of the Adults

Antonio Lopez-Beltran [a,*], *Marina Scarpelli* [b], *Rodolfo Montironi* [b], *Ziya Kirkali* [c]

[a] *Department of Pathology, Reina Sofia University Hospital and Cordoba University Medical School, Cordoba, Spain*
[b] *Institute of Pathological Anatomy and Histopathology, Polytechnic University of the Marche Region, Ancona, Italy*
[c] *Department of Urology, Dokuz Eylul University School of Medicine Izmir, Turkey*

Table 1 – WHO classification of kidney tumors [1]

- Familial renal cancer
  - Renal cell tumors
    - Malignant
      - Clear cell renal cell carcinoma
      - Multilocular clear cell renal cell carcinoma
      - Papillary renal cell carcinoma
      - Chromophobe renal cell carcinoma
      - Carcinoma of the collecting ducts of Bellini
      - Renal medulary carcinoma
      - Xp11 translocation carcinomas
      - Carcinoma associated with neuroblastoma
      - Mucinous tubular and spindle cell carcinoma
      - Renal cell carcinoma unclassified
    - Benign
      - Papillary adenoma
      - Oncocytoma

La palabra “híbrido” en los tumores renales en el congreso USCAP 2010

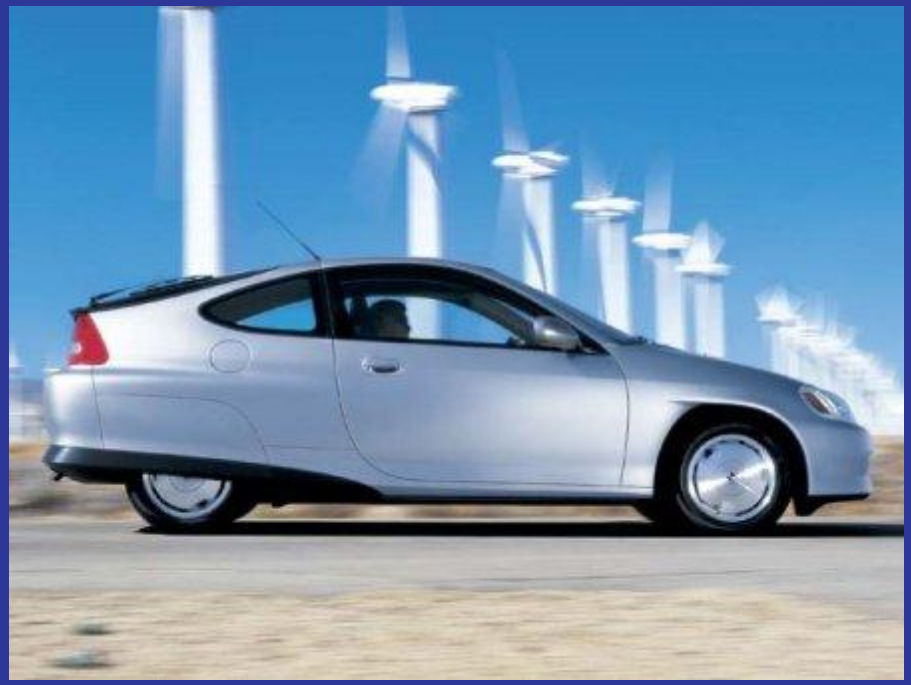
- Eisengart LJ et al. Hybrid oncocytic tumors of the kidney in patients with Birt-Hogg-Bubbe syndrome. Mod Pathol 23 (suppl 1): 188, 2010
- Hes O, et al. Sporadic hybrid oncocytic/chromophobe tumor of the kidney: A clinicopathologic, histomorphologic, immunohistochemical, ultrastructural, and molecular cytogenetic study of 14 cases. Mod Pathol 23 (suppl 1): 186, 2010
- Faraji H, et al. Renal cell carcinoma with hybrid features of conventional and chromophil cytomorphology: A fluorescent in situ hybridization study. Mod Pathol 23 (suppl 1): 191, 2010

Significado de “híbrido”

DEFINICIÓN (RAE)

“Se dice de todo lo que es producto de elementos de distinta naturaleza”

- **indefinido**
- **heterogéneo**
- **impredecible**
- **confuso**
- **inútil**

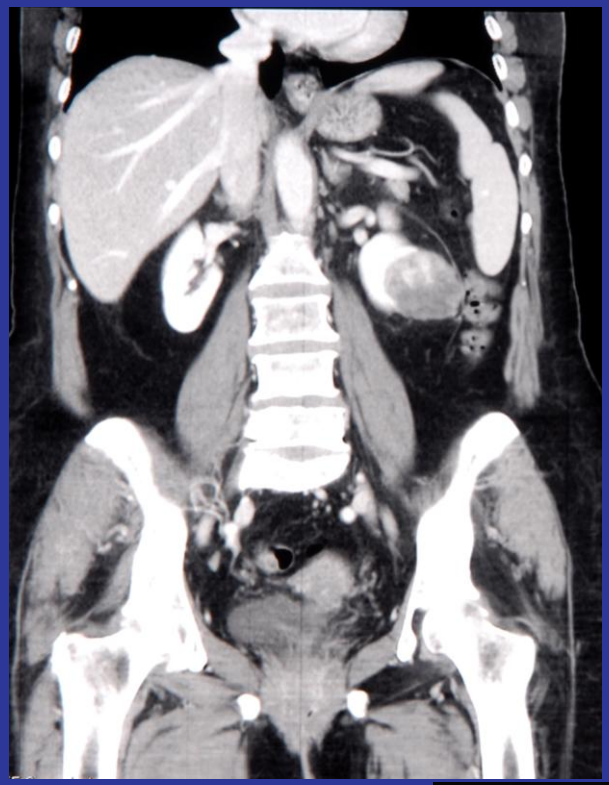


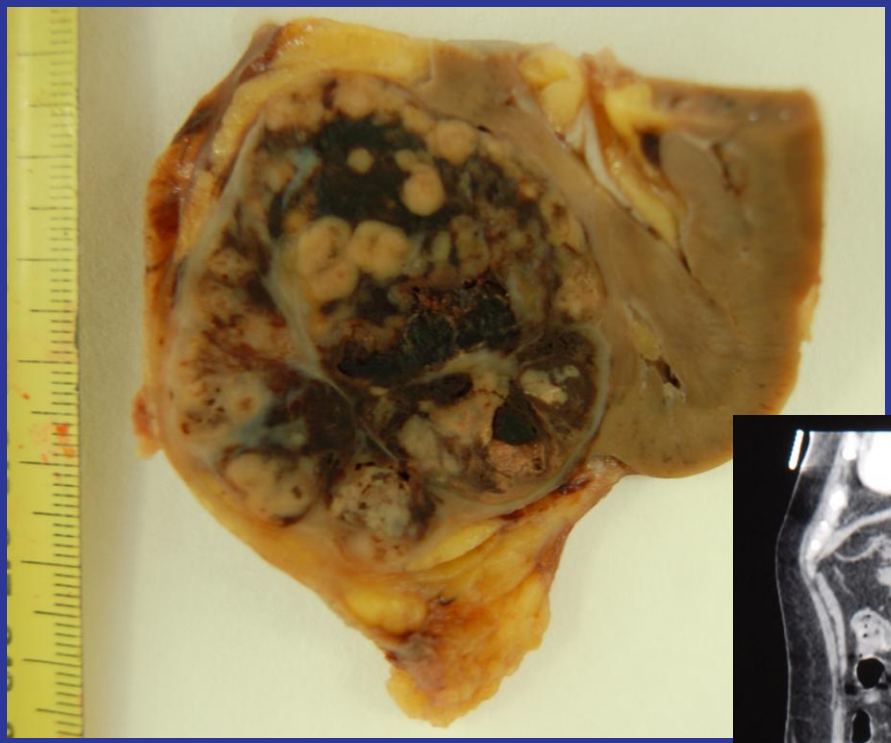
Información intraoperatoria
Tipificación histológica
Grado
Estadificación
Información molecular
Pronóstico

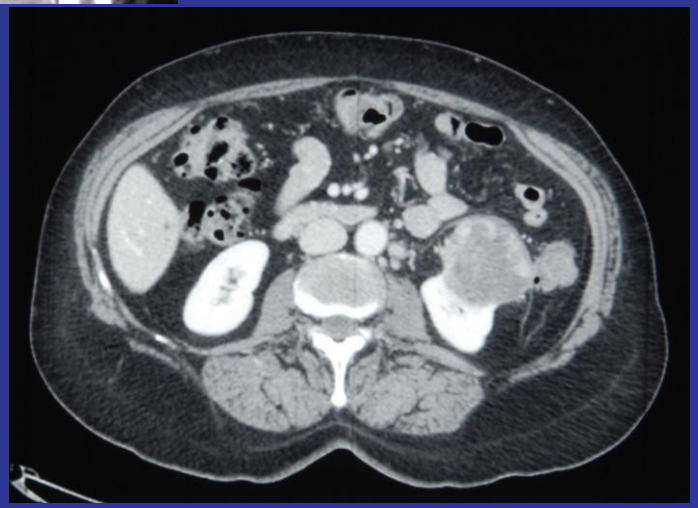
¿Qué tumor es éste?

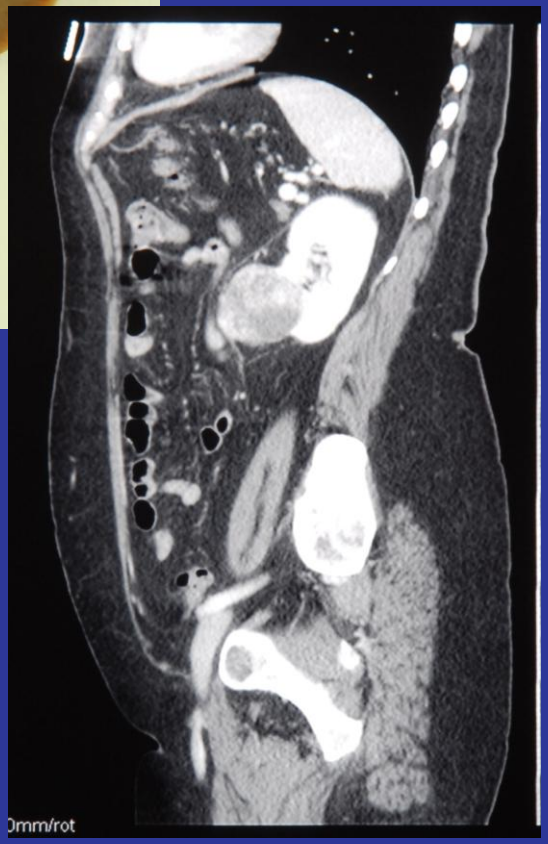
CASO 1 (09B21430)

- 62/F, asintomática.
- Masa renal izquierda (5 cm) descubierta en el estudio radiológico de seguimiento de un cáncer de mama diagnosticado 12 años antes.
- Nefrectomía laparoscópica
- Metástasis adrenal derecha
- Fallece por la enfermedad 3 meses después del diagnóstico





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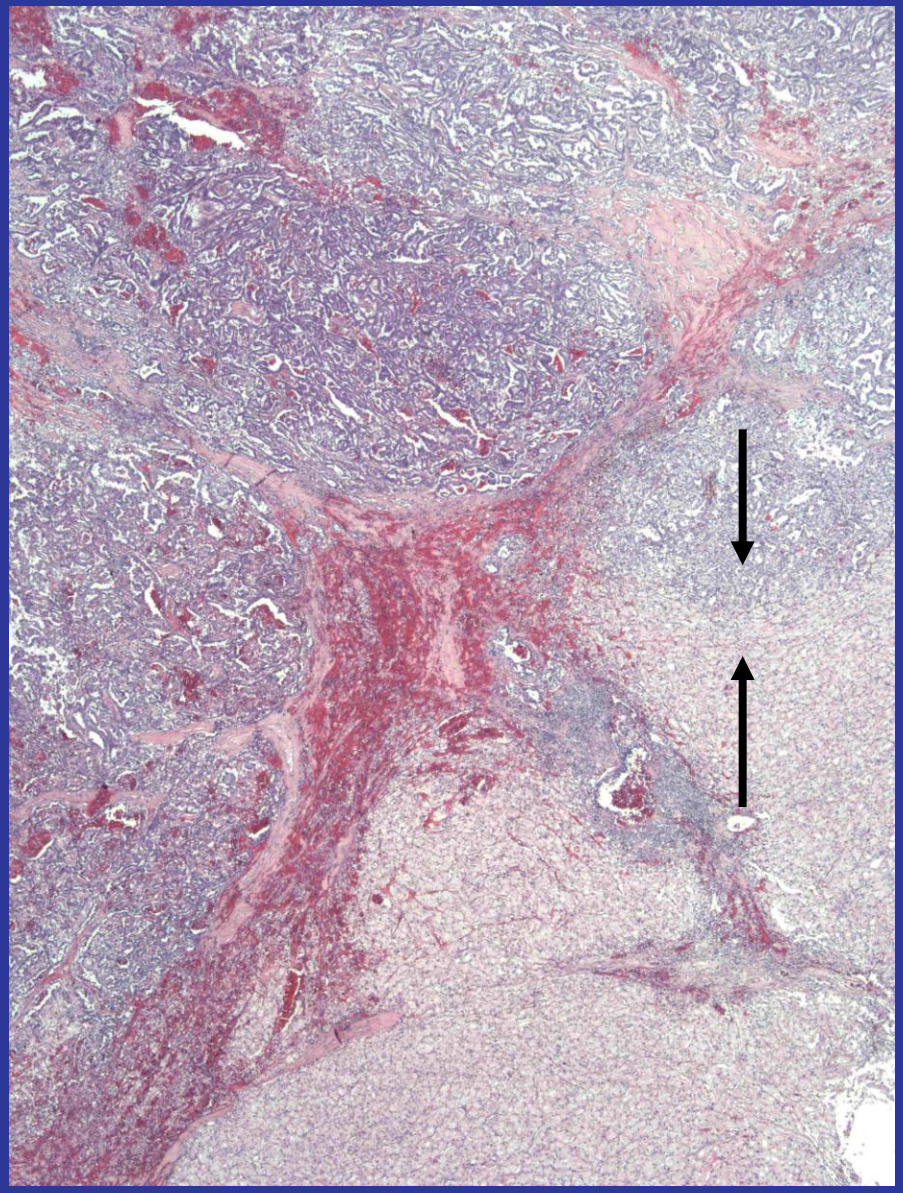
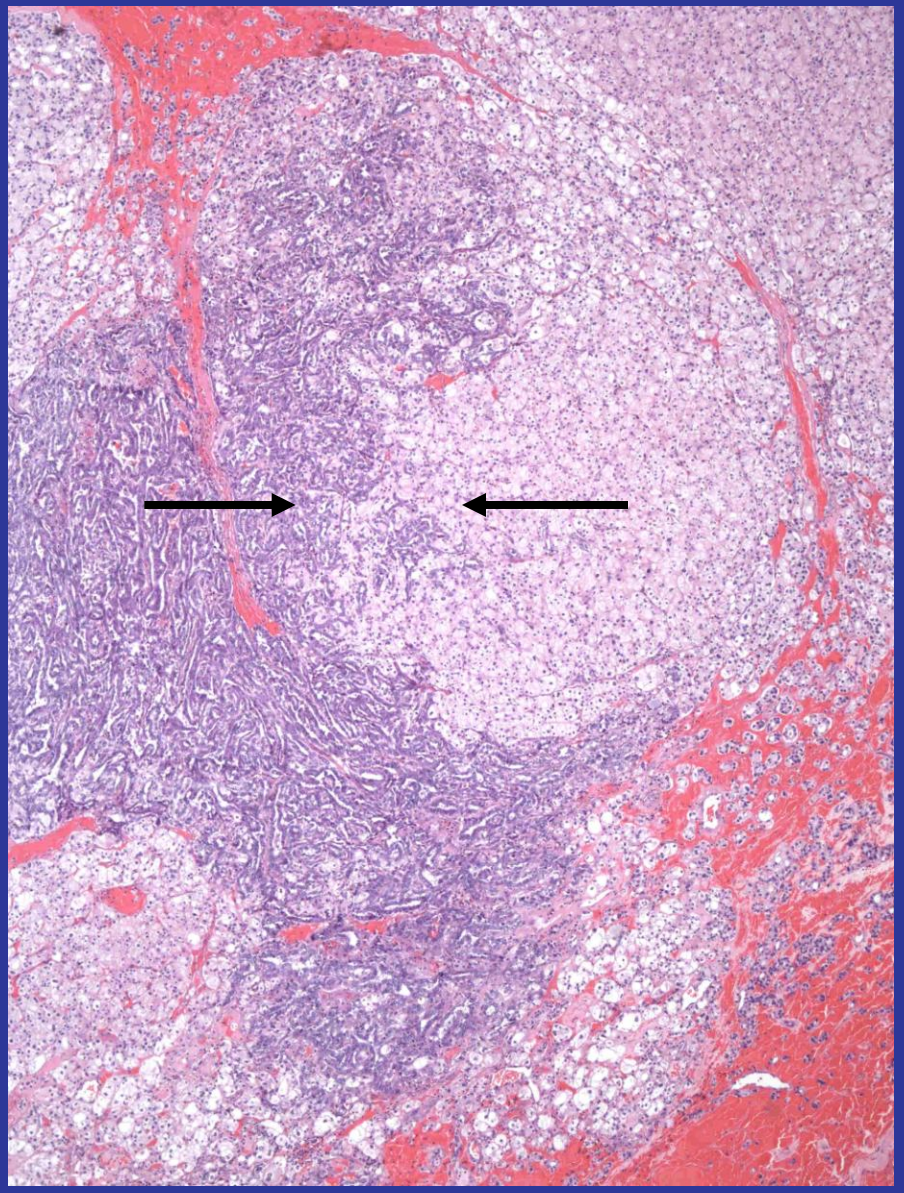
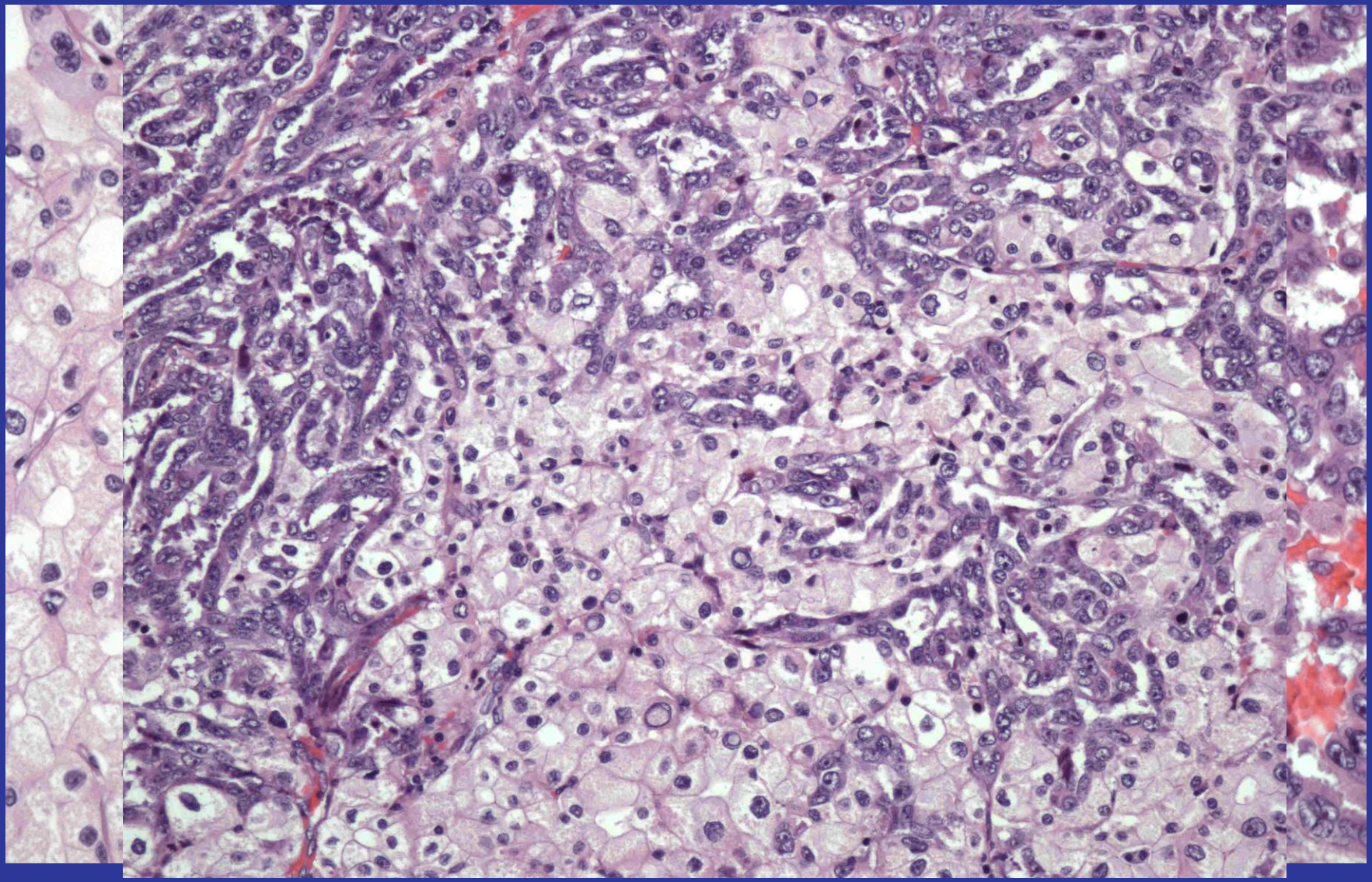
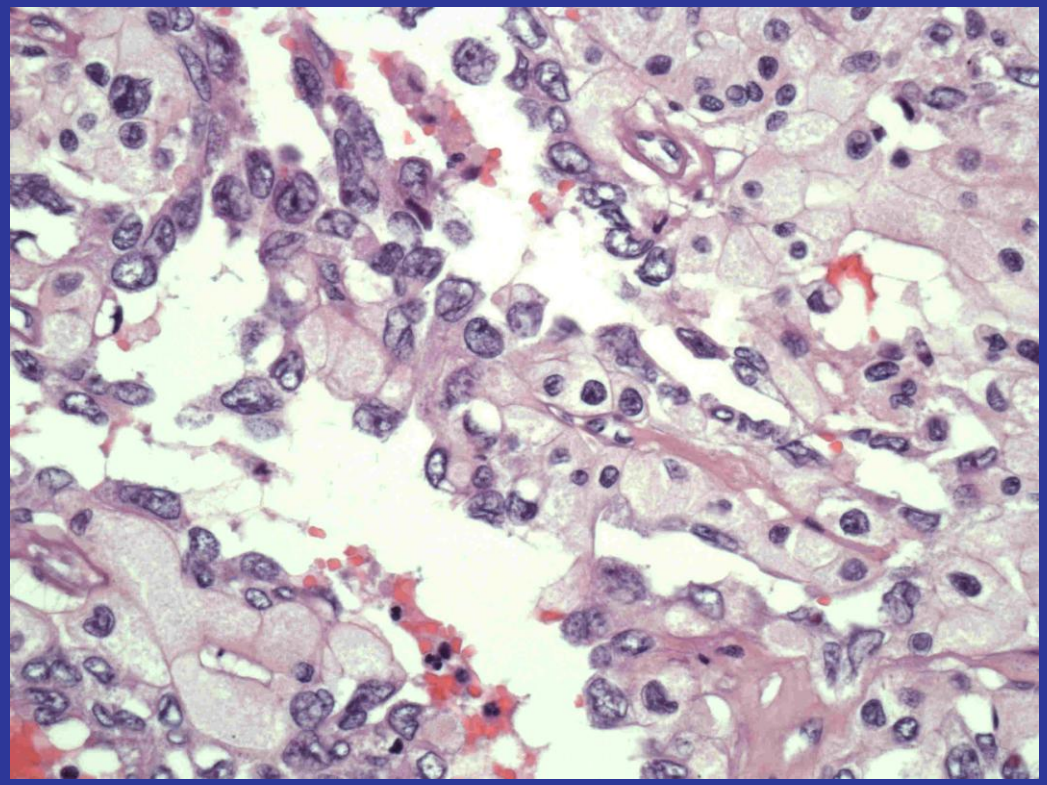


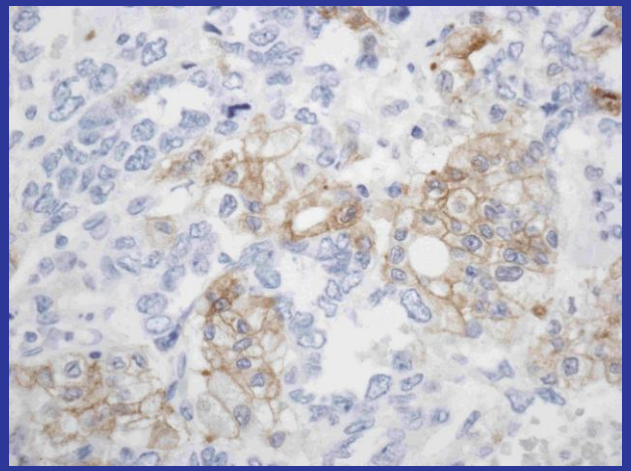


ChRCC

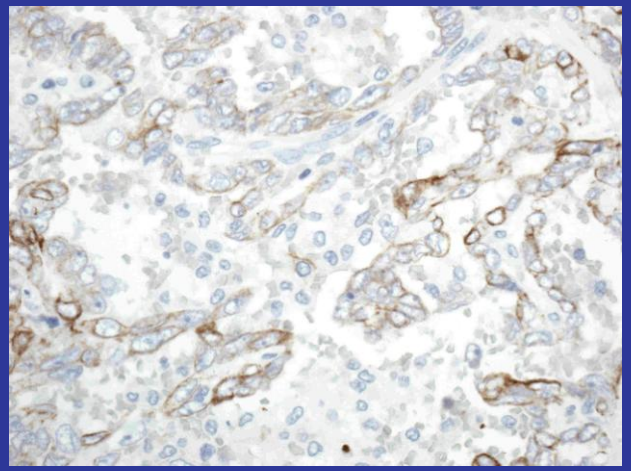
PRCC



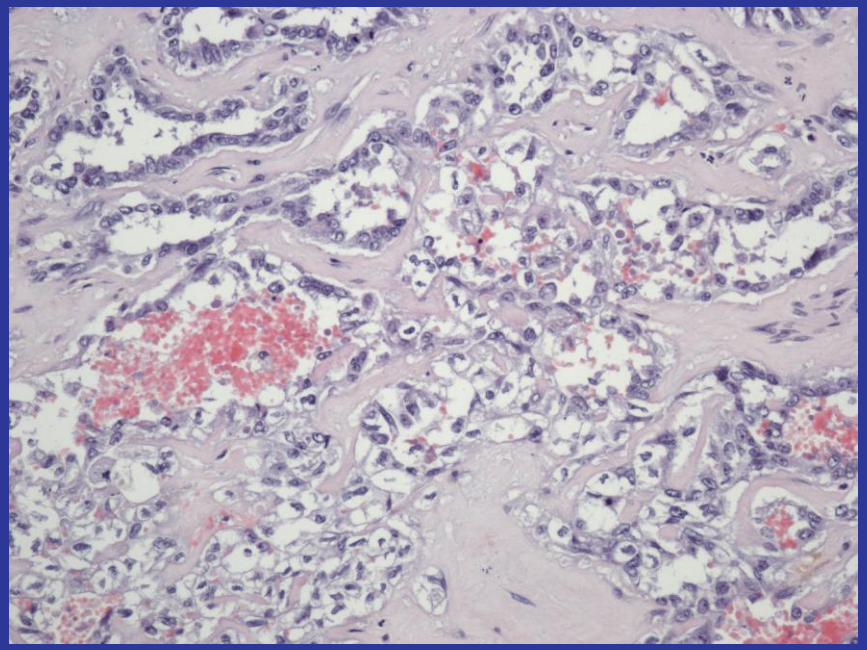


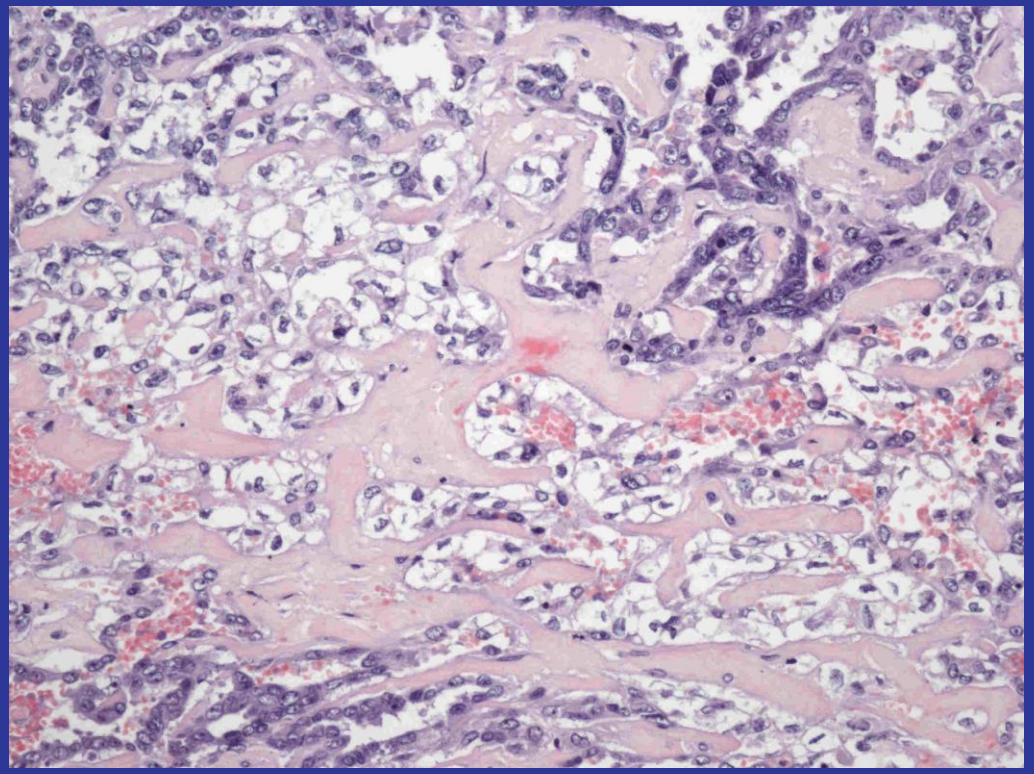


CD117



CK7





Diagnóstico Caso 1

Carcinoma de células renales mixto, papilar y cromófobo

Ca papilar/Tumor oncocítico

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Annals of Diagnostic Pathology 10 (2006) 133–139

Original Contributions

Oncocytic papillary renal cell carcinoma: a clinicopathologic, immunohistochemical, ultrastructural, and interphase cytogenetic study of 12 cases☆

Ondrej Hes, MD, PhD[a], Matteo Brunelli, MD[b], Michal Michal, MD[a,*], Paolo Cossu Rocca, MD[c], Milan Hora, MD, PhD[d], Marco Chilosi, MD[b], Michaela Mina, MD[b], Ludmila Boudova, MD, PhD[a], Fabio Menestrina, MD[b], Guido Martignoni, MD[b,c]

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Cancer Genetics and Cytogenetics 163 (2005) 81–85

Short communication

Renal oncocytoma with loss of chromosomes Y and 1 evolving to papillary carcinoma in connection with gain of chromosome 7. Coincidence or progression?

Tahseen Al-Saleem[a,*], Binaifer R. Balsara[b], Zemin Liu[b], Madelyn Feder[b], Joseph R. Testa[b], Hong Wu[a], Richard E. Greenberg[c]

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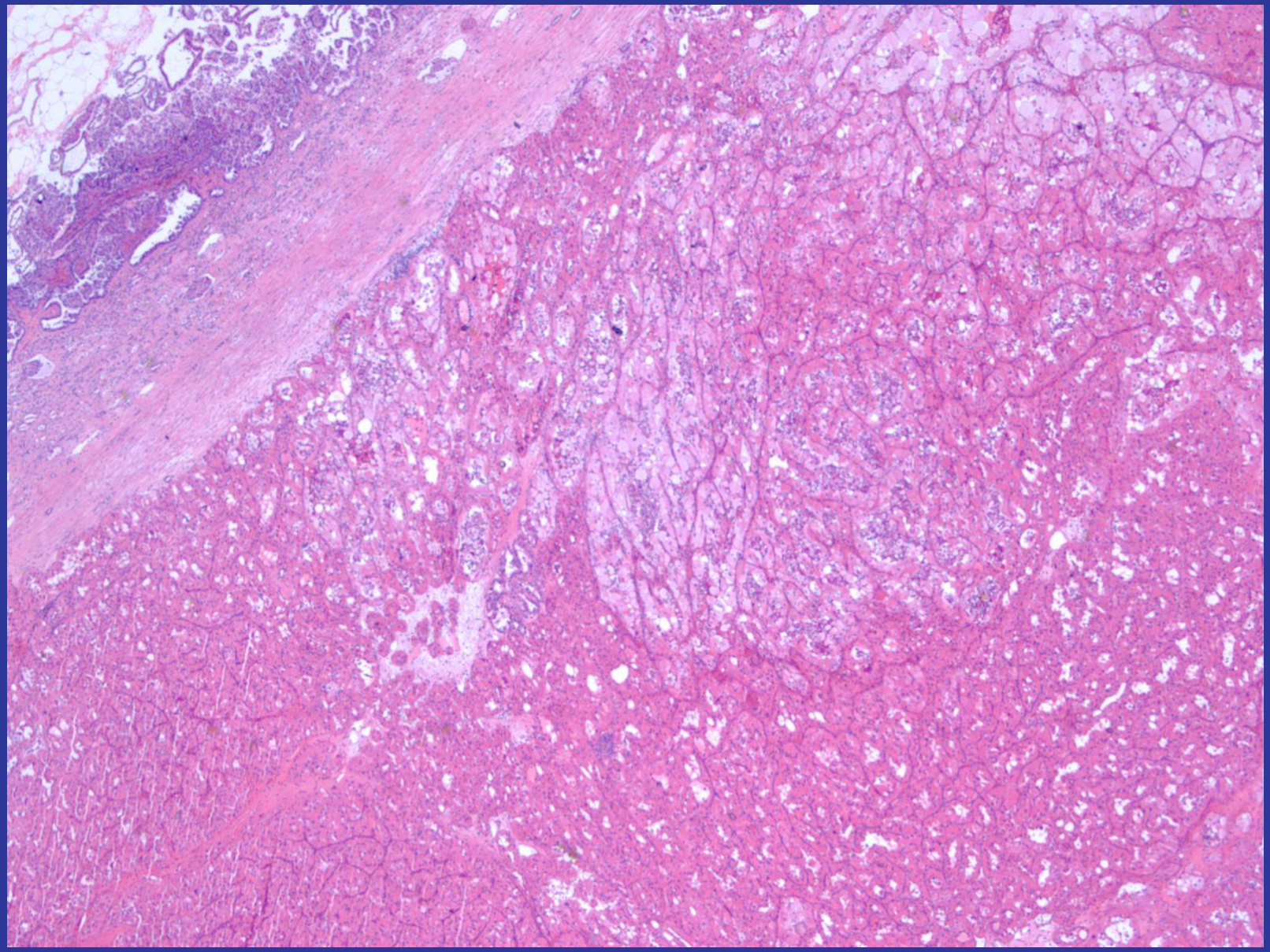
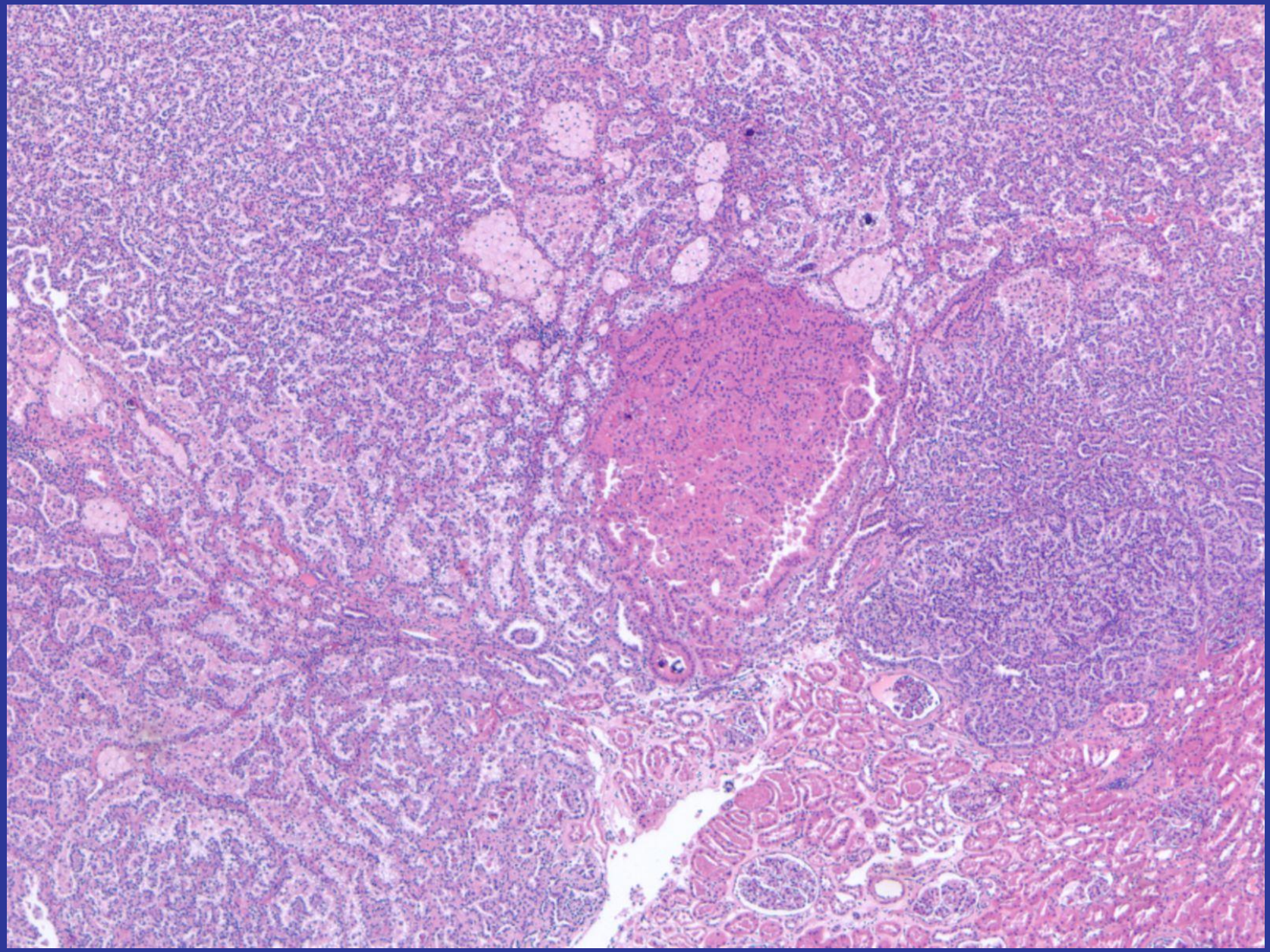
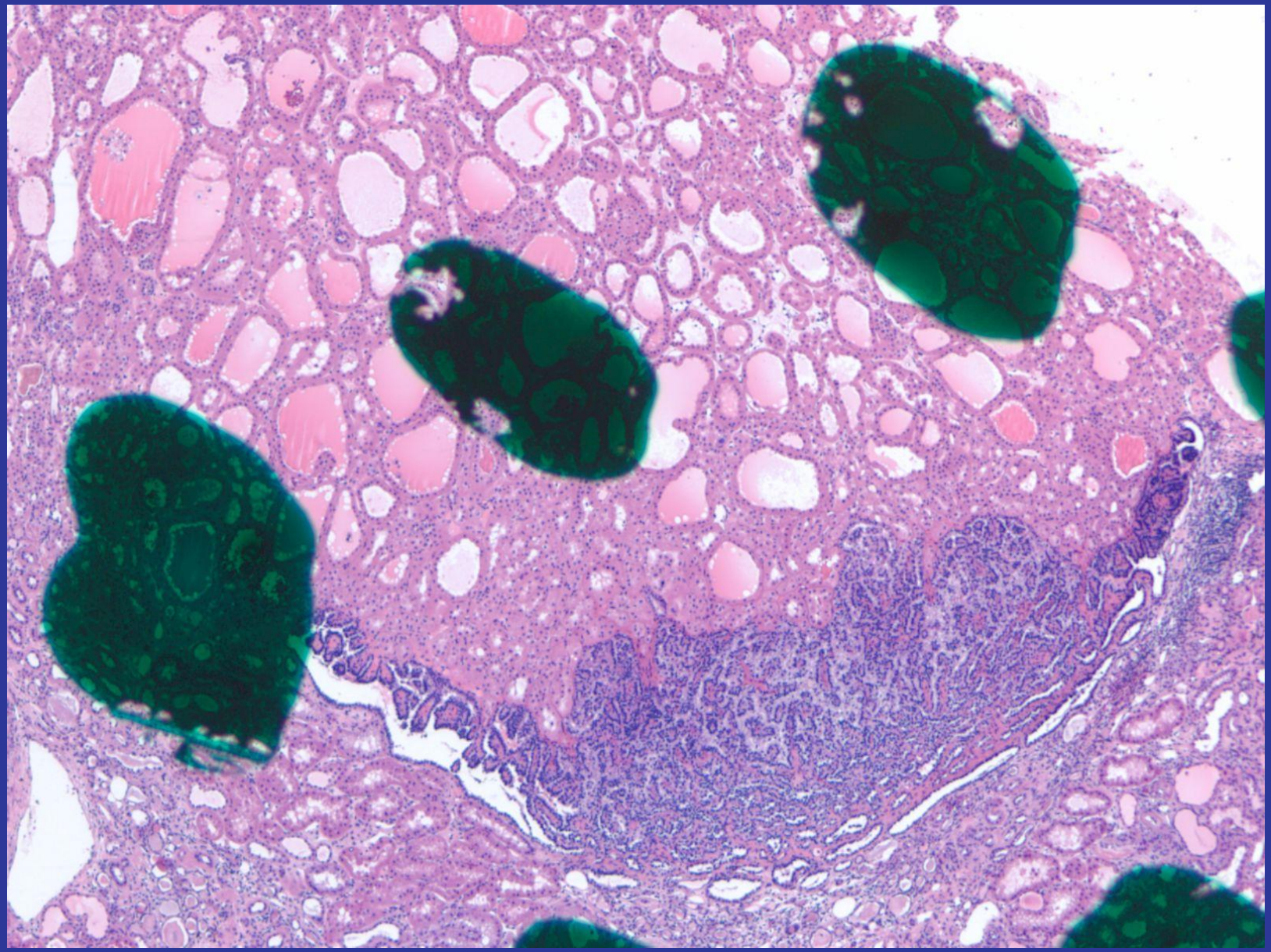
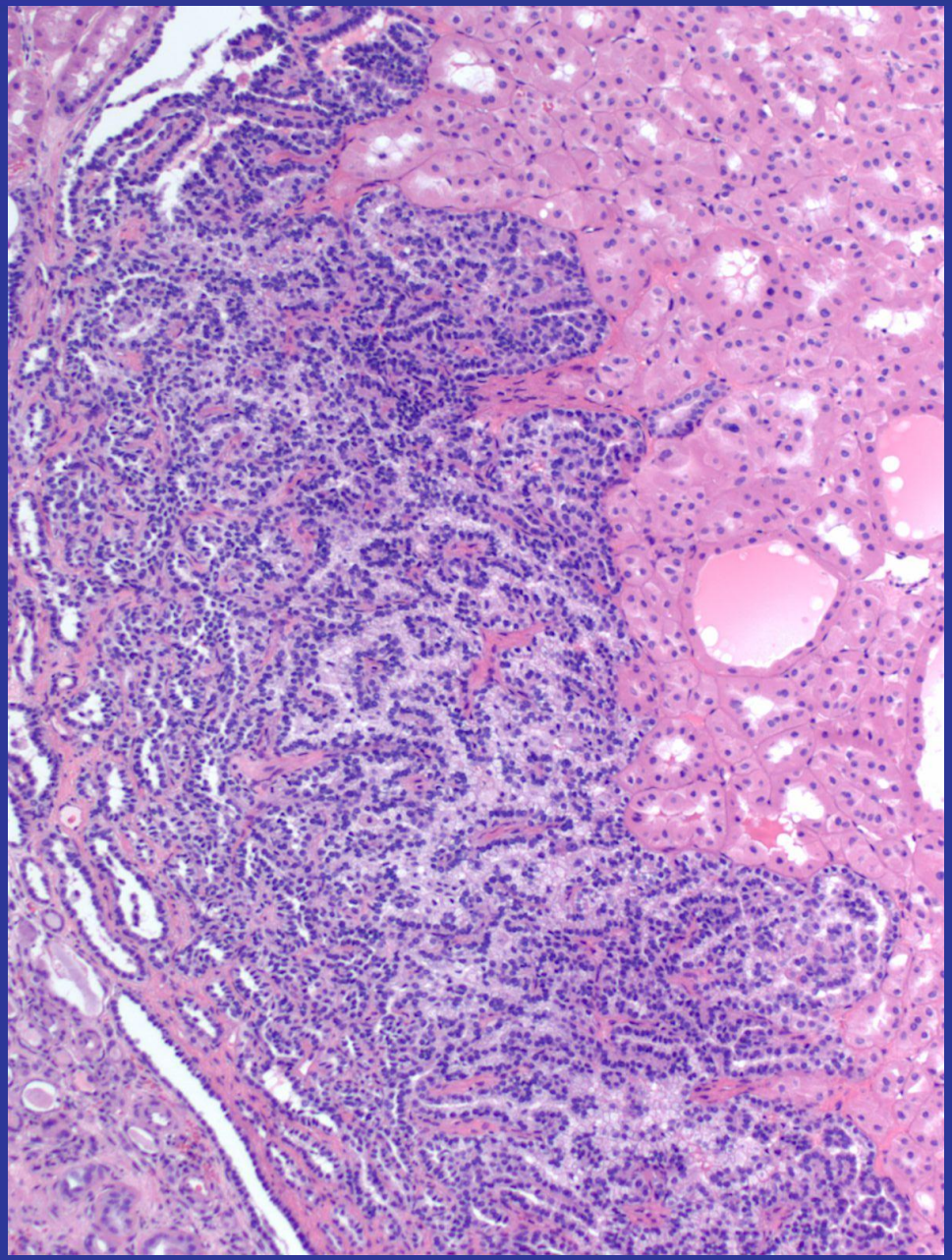
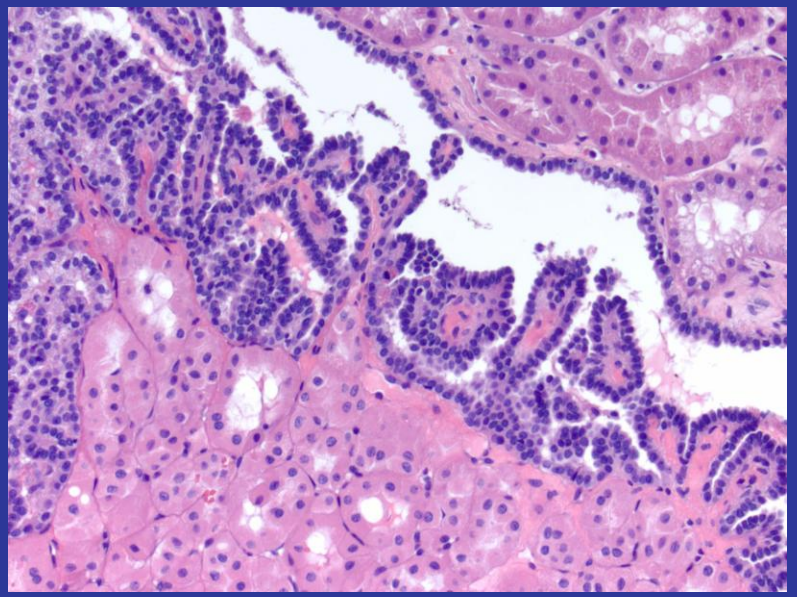
Received 22 April 2005; received in revised form 17 May 2005; accepted 24 May 2005

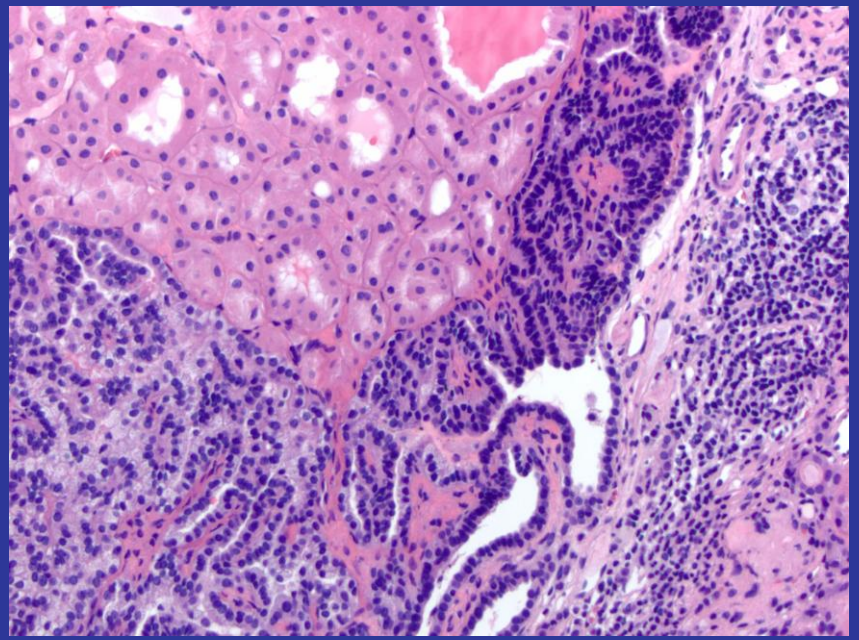


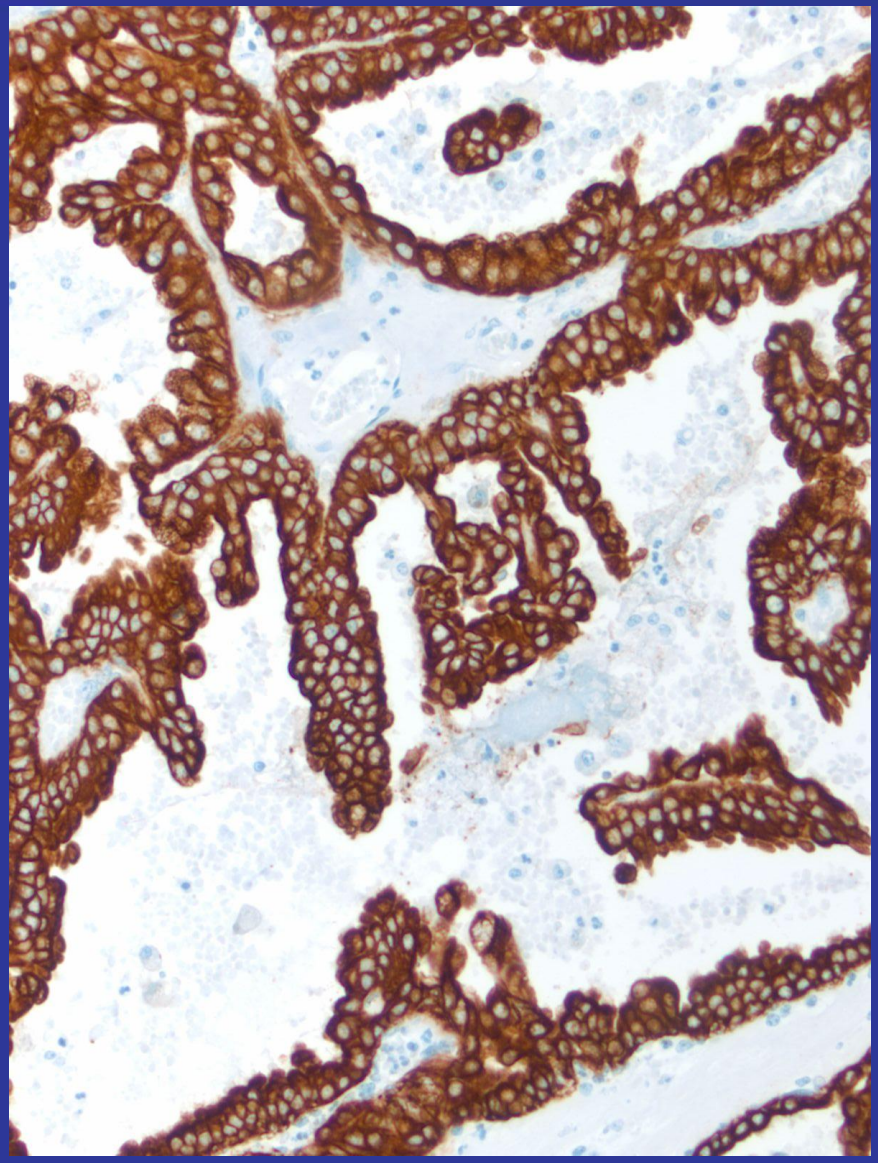






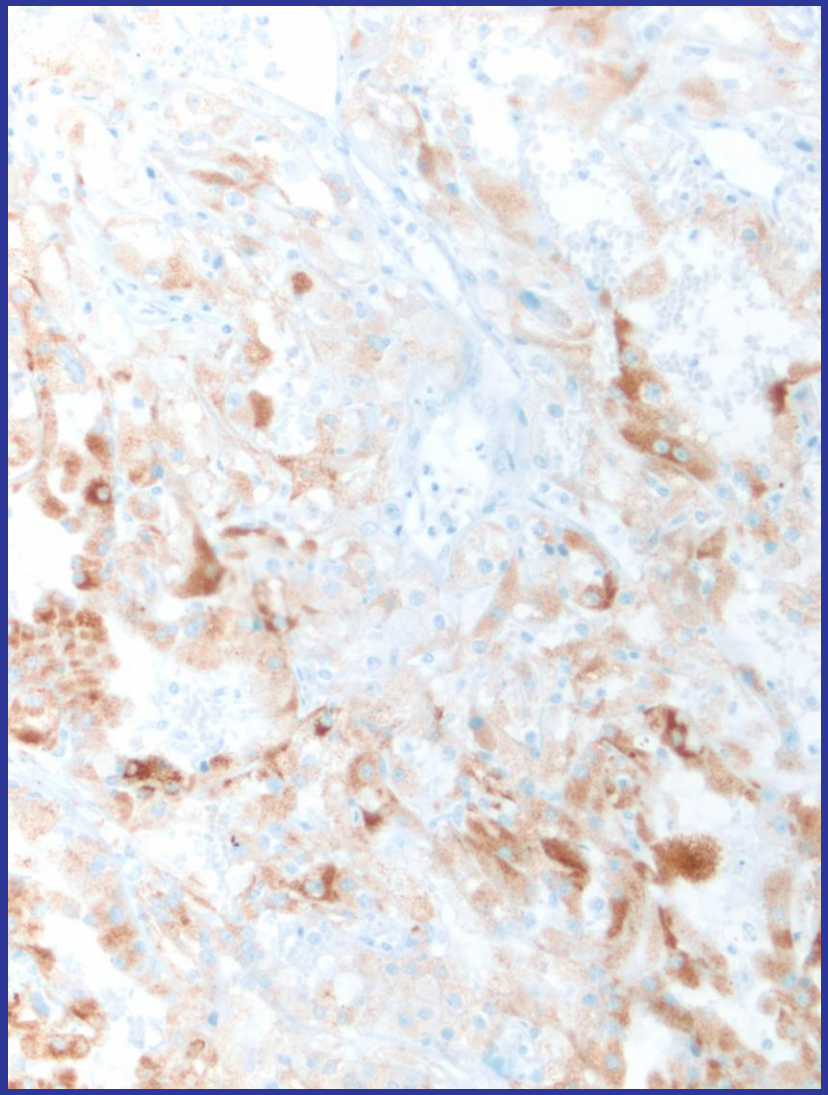


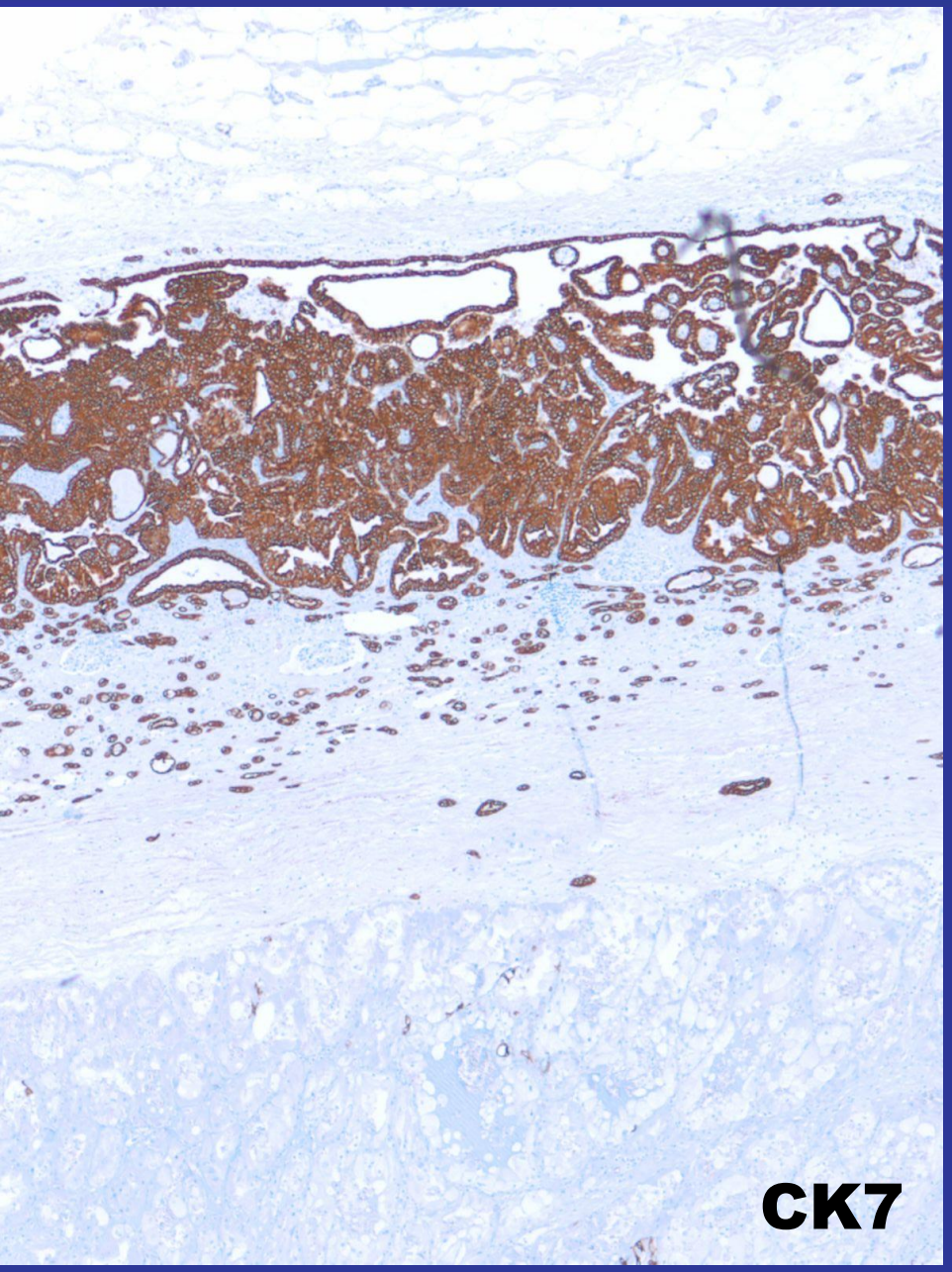


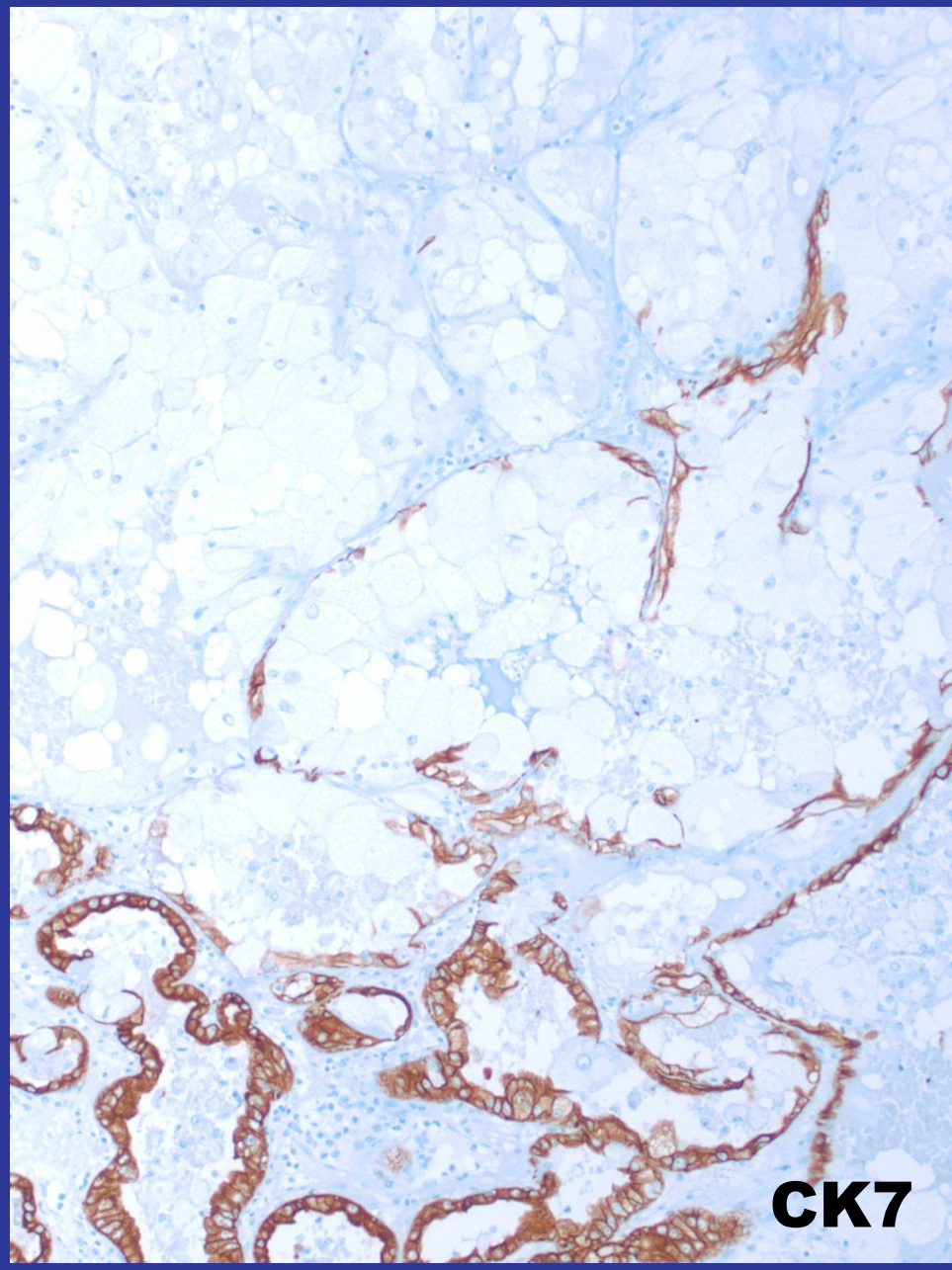


CK 7

AMACR

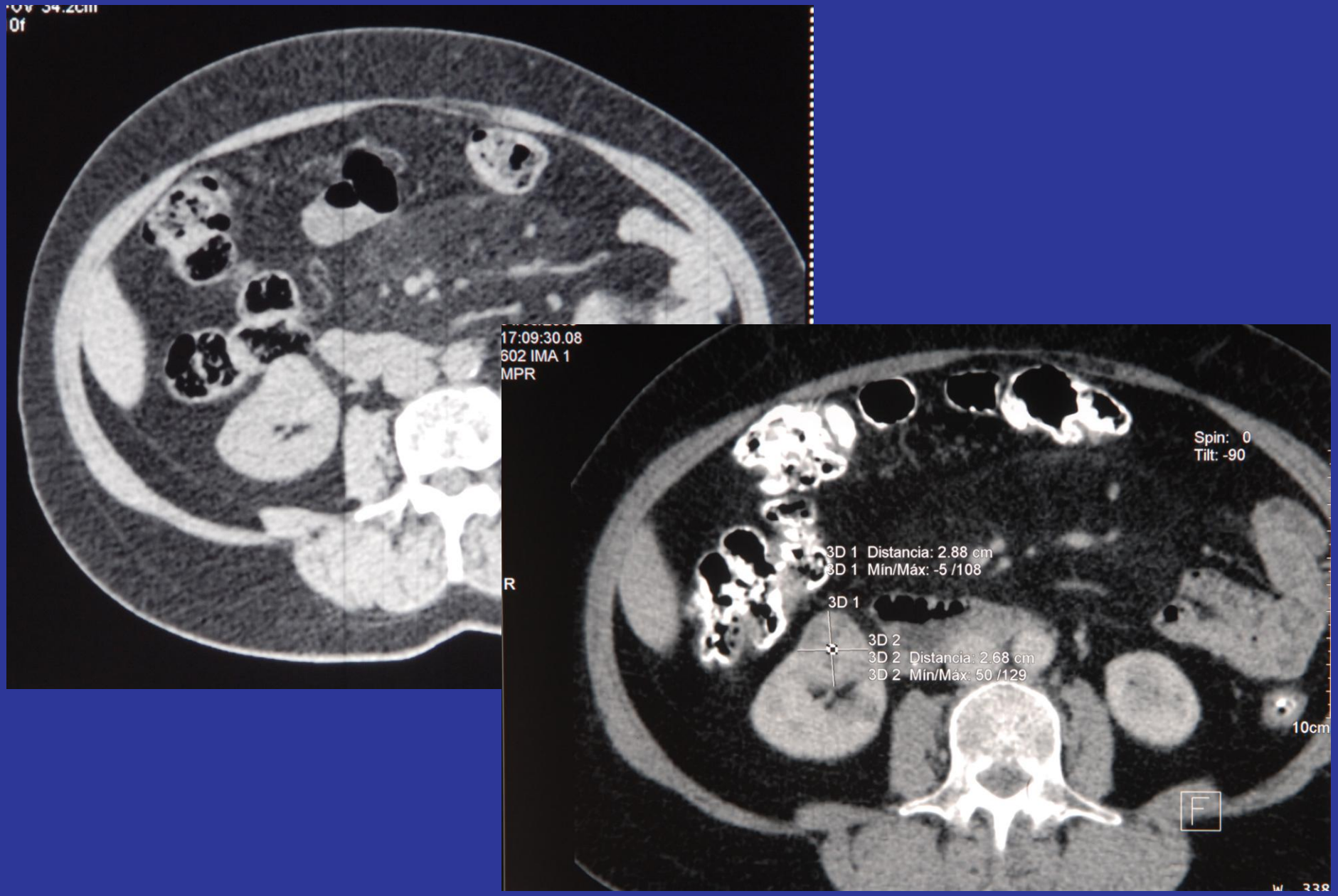



CK7


CK7

CASO 2 (09B16950)

- 65/F, con historia clínica de fibromialgia y dolor persistente en el costado.
- Masa renal derecha (2.8 cm) descubierta en el estudio radiológico de la consulta del reumatólogo.
- Libre de enfermedad 7 meses después del diagnóstico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17:09:30.08
602 IMA 1
MPR
Spin: 0
Tilt: -90
3D 1 Distancia: 2.88 cm
3D 1 Mín/Máx: -5 /108
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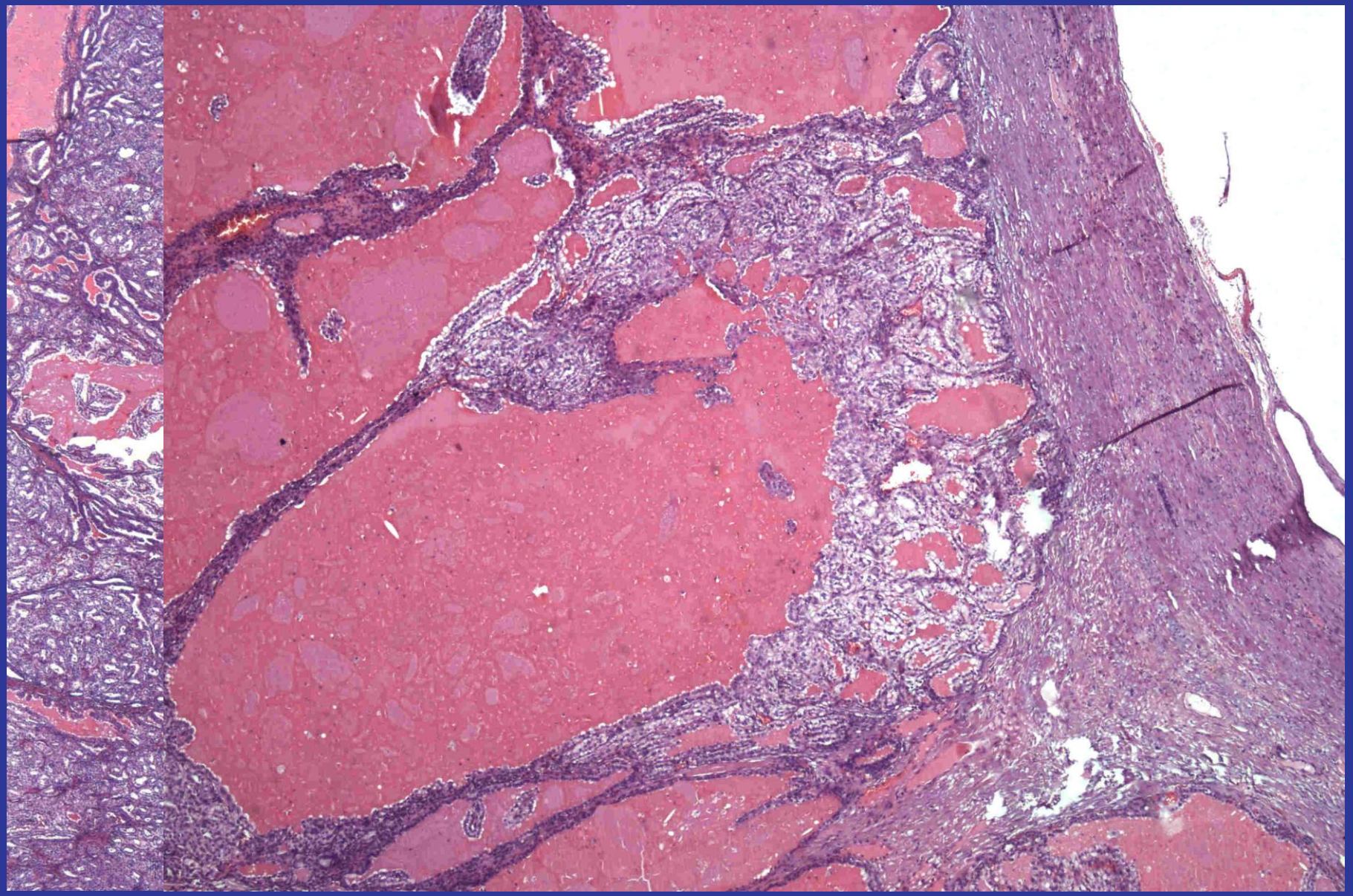
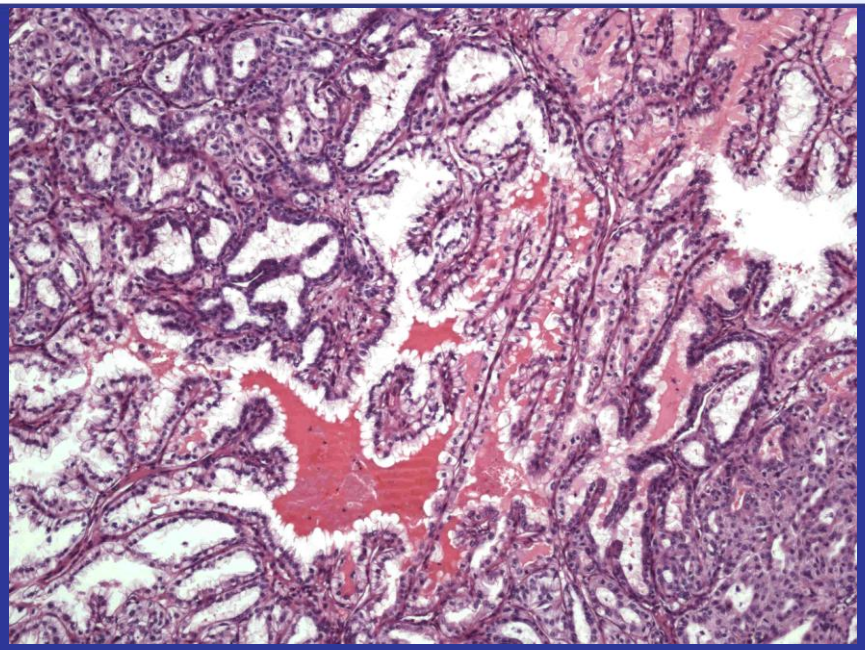
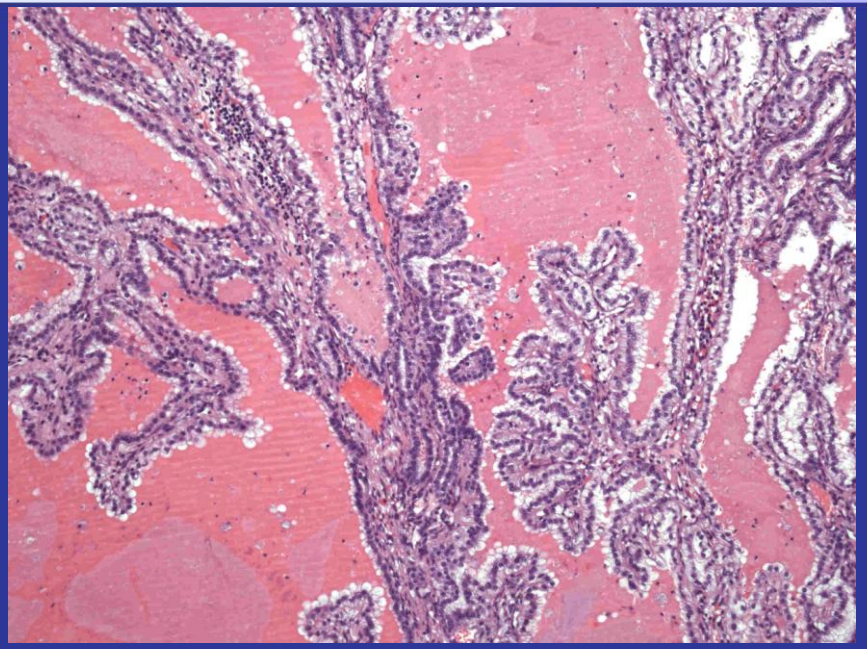
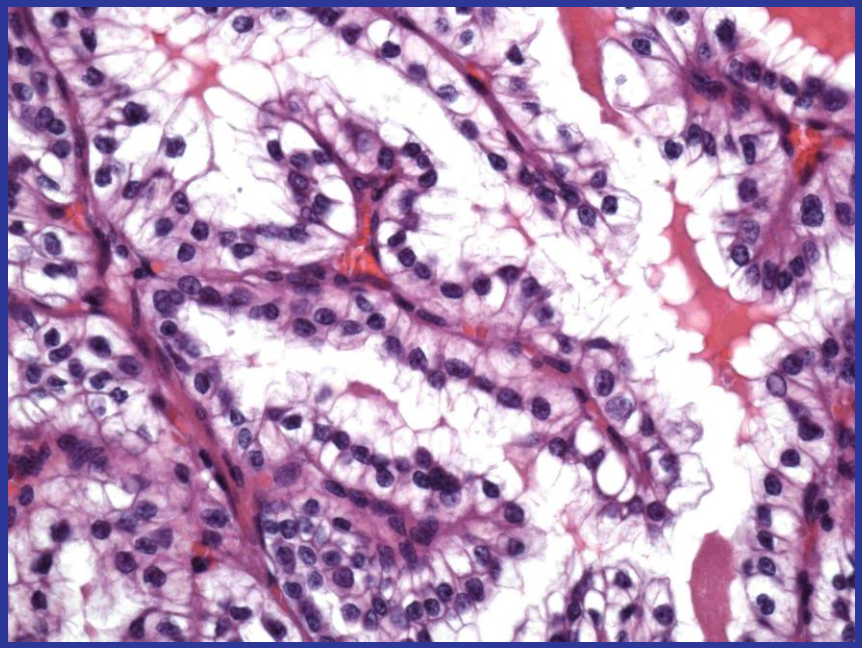
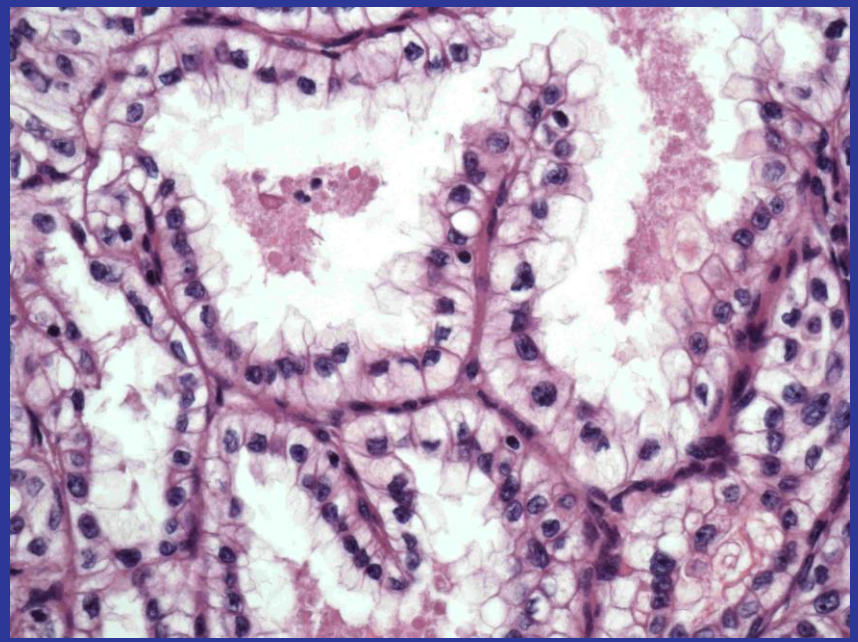
3D 1
3D 2
3D 2 Distancia: 2.68 cm
3D 2 Mín/Máx: 50 /129
10cm
F

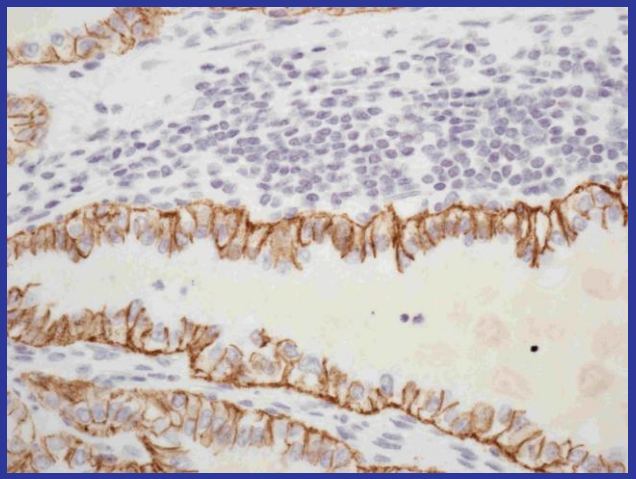




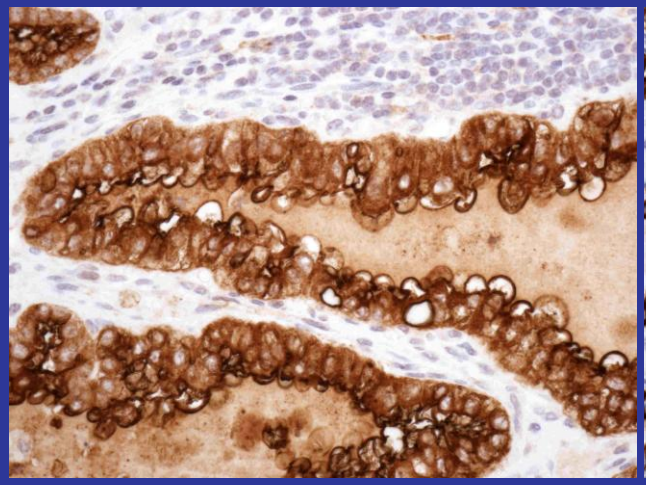




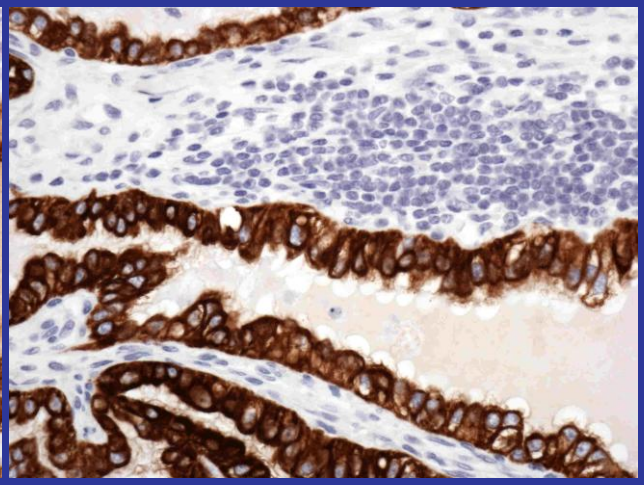




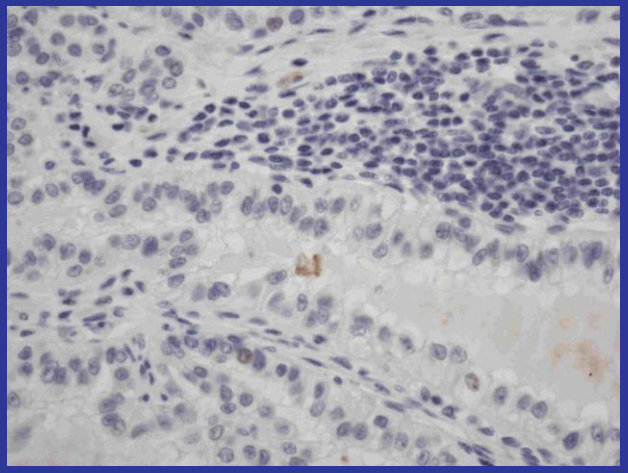
e-cadherin



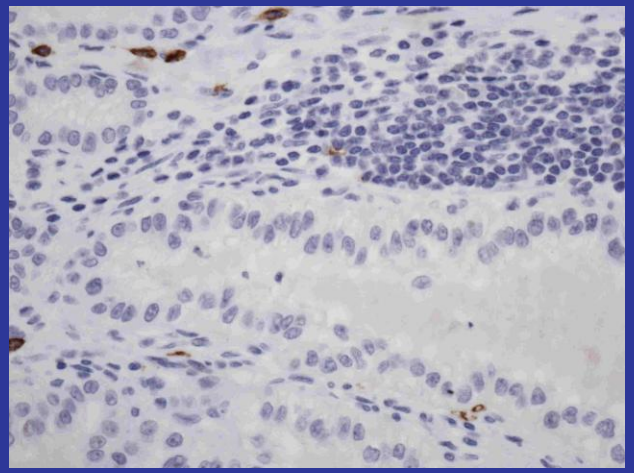
EMA



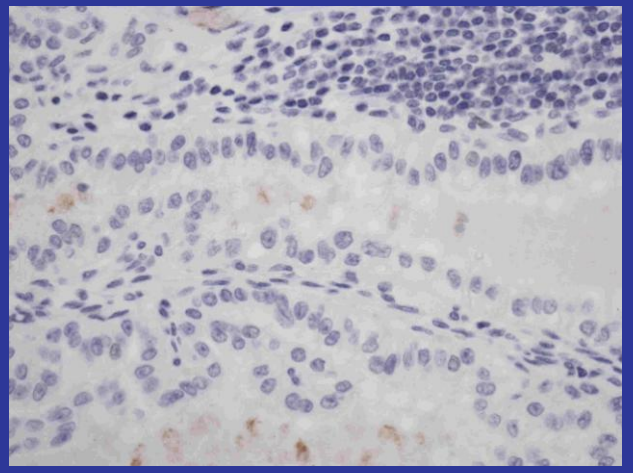
CK7



CD10



CD117



AMACR

Diagnóstico Caso 2

Carcinoma de células renales papilar de células claras

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Available online at www.sciencedirect.com

ScienceDirect

Annals of Diagnostic Pathology xx (2010) xxx–xxx

Annals of DIAGNOSTIC PATHOLOGY

Case Report

Papillary renal cell carcinoma with diffuse clear cells and thyroid-like macrofollicular areas☆

Oluwole Fadare, MD[a,b,*,1], Suzanne Lam, MD[a,c,d], Christopher Rubin, MD[e], Idris L. Renshaw, MD, PhD[e], Craig L. Nerby, MD[a]

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[b]*Department of Pathology, University of Texas Health Science Center at San Antonio, San Antonio, TX 78229, USA*
[c]*Department of Pathology and Laboratory Services, Brooke Army Medical Center, Ft Sam Houston, TX 78234, USA*
[d]*Pathology Program, San Antonio Uniformed Services Health Education Consortium, San Antonio, TX 78236, USA*
[e]*Vanguard Pathology Associates, Austin, TX 73344, USA*

Ca células claras/Ca papilar

Histopathology 1999, 35, 157–161

Papillary renal cell carcinoma with clear cell cytomorphology and chromosomal loss of 3p

L Füzesi, B Gunawan, F Bergmann, S Tack, S Braun & G Jakse[1]
Institute of Pathology and [1]Department of Urology, Medical School of the Technical University, Aachen, Germany

Malignant Papillary Renal Tumors With Extensive Clear Cell Change

A Molecular Analysis by Microsatellite Analysis and Fluorescence In Situ Hybridization

Arch Pathol Lab Med. 2003;127:1176–1181)

Ca células claras/Ca papilar

Bikamunpaka y cols.

Sporadic clear cell renal cell carcinoma with diffuse cytokeratin 7 immunoreactivity. Mod Pathol 21: 148A, 2008

(CK7+ and CD10 and RCC marker negatives)

Shen y cols.

Papillary renal cell carcinoma with clear cell features: A clinicopathologic study of 55 cases. Mod Pathol 21: 181A, 2008

(up to 38% of PRCC show areas with clear cells)

Gobbo y cols.

Renal papillary clear cell tumors is a distinct entity in the spectrum of renal cell neoplasia: An immunohistochemical and cytogenetic study. Mod Pathol 21: 157A, 2008

(sometimes, not always, are associated to renal cystic disease)

Ca células claras/Ca papilar

Malignant Papillary Renal Tumors With Extensive Clear Cell Change

A Molecular Analysis by Microsatellite Analysis and Fluorescence In Situ Hybridization

M. E. Salama, MD; M. J. Worsham, PhD; M. DePeralta-Venturina, MD

• *Context.*—Histologic subtyping of renal cell carcinomas (RCCs) is based not only on cytoarchitectural pattern but also on distinct cytogenetic abnormalities. Some renal tumors demonstrate overlapping morphologic features, rendering histologic subtyping difficult. One such group of tumors is papillary renal neoplasms with extensive clear cell change. Because histologic subtyping has been shown to be of prognostic value, it is important that malignant epithelial renal tumors be accurately subtyped. It is not known if these tumors should be classified as papillary RCC (PRCC) or as conventional/(clear cell) RCC (CRCC).

Objective.—To ascertain if this subgroup of renal neoplasms demonstrates the cytogenetic abnormalities seen typically in PRCC, that is, trisomy 7 and 17 or CRCC, that is, loss of 3p, using microsatellite analysis for loss of heterozygosity (LOH), and fluorescence in situ hybridization (FISH) for trisomies.

Design.—Seven RCCs from 6 patients that showed more than 75% papillary architecture and more than 75% clear cell change were included in the study. Tumor size ranged from 2.5 to 7.0 cm (mean 4.7 cm) and all were confined to the kidney (stage I). DNA was extracted from formalin-fixed paraffin-embedded tissue. FISH was done using In Situ Kits for centromere probes for chromosomes 7 and 17. For LOH, microsatellite analysis using labeled primers for 4 markers in the 3p13 through 3p24.2 region were used. The amplified polymerase chain reaction products were analyzed using an automated DNA sequencer. As compared with normal DNA, LOH in tumor was recognized as a loss of 1 allele, and microsatellite instability as the addition of an extra allele.

Results.—LOH in at least 1 of the markers spanning for 3p13 through 3p24.2 was detected in 6 of 7 specimens (86%), of which 1 also showed concomitant microsatellite instability. FISH did not demonstrate trisomy for either chromosome 7 or 17. Instead, monosomy 7 was observed in 4 of 6 tumors (67%) and monosomy 17 in all tumors (100%).

Conclusion.—Because malignant papillary renal tumors with extensive clear cell change show molecular changes identical to CRCC, this subgroup of tumors may have to be classified as CRCC. This study underscores the utility of molecular studies in refining light-microscopic criteria in accurate histologic subtyping of RCCs.

(*Arch Pathol Lab Med.* 2003;127:1176–1181)

Clear Cell Papillary Renal Cell Carcinoma

A Distinct Histopathologic and Molecular Genetic Entity

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Abstract: A group of renal tumors composed mainly of cells with clear cytoplasm arranged in papillary patterns and arising in end-stage kidneys has recently been identified. The aim of our study is to investigate the cytogenetic and immunohistochemical phenotypes of these unusual renal tumors, and of morphologically similar tumors arising in kidneys unaffected by end-stage renal disease. Seven tumors from 5 patients (age range: 53 to 64 y, mean: 60 y; 3 men and 2 women) were identified. Sections were obtained from paraffin blocks, including the tumors and adjacent non-neoplastic renal parenchyma. Interphase fluorescence in situ hybridization was performed with centromeric probes for chromosomes 3, 7, 17, Y, and with a subtelomeric probe for 3p25. Immunohistochemistry was performed with antibodies against cytokeratin 7, carbonic anhydrase IX, α-methylacyl-CoA racemase, CD10, and transcription factor E3. Four of the tumors were from patients who did not have end-stage renal disease. One patient had end-stage renal disease and presented with 3 morphologically identical tumors, composed of clear cells arranged in a mixture of cystic and papillary structures. Follow-up data were available from all patients and none showed recurrence or metastasis (mean follow-up: 24 mo). All 7 tumors (ranging from 4 to 50 mm in diameter) were stage pT1. All tumors lacked the gains of chromosome 7 and losses of chromosome Y that are typical of papillary renal cell carcinoma. Only 1 tumor showed gain of chromosome 17. Deletion of 3p, usually seen in clear cell renal cell carcinoma, was not detected. All tumors showed strongly positive immunohistochemical staining for cytokeratin 7 and carbonic anhydrase IX and negative immunostaining with antibodies against α-methylacyl-CoA racemase, CD10, and transcription factor E3. In conclusion, clear cell papillary renal cell carcinoma can arise in otherwise normal kidneys and in kidneys with end-stage renal disease. This tumor has immunophenotypic and genetic profiles distinct from those of either classic papillary or clear cell renal cell carcinoma, and should be considered a distinct entity in the spectrum of renal cell neoplasia.

Key Words: kidney, neoplasia, clear cell papillary renal cell carcinoma, end-stage renal disease, classification, immunohistochemistry, cytogenetics, fluorescence in situ hybridization

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Different types of renal epithelial neoplasms have been described in association with end-stage renal disease, with a high prevalence of papillary renal cell carcinomas and clear cell renal cell carcinomas.[9,15–17,20,22,24,25,31] However, tumors arising in kidneys involved by end-stage renal diseases may also show distinctive histologic features not easily classified according to the current World Health Organization (WHO) classification system.[10,28,29] Recently, 2 distinctive renal carcinomas have been described in the spectrum of renal epithelial neoplasms in end-stage renal disease. The most common was designated as "acquired cystic disease associated renal carcinoma" and the second most common as ''clear cell papillary renal cell carcinoma of end-stage kidneys''. The latter is a tumor composed mainly of cells with clear cytoplasm arranged in cystic and papillary patterns.[29] Herein, we investigate the cytogenetic and immunohistochemical phenotypes of 5 papillary renal tumors showing the same peculiar features previously described in clear cell papillary renal cell carcinoma of end-stage kidneys, but arising also in kidneys unaffected by end-stage renal disease.

CCRCC

- Cromosoma 3
  - CA IX
  - Ciclina D1

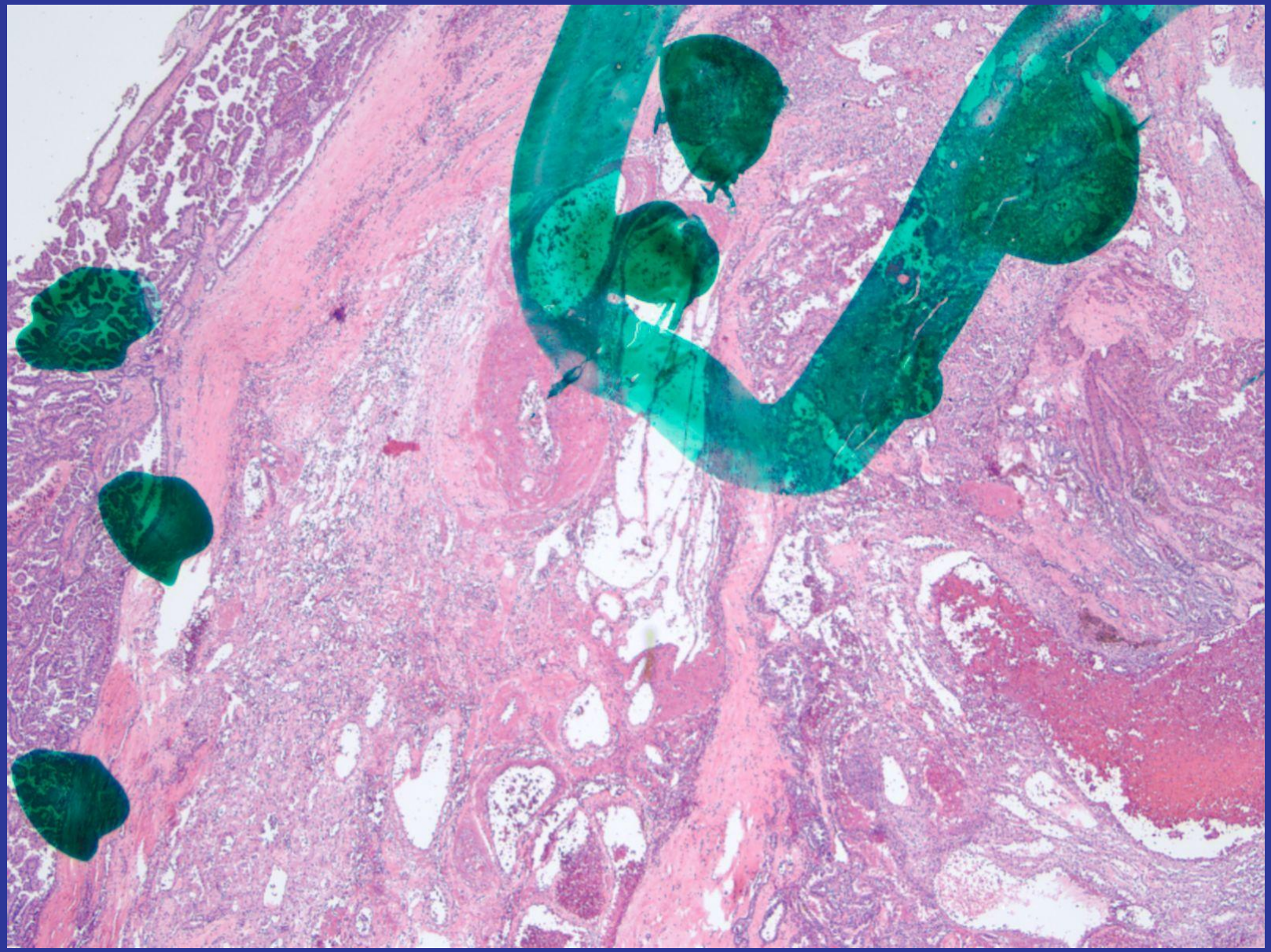
PRCC

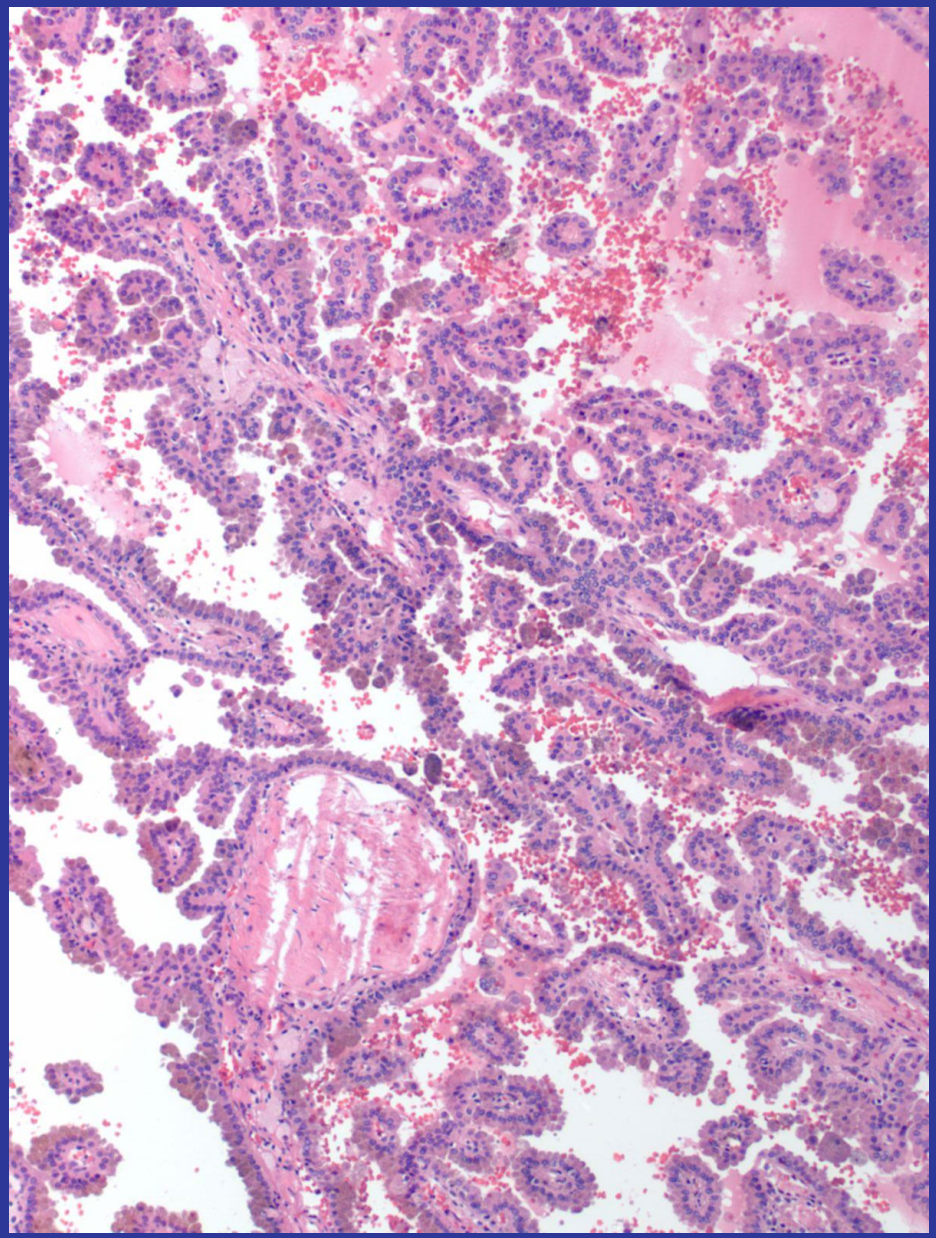
- Cromosoma 7
- Cromosoma 17
- CK7

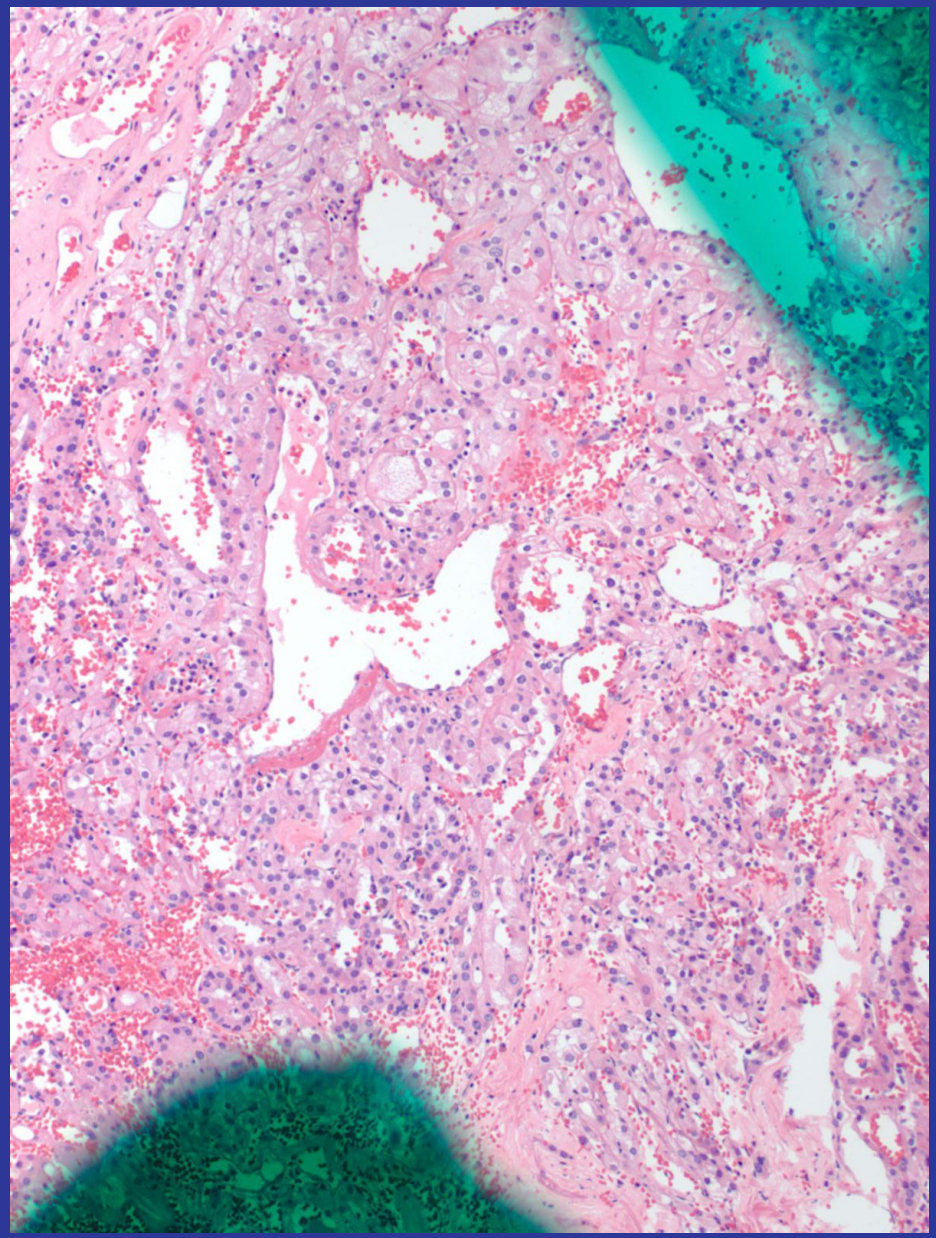
CARCINOMAS DE CÉLULAS CLARAS CON ARQUITECTURA PAPILAR

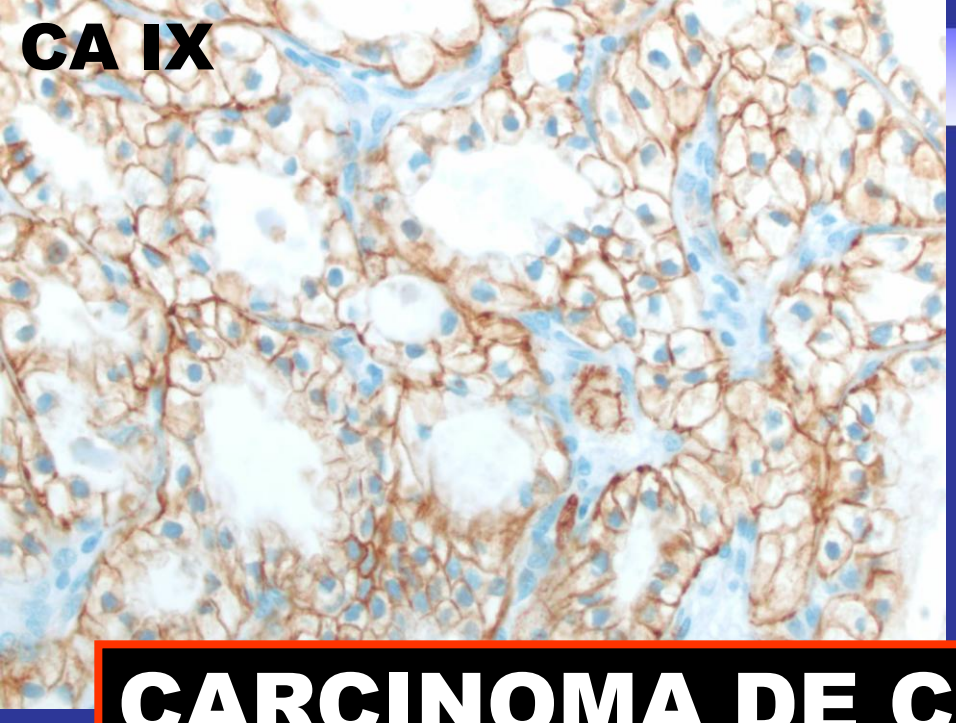
(POTENCIALMENTE DIAGNOSTICADOS COMO CARCINOMAS PAPILARES)

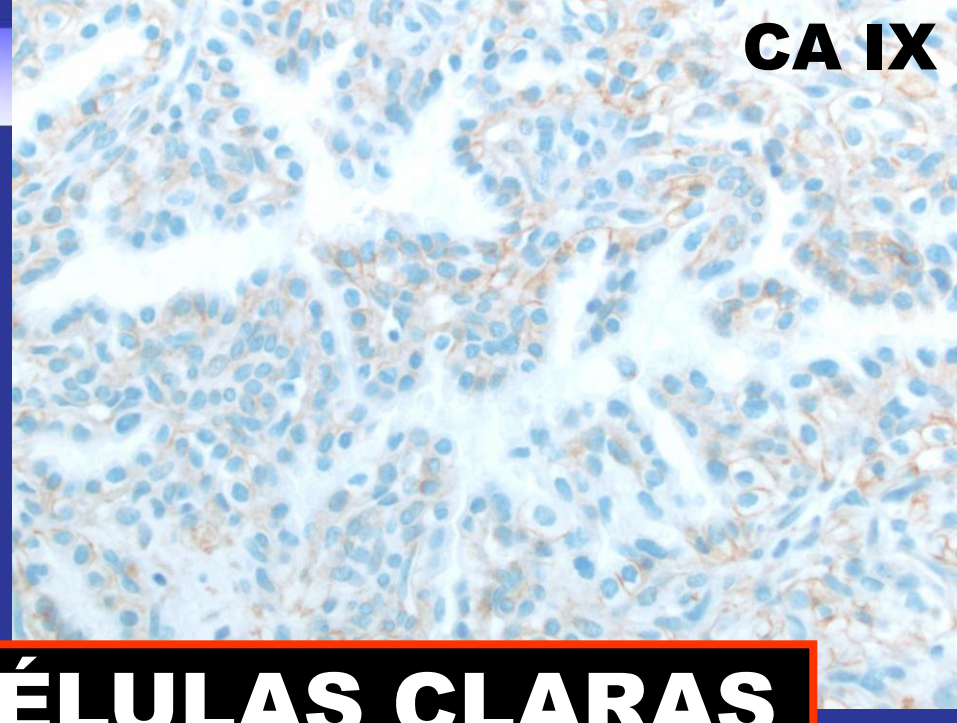
CA IX (+), Ciclina D1 (+), 7 y 17 (dos copias), CK7 (-)



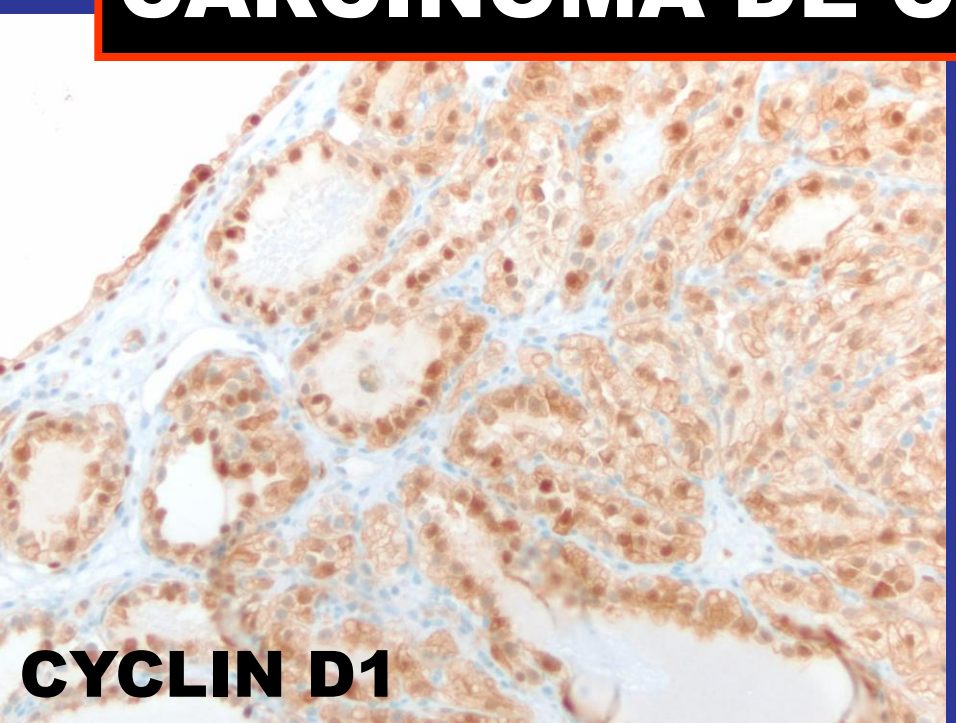


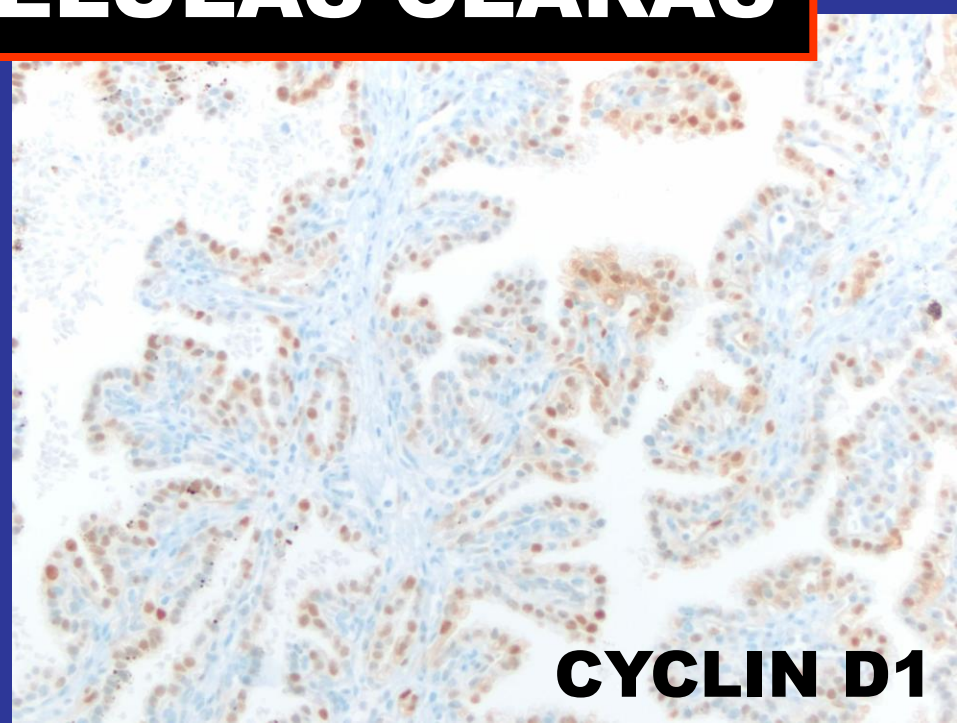






CARCINOMA DE CÉLULAS CLARAS





CCRCC

- Cromosoma 3
  - CA IX
  - Ciclina D1

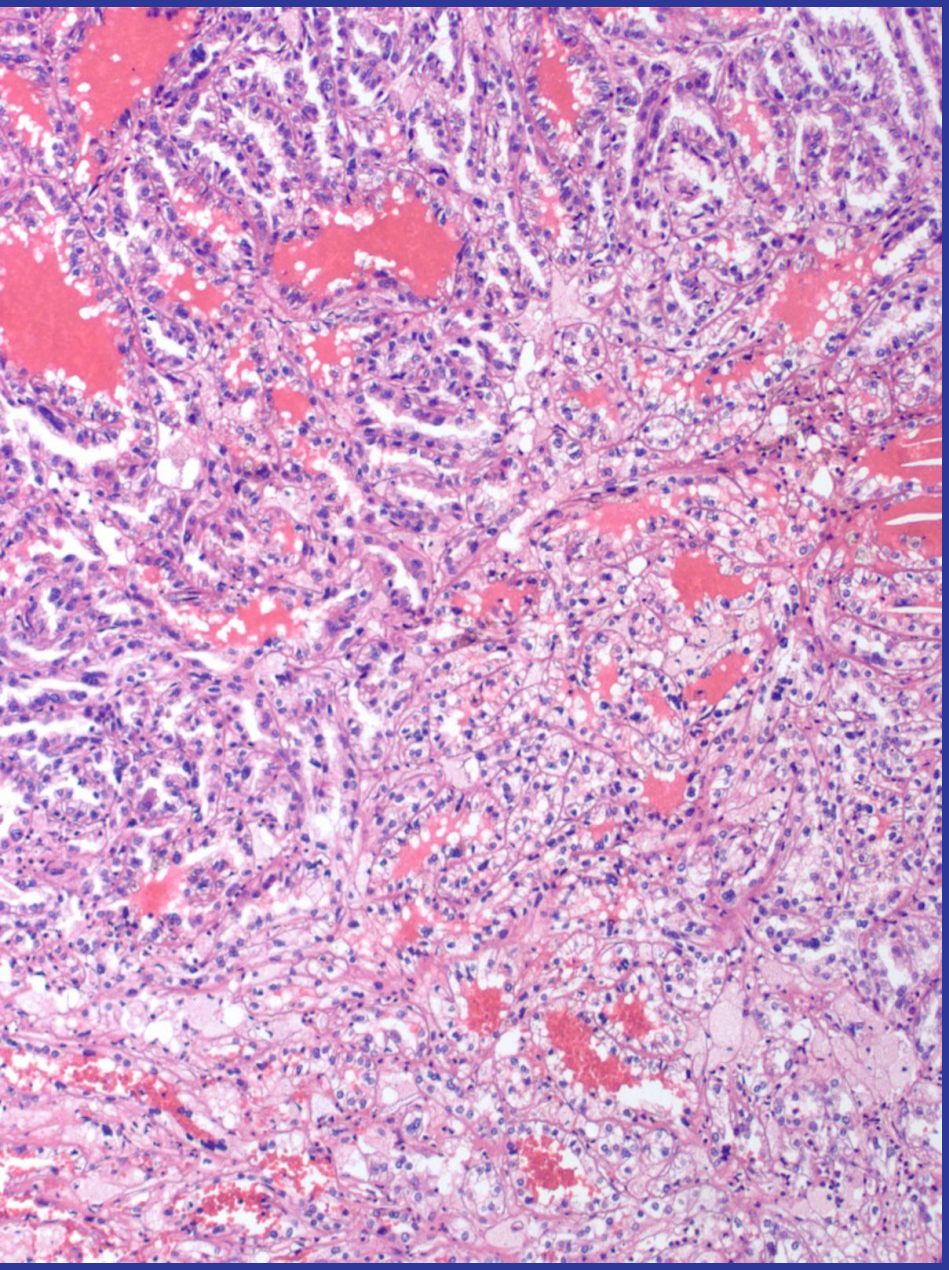
PRCC

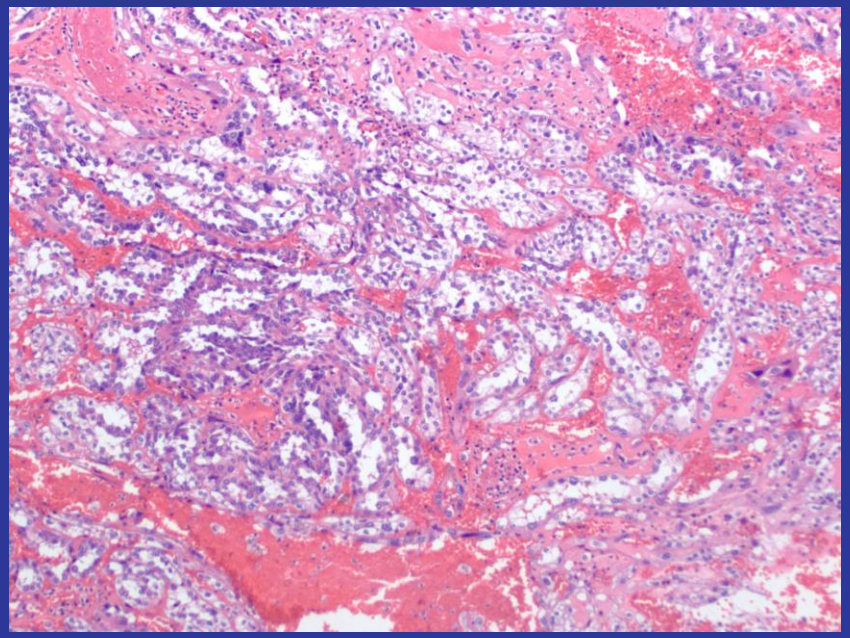
- Cromosoma 7
- Cromosoma 17
- CK7

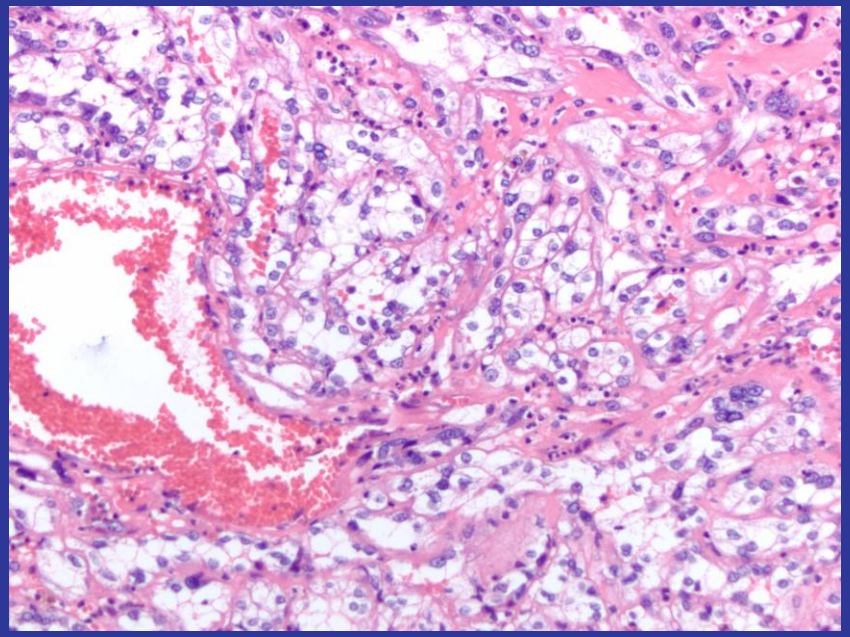
CARCINOMAS PAPILARES CON CÉLULAS CLARAS

(POTENCIALMENTE DIAGNOSTICADOS COMO CARCINOMA DE CÉLULAS CLARAS)

CA IX (-), Ciclina D1 (-), 7 y 17 (tres copias), CK7 (+)



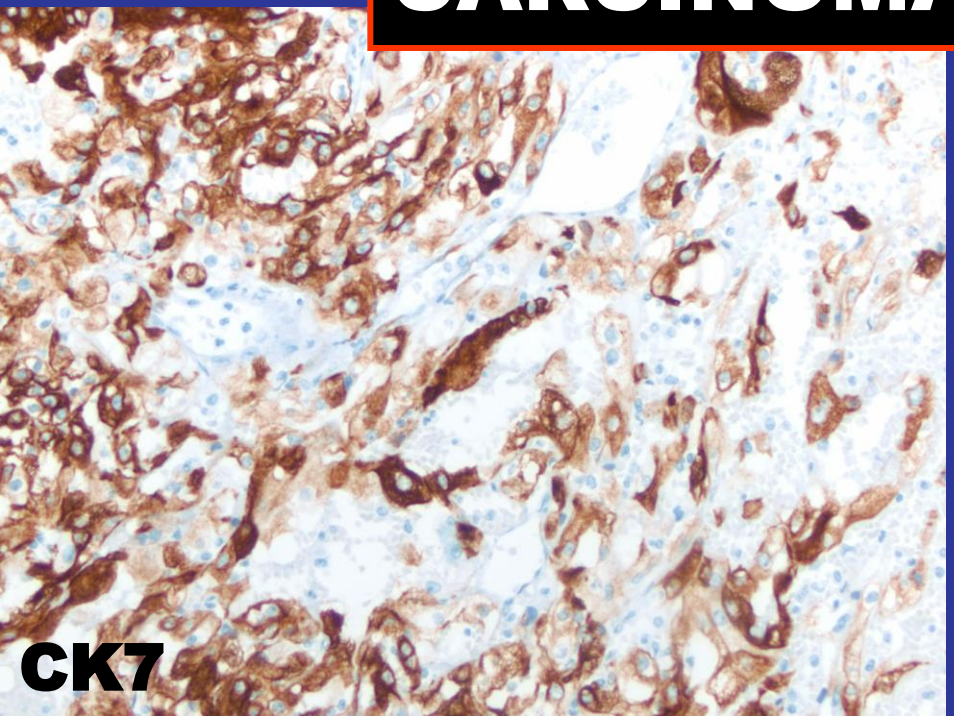




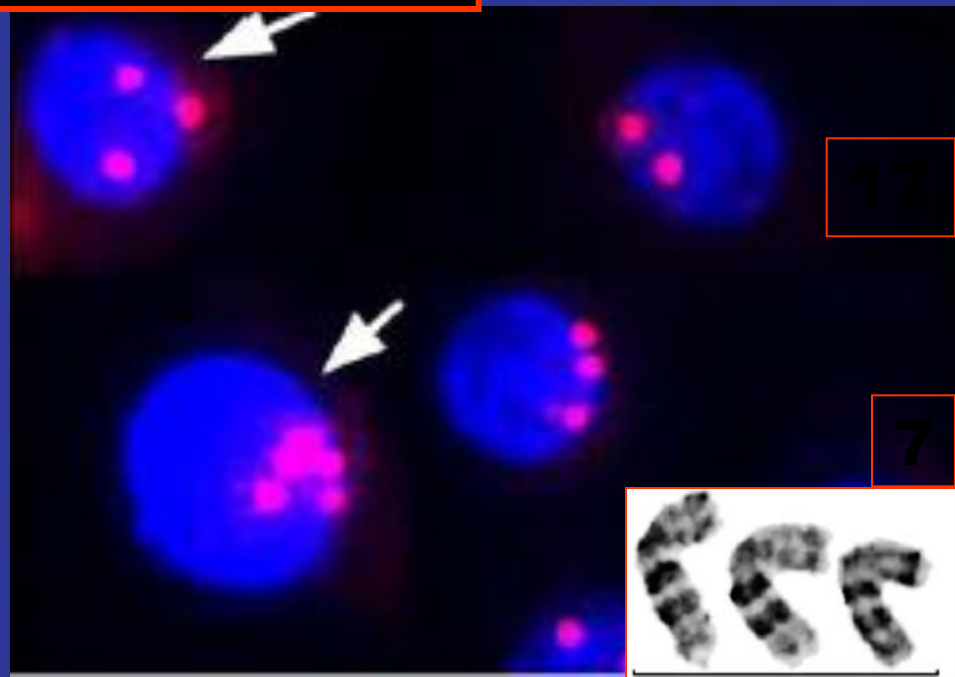
CA IX

CYCLIN D1

CARCINOMA PAPILAR



CK7



CCRCC

- CromosomA 3
  - CA IX
  - Ciclina D1

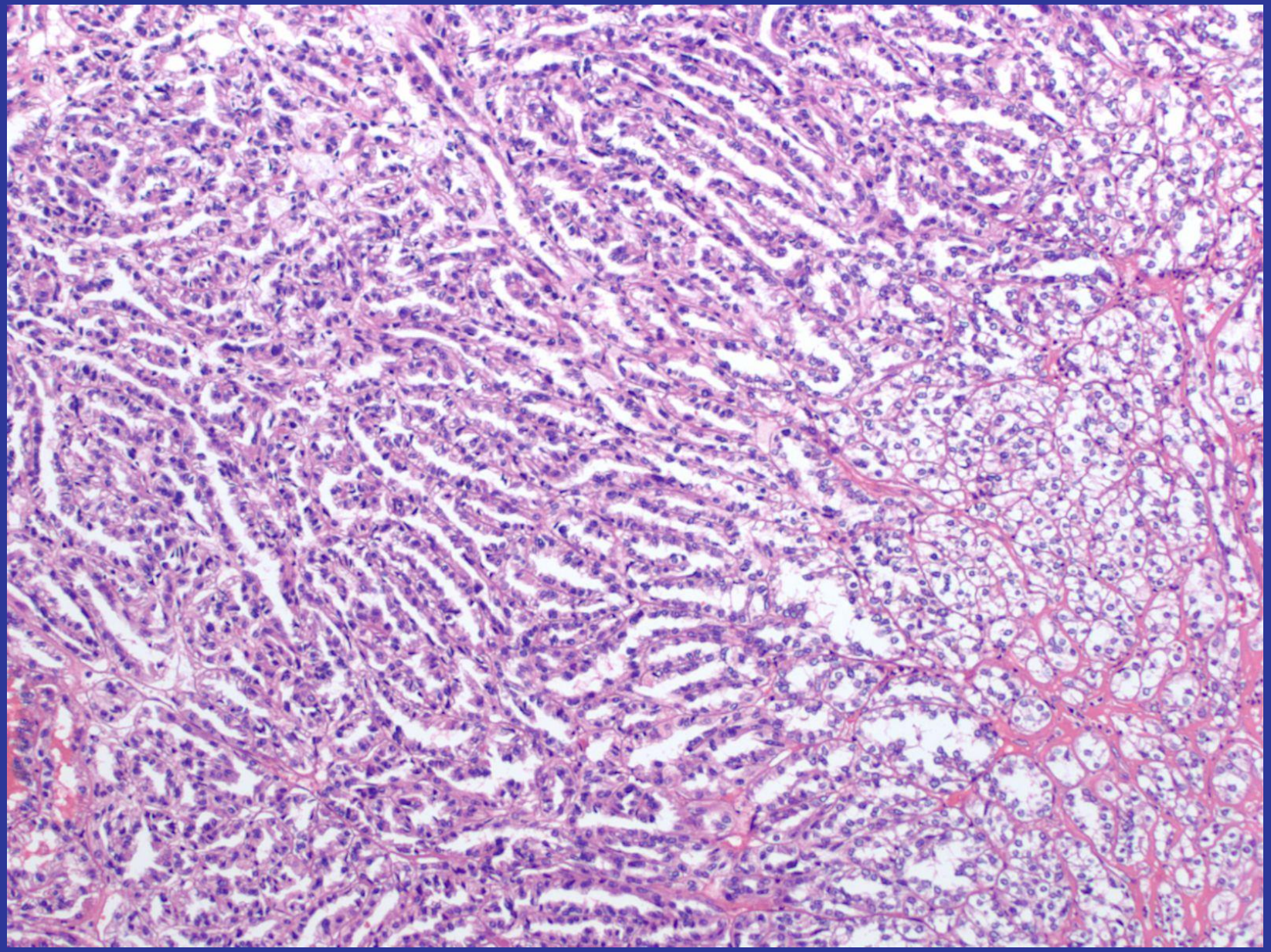
PRCC

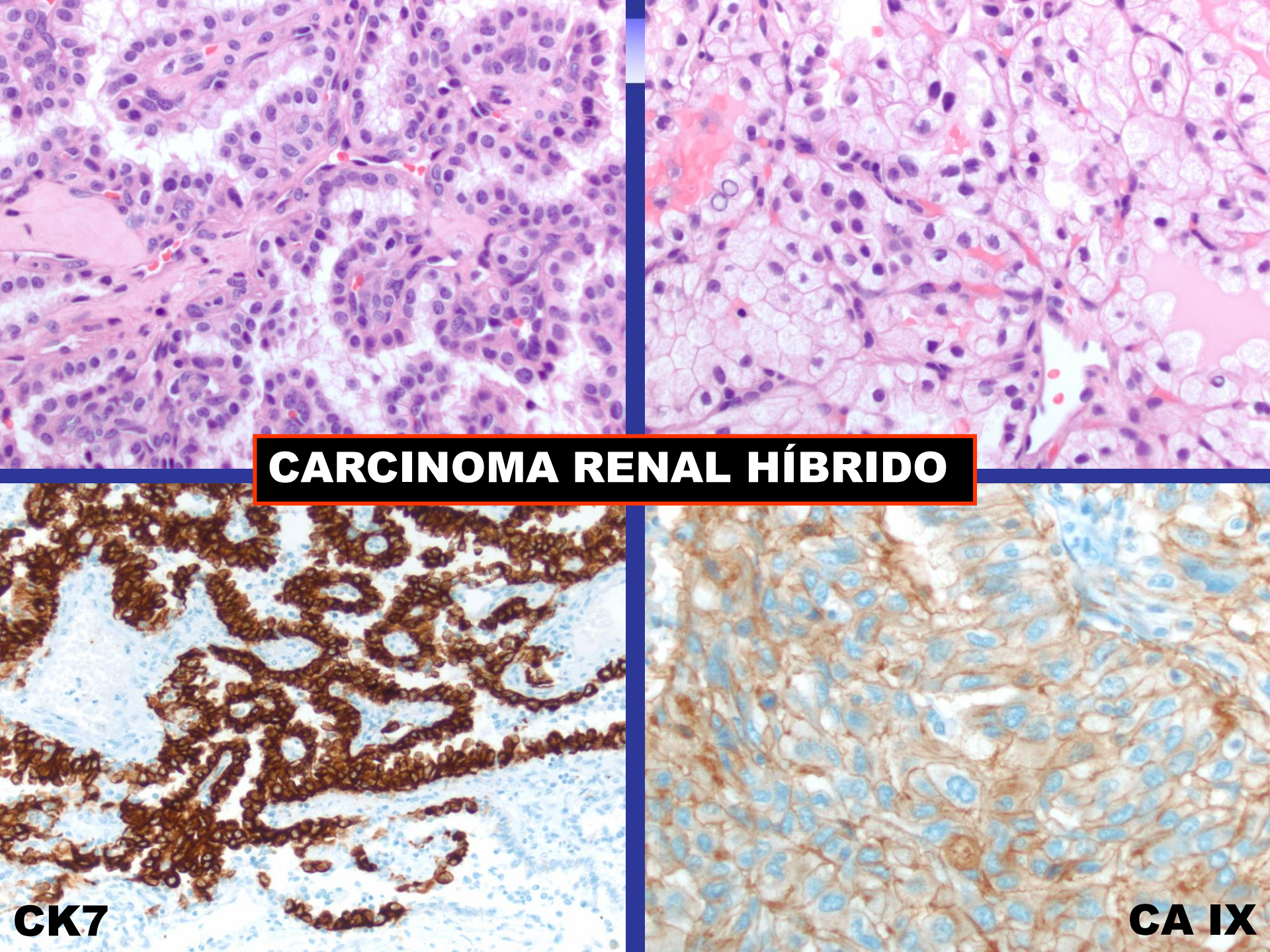
- Cromosoma 7
- Cromosoma 17
- CK7

Carcinoma híbrido, papilar y de células claras

De qué los estamos diagnosticando???

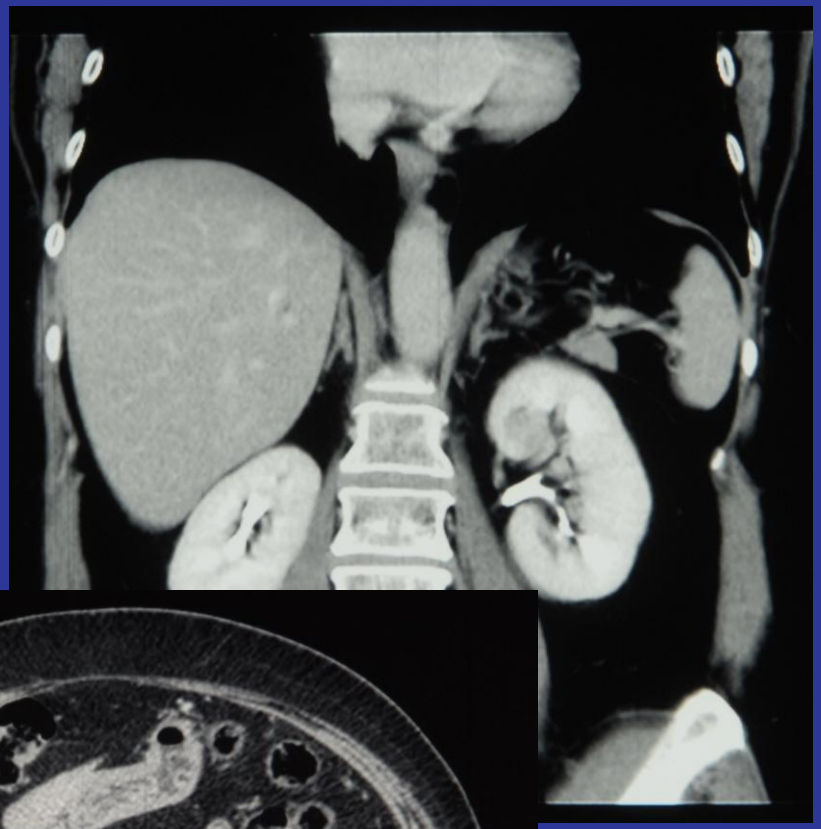
Areas CA IX (+) y Cyclin D1 (+) / areas con 3 copias 7 y 17, CK7 (+)

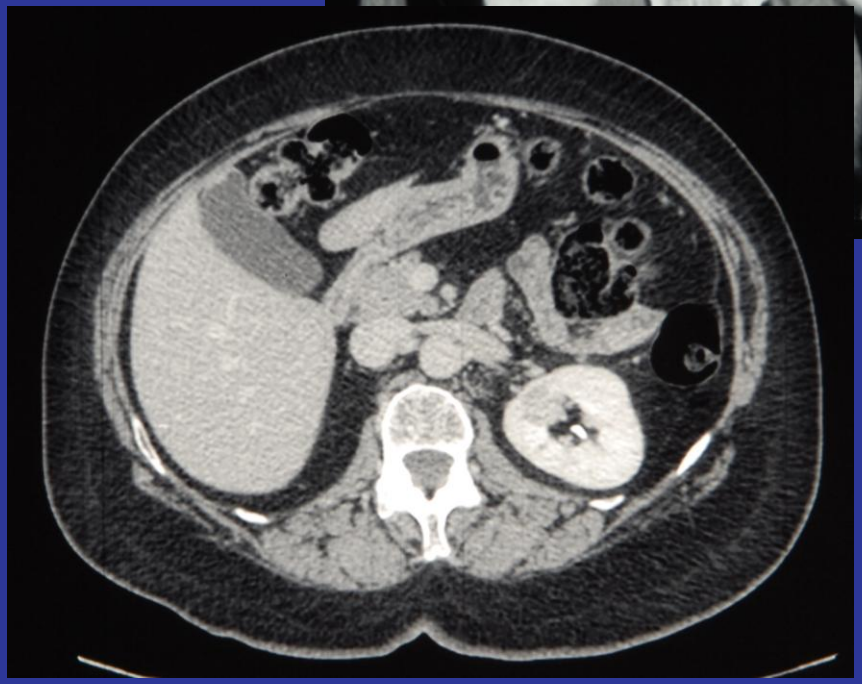


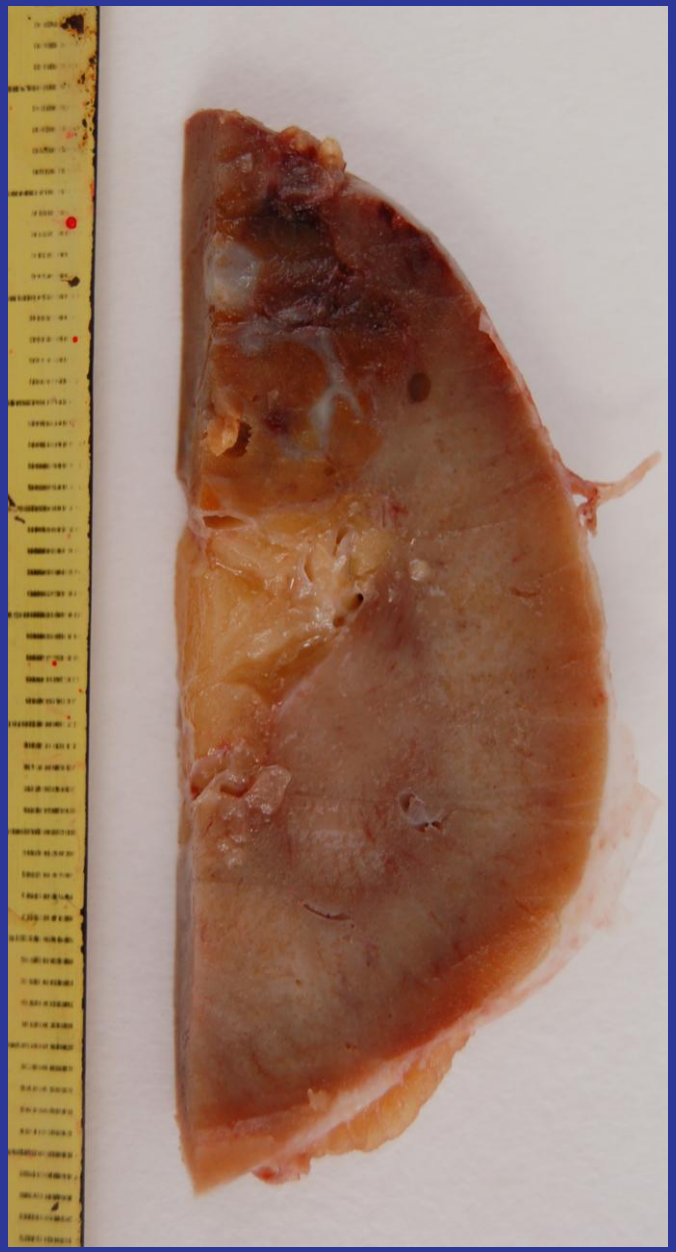

CARCINOMA RENAL HÍBRIDO
CK7
CA IX

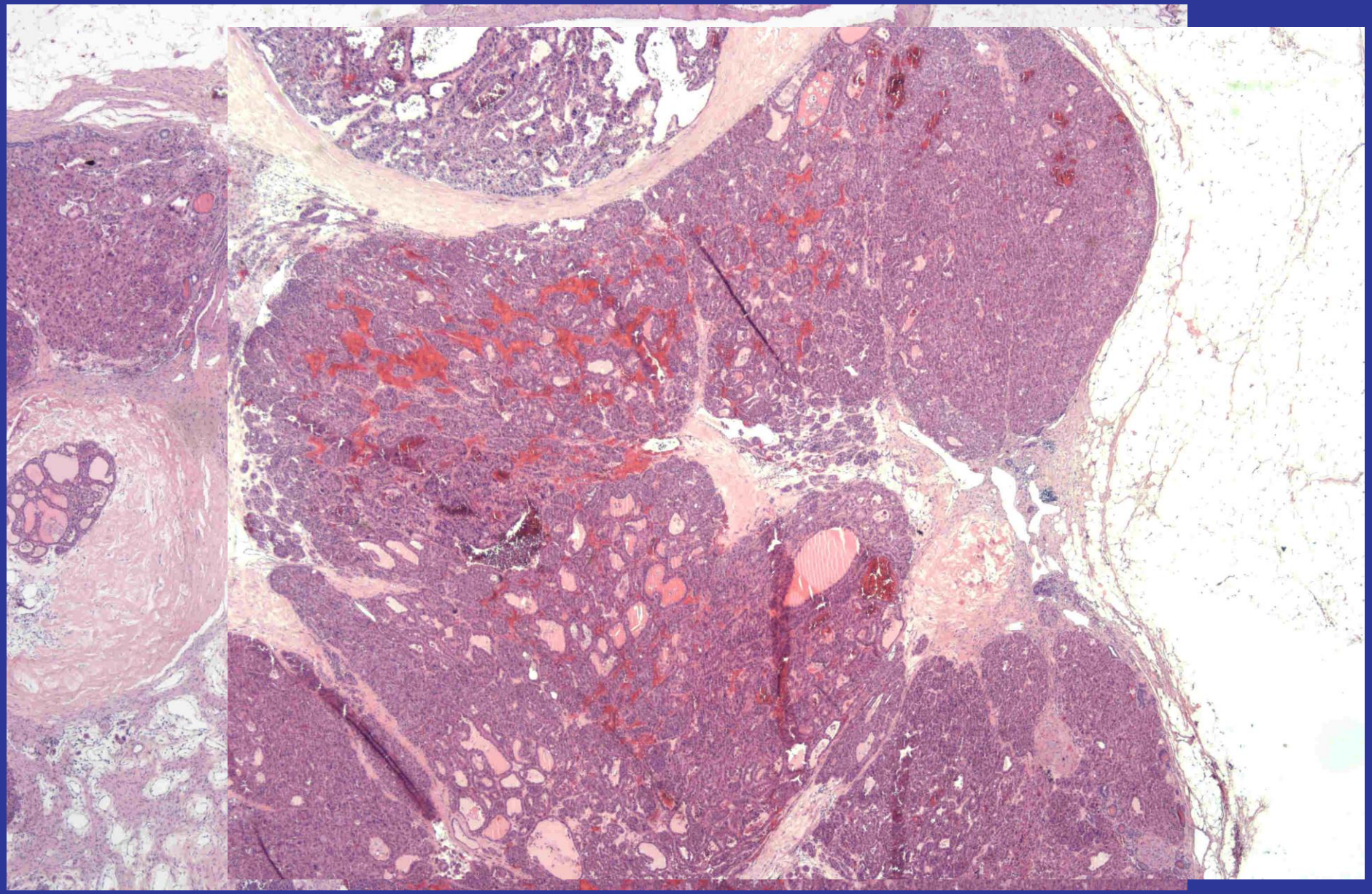
CASO 3 (09B19692)

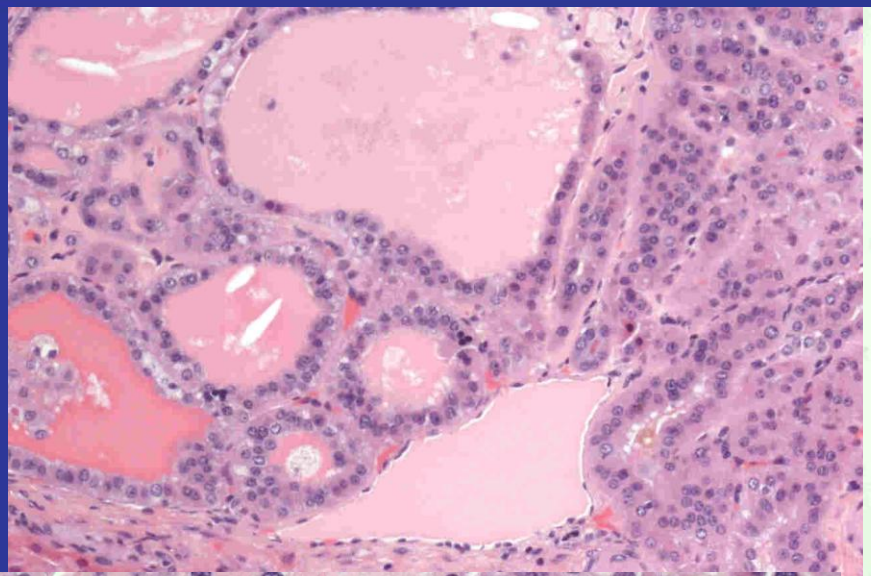
- 55/F, asintomática.
- Masa renal izquierda (2.5 cm) descubierta en el estudio radiológico de una hernia diafragmática.
- Nefrectomía total izquierda.
- Libre de enfermedad 8 meses después

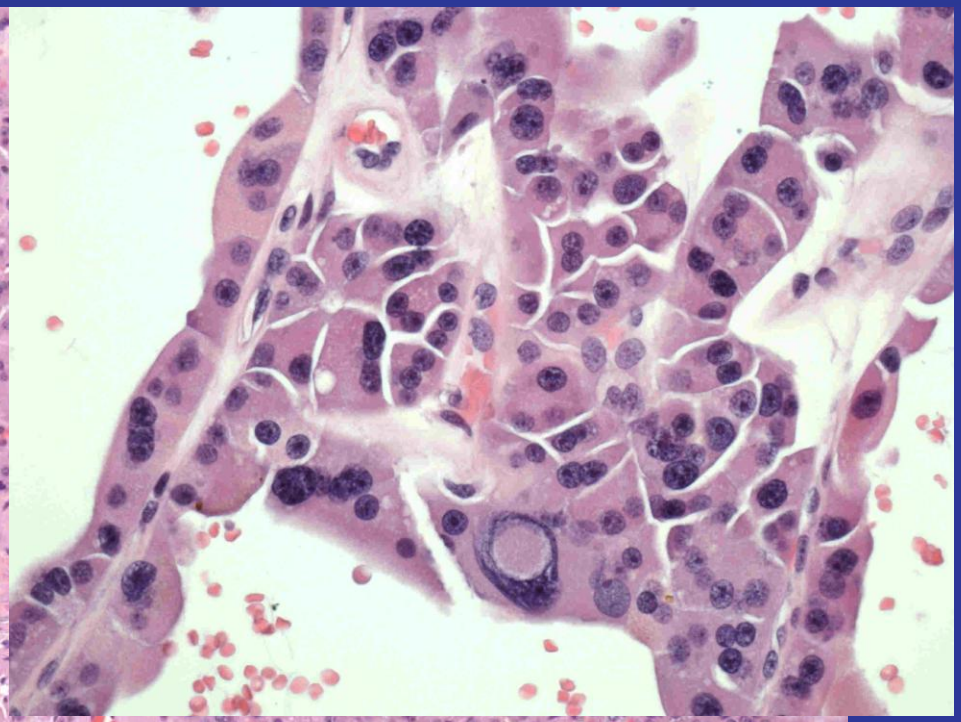


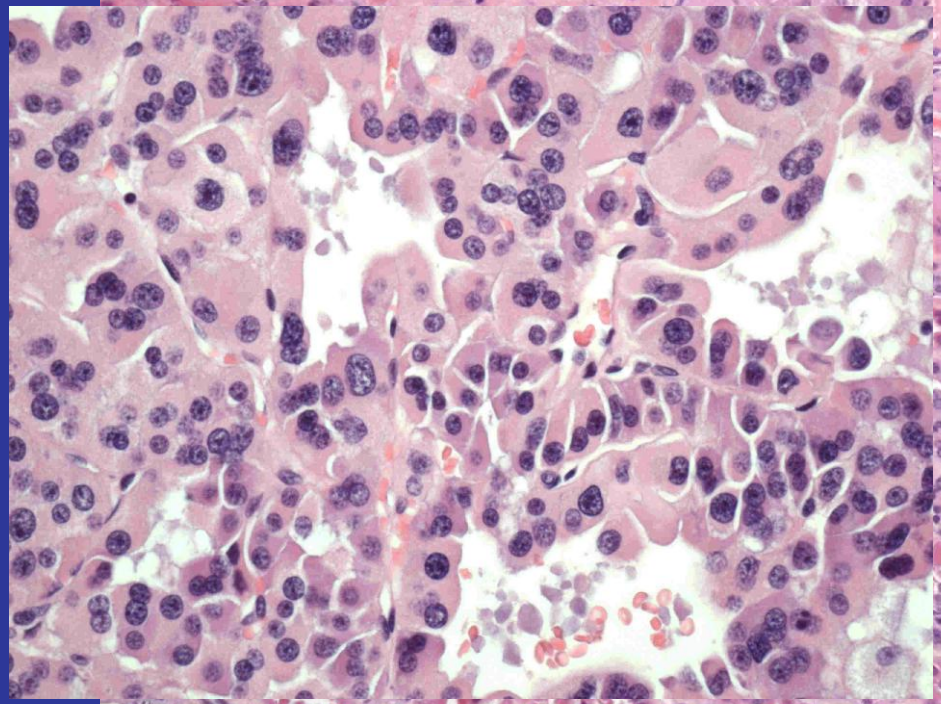


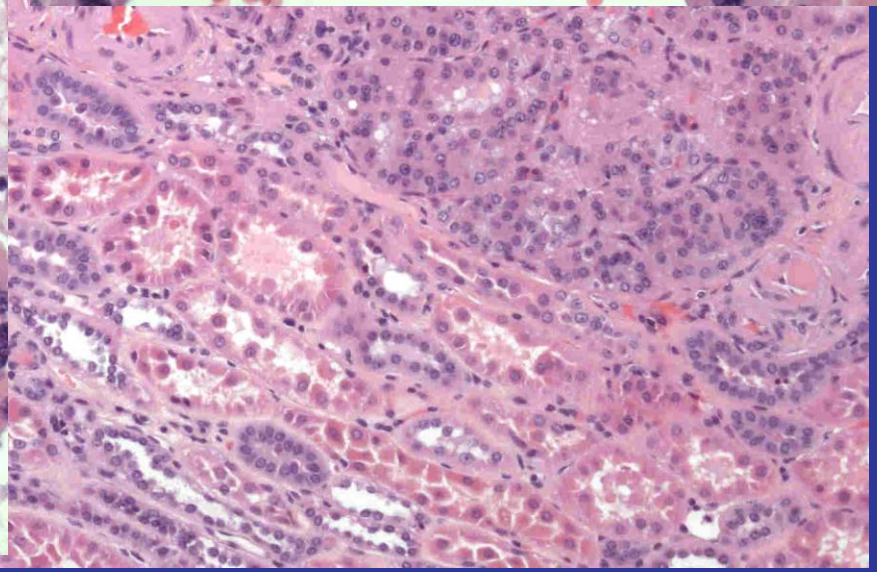


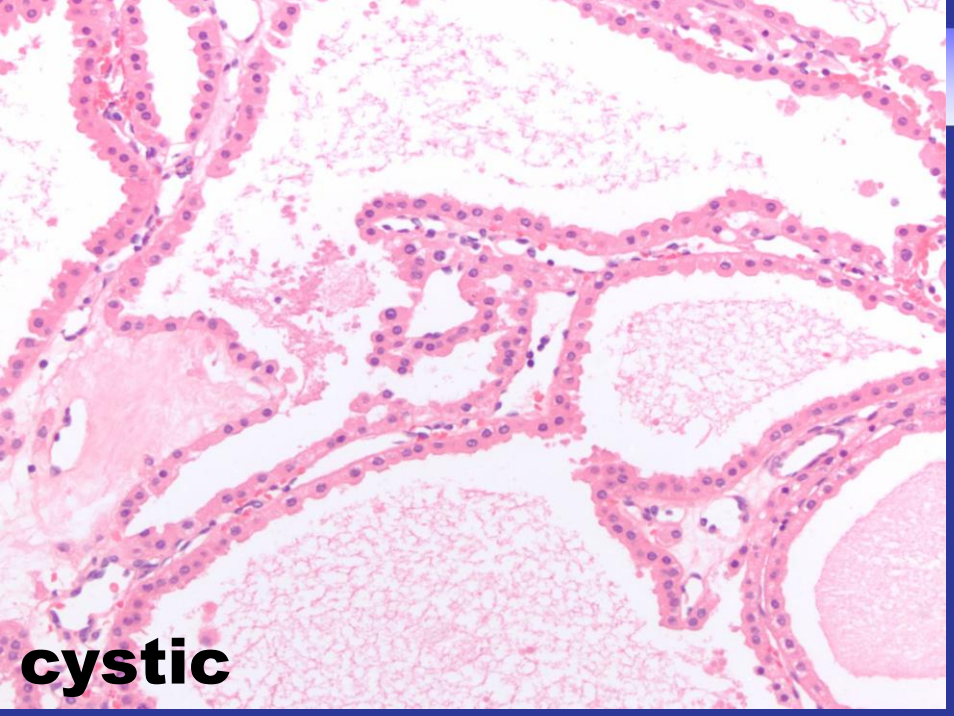


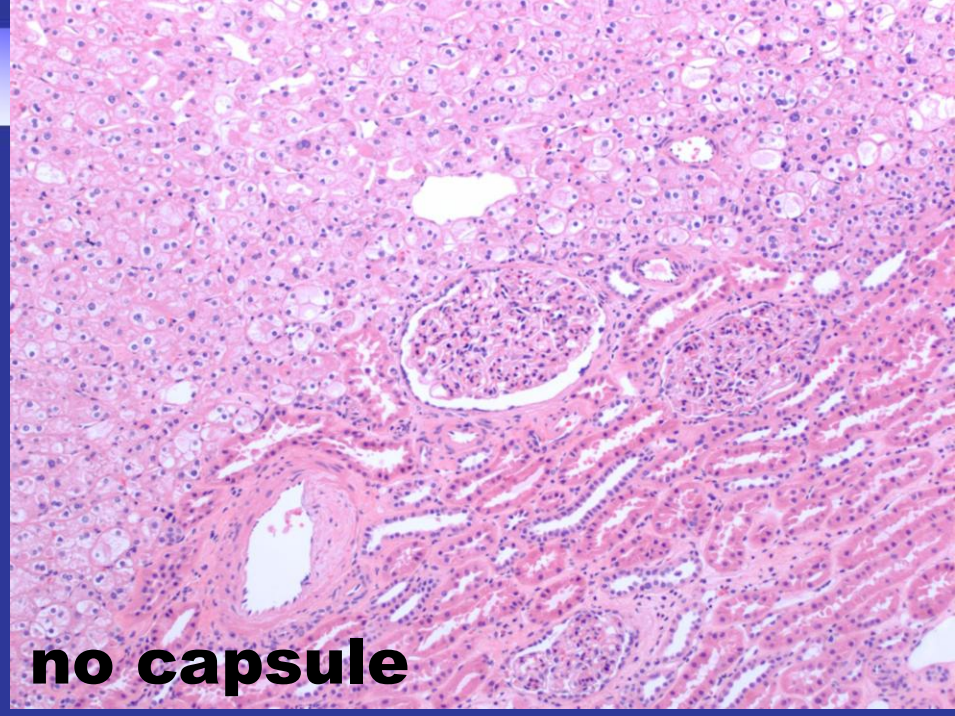


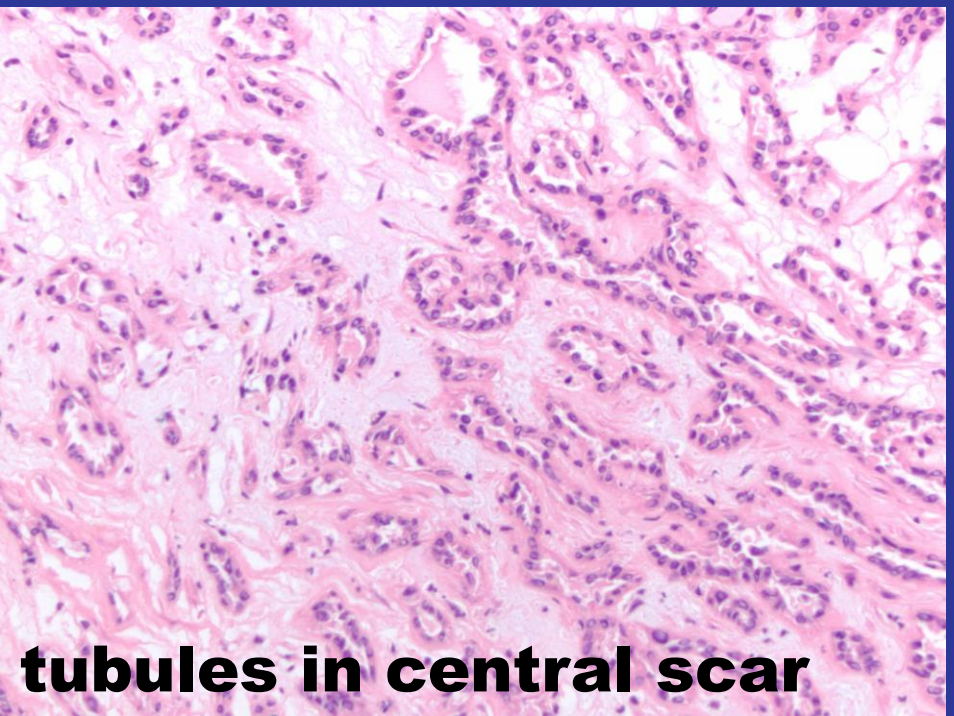


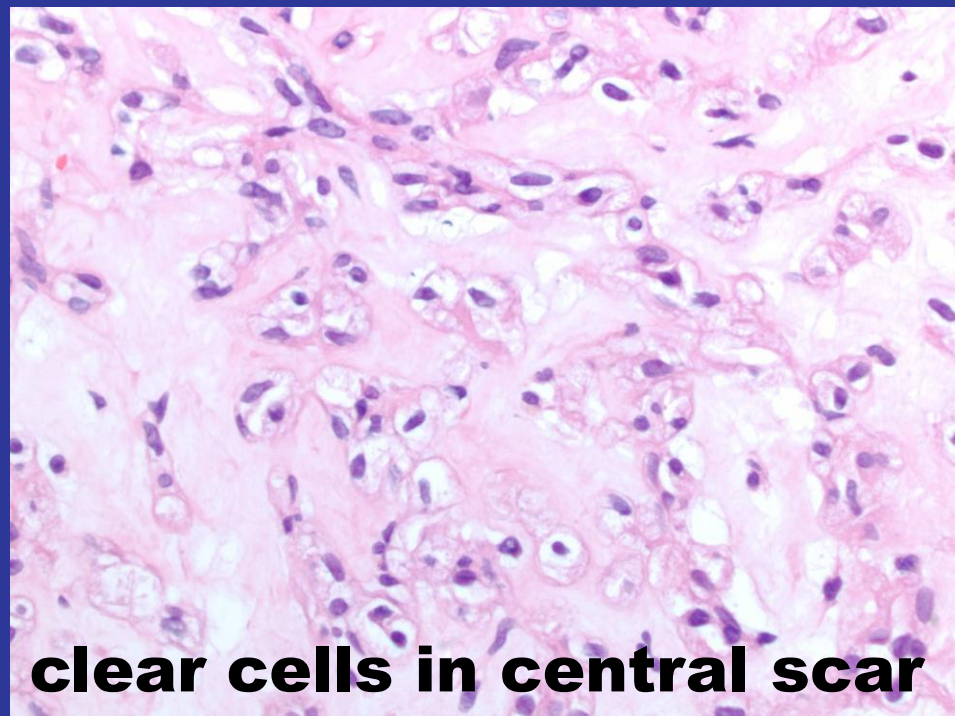


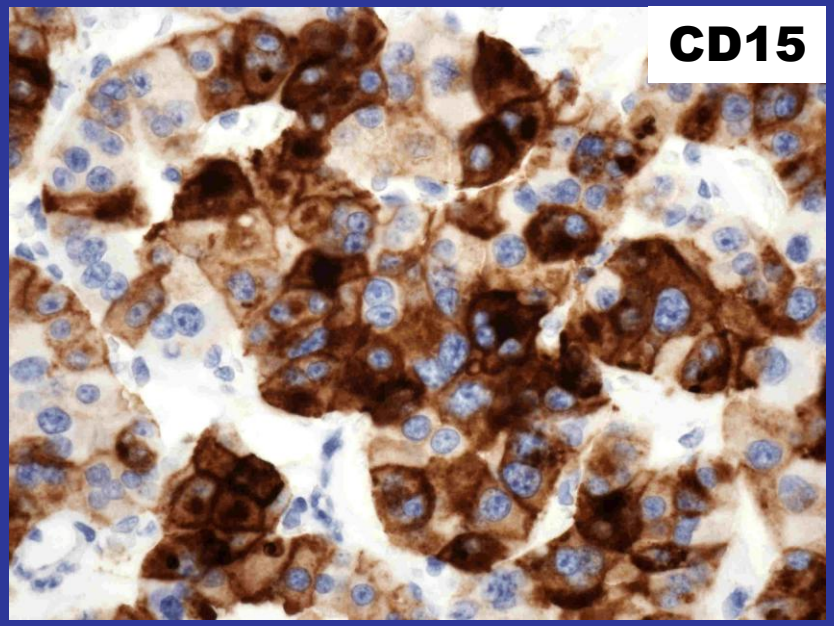


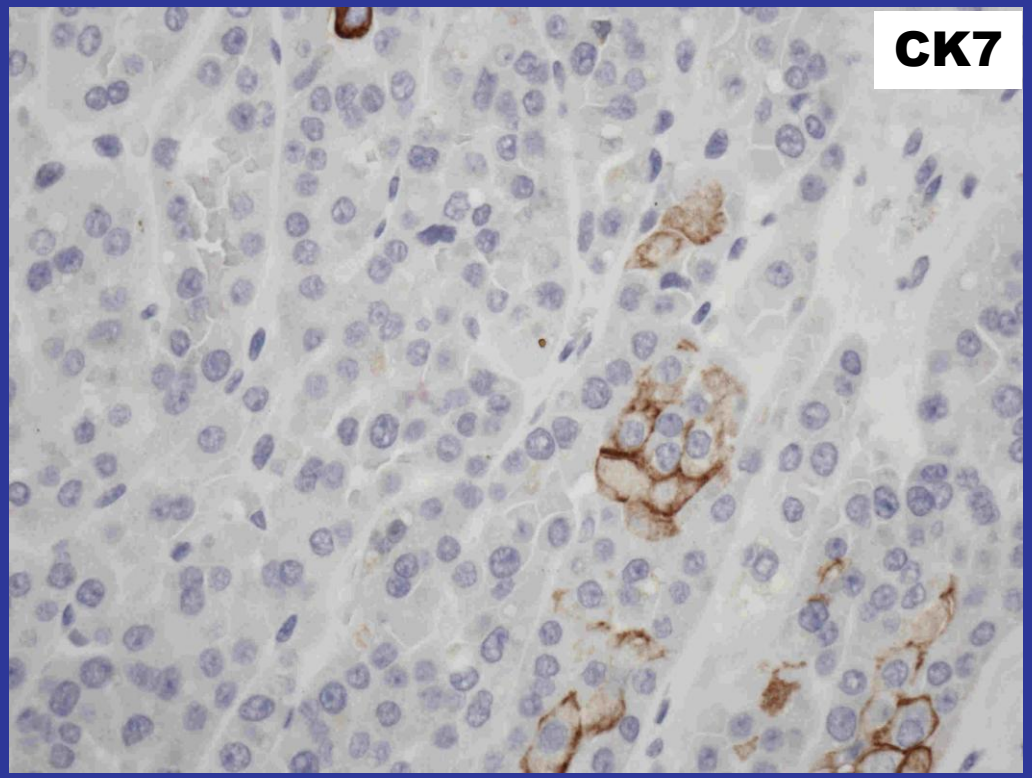

cystic

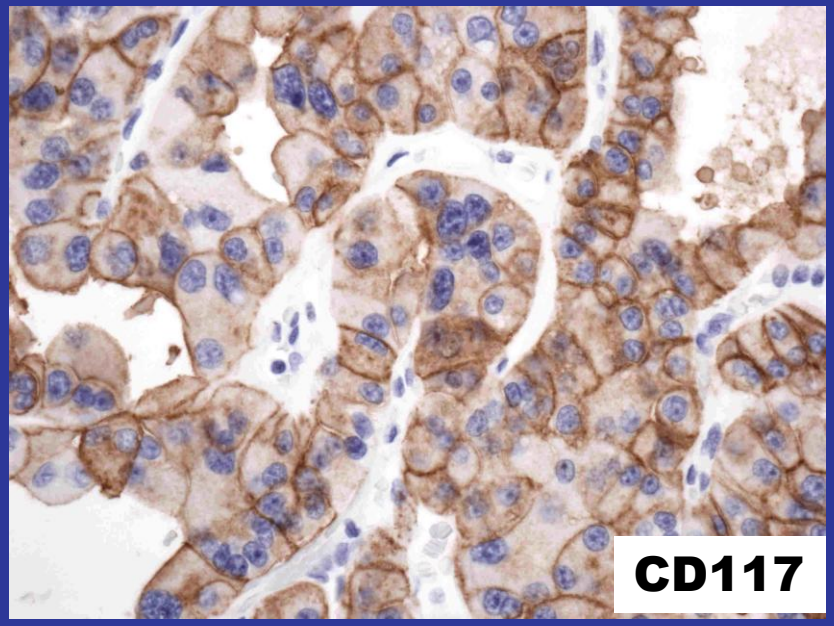

no capsule


tubules in central scar


clear cells in central scar


CD15


CK7

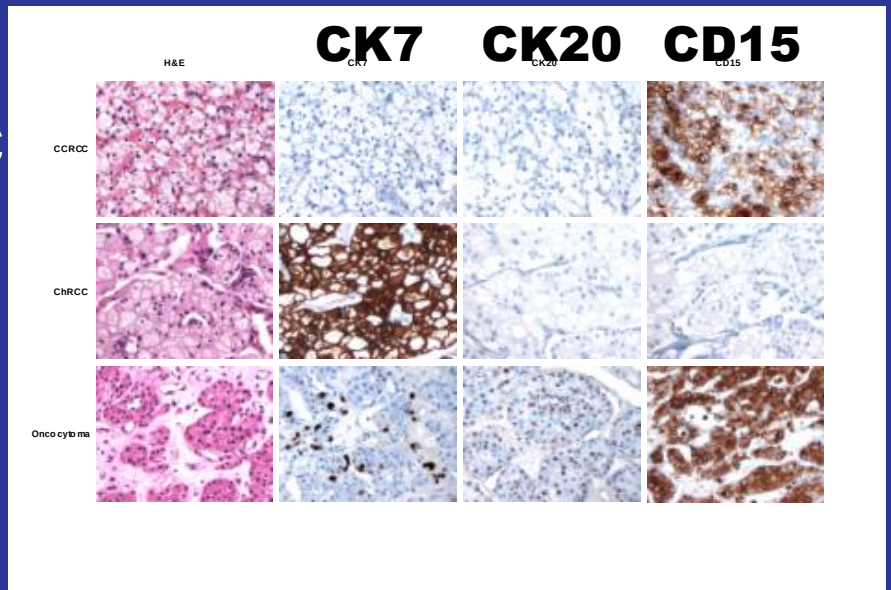

CD117

Ac	CCRCC	ChRCC	Onc
CK7	–	+++	+/-
RCC	++	--	--
CD10	+++	--	--
Vimentina	+++	--	--
CD117	--	++	++
Parvalbumin	--	+	+
e-cadherin	--	++	++
CD15	+	–	+++
CK20	–	–	+++

CCRCC

ChRCC

ONC



Diagnóstico Caso 3

Oncocitoma renal atípico

ONCOCITOMA

ONCOCITOMA ATÍPICO

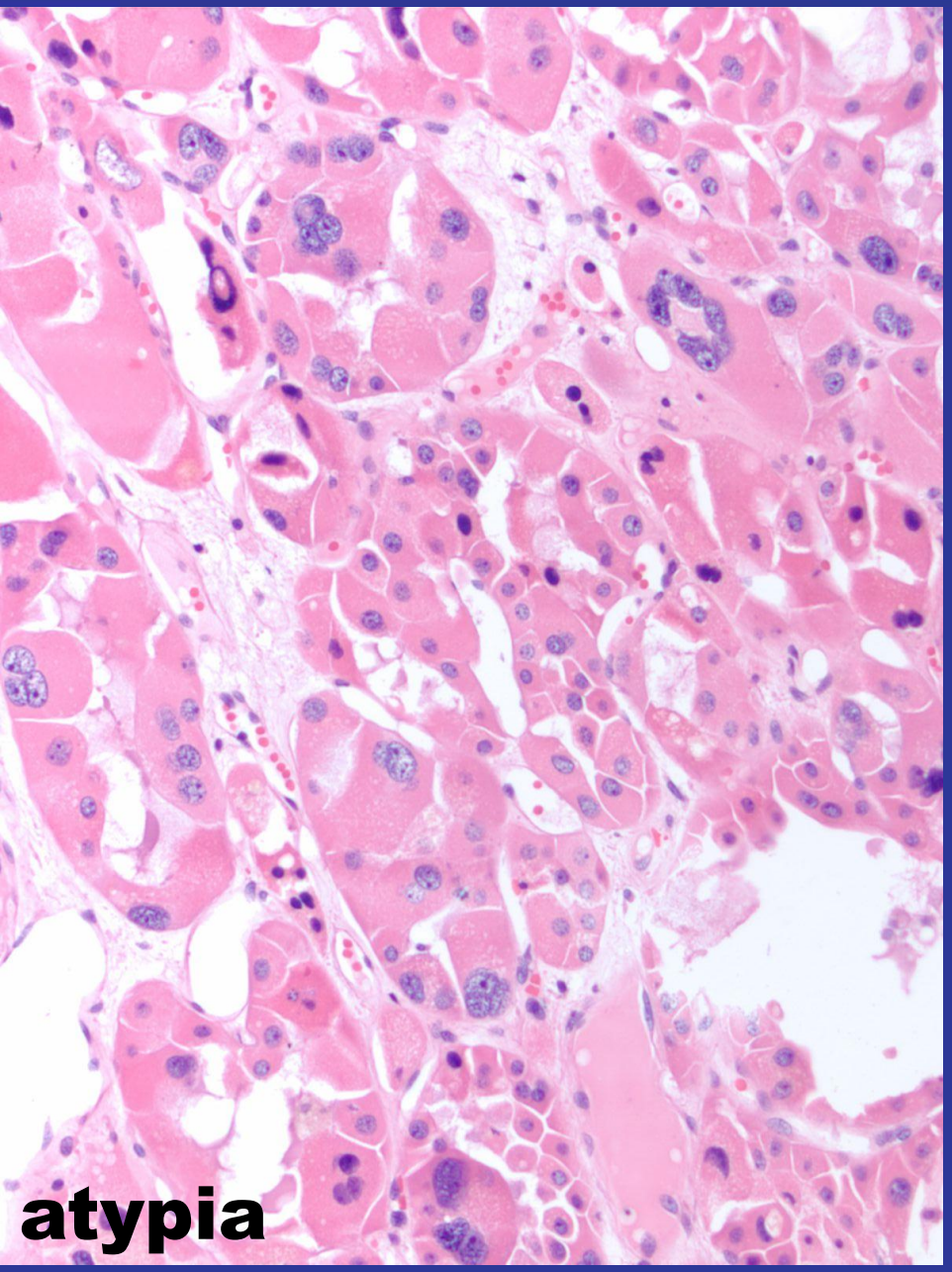
CA RENAL CROMÓFOBO

Oncocitoma atípico

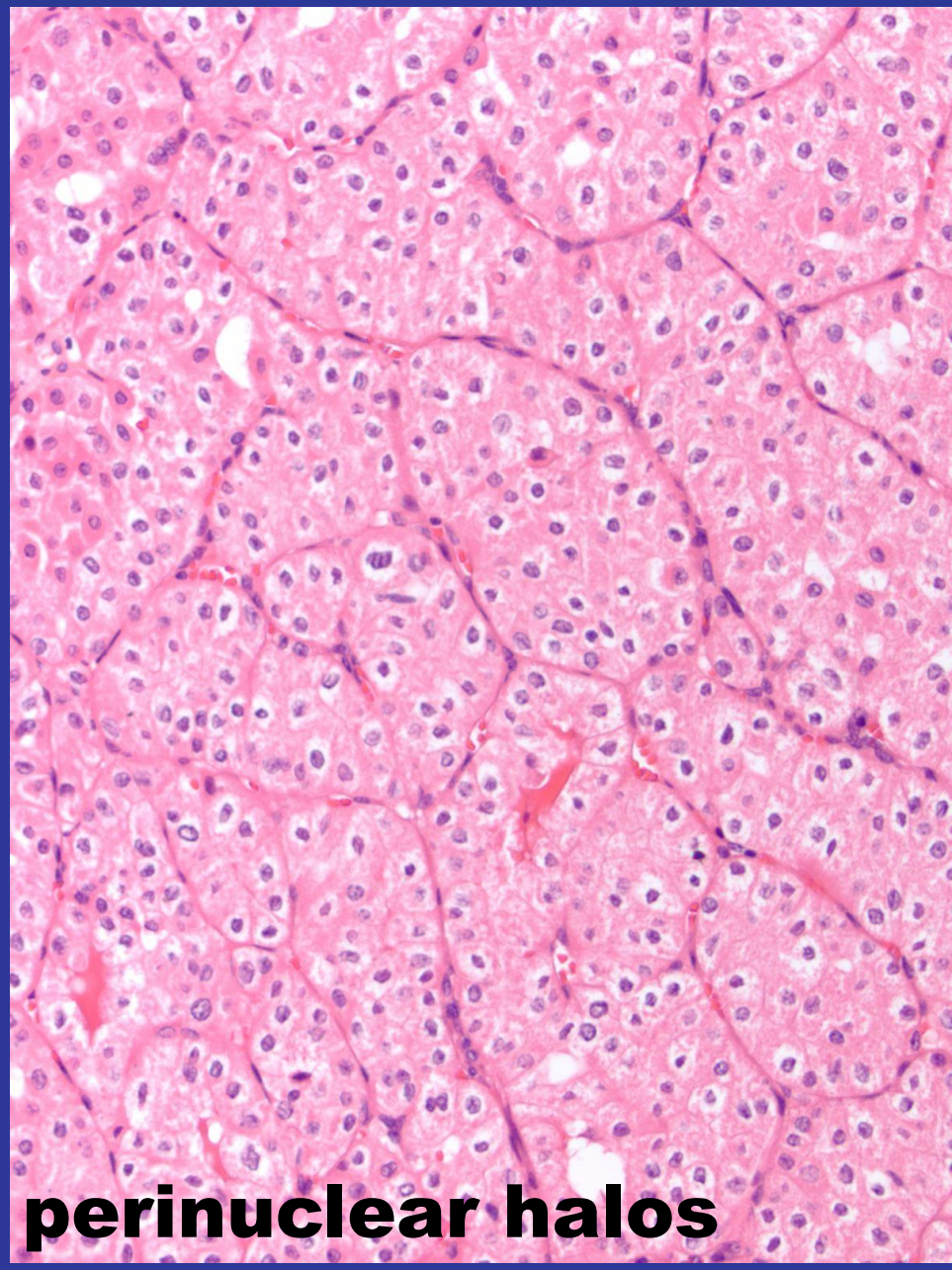
- Patrón sólido en el centro
- Invasión parénquima renal
- Invasión de la grasa perirrenal
- Cápsula
- Invasión vascular
- Hemorragia
- Necrosis
- Calcificaciones
- Bordes citoplásmicos marcados
- Papilas
- Pigmento intracitoplásmico
- Aclaramiento citoplásmico
- Halos perinucleares
- Koilocitosis
- Bi/multinucleación
- Nucleólos (x10)
- Atipia nuclear marcada
- Mitosis
- Cambios xantomatosos
- Vasos hialinizados
- Hendiduras intercelulares
- Multifocalidad

IHC: CK7 (-), CK20 (+), CD15 (+)

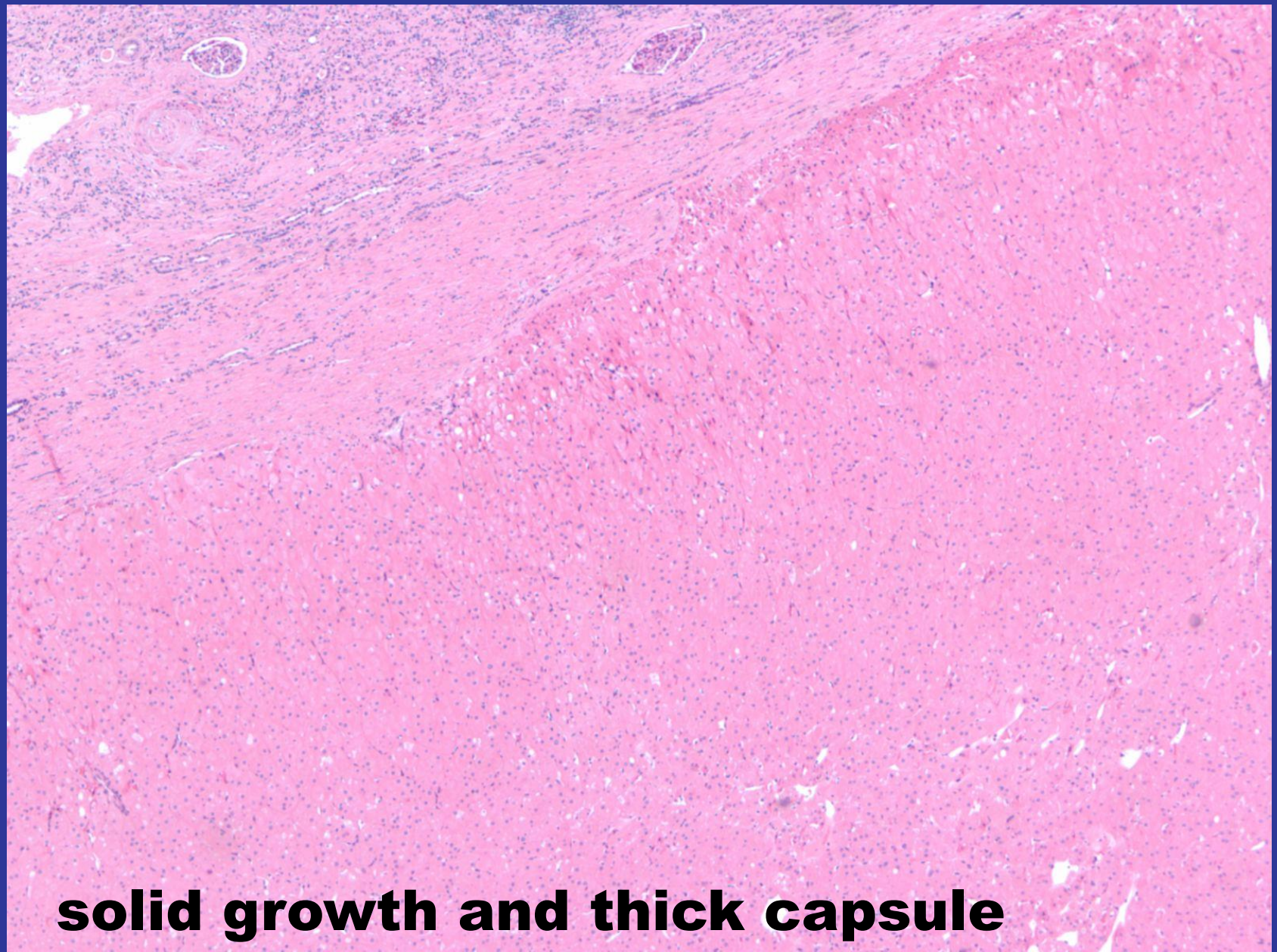
ULTRAESTRUCTURA



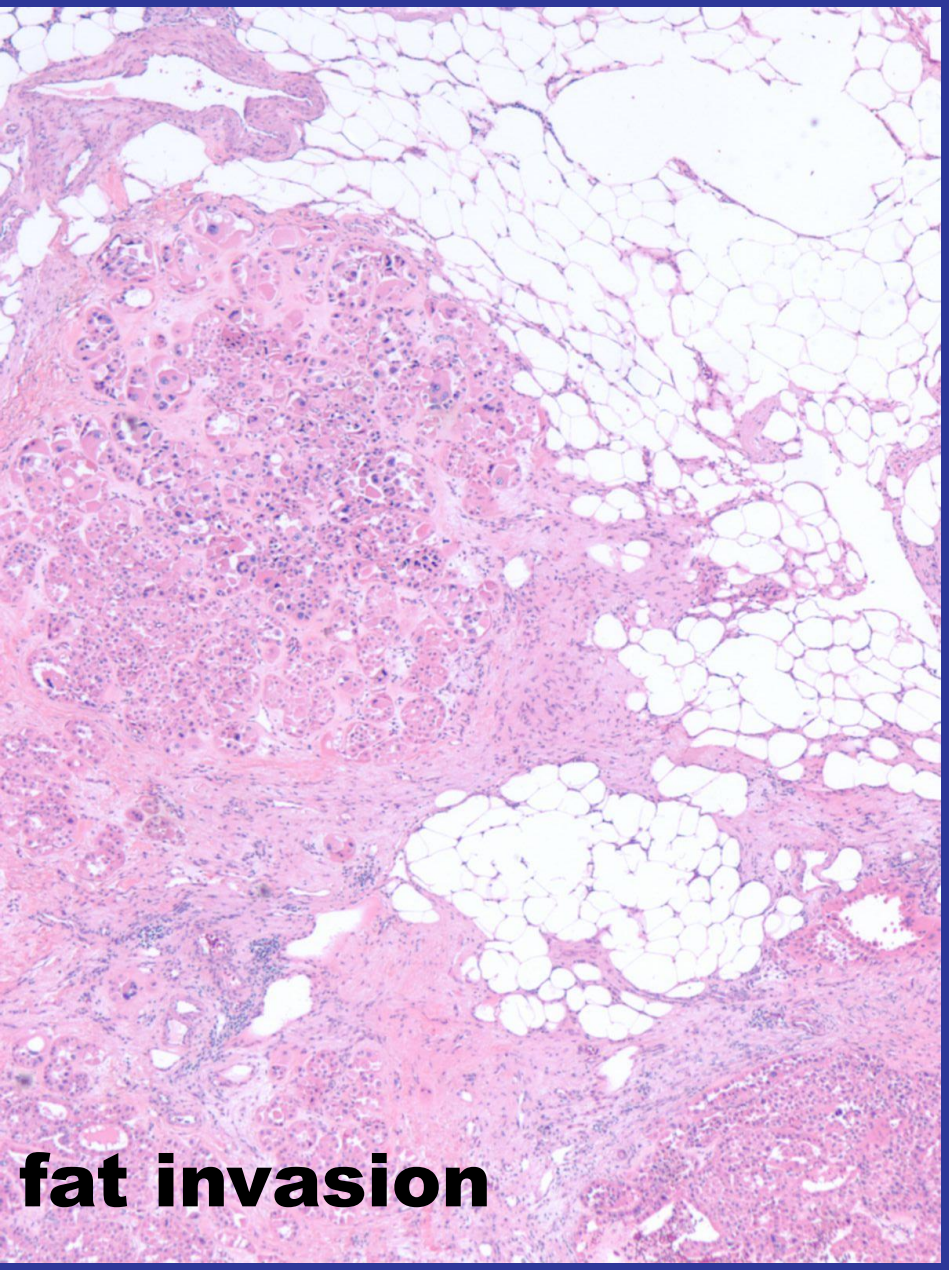
atypia



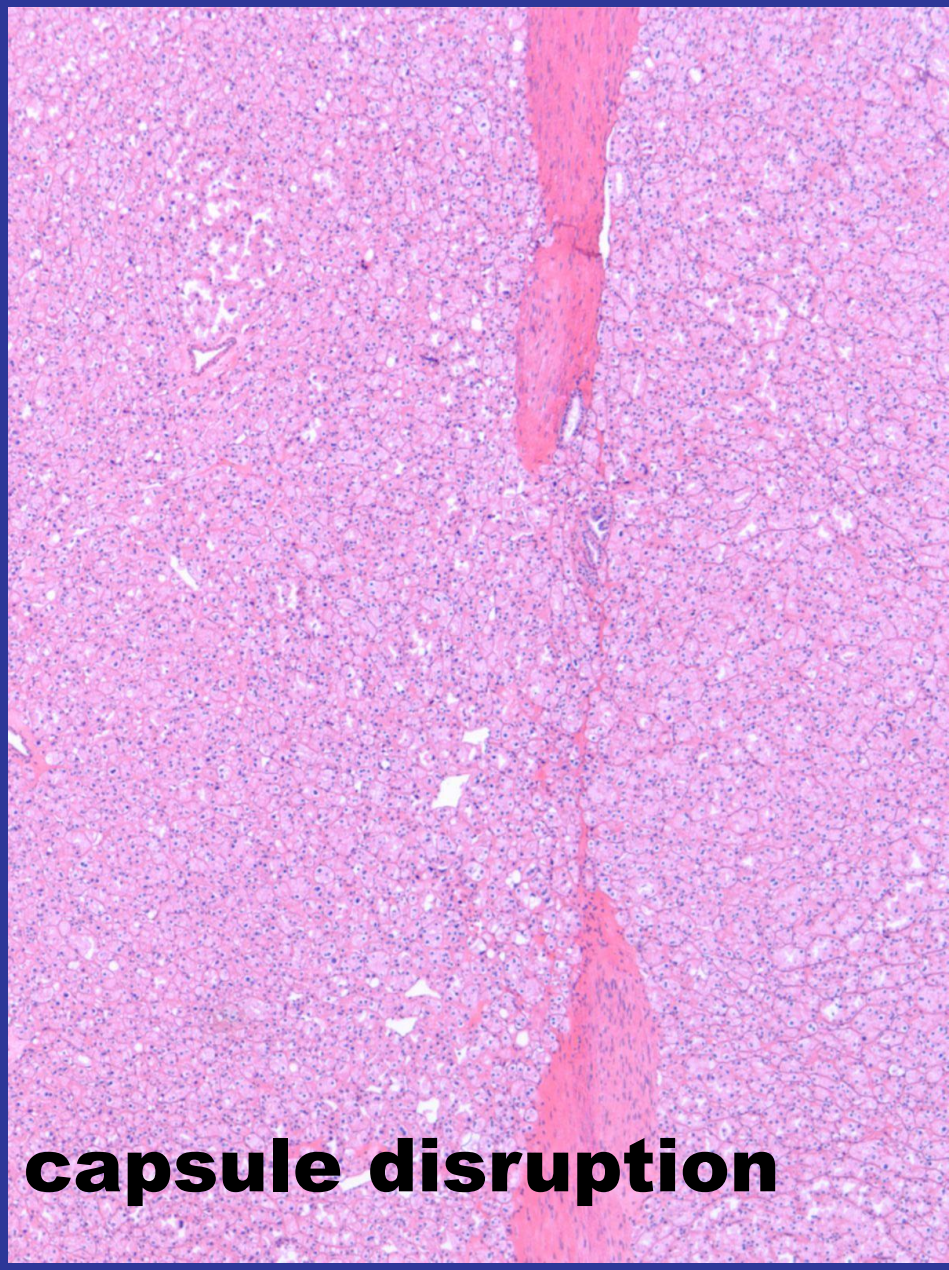
perinuclear halos



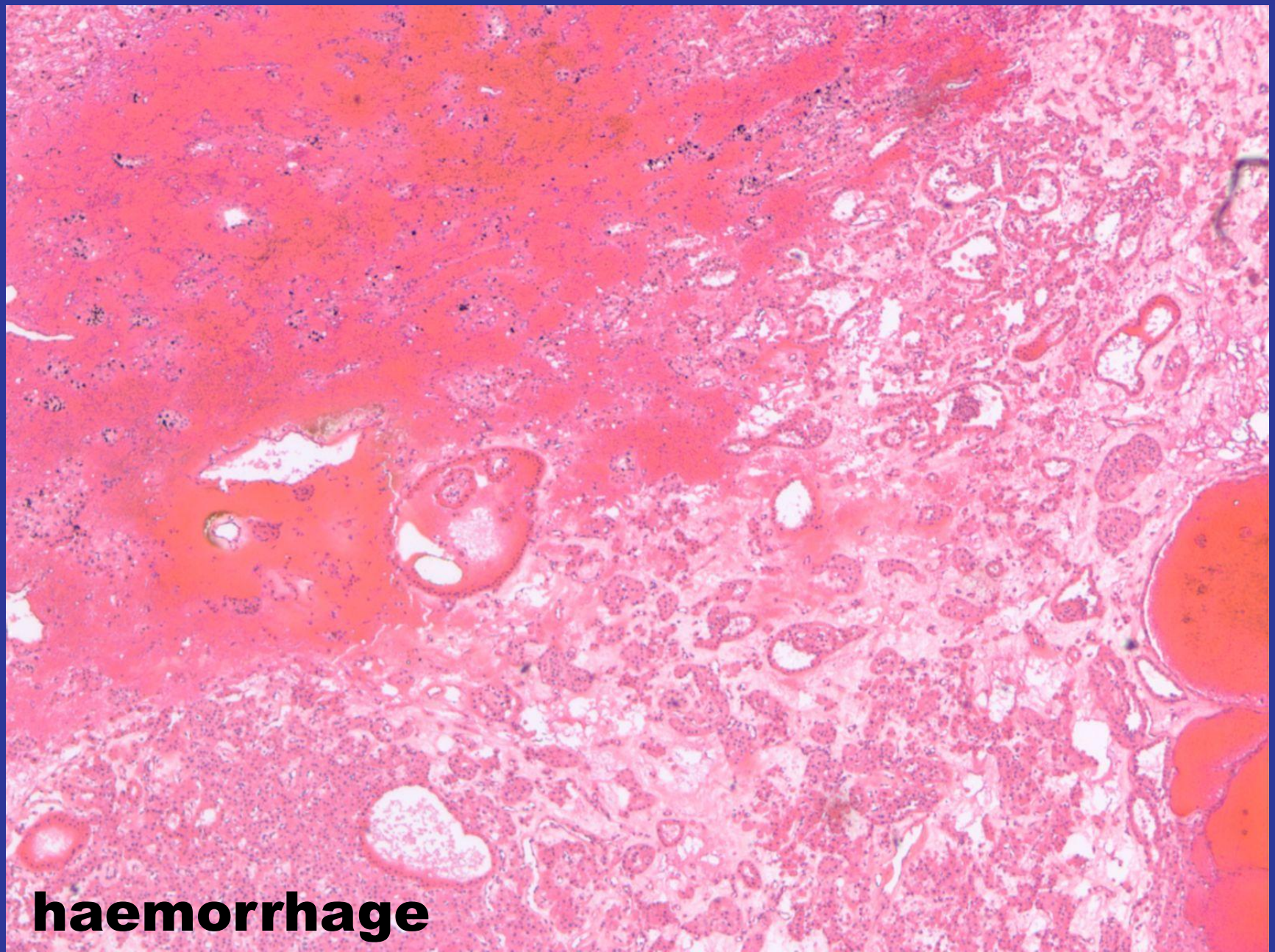
solid growth and thick capsule



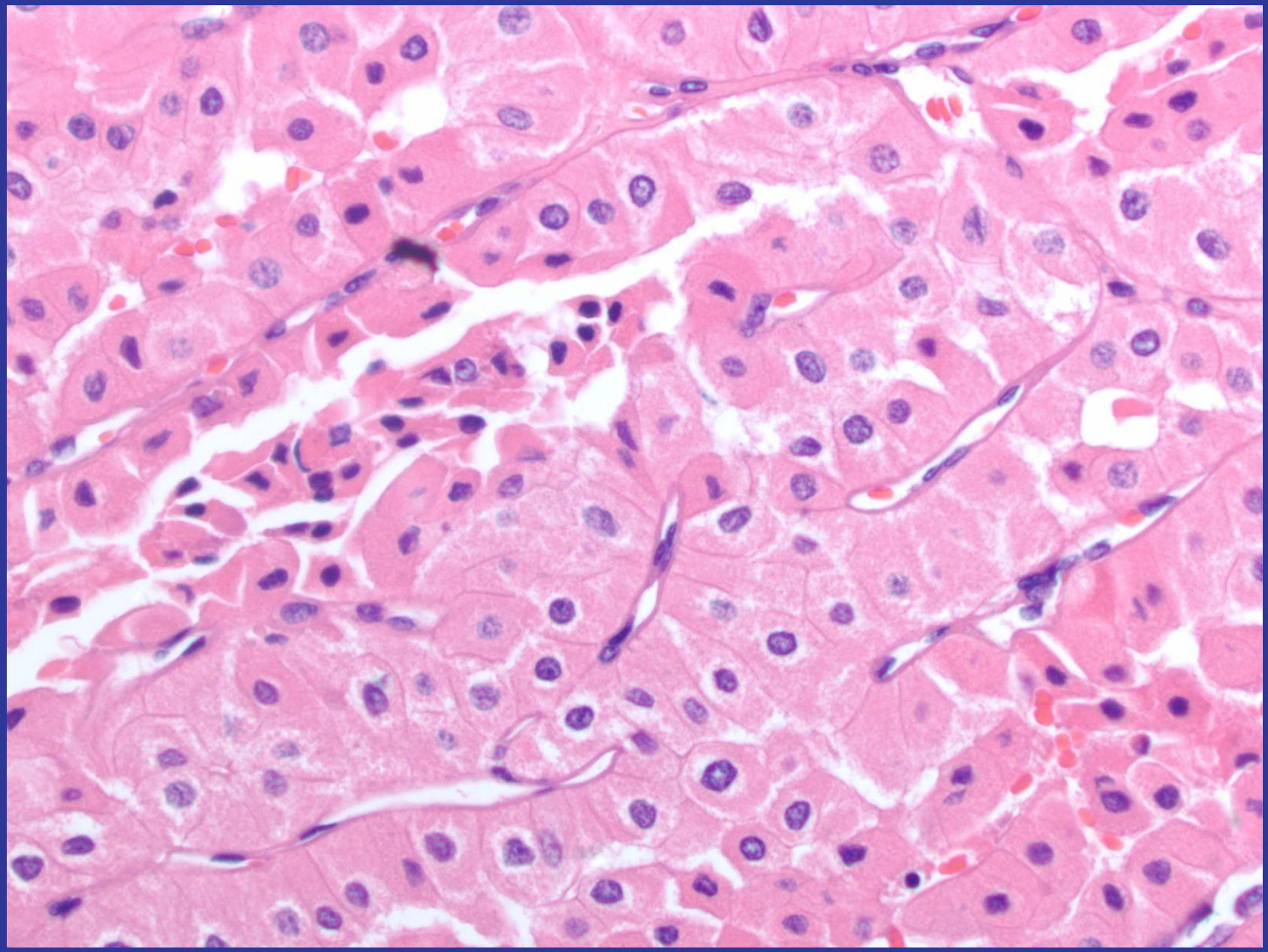
fat invasion



capsule disruption



haemorrhage



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Short communication

Insertion (8;11) in a renal oncocytoma with multifocal transformation to chromophobe renal cell carcinoma

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ORIGINAL ARTICLE

Hybrid chromophobe renal cell neoplasm

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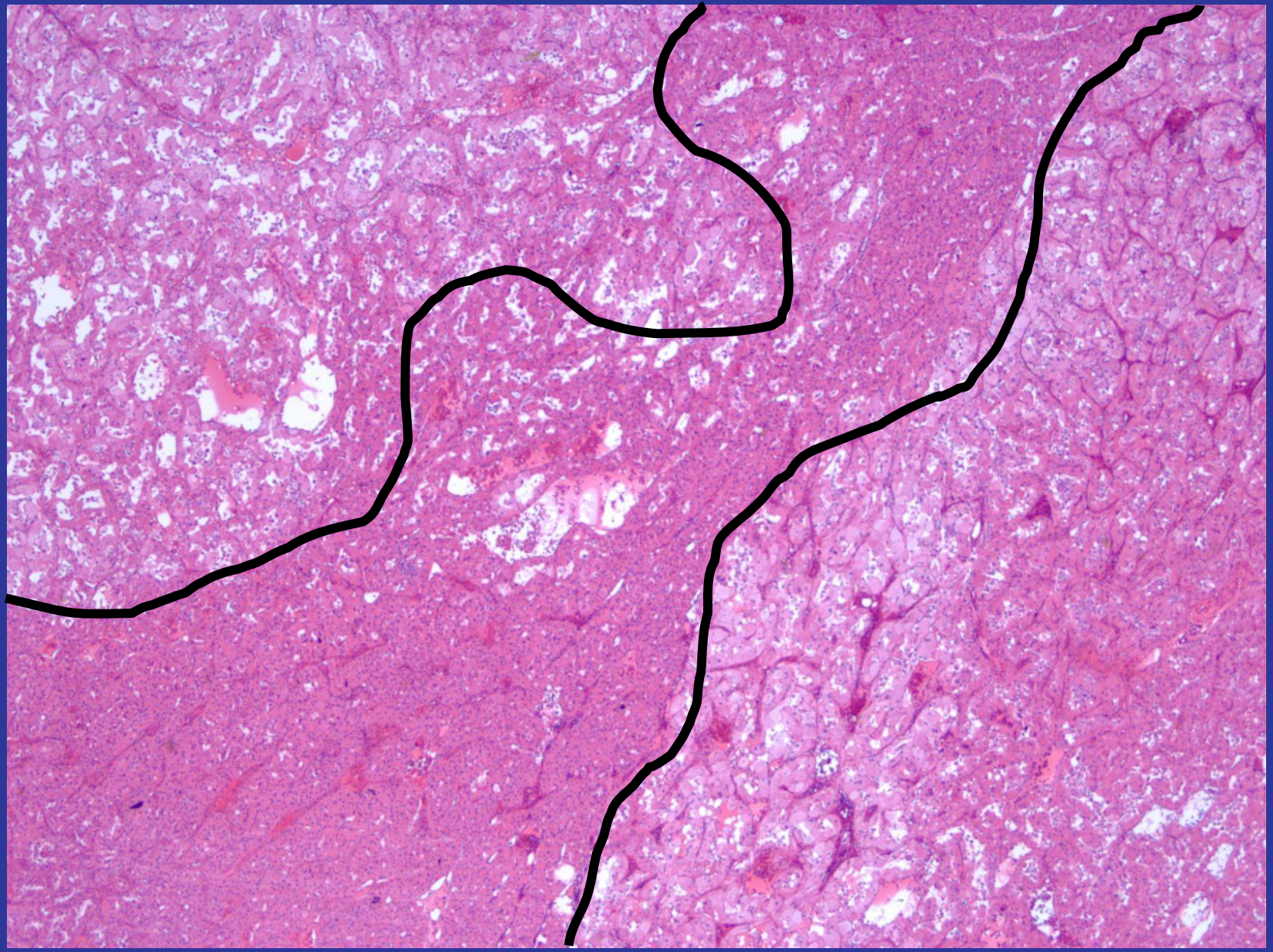

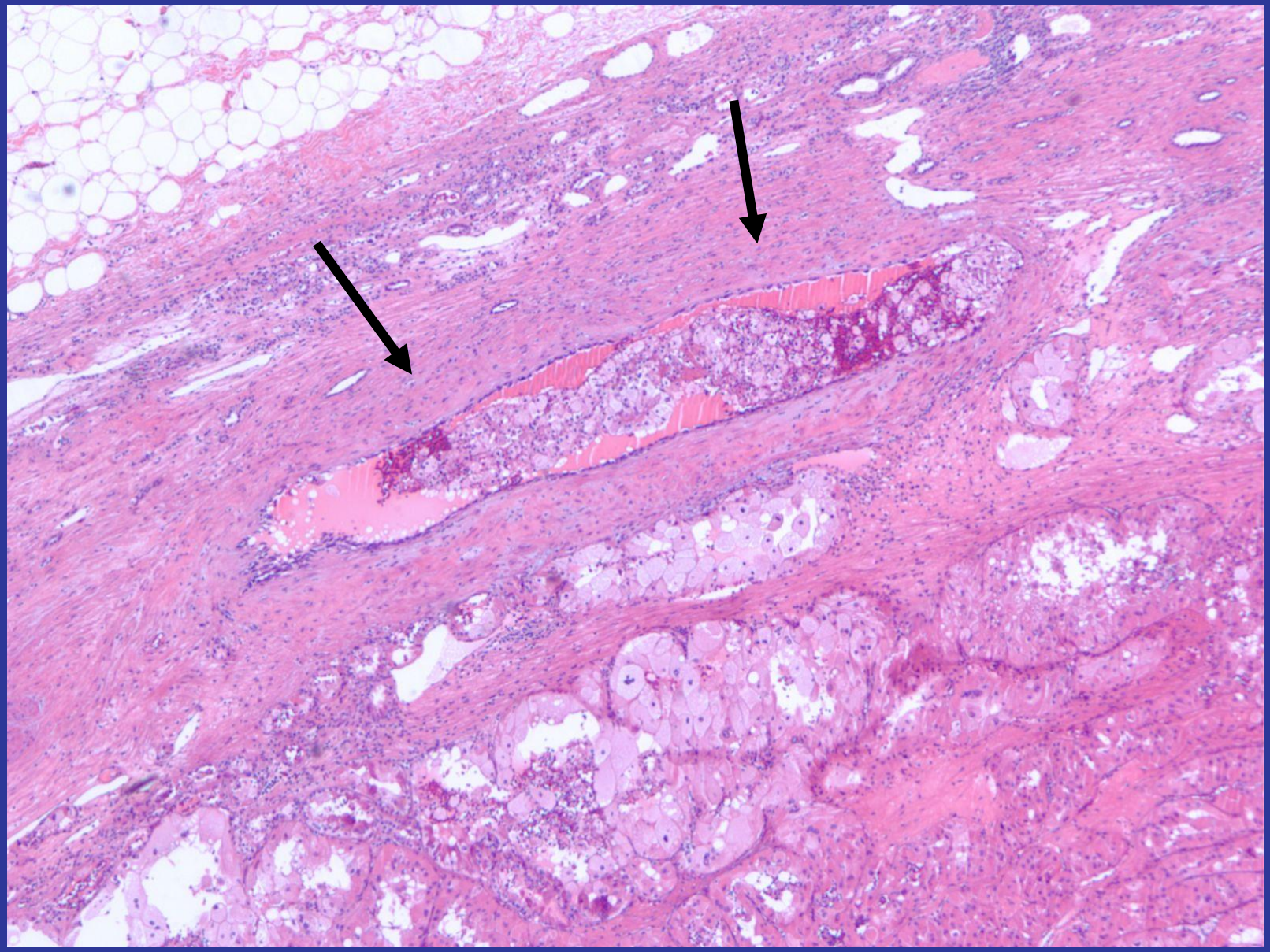

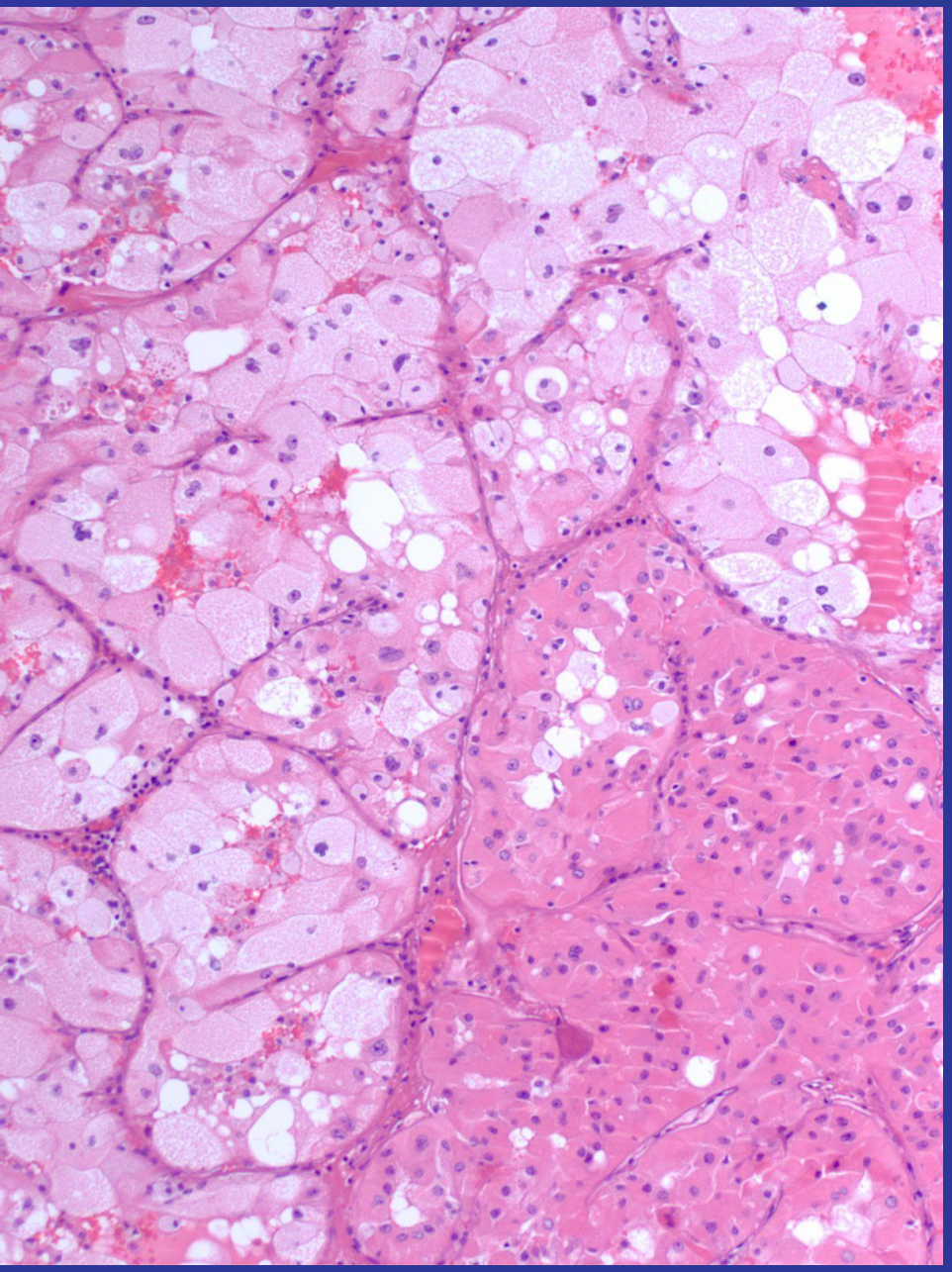

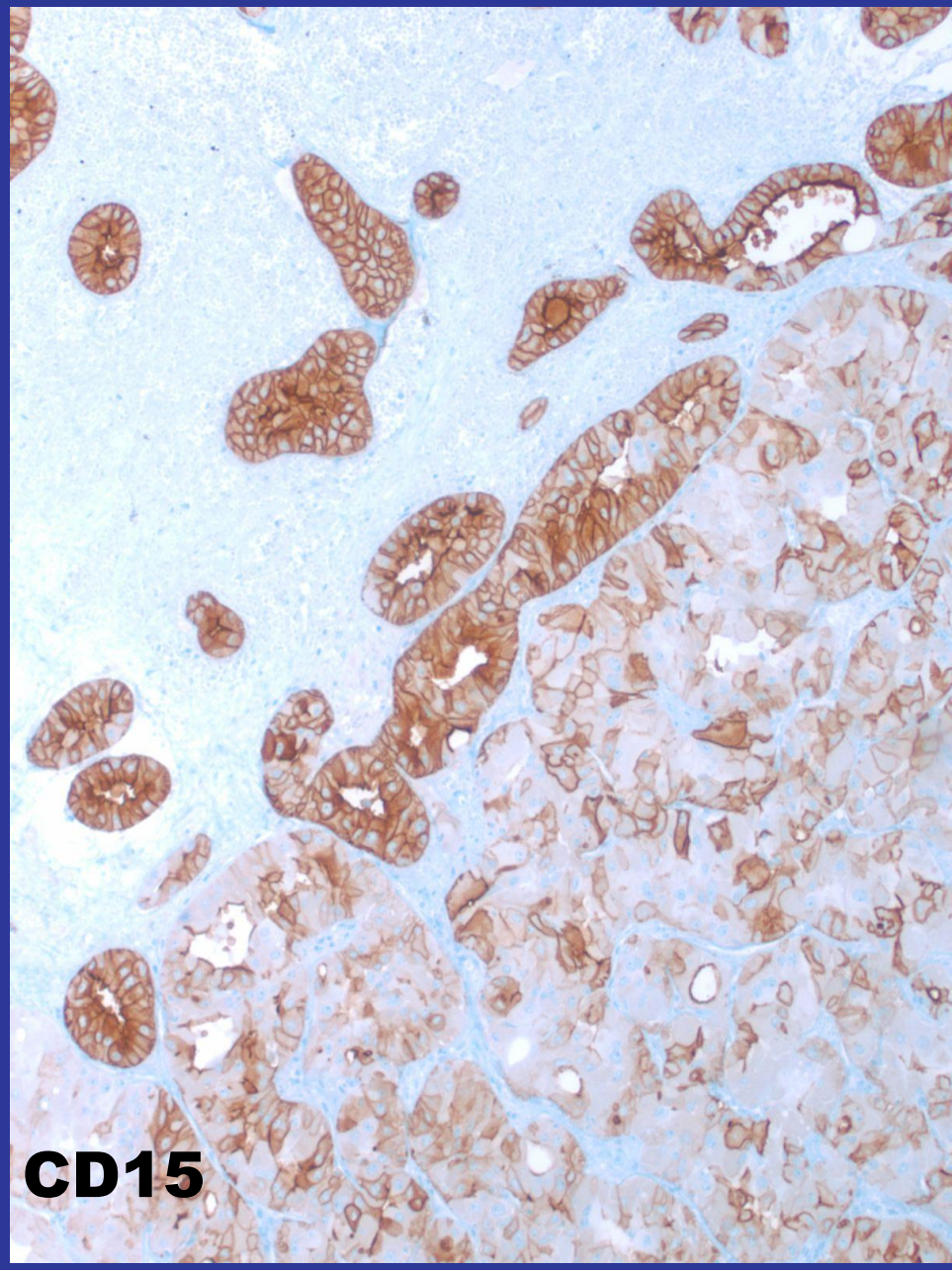
CD15

CONCLUSIONES

CABALLO/ASNA

BURDÉGANO

YEGUA/ASNO

MULO


FunTOOsh.com


STOP

Gurutzeta Ospitalea
Hospital Cruces

Eskerrik asko zuen arretagatik

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