Universitat Autònoma de Barcelona

Vall d'Hebron Hospitals

Sessió Conjunta Societat Catalana d'Anatomıa Patològica – Societat Catalana de Citopatologia

"Seminari de casos de patologia pediàtrica amb correlació cito-histològica"

Punció de tumor renal

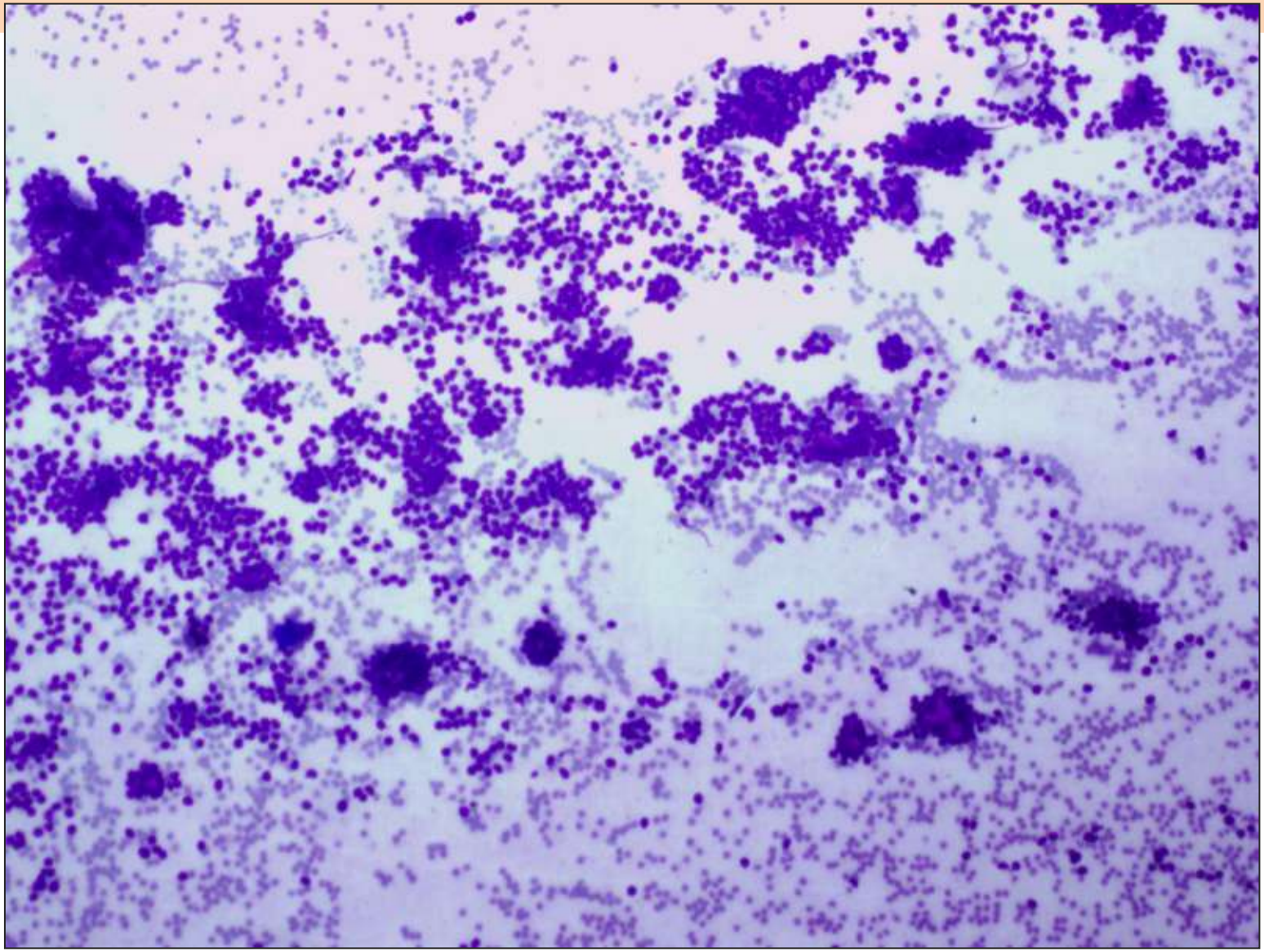
M Carme Dinarès, Joan Carles Ferreres

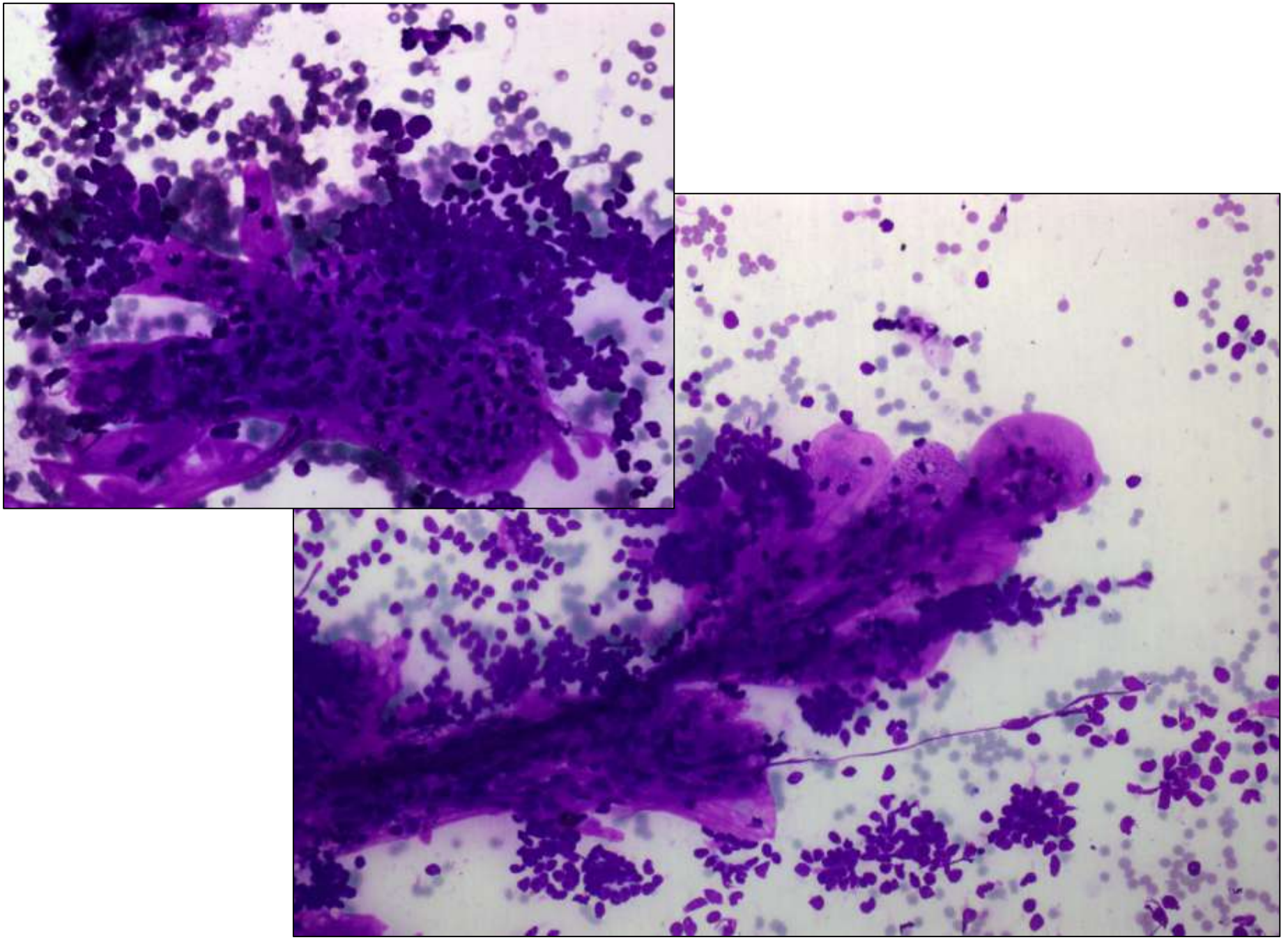
Servei d'Anatomia Patològica. HUVH. UAB

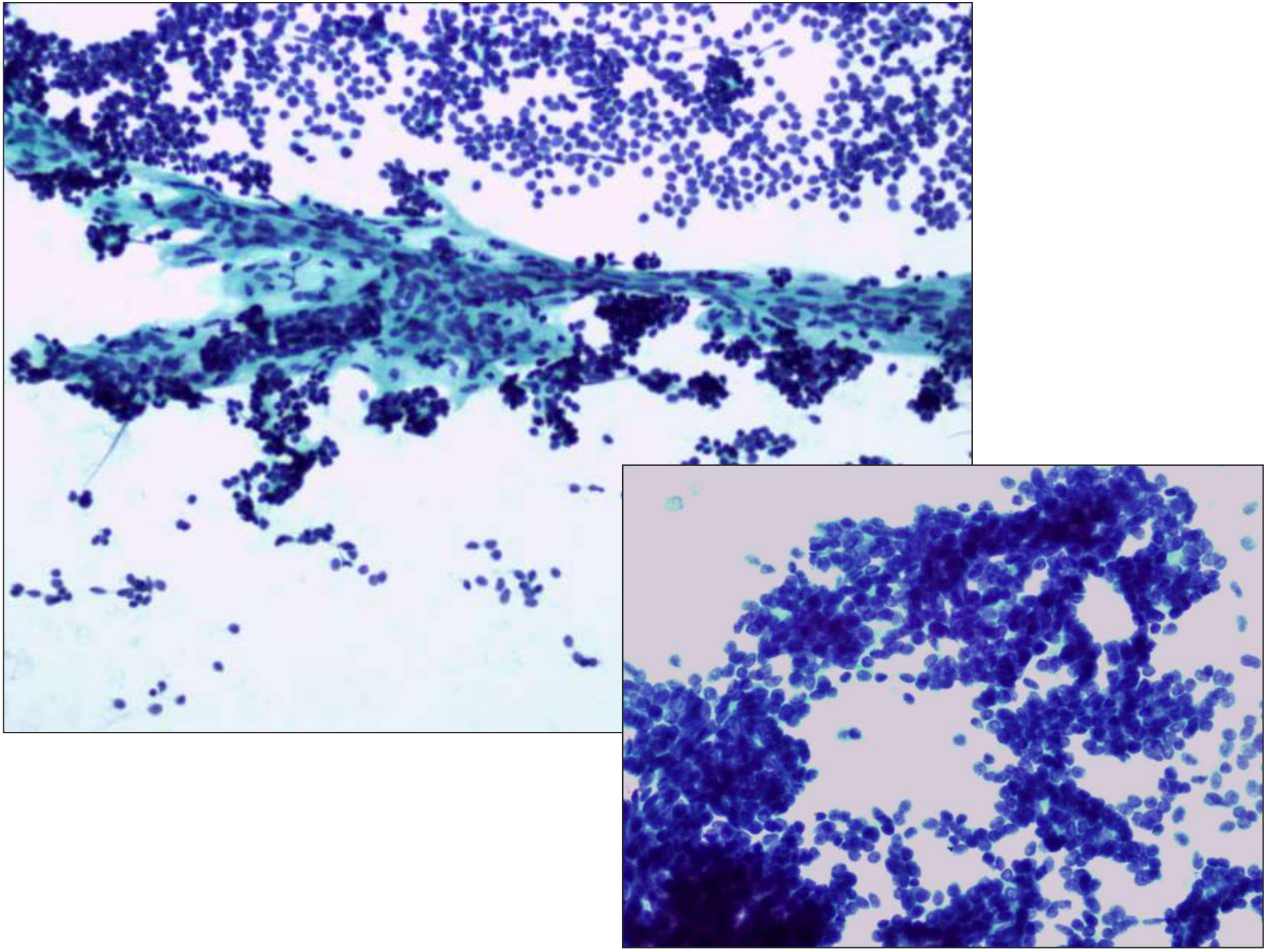
RESUM HISTÒRIA CLÍNICA

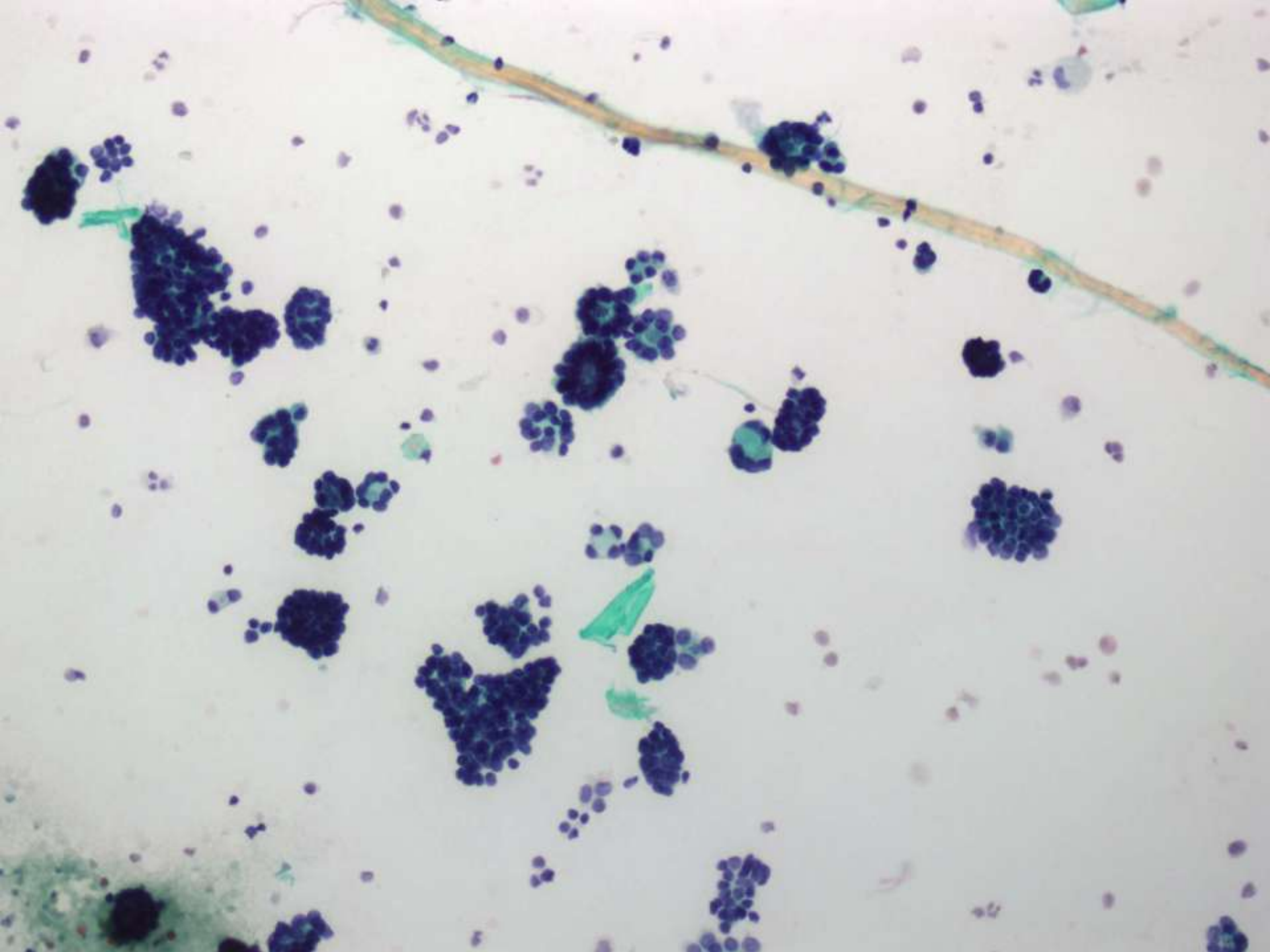
- Nen d'1 any d'edat
- En una ecografia per control d'hidronefrosi esquerra es detecta una tumoració renal d'1,6 cm de diàmetre, ben delimitada, a pol superior de ronyó dret
- No policitèmia
- Realització de PAAF i tru-cut
- Orientació diagnòstica per tècniques d'imatge

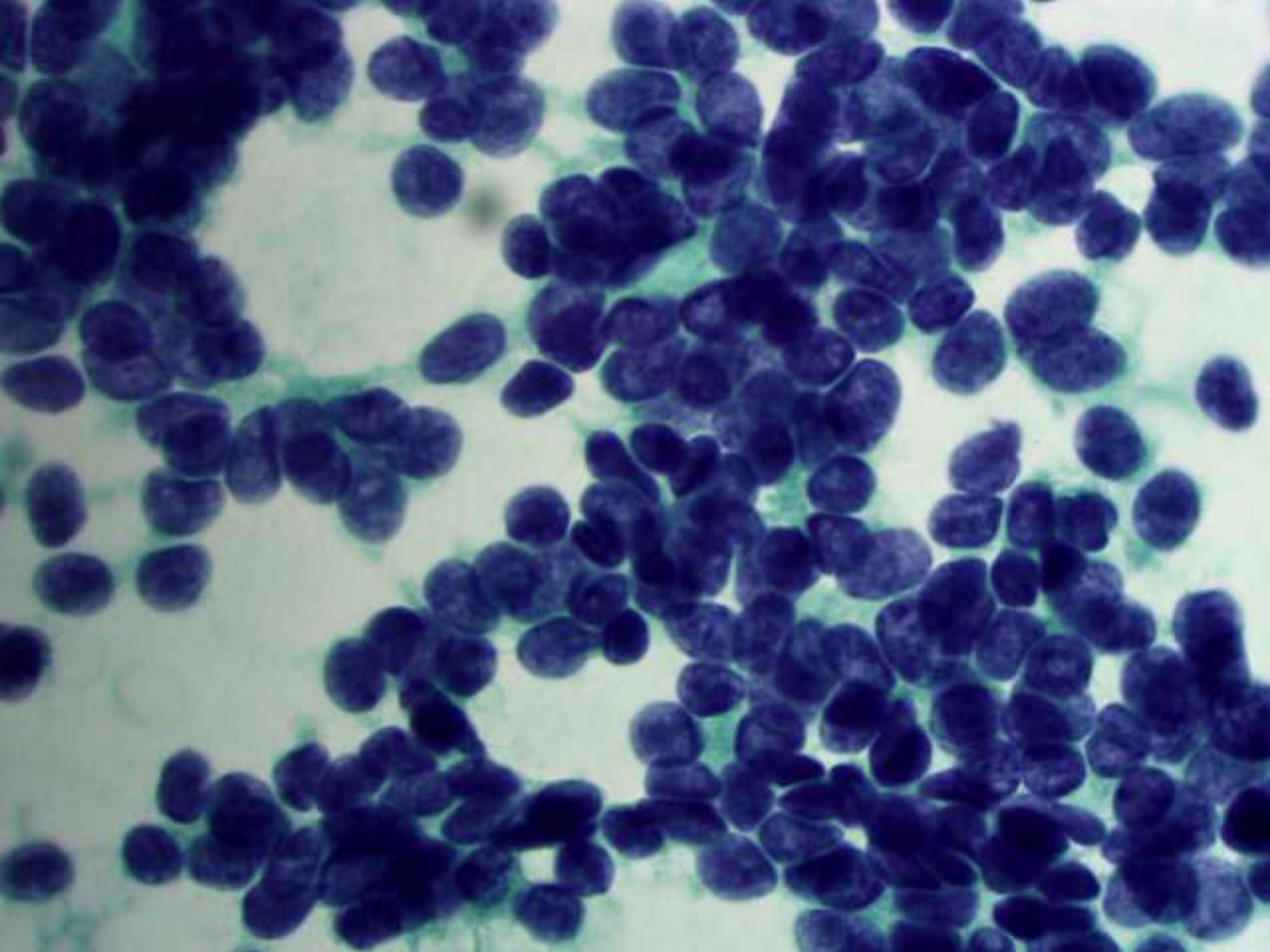
PAAF

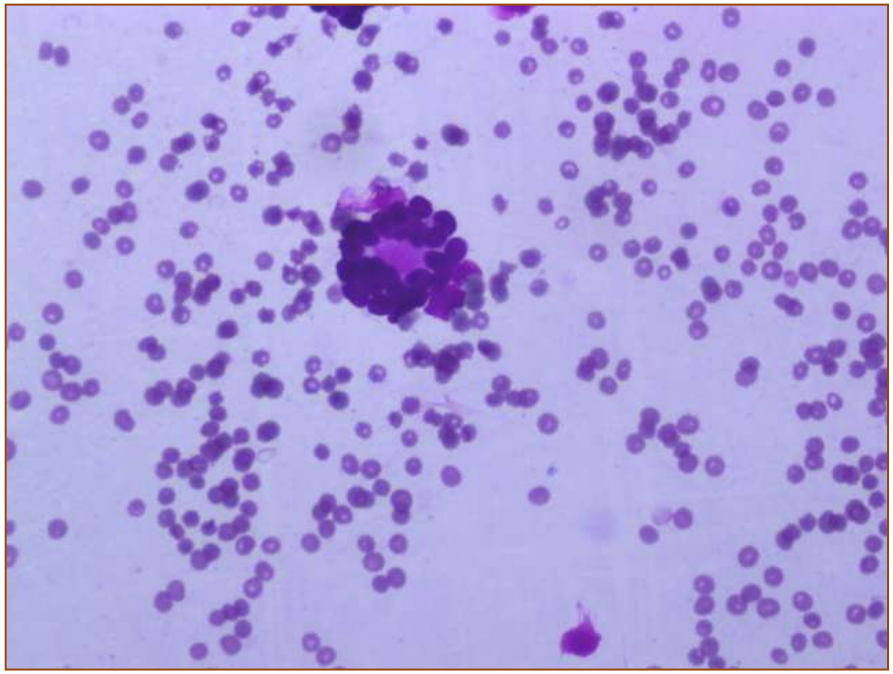


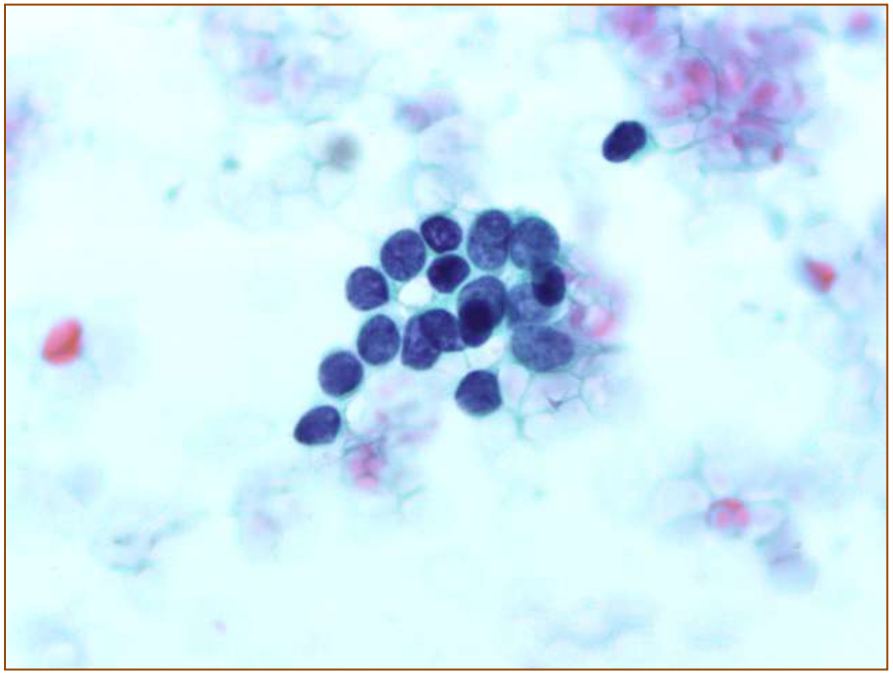


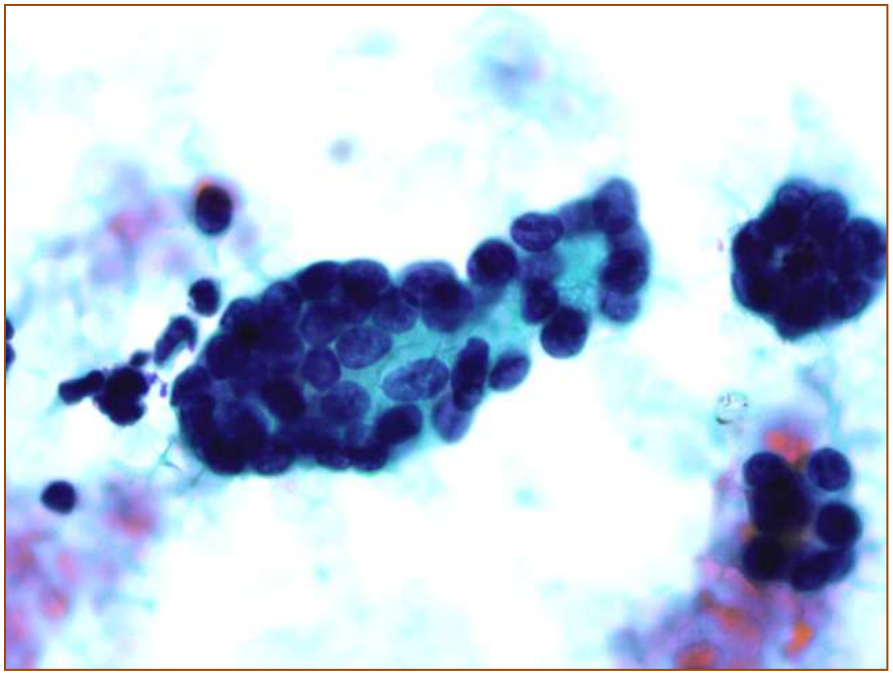


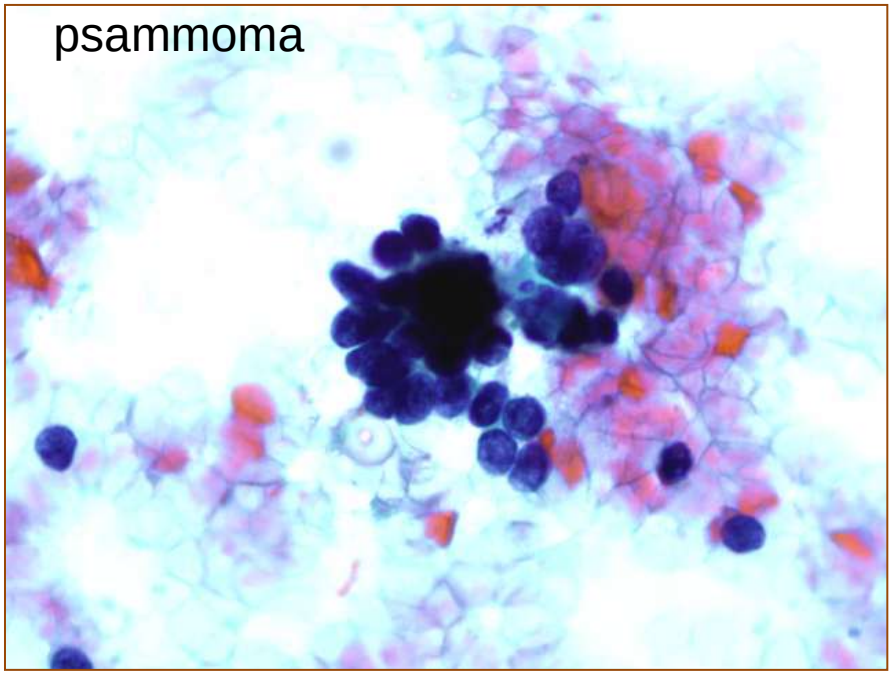











psammoma

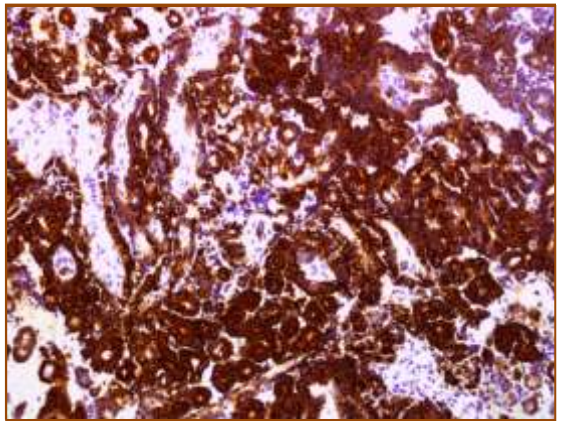
CITOLOGIA I

- Fons net, sense necrosi
- Cel·lularitat abundant de mida petita
- Grans plaques cohesives
- Relació matriu metacromàtica, fibril·lar
- Acinis envoltant material metacromàtic

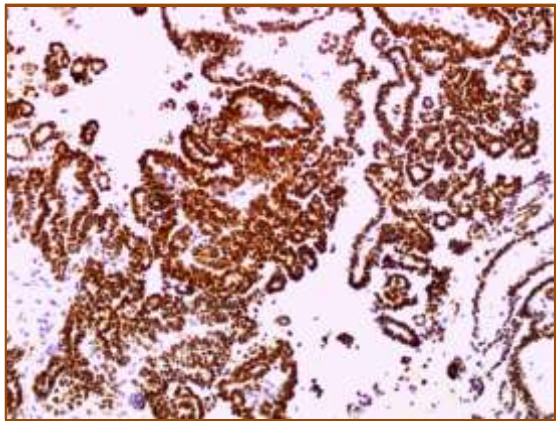
CITOLOGIA II

- Mínima atípia citològica
- Nucli rodó
- Cromatina fina, regularment distribuïda
- No nuclèol evident
- Cossos de psammoma
- No mitosi

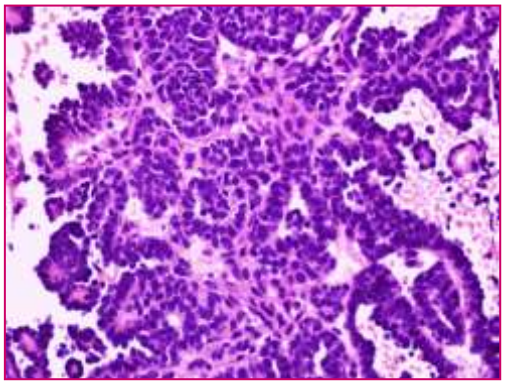
Estudi IHQ sobre bloc cel·lular



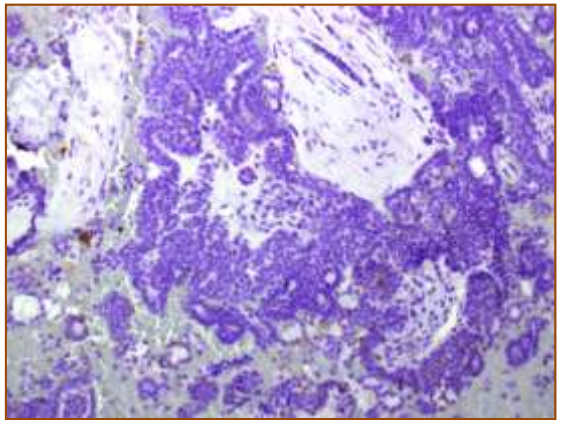
CAM 5.2



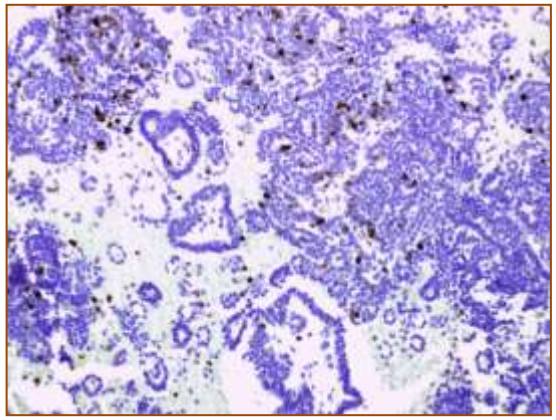
WT1



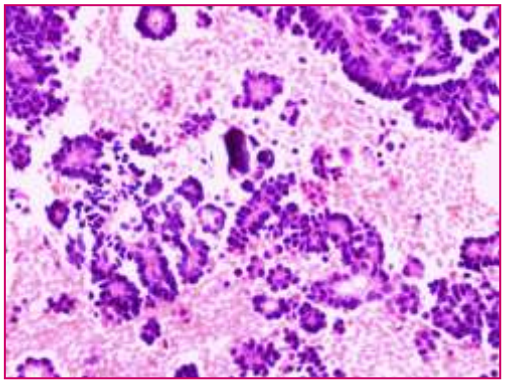
Bloc cel·lular HE



EMA



Ki67



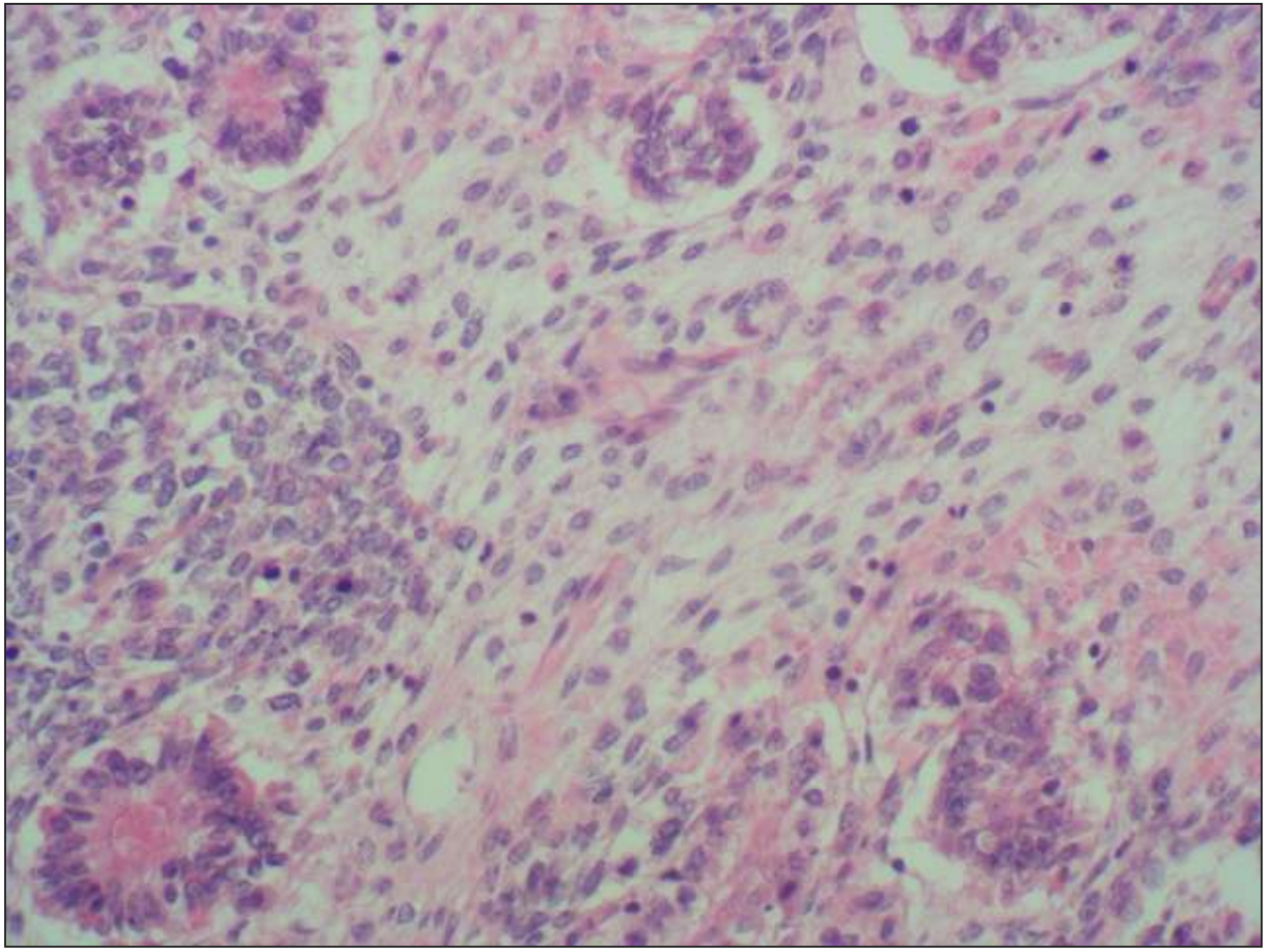
DIAGNÒSTIC PAAF

PROLIFERACIÓ DE CÈL·LULA PETITA I BLAVA DE PATRÓ PAPIL·LAR SUGGESTIVA **D'ADENOMA METANÈFRIC**

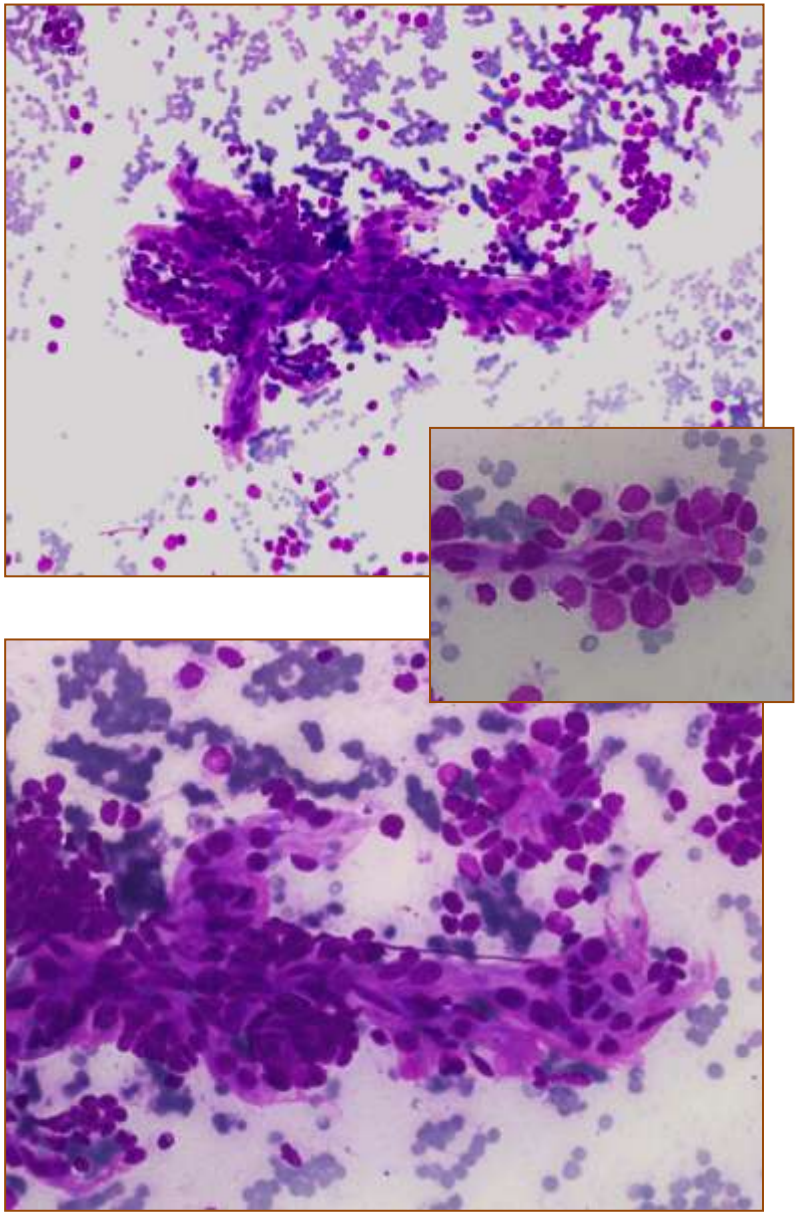
DIAGNÒSTIC DIFERENCIAL

- Tumor de Wilms: predomini epitelial
- Tumors de cèl·lula petita:
  - Neuroblastoma
  - Ewing/PNET
  - Rabdomiosarcoma
  - Limfoma No-Hodgkin
- Carcinoma Papil·lar Renal
- Metàstasis renal d'un carcinoma de tiroides

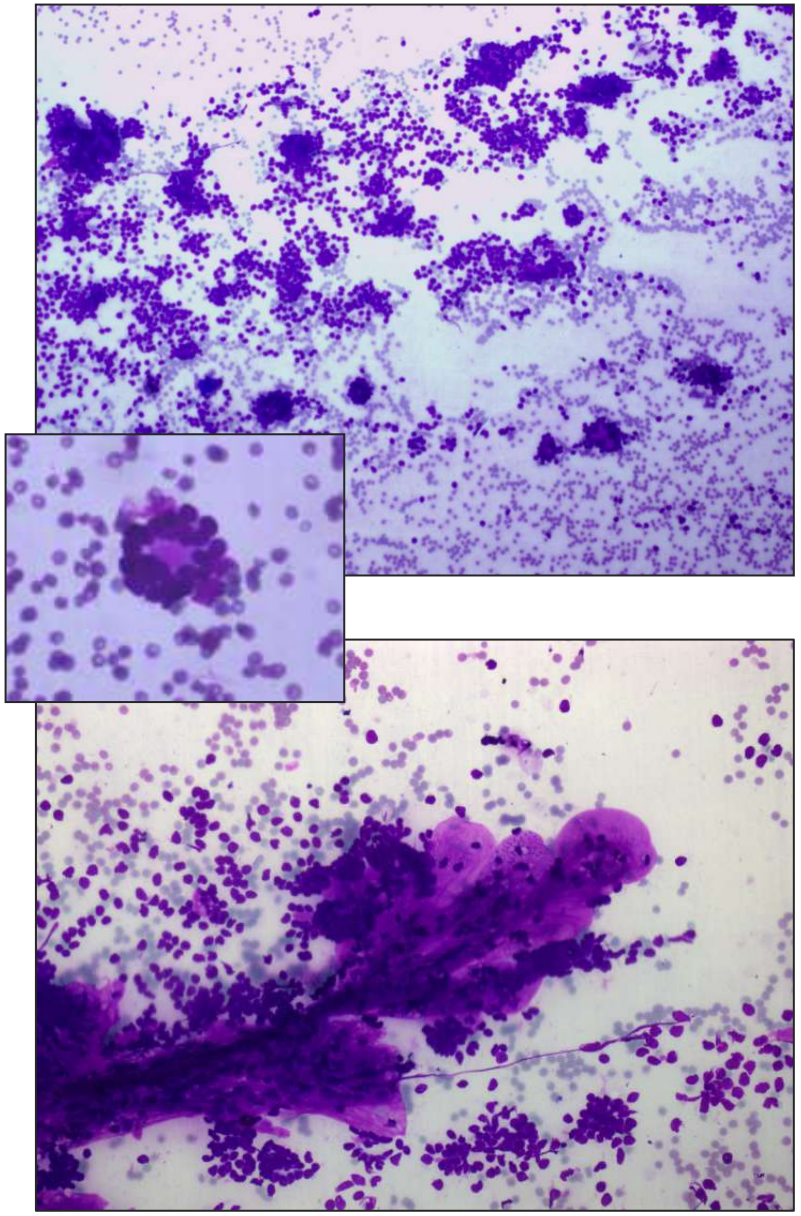
Tumor de Wilms



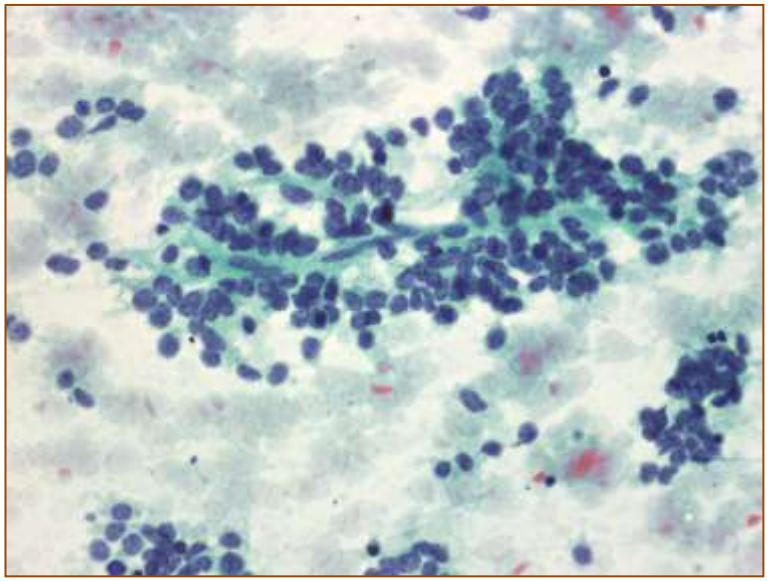
TUMOR DE WILMS

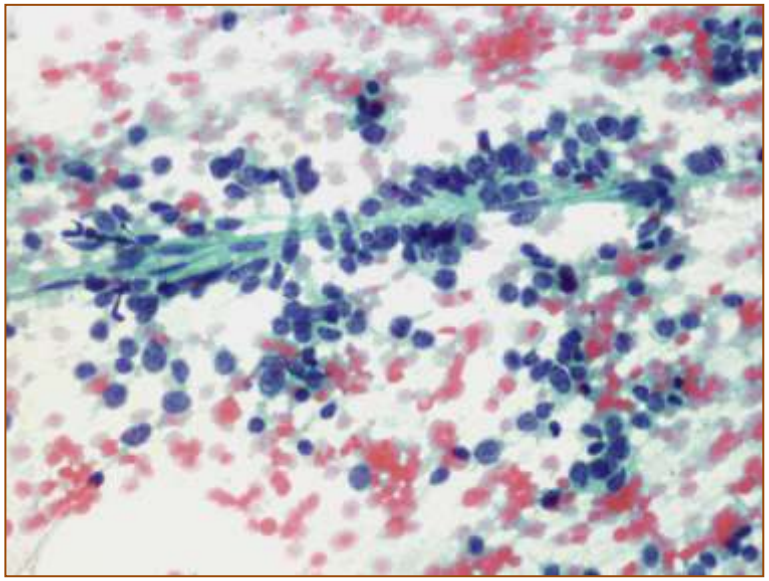


ADENOMA METANÈFRIC

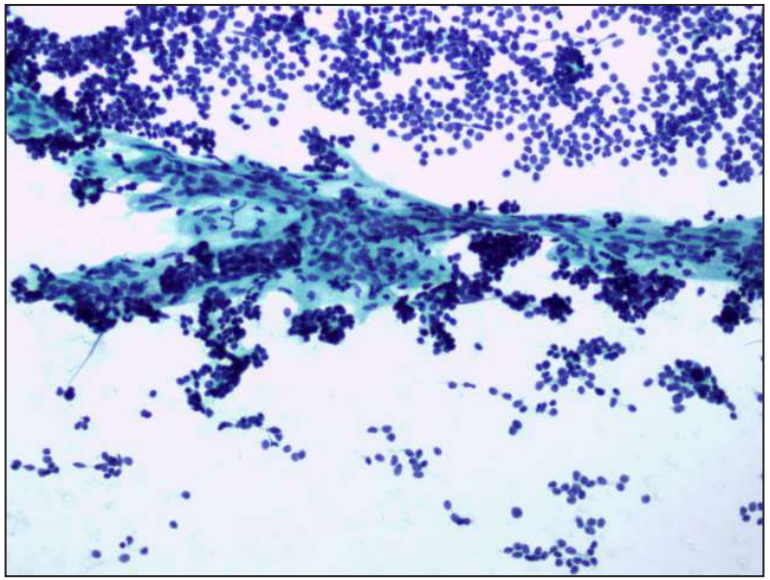


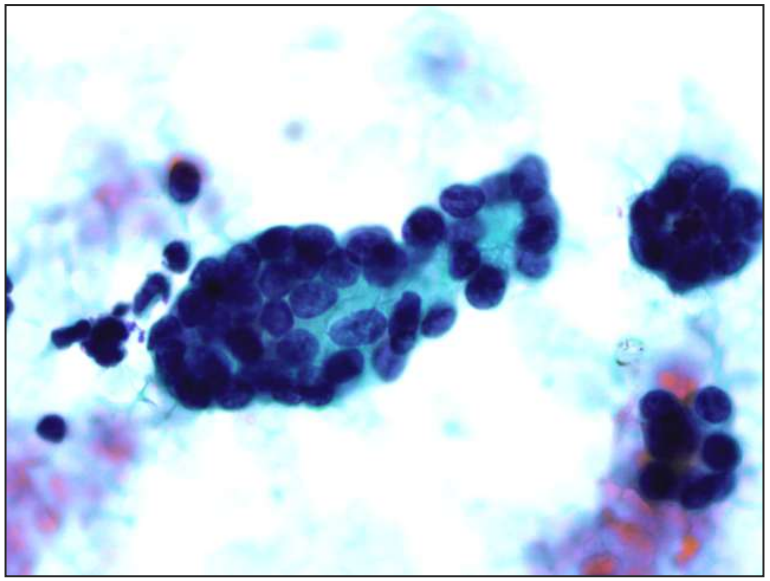
TUMOR DE WILMS



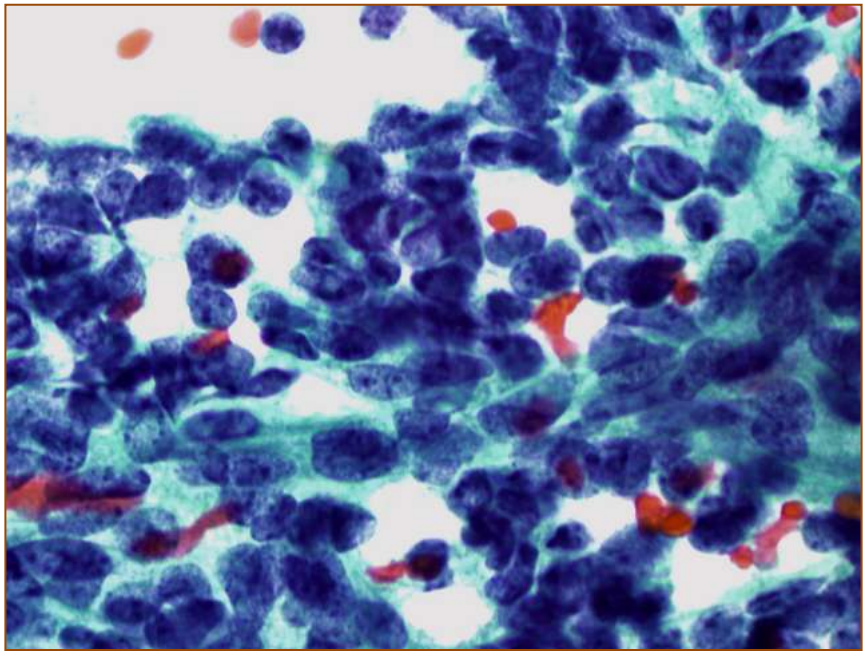


ADENOMA METANÈFRIC

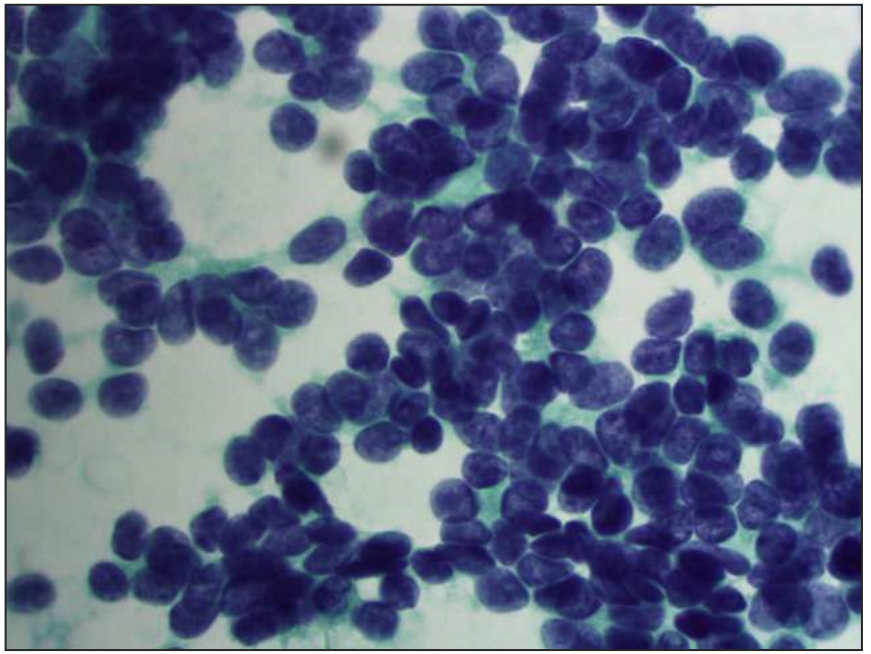




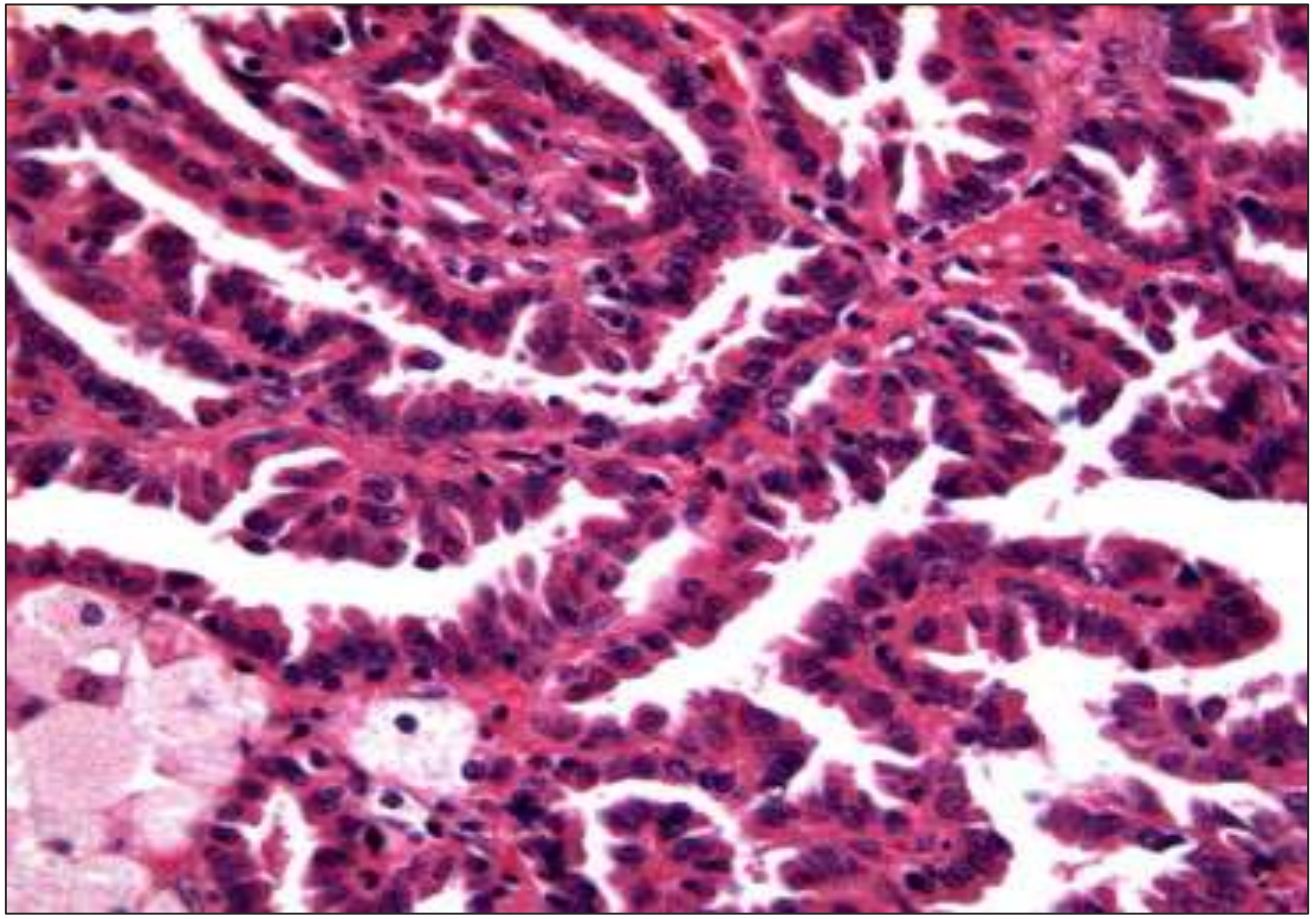
TUMOR DE WILMS



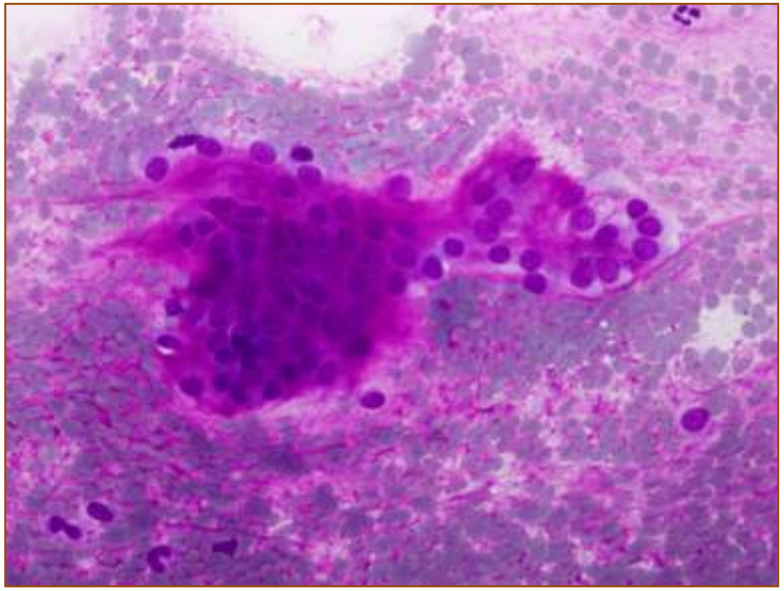
ADENOMA METANÈFRIC

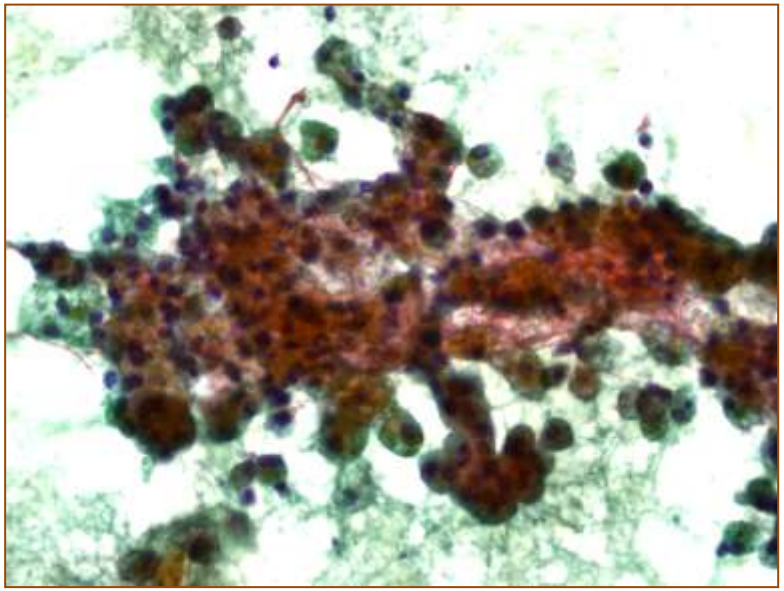


Carcinoma papil·lar renal

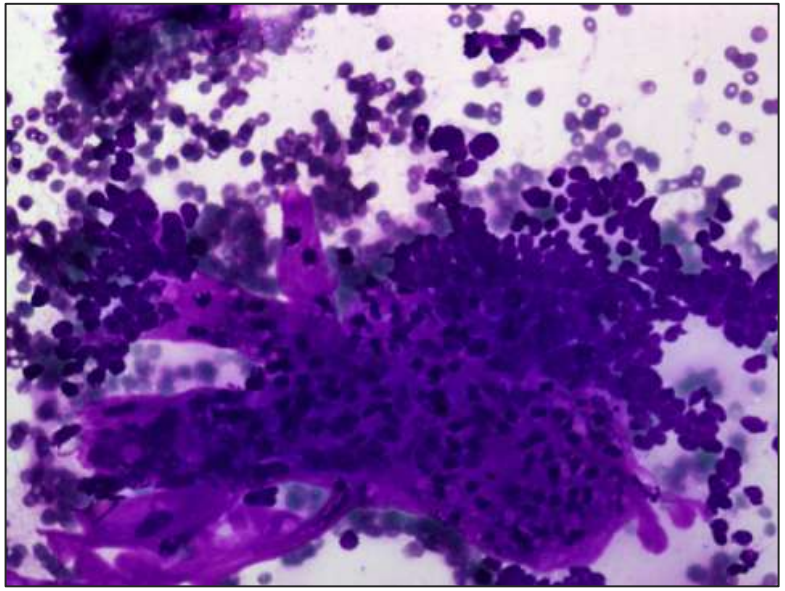


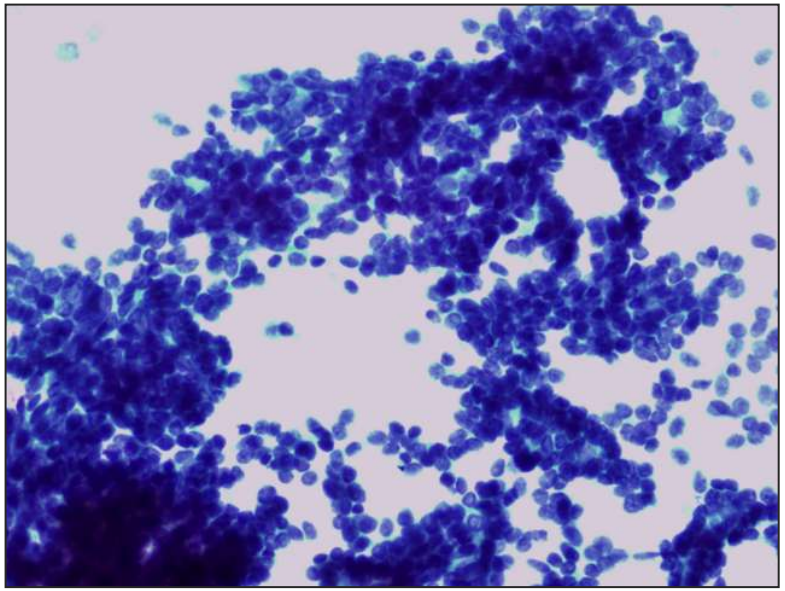
CARCINOMA RENAL PAPIL·LAR





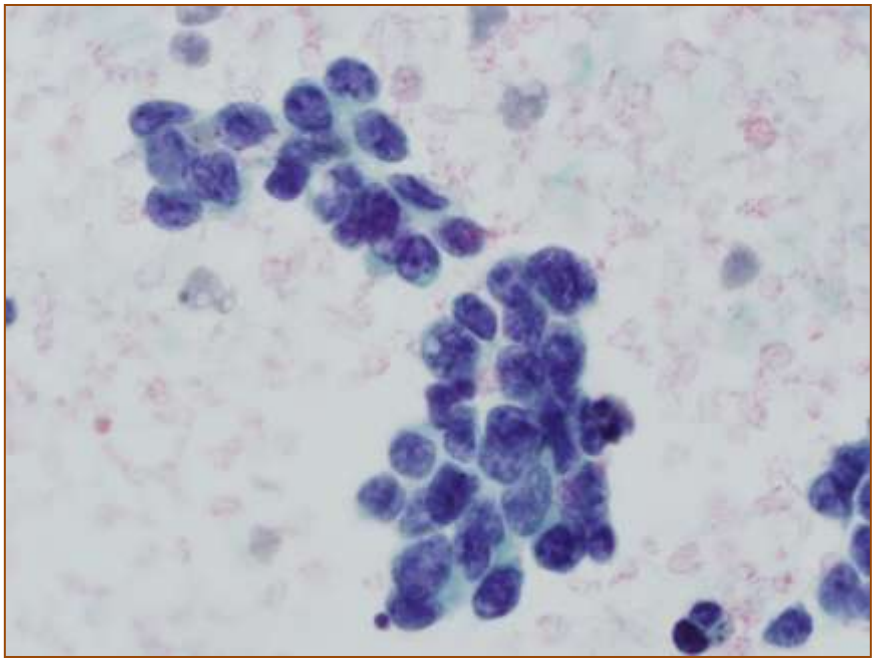
ADENOMA METANÈFRIC





Tumors malignes de cèl·lula petita

- Neuroblastoma
- Ewing/PNET
- Rabdo.Embrionari
- Limfoma No-Hodgkin



Immunohistoquímica

Am J Clin Exp Urol 2014;2(3):266-272
www.ajceu.us /ISSN:2330-1910/AJCEU0000945

Case Report

Differential diagnosis of renal tumors with tubulopapillary architecture in children and young adults: a case report and review of literature

Table 3. Immunohistochemical profiles of Papillary Renal Cell Carcinoma, Epithelial Predominant Wilms Tumor and Metanephric Adenoma

	PRCC	WT	MA
AE1/3	100%	29%	50%
Cytokeratin 7	78%	30%	7%
CD15	100%	0	0
EMA	63%	44%	7%
CD56	0	100%	0
CD57	70%	7%	89%
AMACR	98%	10%	10%
WT-1	10%	81%	82%

Citogenètica

- ADENOMA METANÈFRIC

  - cariotip normal o pèrdua d'al·lels a p13 (56%).
  - guanys en els cromosomes 7 i 17.
  - pèrdua del cr Y en varons

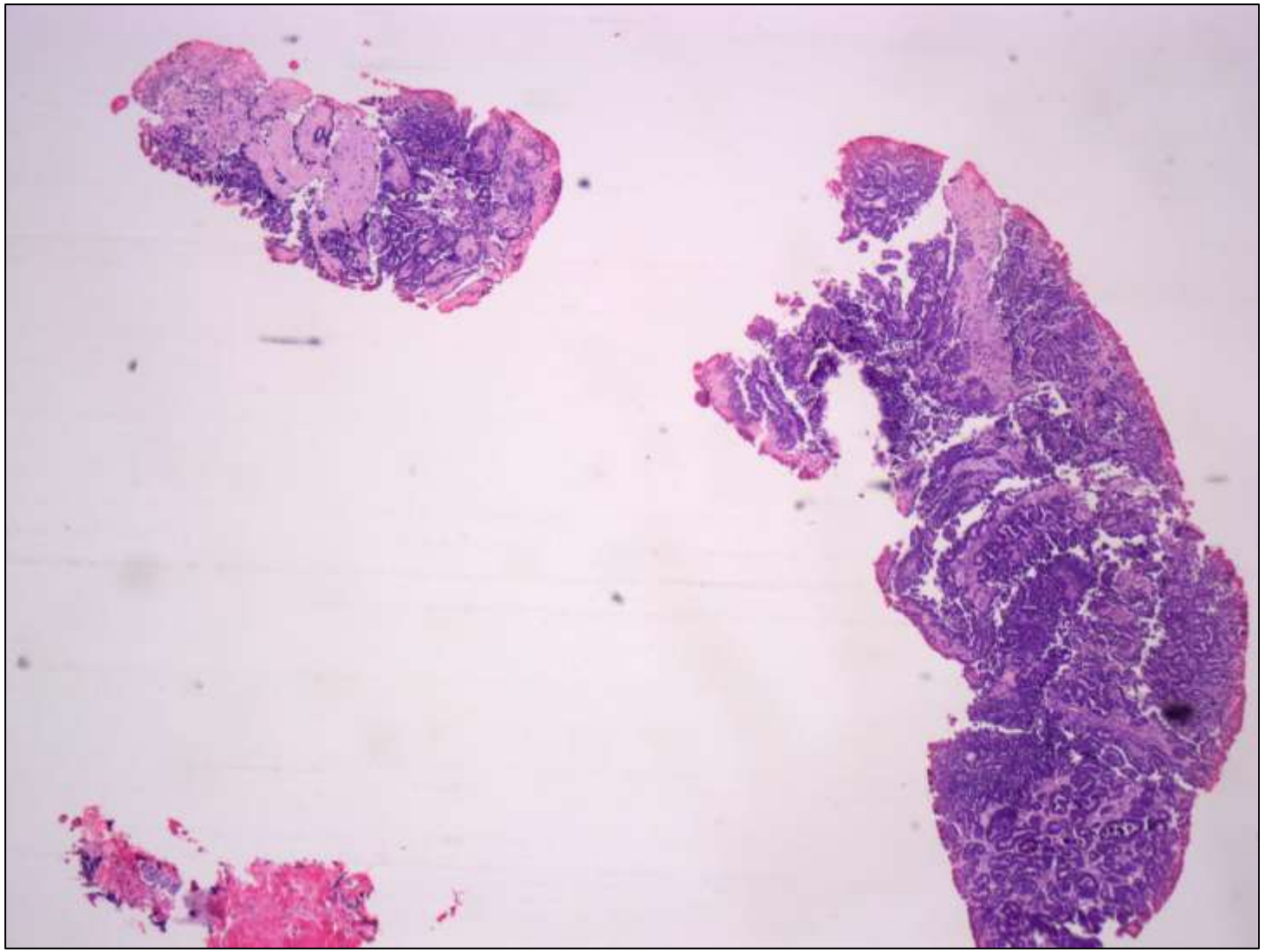
- TUMOR DE WILMS

  - 11p13, 11p15, 1p,1q, 7p
  - trisomies 8,12,18.

- CARCINOMA PAPIL·LAR

  - trisomia 7 y 17
  - pèrdua del cr Y en varons

Tru-cut



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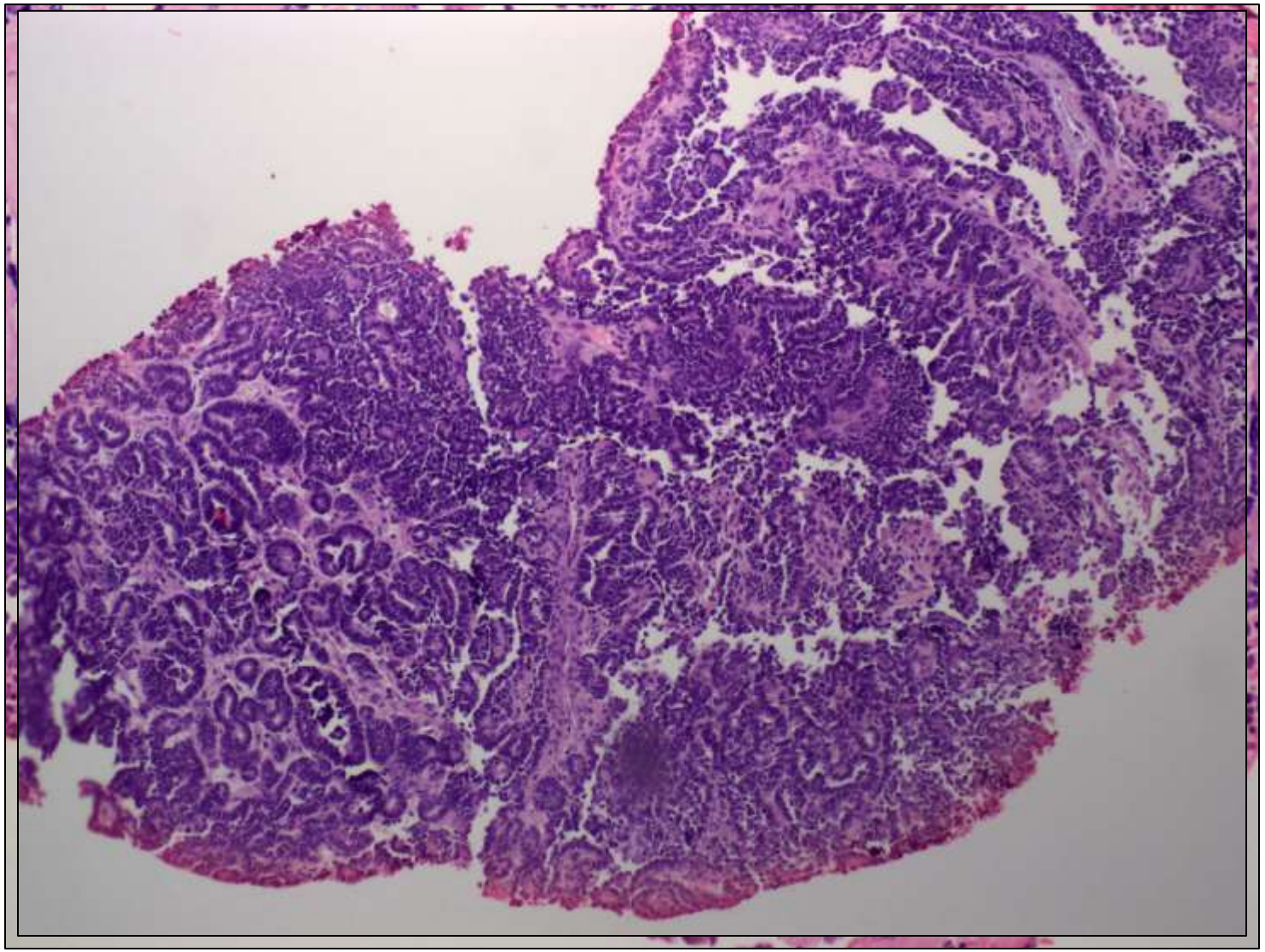

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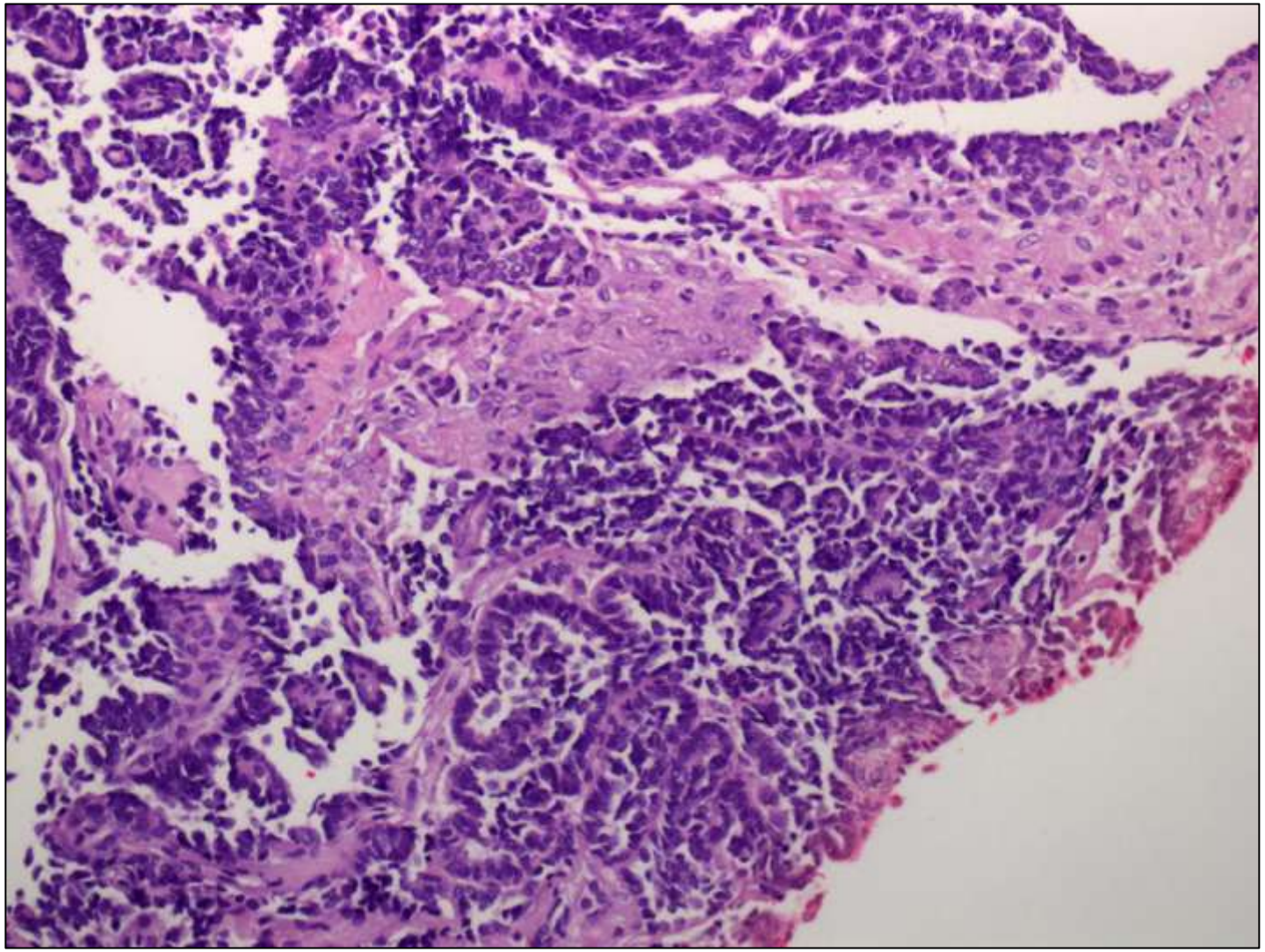

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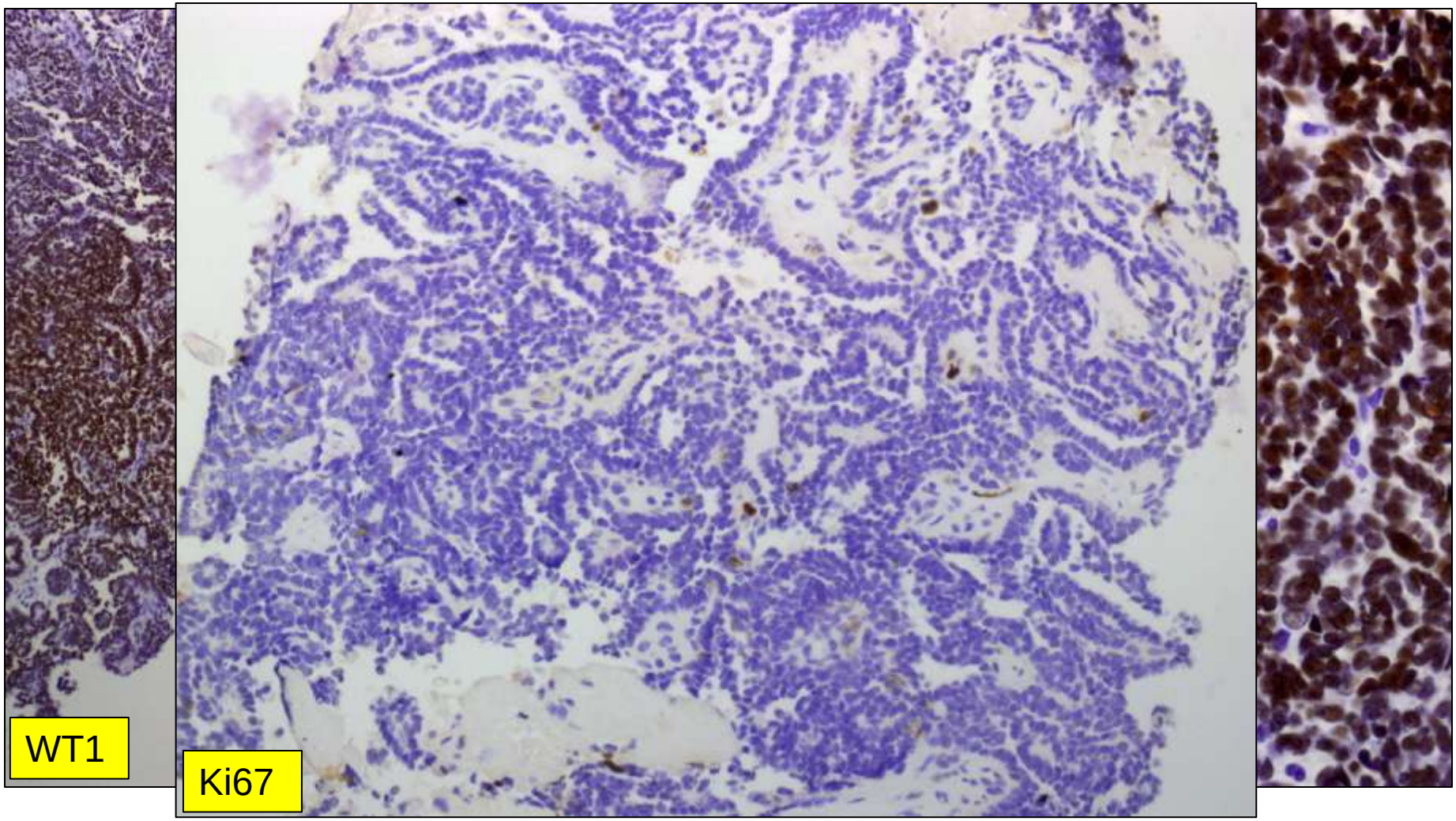


- Diagnòstic tru-cut:

  Compatible amb adenoma metanèfric

Adenoma metanèfric

- Descrit el 1980. Caracteritzat el 1995 en una sèrie de 50 casos (AFIP)[1] i una altra de 7 casos [2]
- Edat: des de 2ª a 9ª dècada, m: 41 a, relació H:D 1:2
- 50% troballa incidental, 10% policitèmia
- "cèl·lules epitelials petites formant petits acinis amb estroma acel·lular… menys freqüentment formant estructures tubulars, glomeruloides, polipoides o papil·lars.
- Mida: 0,3-15 cm
- Mai patró infiltratiu o amb invasió vascular

[1]Davis CJ et al. Metanephric adenoma. Am J Surg Pathol 1995;19:1101-14

[2]Jones EC et al. Metanephric adenoma of the kidney, a clinicopathological, immunohistoqhemical , flow cytometric, cytogenetic and electron microscopic study of seven cases. Am J surg Pathol 1995;19: 615-26

Adenoma metanèfric

- 9 de 50 amb càpsula ben definida; 13 amb càpsula fina i discontínua; 24 no encapsulats
- 6 àrees quístiques
- ½ casos component papil·lar. Un cas “papil·lar pur”
- Cossos de psammoma freqüents en el component papil·lar
- 16 casos amb canvis regressius/cicatricials
- Tots unilaterals
- 2 multifocalitat

[1]Davis CJ et al. Metanephric adenoma. Am J Surg Pathol 1995;19:1101-14

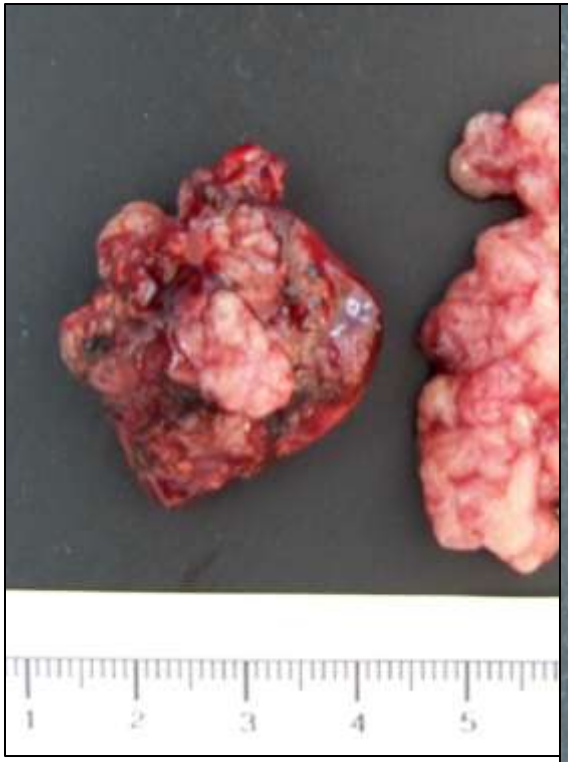
Adenoma metanèfric en nens

- 13 casos d'AM descrits en nens < 12 anys[1,2]
- Clínica de policitèmia, hipertensió, dolor abdominal, hematúria, massa abdominal palpable o troballa casual[1,2]
- Immunohistoquímia: WT1+, CD57+, CD56-, EMA-, CK7 + focal, AE1/AE3 + focal[3]
- 30% AM: WT1-[1,2]

[1]Mei H et al. Metanephric adenoma in a 2-year-old child: case report and immunohistochemical observations. J Pediatr Hematol Oncol 2010; 32:489-93.

[2]Spaner SJ et al. Pediatric metanephric adenoma: case report and review of the literature. Int Urol Nephrol, 2014; 46:677-80.

[3]Muir TE et al. Metanephric adenoma, nephrogenic rests and Wilms' tumor. Am J Surg Pathol 2001; 25:1290-6


1
2
3
4
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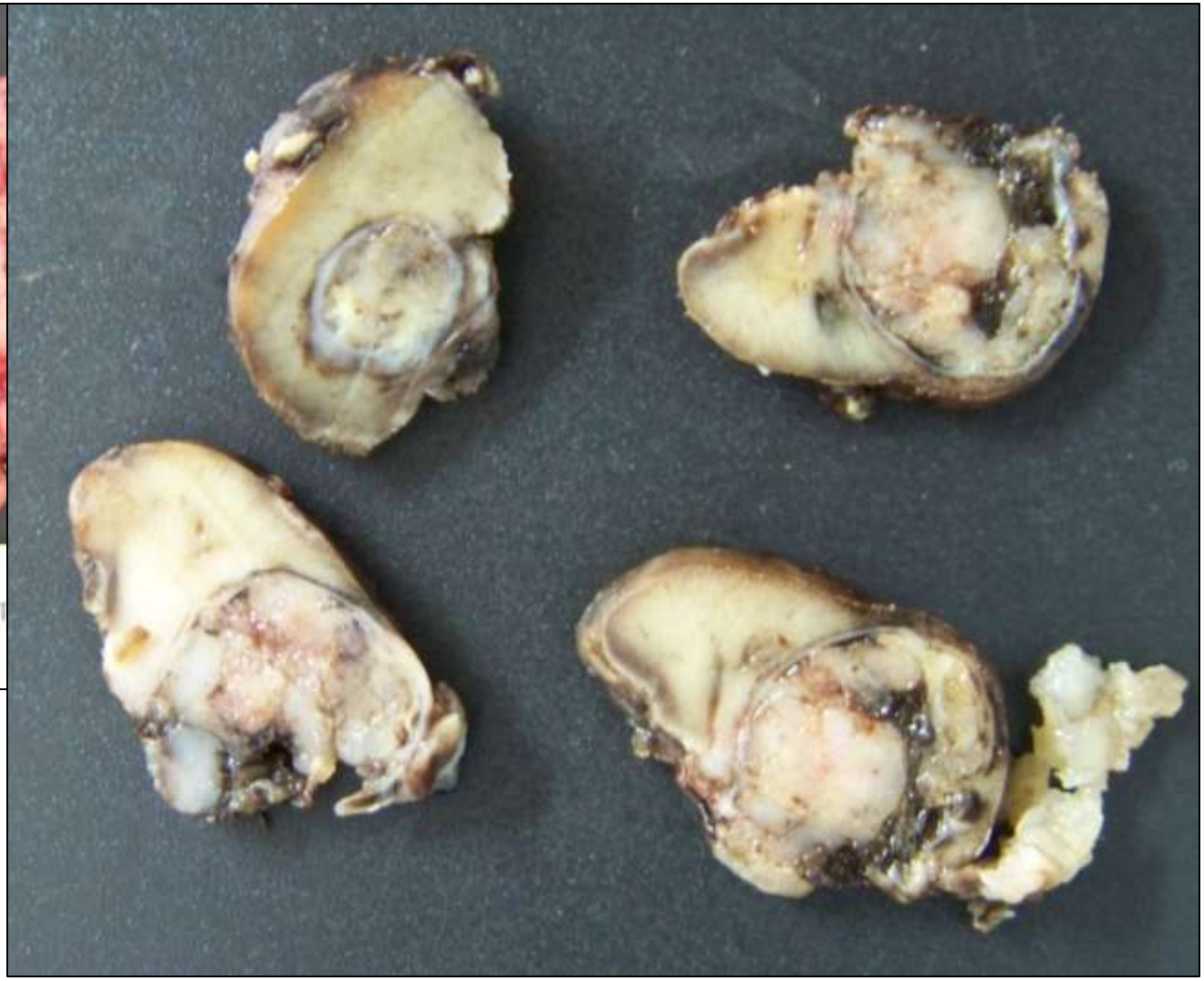
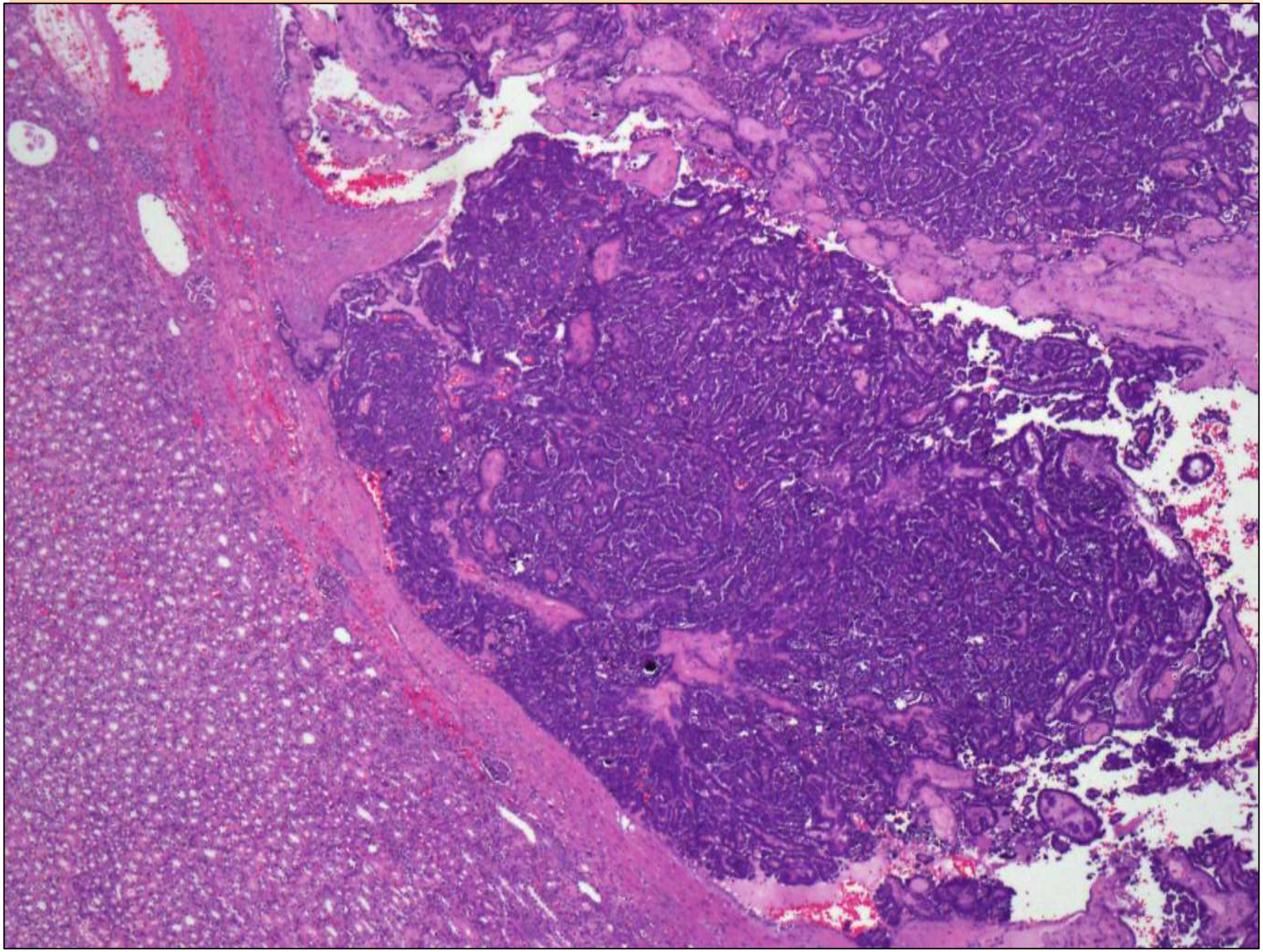
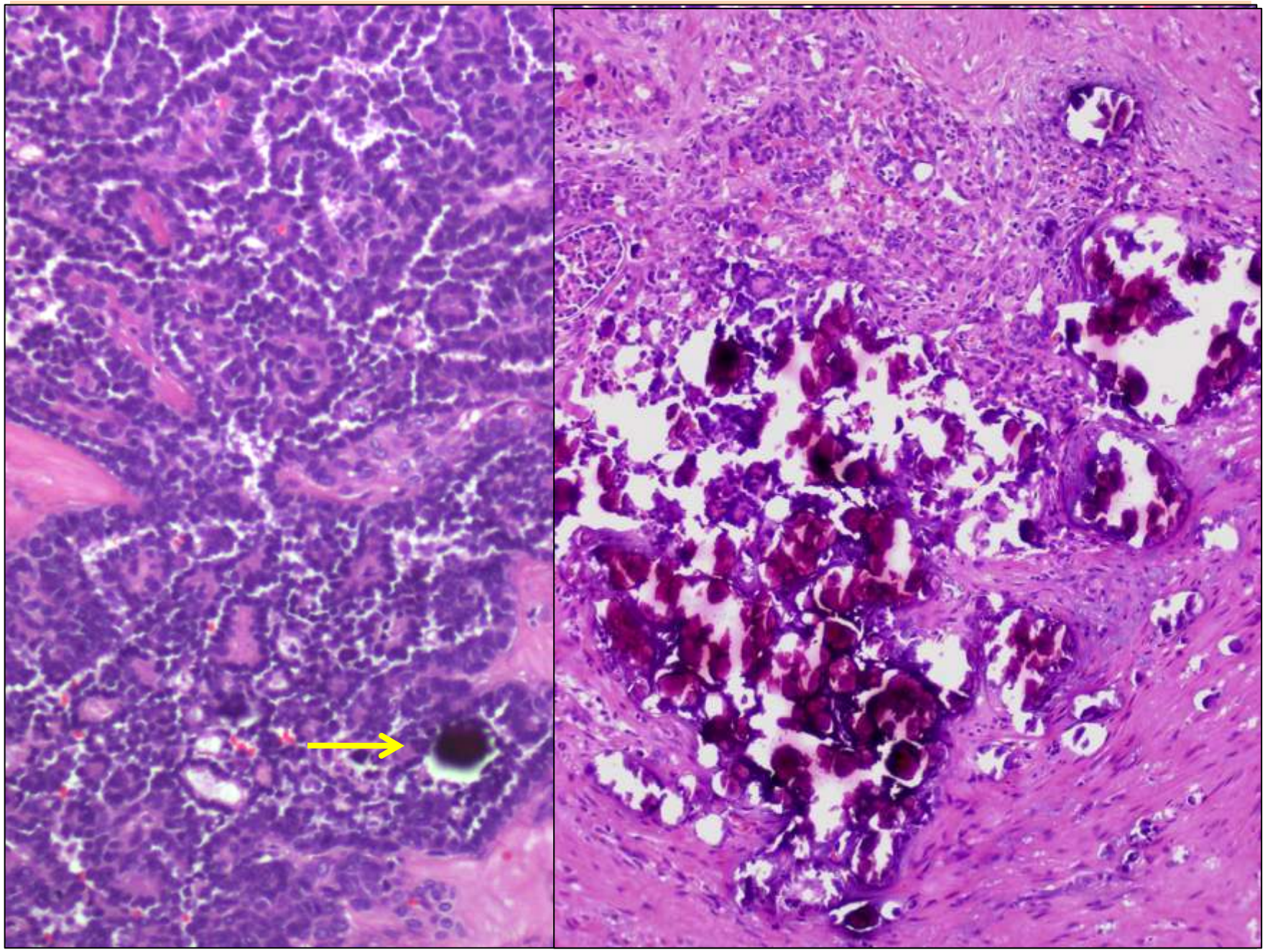
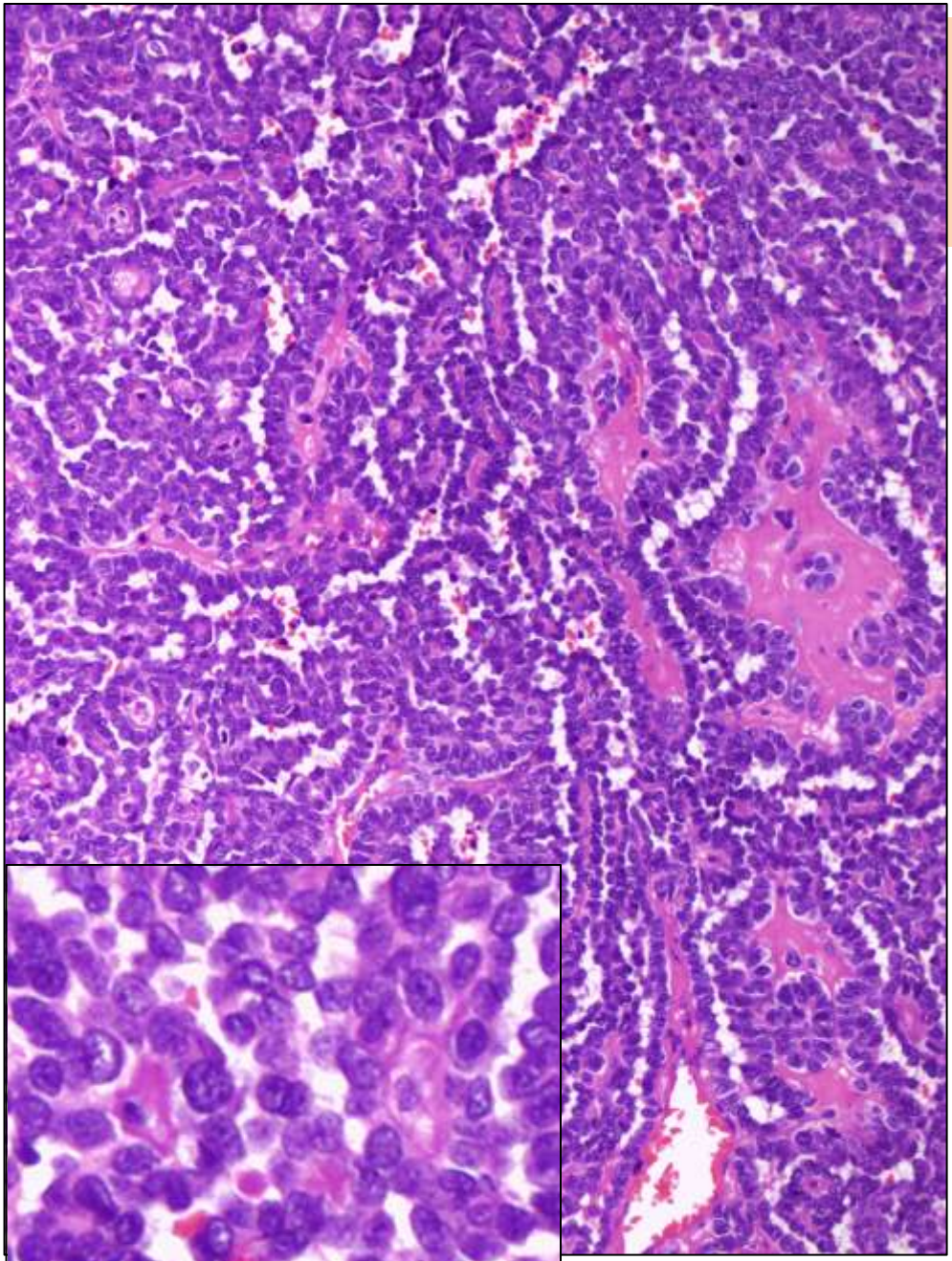
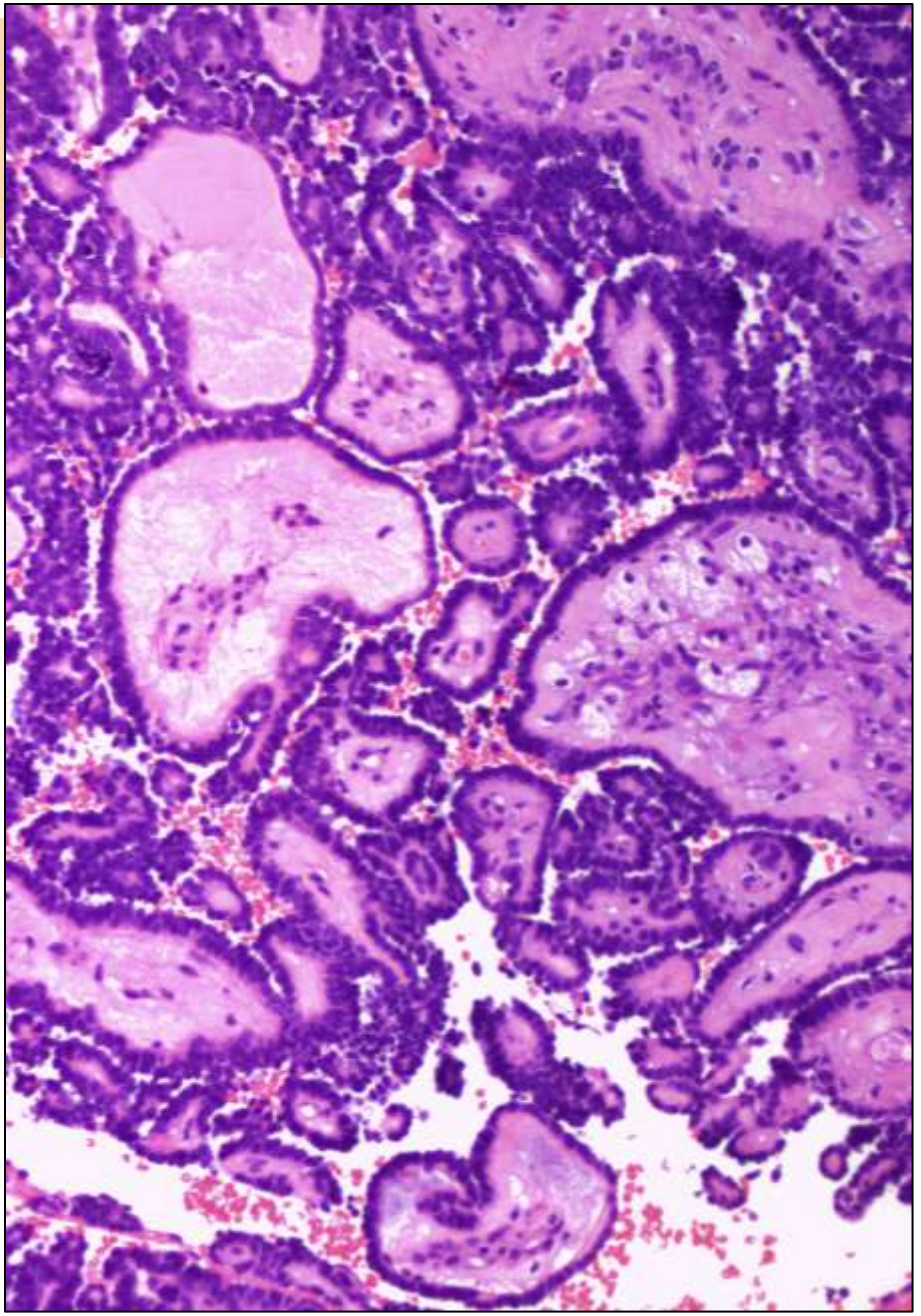
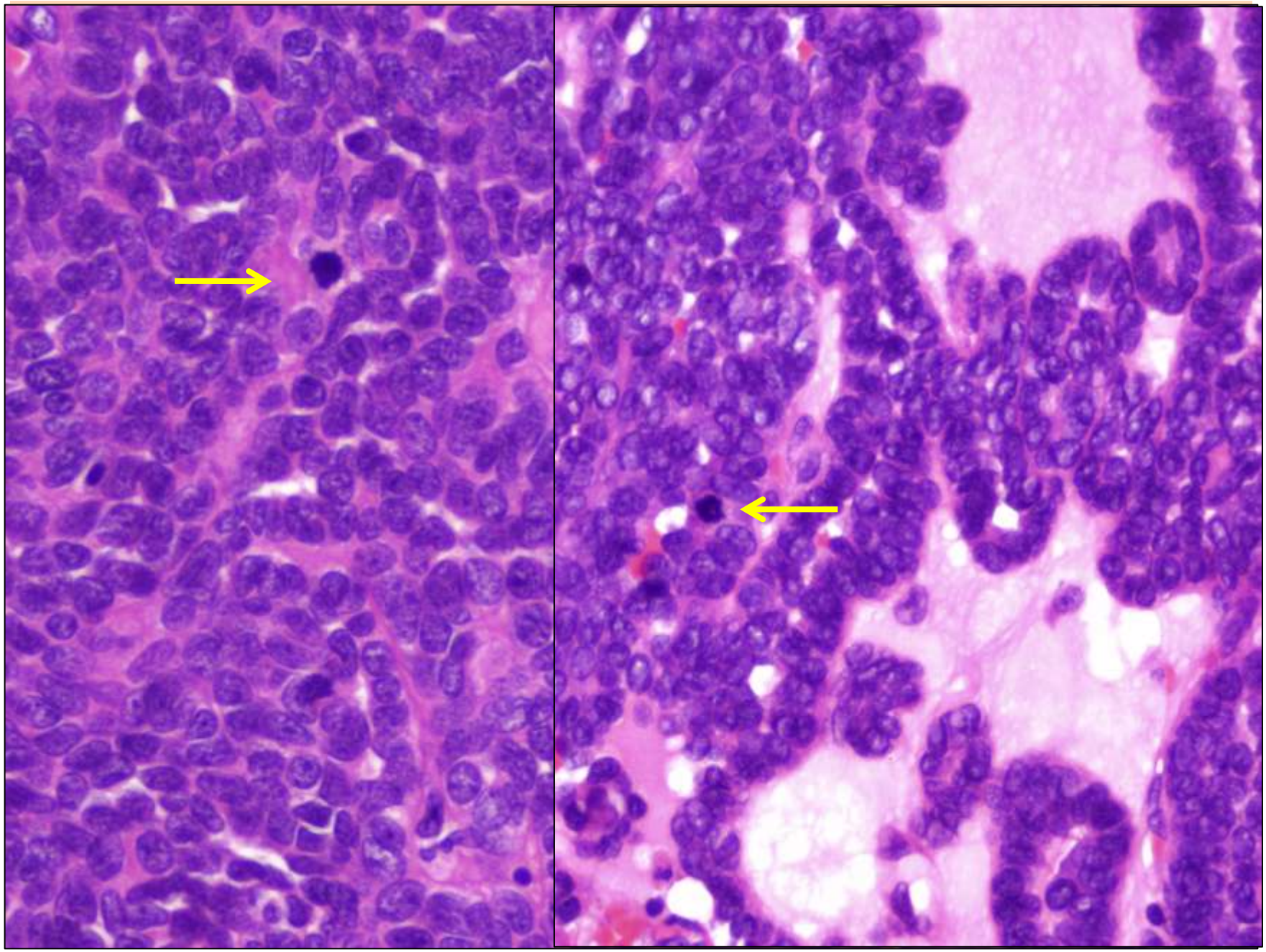


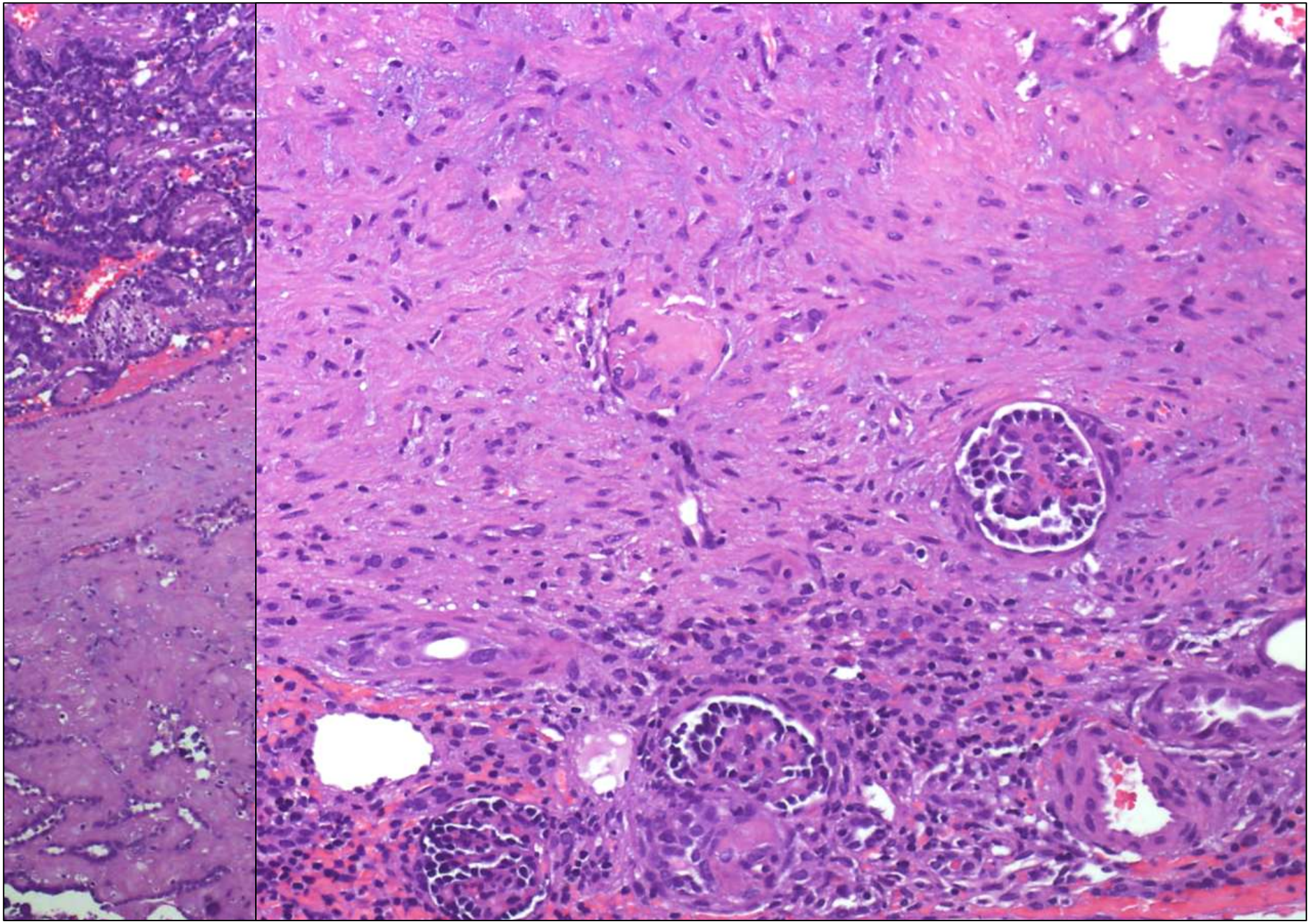


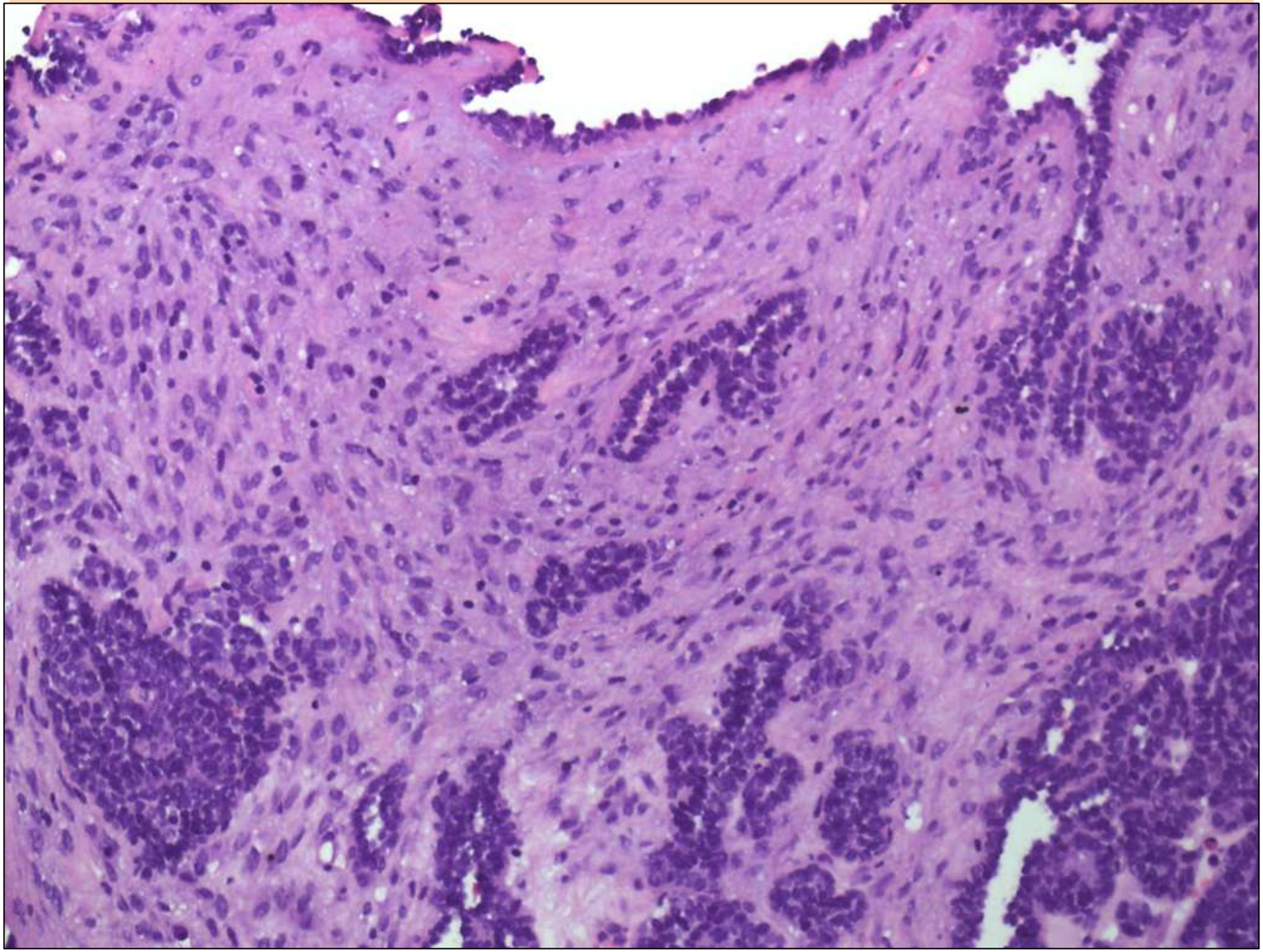


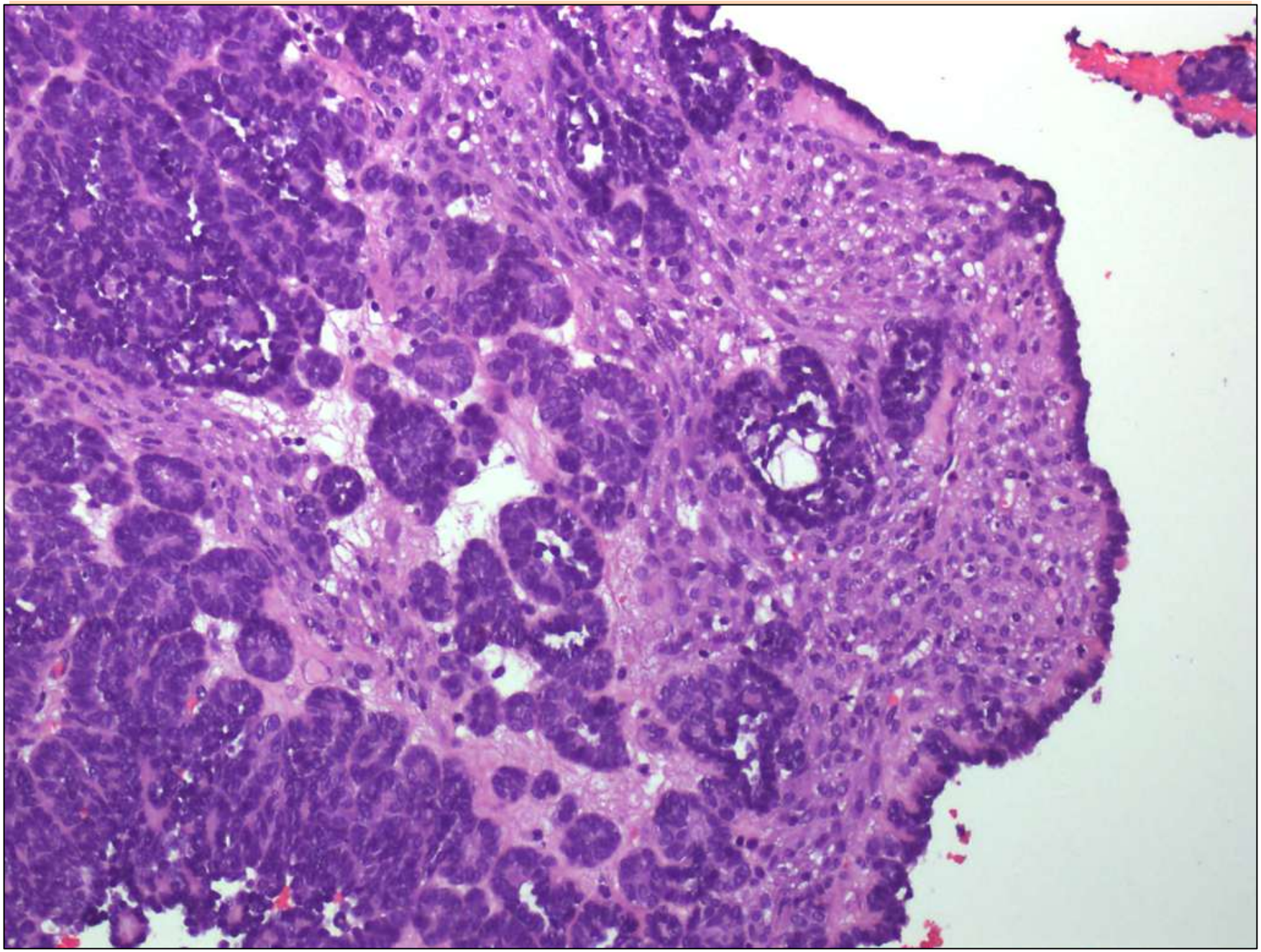


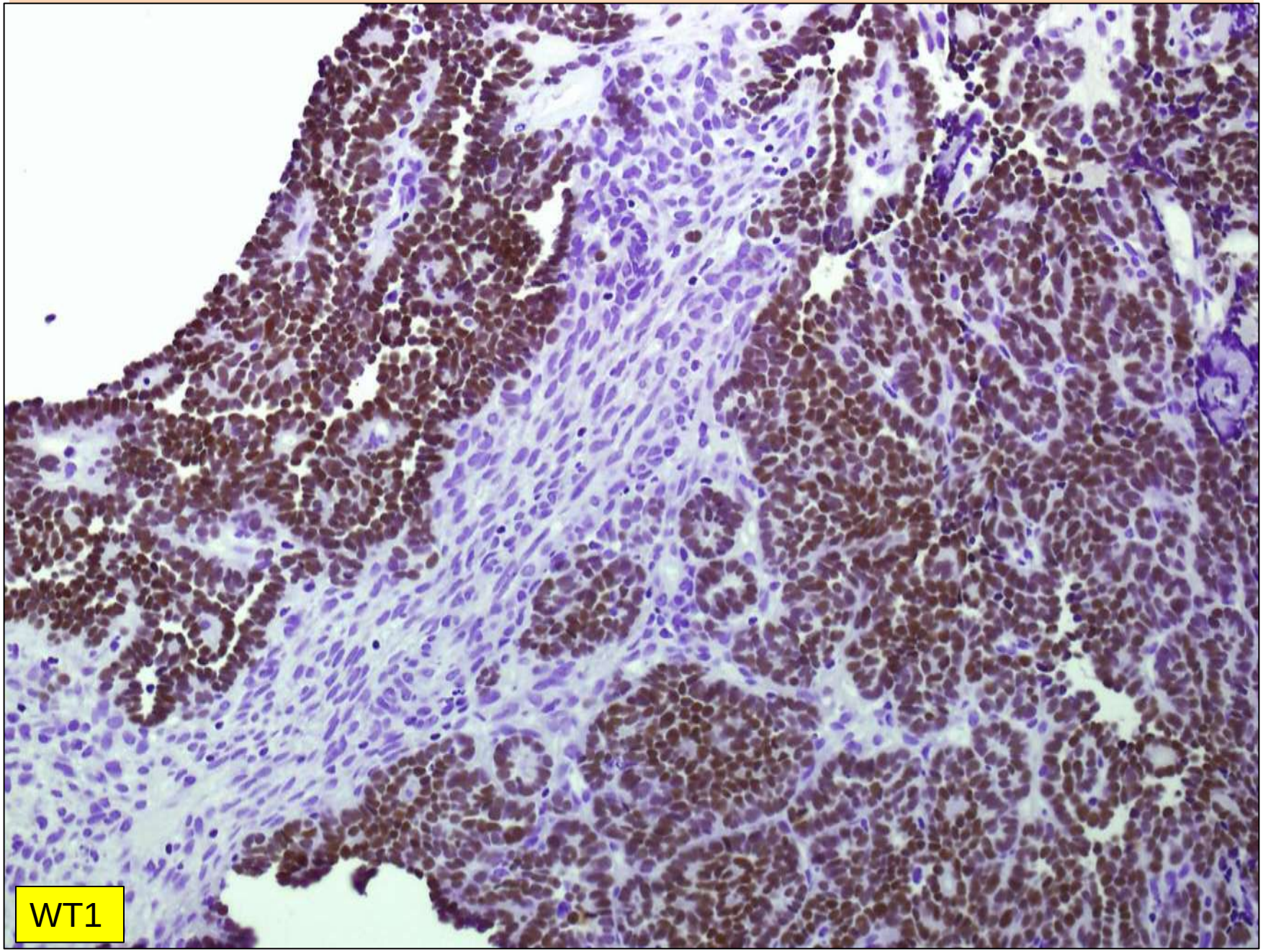


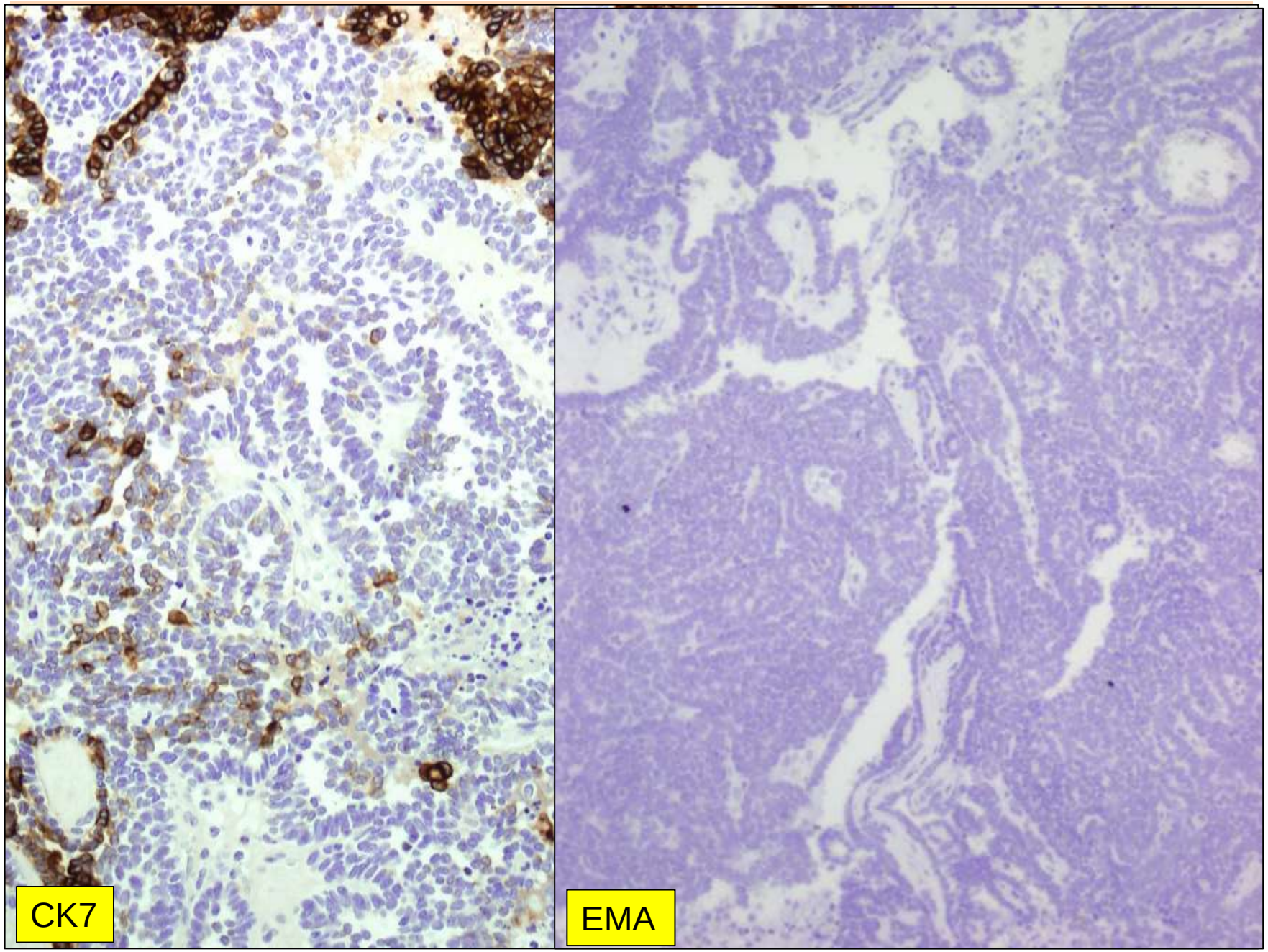


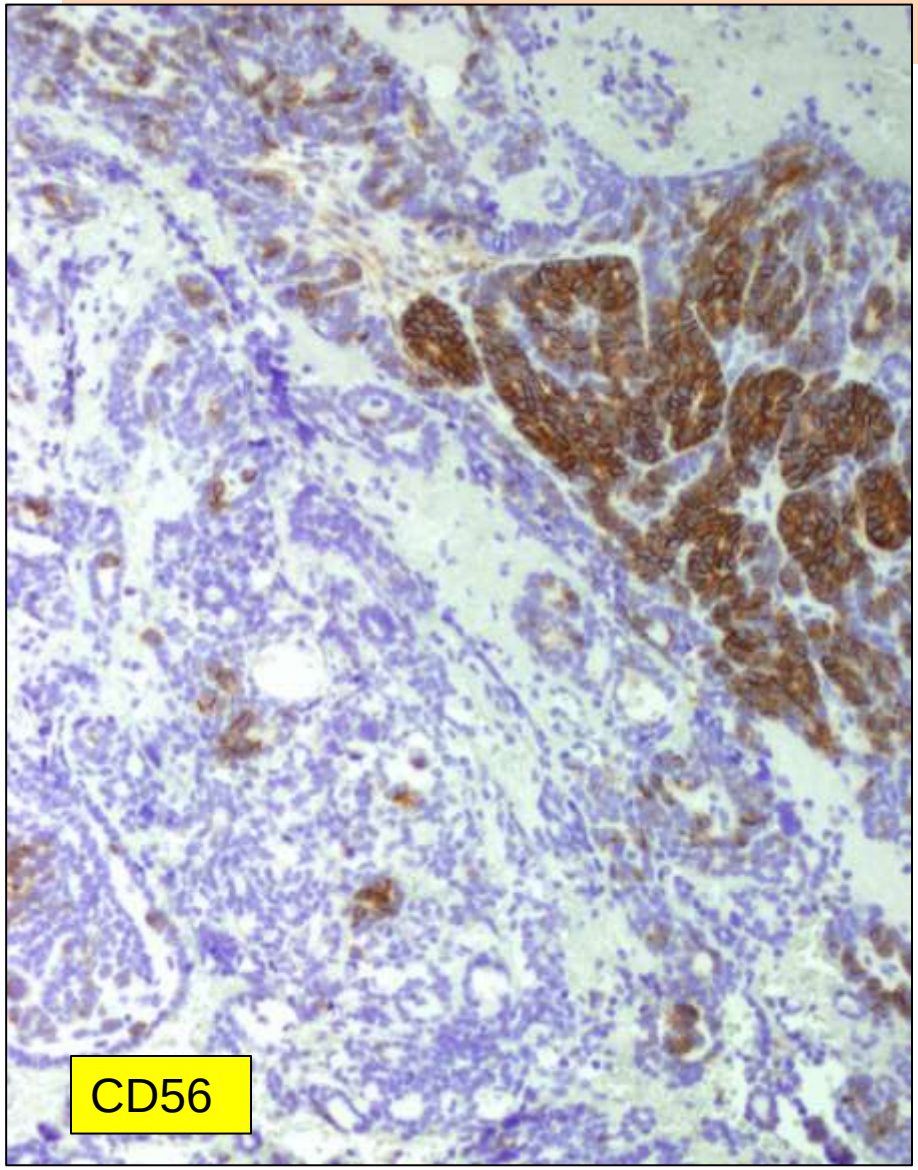


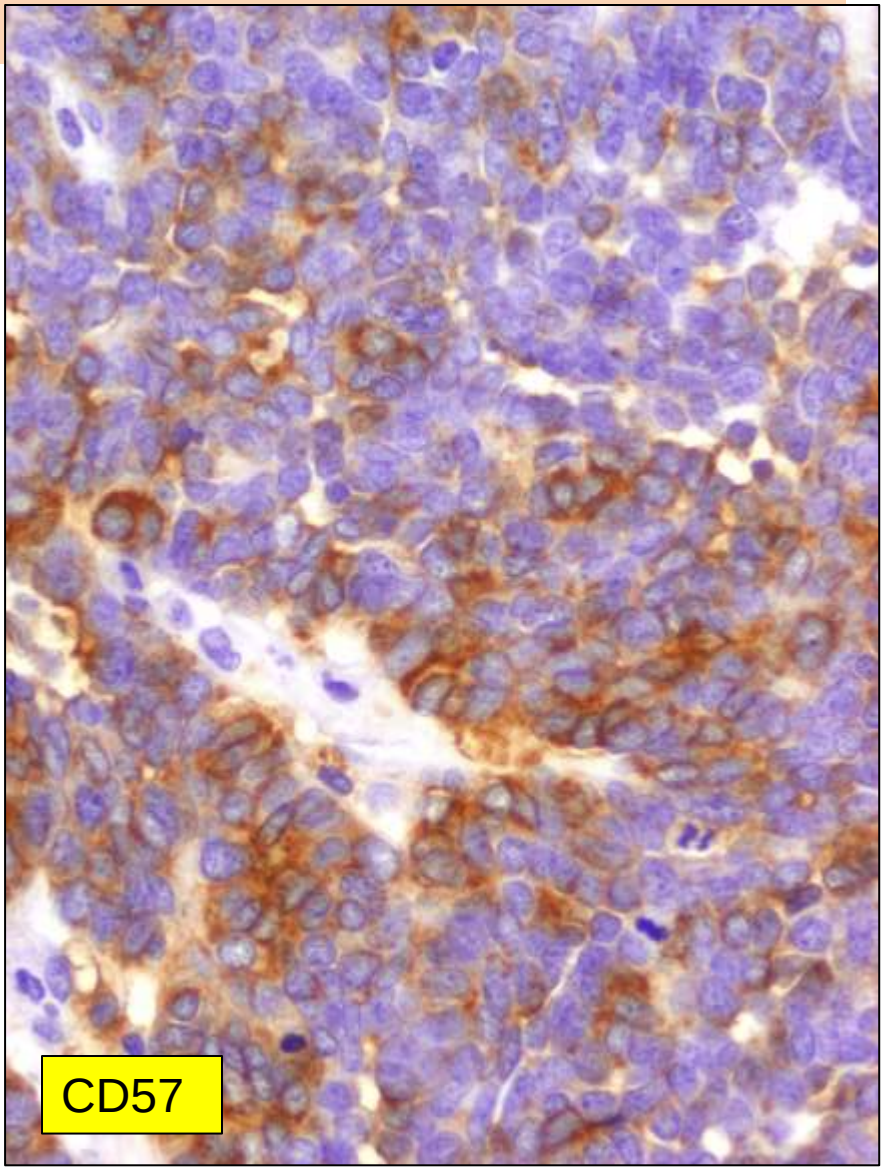





WT1


CK7
EMA


CD56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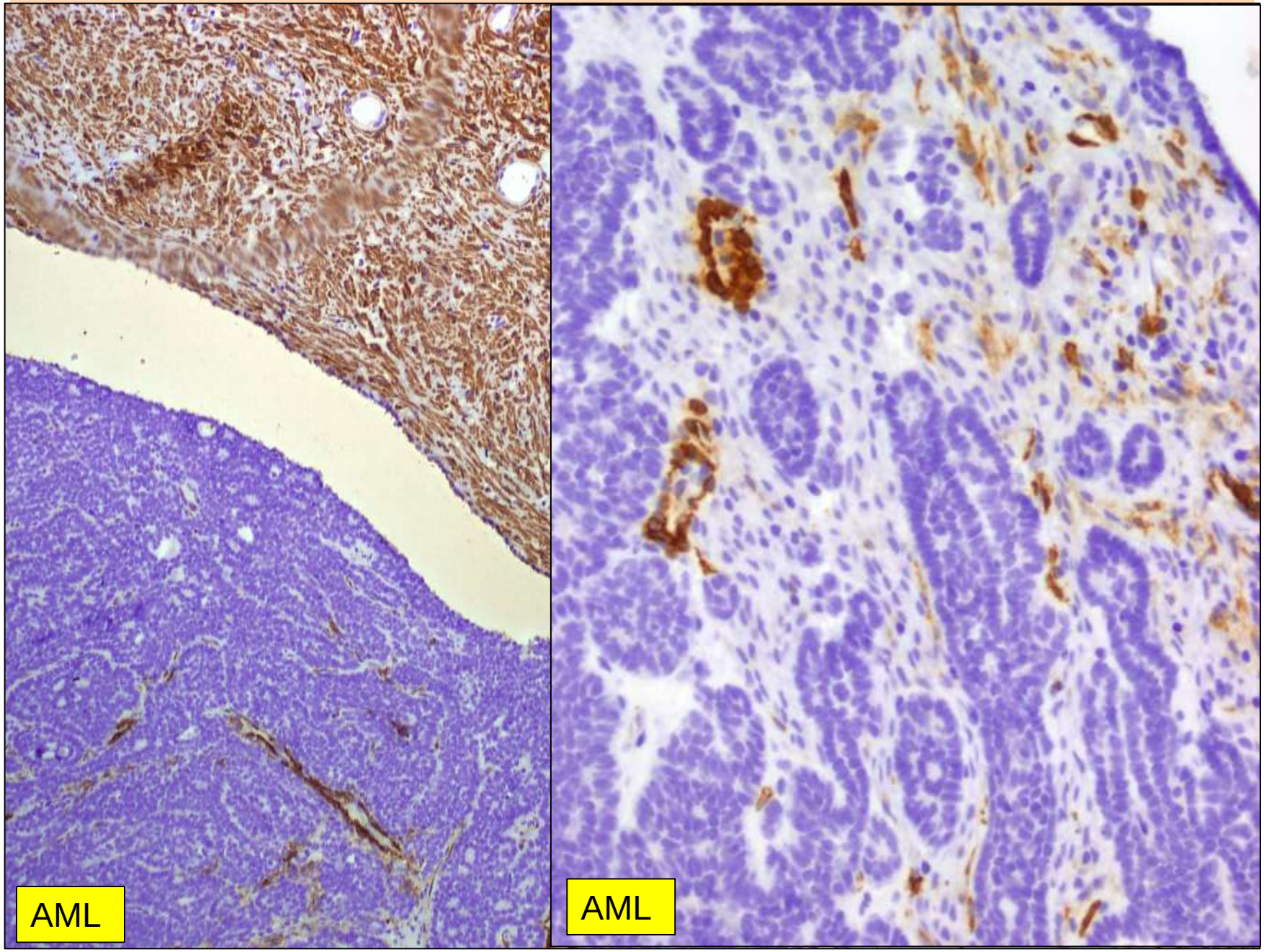
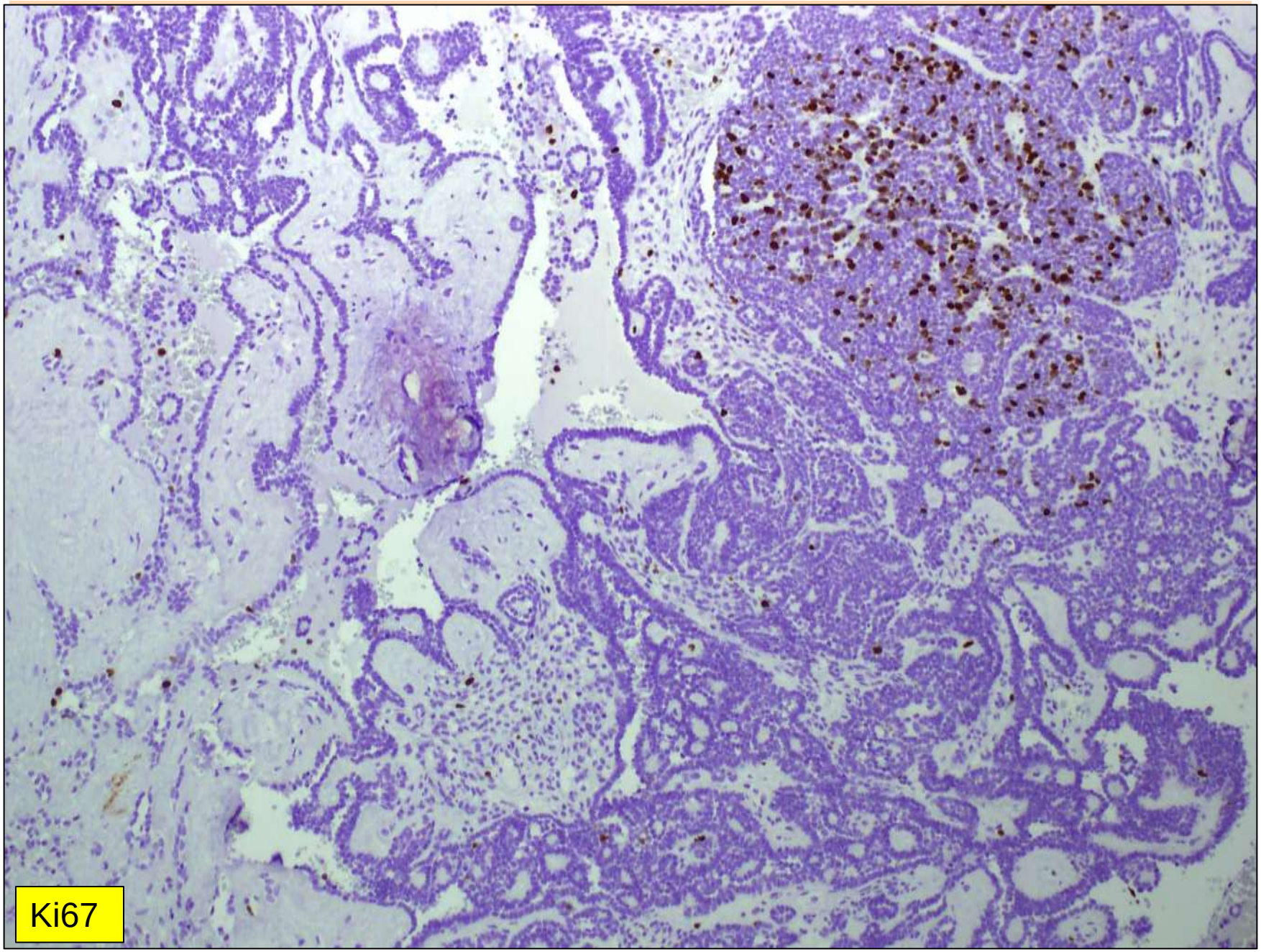

AML
AML


Ki67

- Diagnòstic peça (tumorectomia):

  Adenofibroma metanèfric, mitòticament actiu

- Adenoma, adenofibroma metanèfric i tumor estromal metanèfric: espectre morfològic de la mateixa entitat
- Components estromal i epitelial barrejats o separats[1]

[1]Shek TWH et al. Metanephric adenofibroma. Am J Surg Pathol 1999;23:727-33

Adenofibroma metanèfric

- Descrit inicialment com a adenofibroma nefrogènic[1]
- Pacients joves (m: 14 a; 20 m-35 a). H=D
- Ben delimitat de la resta de parènquima (DxD nefroma mesoblàstic)
- Estroma negatiu per a actina i desmina (DxD nefroma mesoblàstic)
- Policitèmia en 4 de 8 casos publicats el 1999[2]
- Cas publicat[2]: ki67 del 20% en el component epitelial i 5% en el fusocelul·lar

[1]Henningar RA et al. Nephrogenic adenofibroma. Am J surg Pathol 1992;16: 325-34

[2]Shek TWH et al. Metanephric adenofibroma. Am J Surg Pathol 1999;23:727-33

Glubs!

- Revisió nacional (SIOP):

  Adenofibroma metanèfric

- Revisió internacional (SIOP):

  Nefroblastoma epitelial pur,
  “adenoma metanèfric-like” (Dr. Vujanic)

- Existència de càpsula
- Activitat mitòtica/ki67 per sobre de l’esperat

Embolica que fa fort…

- Descripció **d'adenoma metanèfric atípic** (2 casos)
  - Parcialment encapsulat, àrees convencionals, altres hipercel·lulars i amb hipercromàsia, 2 mitosis/10 CGA[1]
  - Mida molt gran (14 cm), no encapsulat, de patró microquístic, cèl·lules moderadament atípiques amb nuclèol prominent, 2 mitosis/10 CGA. Metàstasis òssies als 32 mesos de la nefrectomia i als 6 i 10 anys[2].

[1]Jain M et al. Atypical metanephric adenoma. A case report and review of literature. Int Urol Nephrol, 2007; 39:123-7.

[2]Pins MR et al. Metaneprhic adenoma-like tumors of the kidney: report of 3 malingnancies with emphasis on discriminating features. Arch Pathol Lab Med 1999; 123:415-20.

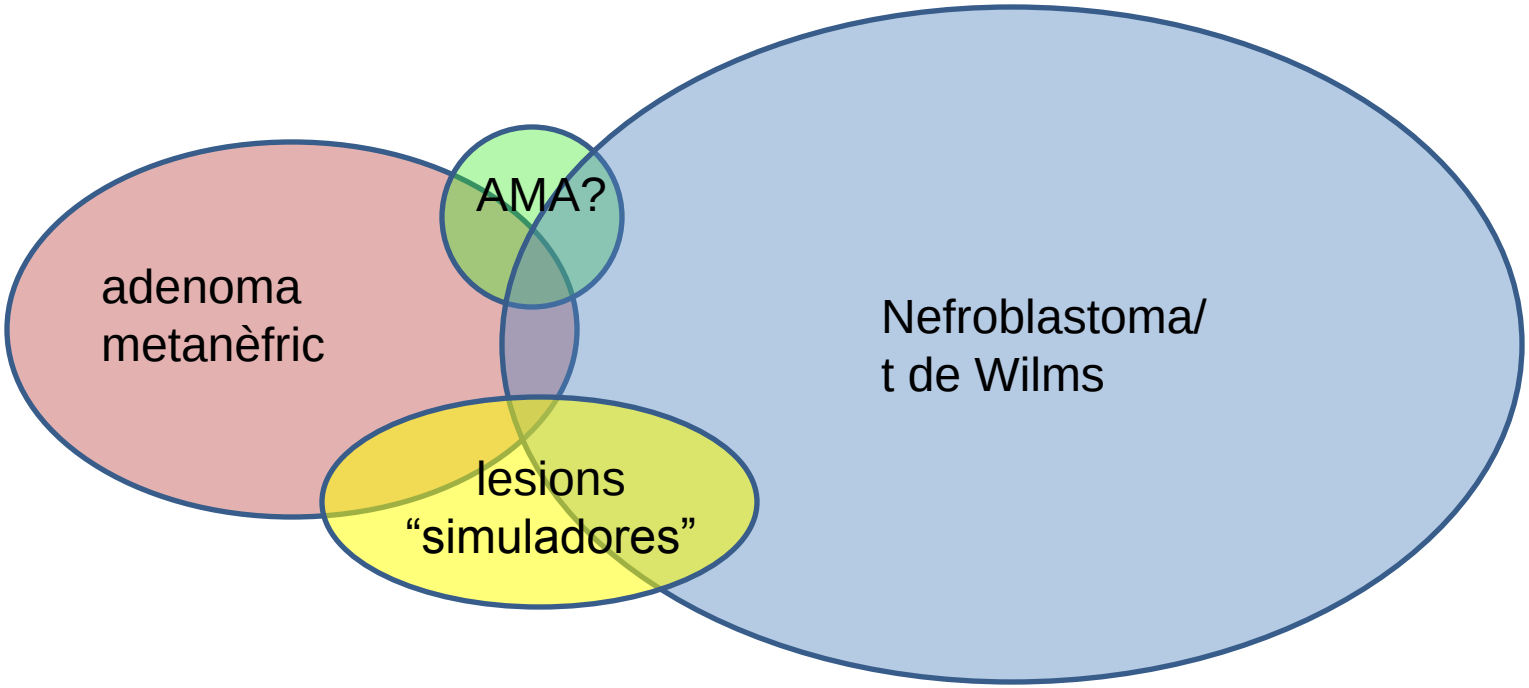
… una mica més encara…

- 3 casos publicats de **metàstasi** en adenoma metanèfric tant convencional[1,2] com atípic[3] (pacients de 7, 11 i 32 anys)
- Importància del DxD amb lesions simuladores d'AM: carcinoma sòlid-papil·lar de cèl·lules renals, metàstasi (carcinoma pobrement diferenciat de tiroide) i t. de Wilms[2]

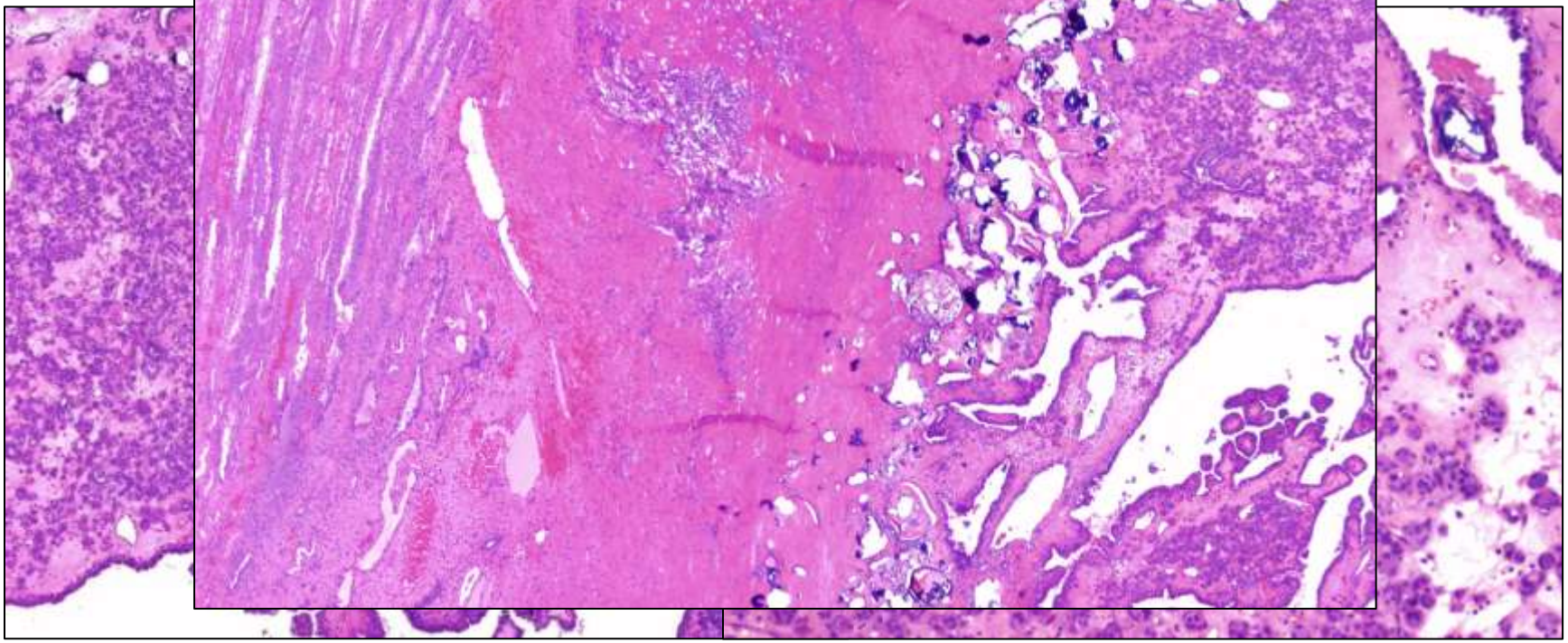
[1]Renshaw AA et al. Metastatic metanephic adenoma in a child. Am J Surg Pathol 2000; 24:570-4.

[2]Drut R et al. Metastatic metanephric adenoma with foci of papillary carcinoma in a child: a combined histologic, immunohistochemical,and FISH study. Int J Surg Pathol 2001; 9:241-7.

[3]Pins MR et al. Metaneprhic adenoma-like tumors of the kidney: report of 3 malingnancies with emphasis on discriminating features. Arch Pathol Lab Med 1999; 123:415-20.


AMA?
adenoma
metanèfric
Nefroblastoma/
t de Wilms
lesions
“simuladores”

- Un a nia) (nen



Evolució

- Realització de tumorectomia amb ruptura intraquirúrgica de la lesió
- No tractament complementari
- Pacient lliure de malaltia als 6 anys de la intervenció

- És el comportament esperat en un tumor de Wilms?
- No, però encara no es pot dir res… s'han descrit casos de metàstasis tardanes, fins a més de 20 anys després del tractament…

I alguna cosa més?

Eur Urol. 2012 Nov;62(5):917-22. doi: 10.1016/j.eururo.2012.05.051. Epub 2012 Jun 9.

BRAF mutations in metanephric adenoma of the kidney.

Choueiri TK[1], Cheville J, Palescandolo E, Fay AP, Kantoff PW, Atkins MB, McKenney JK, Brown V, Lampron ME, Zhou M, Hirsch MS, Signoretti S.

⊕ Author information

Abstract

BACKGROUND: Metanephric adenoma (MA) of the kidney is a rare, indolent tumor that may be difficult to differentiate from other small renal masses (SRMs). Genetic alterations associated with MA remain largely unknown.

OBJECTIVE: We aimed at defining genetic events in MA of the kidney and determining their influence in the management of this disease.

DESIGN, SETTING, AND PARTICIPANTS: Multiplexed mass spectrometric genotyping was performed on 29 MA cases after tumor DNA extraction. We also conducted a mutational screen in an additional 129 renal neoplasms. Immunohistochemistry was performed on the MA cases to assess molecular markers of signaling pathway activation. Patients' baseline characteristics, as well as follow-up data, were captured.

OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: We used descriptive statistics for baseline clinical characteristics and incidence of mutations. The Wilcoxon rank-sum test was used to correlate patient characteristics with mutational status.

RESULTS AND LIMITATIONS: We identified the v-raf murine sarcoma viral oncogene homolog B1 (BRAF) V600E mutation in 26 of 29 MA cases. These results were validated in all cases using the commercially available BRAF Pyro Kit (QIAGEN). In contrast, BRAF mutations were rare in the other 129 non-MA renal neoplasms that were screened. We detected a BRAF mutation (V600E) in only one papillary renal cell carcinoma case. In all MA tumors, we documented expression of phosphorylated mitogen-activated protein kinase and phosphorylated extracellular signal-regulated kinase, accompanied by immunoreactivity for p16 (INK4a). All patients were treated with a partial or radical nephrectomy, and after a median follow-up of 26.5 mo, there were no local or distant recurrences. Limitations include the retrospective nature of this study.

CONCLUSIONS: BRAF V600E mutations are present in approximately 90% of all MA cases, serving as a potential valuable diagnostic tool in the differential diagnosis of SRMs undergoing a percutaneous biopsy. The presence of BRAF V600E and mitogen-activated protein kinase activation in a largely benign tumor supports the necessity for secondary events (e.g., p16 loss) in BRAF-driven oncogenesis.

PMID: 22727996 [PubMed - indexed for MEDLINE]

I alguna cosa més?

V600E,

però tb V600D

Molecular and Immunohistochemical Characterization Reveals Novel *BRAF* Mutations in Metanephric Adenoma

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Abstract: Metanephric adenoma (MA) is a rare benign renal tumor comprised of a neoplastic proliferation of primitive metanephric tubular cells. A previous study identified *BRAF* V600E mutations in approximately 90% of MA and found that similar *BRAF* exon 15 mutations are exceedingly rare in other common renal tumors, including renal cell carcinoma and oncocytoma. A recent follow-up study has validated mutation-specific immunohistochemistry (IHC) for detection of *BRAF* V600E mutations in a small cohort of MA. Here, we extend these findings to a larger, independent cohort of MA, demonstrating an overall 88% sensitivity and 100% specificity for BRAF V600E IHC. In addition, we report 2 cases of MA with novel *BRAF* exon 15 mutations, including a V600D missense mutation and a compound V600D and K601L missense mutation. Finally, we evaluate BRAF V600E IHC in a large tissue microarray cohort of common renal tumors and find no significant expression in several renal cell carcinoma subtypes. These data support a role for BRAF V600E IHC in diagnostically challenging cases of MA and expand the spectrum of *BRAF* exon 15 mutations in this uncommon but unique renal neoplasm.

Key Words: BRAF, metanephric adenoma, immunohistochemistry, V600E, Sanger sequencing

(*Am J Surg Pathol* 2015;00:000–000)

Metanephric adenoma (MA) is a benign, often asymptomatic and incidentally identified renal tumor comprised of primitive metanephric tubular cells.[1–3] Patients commonly present in the fifth to sixth decade of life, and there is a slight female preponderance (F:M = approximately 2:1). Grossly, MA is usually a solid, solitary, unilateral mass that lacks a true fibrous capsule. On average, these tumors measure 5.5 cm in greatest dimension; however, they may be very small (< 0.5 cm) or large (>10 cm). Microscopically, MA usually appears solid at low magnification, although areas of cystic degeneration are sometimes present.[1–3] On higher magnification, these tumors consist of primitive metanephric tubular epithelial cells with scant cytoplasm and monotonous round to oval nuclei with fine chromatin and without nucleoli; these cells are usually arranged in small acinar structures, although areas with papillary, tubular, and glomeruloid growth patterns may be identified. Generally, there is minimal admixed paucicellular or hyalinized stroma, but cases may also demonstrate regressive changes, including dense sclerosis, dystrophic calcification, and/or psammomatous calcification. Mitotic activity is usually very low or absent in MA, and necrosis is very rare.

In the majority of cases, MA can be diagnosed on routine hematoxylin and eosin (H&E) stain; however, the differential diagnosis includes the solid variant of papil-

I alguna cosa més?

... continuarà...