Case of the month
July 2019

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Case Details

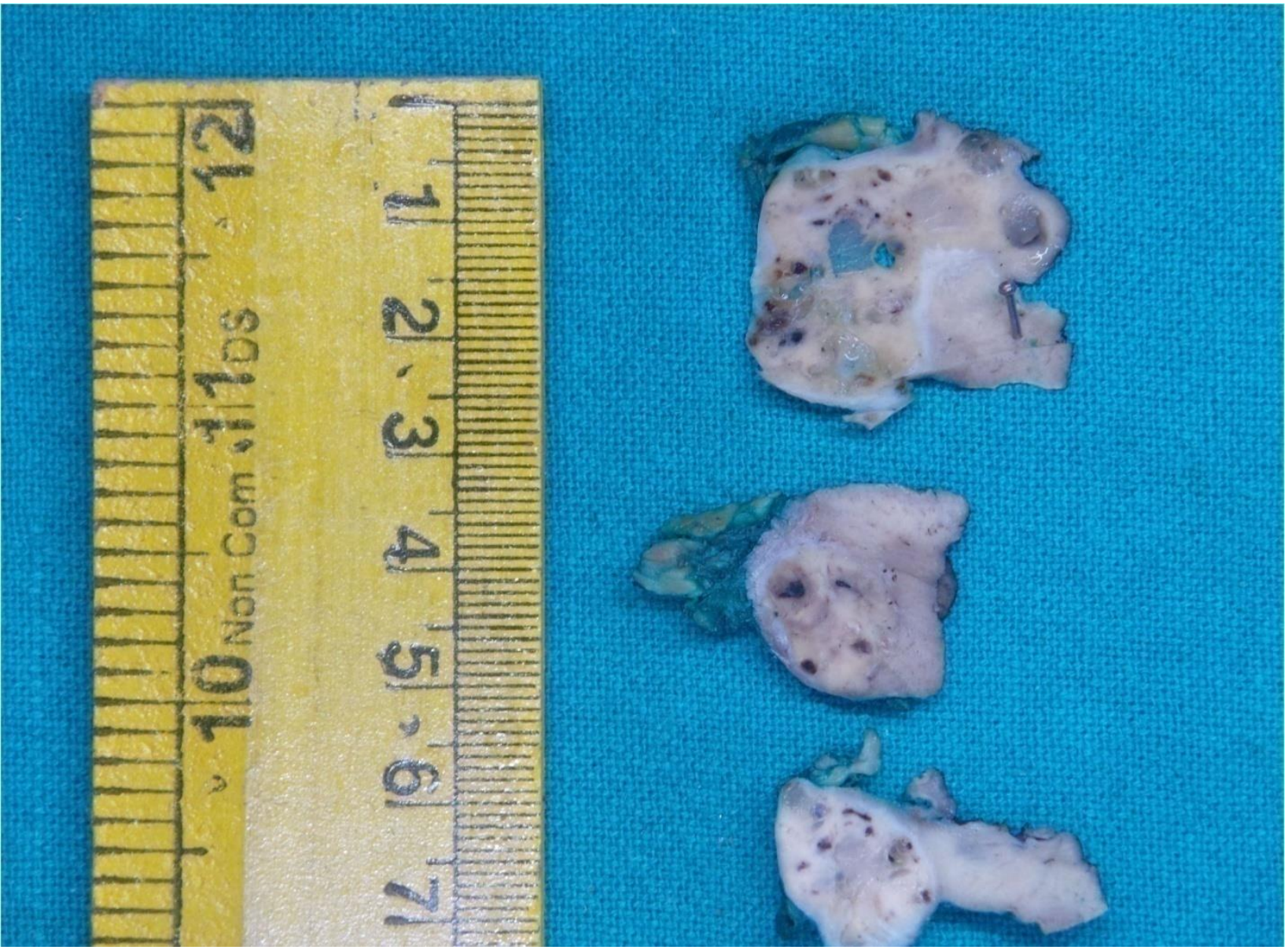
- 55 year old female got herself evaluated for back pain.
- MRI of lumbosacral spine was suggestive of degenerative changes with annular tear and disc herniation at L4-L5 level.
- Incidentally a renal mass lesion was also identified at right upper and middle pole

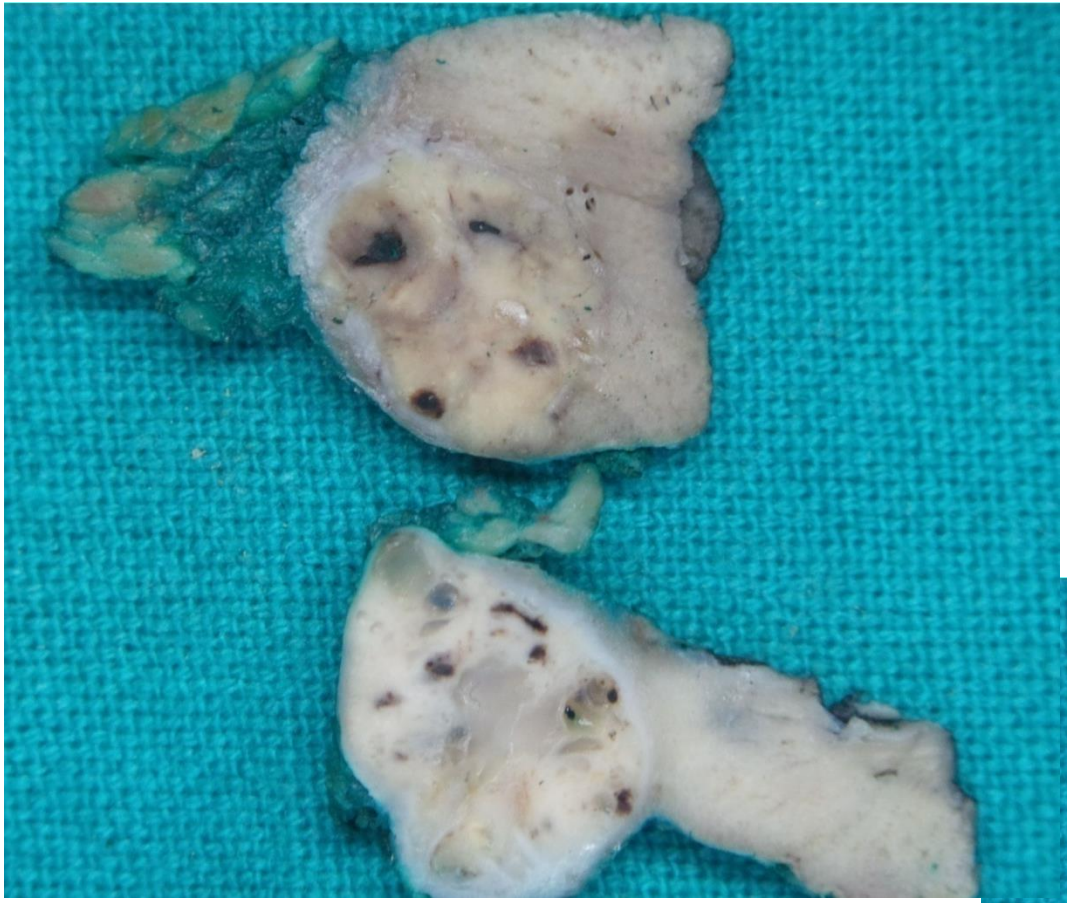
- Then PET scan was done which showed a non-FDG avid enhancing lesion in superior pole of kidney.
- No other lesion was seen in rest of the body
- Patient underwent Right Robotic Nephron Sparing Surgery (NSS)

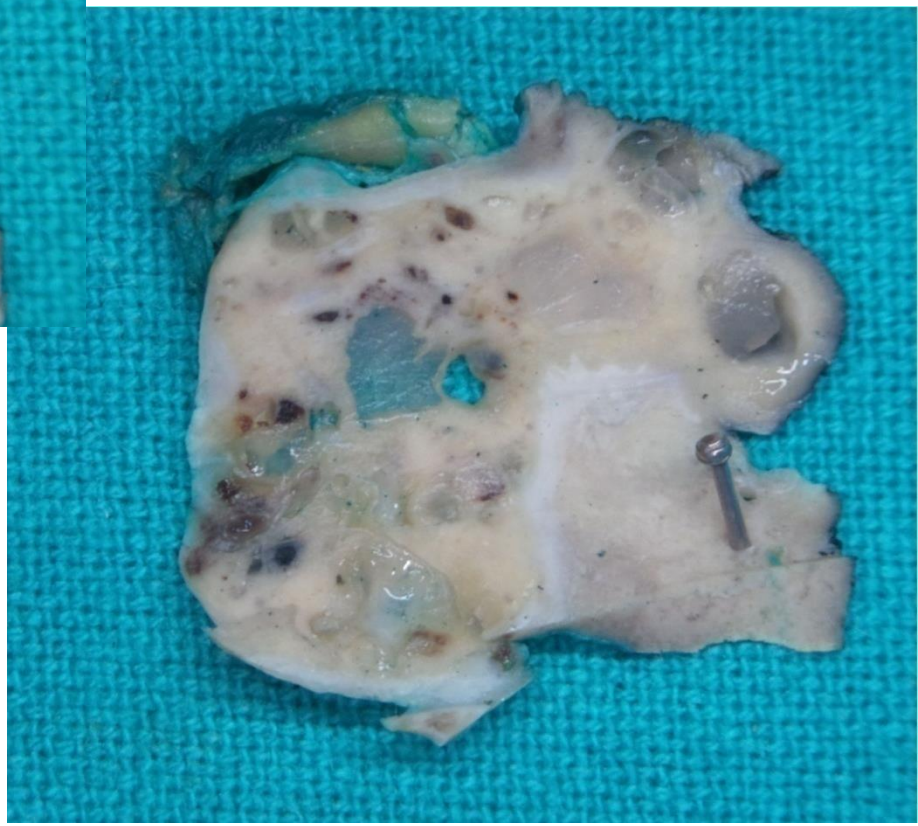
Macroscopic Examination

- Right NSS specimen
- Cut surface showed a solid and cystic tumor mass measuring 2.7 x 2 x 1.5 cm
- Tumor was yellowish to pale brown in colour with few haemorrhagic areas. Varying sized cysts were seen (0.3 to 0.5 cm)

Yellowish to pale brown solid and cystic kidney tumor





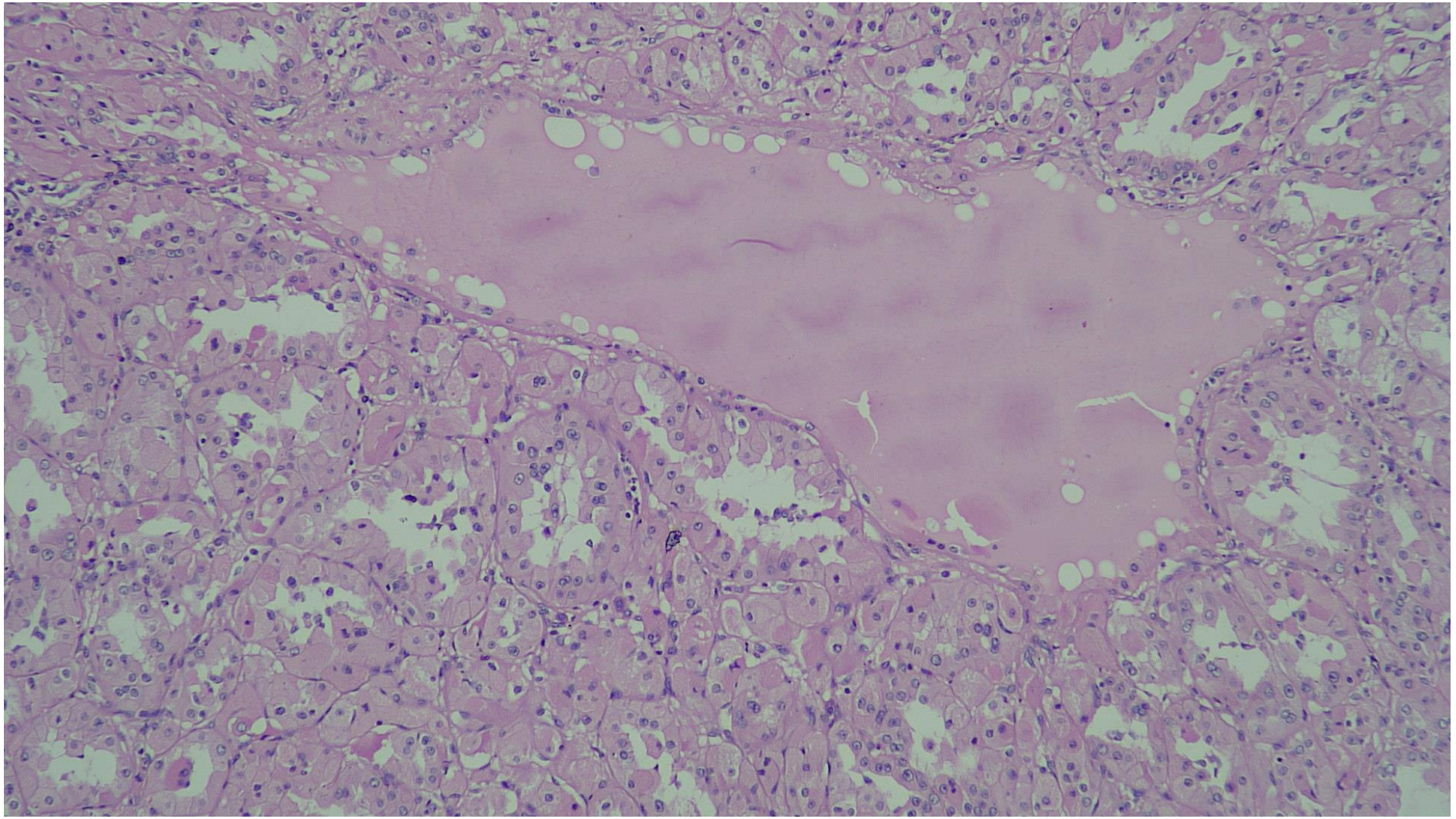


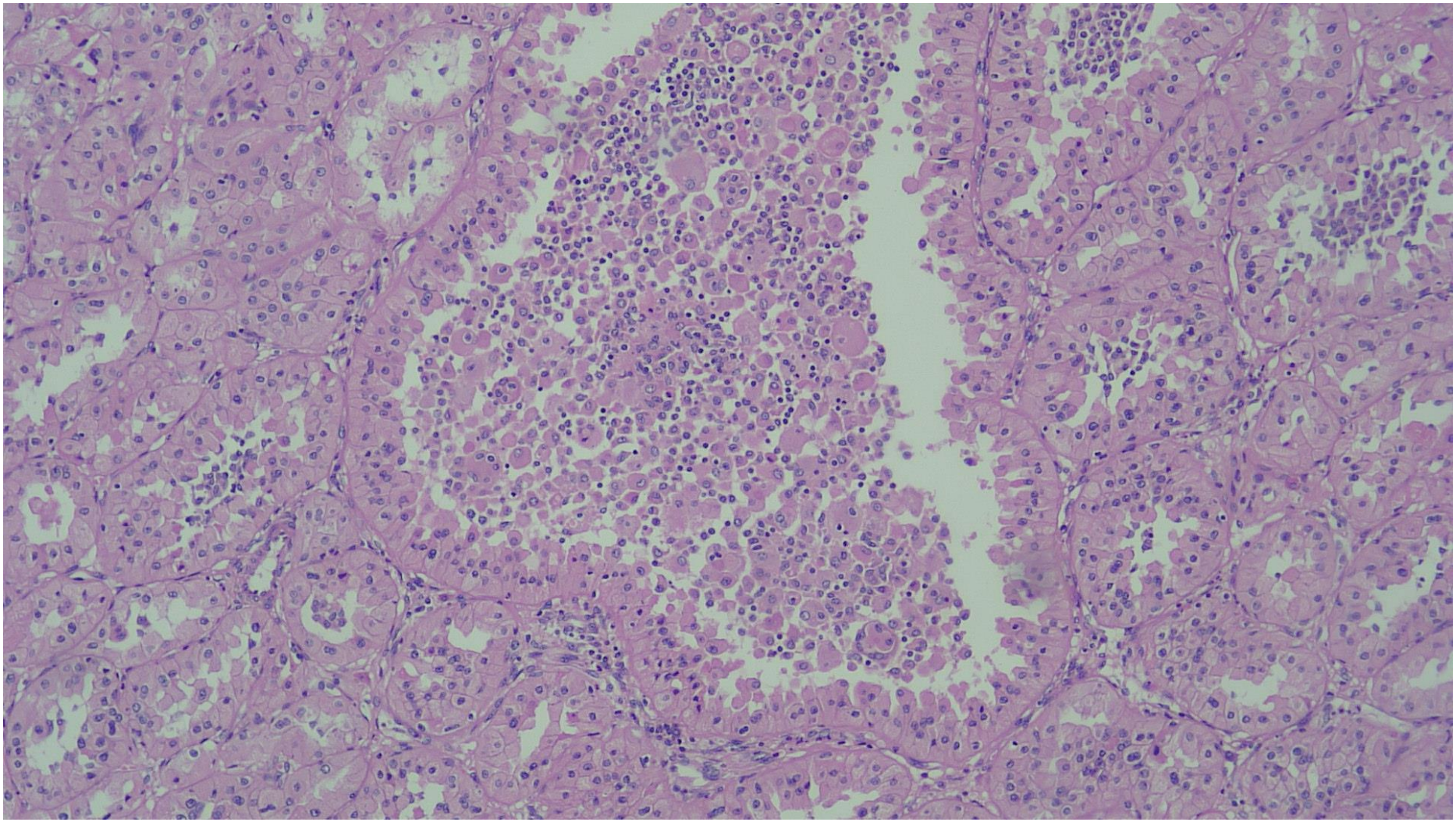
Microscopic Examination

- Tumor shows solid and cystic areas, with large polygonal cells having abundant eosinophilic granular cytoplasm , central nuclei and inconspicuous nucleoli (WHO/ISUP Grade 2)
- Many cystic areas were lined by hobnailed cells.
- Occasional mitotic activity was seen.

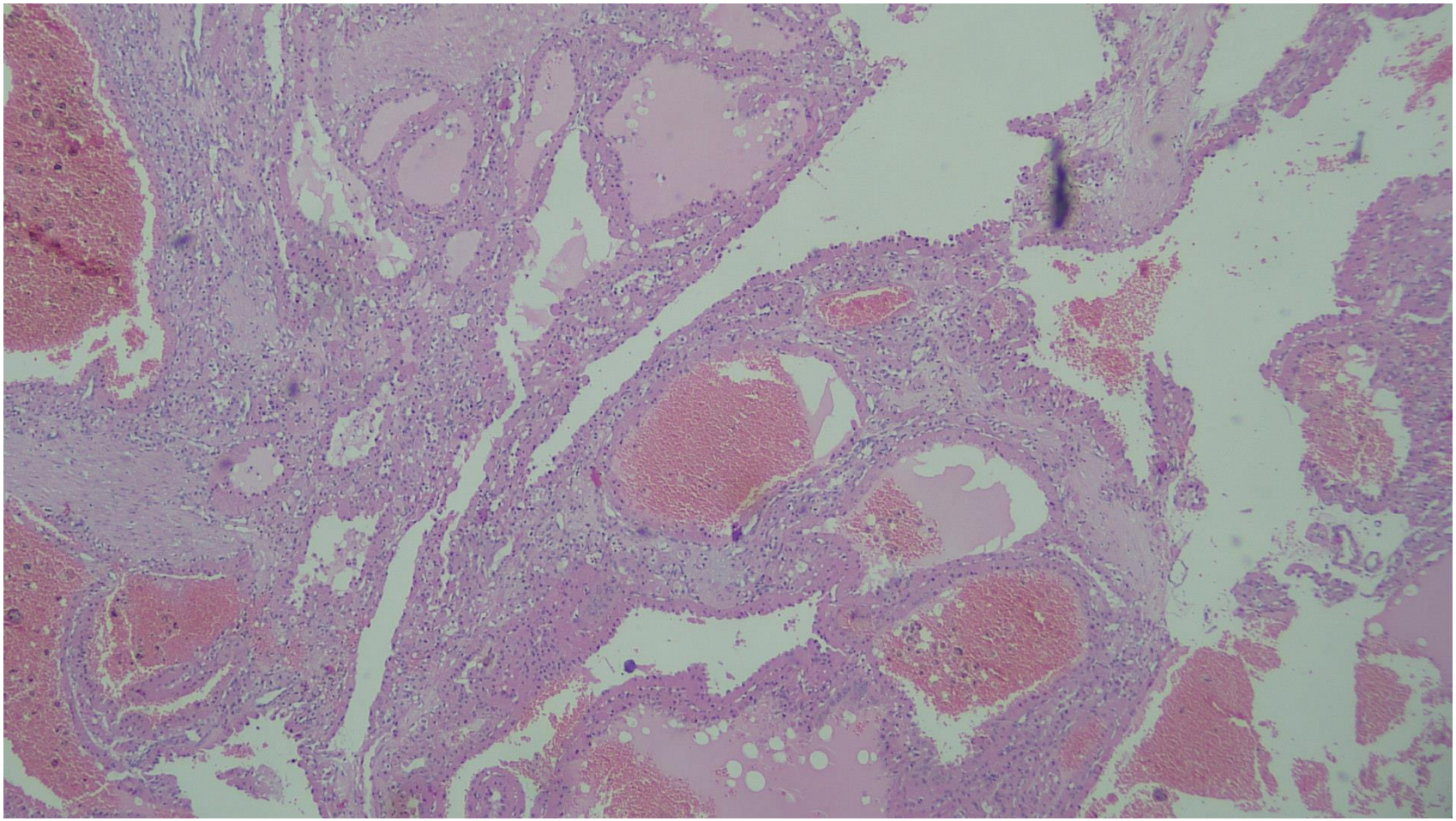
- Sarcomatoid and rhabdoid features: not identified
- Tumor necrosis: not identified
- Renal parenchymal margin : tumor is 1mm away
- Renal capsular margin : free of tumor
- Lymphovascular invasion : not identified

Solid and cystic areas of tumor; solid areas show neoplastic cells in nests and tubules

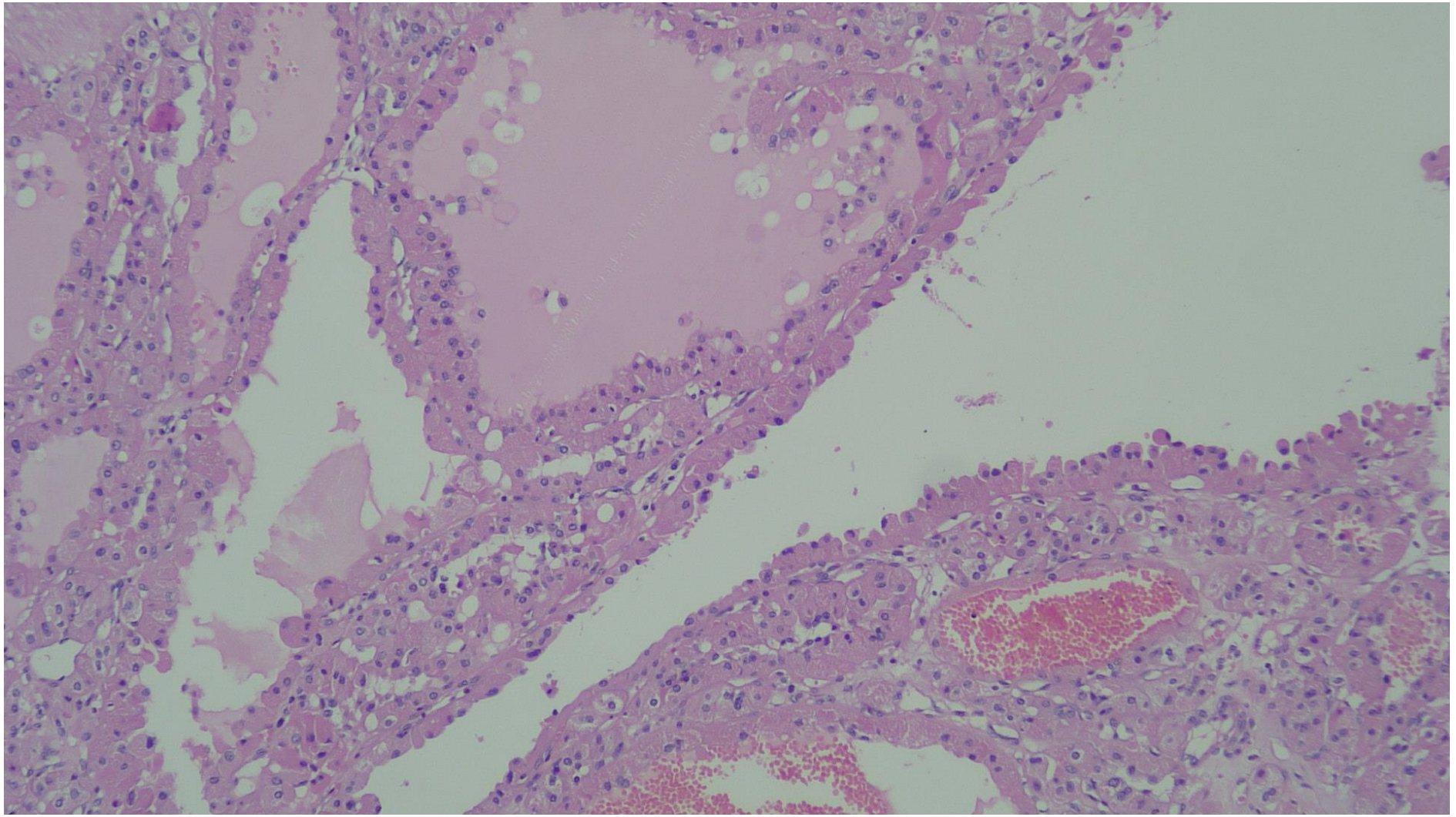




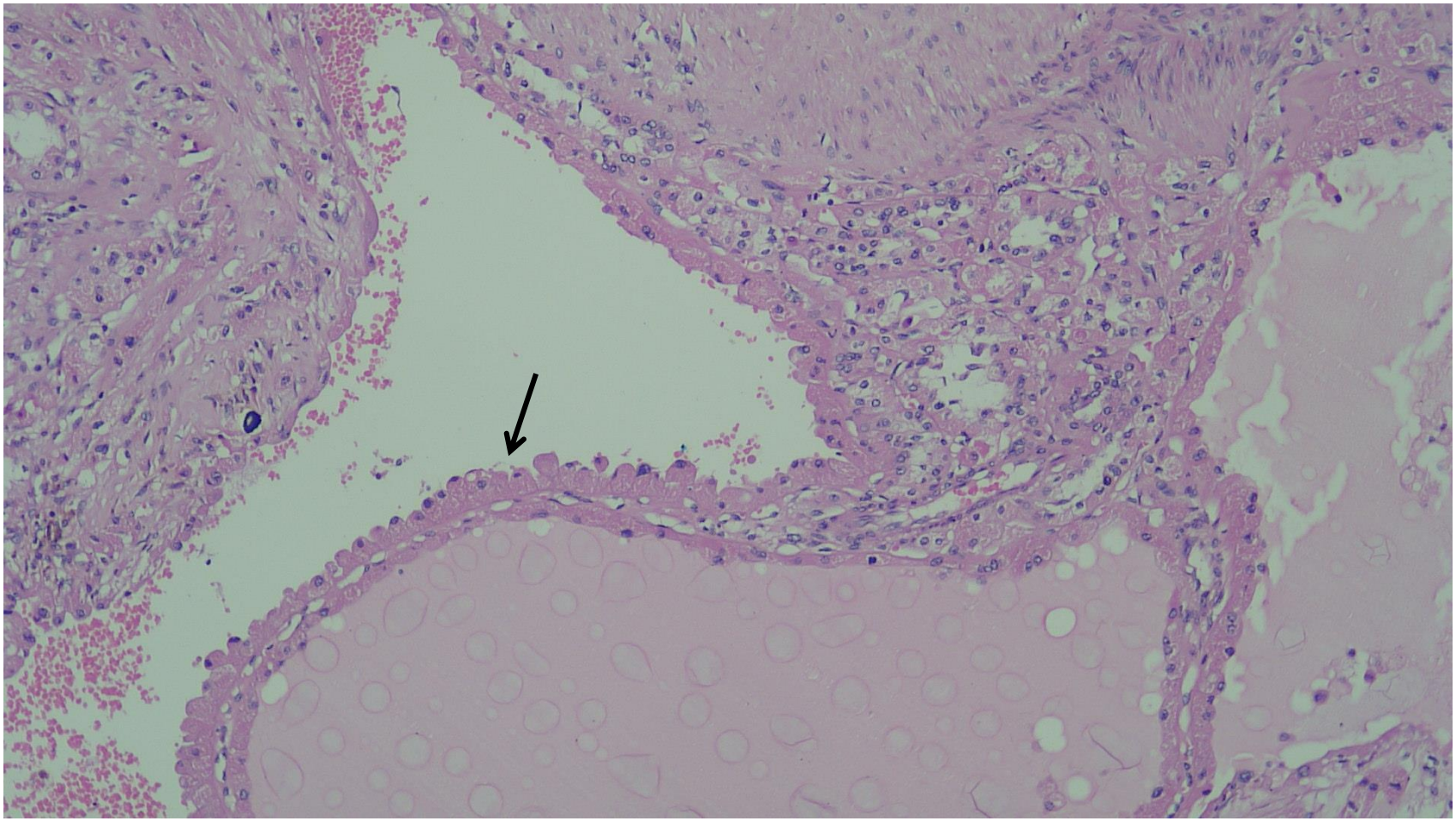
Cystic areas of tumor



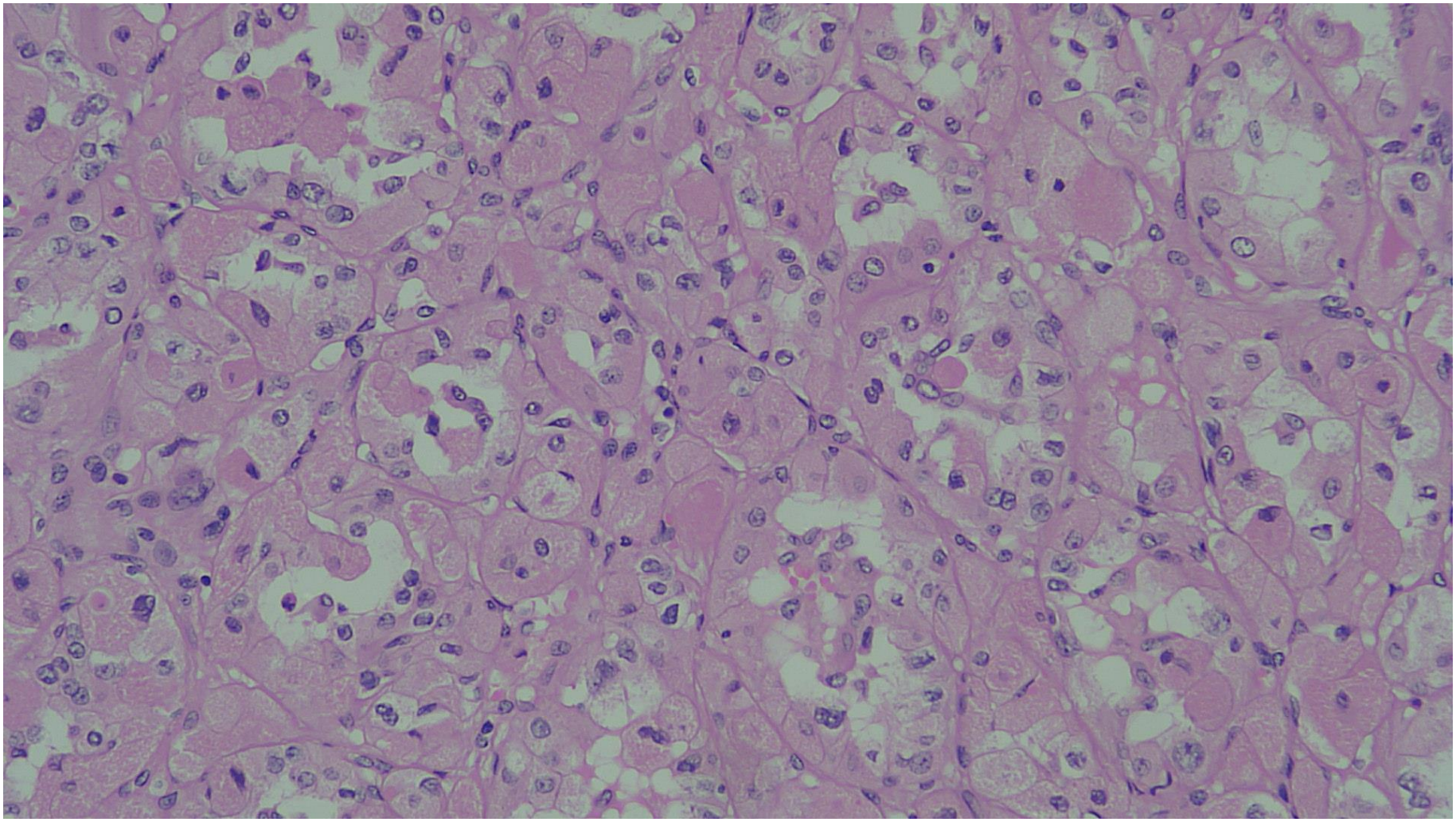
Cystic areas lined by hobnailed neoplastic cells

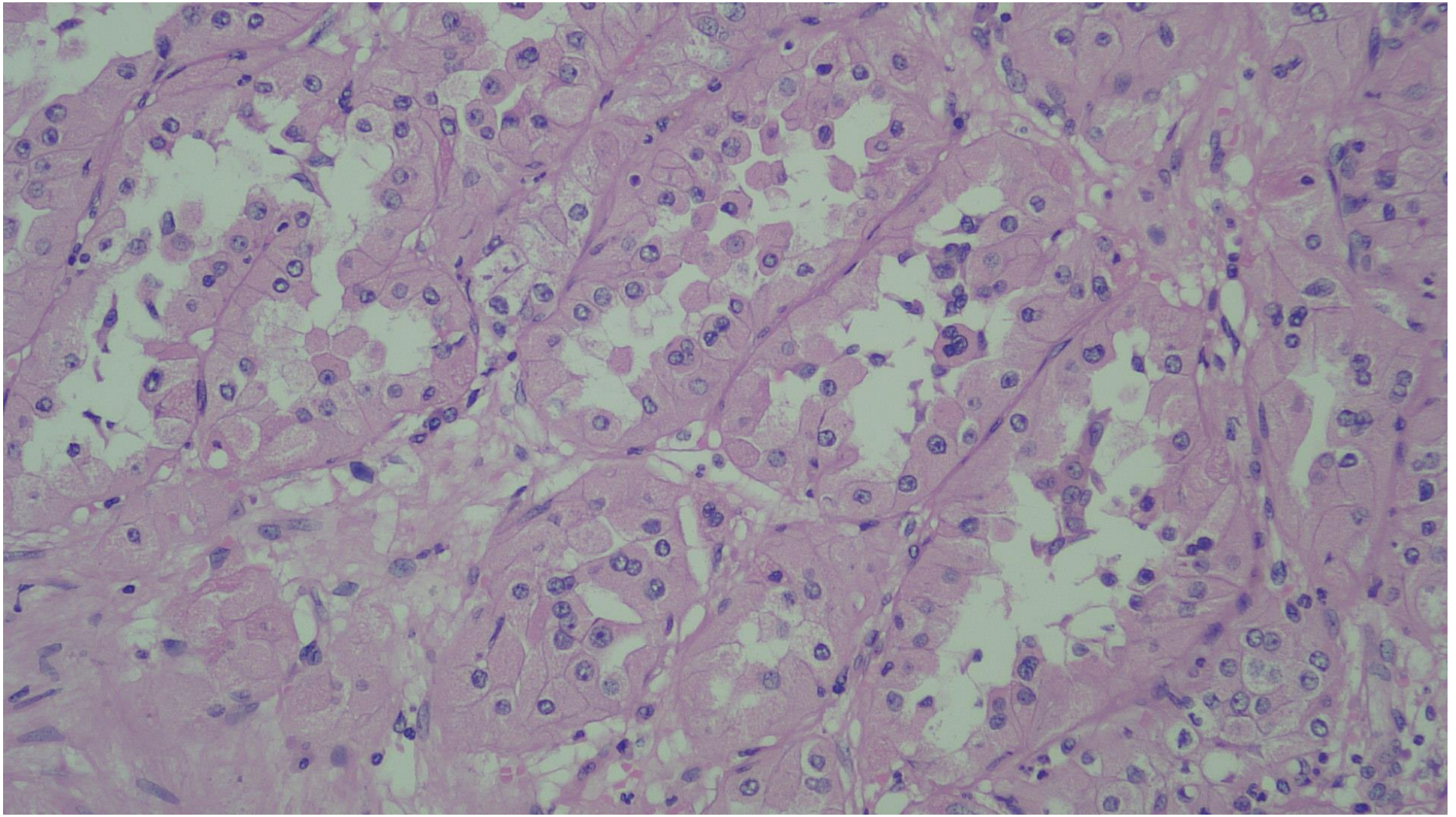


Cystic area lined by hobnail cells (arrow)

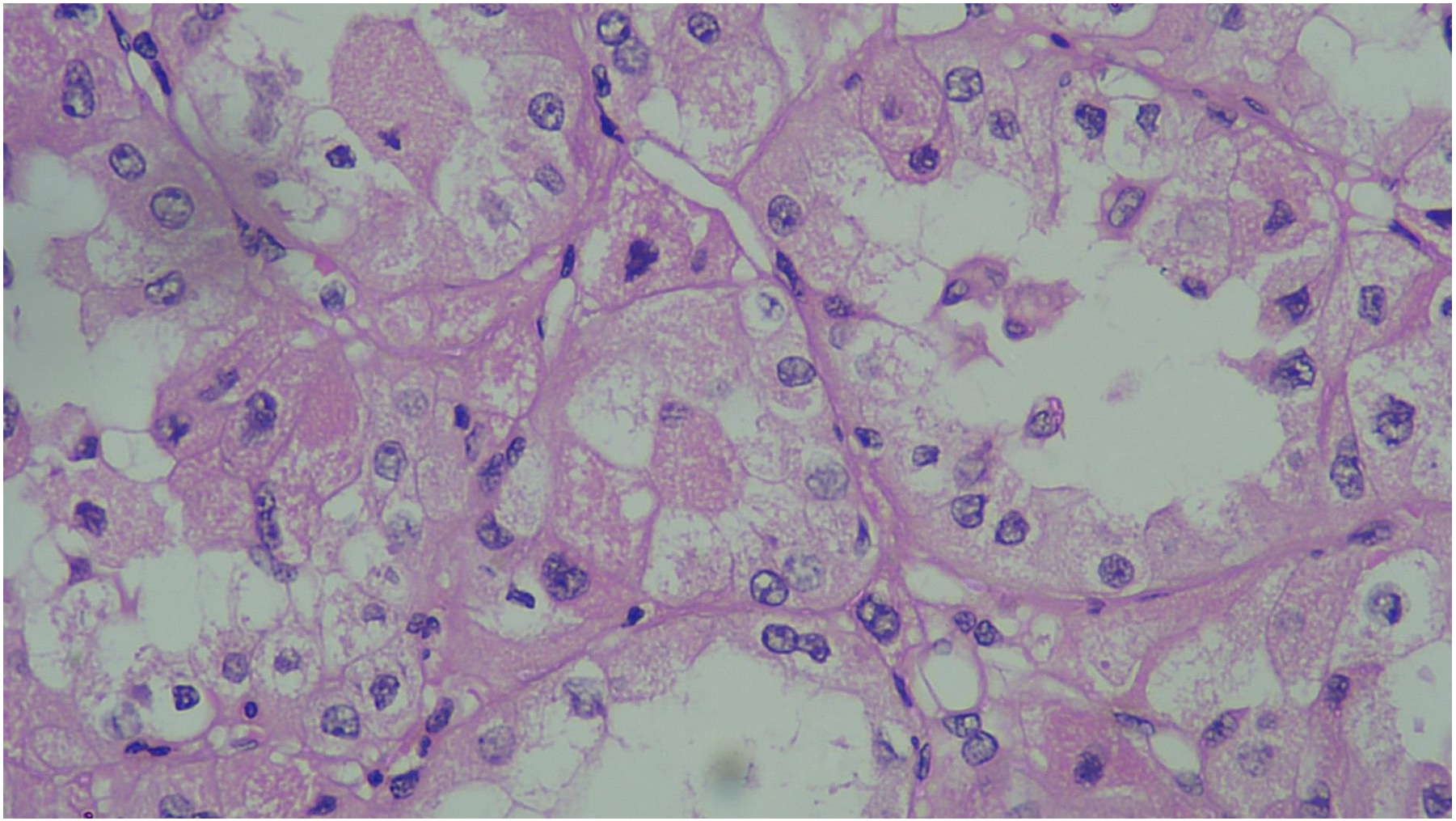


Nested and tubular area of tumor with large polygonal cells having eosinophilic granular cytoplasm

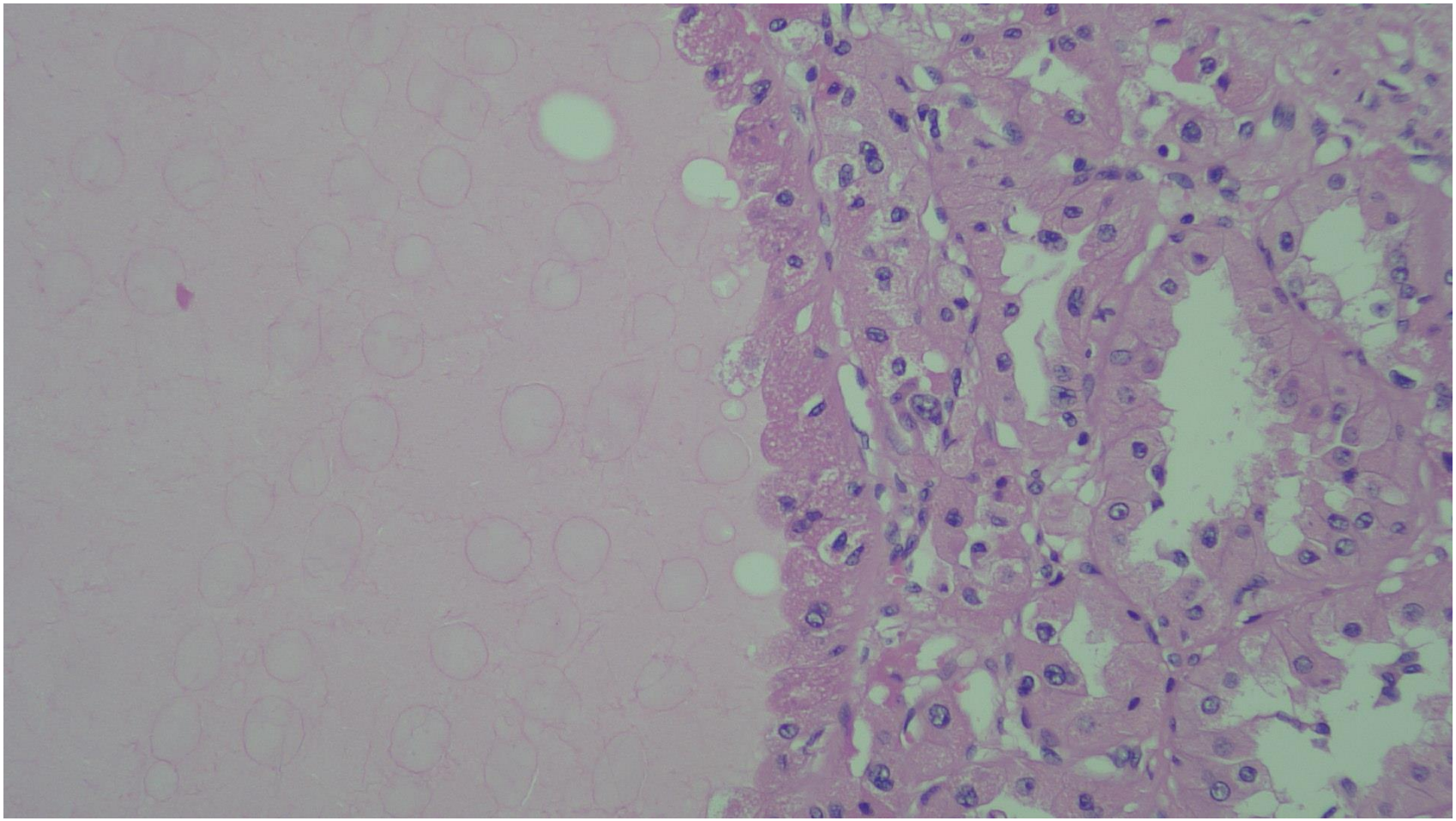




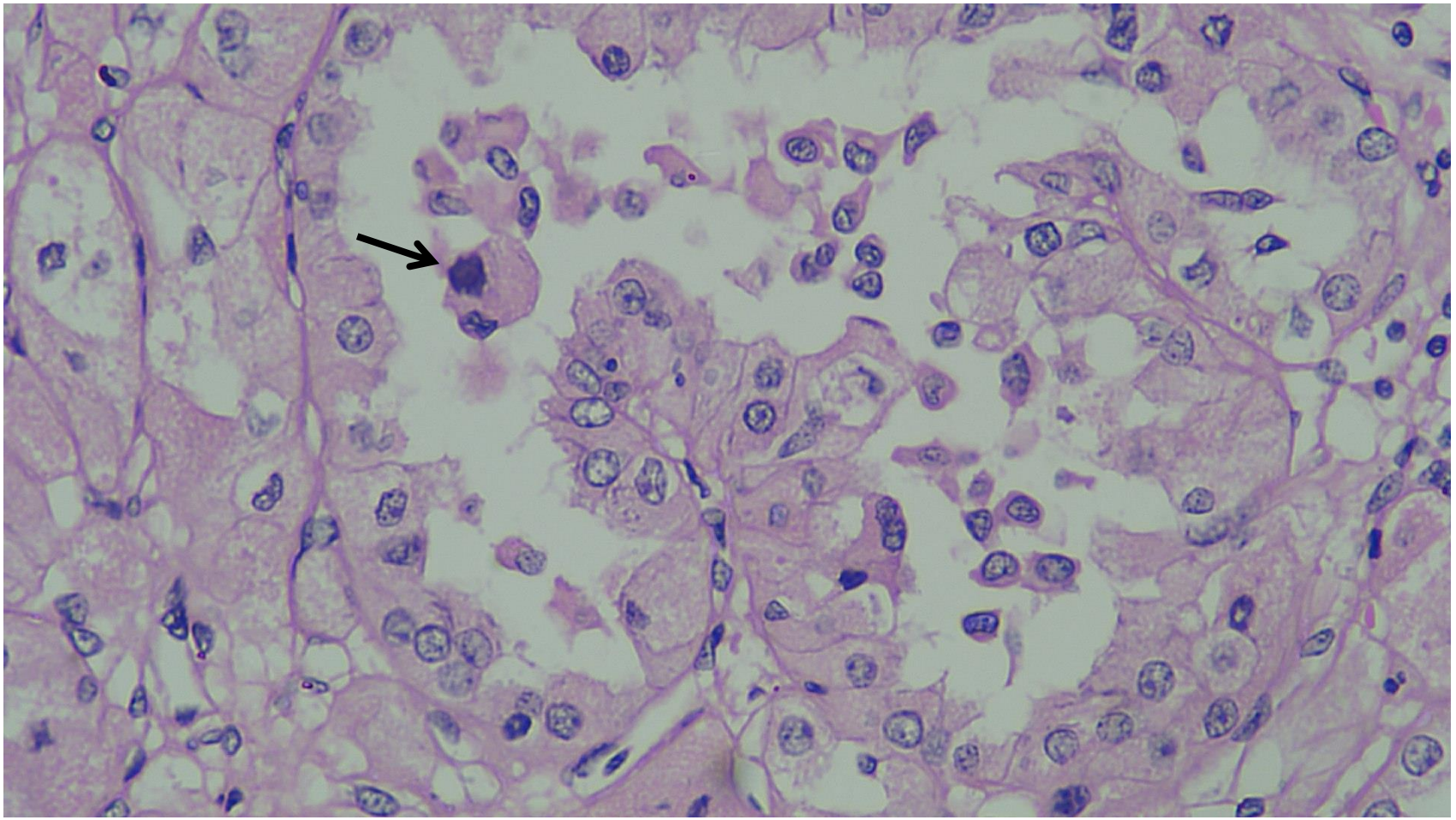
Large polygonal cells with eosinophilic granular cytoplasm



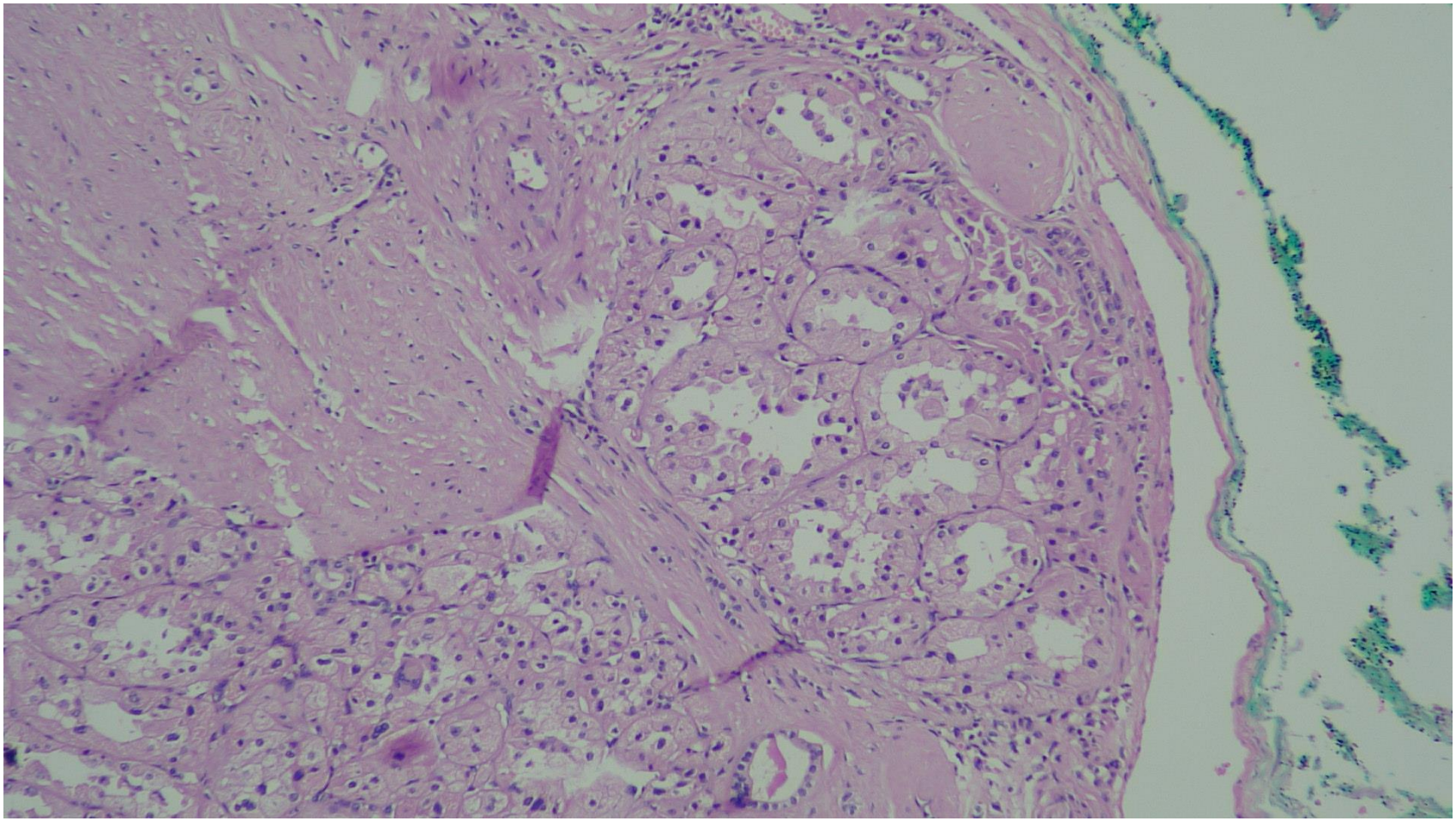
Cyst lined by hobnail cells

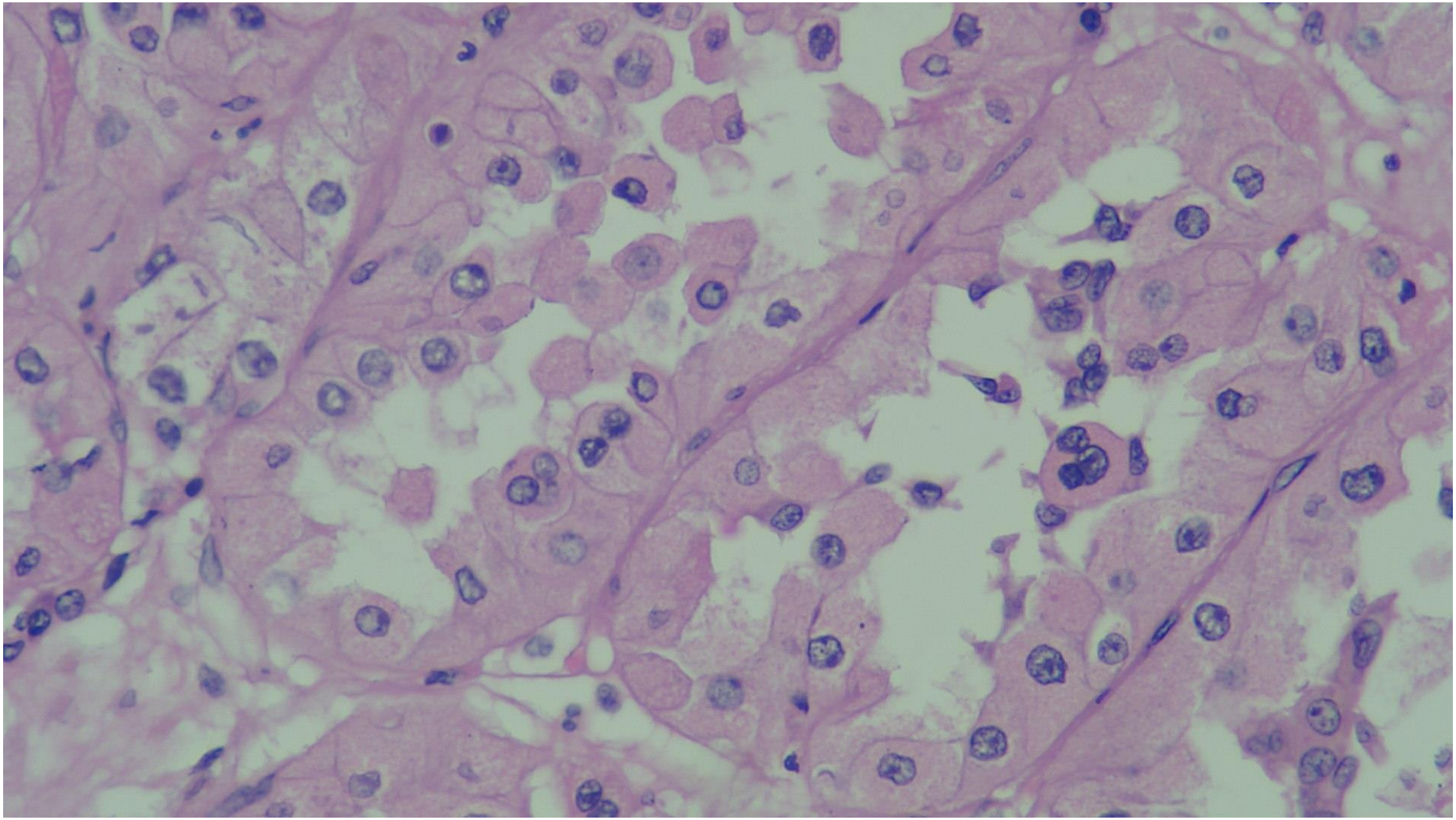


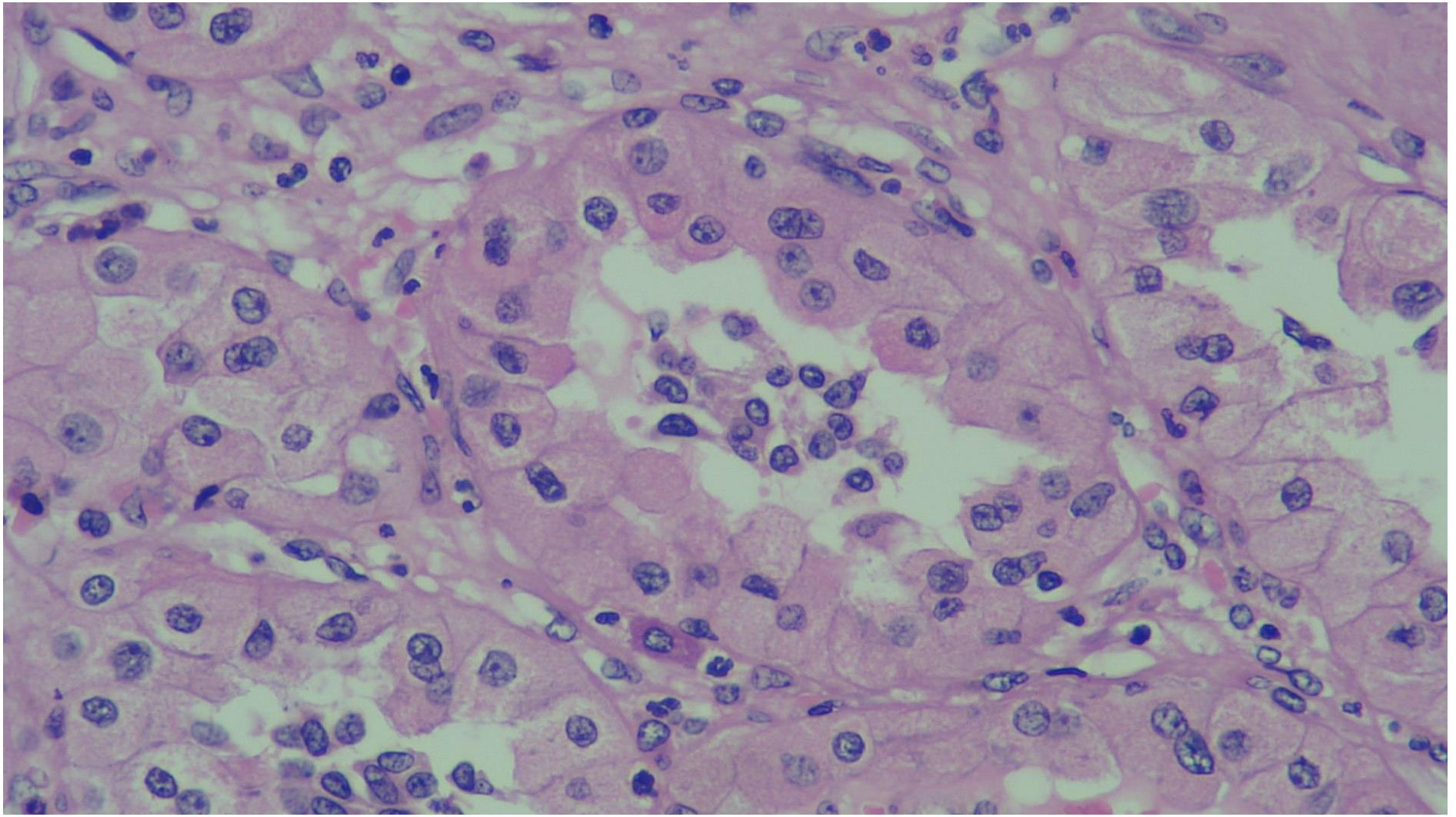
Occasional mitotic activity is seen



Capsular mushrooming seen focally



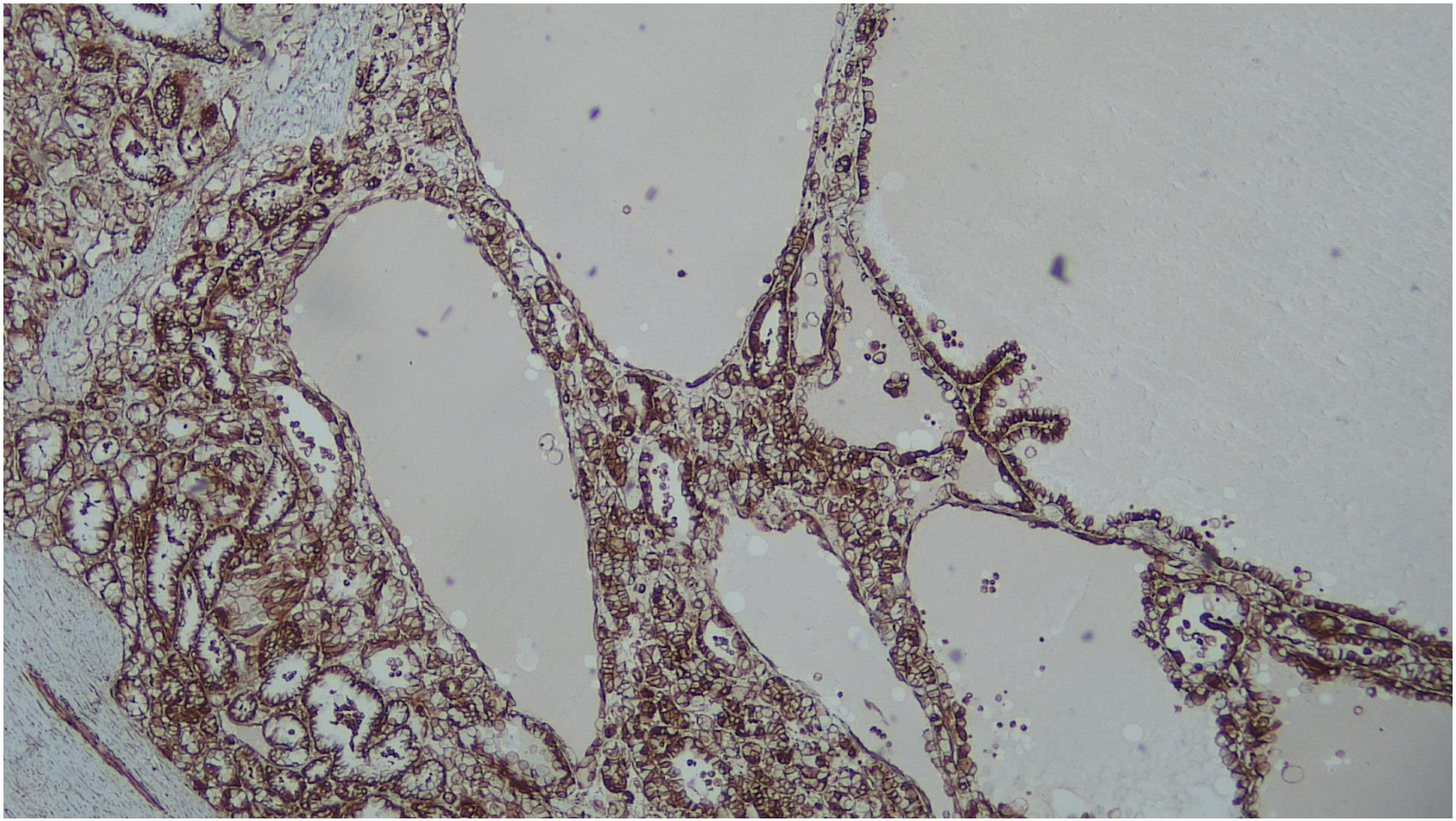




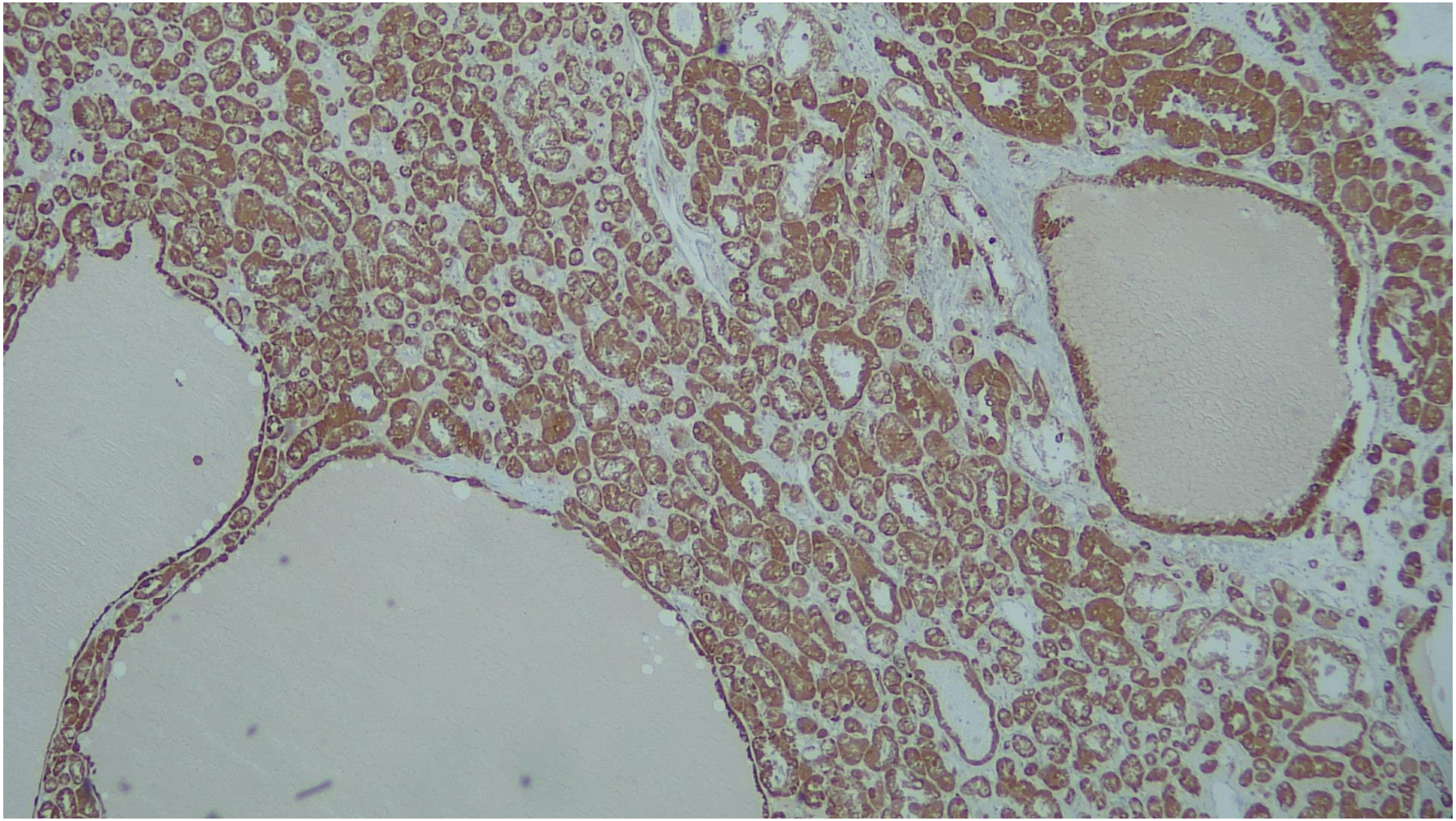
Morphologic Differentials considered

- Eosinophilic CCRCC
- Oncocytoma (although presence of mitotic activity was not in favour)

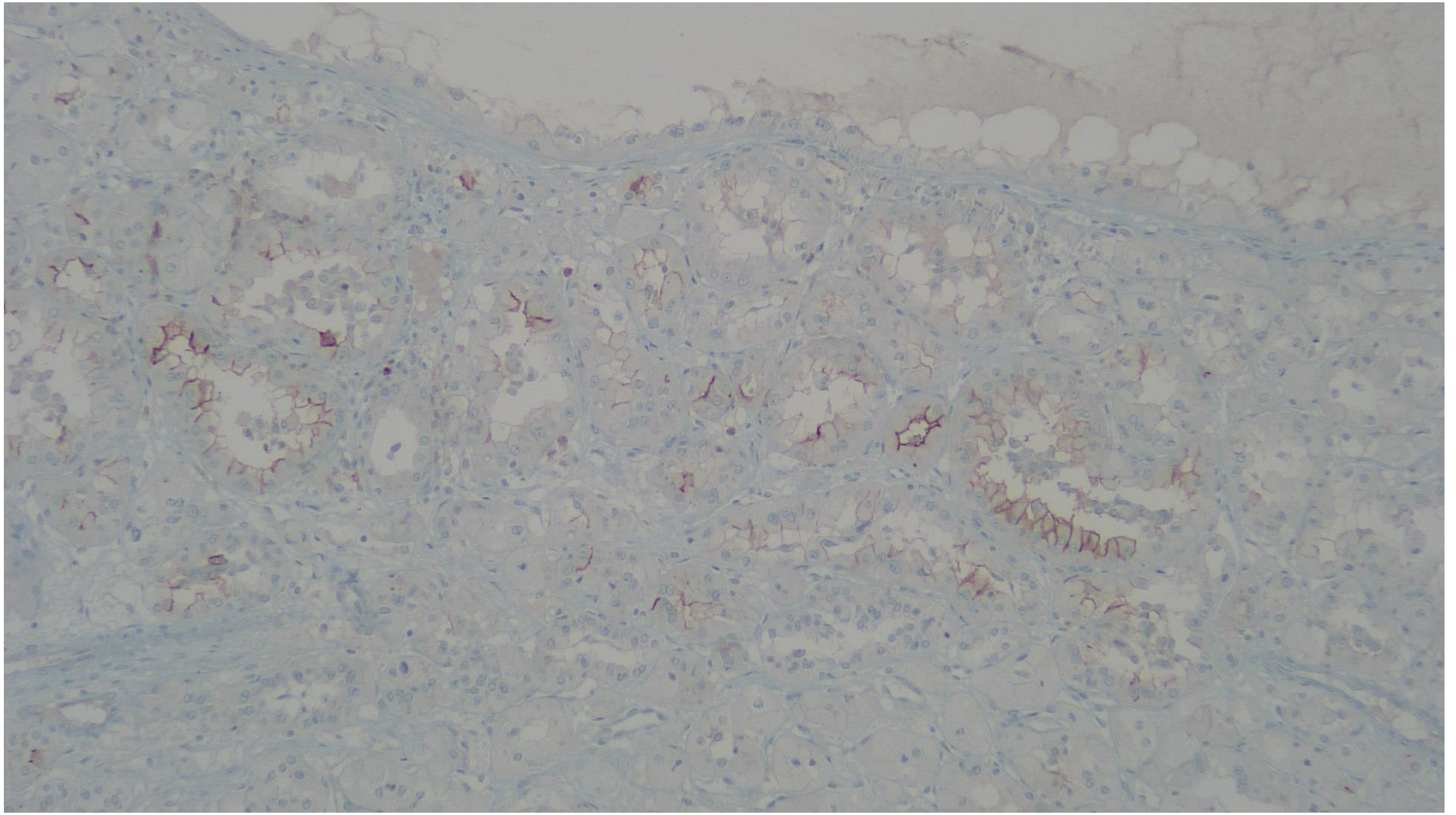
IHC for CK – diffuse positive



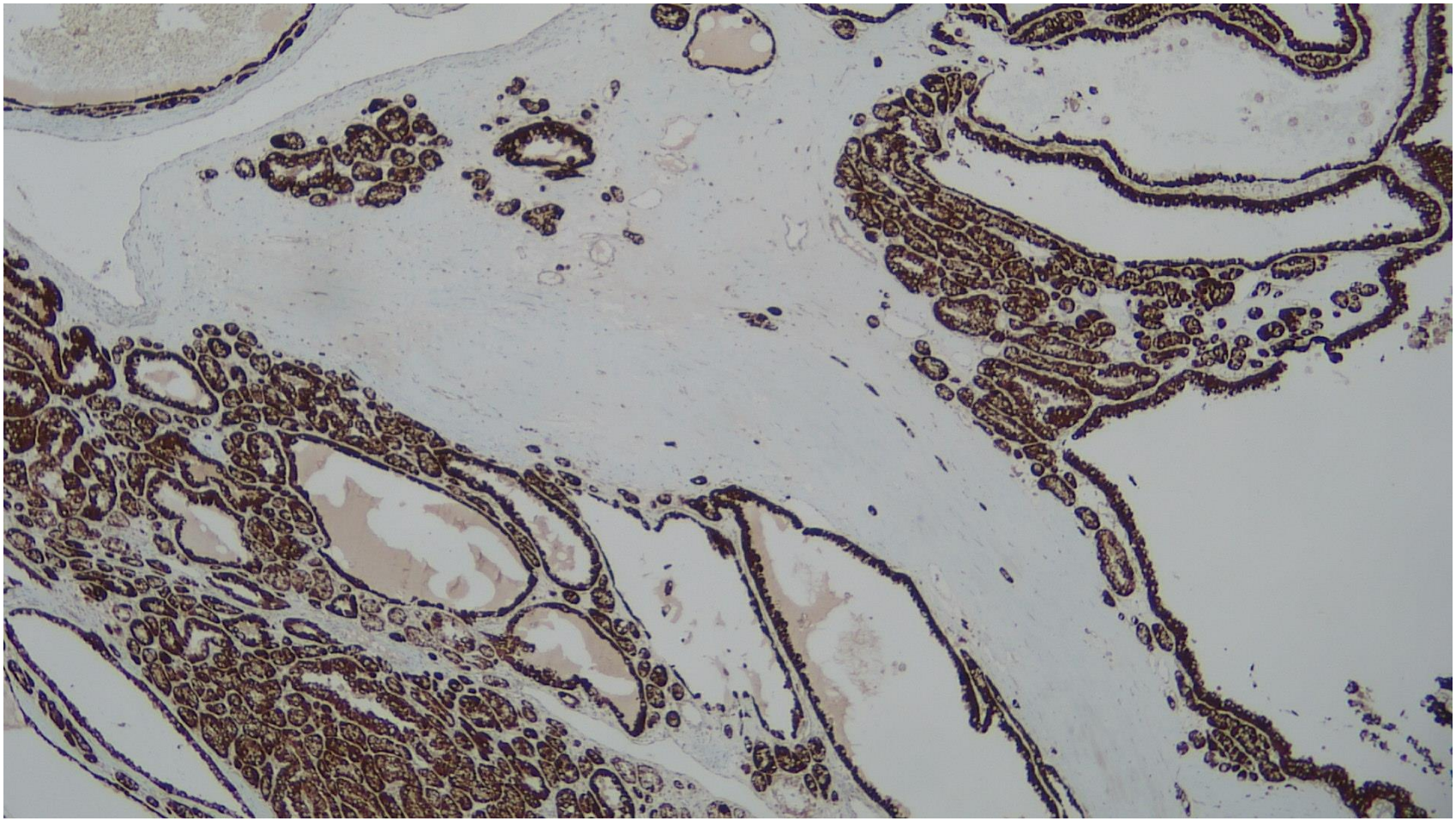
IHC for AMACR: diffuse cytoplasmic granular positivity



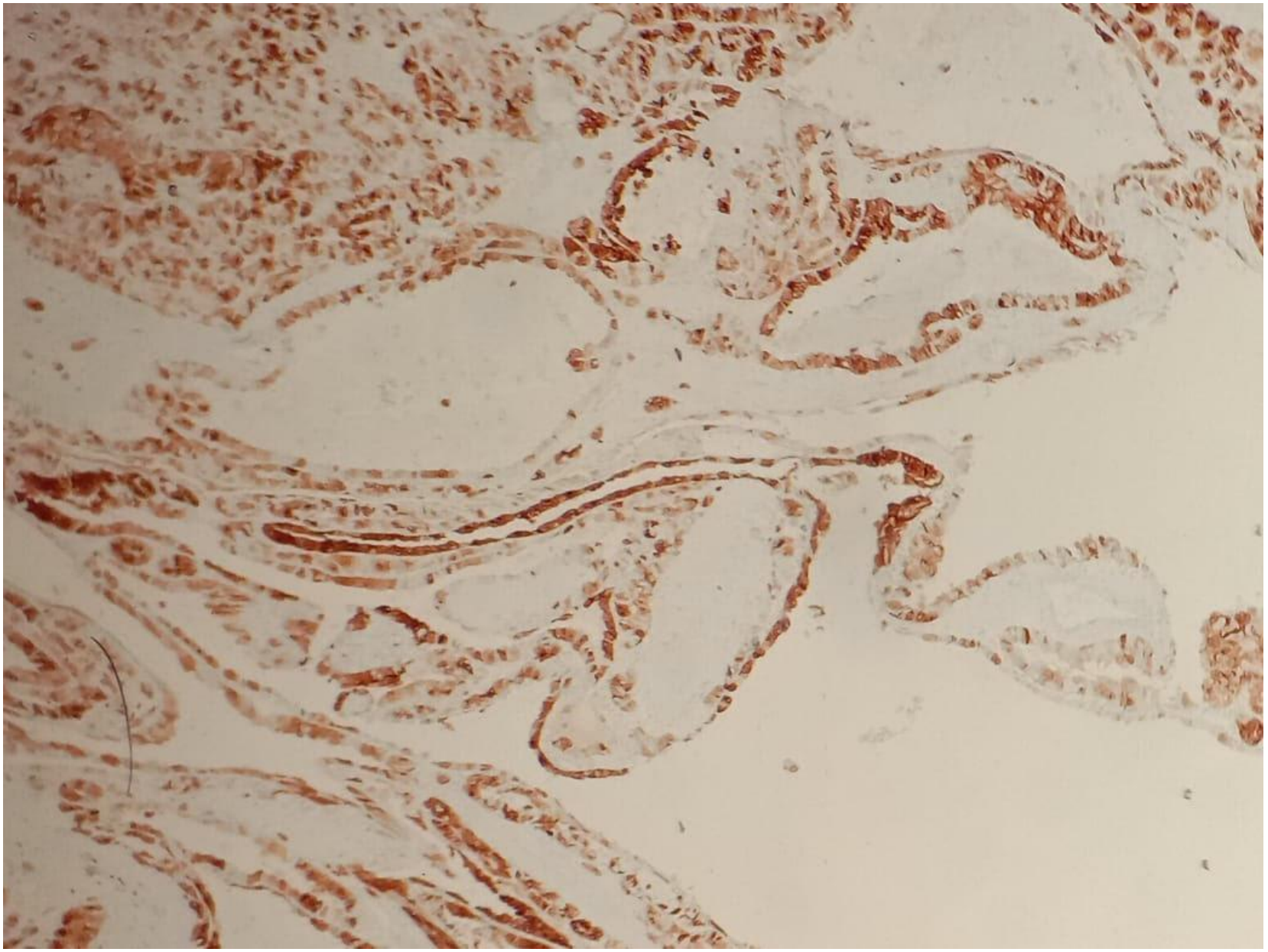
IHC for CD10 was focal positive only



IHC for Vimentin – diffuse positive



IHC for Melan A- diffuse positive



Summary of Immunohistochemical Profile

- **Positive markers:**
- CK (diffuse)
- PAX-8 (diffuse)
- Vimentin (diffuse)
- AMACR (diffuse)
- Melan-A (diffuse)
- CD10 seen focally
- SDH-B and FH is retained in the tumor cells.

- **Negative markers:**
- EMA
- CA-IX
- CK7
- TFE-3
- CK20
- CD-117
- HMB-45

Diagnosis

- **Eosinophilic solid and cystic renal cell carcinoma, right kidney**

- **pStage : pT1aNx**

Eosinophilic Solid and Cystic (ESC) RCC

Incidence

- First case of ESCRCC was reported in 2016
- Not currently included in 2016 WHO classification
- Current incidence of ESRCC is unknown as they were previously labelled as unclassified RCC or unclassified RCC with oncocytic or eosinophilic morphology
- A total of ~60 cases have been reported in literature till now
- An incidence of ~0.2% has been reported by an institution, in the largest series of 19 cases
- Usually in adult females

Behaviour

- Majority of ESRCC show indolent behaviour
- Most present in Stage pT1a or pT1b
- In a study 4 cases (<10%) have been reported with metastatic disease
- Usually in adult females, with low stage, U/L tumors, good prognosis, no recurrence or mets

Macroscopy

- Usually solitary tumor, rarely multifocal
- Yellow-grey (tan) colour with median size of 31mm (12-135mm)
- Cut surface:
  - Solid & cystic tumor with variably sized macrocysts and microcysts
  - Grossly solid tumors also show scattered microcysts

Microscopy

- Cysts are lined by cells in hobnail pattern
- Cells have voluminous eosinophilic cytoplasm, coarse cytoplasmic granules(stippling)
- Cells in solid areas show diffuse compact acinar or nested growth, admixed with small foci of histiocytes and lymphocytes
- Nuclei are round to oval, often irregular, focal prominent nucleoli (WHO-ISUP grade 2-3)
- Some cells may also show densely eosinophilic to purple cytoplasmic globules, surrounded by delicate rims, reminiscent of leishmania bodies

- Some *focal* architectural and cytological variations that can be seen
  - Intracytoplasmic vacuolisation (micro or macro)
  - nested, insular, tubular or clear cell areas
  - Multinucleation
  - Calcification
  - psammoma bodies
- On Electron Microscopy- aggregates of rough endoplasmic reticulum

Differential Diagnosis

CCRCC	**Focal clear cell areas, delicate vasculature, may contain macrocysts**	**CA-IX+, CK20-**
Papillary RCC, oncocytic	**Papillary formations (at least focal), uniform cytology**	**CK7+, CK20-**
Oncocytoma	**Uniform cytology, lacks macrocysts**	**CD117+, CK7 /+, CK20-**
Eosinophilic chromophobe RCC	**Solid and uniform architecture, irregular nuclear membranes, perinuclear halos**	**CD117+, CK7+, CK20-**
Thyroid like follicular RCC		**PAX-8+, CK7+, TTF-1 -, Thyroglublin-,**

Differential Diagnosis

Epithelioid angiomyolipoma	**Epithelioid cells that may be pleomorphic, lacks macrocysts**	**PAX8-, HMB45+, PanCK-, CK7-, CK20-**
MiTF RCC (TFEB)	**Large cells with clear (or eosinophilic) morphology, focal papillary and nested growth, lack cysts (usually)**	**TFE3+, TFEB+, HMB45+, PanCK-**
SDH-B deficient RCC	**Lacks macrocysts, uniform low-grade oncocytic cells with flocculent to densely eosinophilic cytoplasmic vacuoles**	**CD117-, SDHB-, SDHA+, CK20-**

Immunohistochemical profile

- PAX-8 +
- AE1/AE3 +
- CK8/18 +
- CK20 +/CK7-
  - CK20+ in ~80% cases
  - CK7-/focal
  - CK20-/CK7+ IHC never seen
- Vimentin +
- Cathepsin-K + in some
- Melan-A + in some
- AMACR
- CA-IX

- CK7 – or focal +
- CD117 –
- Variable AMACR (patchy), CA-IX, vimentin, CD10

Genetics of ESCRCC

- Most of ESCRCC are sporadic
- 10% occur in patients with documented tuberous sclerosis complex (TSC)
  - Somatic biallelic loss or mutation of TSC genes, specifically TSC1 or TSC2
- Molecular karyotype profile of recurring CN alterations seen and variable set of genomic alterations, different from other RCCs

Genetics

- Frequent CN gains
  - On 16p13-16q23, 7p21-7q36, 13q14, 19p12
- CN loss
  - At Xp11.21 & 22q11
- LOH alterations
  - At 16p11.2-11.1, Xq11-13, Xq13-21, 11p11, 9q21-22, 9q33
- LOH alterations at TSC1 in 33%
- CN gains at TSC2 in 42%

Largest series of 19 cases (Trpkov et al,2017)

Eosinophilic Solid and Cystic Renal Cell Carcinoma (ESC RCC)

Further Morphologic and Molecular Characterization of ESC RCC as a Distinct Entity

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(*Am J Surg Pathol* 2017;00:000–000)

- Incidence of ~0.2%
- All females
- None had clinical features of TSC
- Median age 55 years
- Size mean 42mm
- 4 cases (<10%) have been reported with metastatic disease

- CK+ in all
- EMA focal in 33%
- PAX-8 uniformly positive
- CK20 + in 74%
- CK7 focal in 31%
- AMACR in 84% but mostly focal
- CD10 focal in 79%
- CD117-
- CA-IX-
- Vimentin + in 90%
- HMB45/Melan A not seen

THANK YOU