21. ULUSAL PATOLOJİ KONGRESİ

Slide Seminar

SMALL ROUND CELL TUMORS OF CHILDHOOD

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8 years old, female

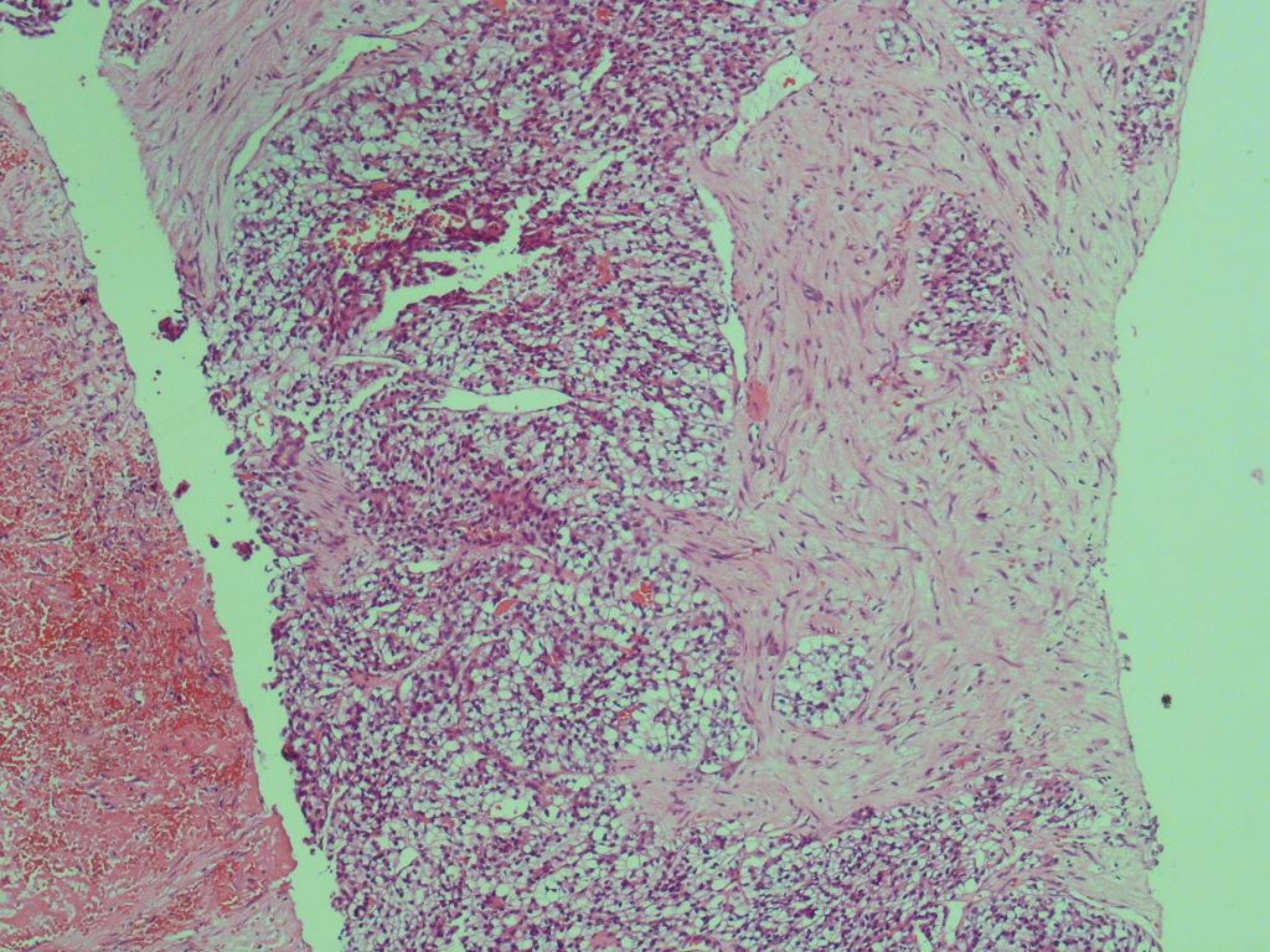
abdominal pain, jaundice, December 2009

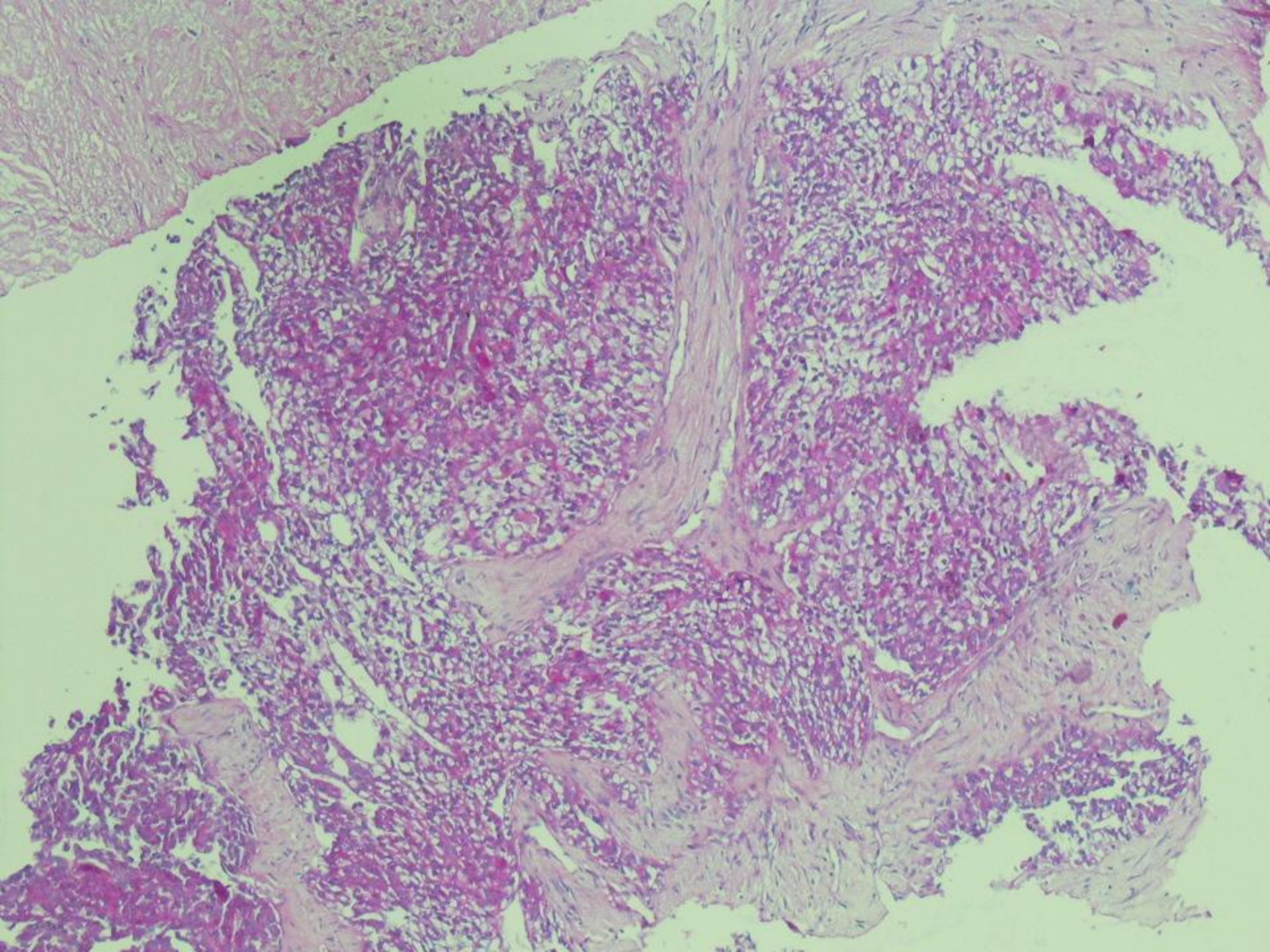
USG: liver and pancreatic mass

tru-cut biopsy from liver mass in local health center:
hepatoblastoma

no regression after 4 cycles of PLADO and 3 cycles of Carboetoposide

- referral to our hospital: abdominal pain, jaundice, hepatomegaly, good general performance
- CEA: N Ca19.9: N AFP: N
- USG: 73x43 mm solid, heterogeneous and hypoechoic mass with lobulated contours localized to pancreatic head + multiple ill defined liver nodules (GD: 68x45 mm) with blurred border between one hepatic and pancreatic mass
- CT: Portal hilar infiltration, protrusion into bulbus, minute calcifications





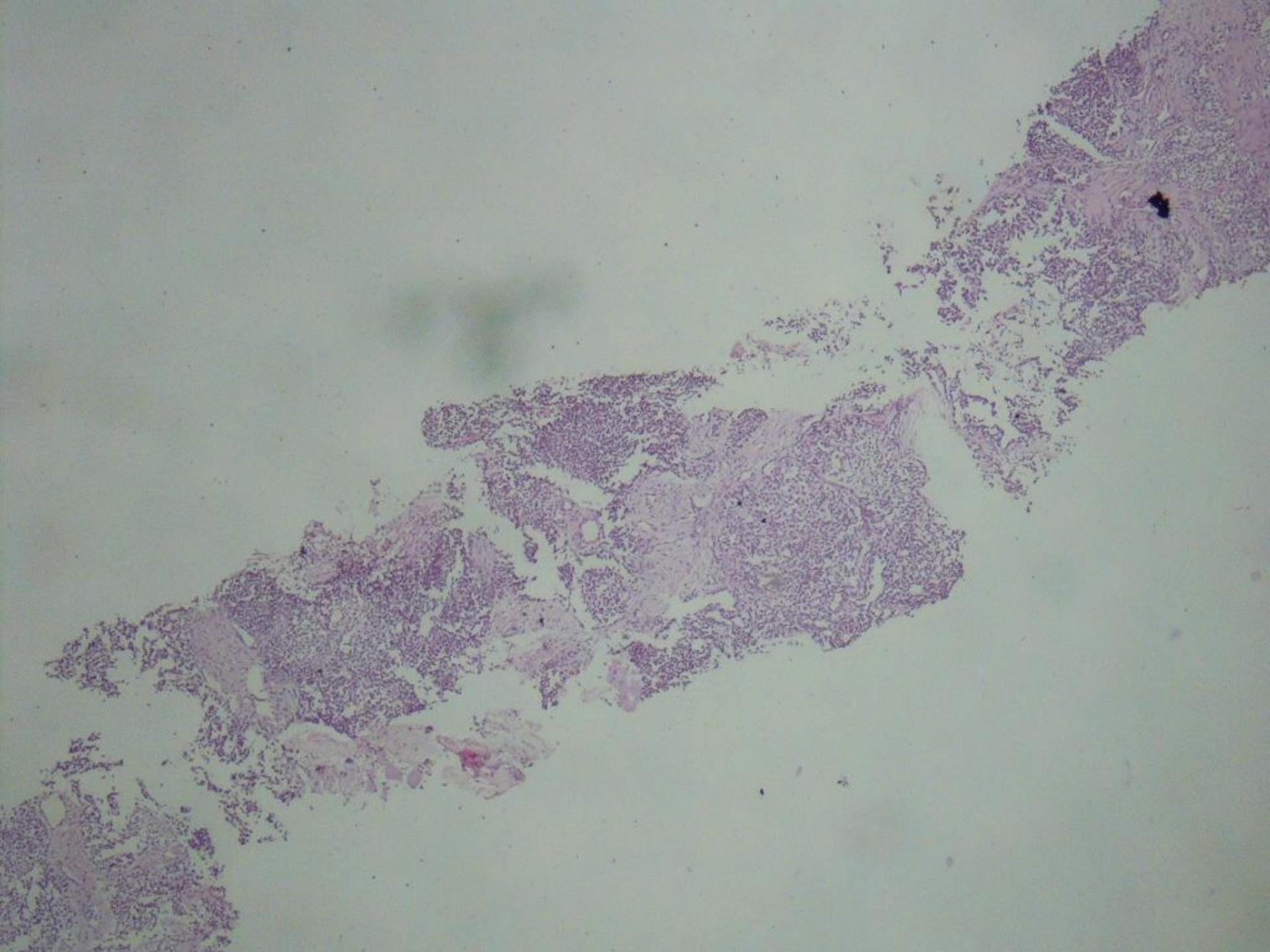
Immunohistochemistry

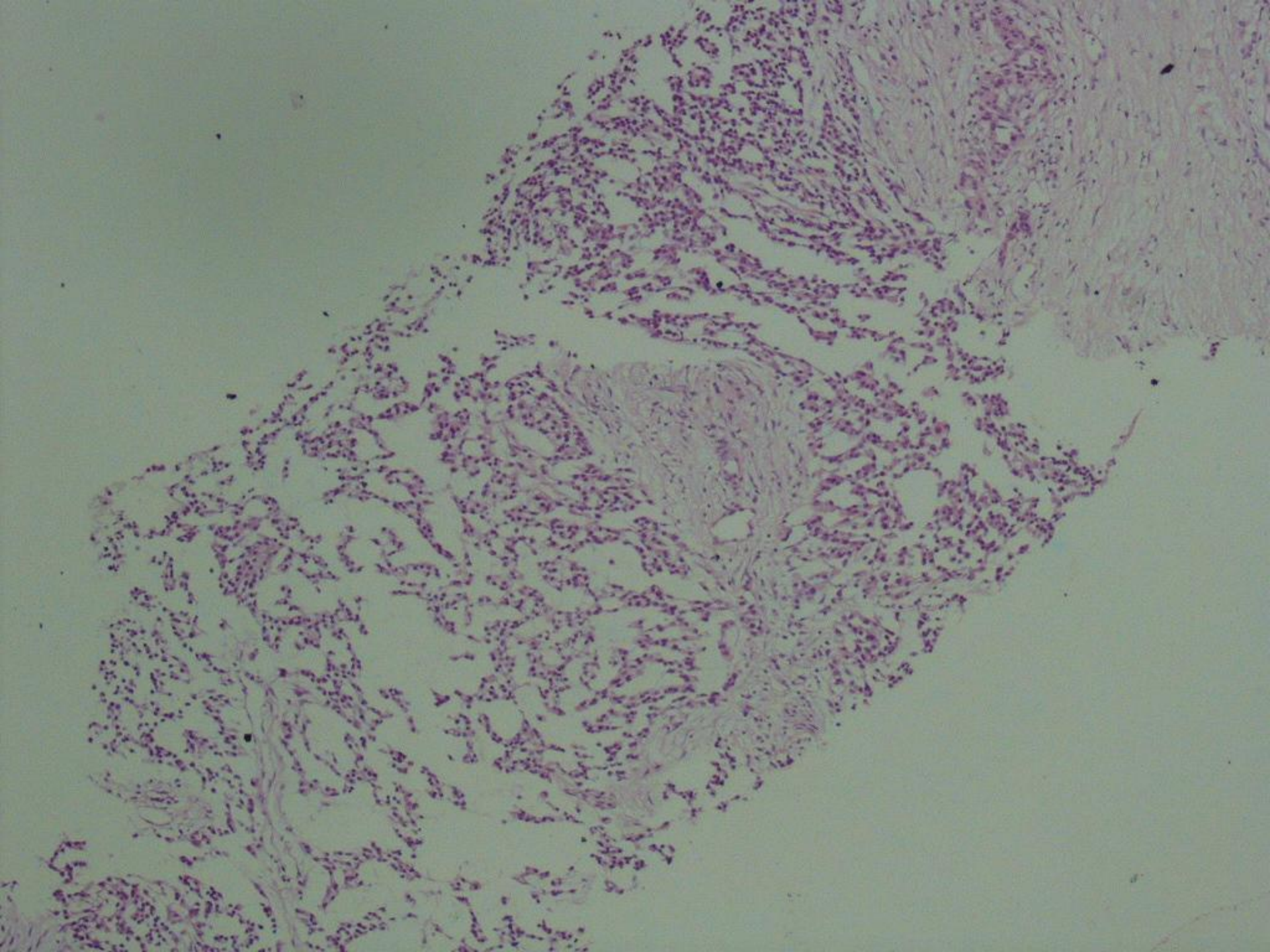
- EMA +
- CK (AE1-AE3) +
- Vimentin +
- AAT +
- AFP -
- CD34 -
- Desmin -

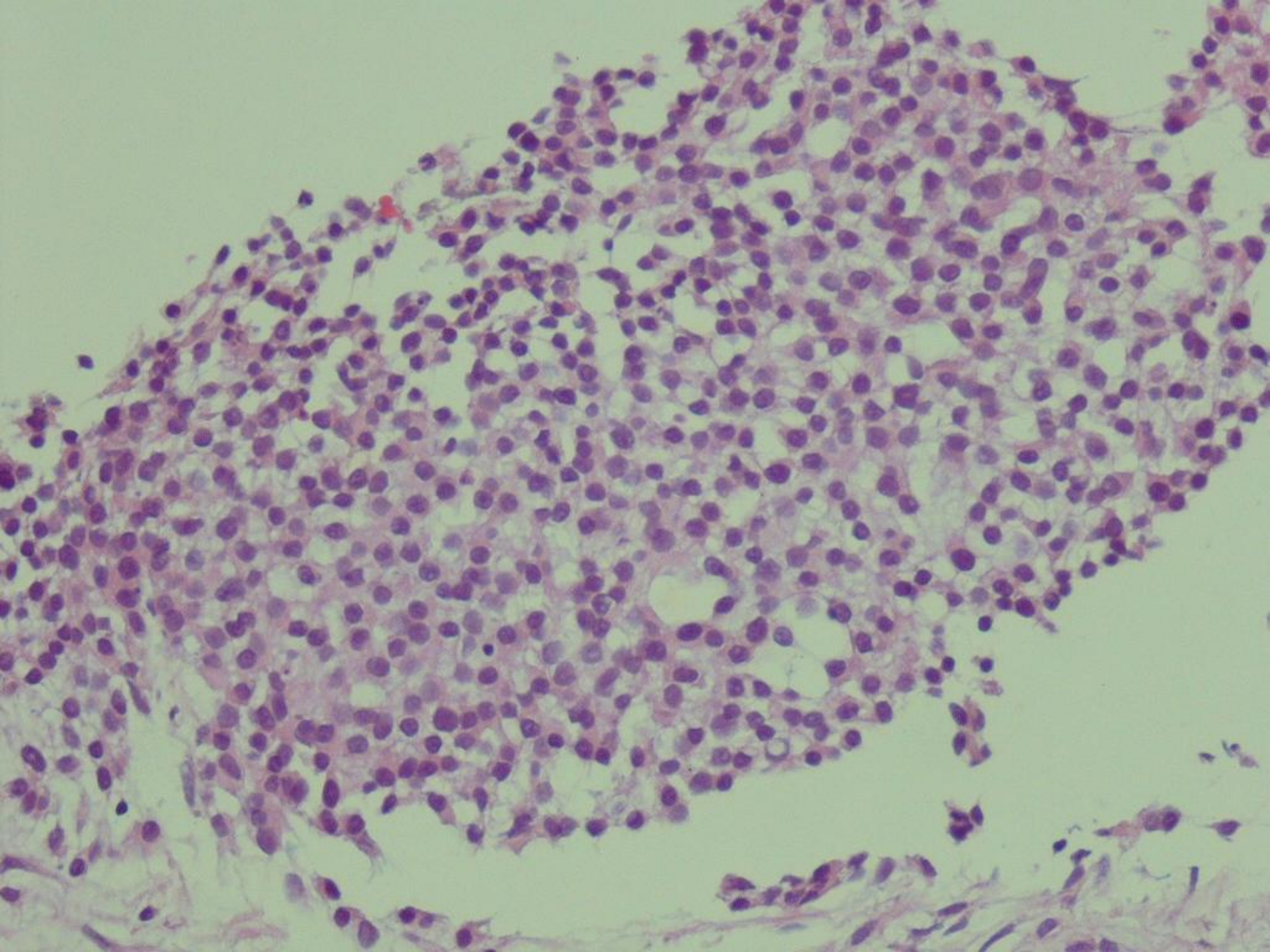
First report:

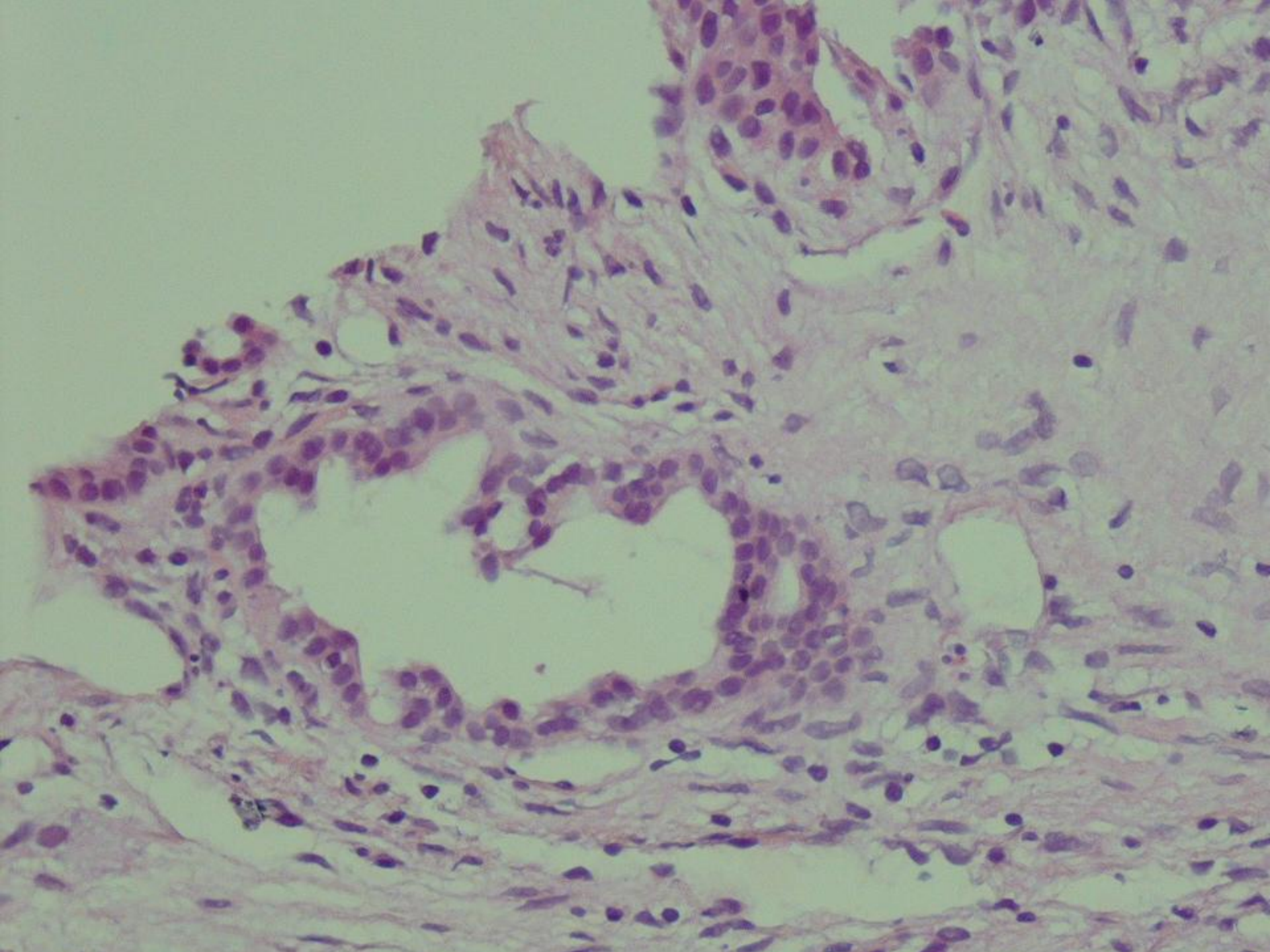
Primitive embriyonal tumor; HB can not be excluded, sample not sufficient for further differential diagnosis

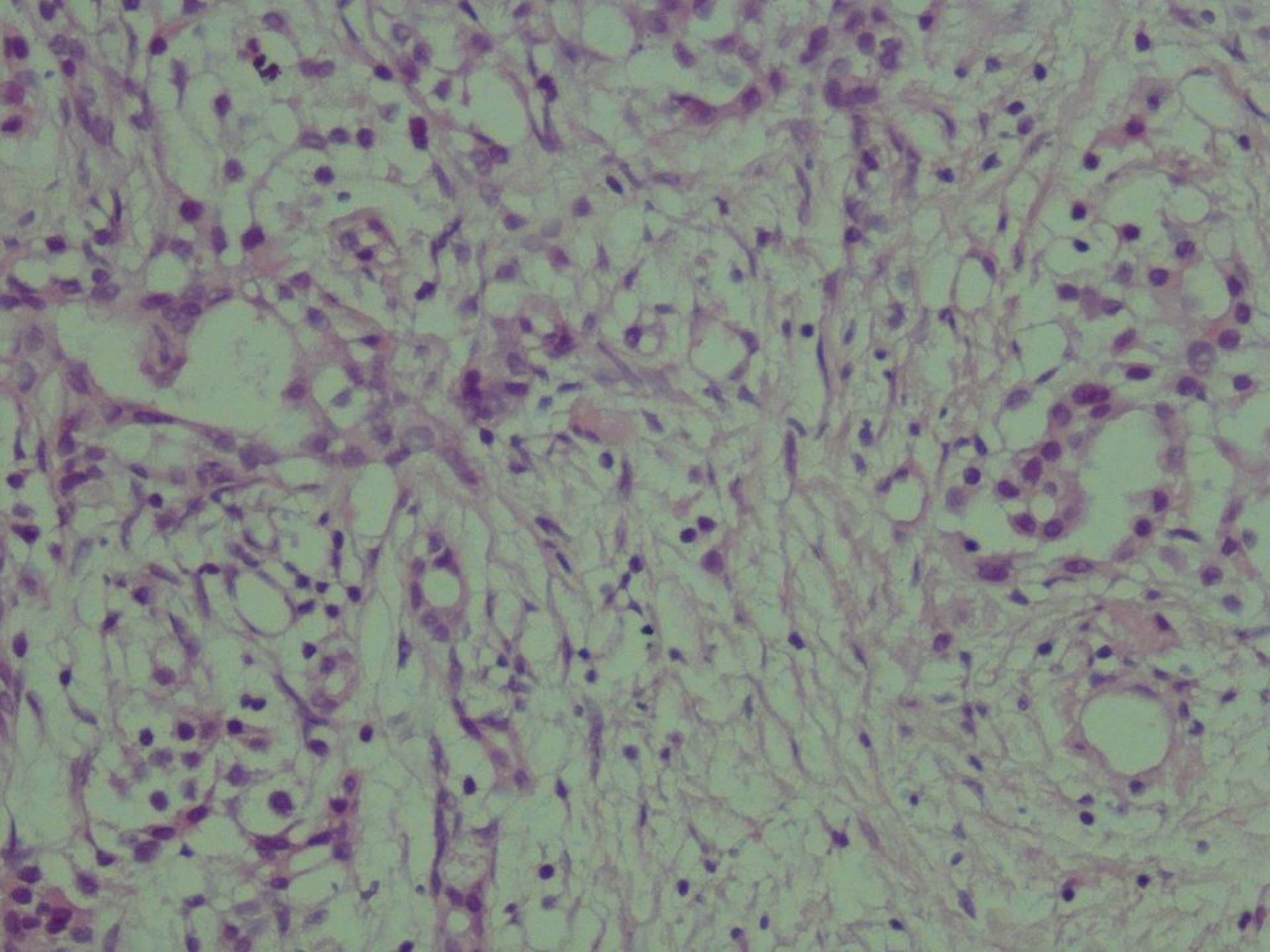
- jaundice 
- No response to treatment (ifosfamid+MESNA + carboplatin)
- tru-cut biopsy from pancreatic mass

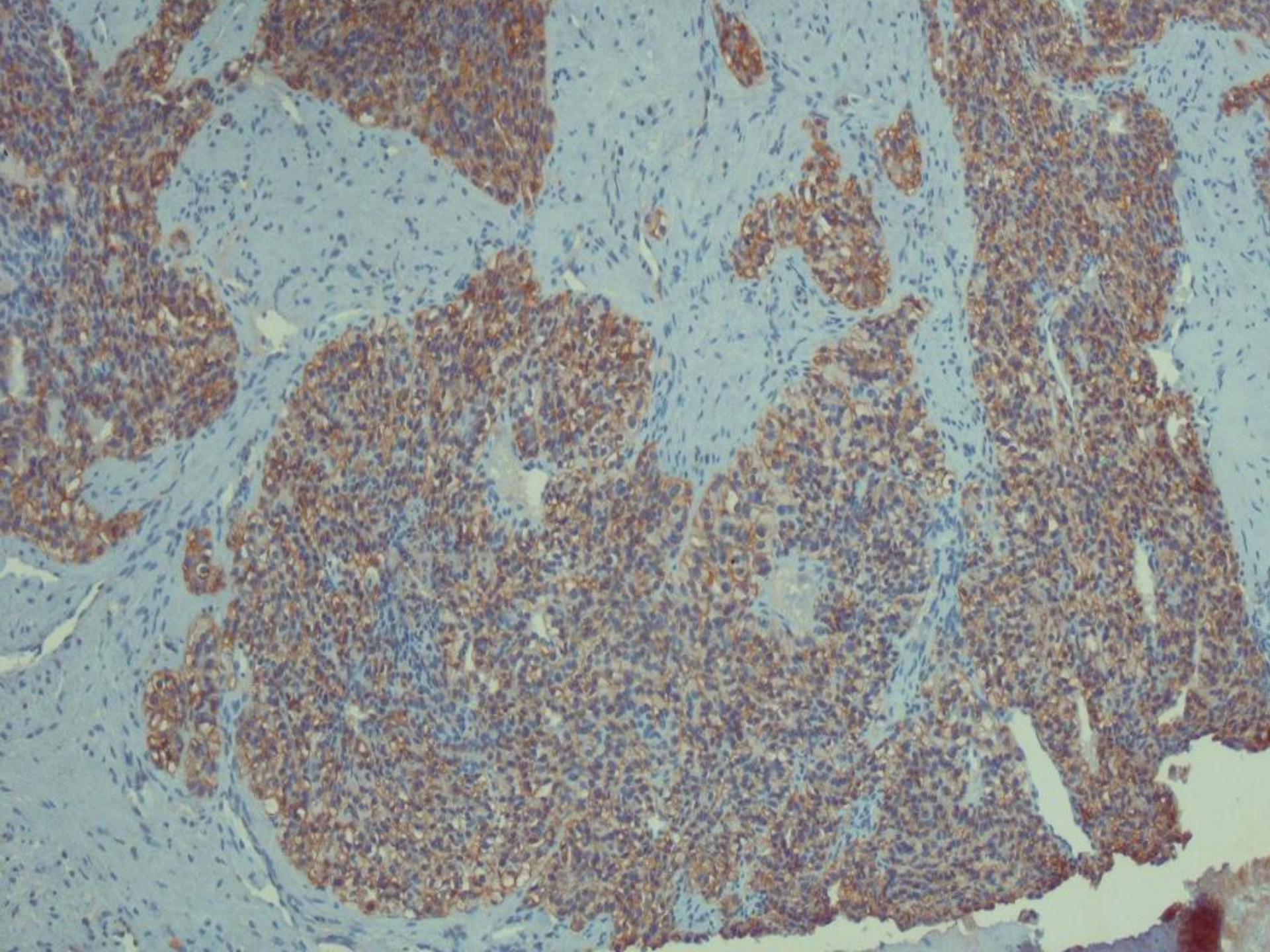


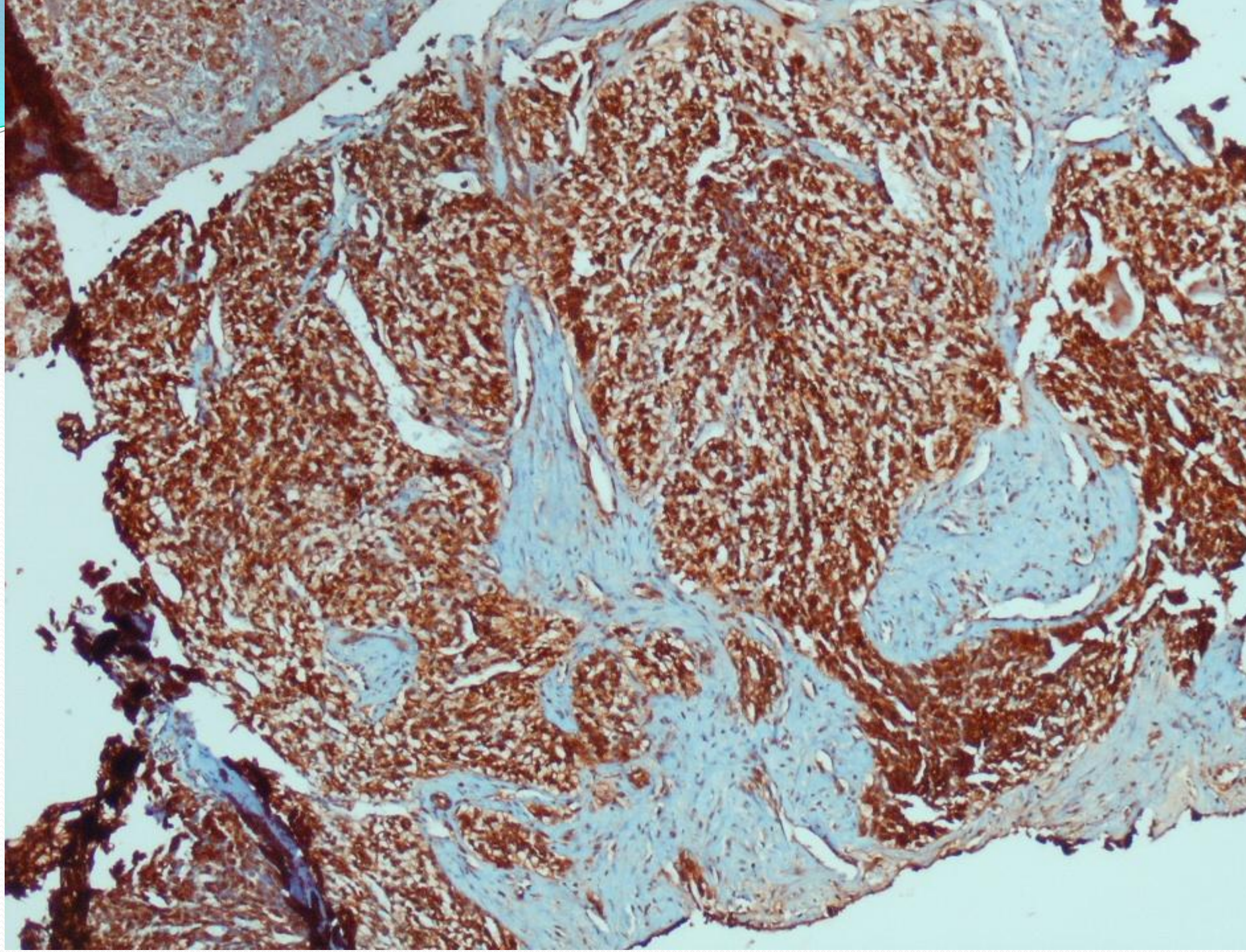


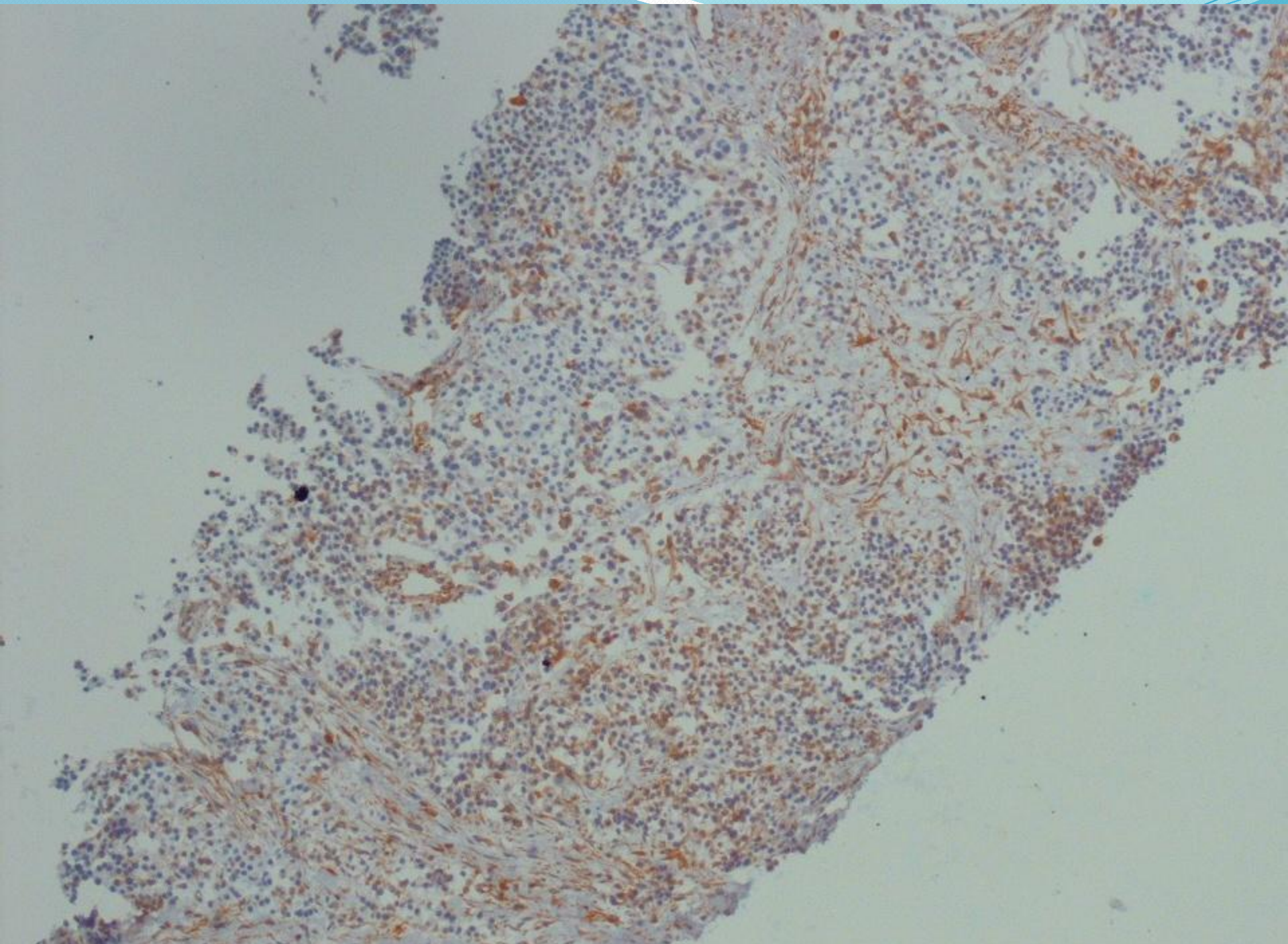


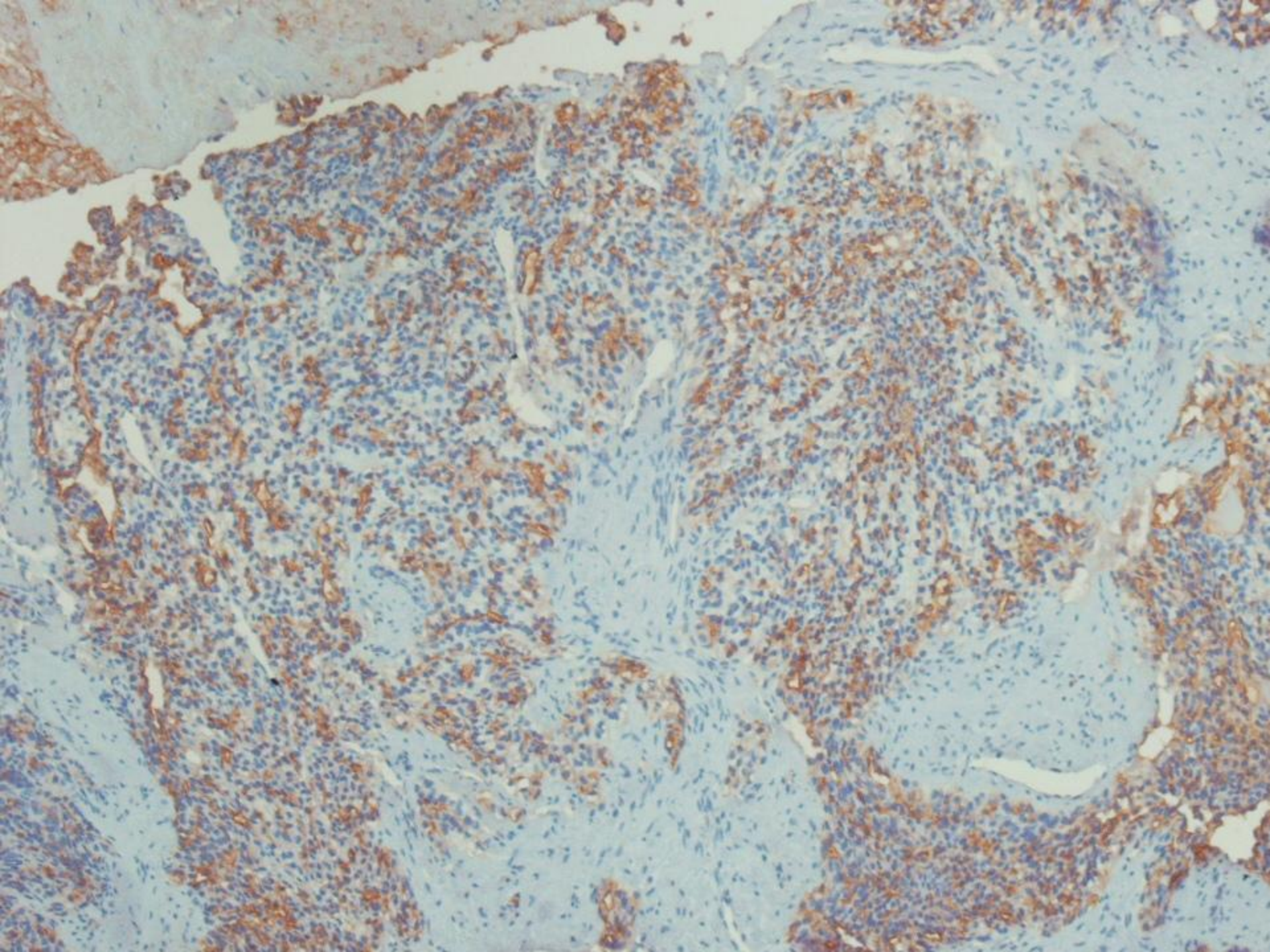


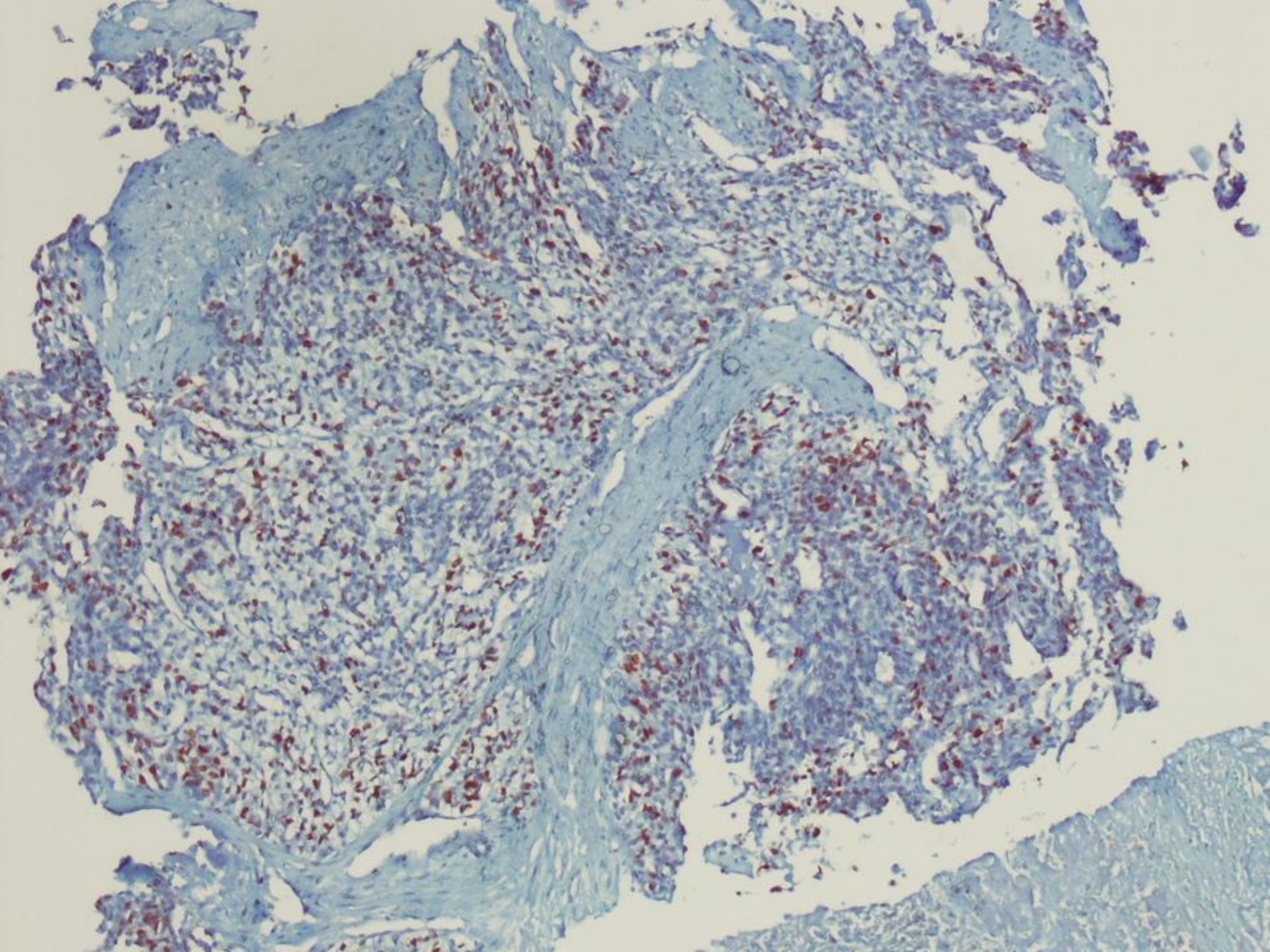


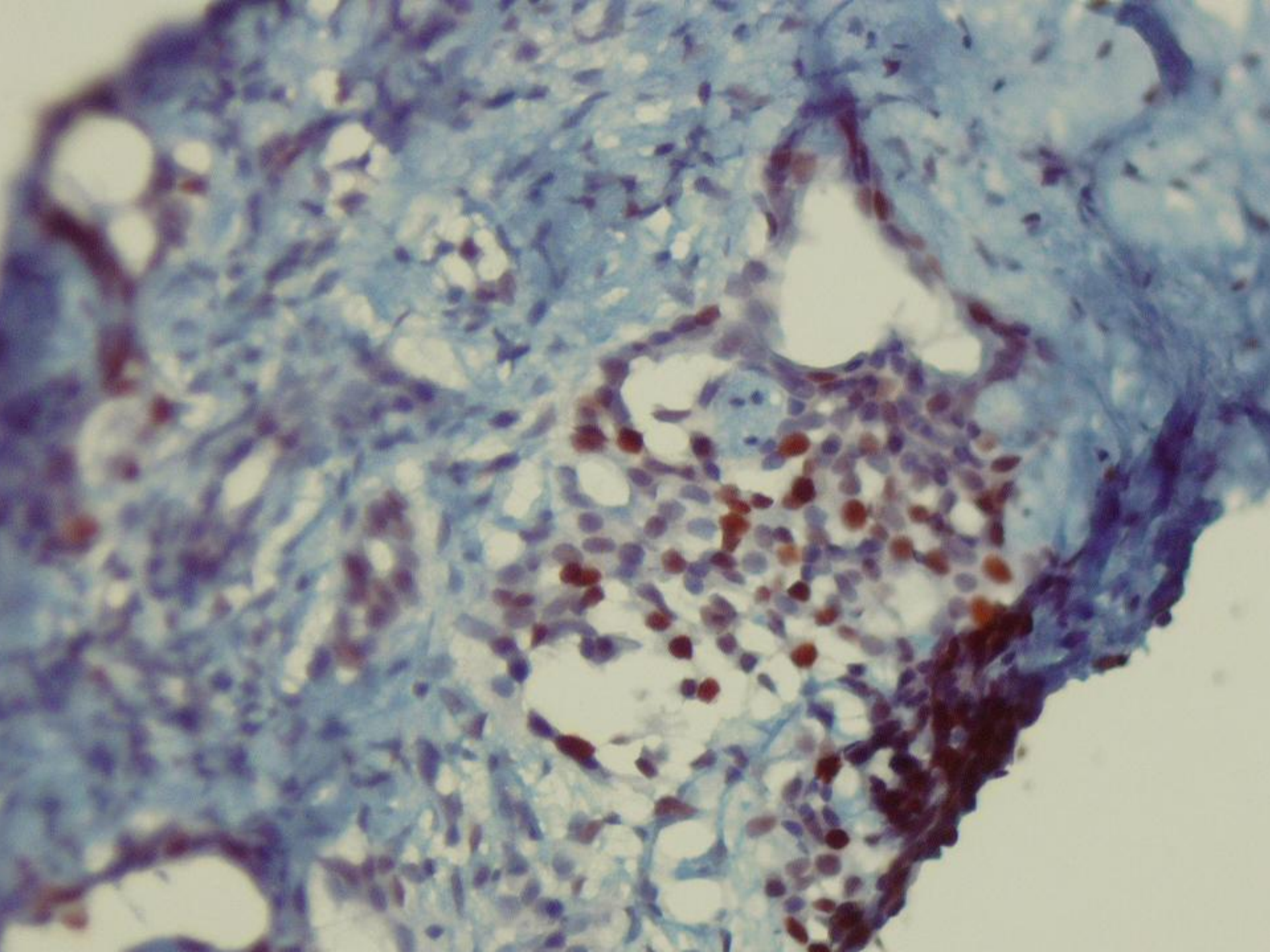












Immunohistochemistry

AAT	+
CK (AE1-AE3)	+
Vimentin	f+
P53	f+
β-catenin	f+ (cyt+memb)
Synaptophysin	f+
EMA	+
CD10	-
Chromogranin	-
NSE	-
CK7	-
mCEA	-
AFP	-
Desmin	-

Primitive epithelial tumor with duct-like structures

involving liver + pancreatic head

Differential Diagnosis

- Hepatoblastoma
- Pancreatoblastoma
- Acinar cell carcinoma
- Neuroendocrine tumors of pancreas
- Desmoplastic small round cell tumor
- ES/PNET
- Pancreatic ductal carcinoma

Pancreatic Tumors That May Occur in Children

- ***Epithelial tumors***

  Acinar cell origin — **Pancreatoblastoma**; **Acinar cell carcinoma**

  Ductal cell origin (exceedingly rare) — Ductal adenocarcinoma

  Endocrine cell origin — Uncertain origin: **Solid-pseudopapillary tumor**

- ***Nonepithelial tumors (exceedingly rare)***

  Lymphoma, particularly Burkitt

  Sarcomas, particularly rhabdomyosarcoma

  Dermoid cyst

  Lymphangioma

  Hemangioendothelioma

DD: Acinar Cell Carcinoma

- No clear-cut acinar pattern, no basal polarisation,
- Clear cytoplasmic features
- Prominent fibrotic stroma
- Positive P53 staining

- **DD: NET-NEC**

Rare in childhood, clinical syndrome, vast majority strongly(+) for at least two NE markers

- **DD: Desmoplastic Small Round Cell Tumor**

Desmin positivity

- **DD: Solid pseudopapillary neoplasm**

No true luminal structures, hyaline globules, pseudopapillae, nuclear β-catenin positivity, negative P53 staining

- **DD: ES/PNET**

Some related to small cell HB? Clear cell features and CK positivity described in liver localisation

- **DD: Ductal adenocarcinoma**

DD: Pancreatoblastoma

- Most frequent pancreatic tumor of childhood
- Well defined heterogeous mass localized to head and tail of the pancreas
- Invasion to adjacent structures
- Metastases at the time of diagnosis in 20-35% (liver, LN, lung, bone)
- Well defined epithelial islands (predominantly acinar and solid) separated by fibrous stroma producing a geographic low power appearance
- Acinar, endocrine and ductal differentiation with distinctive **squamoid nests**
- PAS-D+ cytoplasmic granules indicating acinar differentiation
- Immunohistochemical labelling for trypsin, chymotrypsin and lipase

PB has certain similarities to HB

- Embryonically related structures-liver and pancreatic cells appear to keep a considerable plasticity in that they can transform to each other in the post-organogenetic period
- A tumor found in an identical age group with a

  closely related morphological appearance
- Both occur in association with the Beckwith-Wiedemann syndrome and Familial Adenomatous Poliposis
- Often exhibit elevated plasma levels of AFP
- No distinct immunohistochemical profile, the diagnosis requires a combination of the clinical, imaging and pathologic findings
- Similar molecular alterations (LOH 11p, β-catenin/APC pathway)

Difficulties in diagnosing Hepatoblastoma

- Small sample size
- Low serum AFP level with complete IHC negativity
- Extremely rare pancreatic metastasis/invasion by HB
- **Fetal** no obvious similarity to hepatic parenchyma, absence of sinusoidal or canalicular pattern (CD34), no extramedullary hematopoiesis
- **mixed fetal and embryonal** no blastema-like areas
- **Macrotrabecular** no trabecular pattern, monomorphic appearence
- **SCUD** ample cytoplasm, presence of glandular differentiation
- **Rhabdoid** no convincing cytomorphologic detail
- **Mesenchymal**

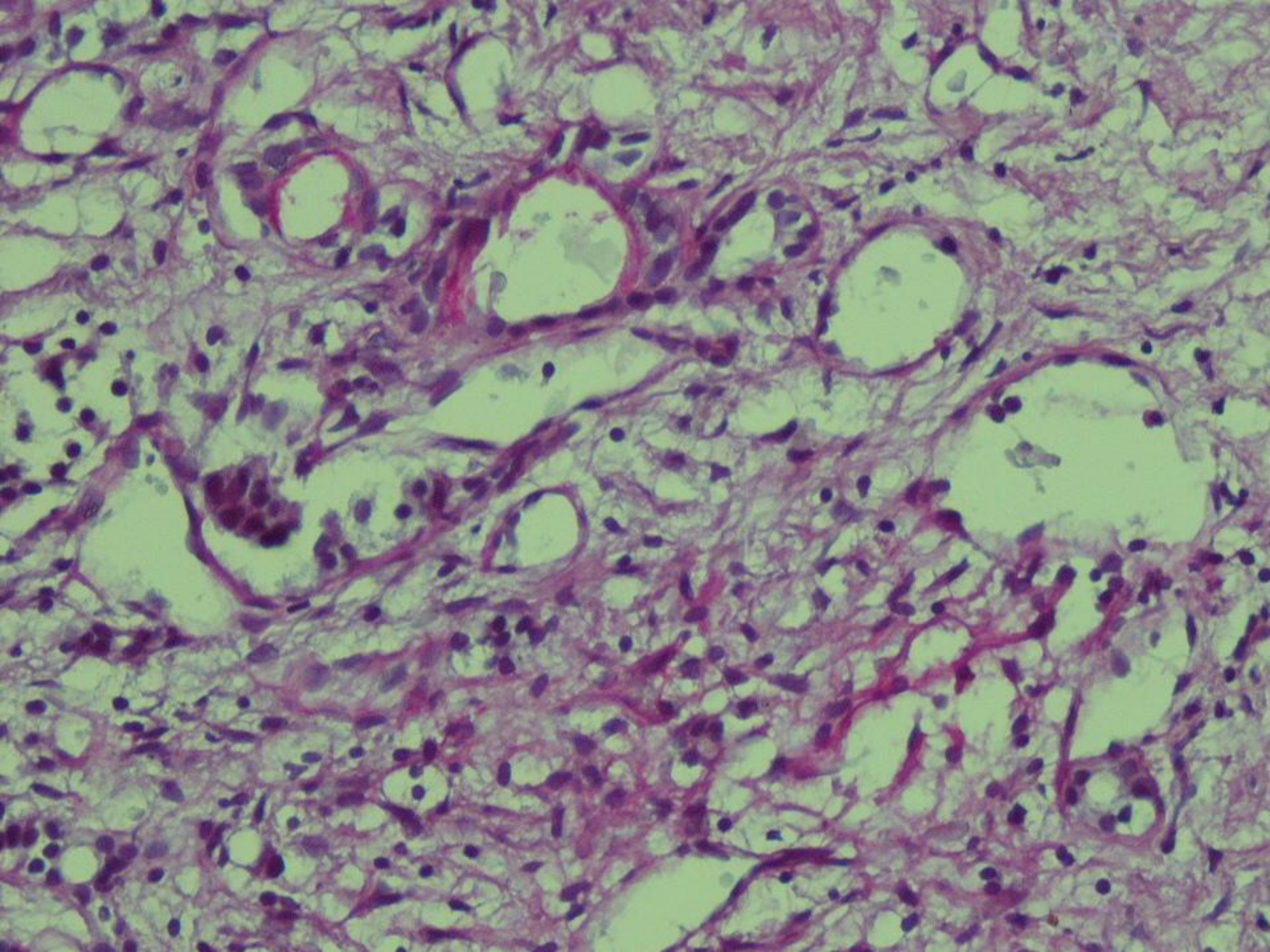
- Pancreatic extension of a hepatoblastoma?
- Pancreatoblastoma metastatic to liver?

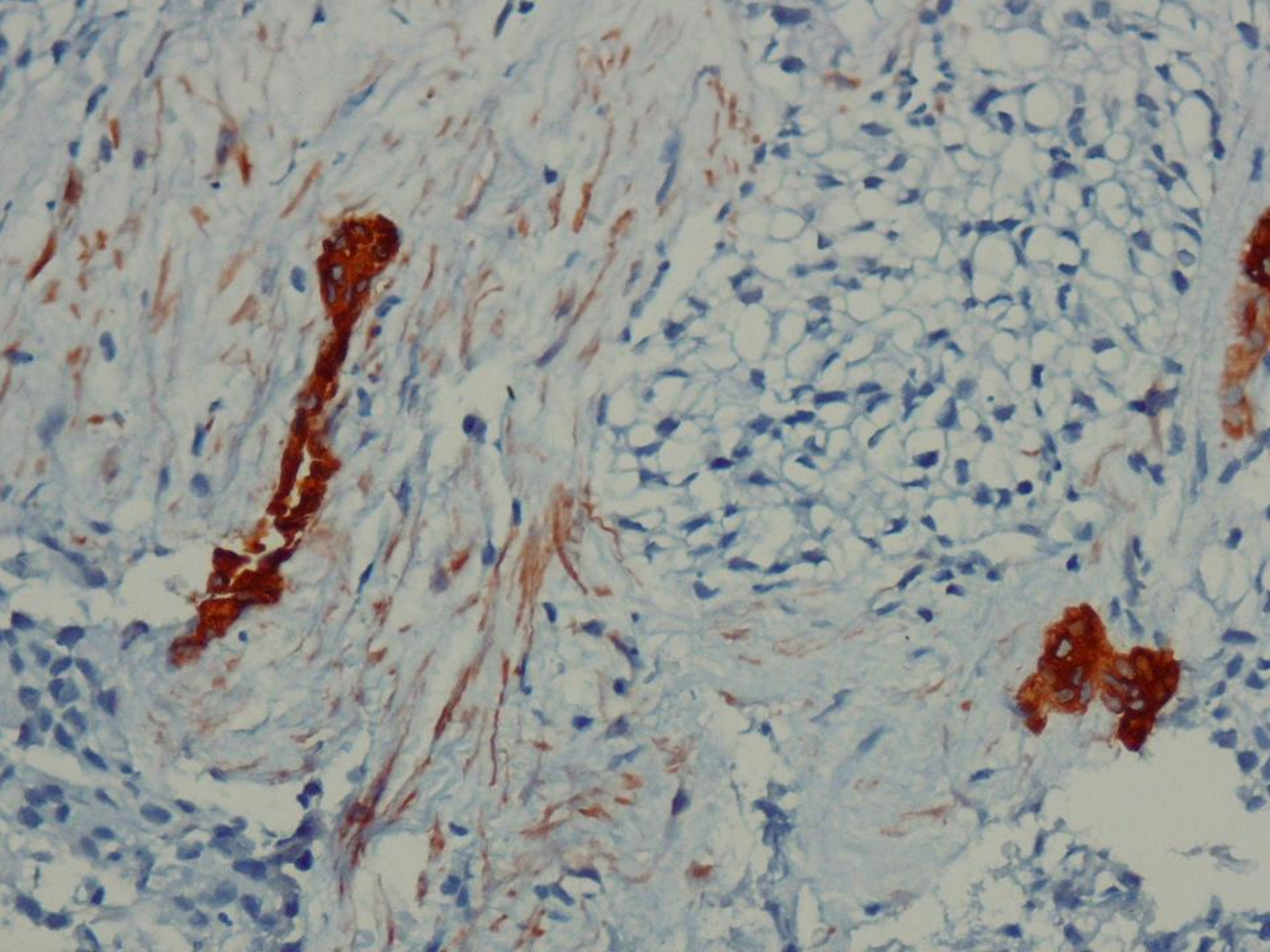
Presence of individual duct-like structures in continuity with the solid nests

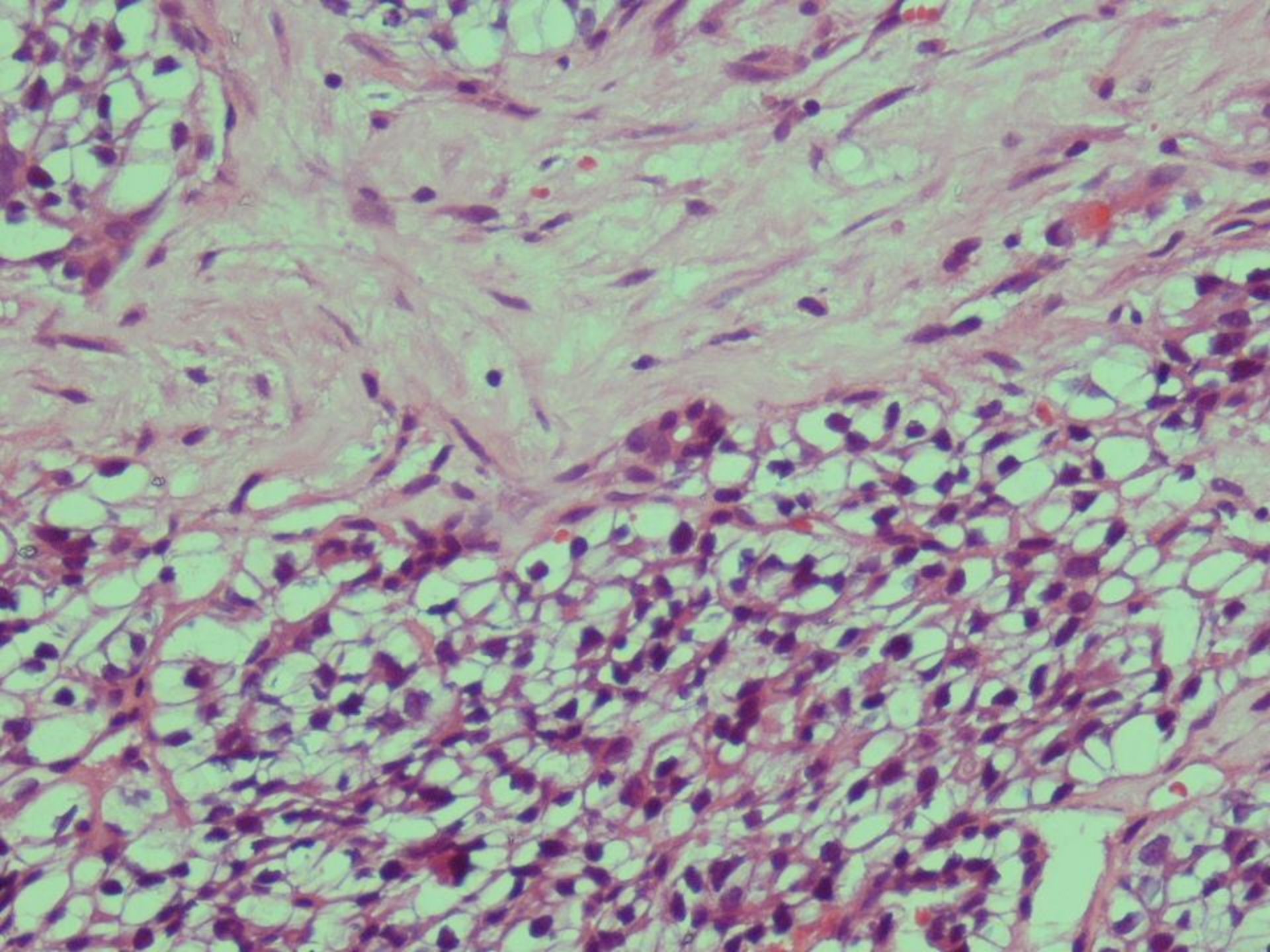
Pancreatoblastoma with ductular differentiation?

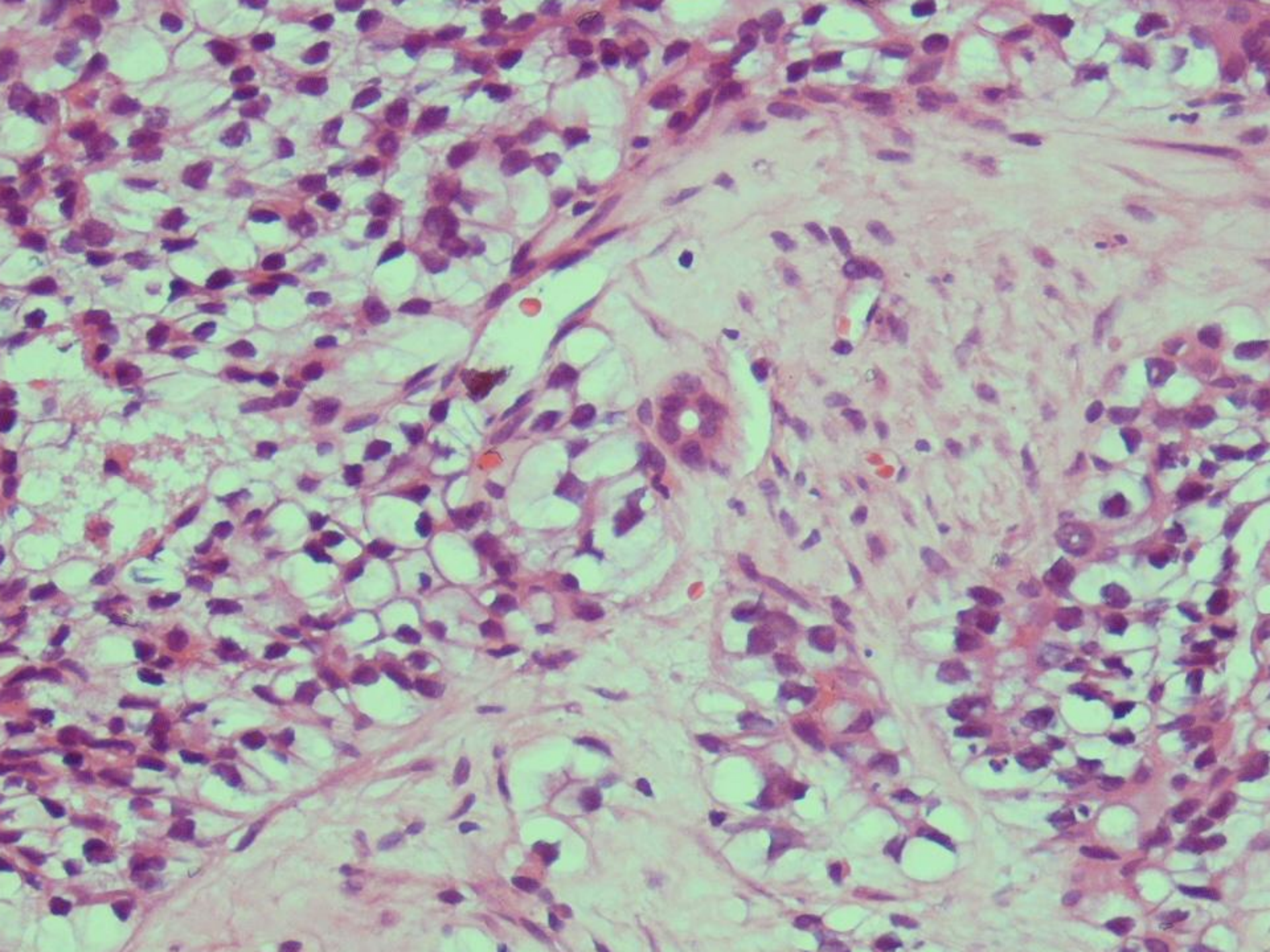
Hepatoblastoma with cholangioblastic features?

Presence of DPAS positivity in tubular BMs as well as in tubule cytoplasm focally: acinar differentiation? cholangiolar proliferation? entrapped pancreatic tubules?









- Presence of PAS tumor sheets with light and dark cytoplasm
- No predominant acinar pattern
- Non-visualisation of squamoid corpuscules

- Biphenotypic expression of intermediate filaments (vimentin + CK)
- Negative staining of tumor with CK7, mCEA
- CK7 + ductular component in continuity with solid component

- P53 positivity (both in solid and ductular components)

HEPATOBLASTOMA WITH CHOLANGIOBLASTIC FEATURES

Hepatoblastoma with a low serum alpha-fetoprotein level at diagnosis: the SIOPEL group experience

De Loris M et al,

Eur J Cancer 2008

Low serum AFP

Multifocal tumors with extrahepatic extension

Poor prognosis

- **HIGH RISK FACTORS IN HB**

- High initial (PRETEXT) stage
- Low serum AFP
- Vascular invasion
- Histologic subtype (SCUD, rhabdoid, TLCT)

- Polo-kinase 1 expression
- RASSF1A methylation

- **STANDARD RISK FACTORS IN HB**

- Low stage
- Purely fetal morphology

Conclusions

- Hepatoblastoma diagnosis difficult in needle-biopsy due to highly variagated histopathological appearance of the tumor from field to field- adequate sampling is mandatory even for resection specimens, rebiopsy may need to be performed if the biopsy contains only one of the patterns

- Special attention has to be paid to liver tumors with unusual features (low serum AFP, small cell, macrotrabecular, myxoid, cholangioblastic variants, tumors with rhabdoid features)

- No distinct immunohistochemical and genetic profile is available- diagnosis should be based on combination of the clinical, radiological and morphologic findings