CASE 1 (Patient A, slides 1-3; Patient B slides 4-6): **Autoimmune Hepatitis**

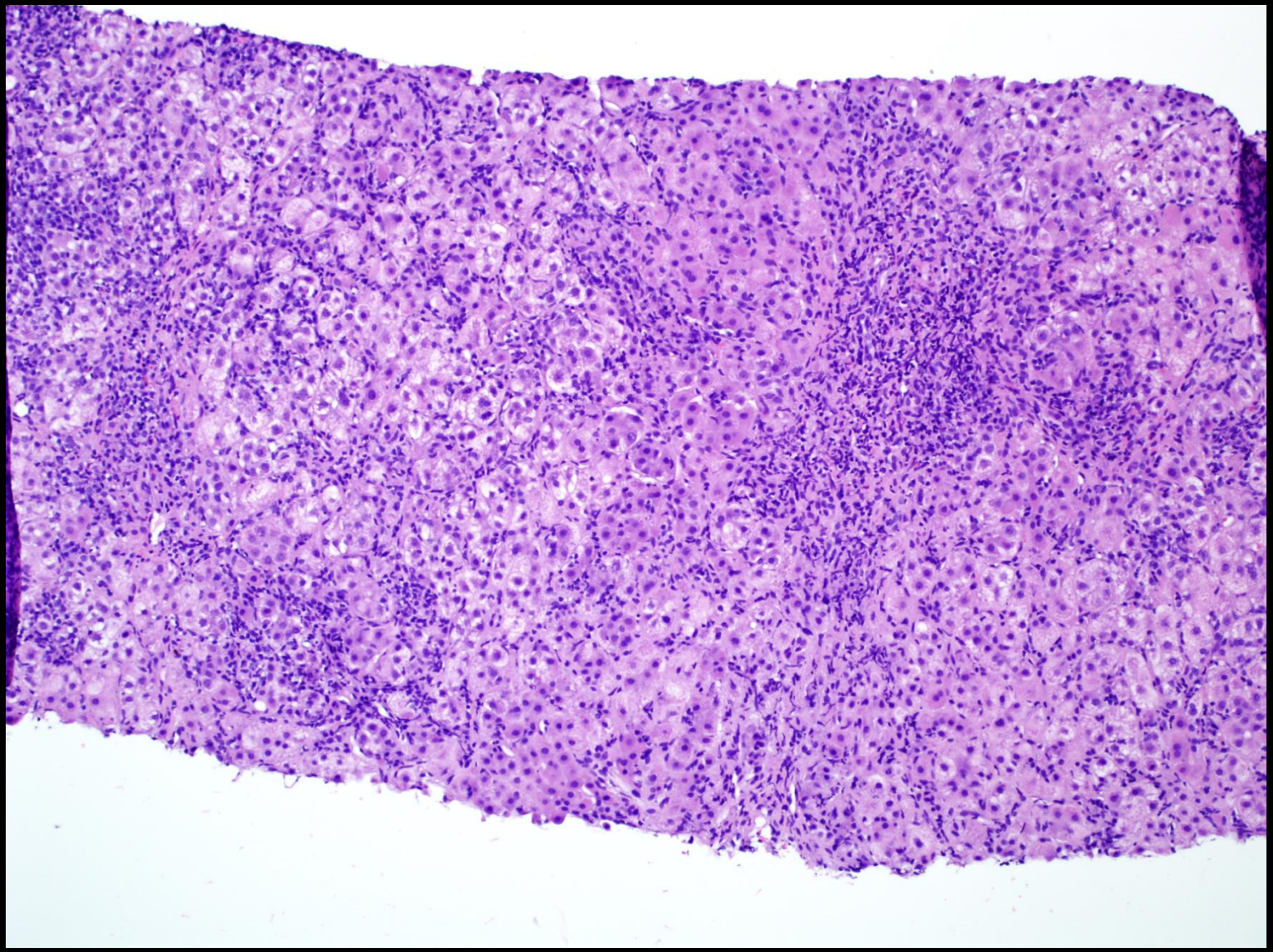
Patient A: 15-year-old girl who experienced uncharacteristic muscle pain, soreness, and fatigue during exercise.

AlkPhos	114	(40-150 U/L)
AST	385	(0-35 U/L)
ALT	460	(0-50 U/L)
IgG	7340	(695-1620 mg/dL)
F-Actin IgG	95	(> 31 units = positive)
Smith SSA (Ro)	>8.0	(0-0.9 AI).

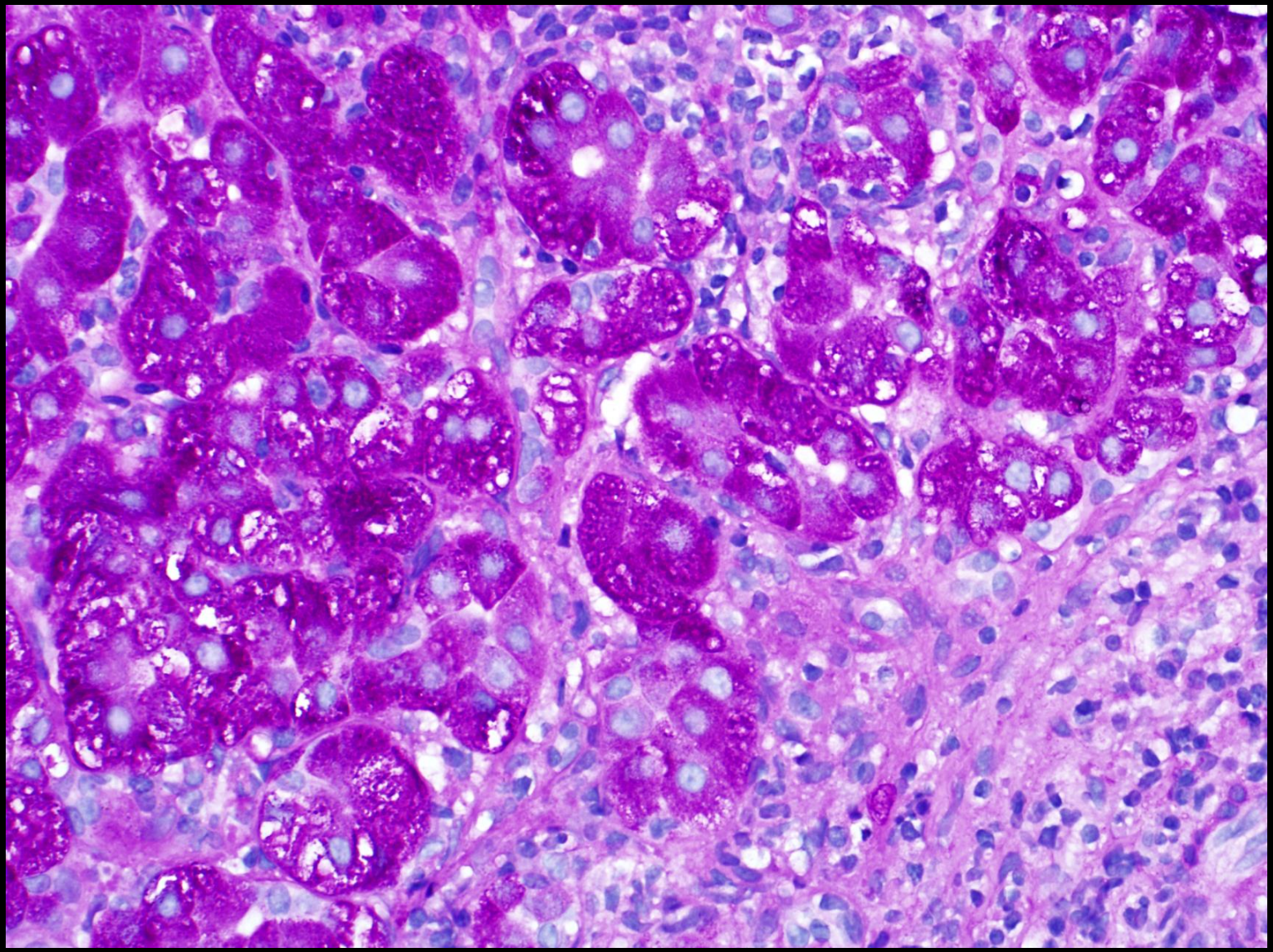
Negative for Scleroderma Scl-70 ENA, SSB (La), Smooth Muscle Antibody (SMA), RNP Antibody IgG, Jo 1 Antibody IgG, LKM Antibody, Hepatitis B and C.

Patient B: 13 year old girl with a painless left sided abdominal mass for 3 months prior to presentation with left sided pain and thrombocytopenia. Imaging showed splenomegaly and a diagnosis of immune thrombocytopenia was made.

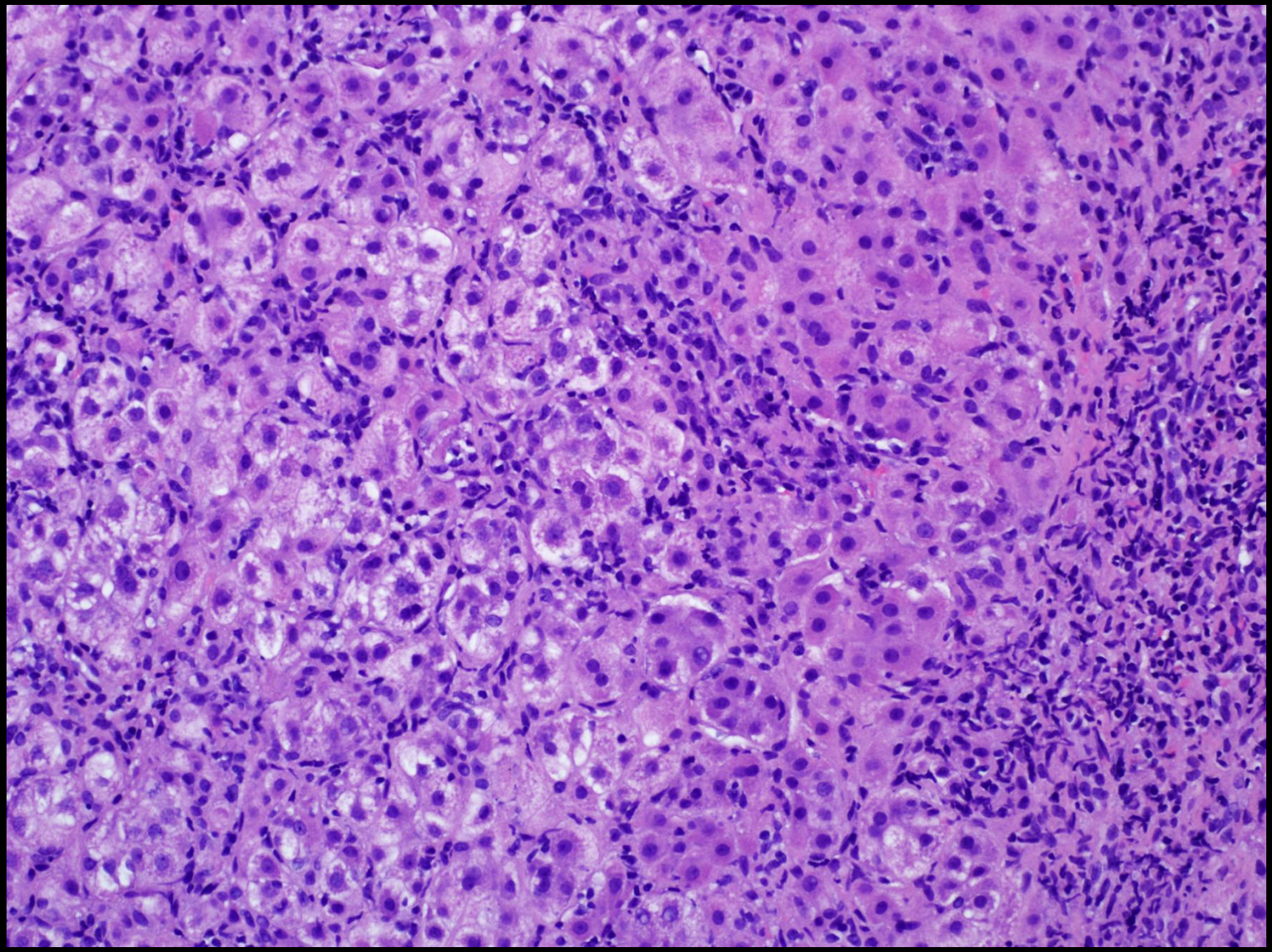
AlkPhos	232	IgG	3502	
AST	617	SMA	93	(0-19)
ALT	712	ANA	negative	



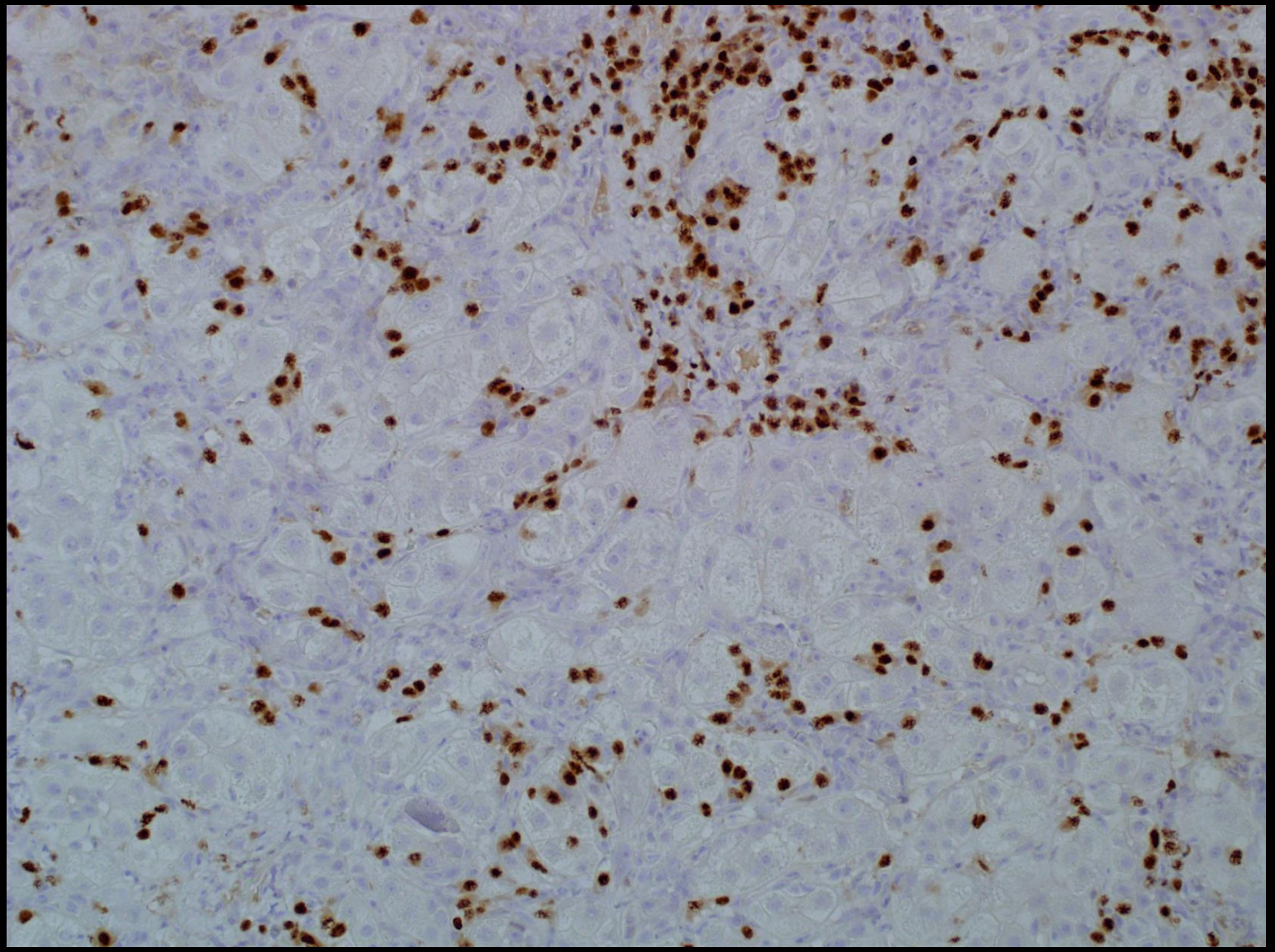
Architecture disrupted by lymphocytic infiltrate filling portal area and extending into lobule.



PAS highlights the “rosette formation” of hepatocytes.

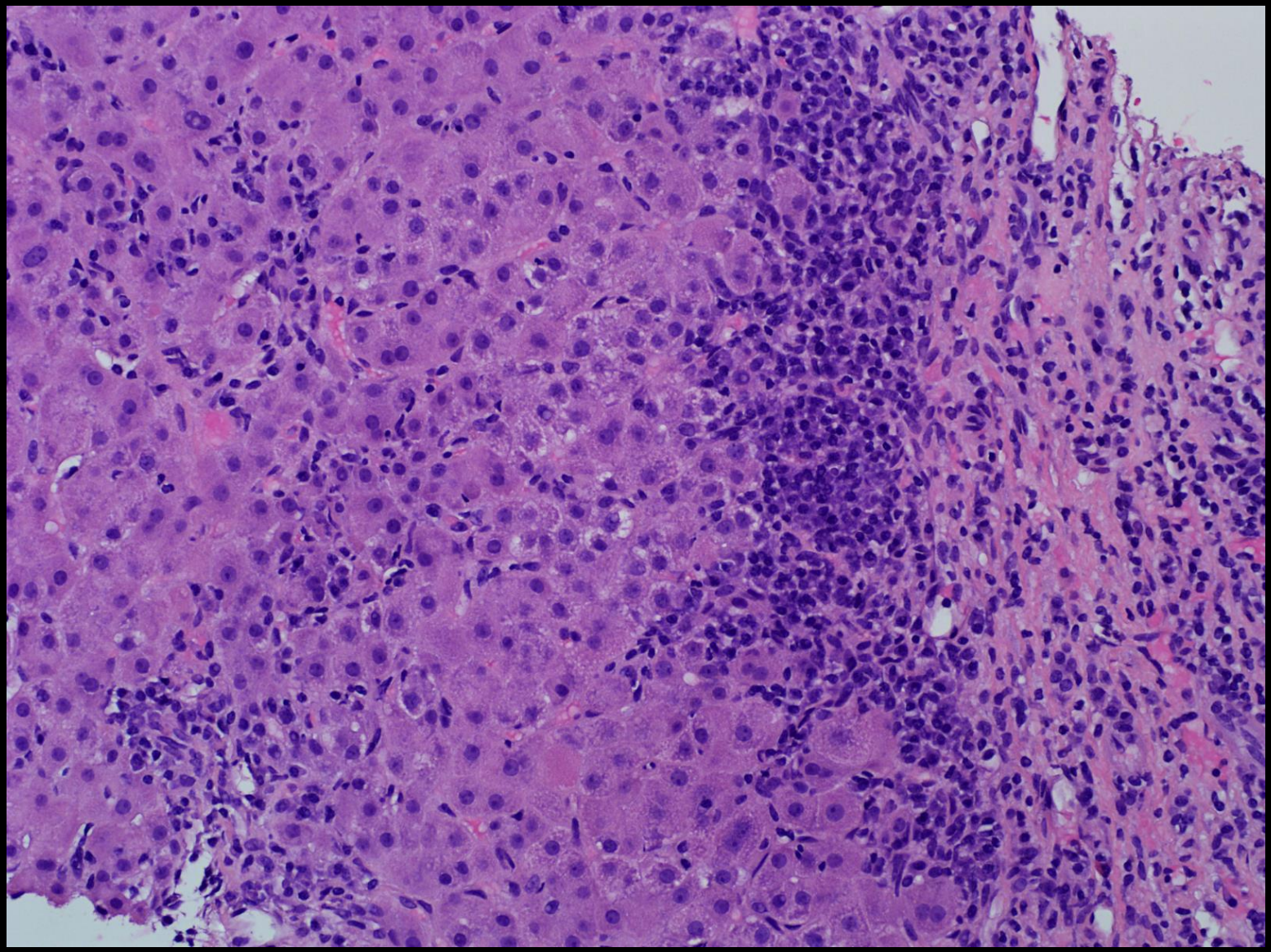


Lymphocytic infiltrate filling portal area and extending into lobule.

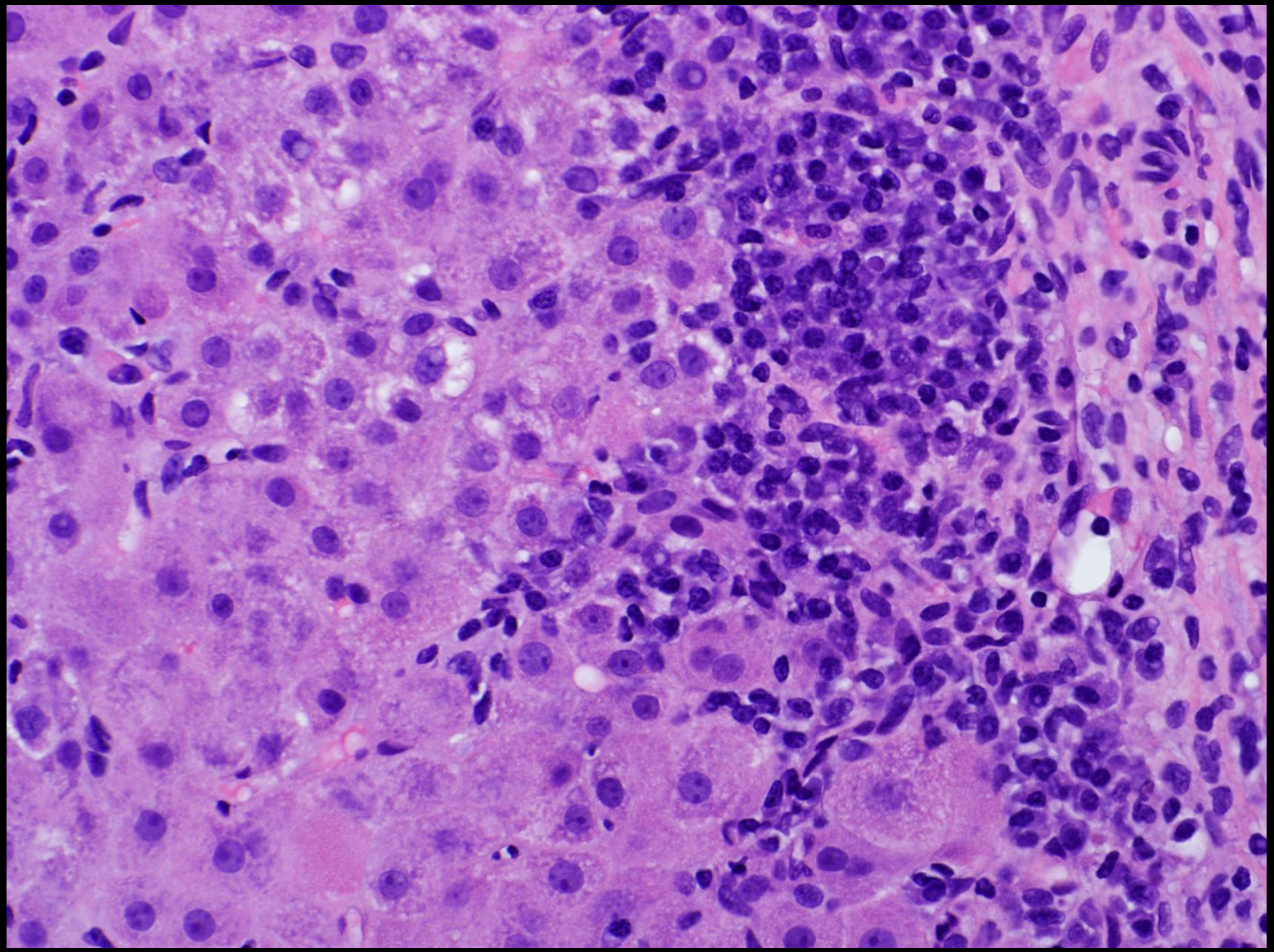


Extension of Mum-1 positive cells into the lobule.

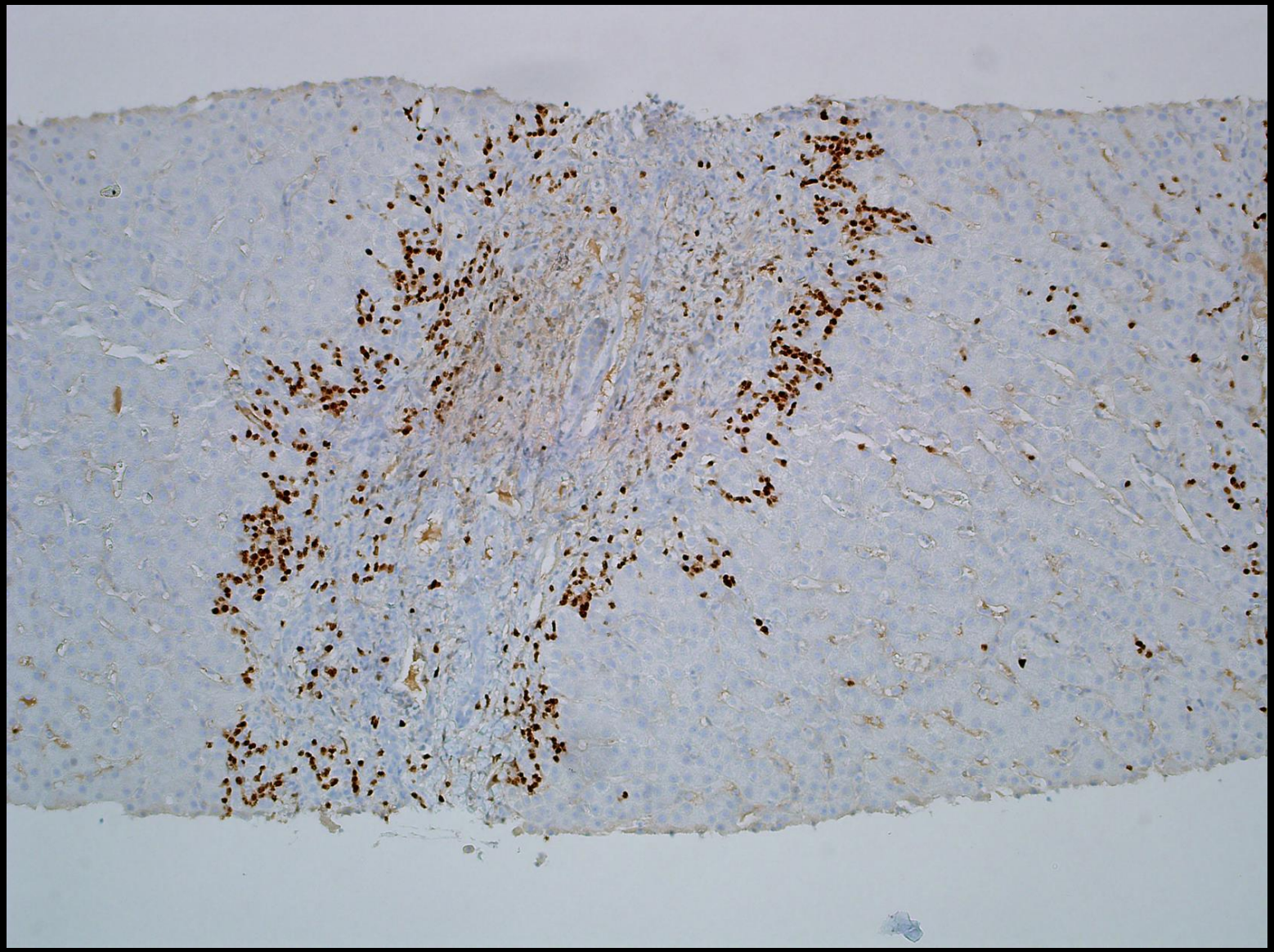
Mum-1 is positive in plasma cells and plasma cell precursors.



Lymphocytic infiltrate focused on the limiting plate and extending into the lobule.



Difficult to resolve plasma cells in dense infiltrate.



Mum-1 stain shows the inflammation focused on the limiting plate.

CASE 2 (Slides 7-8): **Wilson's Disease**

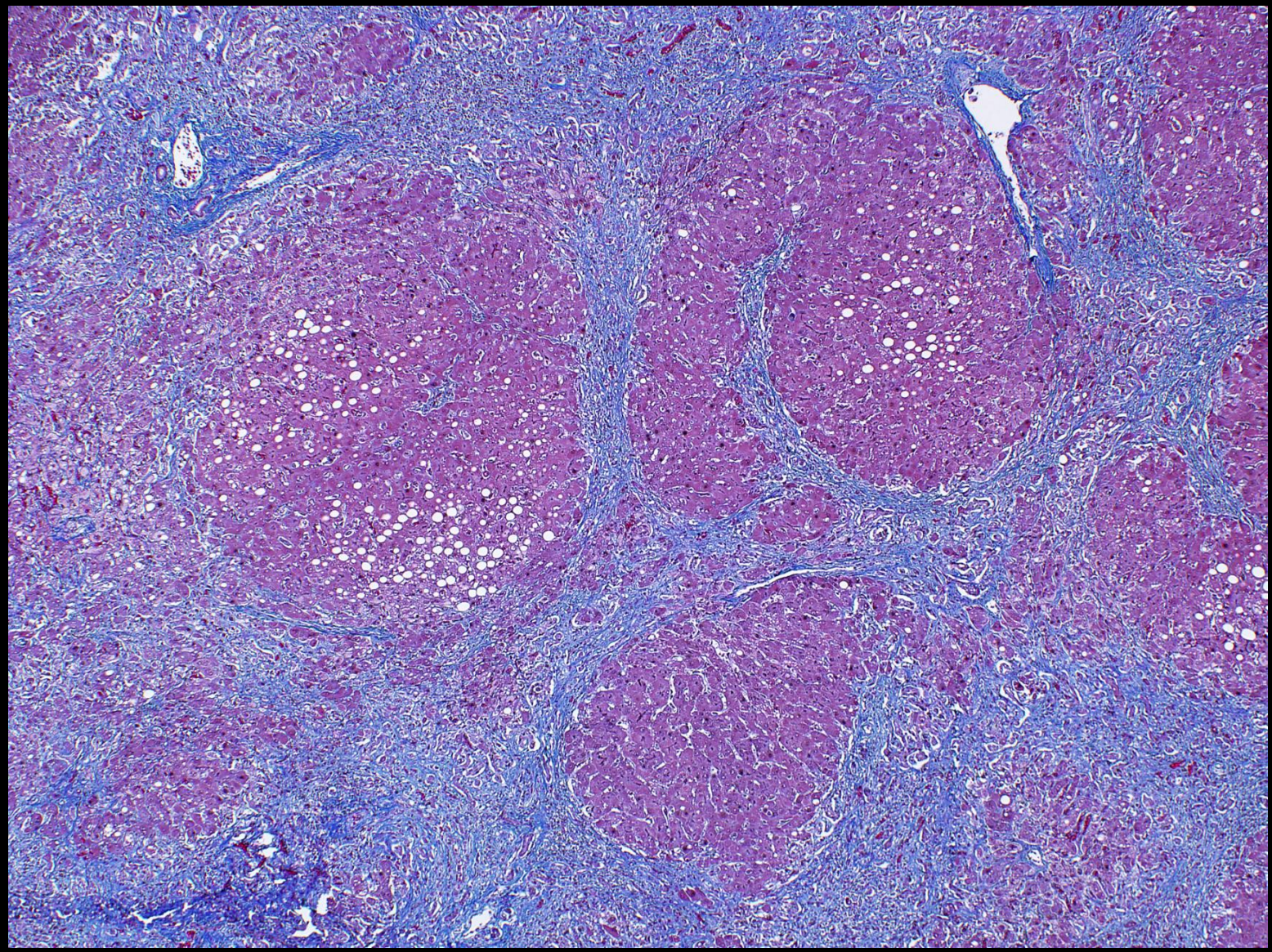
16 year old girl without prior medical problems presents with abdominal pain, vomiting and bloody stools for last few days and was anuric. Initial impressions were hemolytic anemia, liver dysfunction, and renal failure, suspect Hemolytic Uremic Syndrome. The patient was seen by Pediatric Critical Care, Pediatric Hem-Onc, Pediatric Nephrology, and Pediatric Gastroenterology. Pedi GI suspected Wilson's disease and consulted Ophthalmology. Kayser Fleischer rings were noted bilaterally. Using the Leipzig Wilson's Scoring System, a clinical diagnosis of Wilson's disease was made. An emergent liver transplant was done 3 days after admission.

BUN	93	(7-19 mg/dL)	AlkPhos	19	(40-150 U\L)
Creatinine	7.1	(0.5-1.0 mg/dL)	ALT	33	(0-50 U\L)
Bilirubin,total	17.3	(0.2-1.3 mg/dL).			
Bilirubin,direct	11.3	(0.0-0.2 mg/dL).			
Ammonia	97	(10-50 umol/L)			

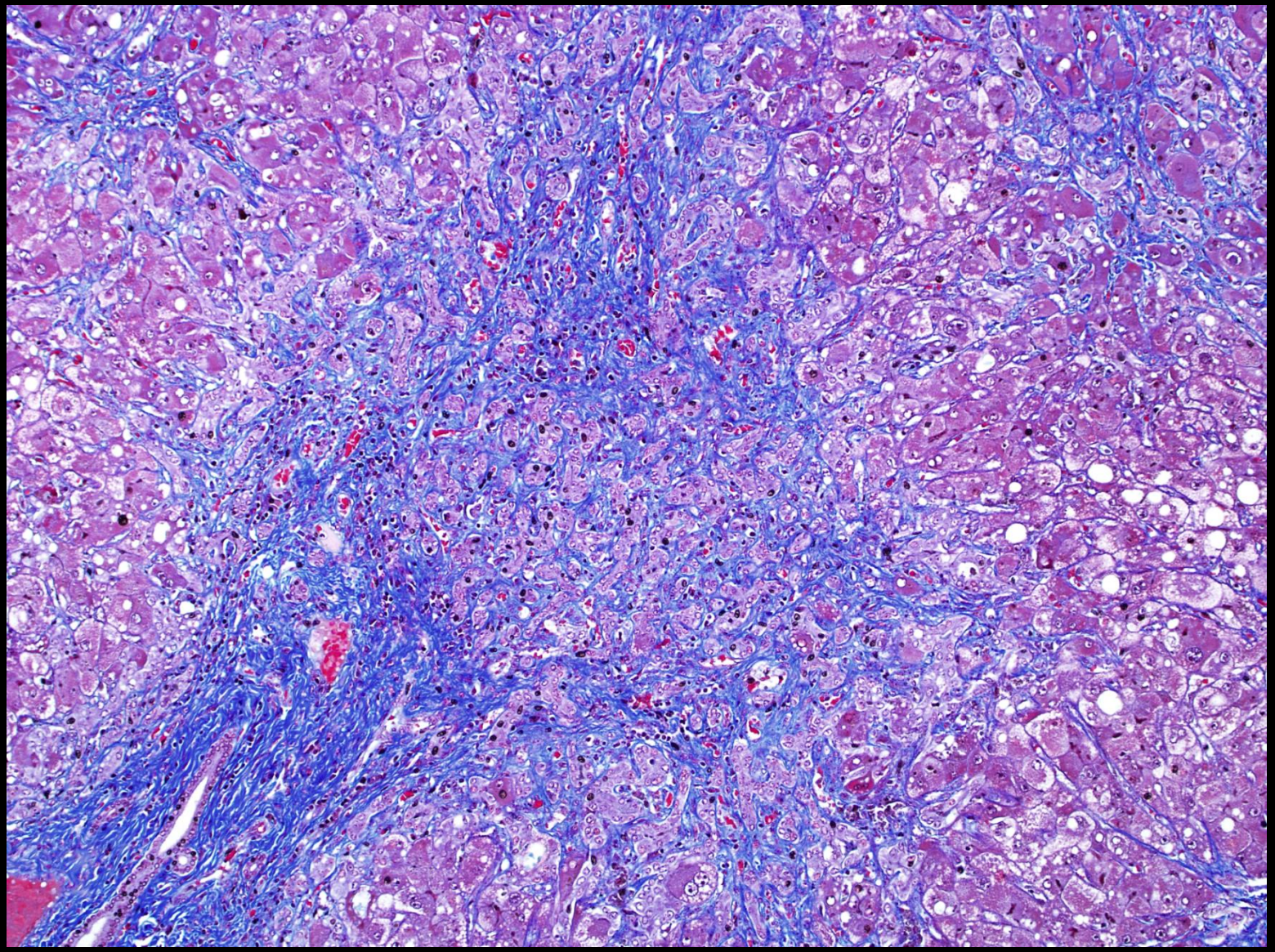
CLUES:

Target Organs: Liver, Kidney, Brain

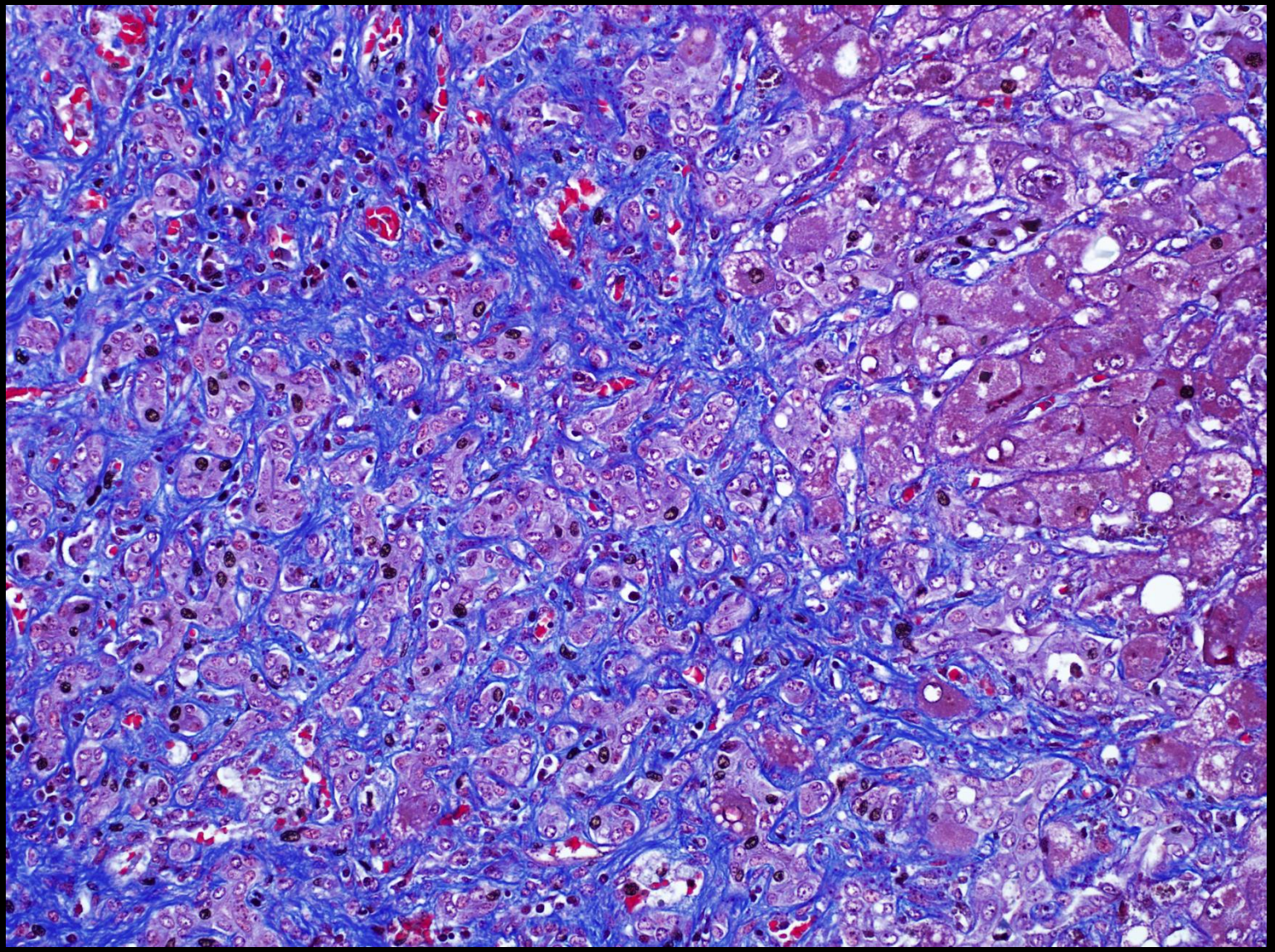
- > 5 yrs old with unexplained liver disease or hemolytic anemia.
- Older children with unexplained neurologic symptoms.
- Low AlkPhos and AlkPhos/Bilirubin < 2
- Low ceruloplasmin and high urinary copper.



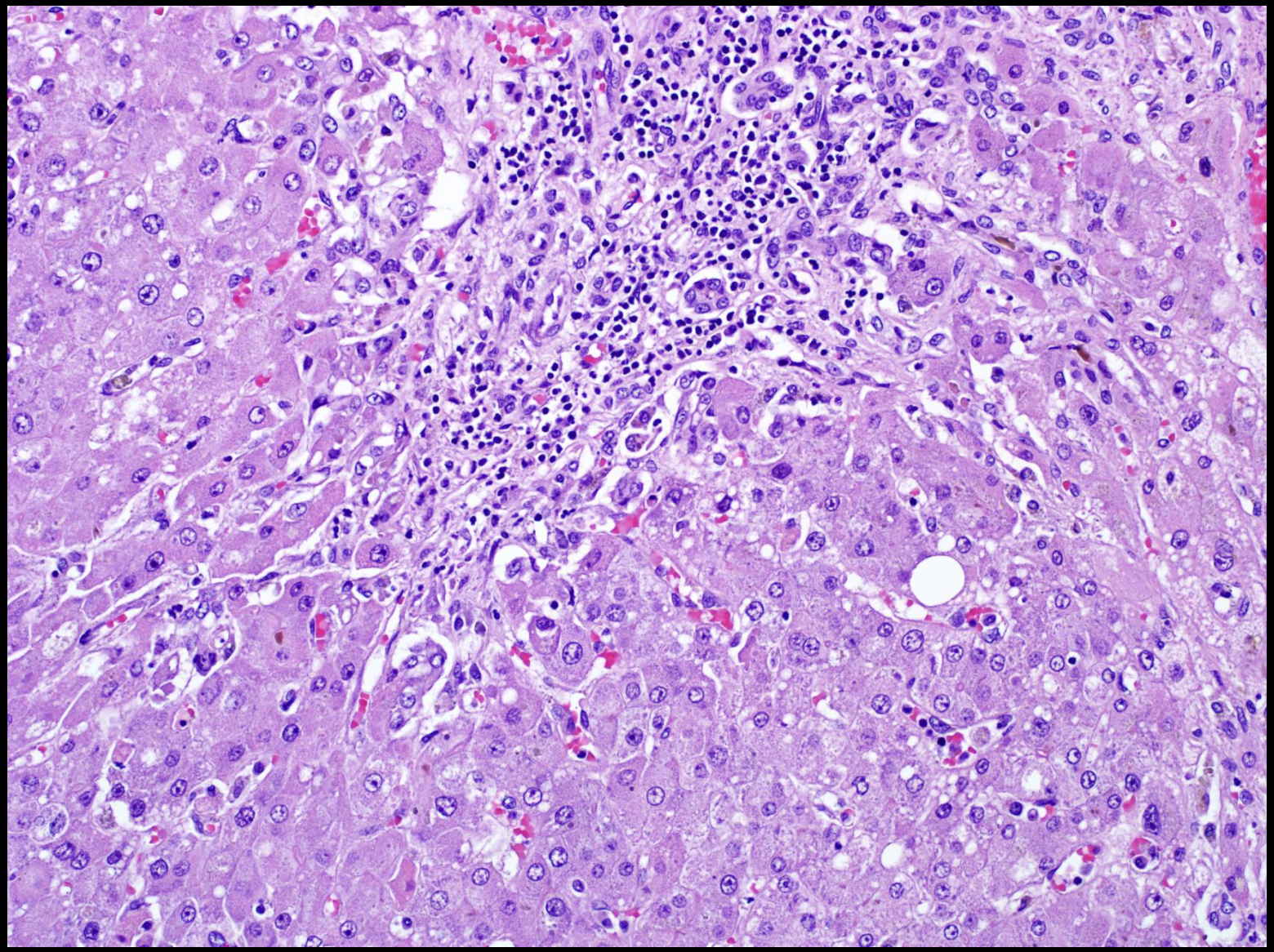
Trichrome stain shows cirrhosis.



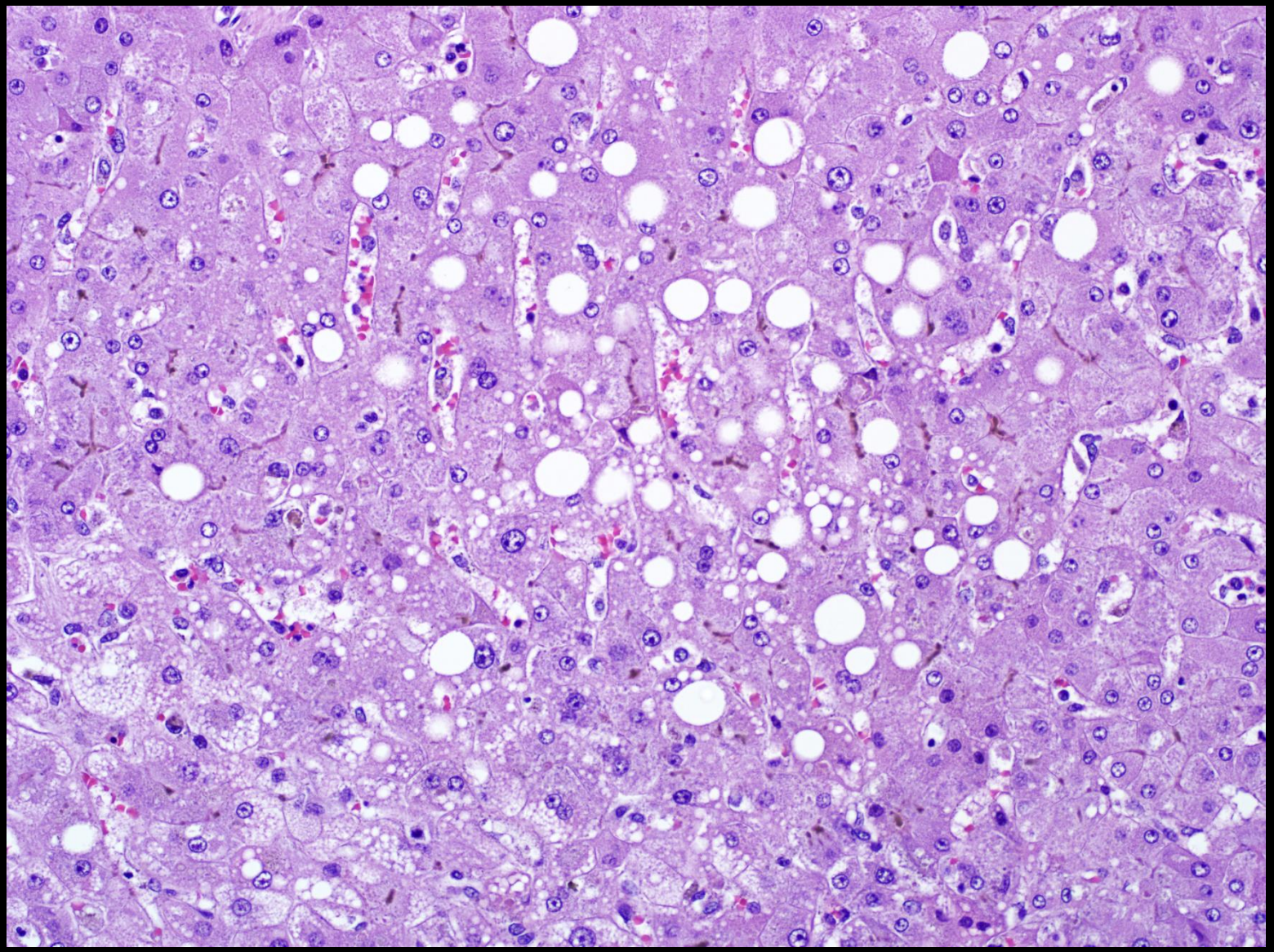
Lobular collapse and fibrosis.



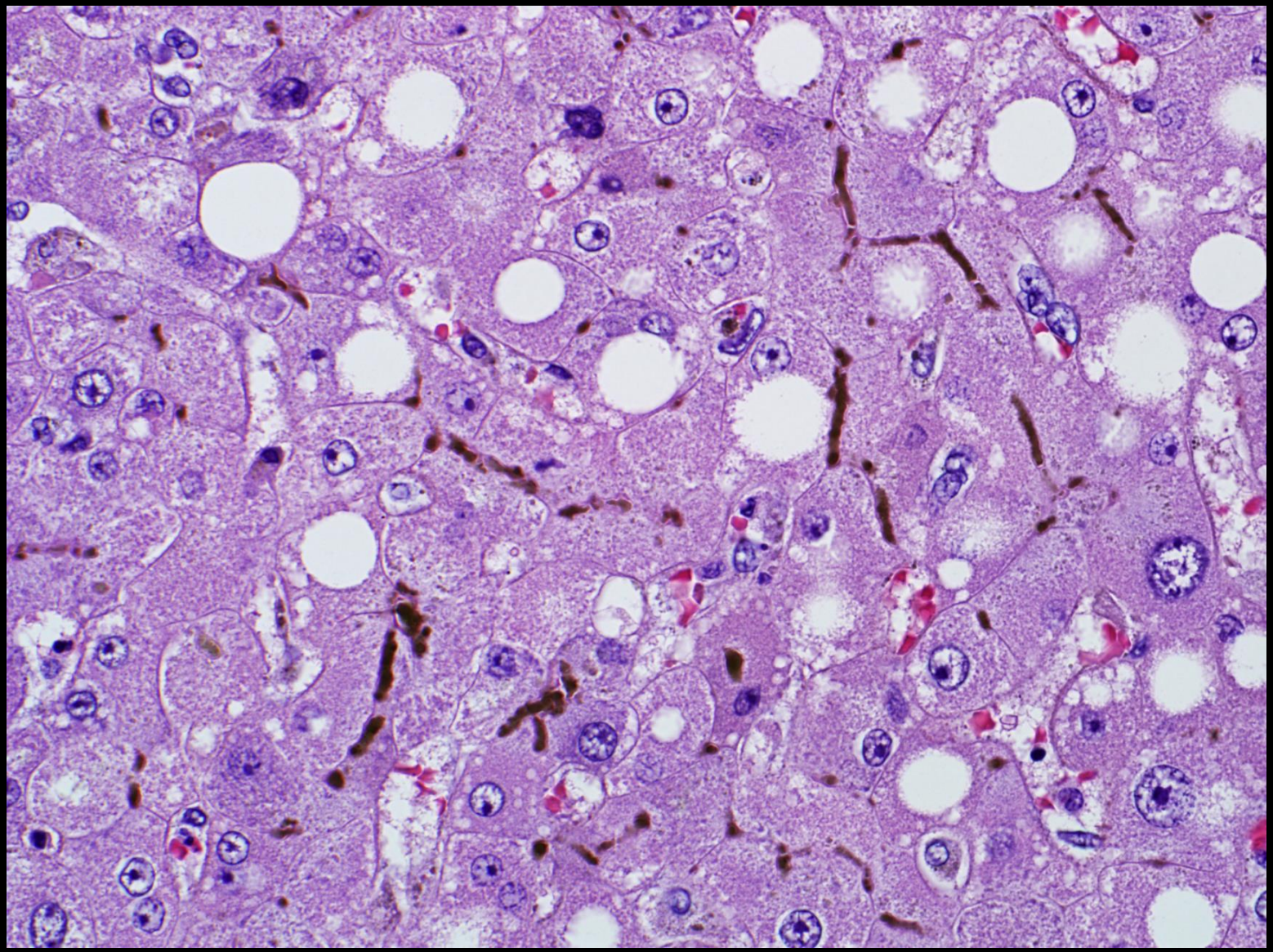
Lobular collapse and fibrosis.



Portal lymphocytic infiltrate.



Steatosis.

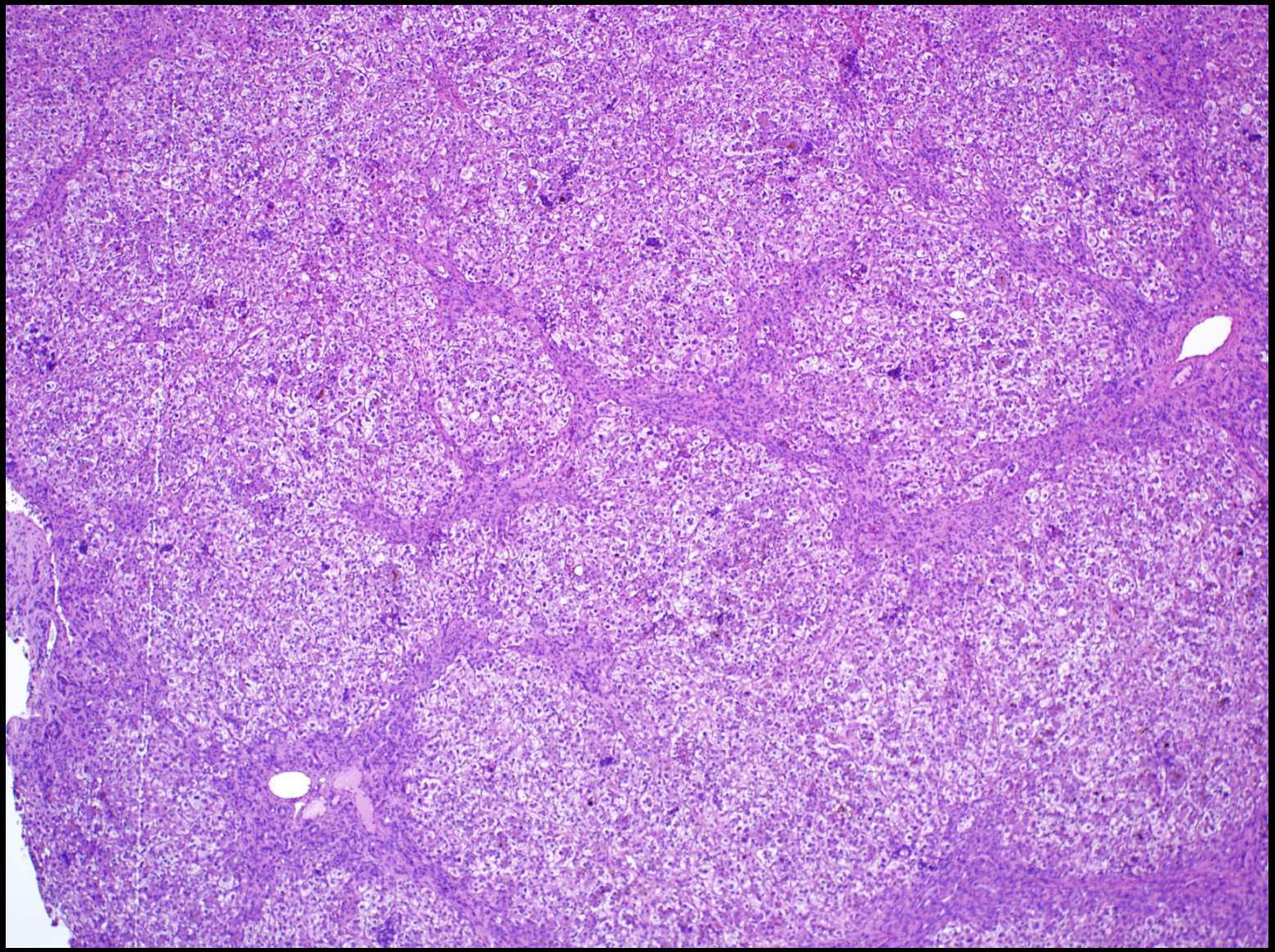


Marked canalicular cholestasis.

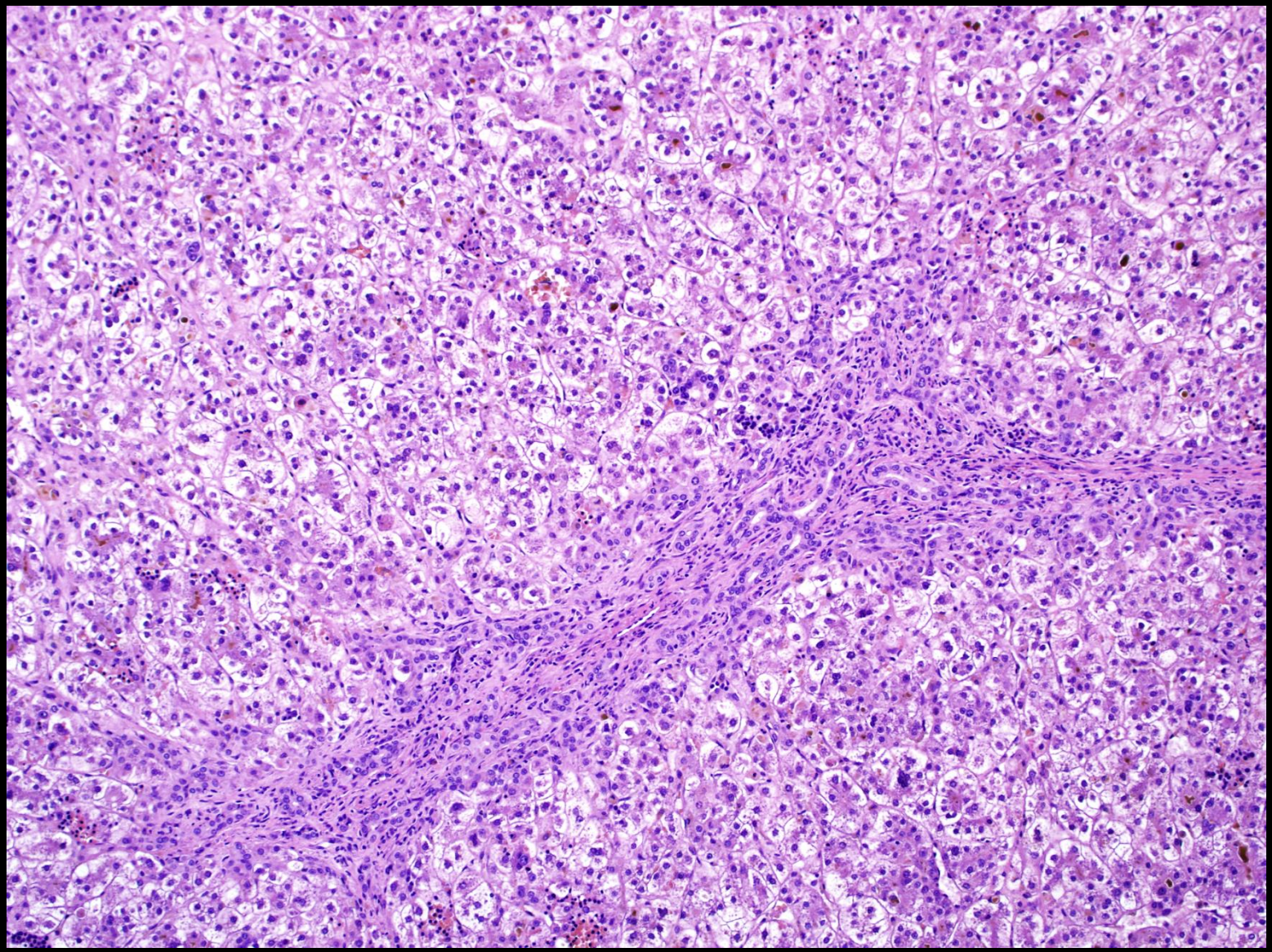
CASE 3 (Slides 9-10): **TPN effect**

6 month old boy born at 23 weeks gestation with a history of necrotizing enterocolitis and a bowel perforation in the first 2 weeks of life; reanastamosed at 4 months of life. He has generalized bowel dysmotility, and a rectal biopsy for Hirschsprung's disease at 5 months of age was normal. A liver biopsy was done during a laparotomy for lysis of adhesions (causing bowel obstruction) because the surgeon thought the liver looked abnormal.

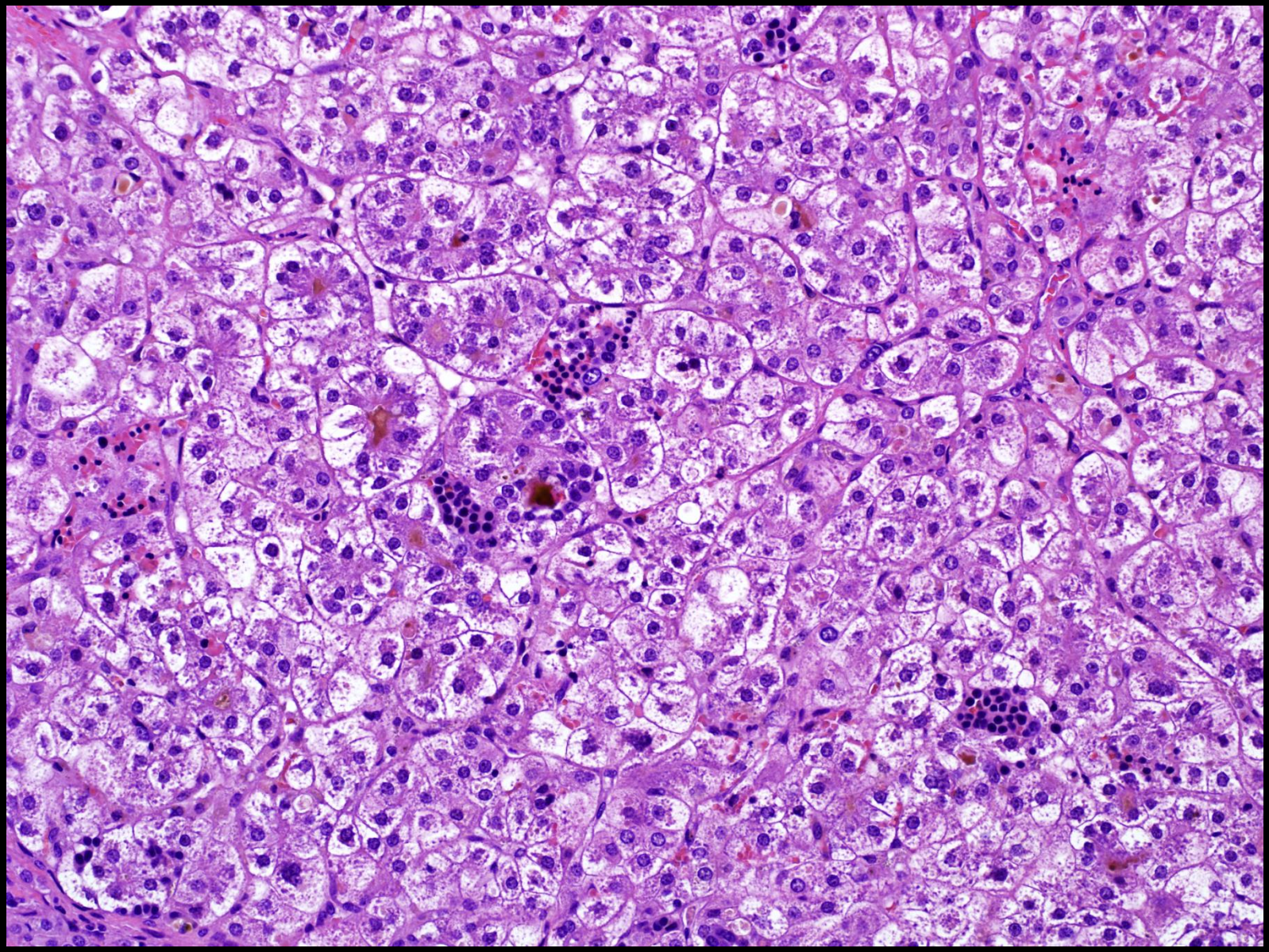
Albumin	2.2	(2.6-4.2 g/dL)
Bilirubin,total	23.4	(0.2-1.3 mg/dL),
Bilirubin, direct	18.7	(0-0.2 mg/dL),
AlkPhos	493	(110-320 U/L),
ALT	118	(0-50 U/L)
AST	281	(20-65 U/L),
GGT	179	(0-65 U/L).



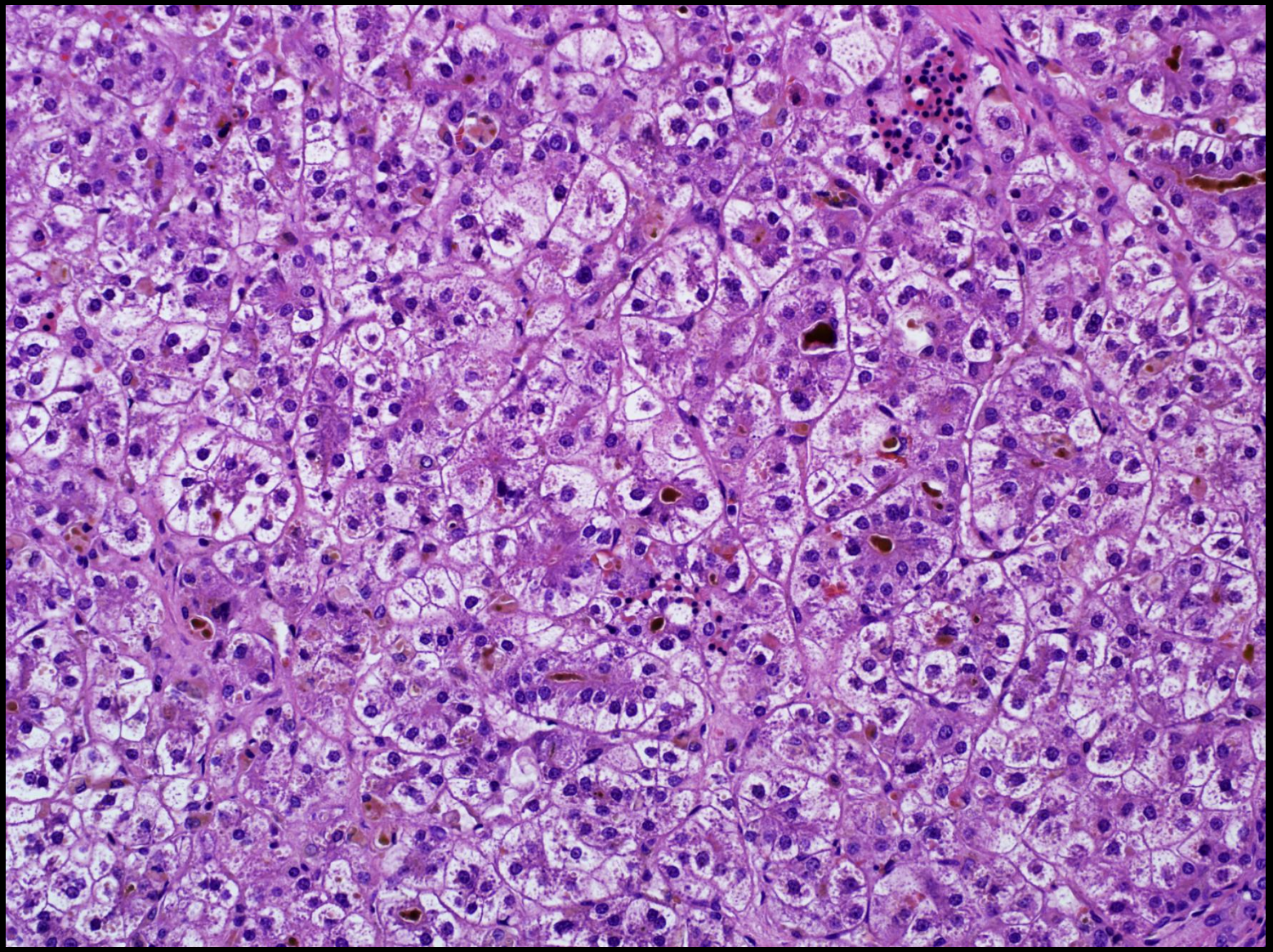
Low power shows bridging fibrosis.



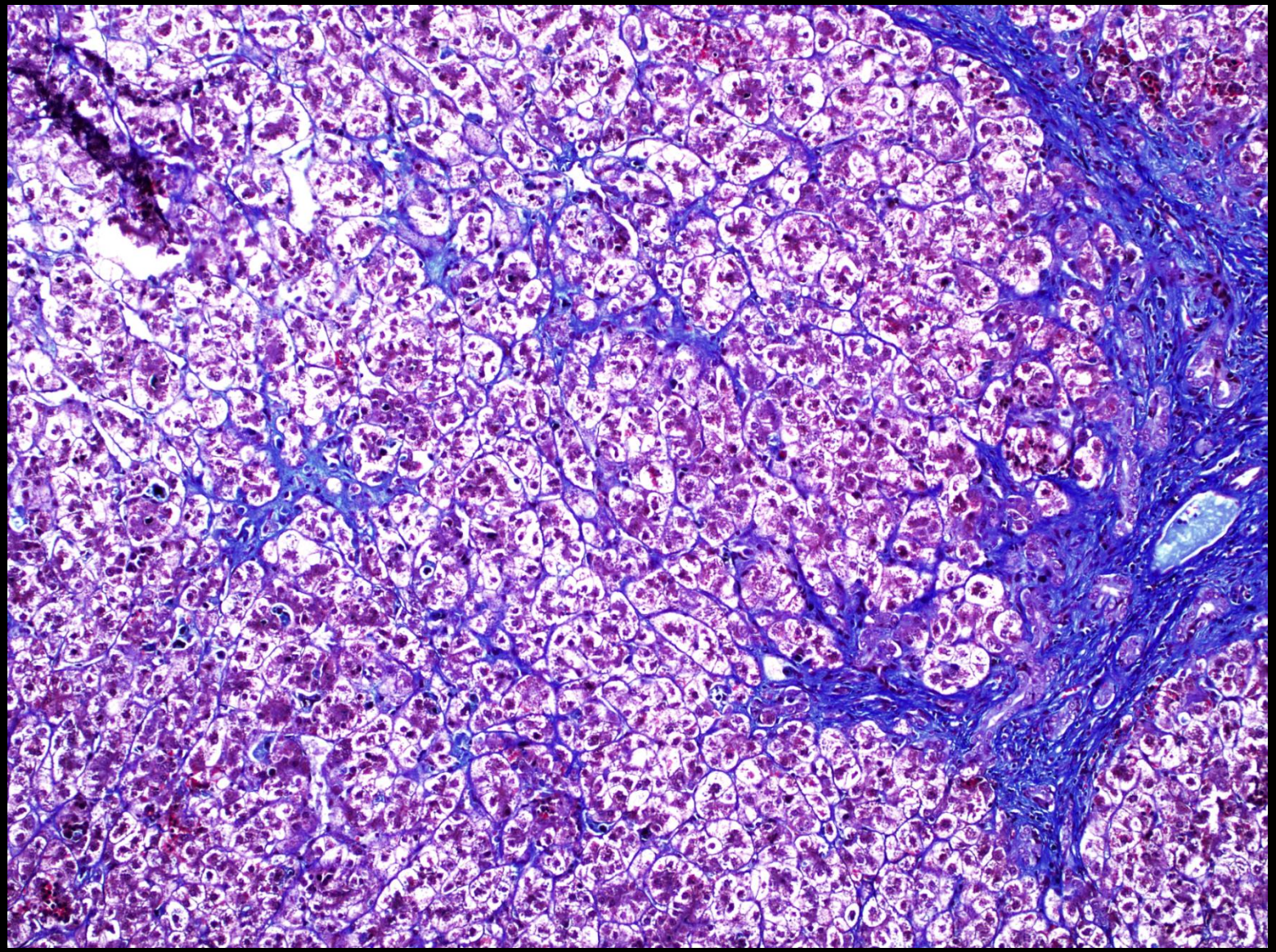
Bridging fibrosis and cell clusters in the lobule.



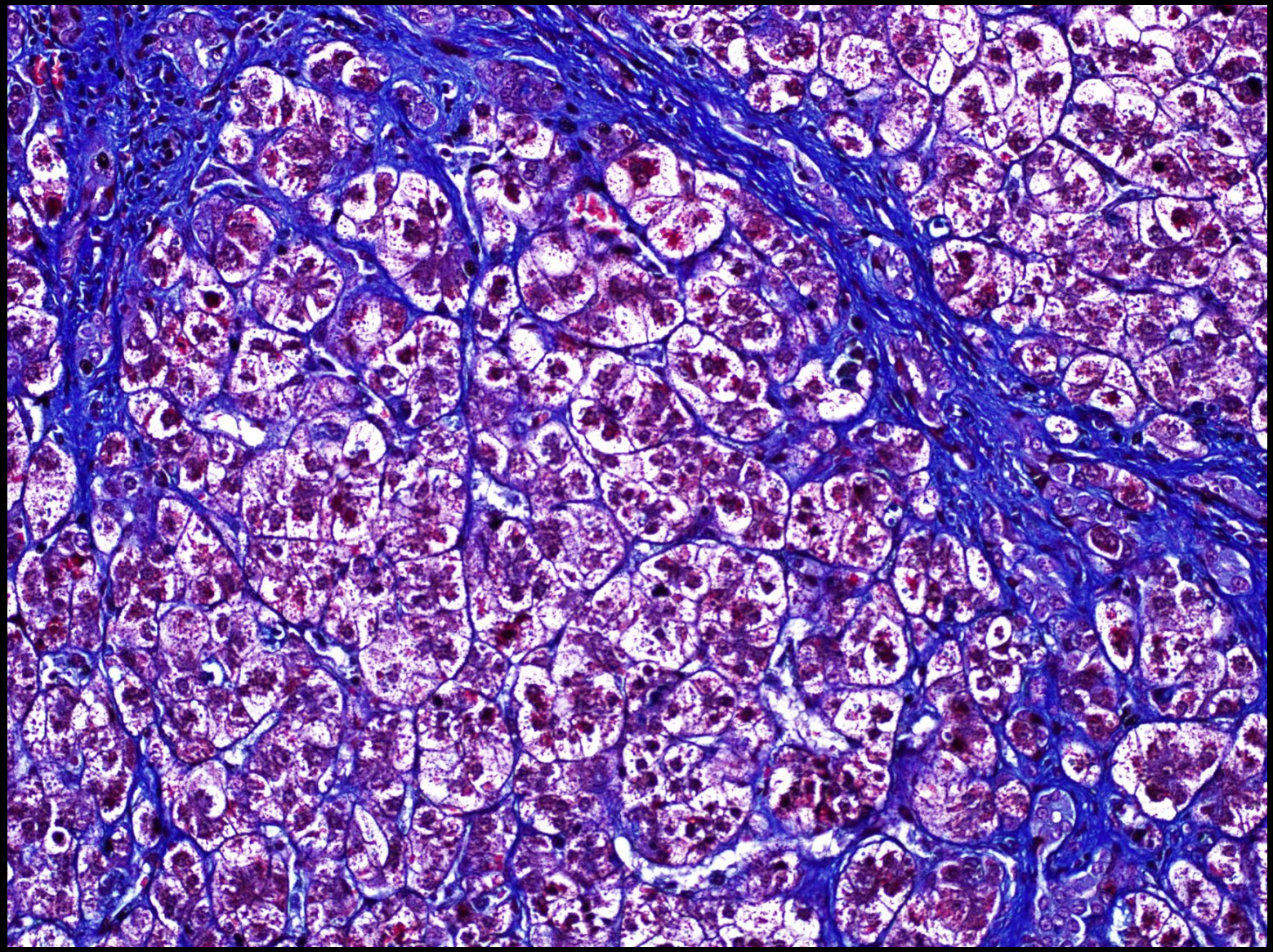
Cell clusters are islands of erythropoiesis due to immaturity (premature birth).



Canalicular cholestasis.



Trichrome shows sinusoidal extension of fibrosis.



Sinusoidal fibrosis.

CASE 4 (Patient A, slides 11-15; Patient B slide 16):

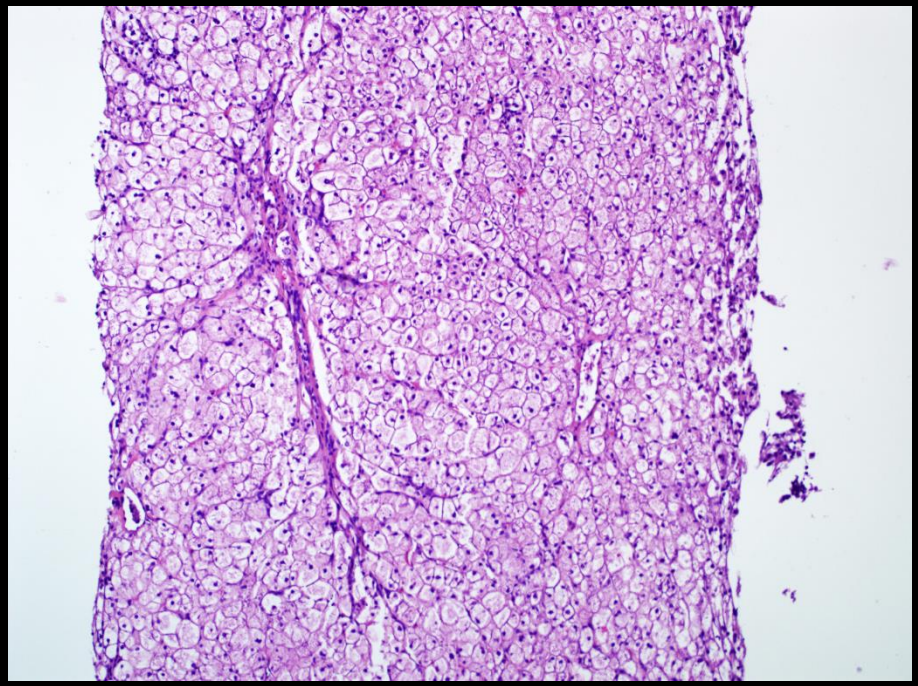
Glycogen Storage Disease Type III ; Type I Diabetes Mellitus

Patient A: 8 month old boy presenting with hepatomegaly and elevated liver enzymes. He was suspected of having Glycogen Storage Disease, but a broad differential was ackowledged (hepatitis, other storage disorders, malignancy, biliary tract disorders, and hepatic venous outflow.

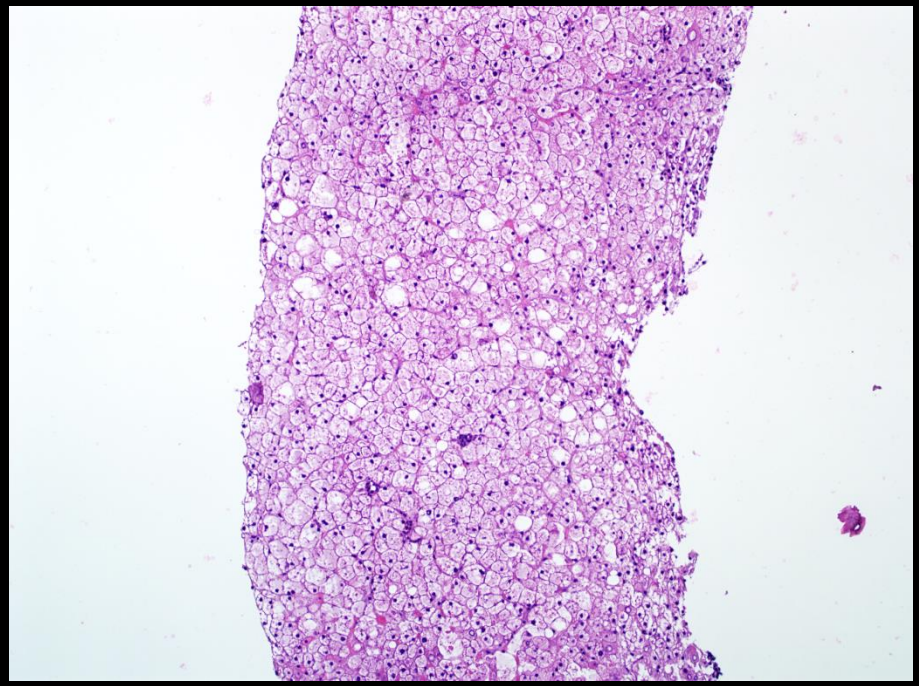
AlkPhos	212	(110-320 U/L)
ALT	548	(0-50 U/L)
AST	708	(20-65 U/L)
Triglycerides	745	(<75 mg/dL)

Normoglycemic

Patient B: 18 year old female with elevated liver enzymes, Type 1 diabetes mellitus and Crohn's disease.



Glycogen.Storage Disease Type III



Type I Diabetes Mellitus

Both biopsies show excessive glycogen storage, and both would be in the glycogen storage disease range if a determination of wet weight glycogen was done. Knowing the history of diabetes prevents additional costly studies to type the glycogen storage disease.

Case 5 (slides 17-20): **Clinical Diagnosis of NAFLD (Non-alchoholic fatty liver disease)**

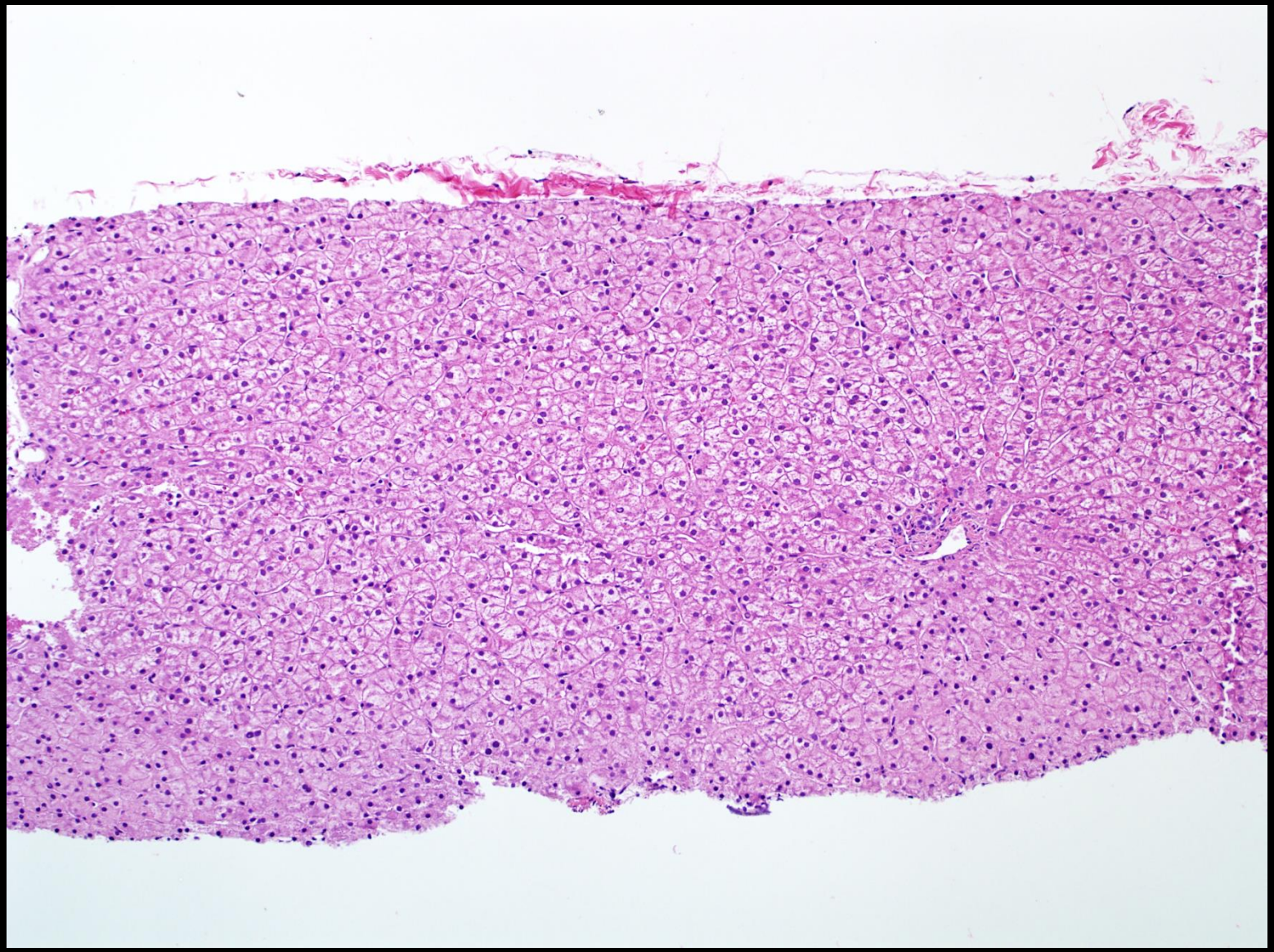
9 year old boy,

- BMI at 91st percentile for age
- Elevated AST 153 (0-50 U/L)
- Ultrasound consistent with steatosis (liver diffusely hyperechoic vs kidney).

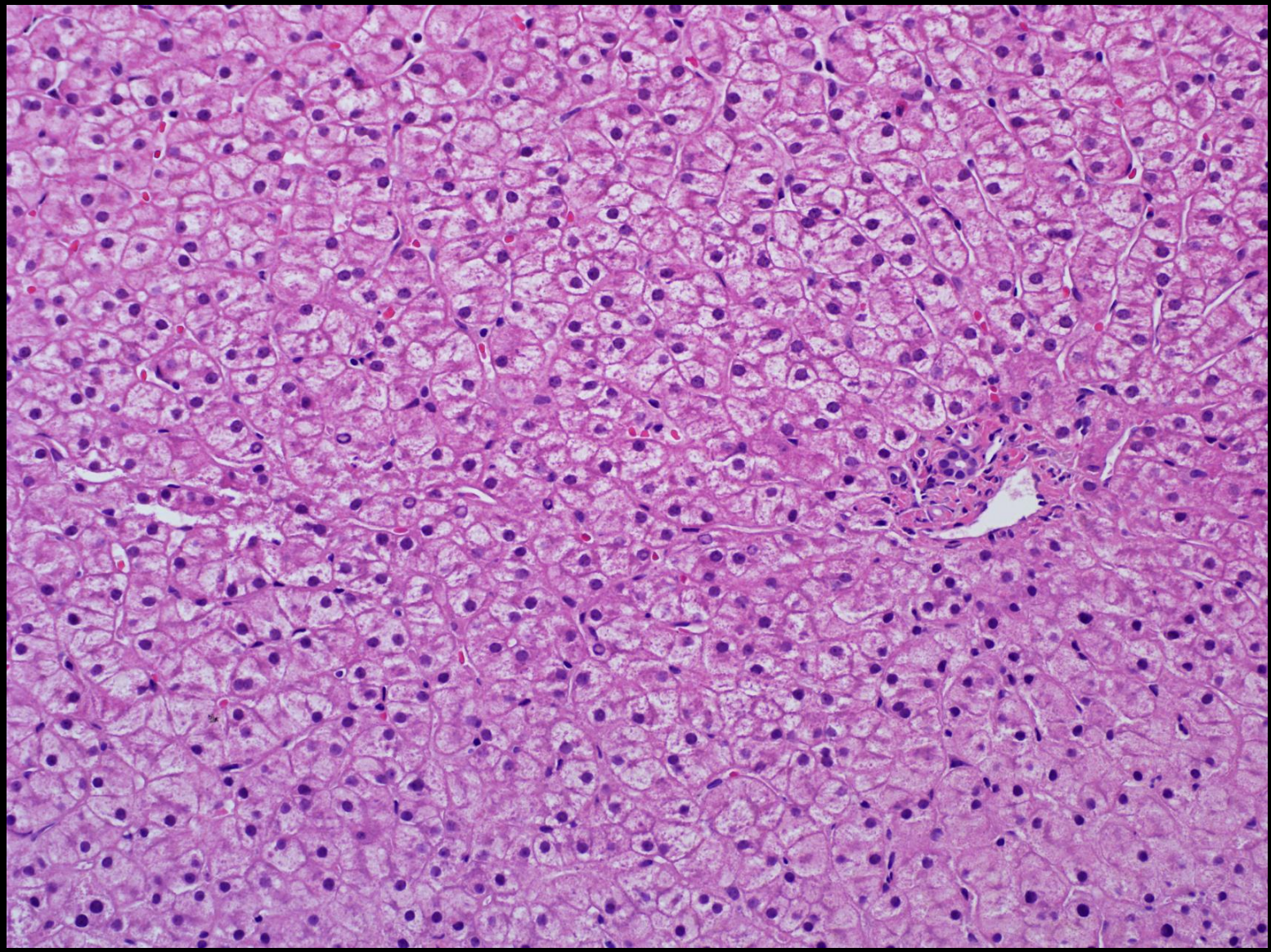
History on pathology requisition: "Abnormal lab values"

Diagnosis from Biopsy: "No Pathologic Diagnosis"

- 7 months after the biopsy, the clinician calls to ask if I am sure there is no steatosis.
- I requested re-evaluation of Ultrasound; Difficult to interpret due to technical complexities.
- Clinician alerted to consider a storage disorder.



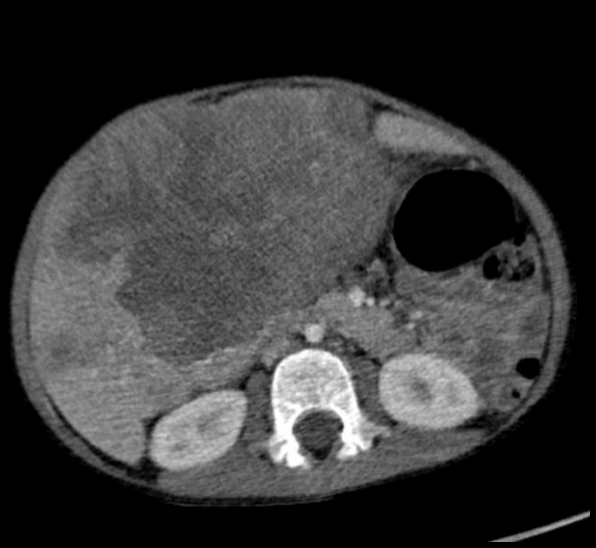
No evidence of steatosis. Hepatocytes appear clear.

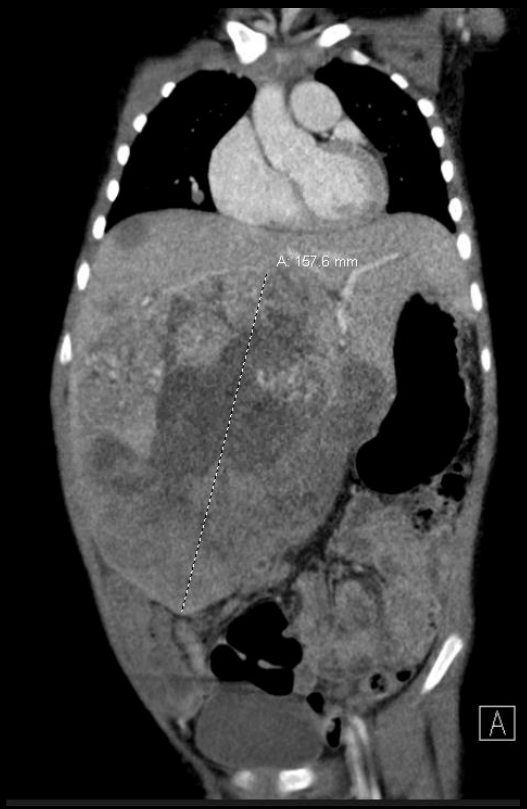


Possible excess glycogen or mucopolysaccharide?

CASE 6 (Slides 21-25 are primary tumor, slide 26 is peritoneal implant, 1 yr later): **Hepatoblastoma**

6 year old boy presents with liver mass and pulmonary nodules. Alpha Fetoprotein 288,067 (0-8 ug/L)





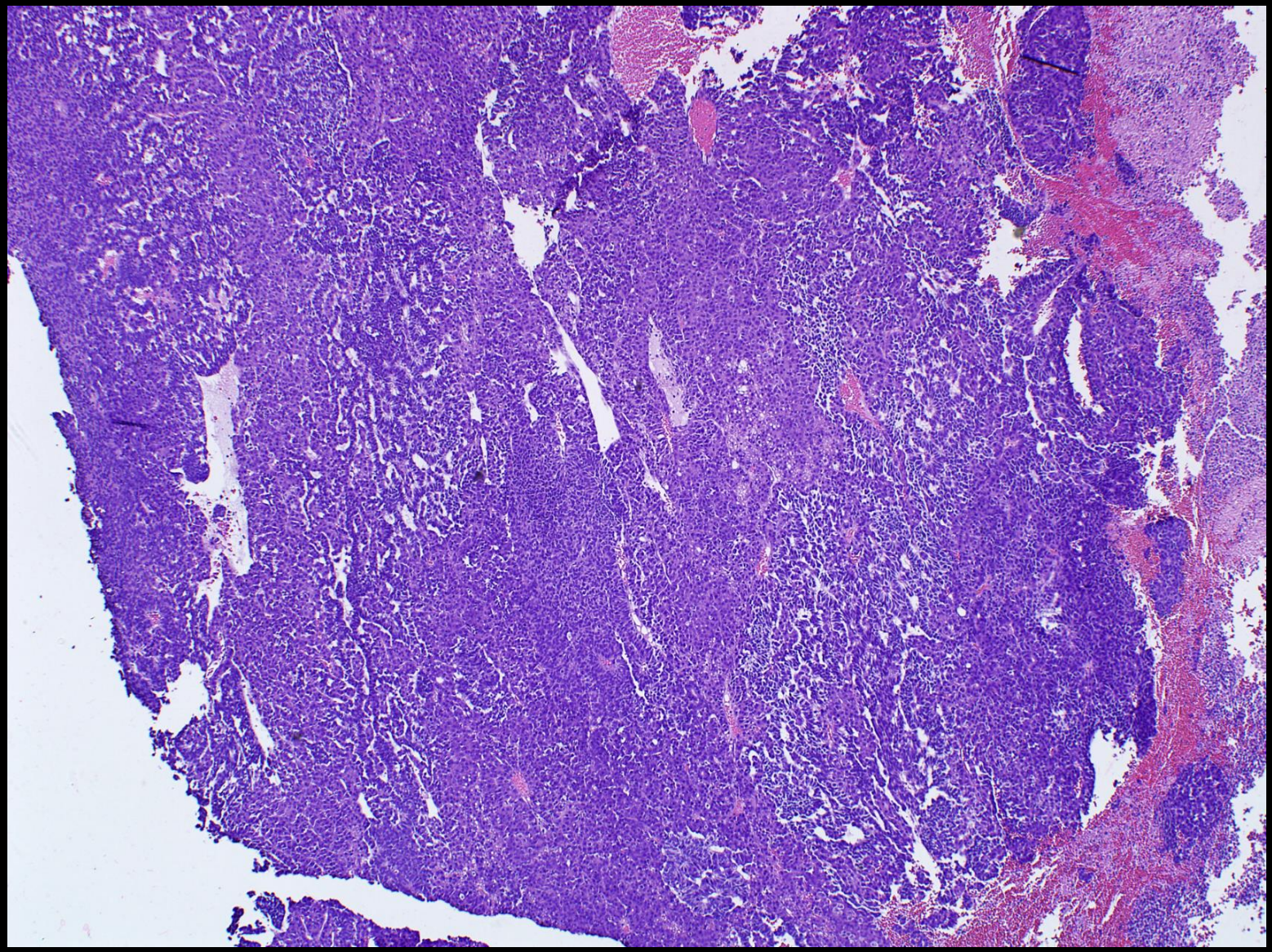
Hepatoblastoma

Hepatocellular Carcinoma

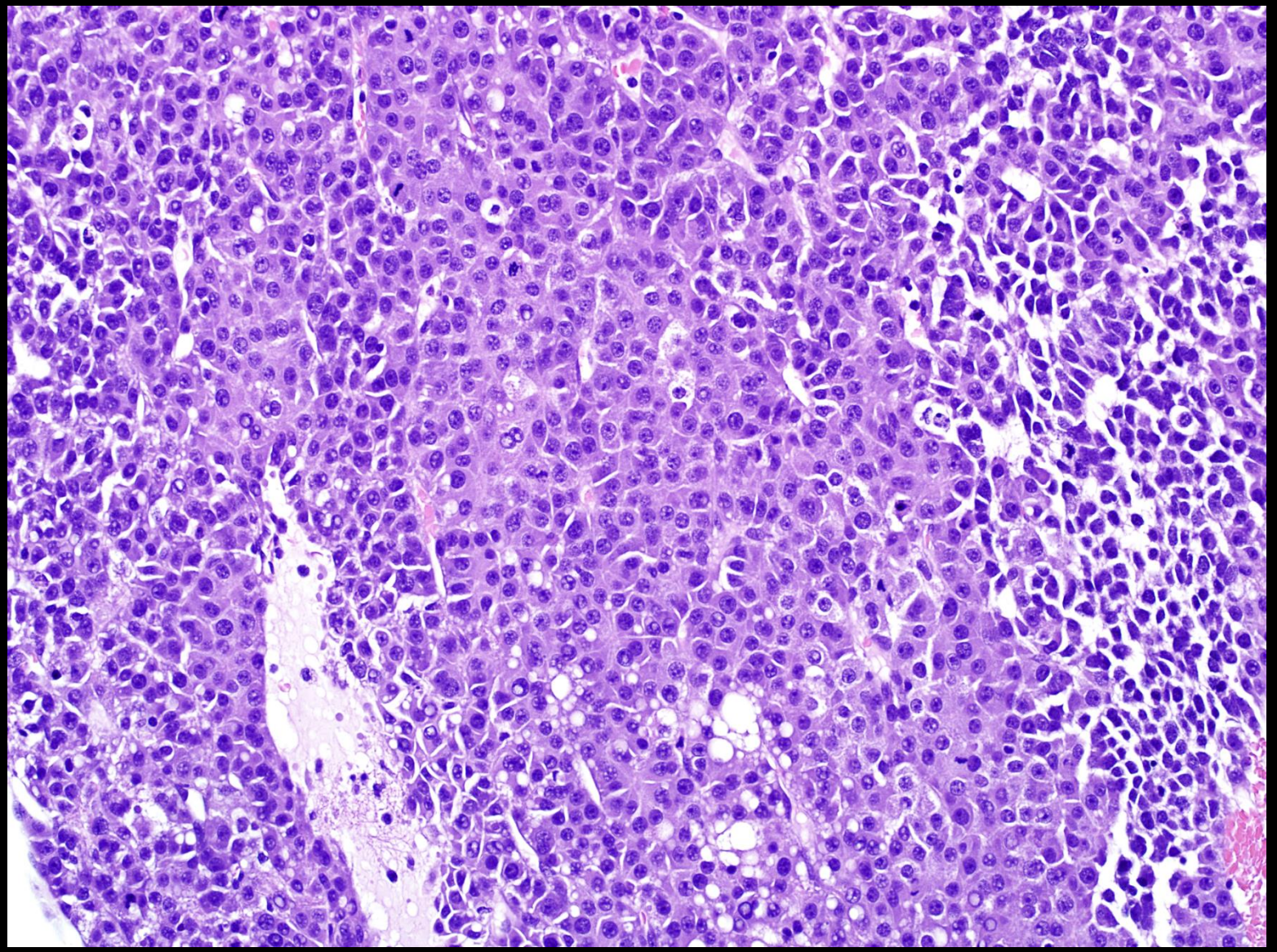
Germ Cell Tumor

Small Cell Variant of Hepatoblastoma is negative for AFP.

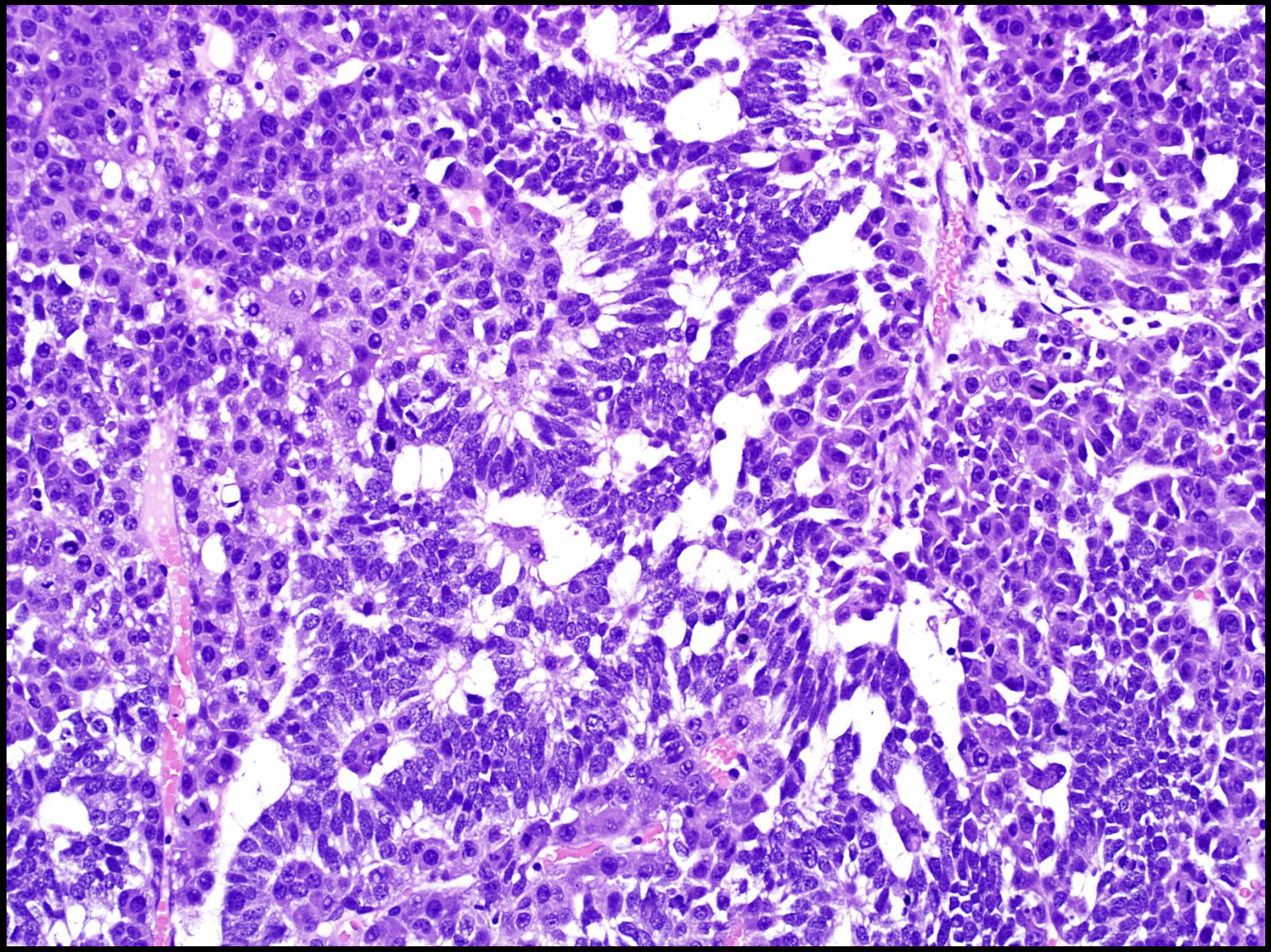
- Ini-1 lost
- ? Rhabdoid tumor



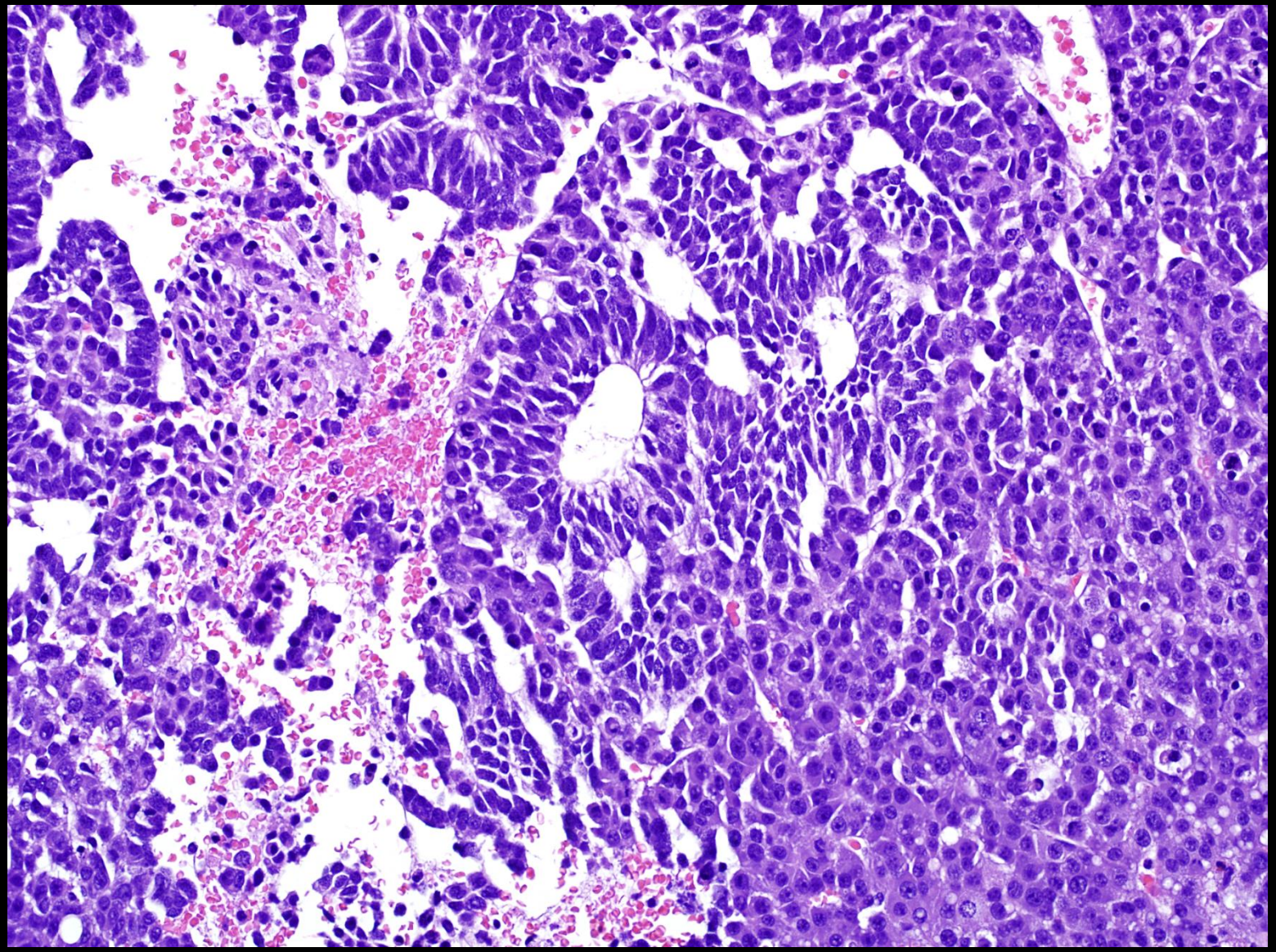
Low power shows heterogeneous morphology.



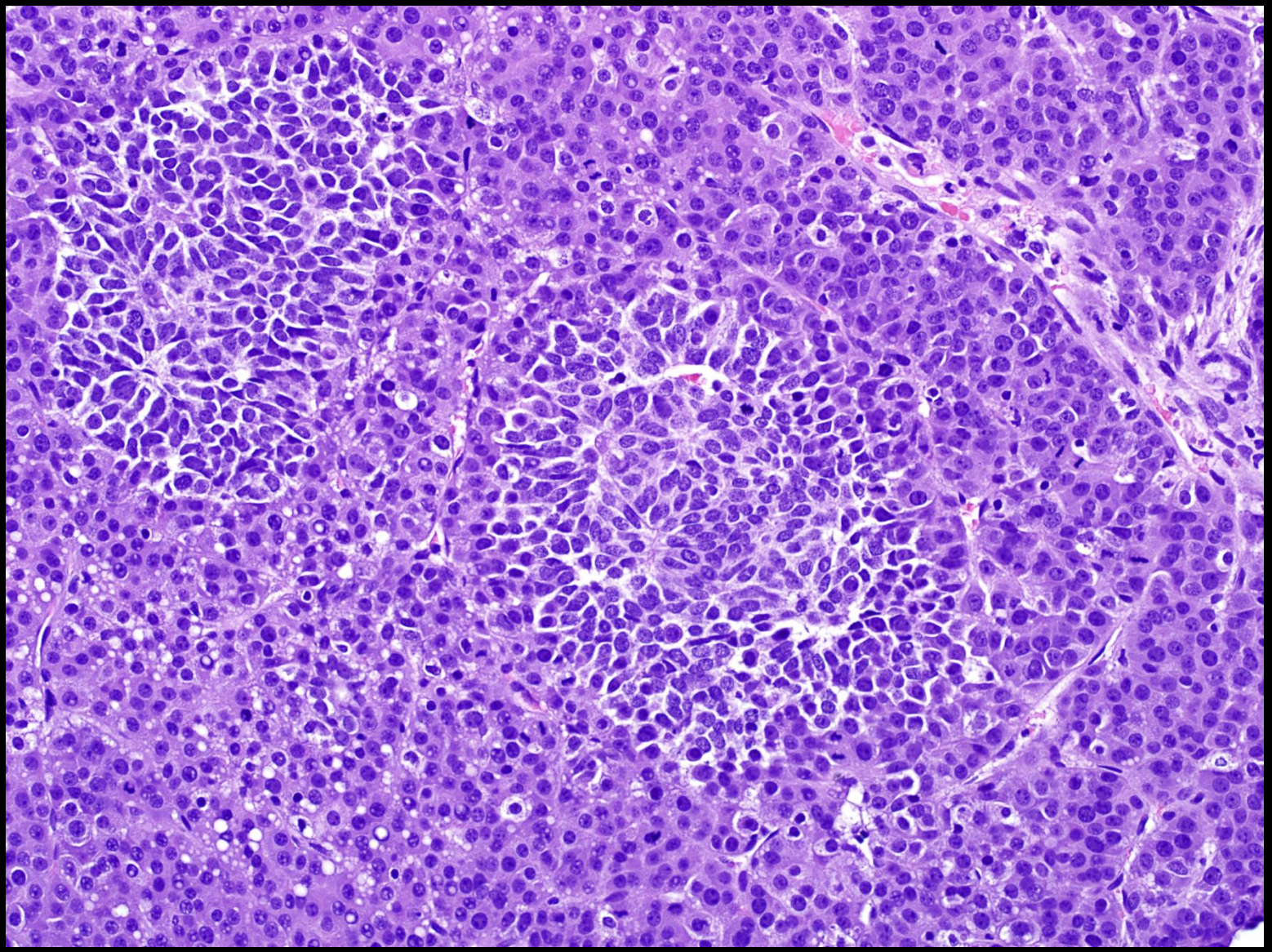
Epithelial and embryonal cell types.



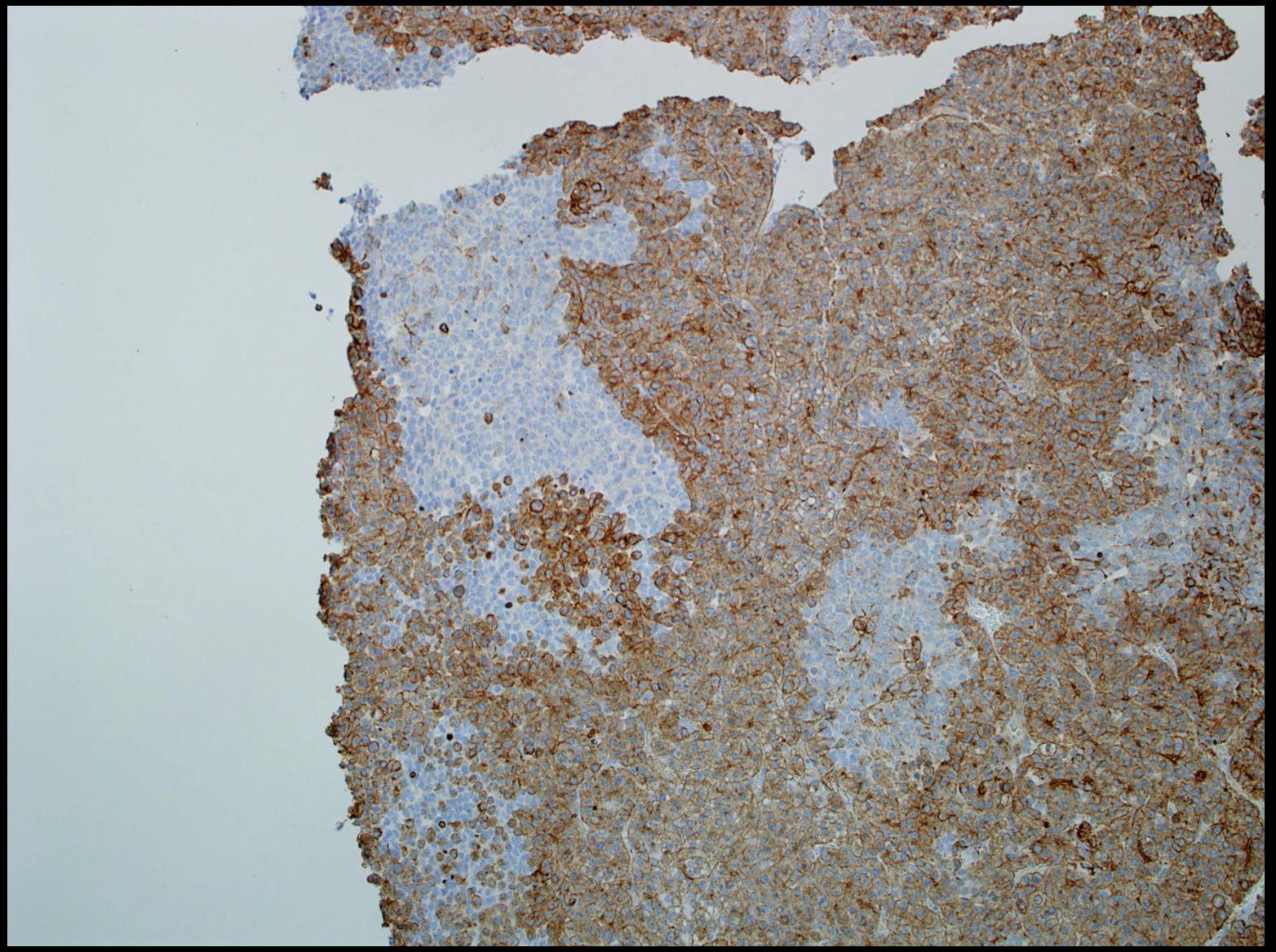
Festooning bands of cells (range from embryonal to epithelial in morphology).



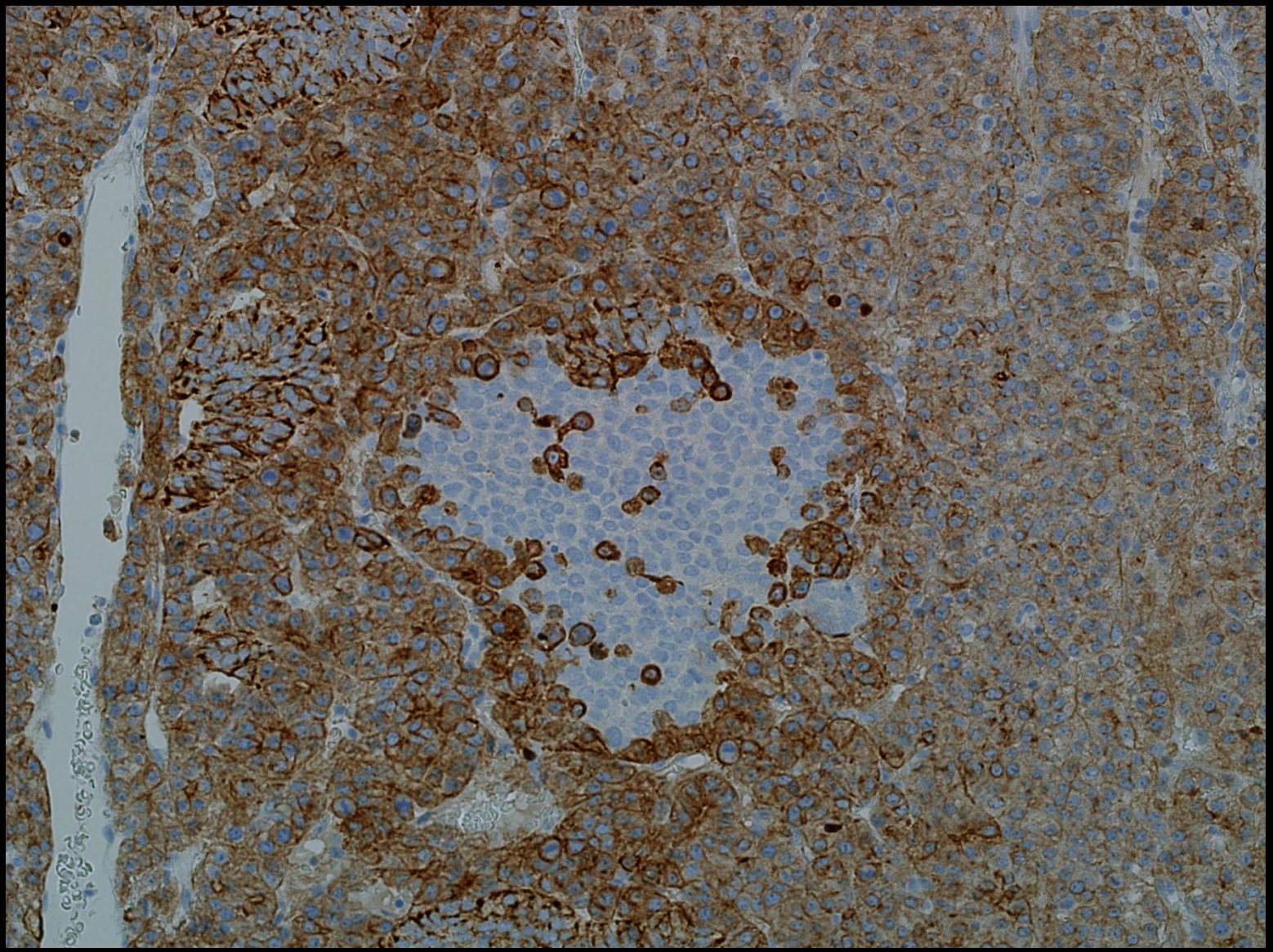
More distinctly glandular.



Small cell focus.



Small cell foci are cytokeratin (AE1/AE3) negative.



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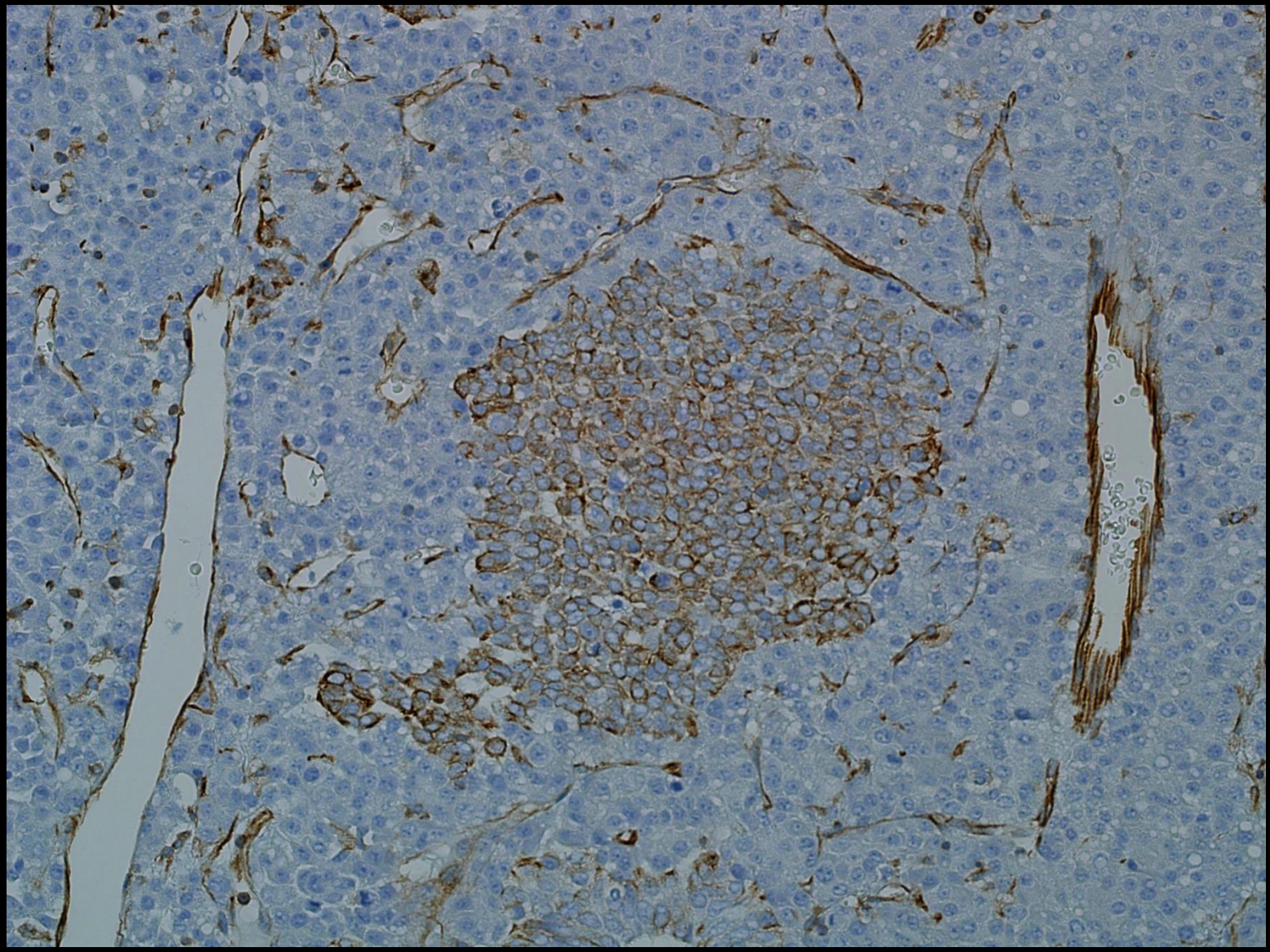
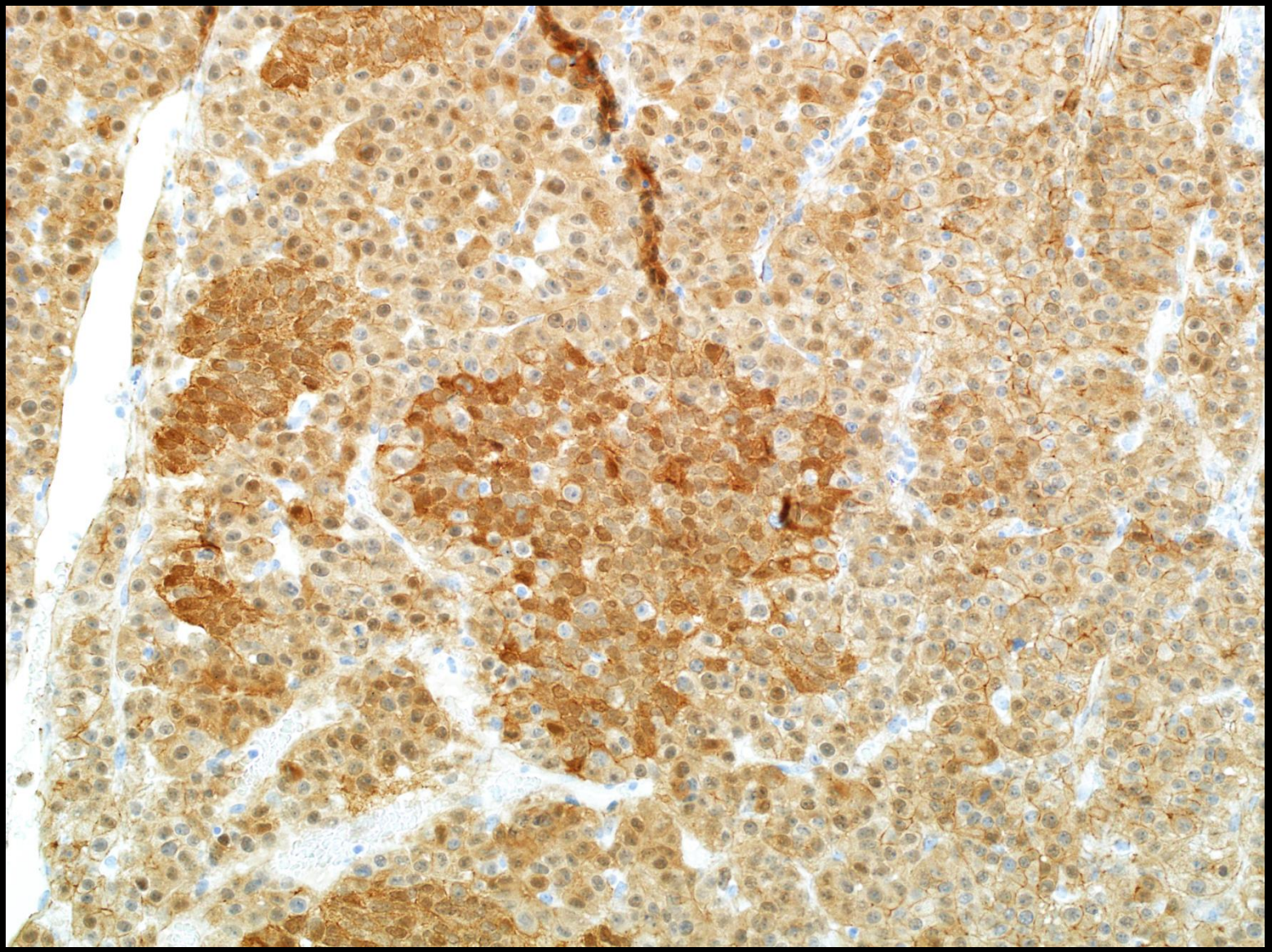
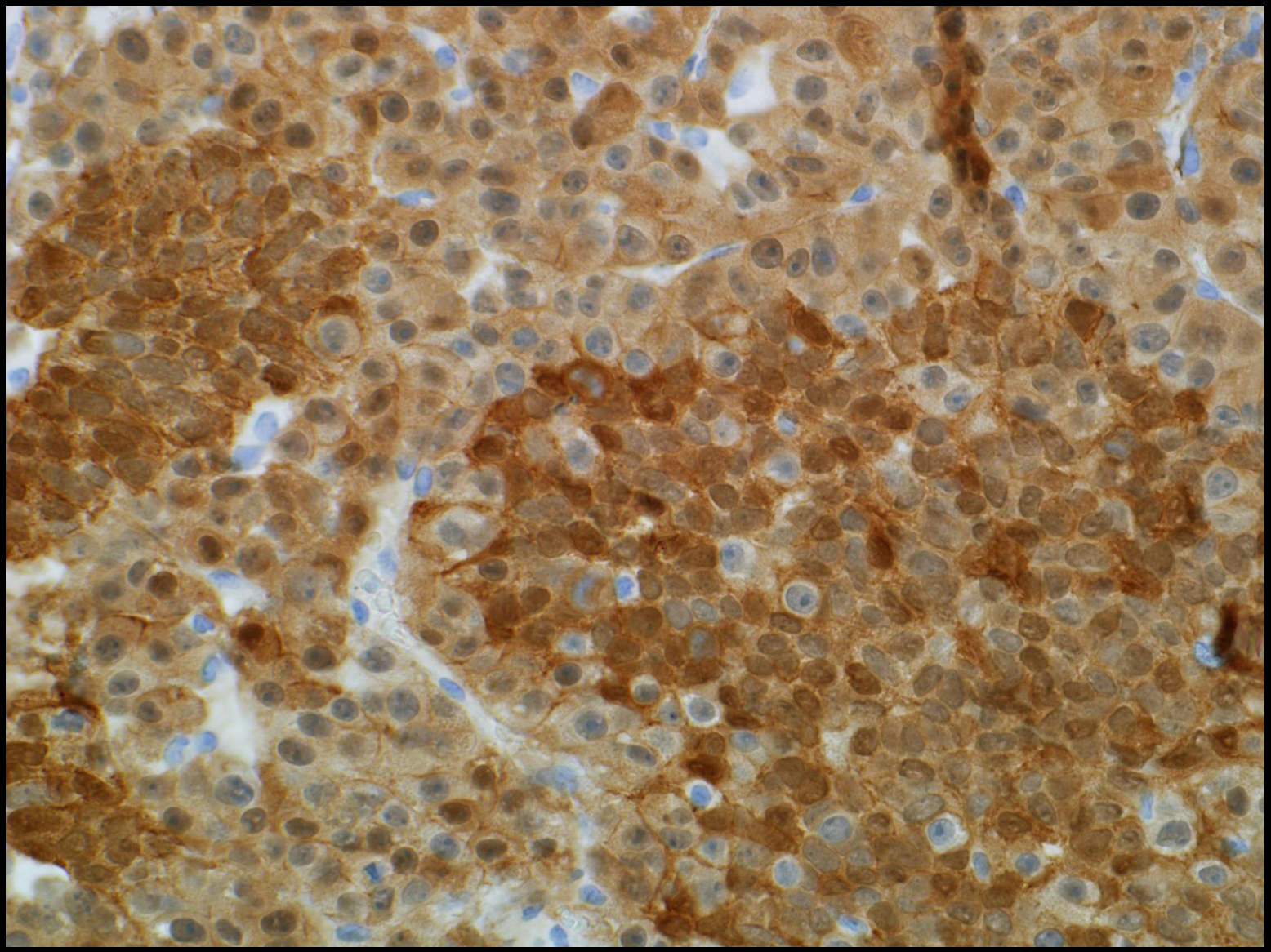


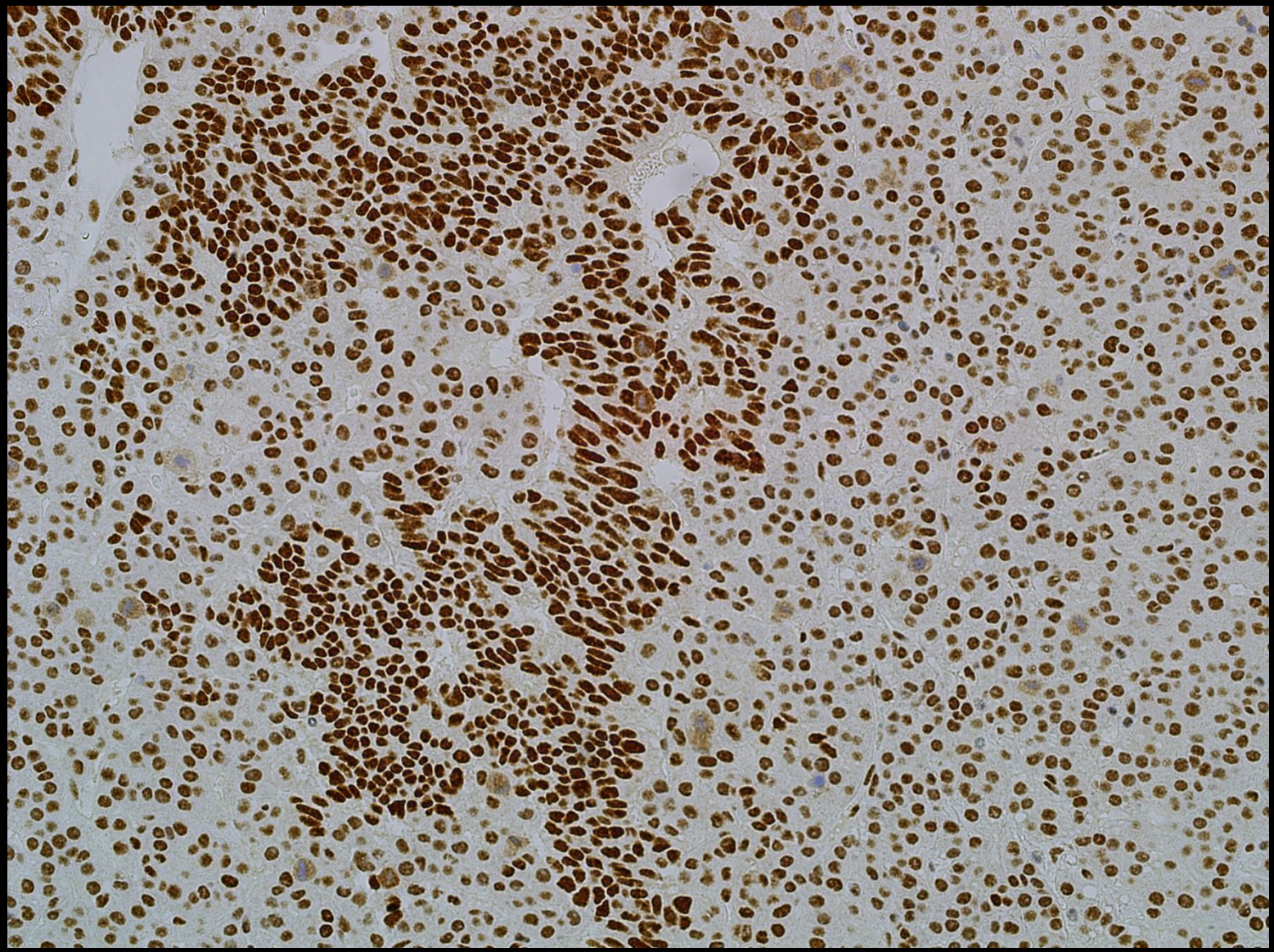
Small cell foci are vimentin positive.



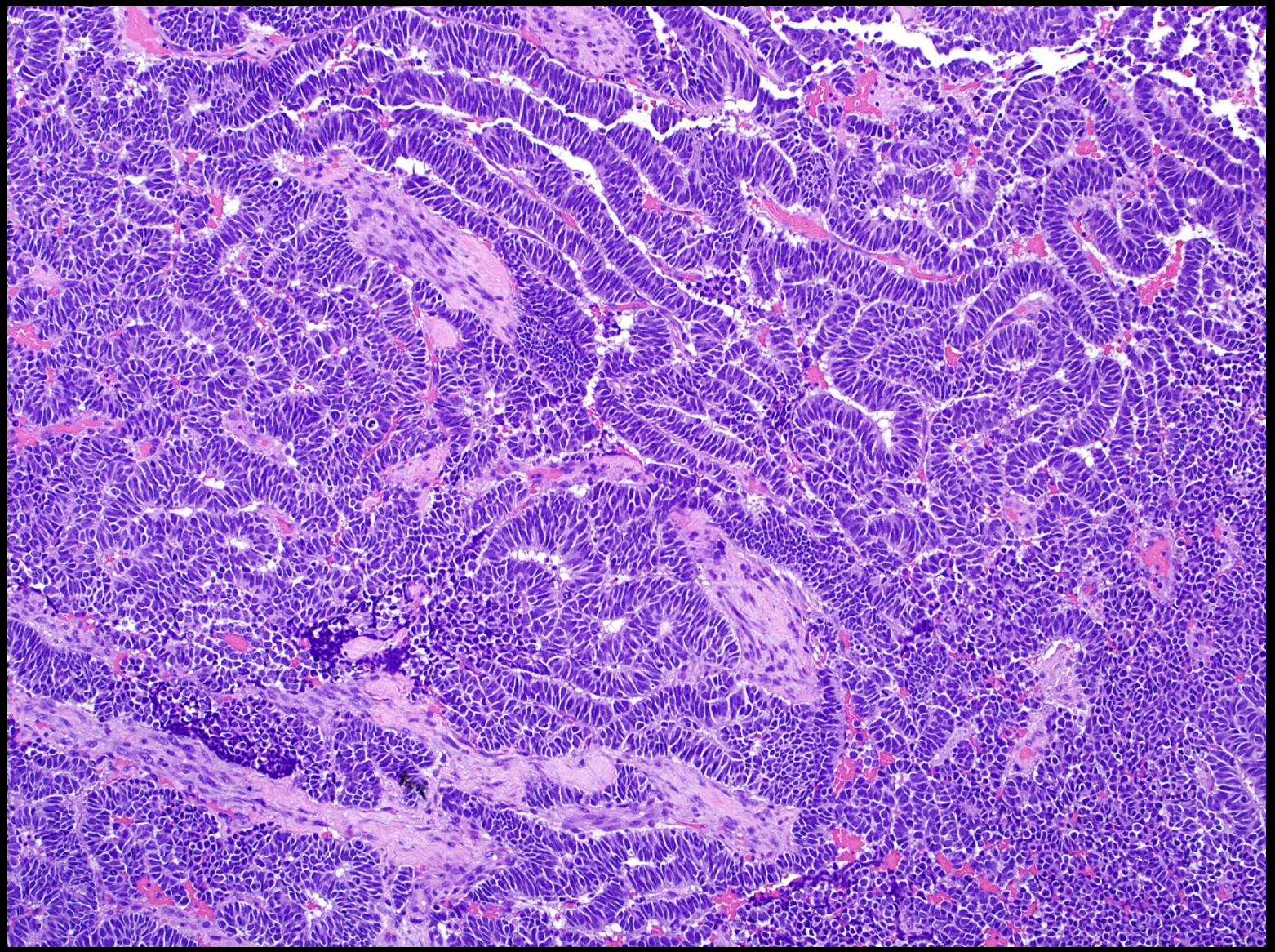
Small cell foci have positive nuclei with beta-catenin stain.



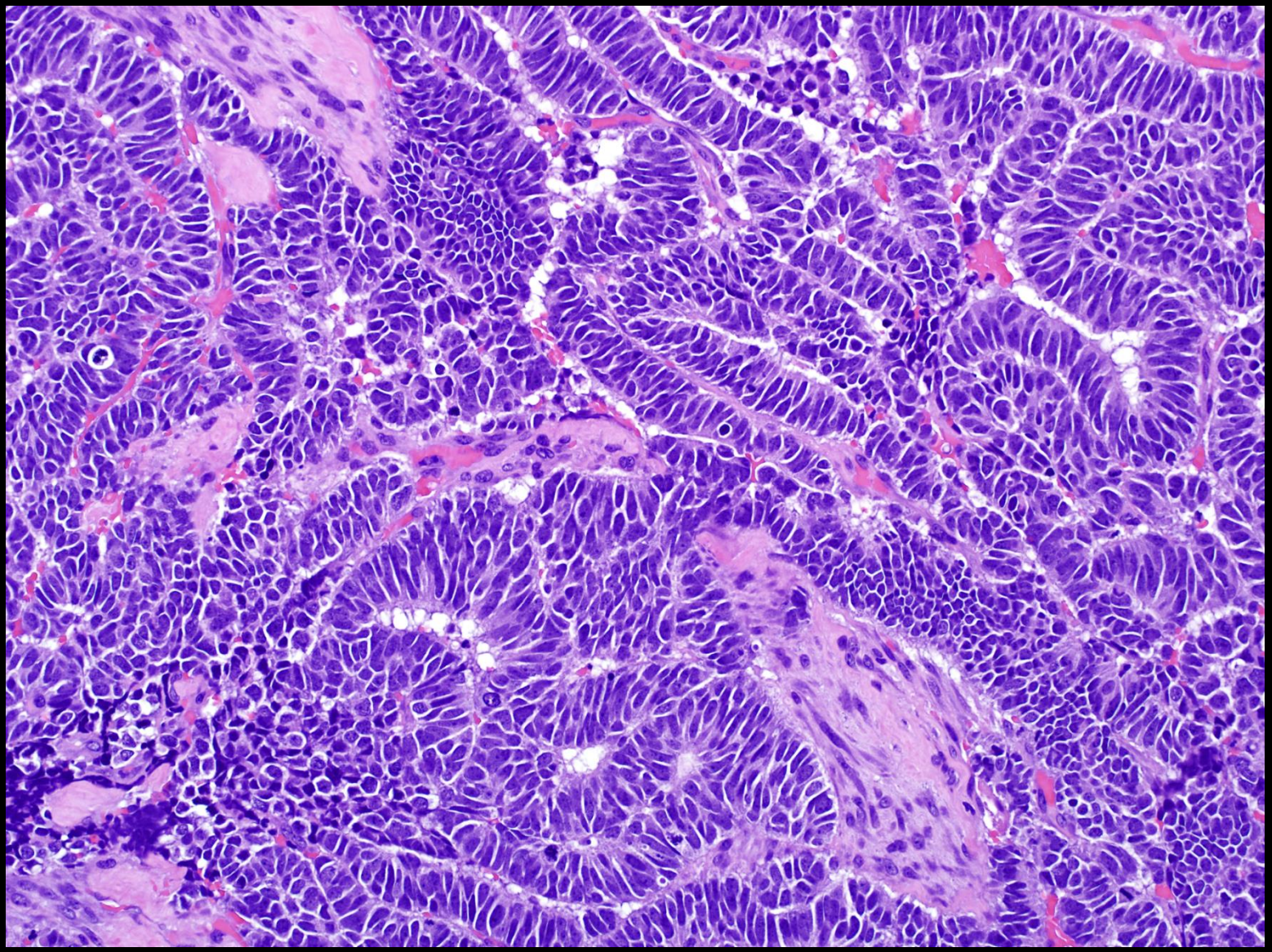
Small cell foci have positive nuclei with beta-catenin stain.



Small cell foci in this case retain nuclear Ini-1.



All of the recurrent lesions (peritoneal implants) are predominantly the festooning band pattern.



Collumnar epithelial appearance.

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Lecture posted at:

Ibdregistry.net