BLTG meeting 2017 Coventry: Leeds case

- Female 48 years

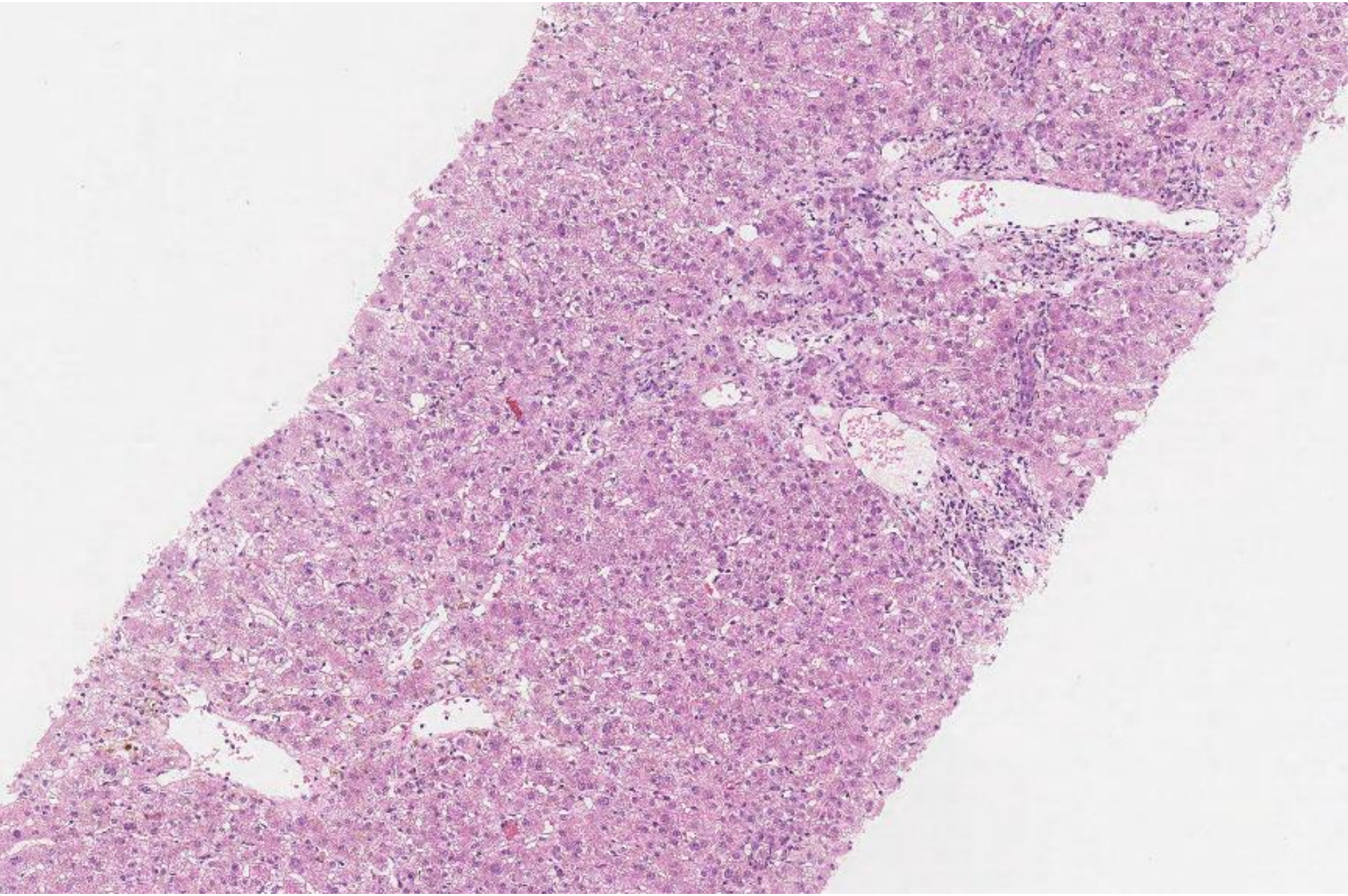
  DBD transplant for ALD/HCV cirrhosis in May 2017.

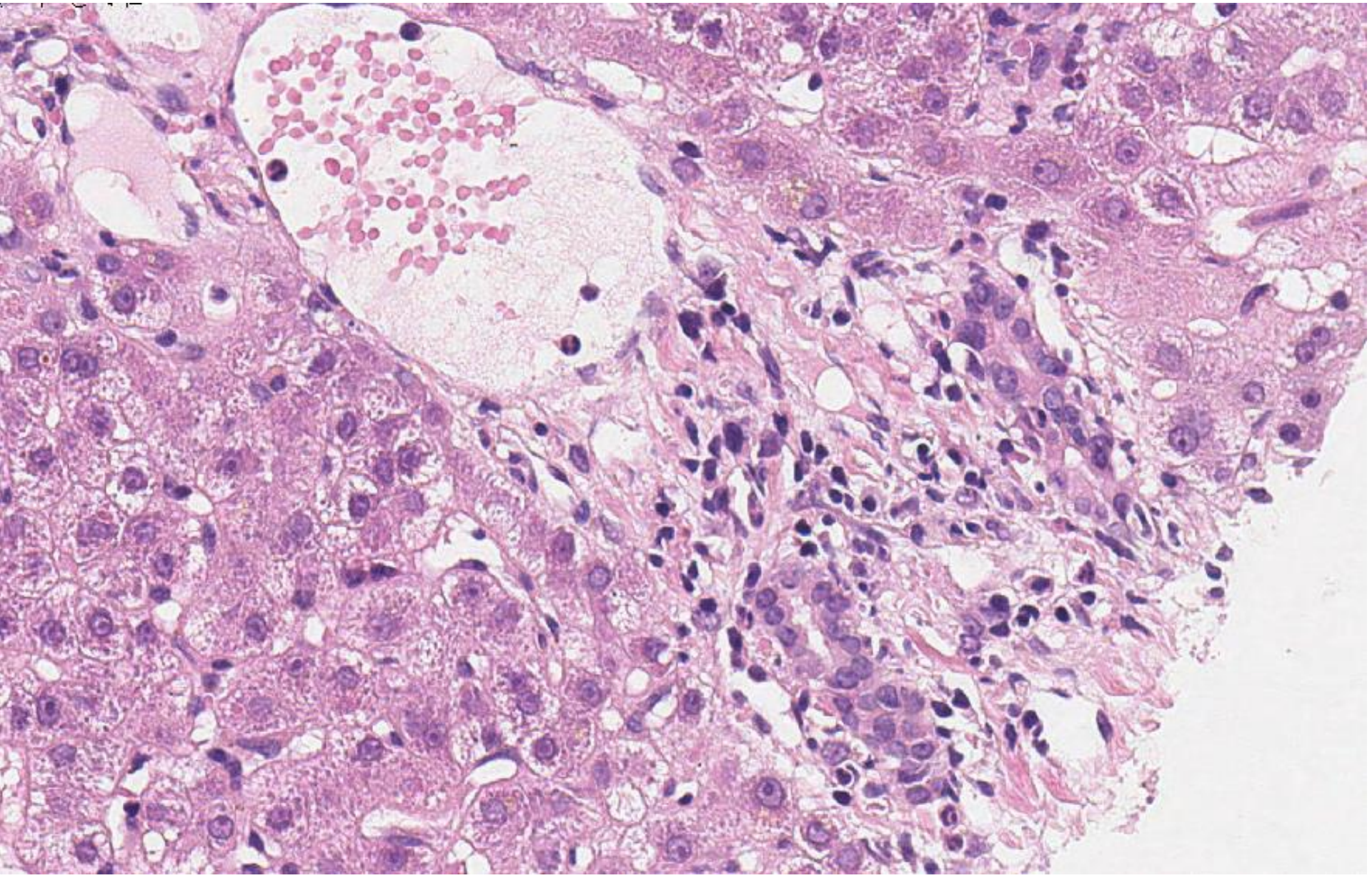
  (Hep C type 3a, treatment naïve)

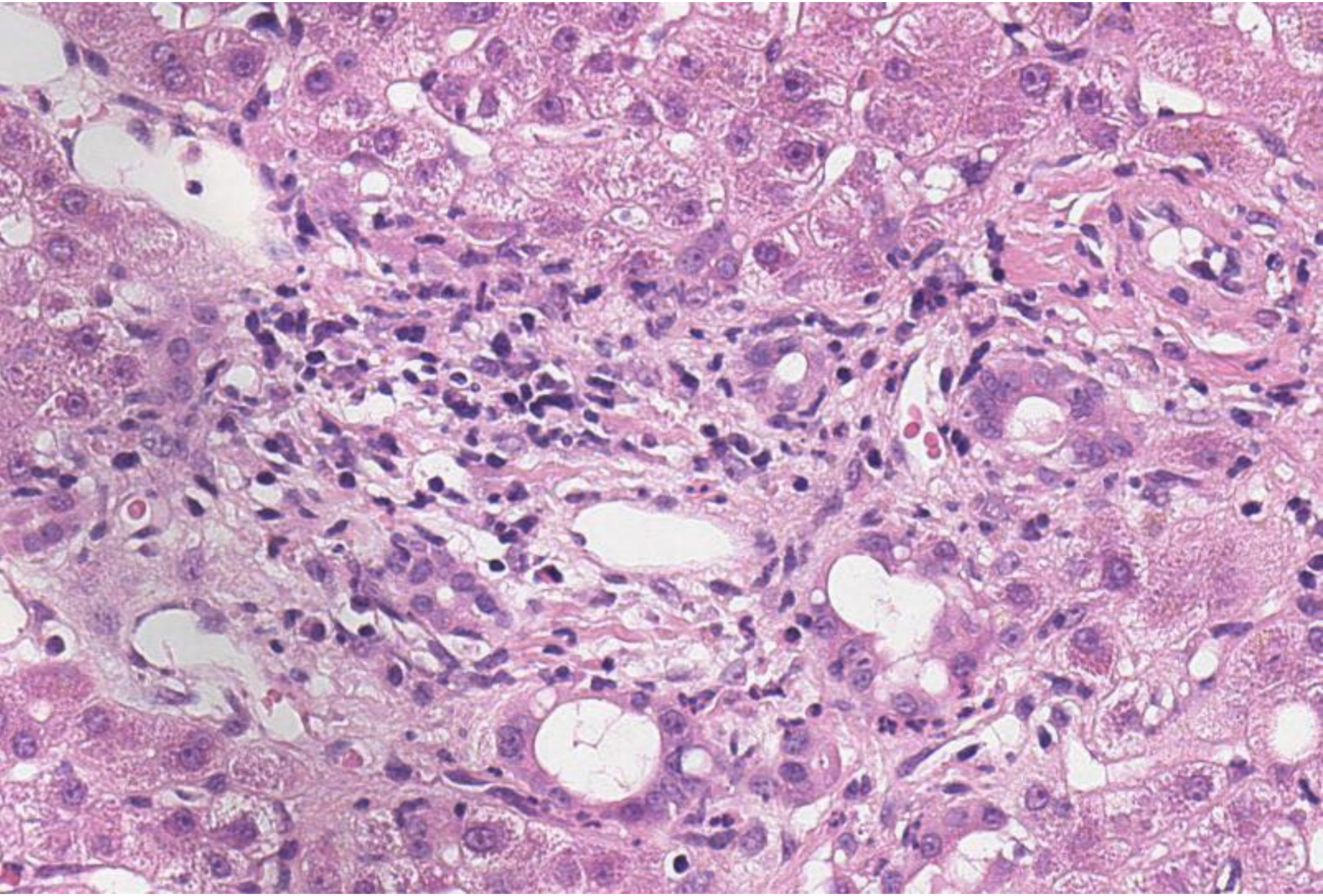
- Deranged LFTs with recent MRCP ruling out an obstructive cause with patent vessels.

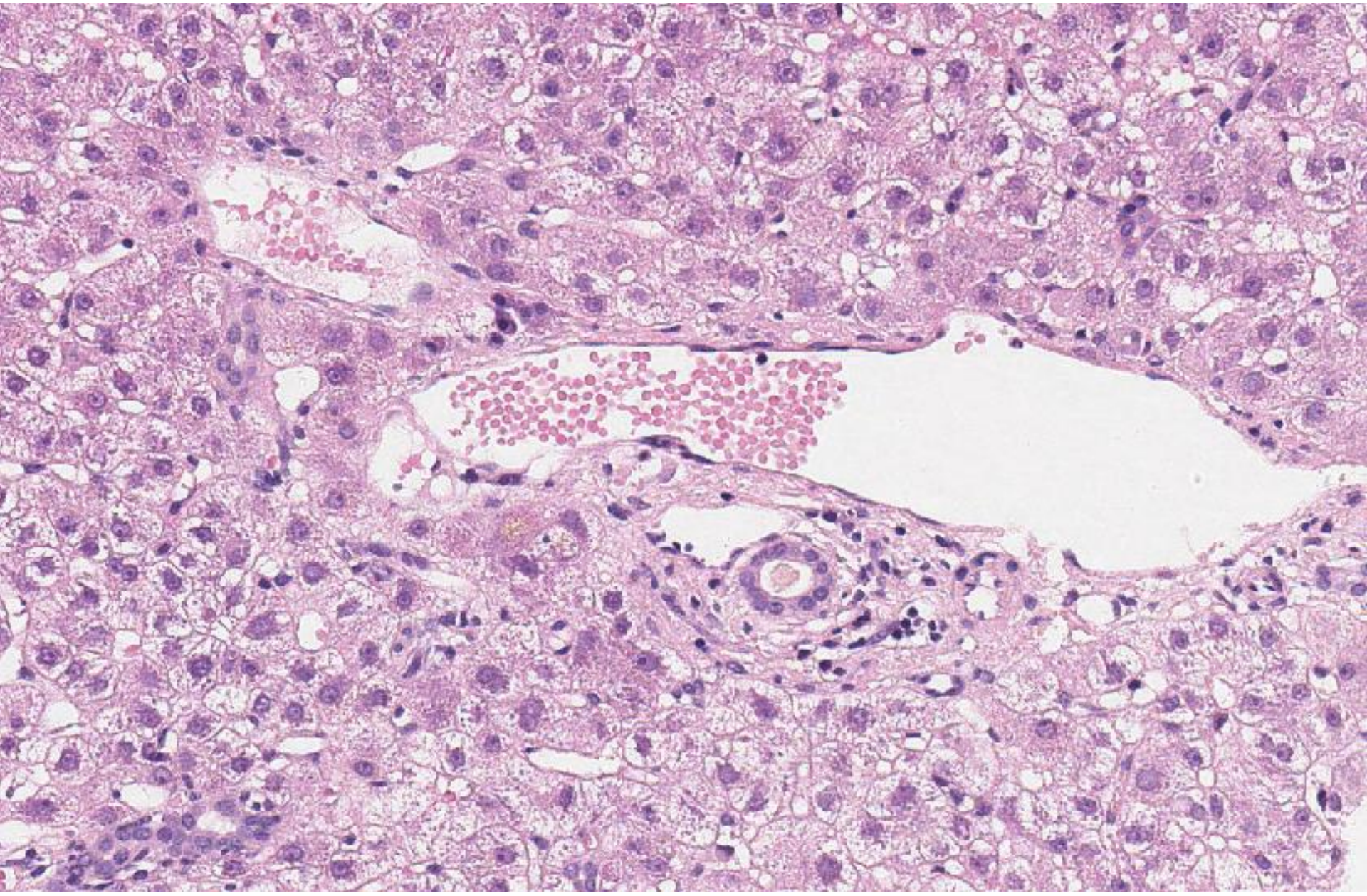
- This biopsy day 18 post transplant
  when LFTs were:

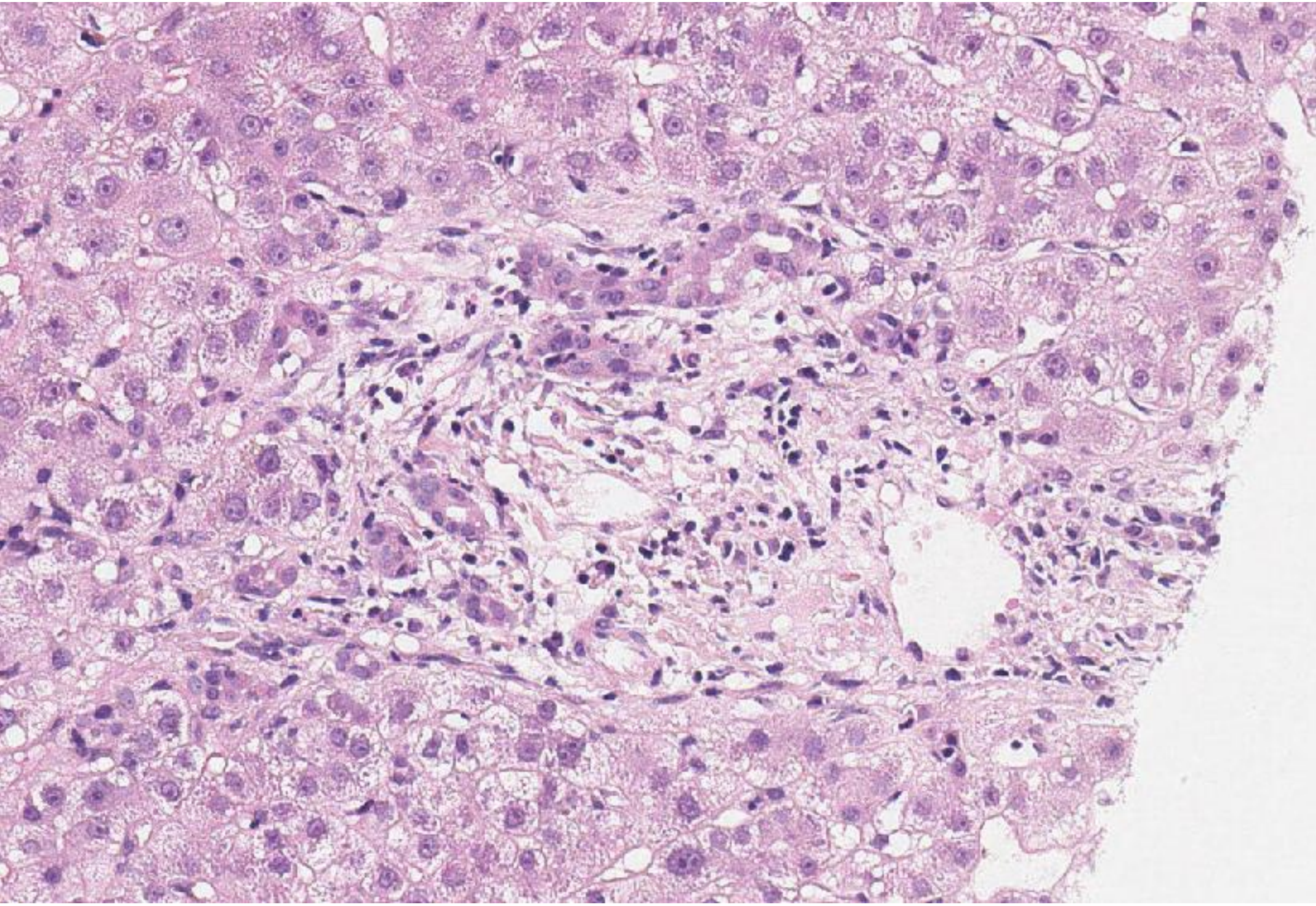
  ALT 63, bili 55, alk phos 876.

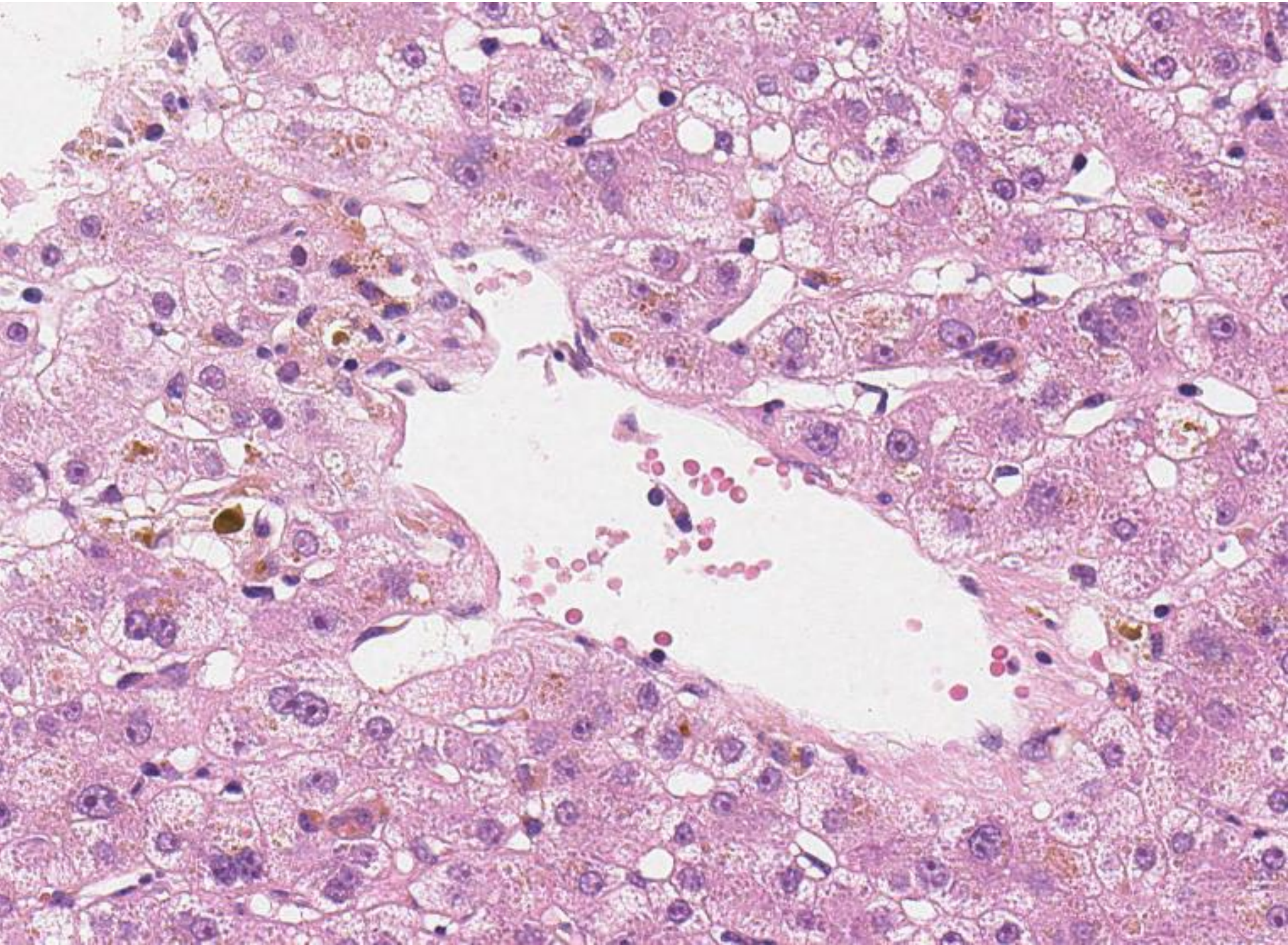


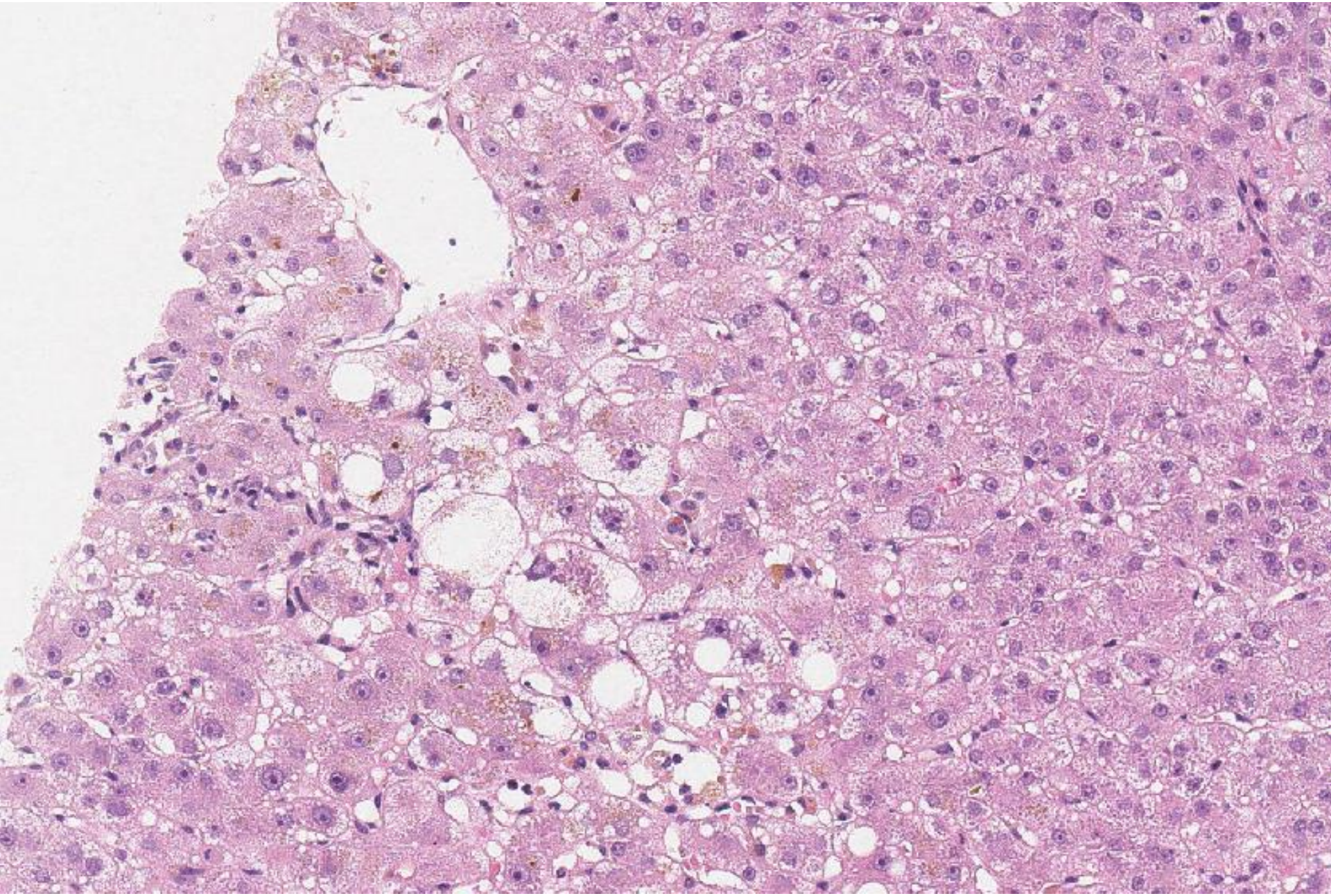












Leeds case. Biopsy day 18 post transplant

Core biopsy 28mm long; 20 portal tracts.

Portal tract very mild inflammation with neutrophils; cholangiolitis, some dilated ductules, not endotheliitis, not ascending cholangitis.

Canalicular cholestasis, perivenular hepatocyte swelling and some drop out. Minimal inflammation. Slight hepatic vein endotheliitis.

Result phoned: predominant feature is portal oedema, cholangiolitis and cholestasis; ? Sepsis, obstruction.

Not typical features of acute rejection - immunosuppression had been intensified prior to biopsy and liver function tests are improving.

MRCP showed ? Ischaemic duct stenosis.

Leeds case. Biopsy day 18 post transplant

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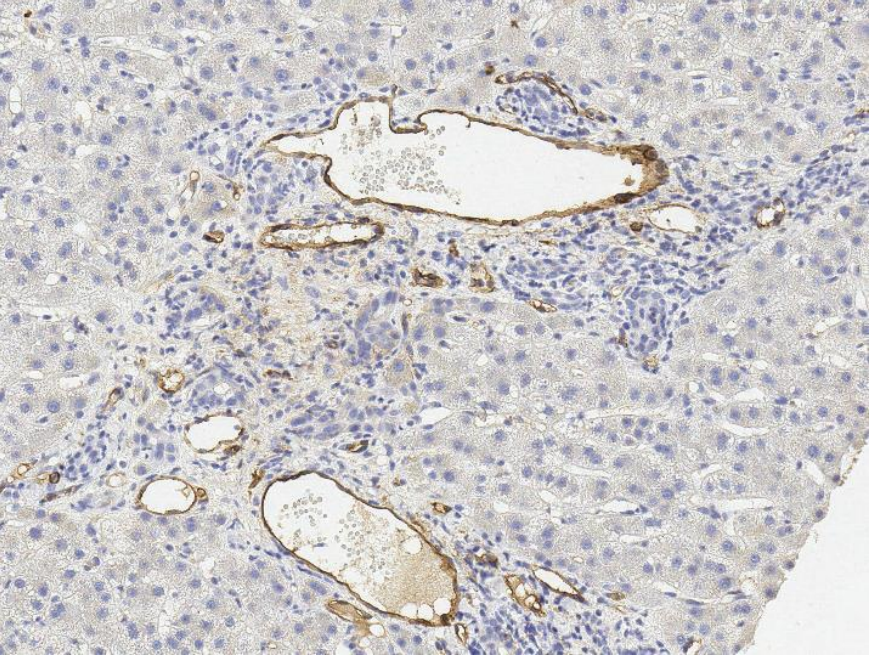
Not features of T cell mediated rejection.

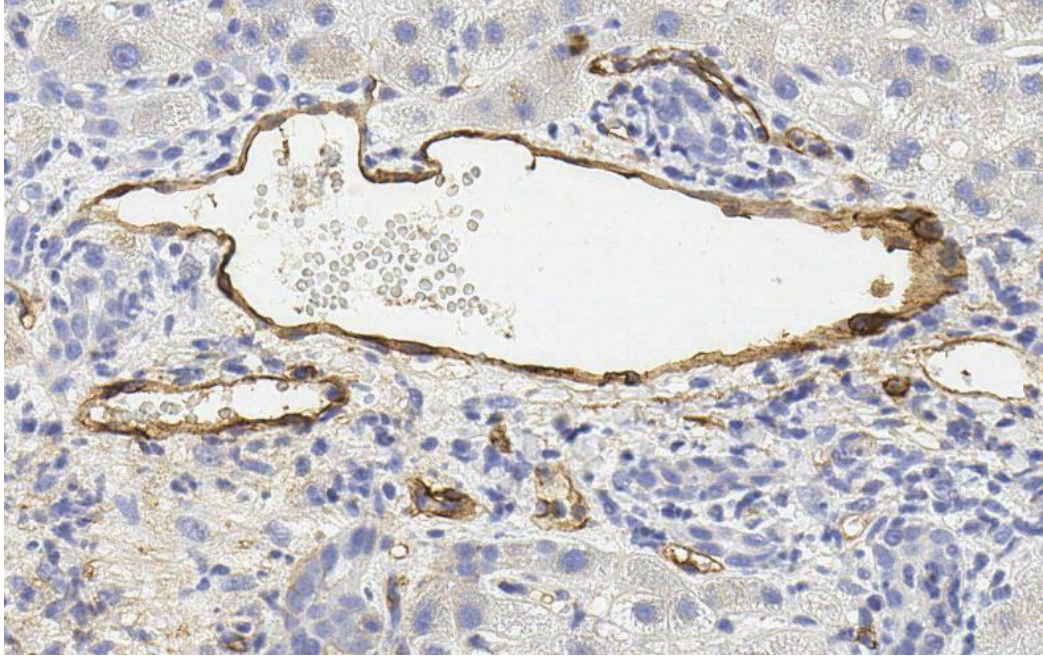
Requested C4d in view of portal changes –

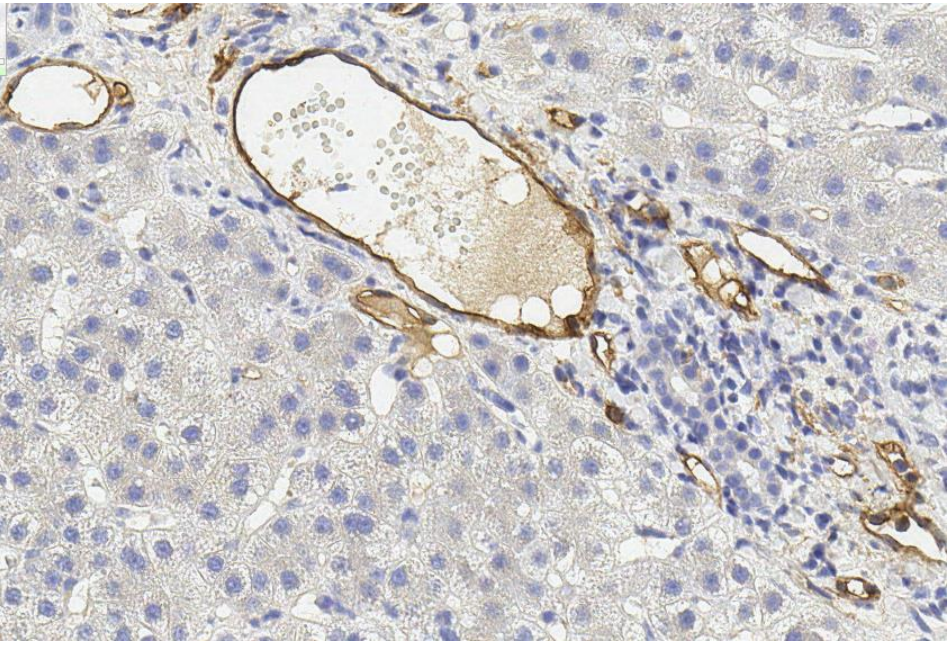
AMR in ABO-compatible allografts:

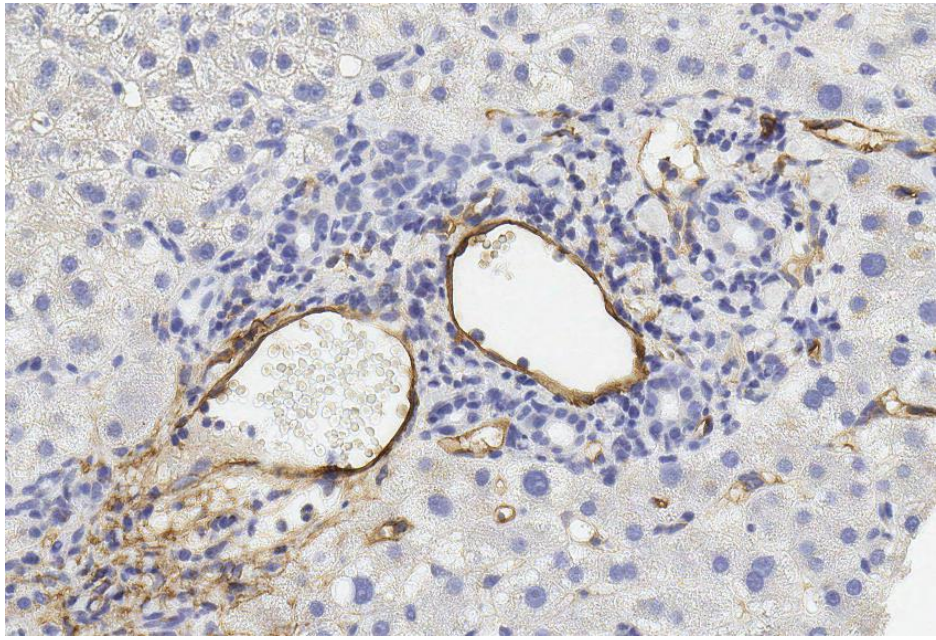
Endothelial hypertrophy and cytoplasmic eosinophilia, capillary dilatation, leukocyte sludging/margination.

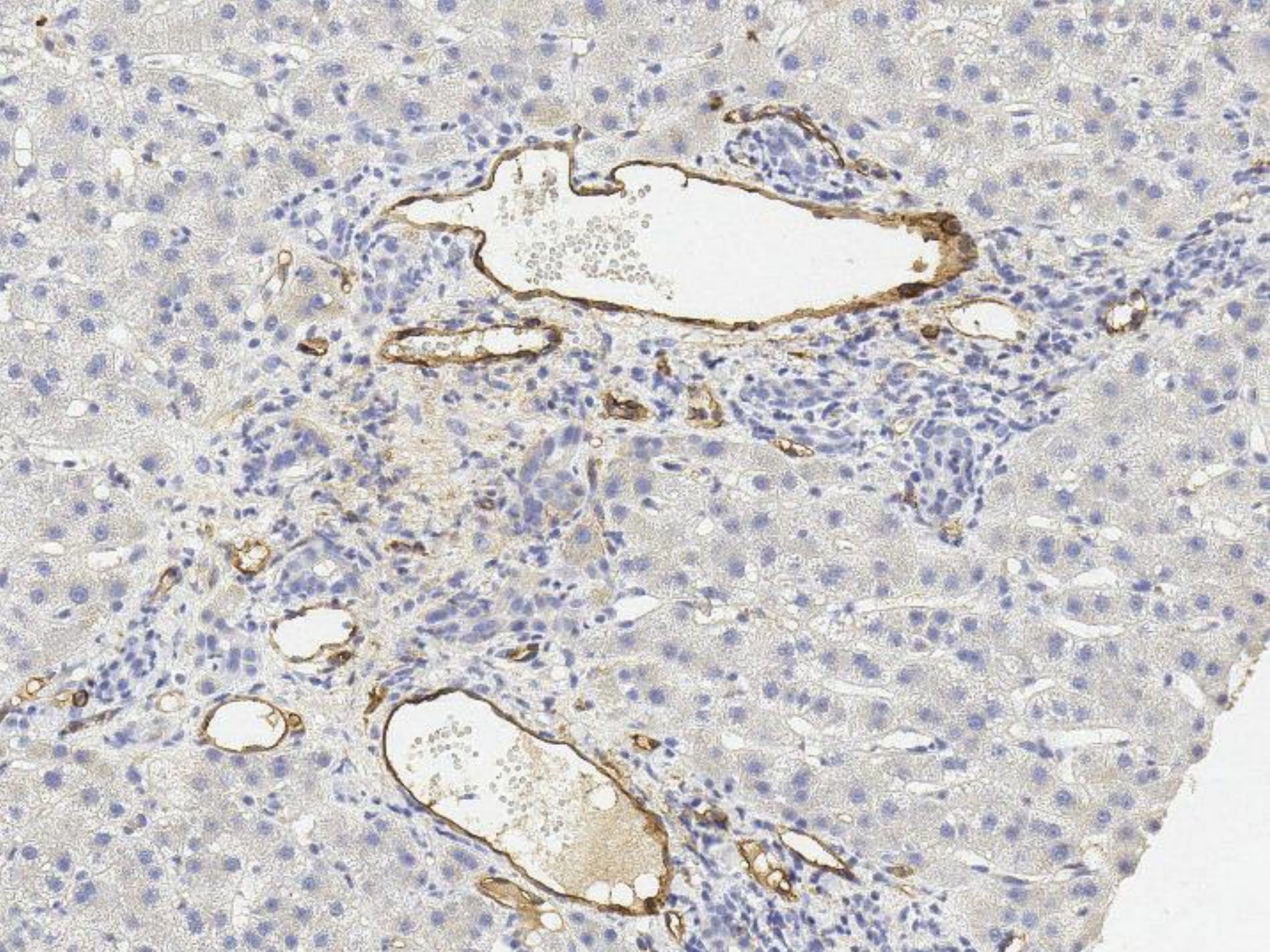
Other changes: portal oedema, ductular reaction, hepatocyte apoptosis, centrilobular hepatocellular swelling and hepatocanalicular cholestasis.

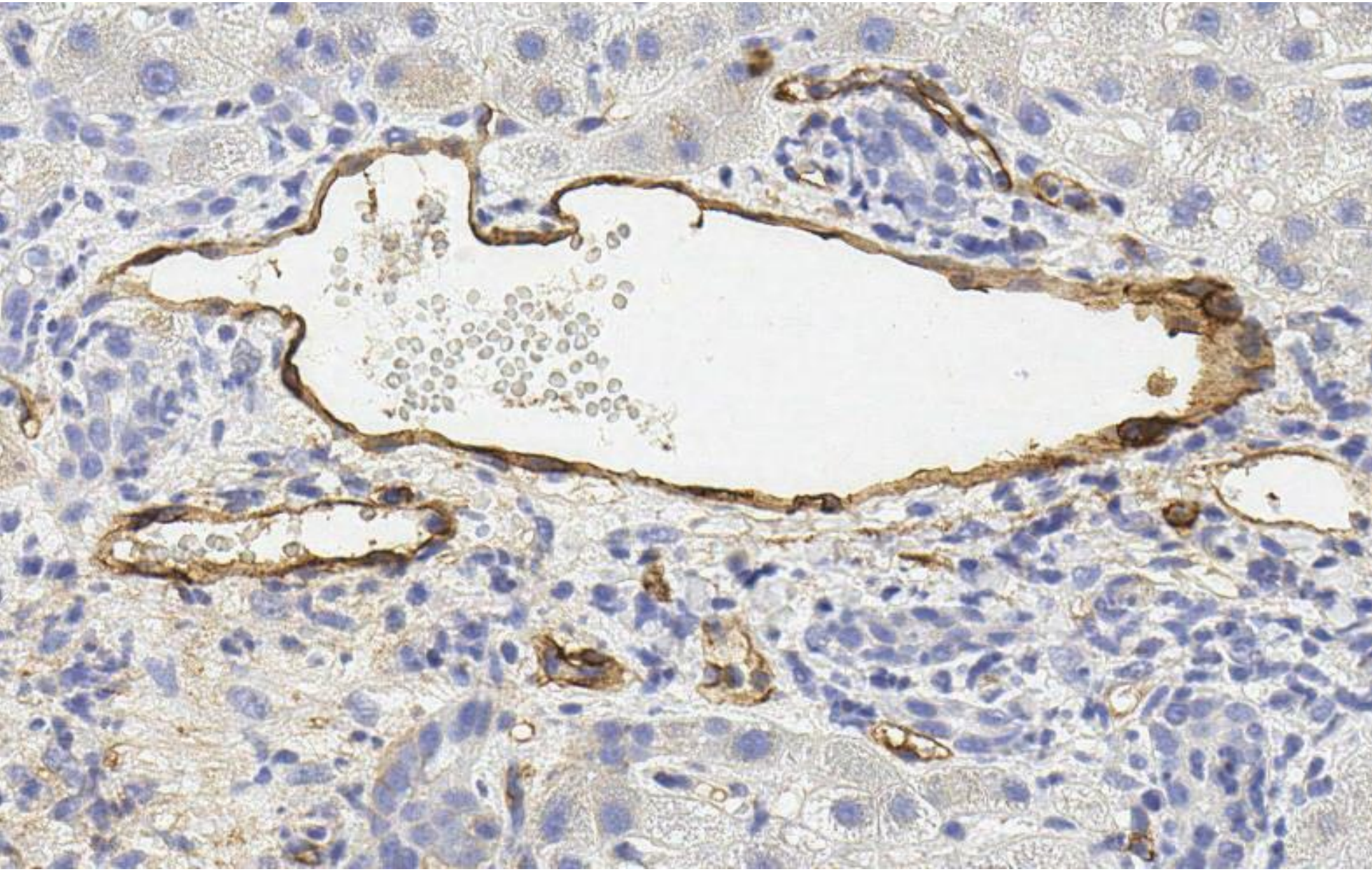


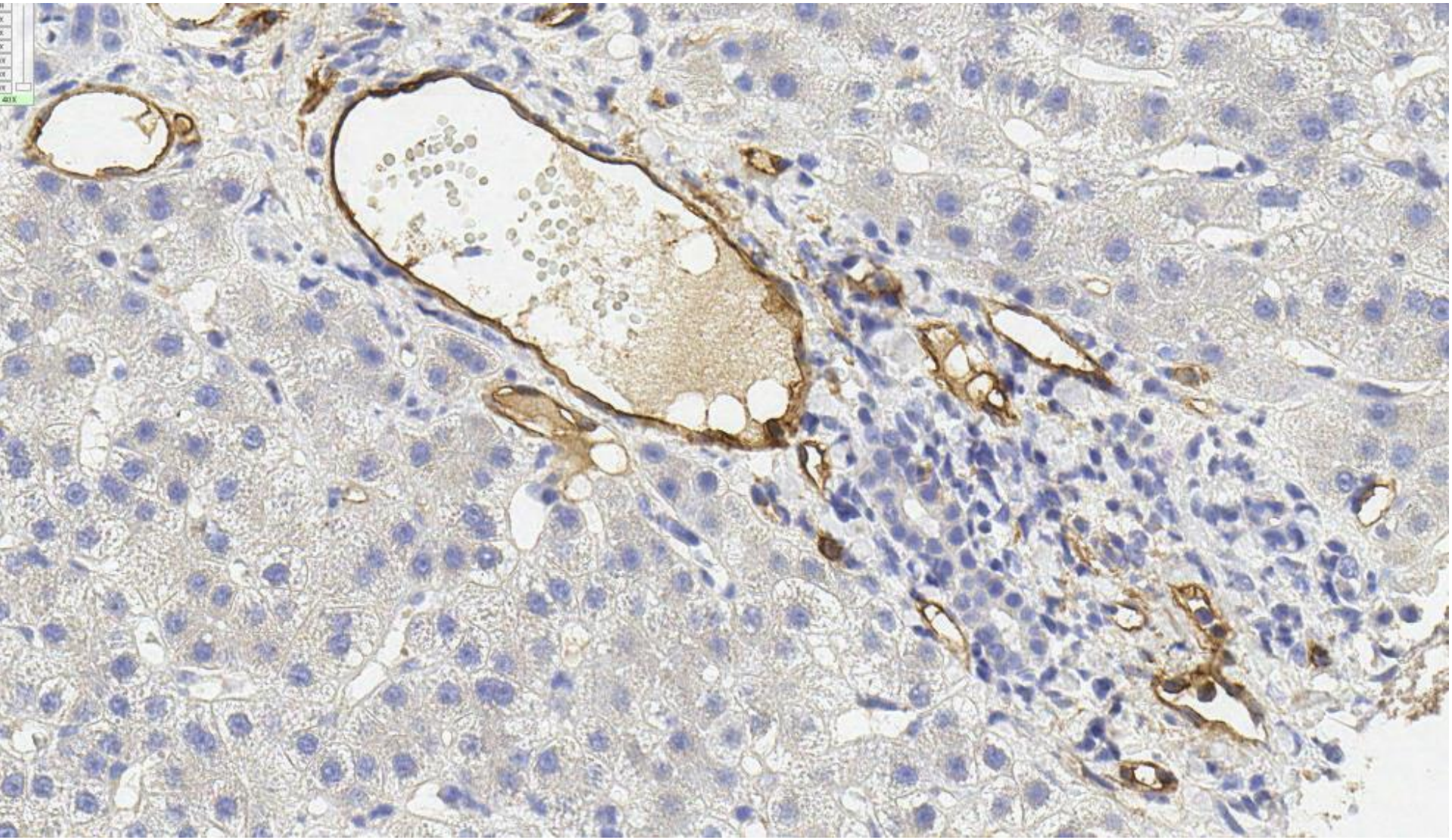


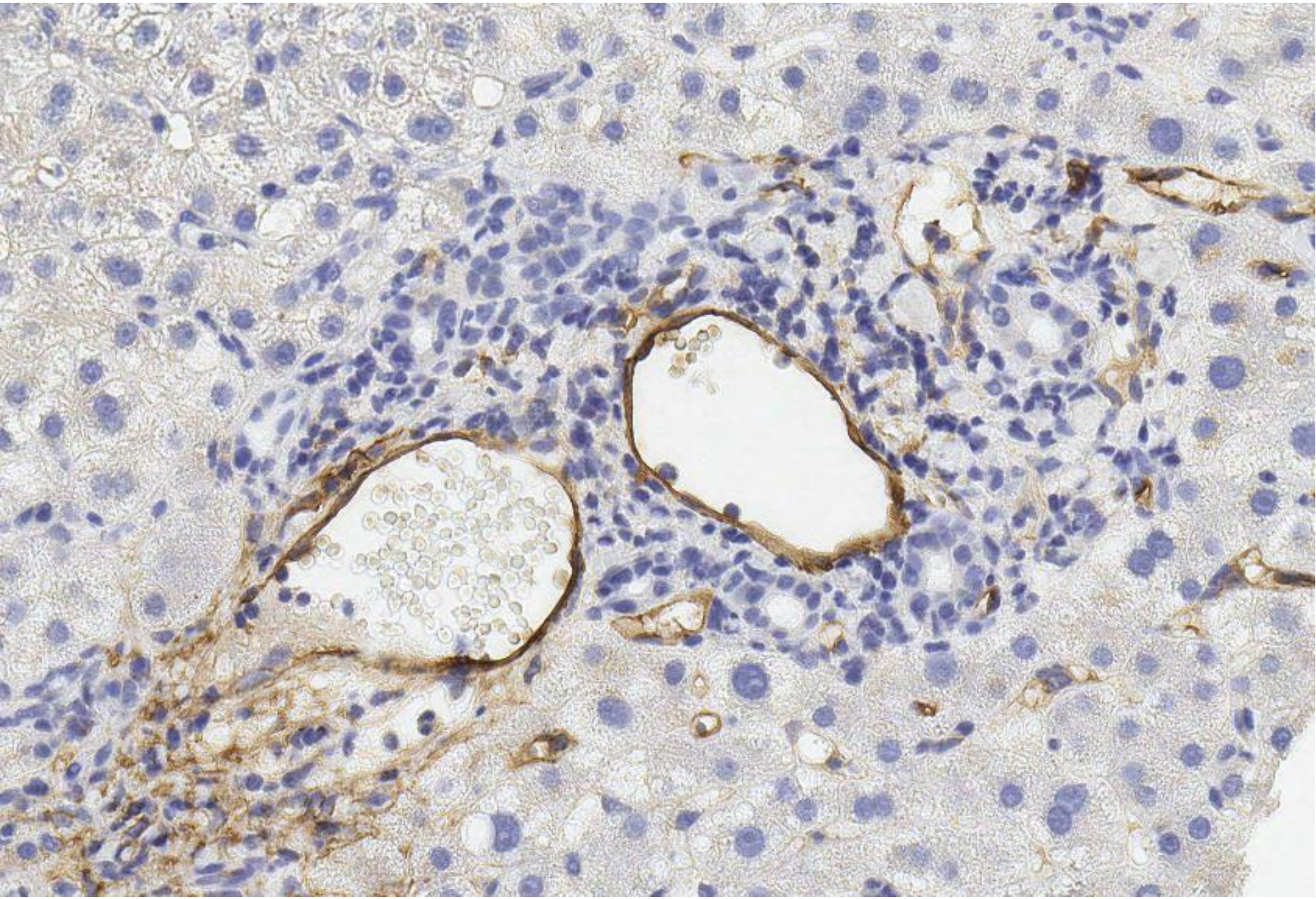


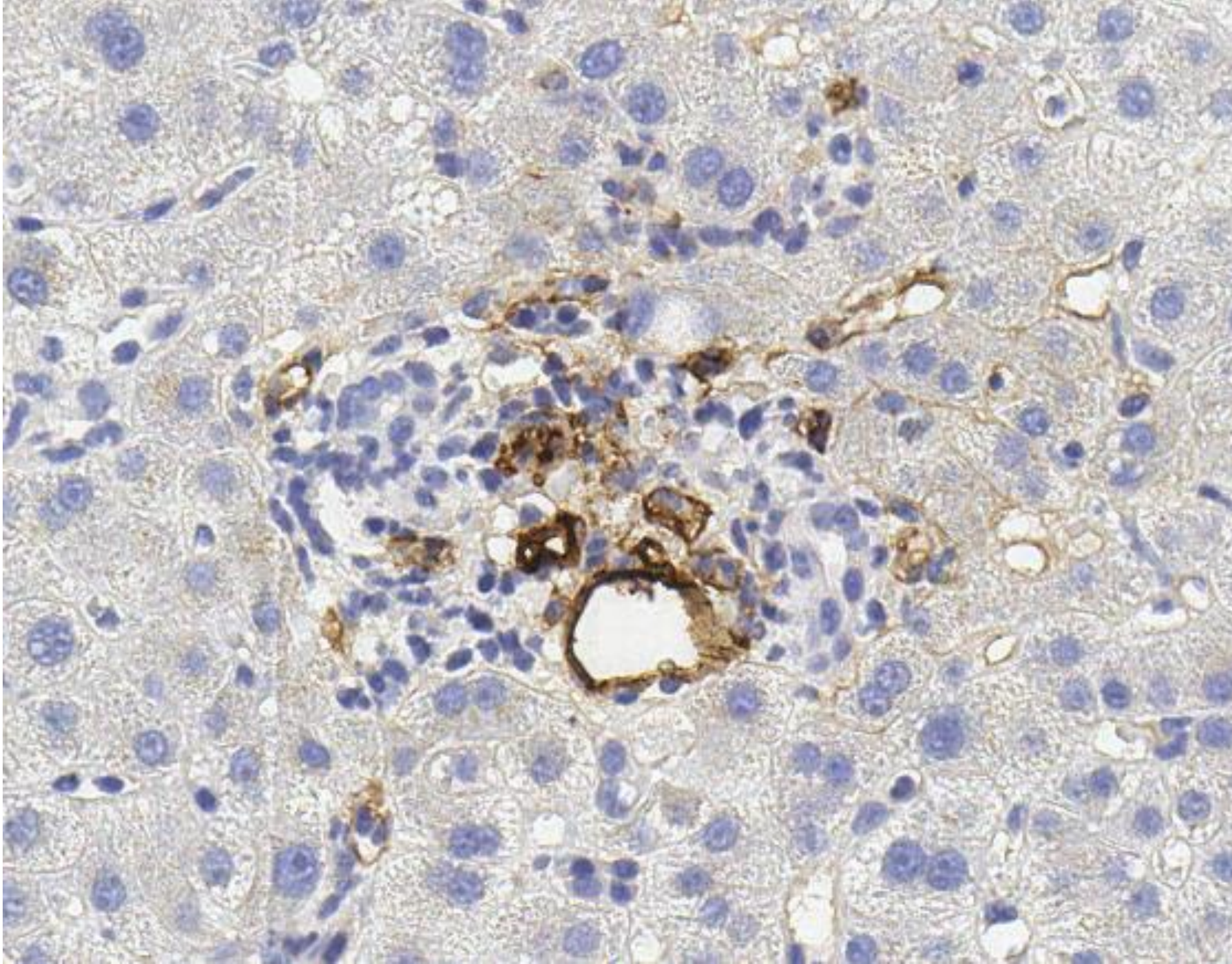


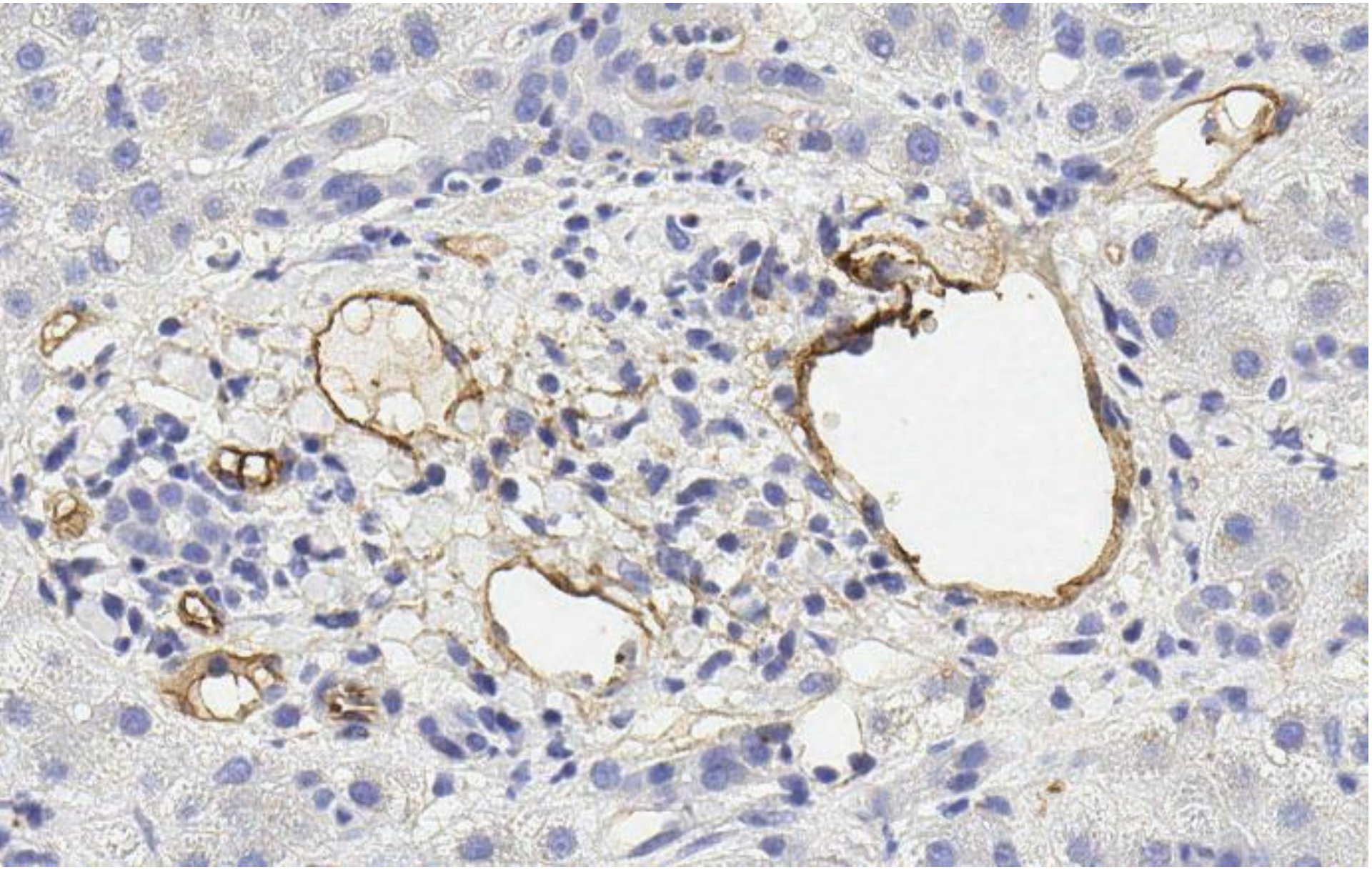




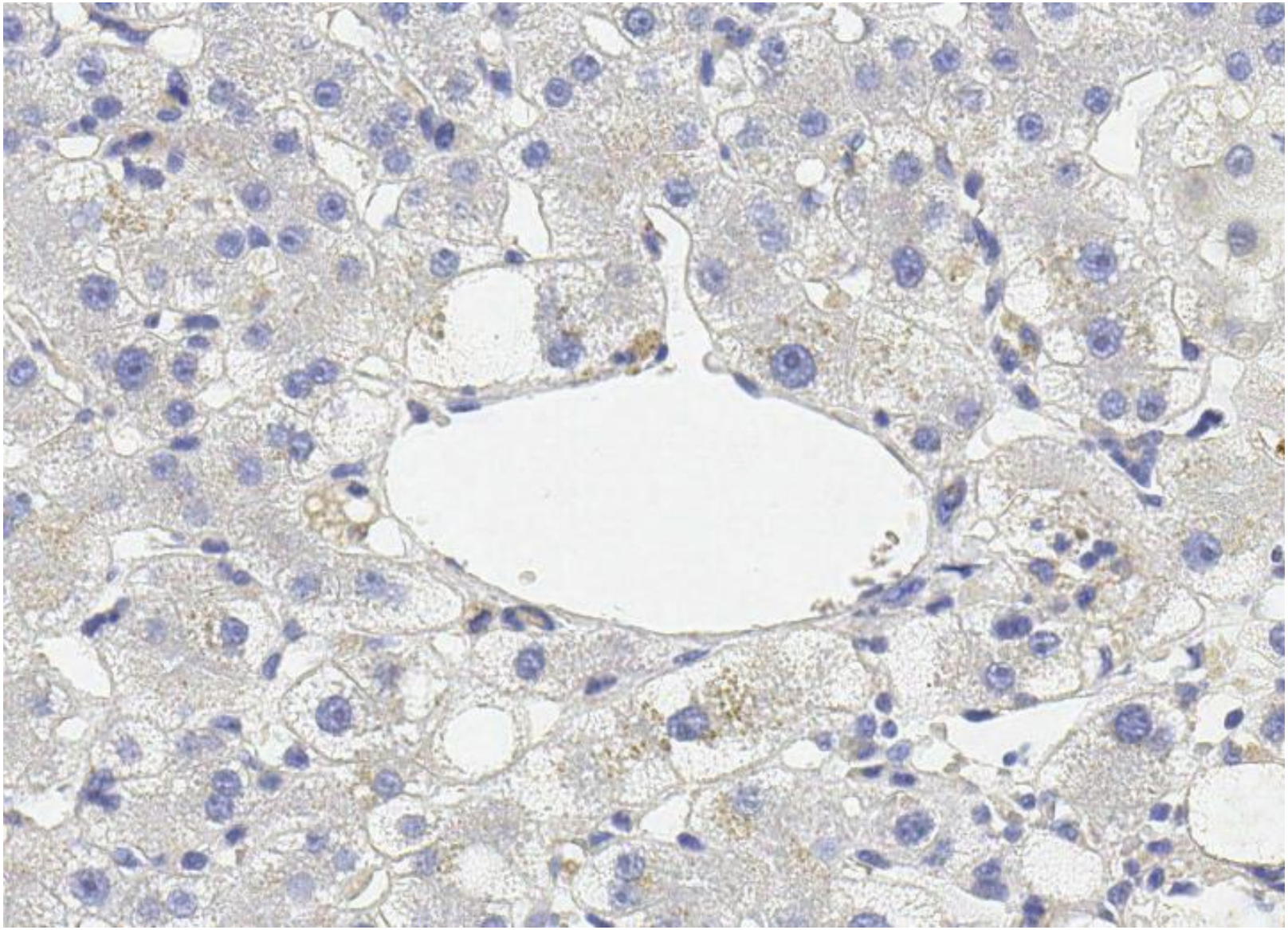


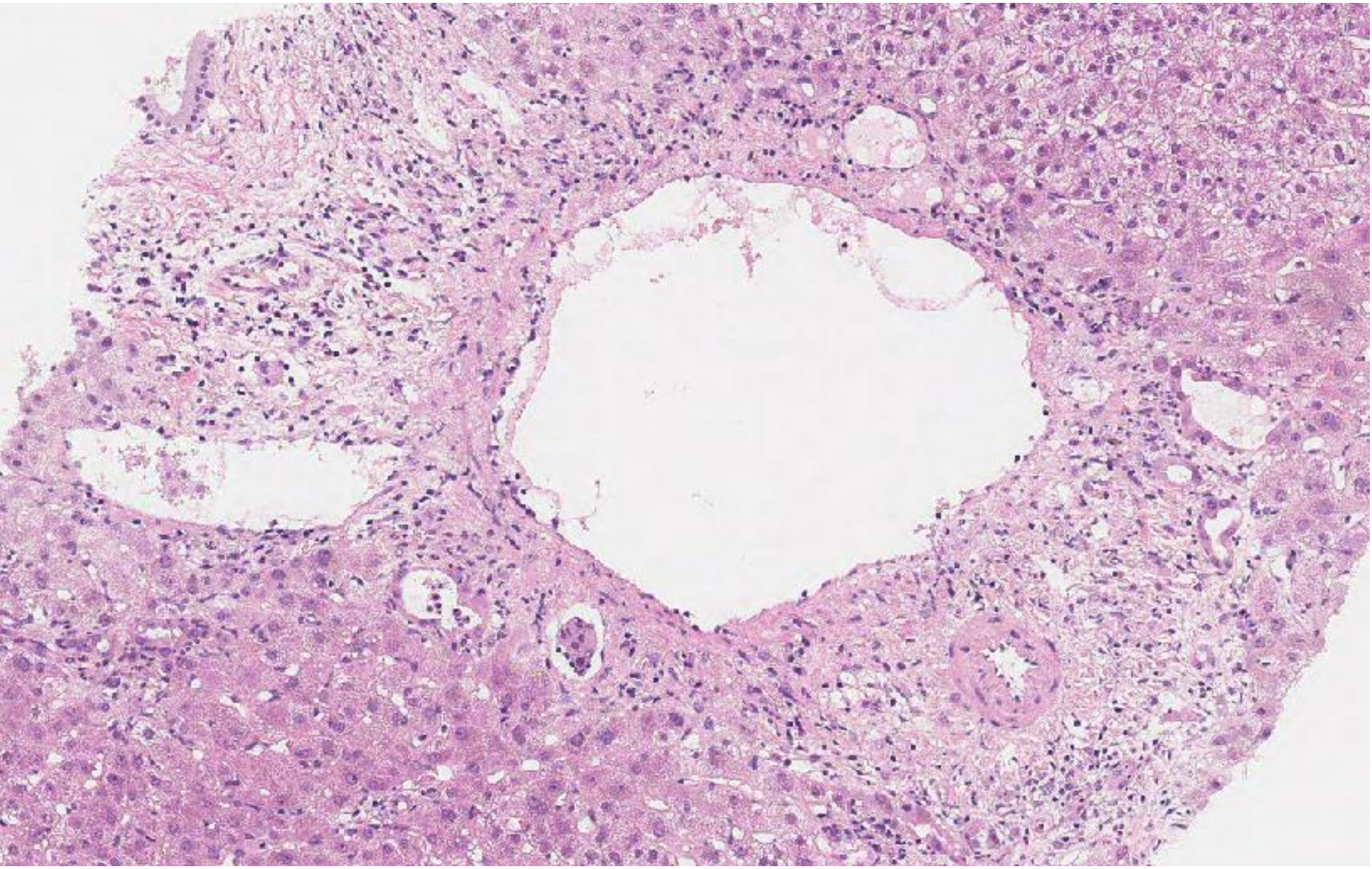


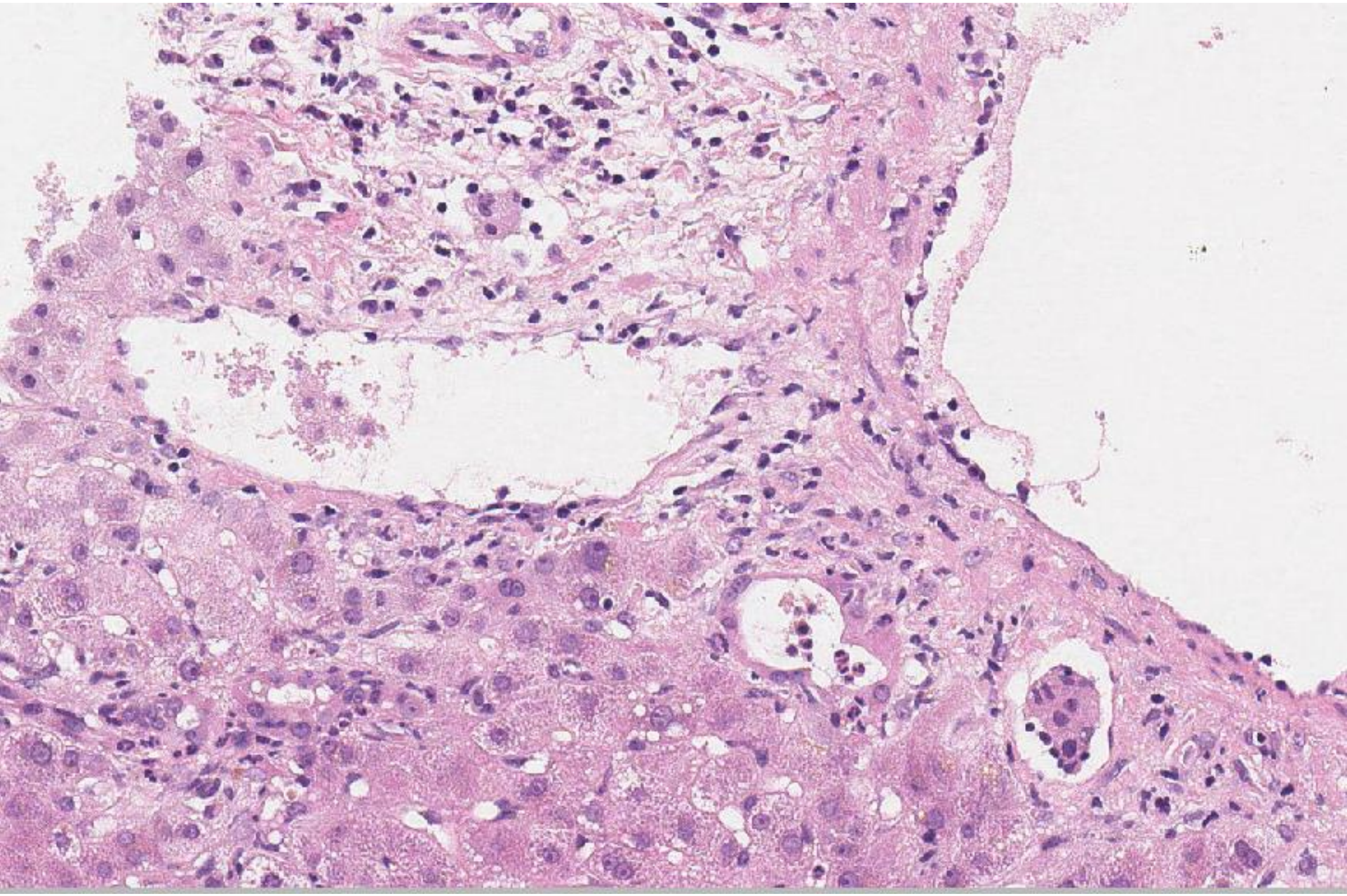


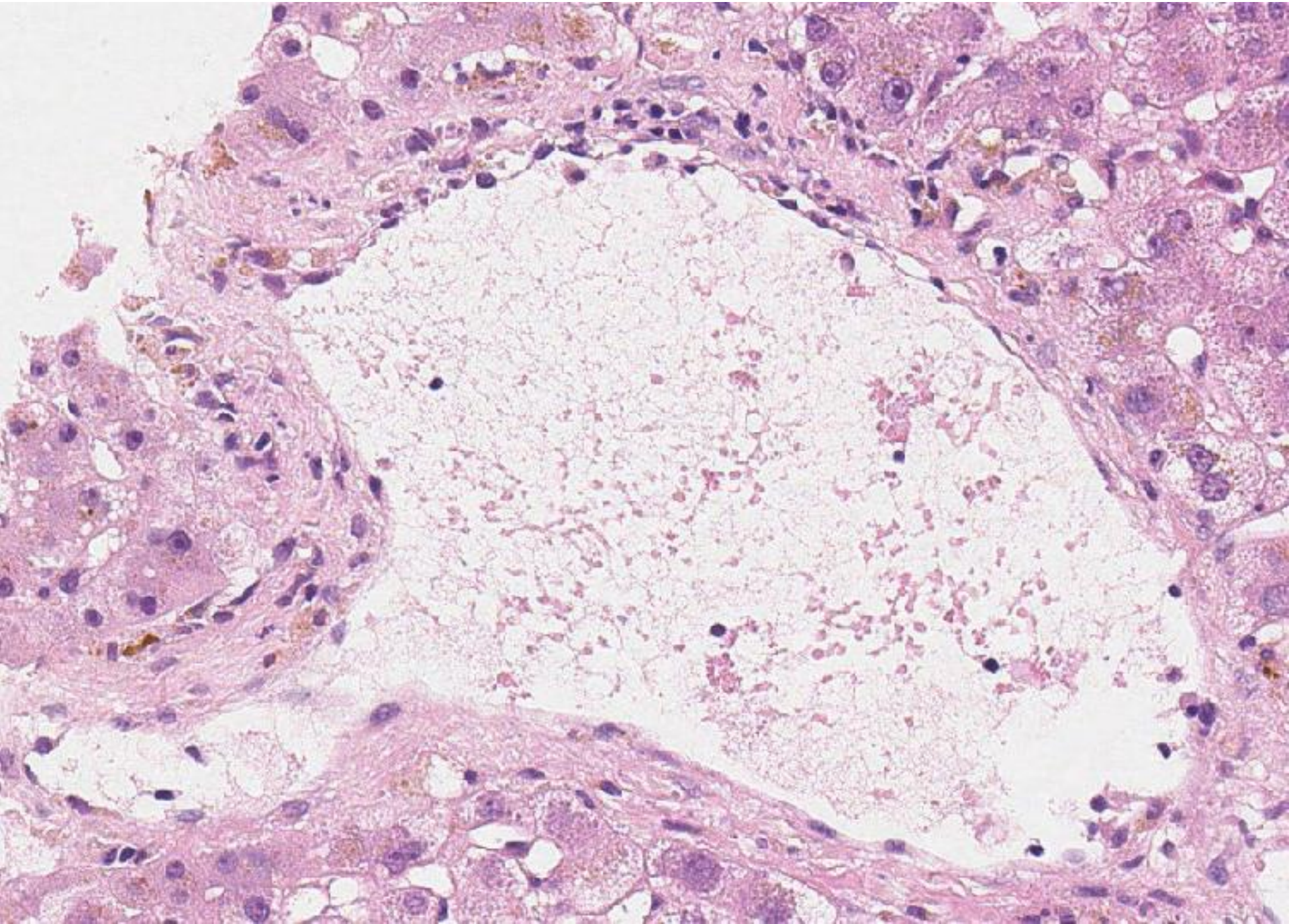


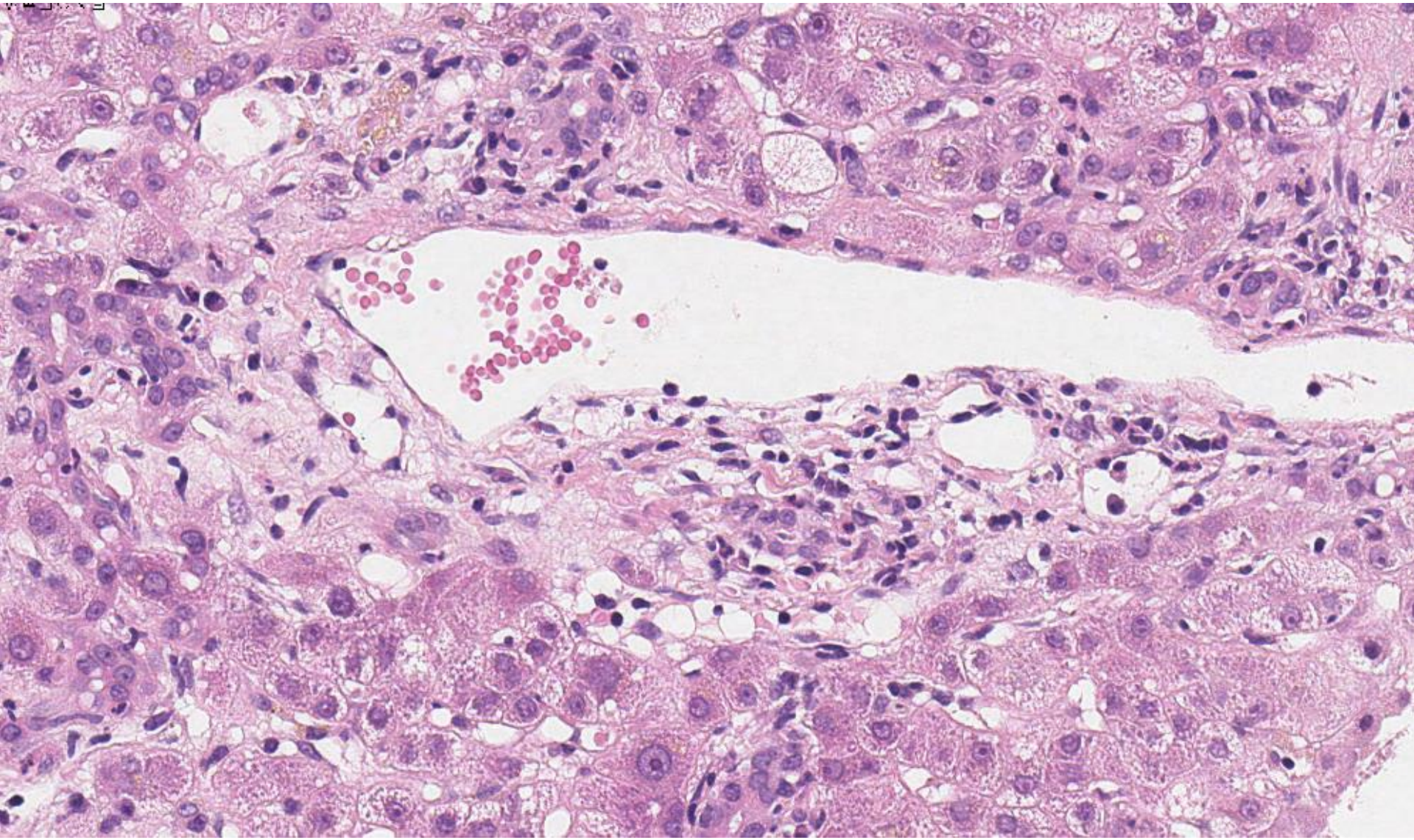
No positivity in hepatic vein or perivenular sinusoidal endothelium

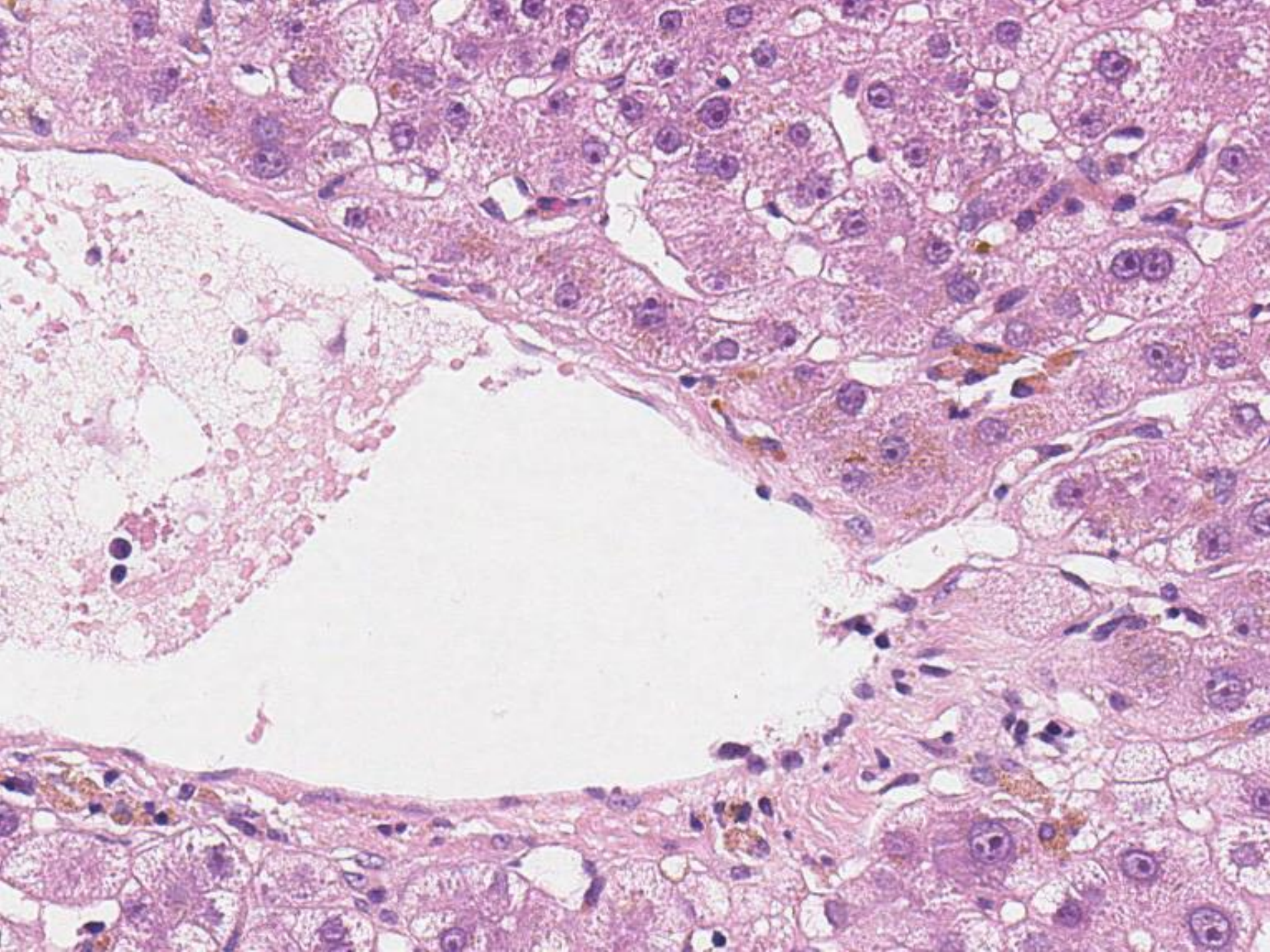


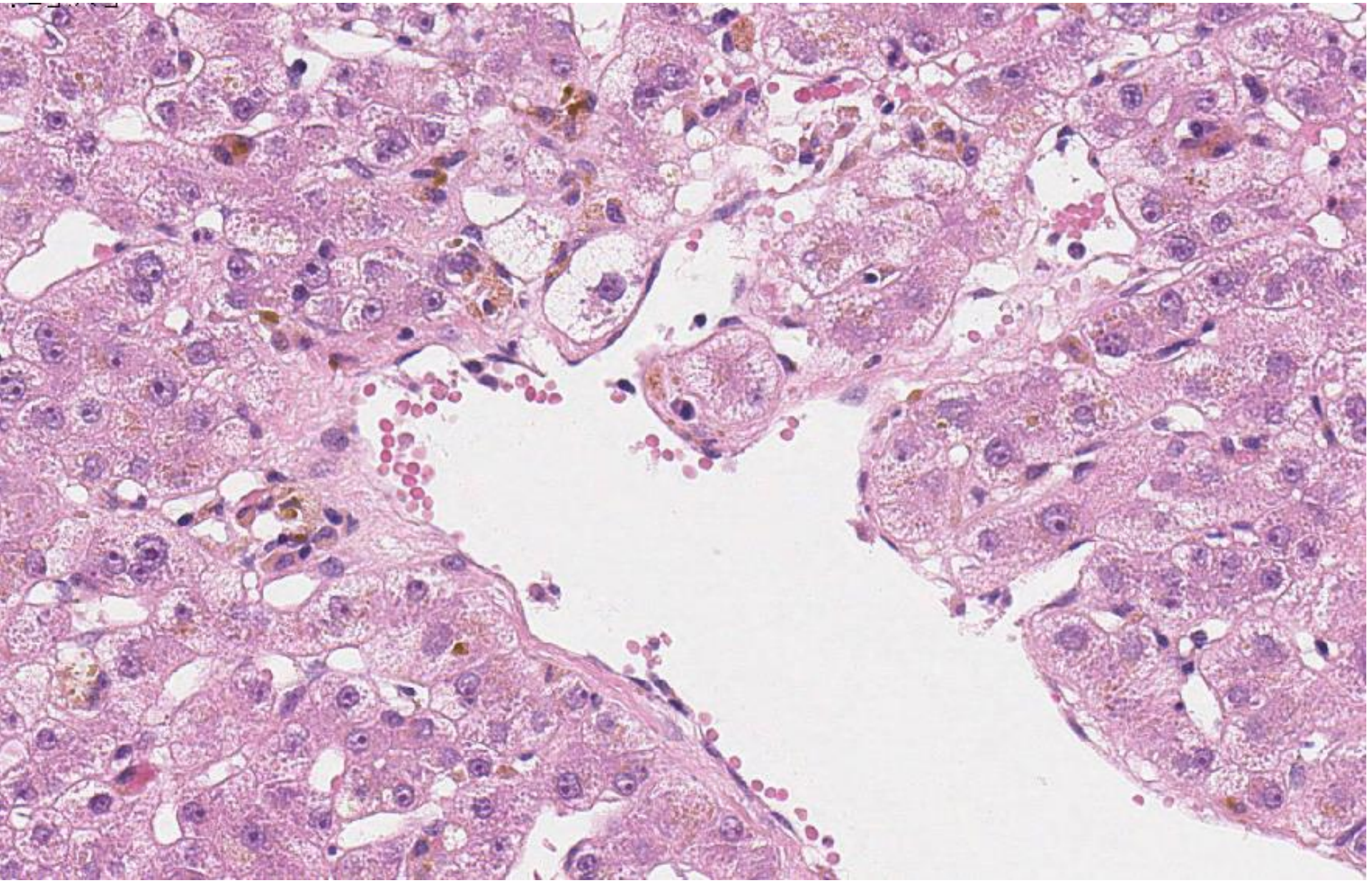












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AMR in ABO-compatible allografts:

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- Deranged LFTs with recent MRCP ruling out an obstructive cause with patent vessels.
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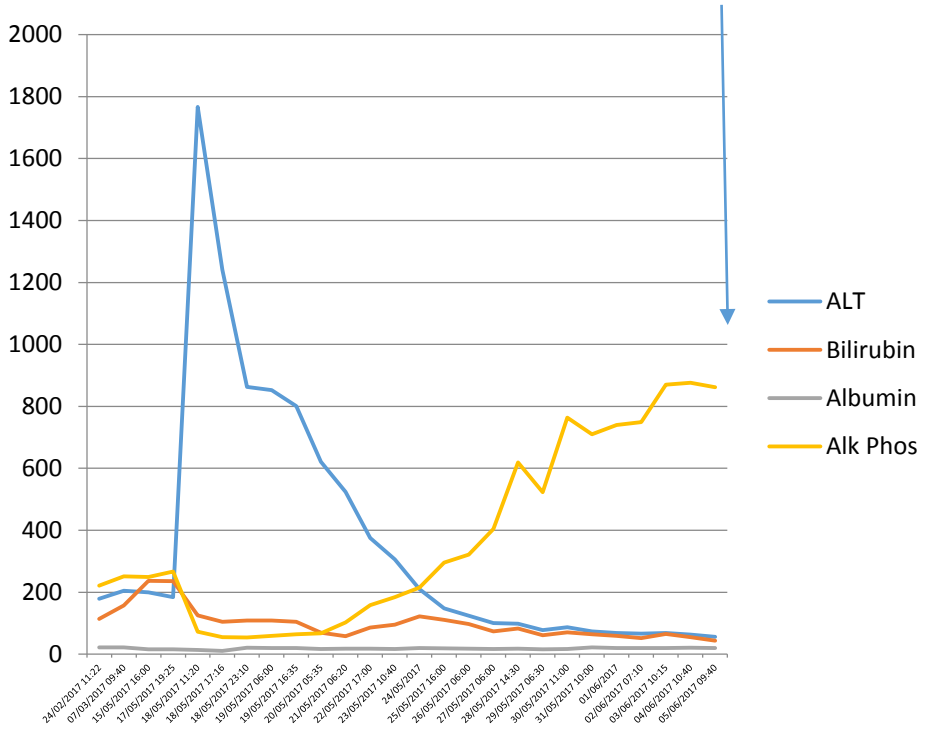
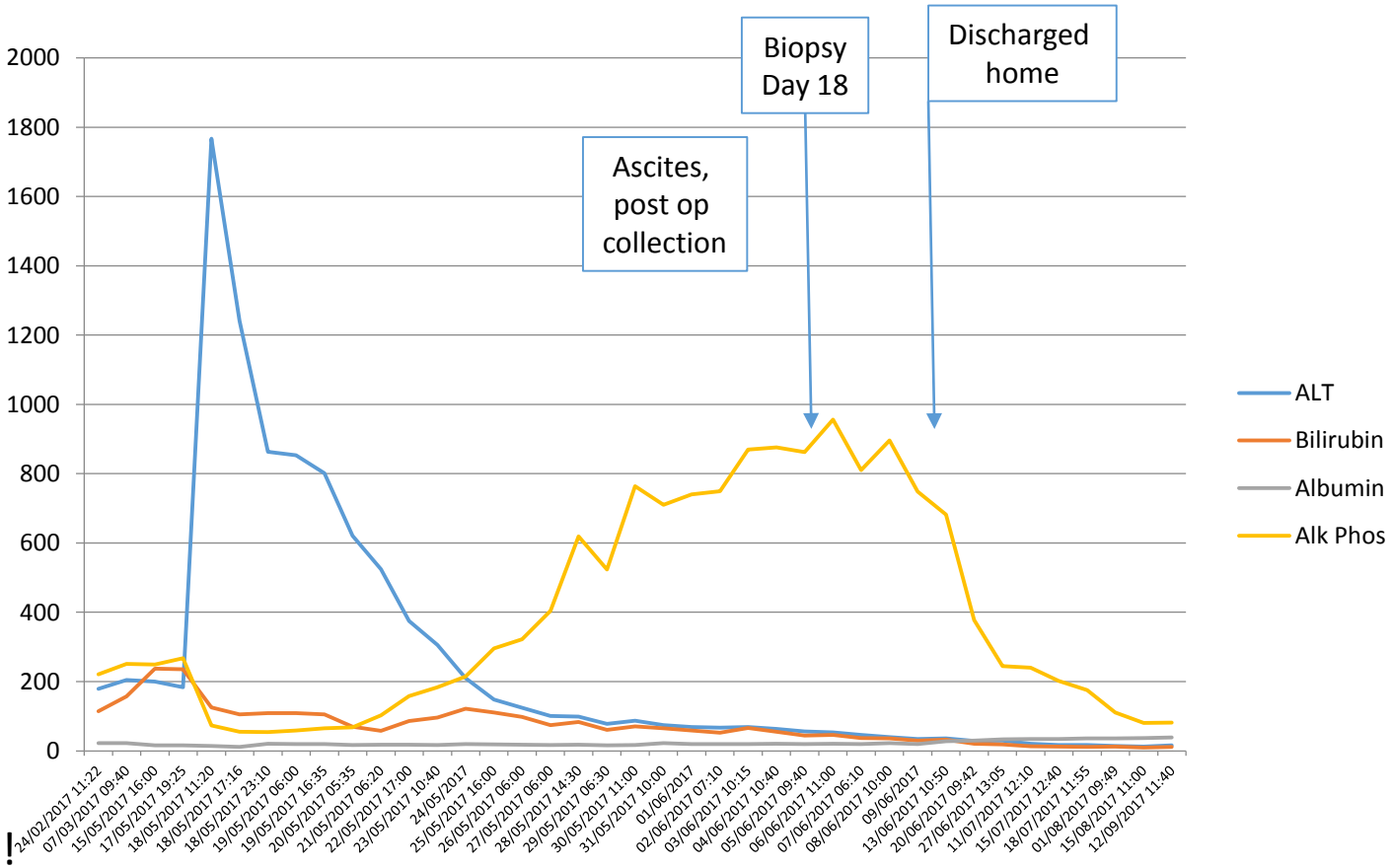


Leeds case. Biopsy day 18 post transplant

What happened next:

Decided against ERCP, discharged 4 days later,

Uneventful follow up.



Date of LFT

– non-linear scale!

Experience of C4d in Leeds?

- Word search of CoPath for 'C4d' since Jan 2014
  – mentioned in 37 biopsies from 32 patients (but not the case presented – so doesn't find all cases).

- Of these, 6 reported C4d +ve
  (time post Tx 6d,7d, 8d, 24d, 1m, 72m).

- Of these, 2 had DSA+ve (6d and 1m),
  1 DSA –ve, 3 not tested.

- One other DSA+ve tested on day 9, not C4d endothelial +ve but lots in Kupffer cells.

  Tx for acute hepatitis. Retransplant for haemorrhagic necrosis but died post re-transplant.

specnum_formatted	pathologist	post Tx	C4d	diagnosis	HLA Ab %	DSA	comment
LH14-141	JW	2m	-	resolving acute rejection	2		HLA C1 (IgG)
LH14-907	DT	8m	-	late ac rejection			
LH14-2435	OR	8d	+	ACR 8-9/9			
LH14-4633	DT	5m	-	perivenulitis	1		class II, PRA IgG, HLA DQ A1....
LH14-11659	DT	3m	equiv	min non-spec (age 1)			neg
LH14-13207	OR	7d	+	ACR			not tested
LH14-16296	JW	6d	-	ACR inad for grade	7		class 1 4% HLA DQ7 is a DSA
LH14-18788	DT	20m	-	improving rejection, bridging necrosis			
LH14-22389	JW	4m	equiv	cholestasis ? FCH	0		HLA not detected
LH14-24142	JW	4m	equiv	cholestasis, acute rejection, C4d not endothelial	21		class II 21%
LH14-43276	OR	6d	+	severe endotheliitis	40%	DSA	class I 22%, class II 40% - around 6 different HLAs
LH14-44592	JW	14d		improving rejection byt ALT increased during methyl pred also perivenular necrosis			
LH14-46378	DT	24m	-	infl and necrosis, probably rejection			
LH14-52281	JW	2m	-	11 days after prev biopsy, ongoing rejection			not detected
LH15-2751	DT	7d	inad	ACR 8/9, small biopsy			
LH15-2879	DT	3m	-	perivenulitis			
LH15-6654	JW	72m	+	early chronic rejection			
LH15-10826	DT	9d	-	necrosis and mild rejection - ? Re-transplanted	8	DSA	HLA B8, DSA
LH15-33954	DT	explant	req	haemorrhagic necrotis, histology thrombotic microangiopathy. DSA said to be +ve in histology reprot			DSA -ve in immunol report - but said to be +ve in histo report
LH15-34717	JW	7m	-	perivenulitis, NRH			
LH15-38180	DT	4m	-	perivenulitis			HLA -ve
LH15-40124	JW	8m	equiv	ACR 7-8/9			none detected
LH15-44961	JW	24d	+	lobular hepatitis, not features of acute rejection	2		does not include DSA
LH15-53734	OR	12d	-	ACR 6/9 and necrosis, no respnse to Rx			
LH15-54732	JW	17d	-	still rejection, cholestasis, duct inflammation			
LH15-56791	OR	1m	equiv	increasing cholestasissick ducts, C4d questionnable in CPC comment	12	?	class II HLA DQ3
LH16-29939	JW	1m	-	ACR 5/9	3		HLA class I
LH16-32038	DT	1m	+	ACR 6/9 and necrosis, no respnse to Rx	38	DSA	class I 38%, HLA DQ [illegible] on 4/8/16 - retested
LH16-33116	JW	1,5m		improved but still hepatic vein endotheliitis	46		DSA not detected, 46% class I, 11% class II
LH16-34114	JW	3m	-	acute rejection, perivenulitis, PT oedema			none detected on 05/08/16
LH16-35954	OR	4m	-	improving, BD injury	10		all class II, no donor HLA available, on 11/08; also 10% on 19/08/17
LH16-49815	DT	10d	-	ACR 6/9 and necrosis, no respnse to Rx			
LH16-52012	DT	96m	-	recent 8/9 rejection, improved but chronic rejection			
LH16-56816	DT	5d	-	bilirubinostasis, ? Sepsis - subsequent biliary stent			not tested - wrong tube used
LH17-1793	DT	28m	-	multiacinar necrosis, ? Cause	11		class I, no DSA
LH17-13202	JW	14d	-	cholangiolitis, with differential diagnosis plan MRCP			
LH17-27817	JW	24d	-	ACR has improved, C4d -ve both biopsies.			

C4d +ve

DSA +ve

DSA not tested

C4d -ve

AMR Case 1

Haemorrhagic necrosis

AMR Case 2

Experience of C4d in Leeds?

Two patients with diagnostic criteria for acute AMR

Case 1: KS Oct 2014, 35F transplant for PBC.

Day 6, Banff 7-8/9 acute cellular rejection, with very severe hepatic vein endotheliitis. Received 5 days methyl pred, and increased other immunosuppression.

- re-biopsy day 14, portal inflammation resolved but hepatic vein endotheliitis still prominent.

Discharged on enhanced immunosuppression. Good post transplant course.

Experience of C4d in Leeds?

Two patients with diagnostic criteria for acute AMR

Case 2: LS July 2016, 49F, transplant for PSC.

Known to have preformed class II antibodies, which prevented live donor from her husband. Right lobe graft, DBD.

Did well, discharged at 3 weeks on enhanced immunosuppression.

One week later ALT rising, after MMF lowered for side effects.

day 30 biopsy: acute rejection 6/9, with necrosis, no biochemical response to treatment.

Re-biopsy day 37, improved but still hepatic vein endotheliitis.

Diagnosis: acute TCMR and AMR – maintain goodmmunosuppression.

ALT was 16 on day 55 and has not been raised since.

Experience of treating AMR in Leeds?

- No patient has had plasmapheresis or retuximab
- Steroids and enhance triple immunosuppression
- We are not aware of any lost grafts as a result.
- Only two patients fulfilling all three criteria for AMR

= histology, C4d, DSA

Both responded to increased standard immunosuppression and remain well at 35m and 15m.