Histopathology Workshop
Liver Pathology

RCPath April 5th 2019

Medical liver biopsies
Cases for Discussion

Dr Jl Wyatt

Histopathology Workshop
Liver Pathology

Where have we got to?

Stefan Hubscher – liver tumours

Sue Davies – medical biopsies

– biliary and fatty

Judy Wyatt – medical diseases

– acute and chronic hepatitis, vascular

JIW 1 43/M

Acute hepatitis presentation

- Mr DB 43M, caterer
- Fit, runs with dog,

- February 2012 – cough, congested feeling,
- Diagnosis ? Reflux, prescribed lansoprazole
- 4 weeks later lethargy, nausea, no fever

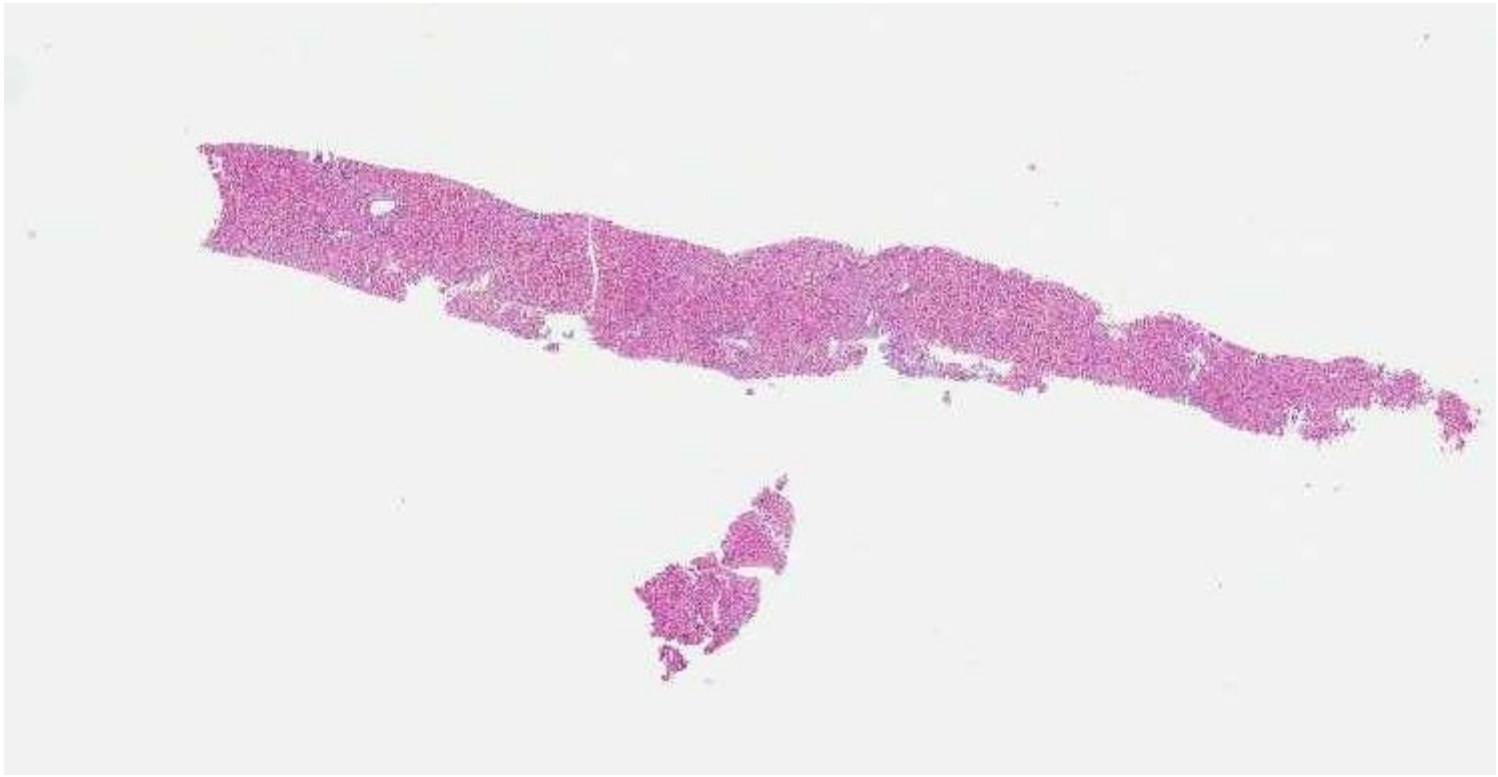
- ALT 3714 (X 93 ULN) Alk phos 301 (= ULN)
  bilirubin 92
- Viral serology, autoantibodies –ve, IgG 9.4 (6-16)

JIW 1 43/M

Unwell for 1 week with lethargy, nausea. No fever. Deranged LFT (ALT - 3407).

Ultrasound = normal liver

Liver screen - normal.



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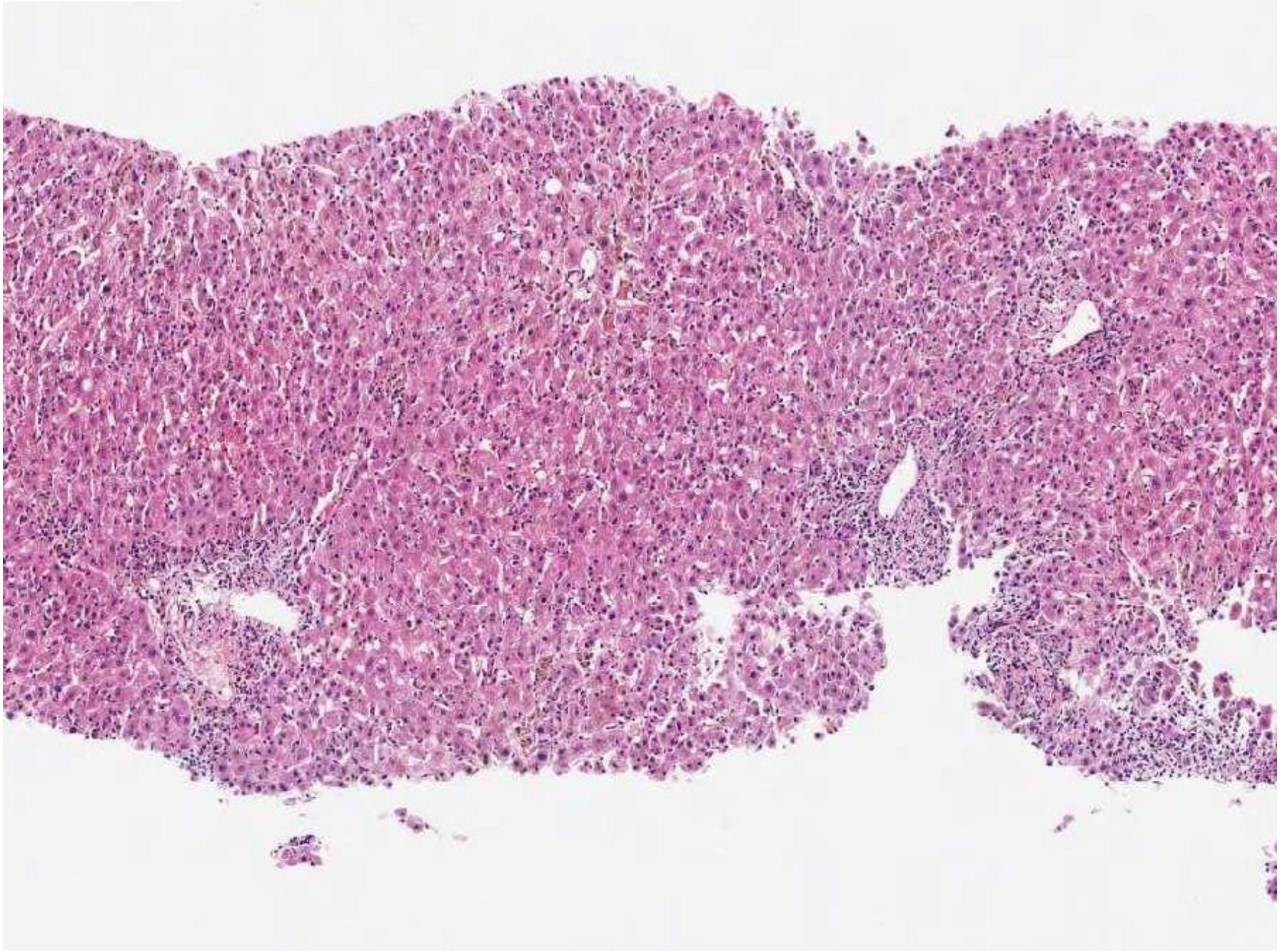

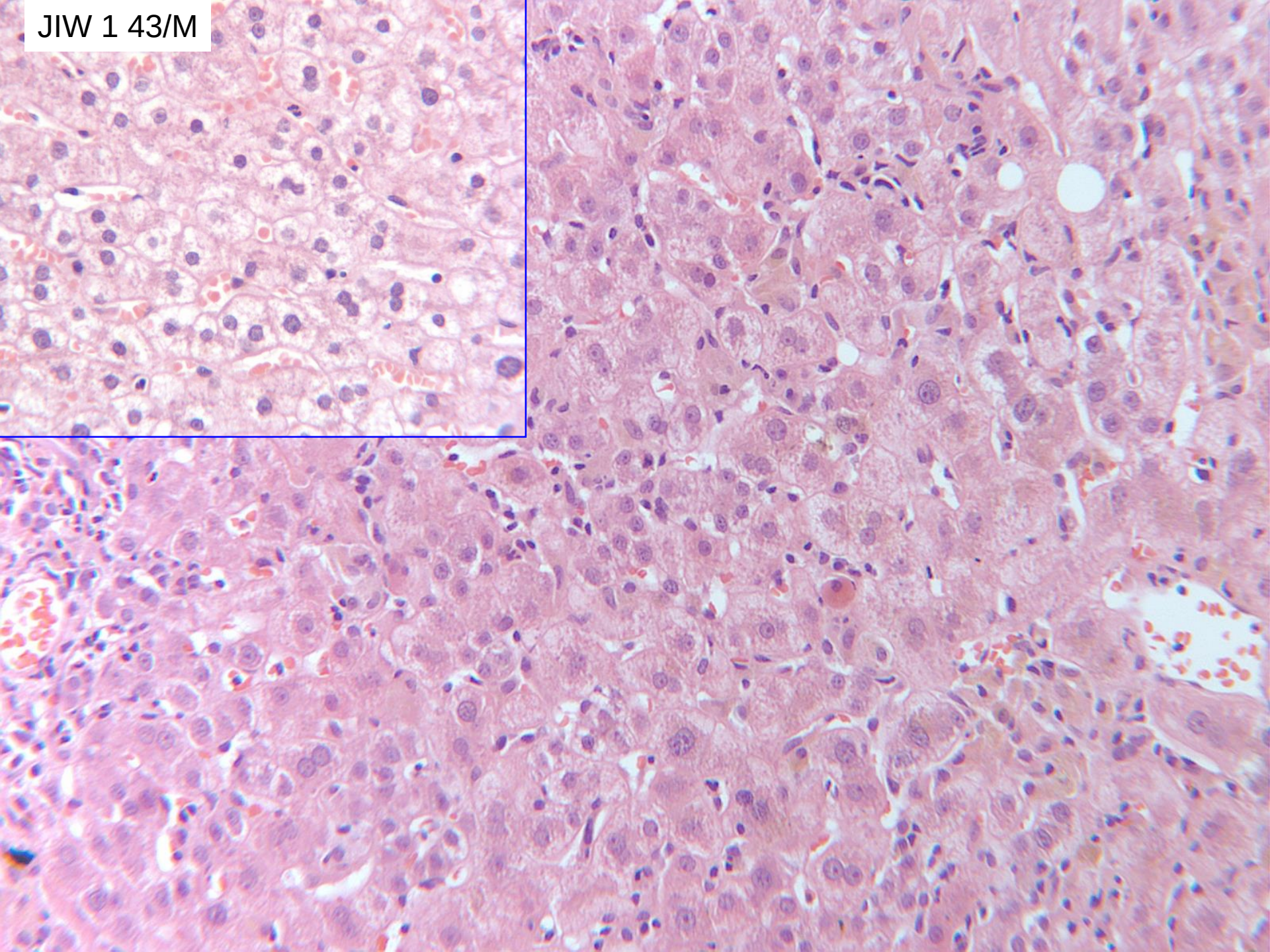
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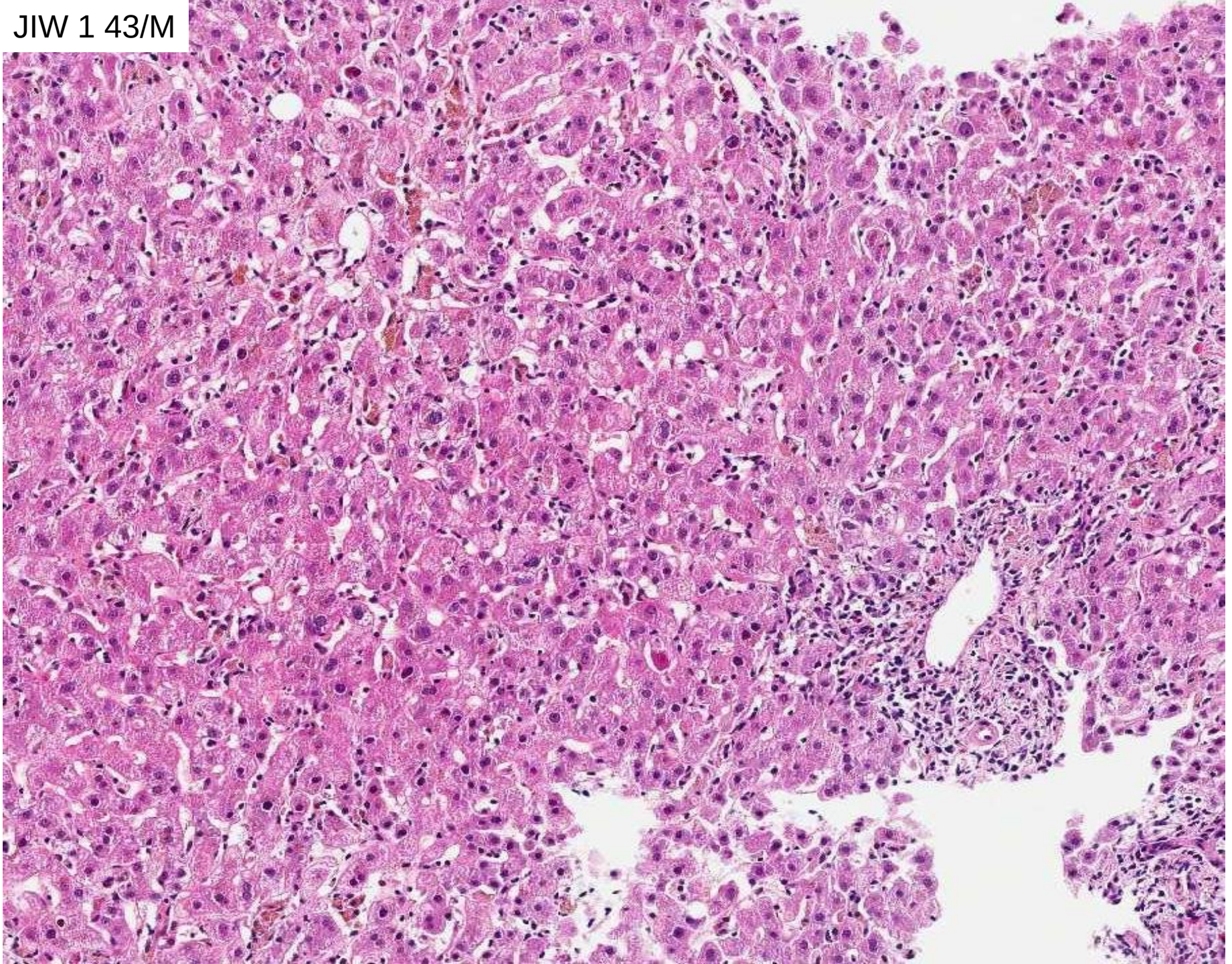
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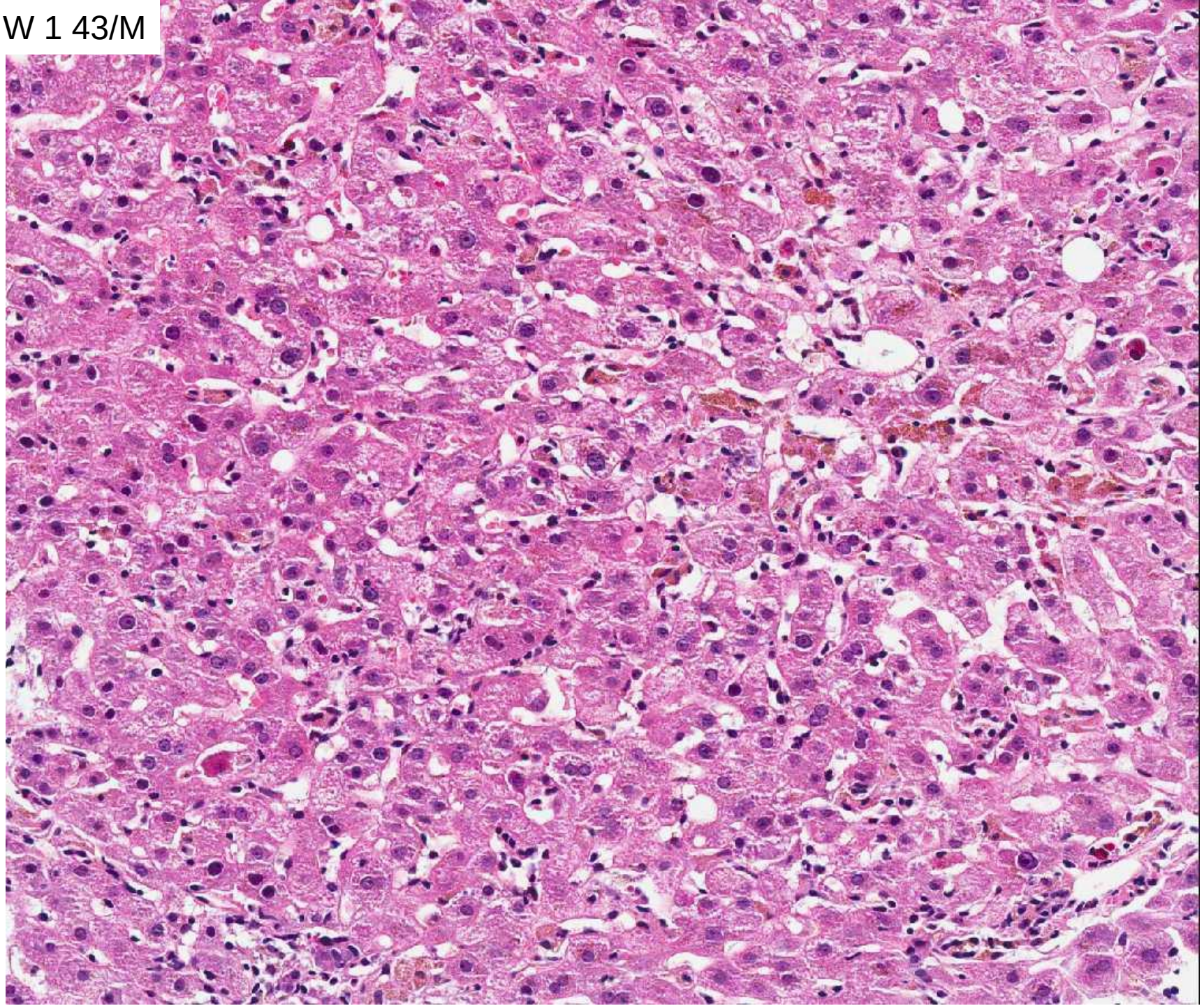

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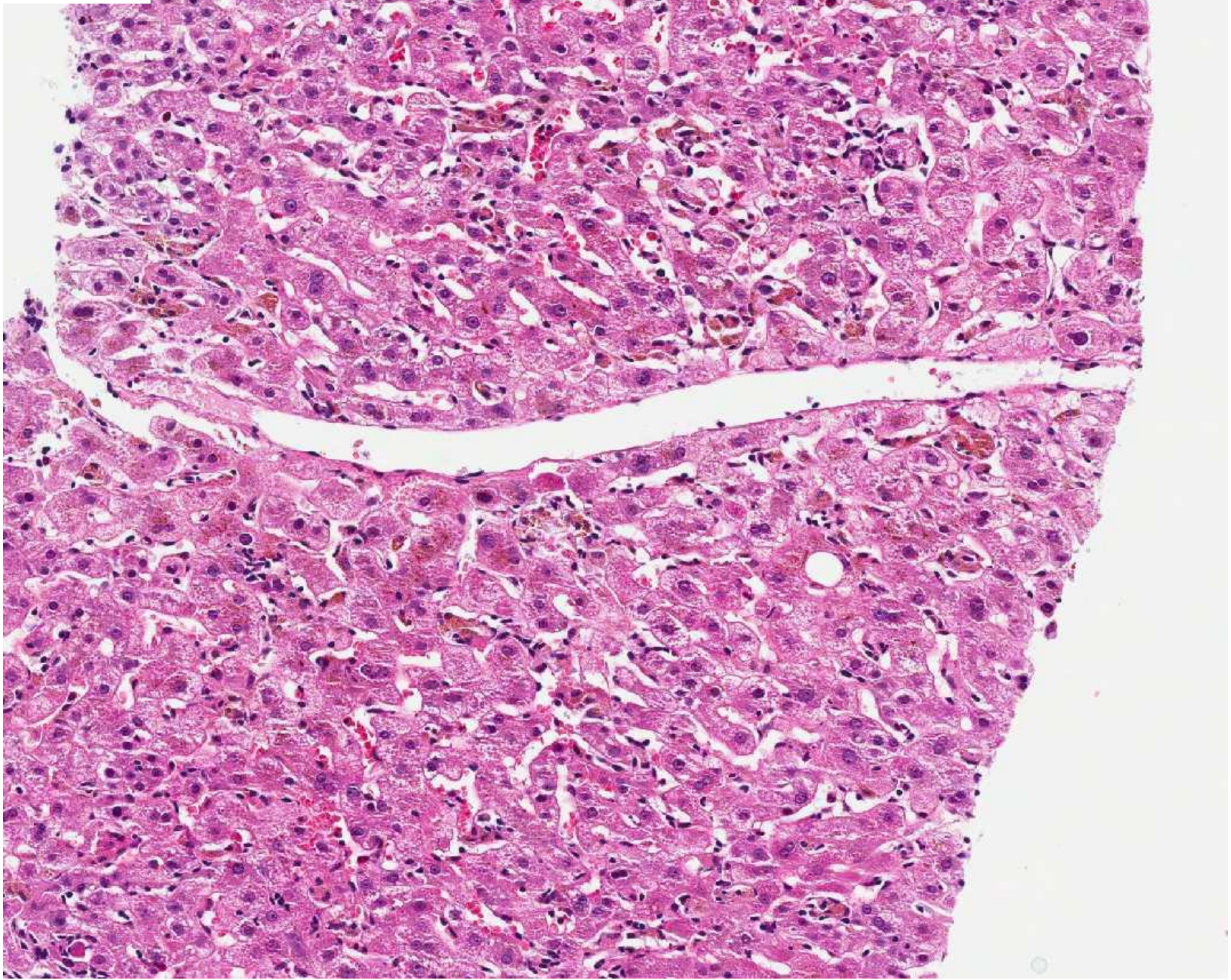

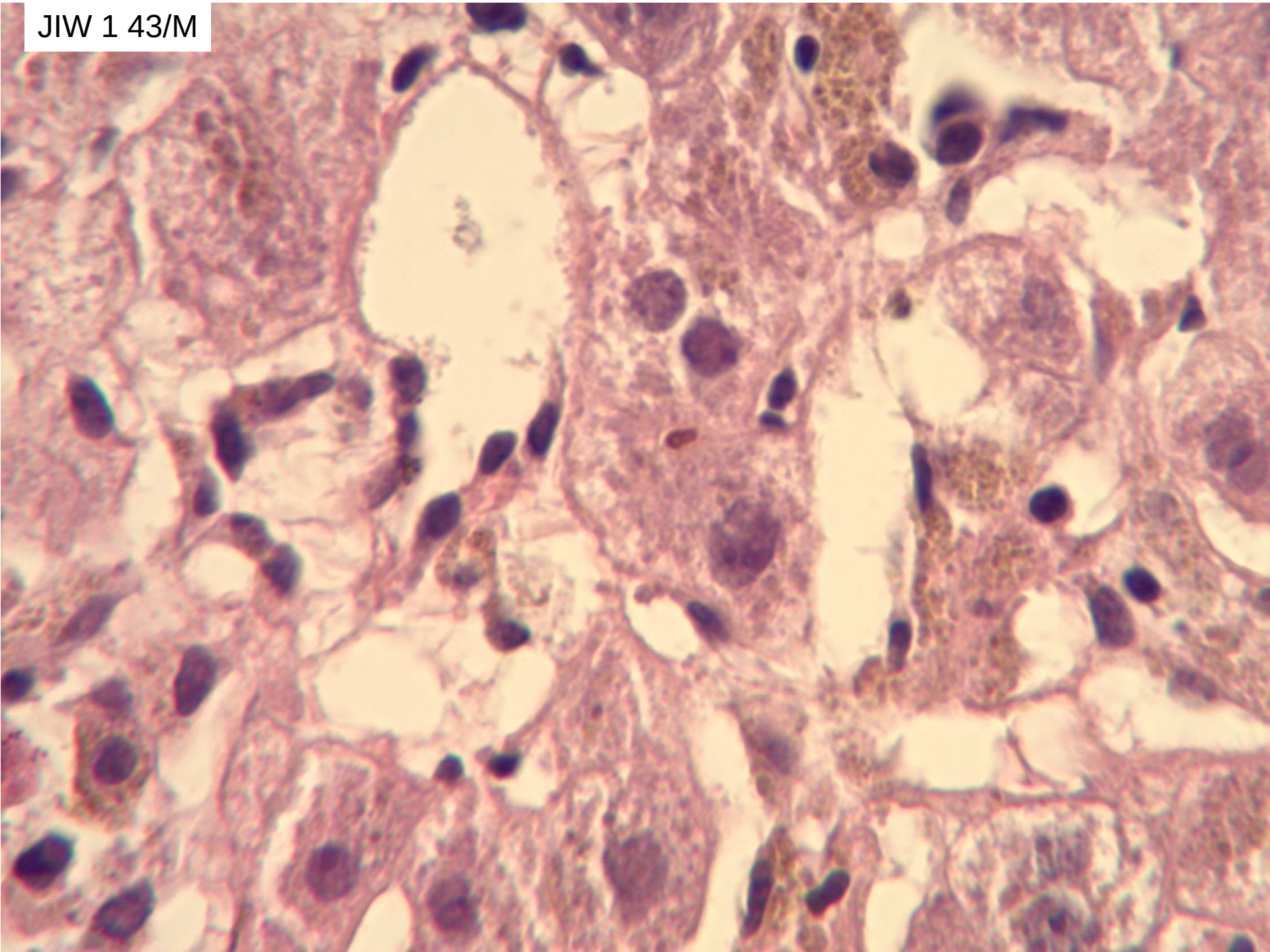
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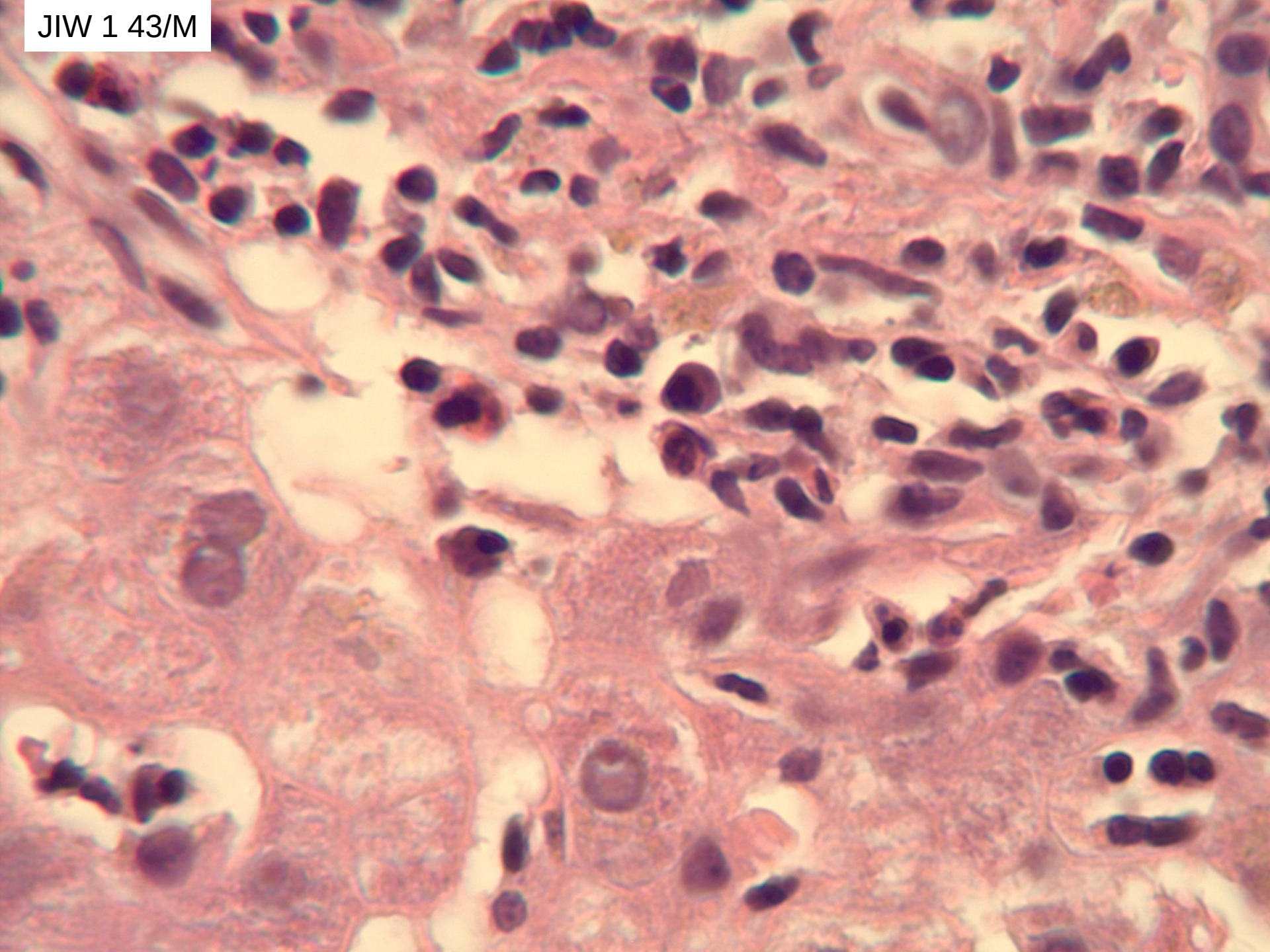
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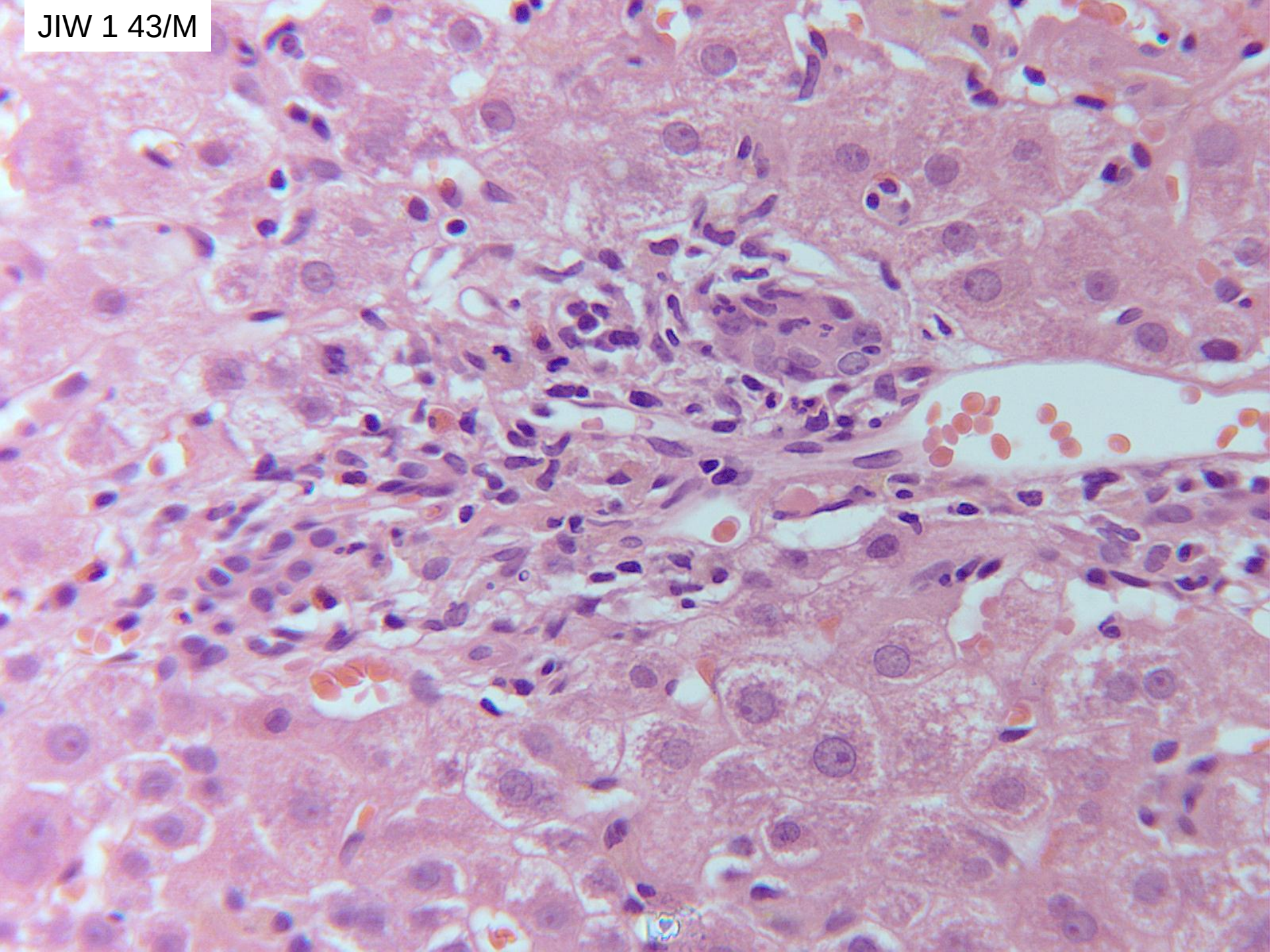
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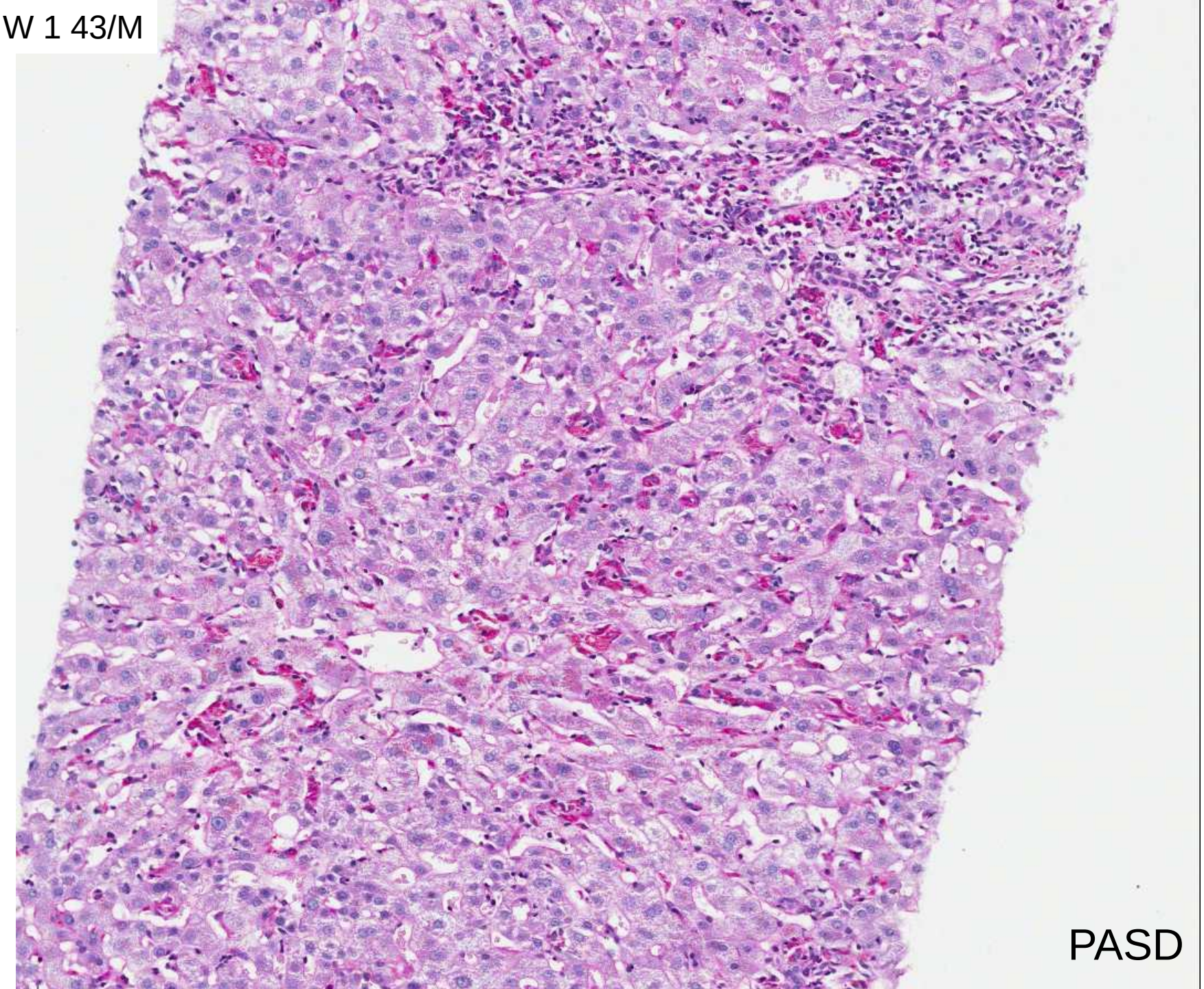
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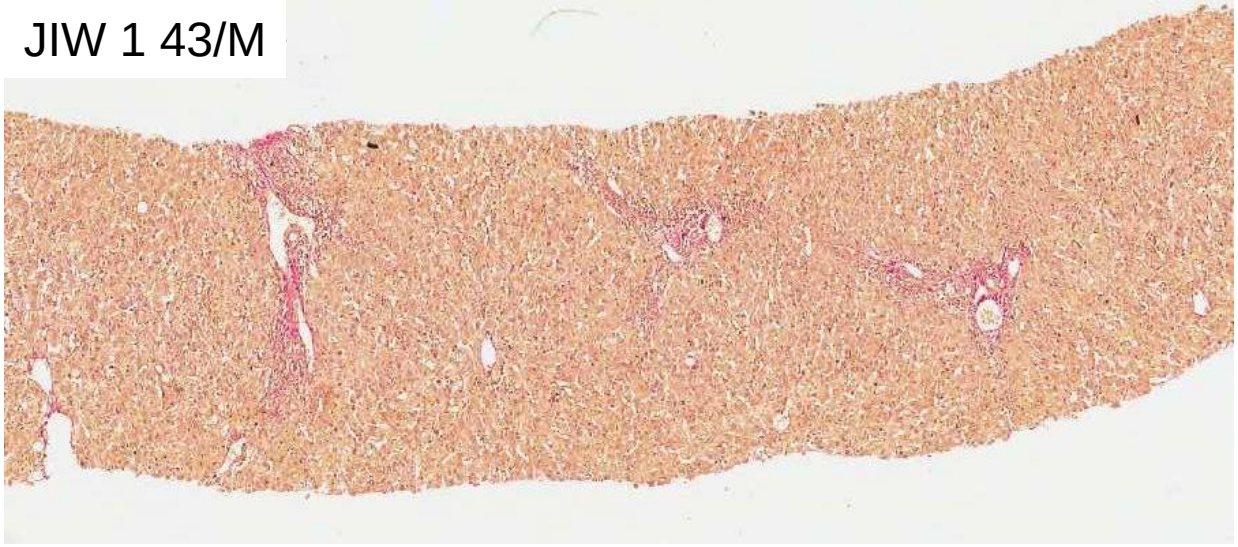
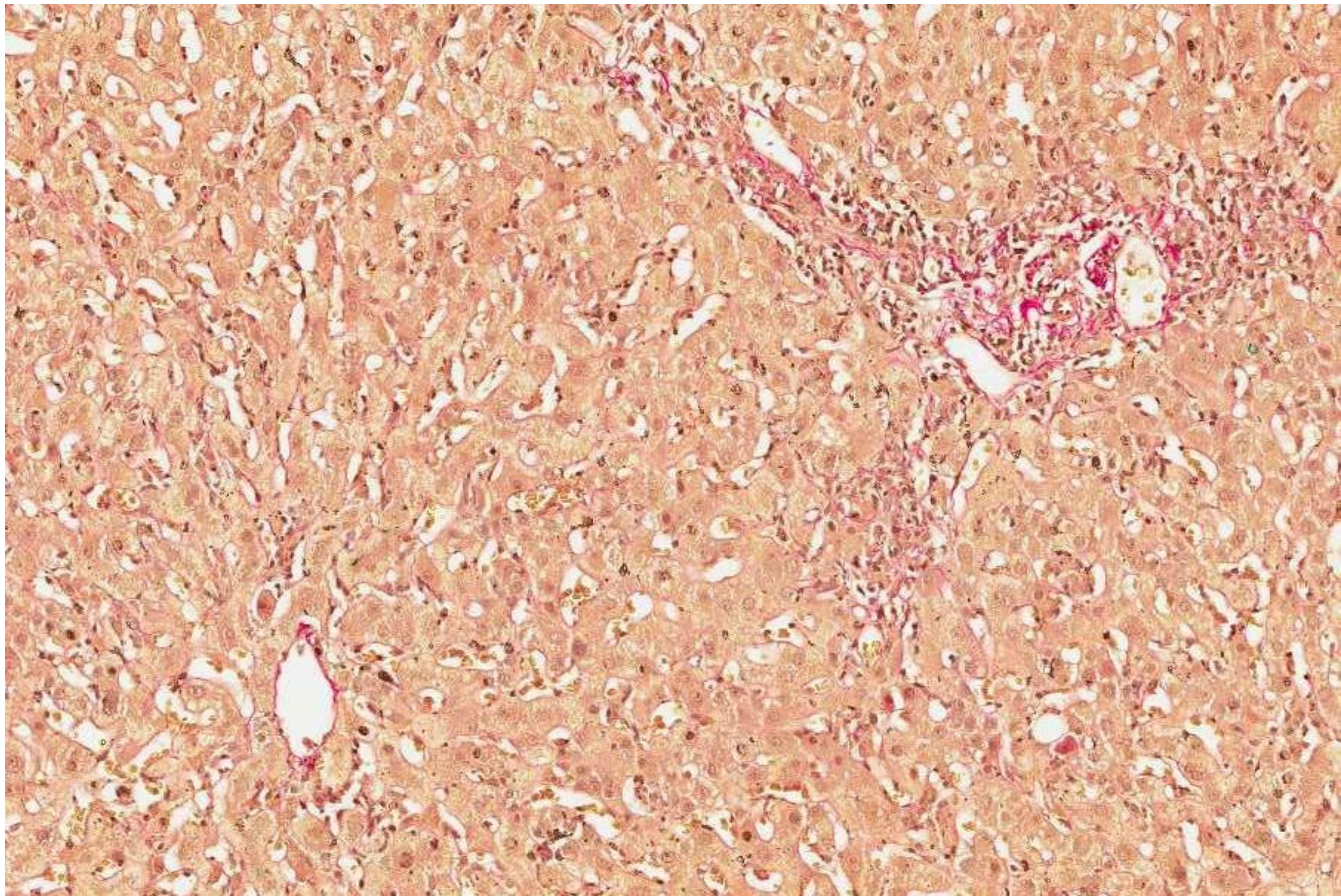
JIW 1 43/M





Sirius Red

JIW 1 43/M

Unwell for 1 week with lethargy, nausea. No fever. Deranged LFT (ALT - 3407). ultrasound = normal liver Liver screen - normal.

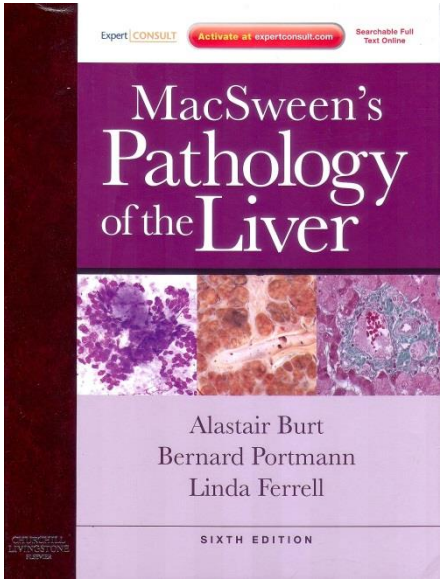
Comment: This liver biopsy shows features of cholestatic hepatitis without confluent necrosis, with mild portal inflammation that includes both plasma cells and eosinophils.

The differential diagnosis includes viral hepatitis, autoimmune hepatitis and drug induced hepatitis.

Diagnosis: acute cholestatic hepatitis

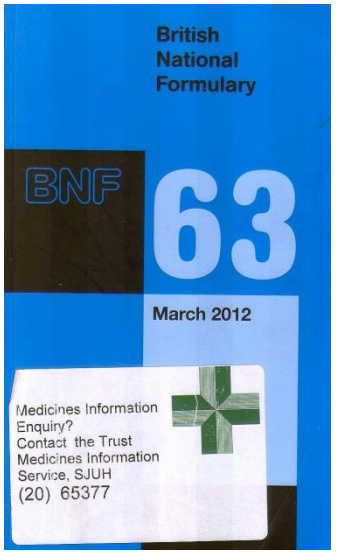
Patient had taken lansoprazole – ? Cause of hepatitis.

JIW 1 43/M



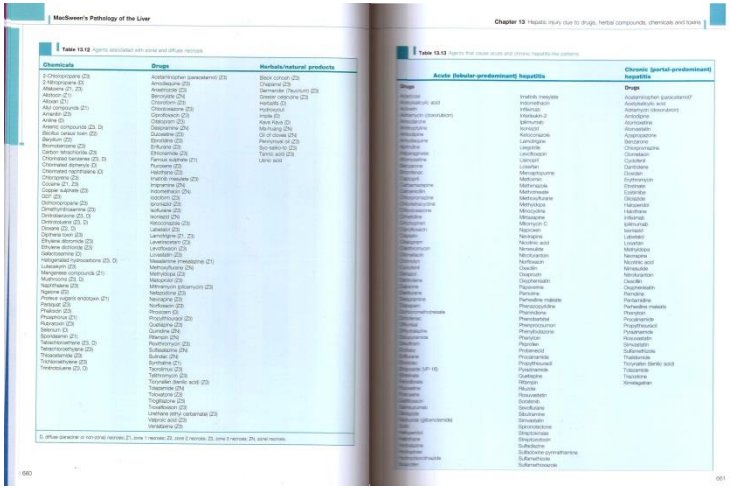
Lansoprazole?

Clinicians thought unlikely but



'at least two cases of hepatotoxicity related to omeprazole have been reported'

'other side effects of PPIs reported rarely or very rarely include …
….hepatitis, jaundice, …..



Reporting DILI
-under-reported for common drugs
-over-reported for new drugs

- **Only a small number of cases of clinically apparent liver disease due to lansoprazole have been published and most have been anicteric and mild.**
- **In most instances, the time to onset was within 2 to 4 weeks and the pattern of enzyme elevations was hepatocellular or mixed.**

- **Clinically apparent liver injury due to lansoprazole, however, generally calls for prompt withdrawal of the agent.**
- **Severe injury is uncommon and most cases resolve promptly upon withdrawal.**
- **Cases of acute liver failure due proton pump inhibitors have been described, but they are exceedingly rare.**

What happened next?

- Treated with steroids,
- ALT fell rapidly then gradually to normal over next 9 months

  = steroid responsive seronegative hepatitis.

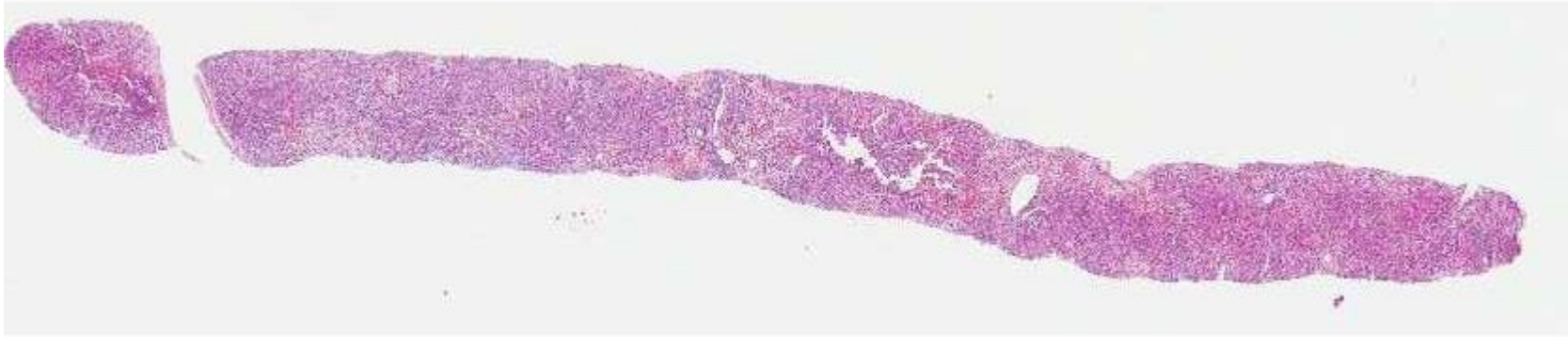
- Repeat biopsy because became SMA+ve but normal LFTs and Igs
- Biopsy near normal, some macrophages in portal tracts
- Remains normal LFTs over the next year without further treatment

JIW 2 26/M

Acute illness, unwell, lethargy, vomiting.
Bilirubin >250. ALT >3500.

Liver screen so far negative. Cocaine use over 4 months ago, nil recently. Has been having nurofen for headaches.

? cause of LFT disturbance.
History of high alcohol intake



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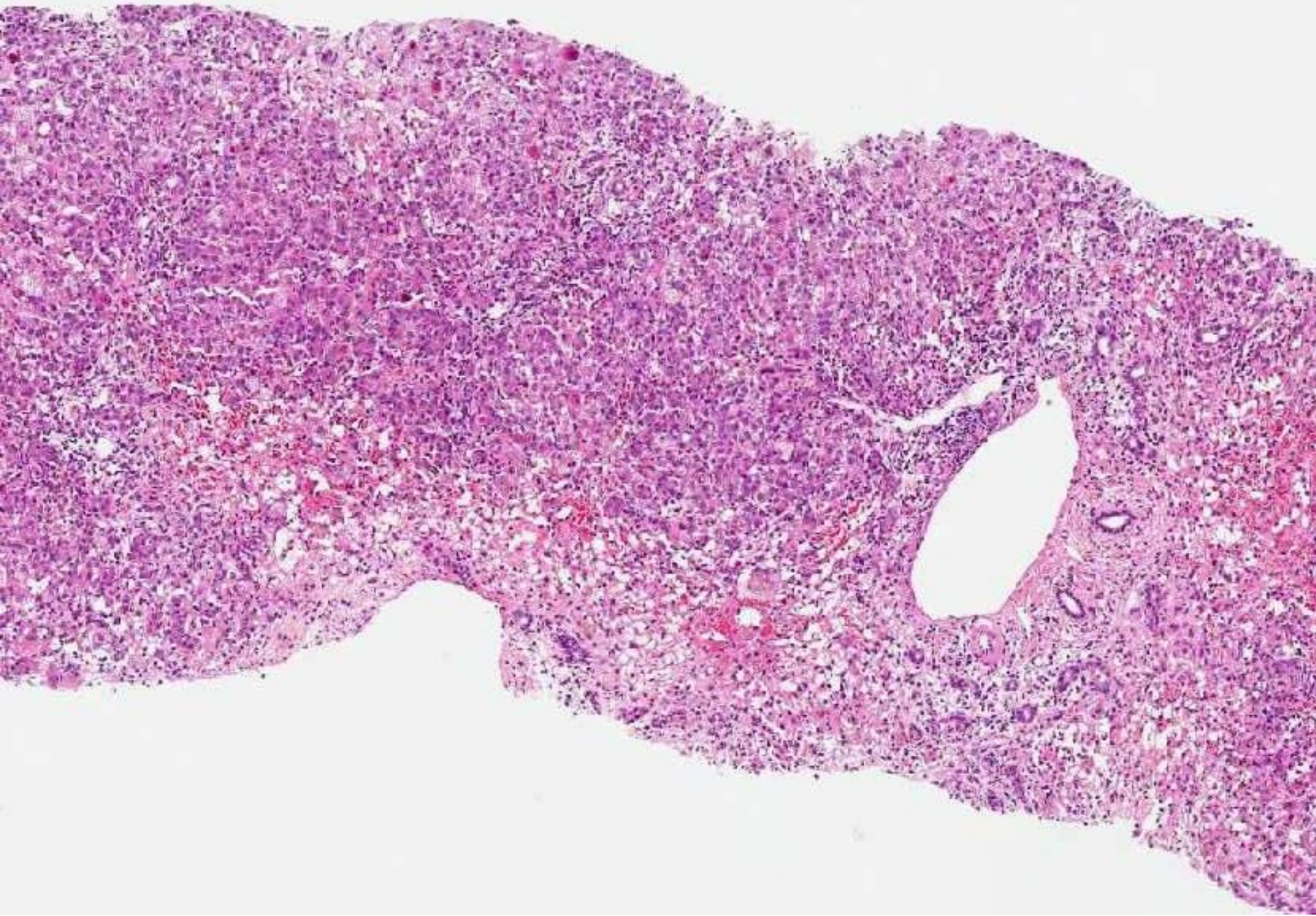

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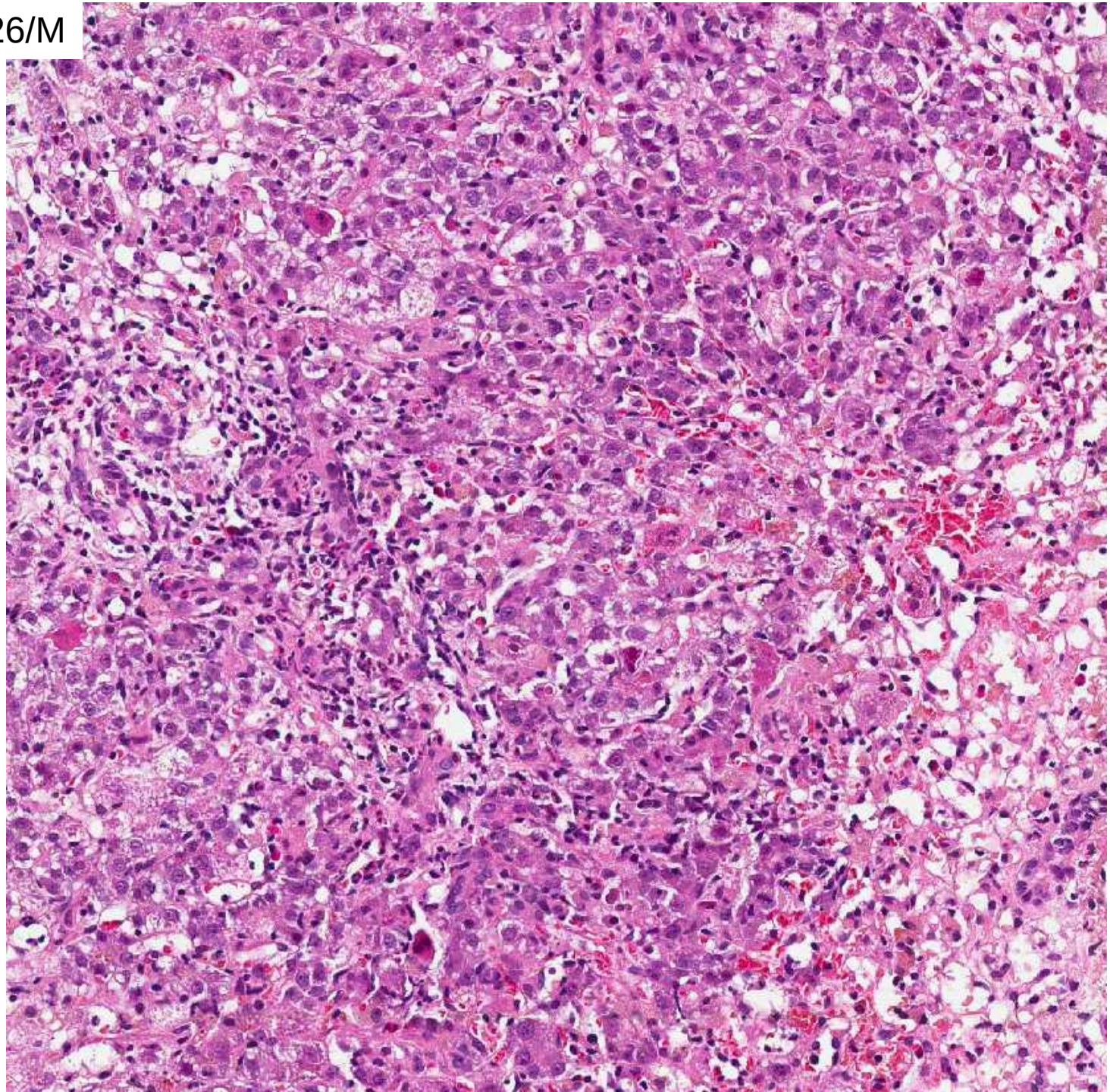

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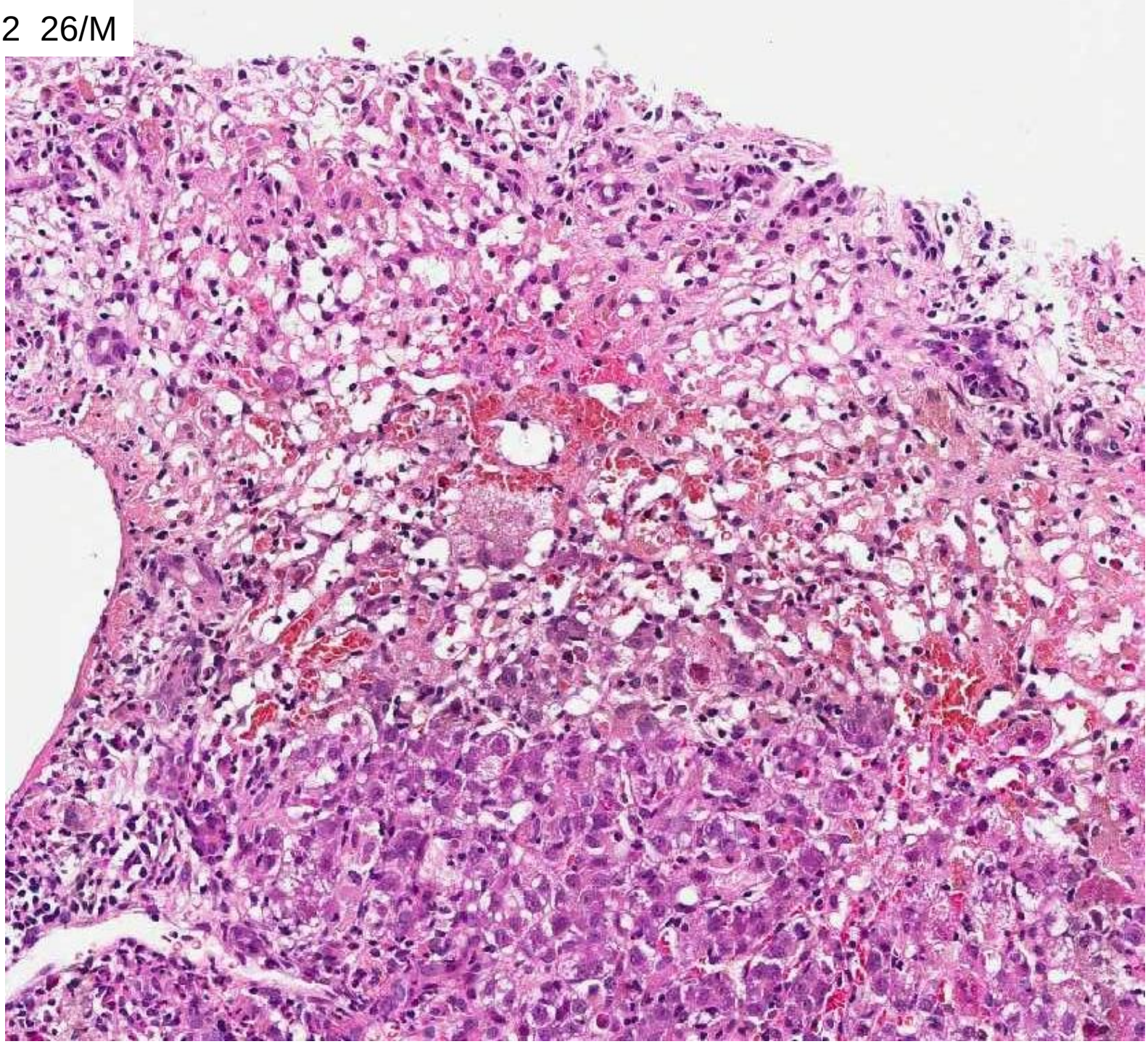

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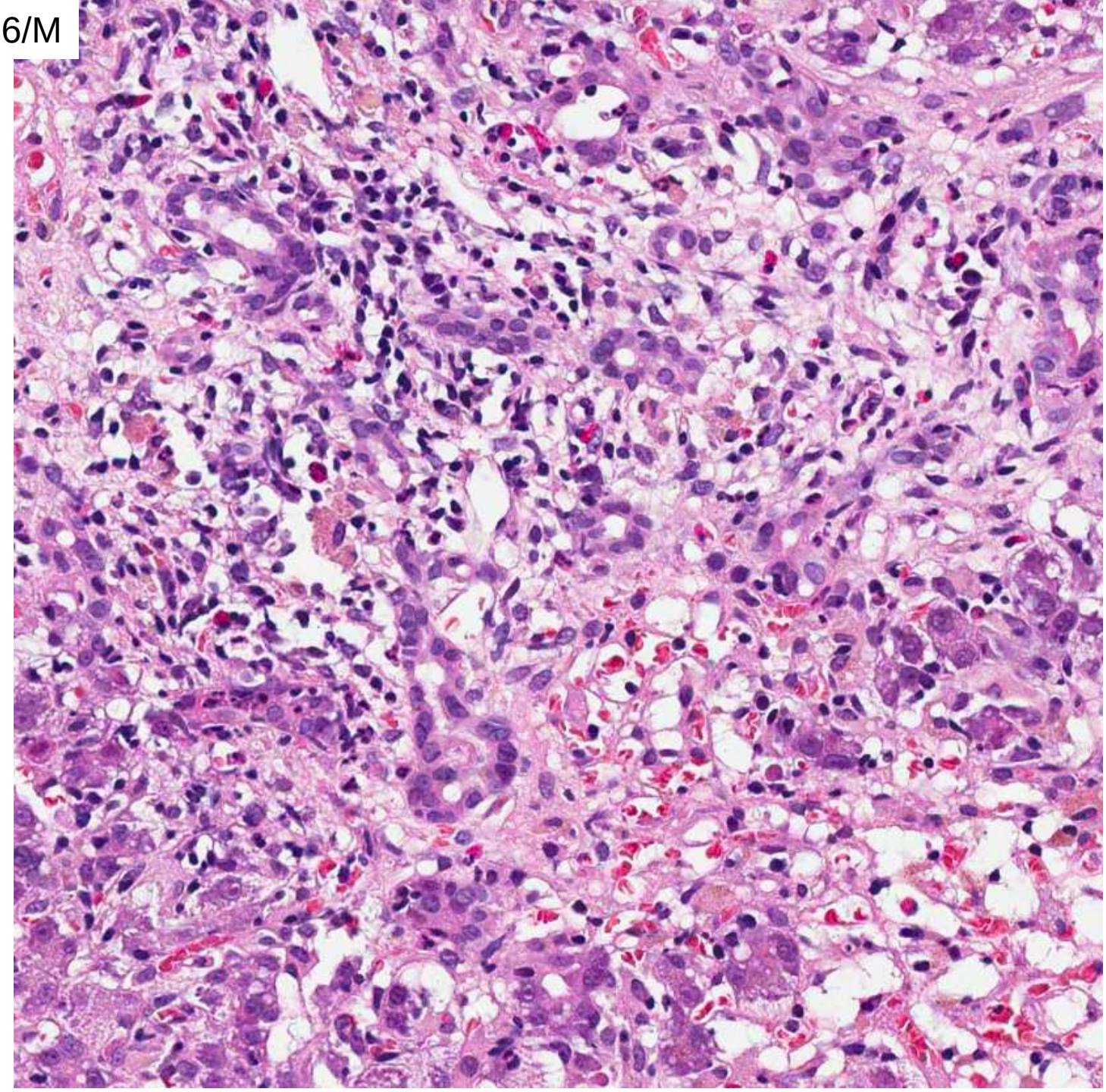

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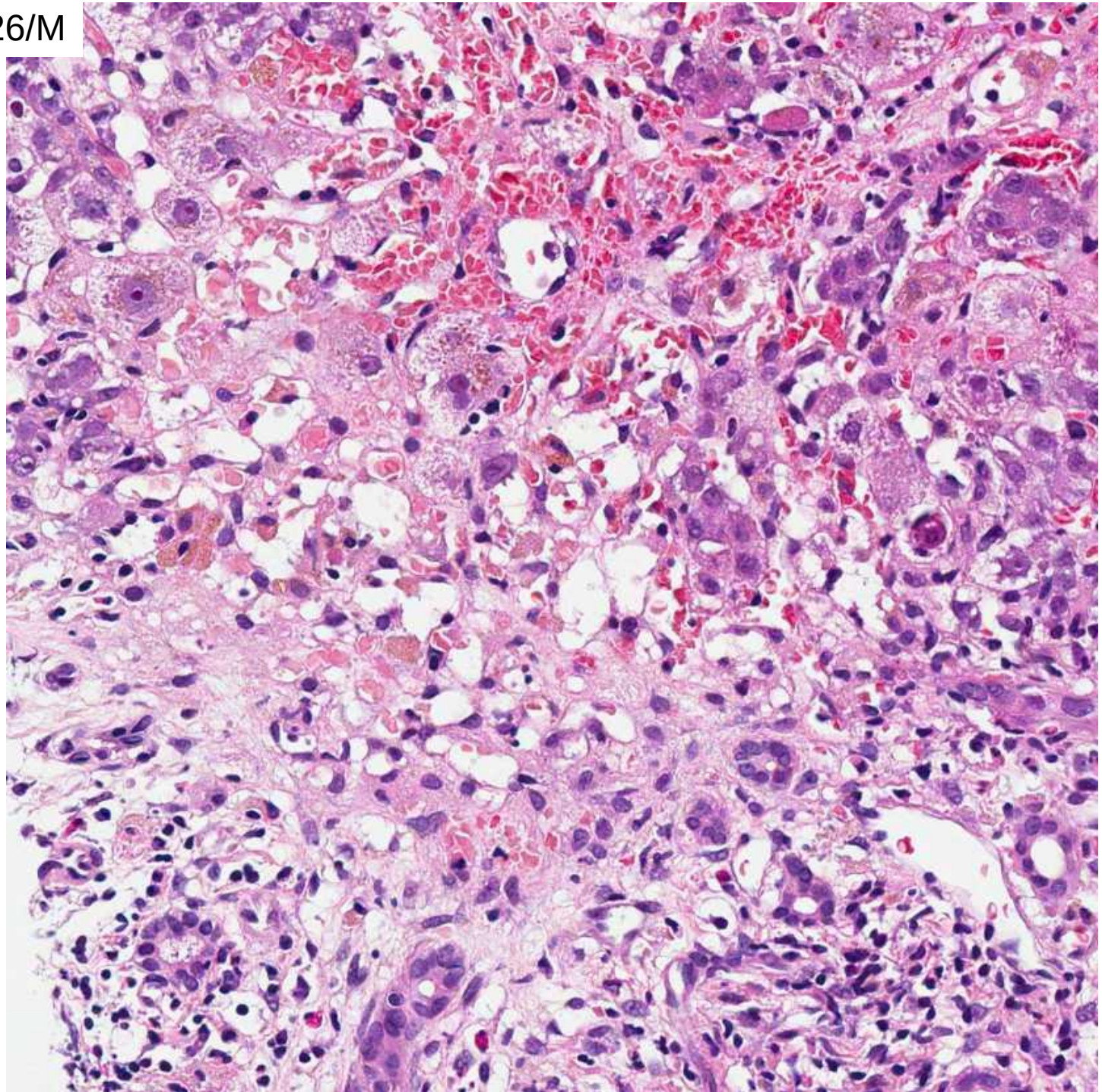

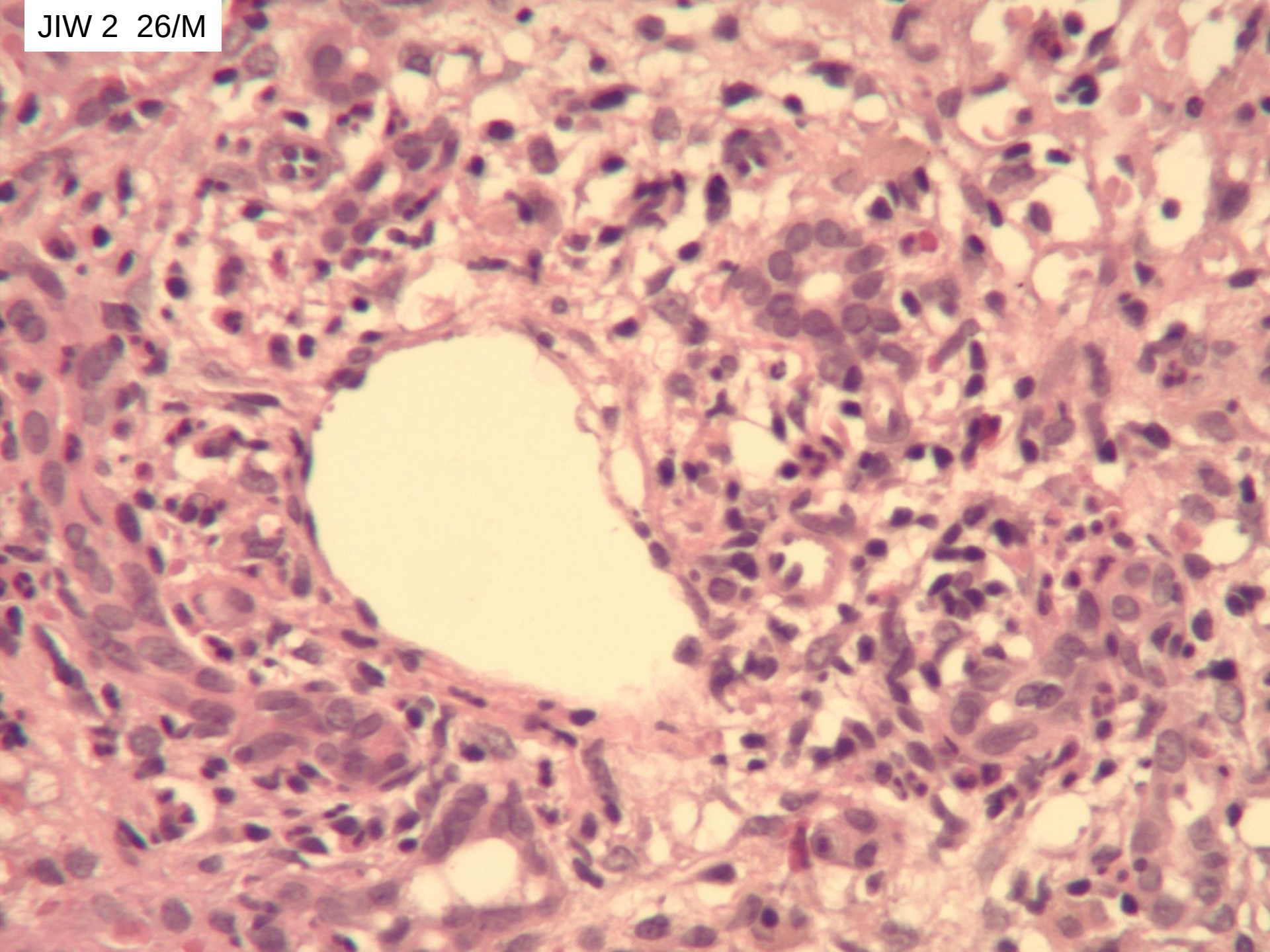
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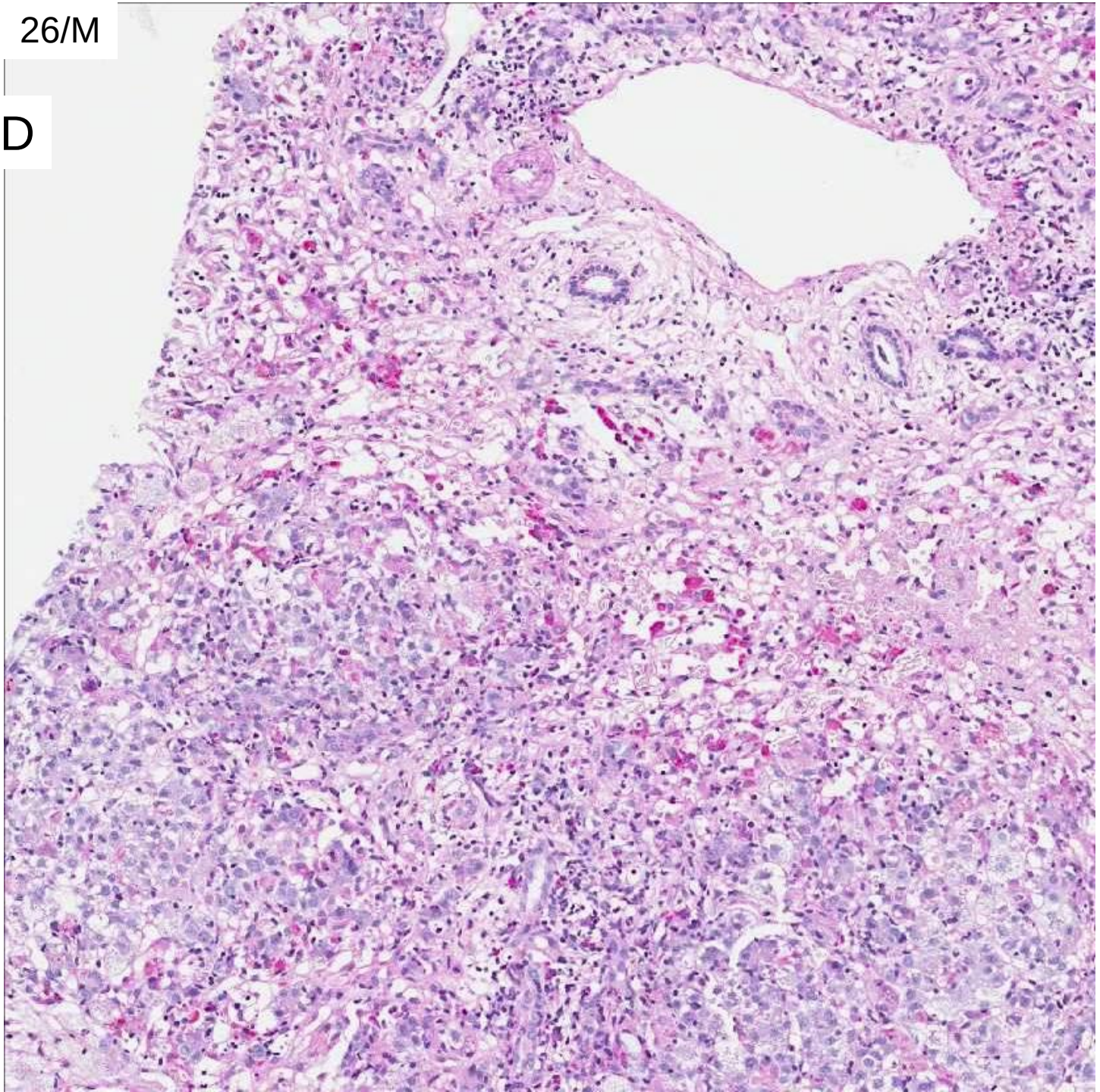

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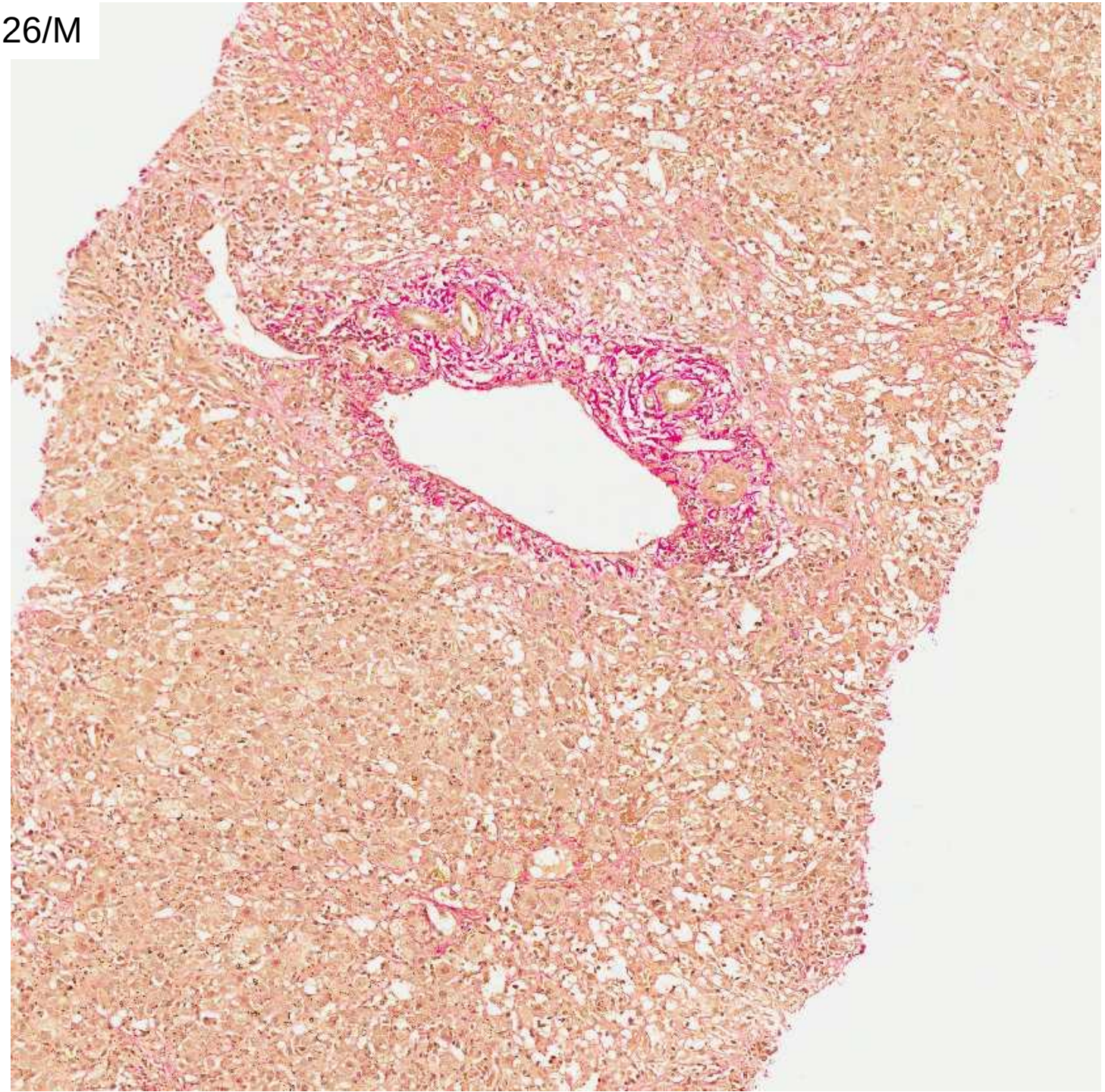

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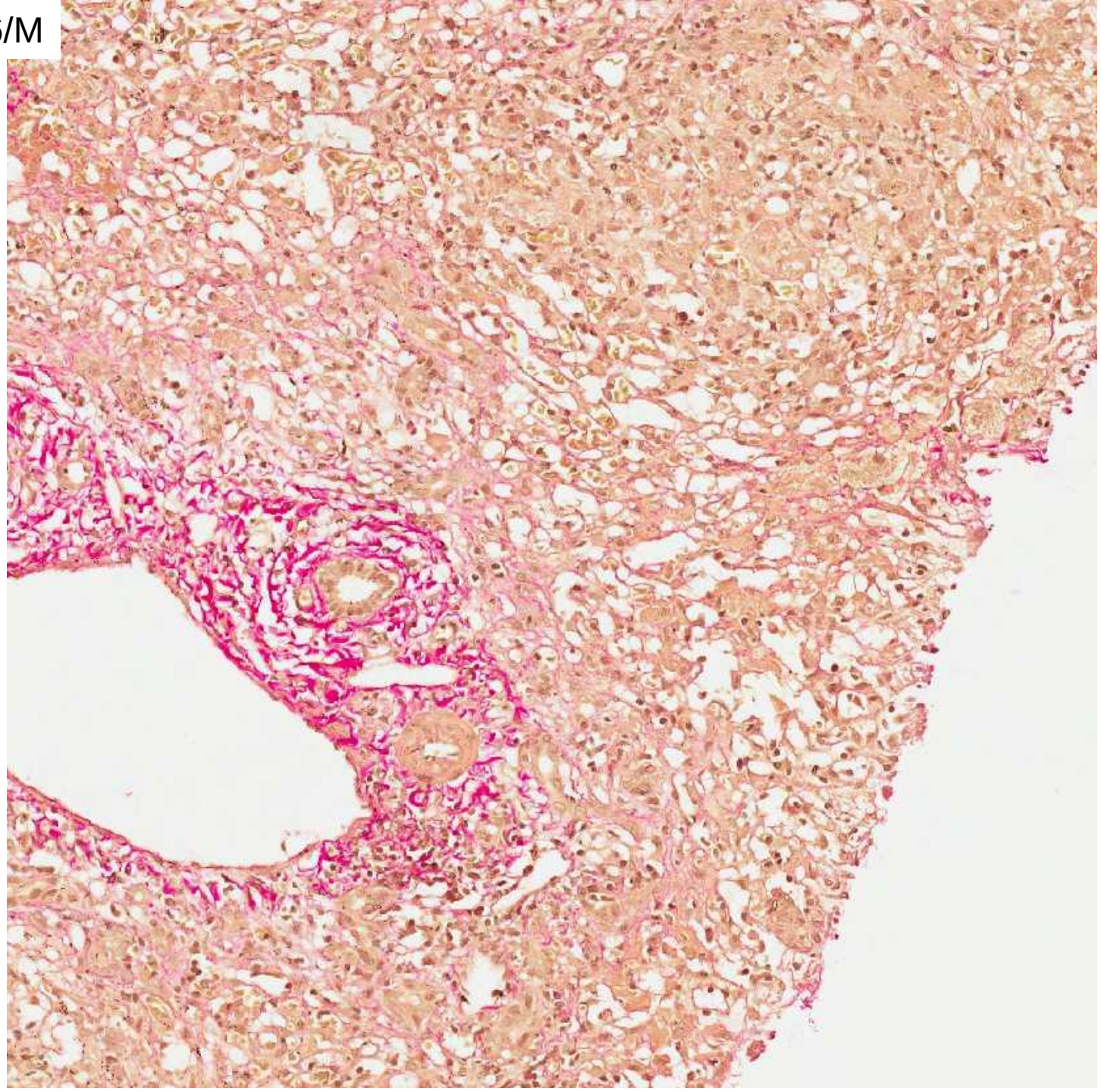

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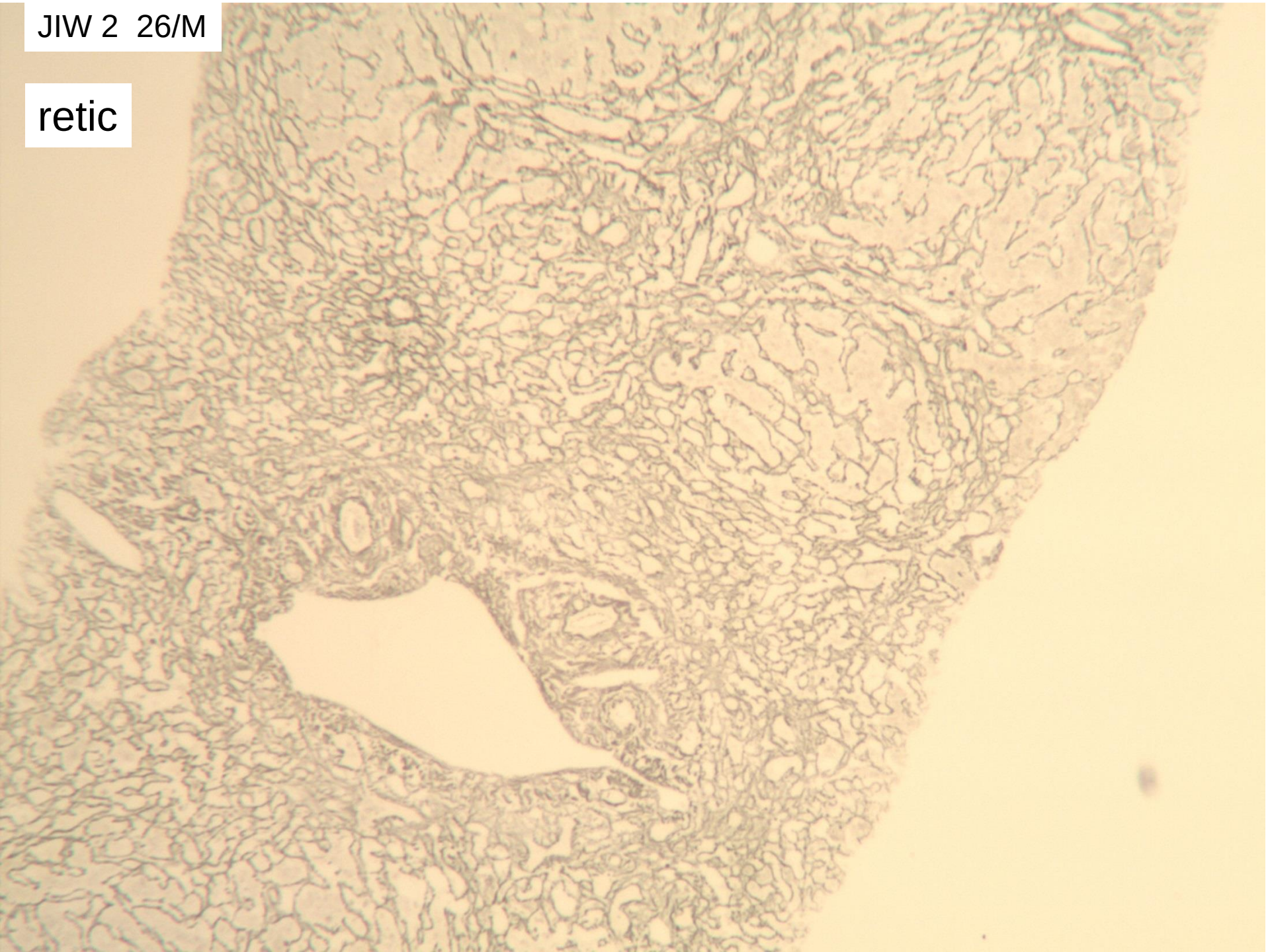


JIW 2 26/M

Acute illness, unwell, lethargy, vomiting. Bilirubin >250. ALT >3500.

Liver screen so far negative. Cocaine use over 4 months ago, nil recently. Has been having Nurofen for headaches.

? cause of LFT disturbance. History of high alcohol intake

Biopsy: severe hepatitis with bridging and focally pan-acinar necrosis.

Absence of portal inflammation/PCs

No features of alcoholic liver disease.

Additional information from clinicians – also Disulfiram 3/52.

c/w Disulfiram-induced liver injury.

- Idiosyncratic, clinically apparent liver injury due to **ibuprofen** is very rare (estimated to occur at a rate of 1.0-1.6 cases per 100,000 prescriptions). However, several convincing reports have been published of acute liver failure and death attributed to ibuprofen, usually after presentation with an immunoallergic-like reaction within days of starting

- **Cocaine** is not an infrequent cause of sudden "unexplained" death in young adults. Hepatotoxicity usually arises hours to a few days after an acute overdose, generally following or accompanying other major organ involvement.

- **Disulfiram** is a well established cause of clinically apparent liver injury, which can be severe and even fatal.

Disulfiram hepatotoxicity with jaundice is associated with high mortality and appearance of symptoms or signs of liver injury should lead to its immediate discontinuation.

JIW 2 26/M

Disulfiram induced liver injury – 82 cases from Swedish DILI registry

cases present within 60 days of commencing drug:

10% mortality/transplantation

Two patterns –

- Bridging and panacinar necrosis – high risk of liver failure
- Eosinophilic infiltration

Bjornsson *et al.* H Hepatol 2006;44;791-797

Follow up –

ALT peaked at 3,694, bili 379 on day of biopsy,

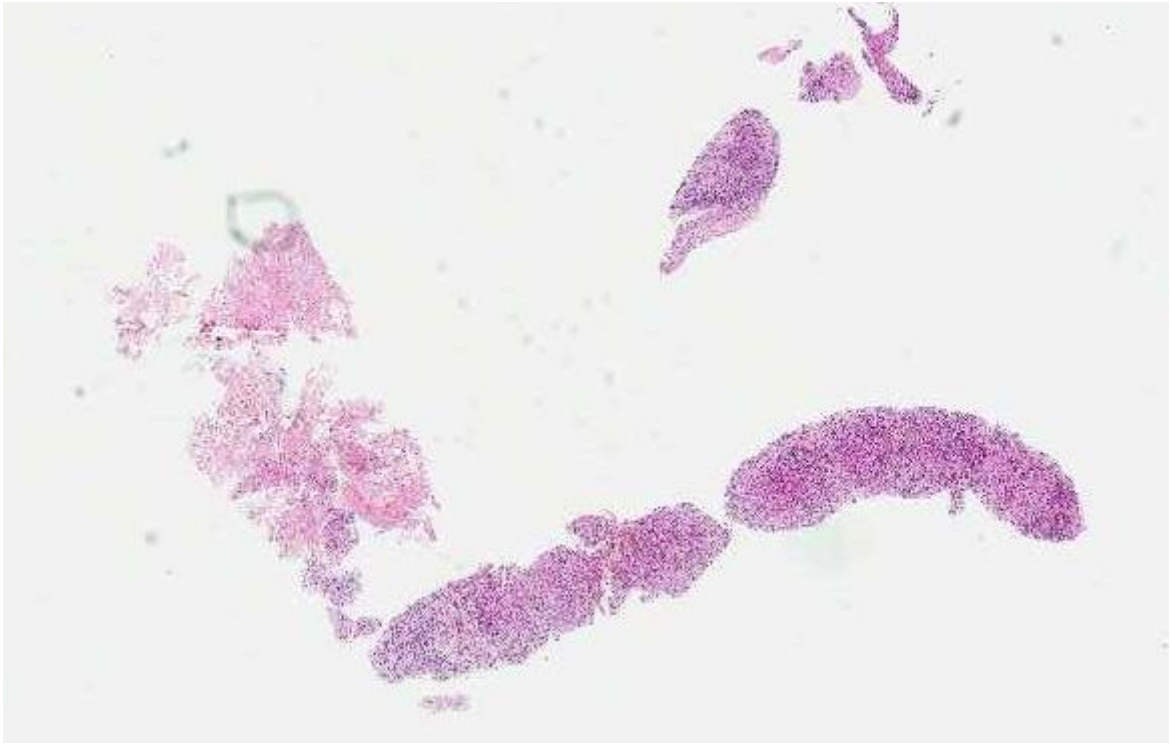
Treated with steroids

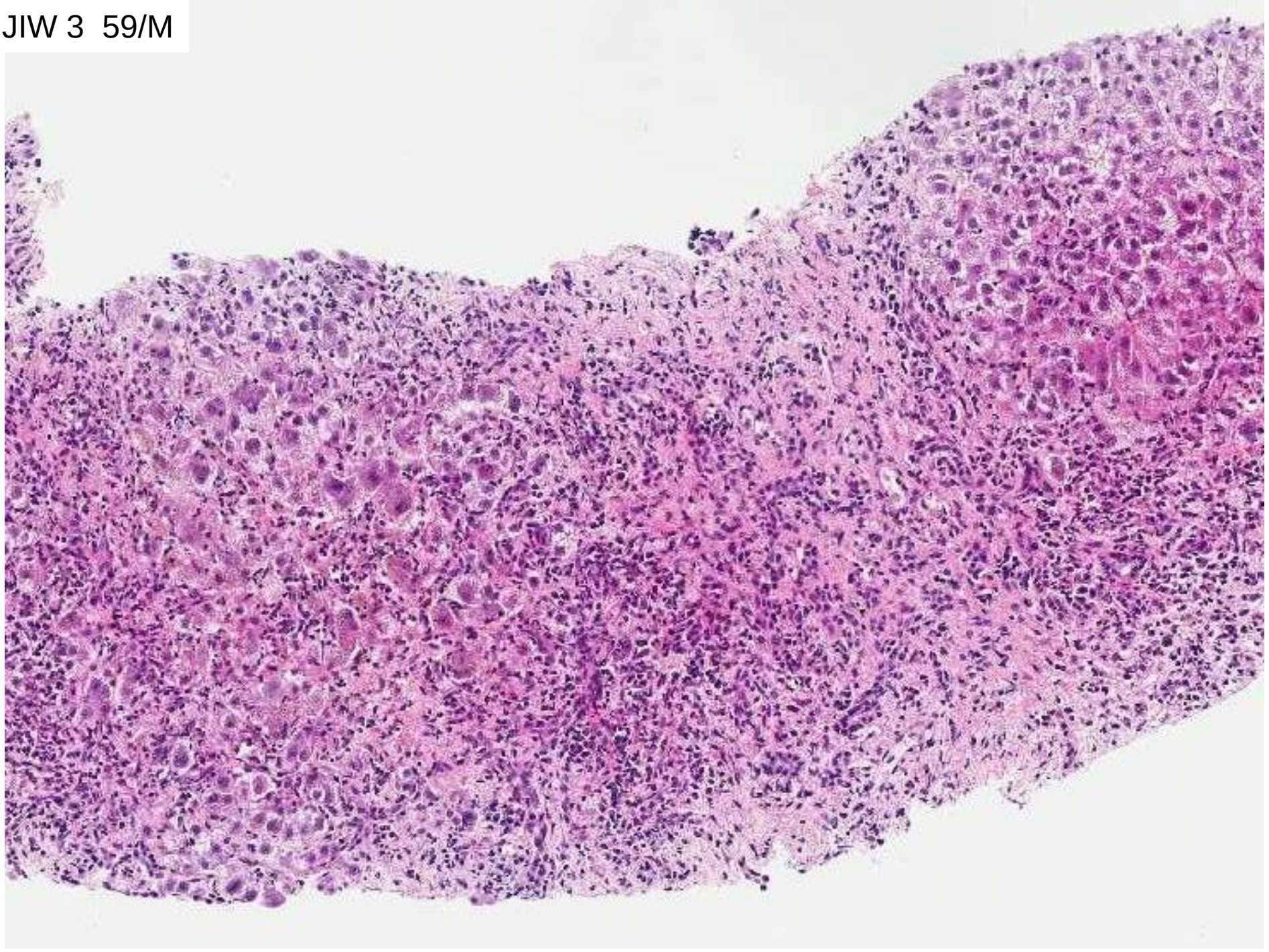
1 month later ALT = 806, 2 months later ALT = 60.

Steroids weaned and stopped, ALT remains normal.

JIW 3 59/M

Two weeks history of jaundice. Coagulopathic, ALT >1000, bilirubin >500. Taken nitrofurantoin recently.

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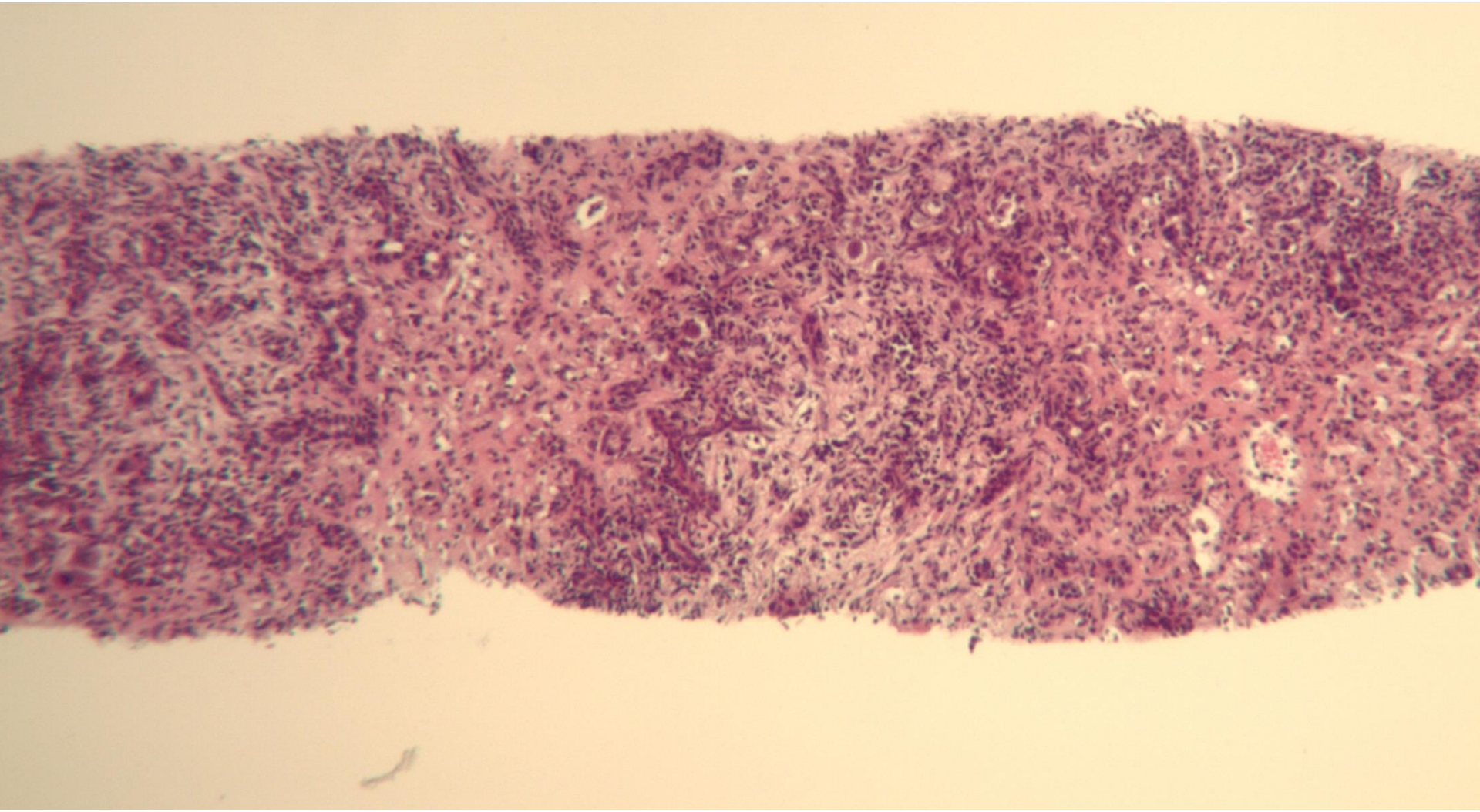

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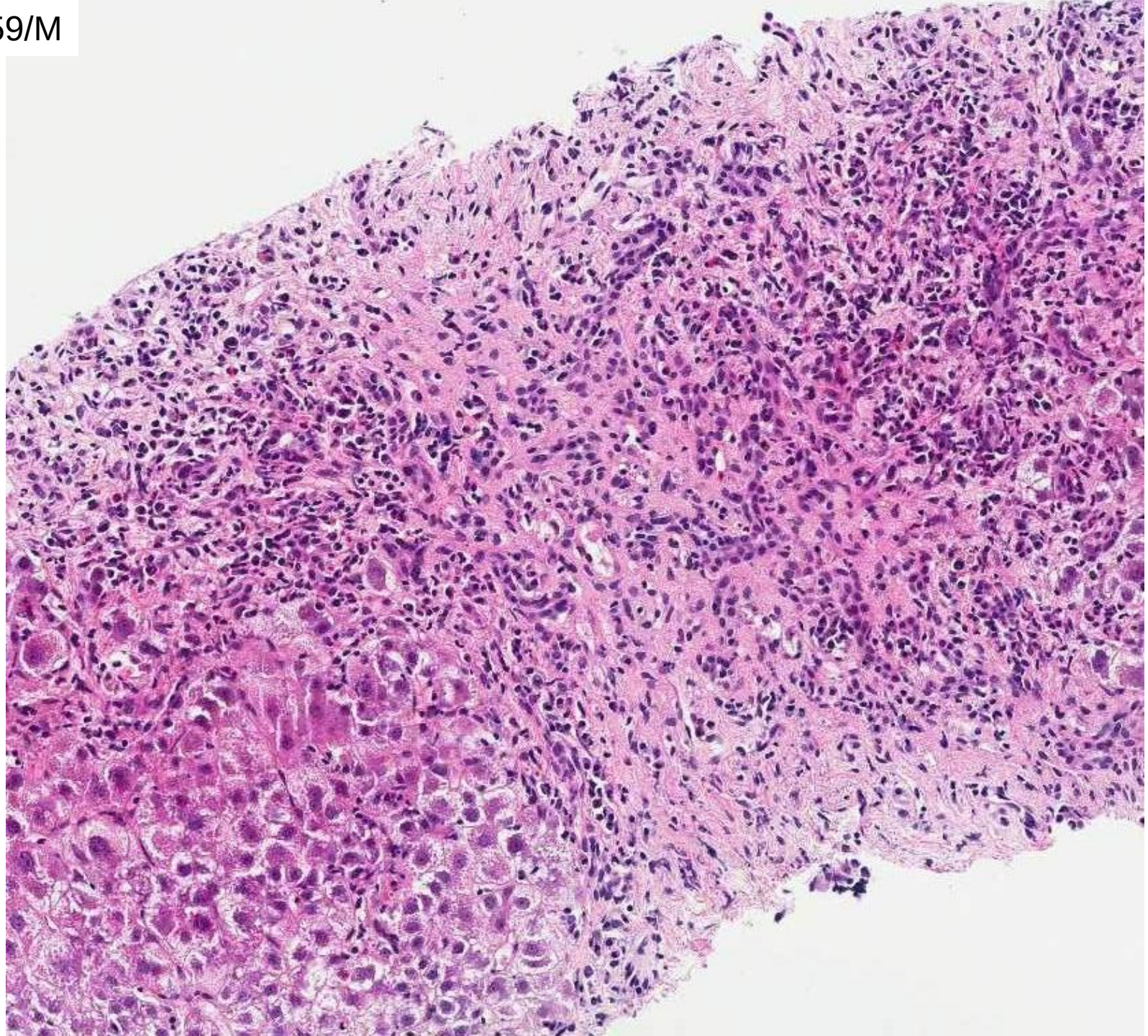

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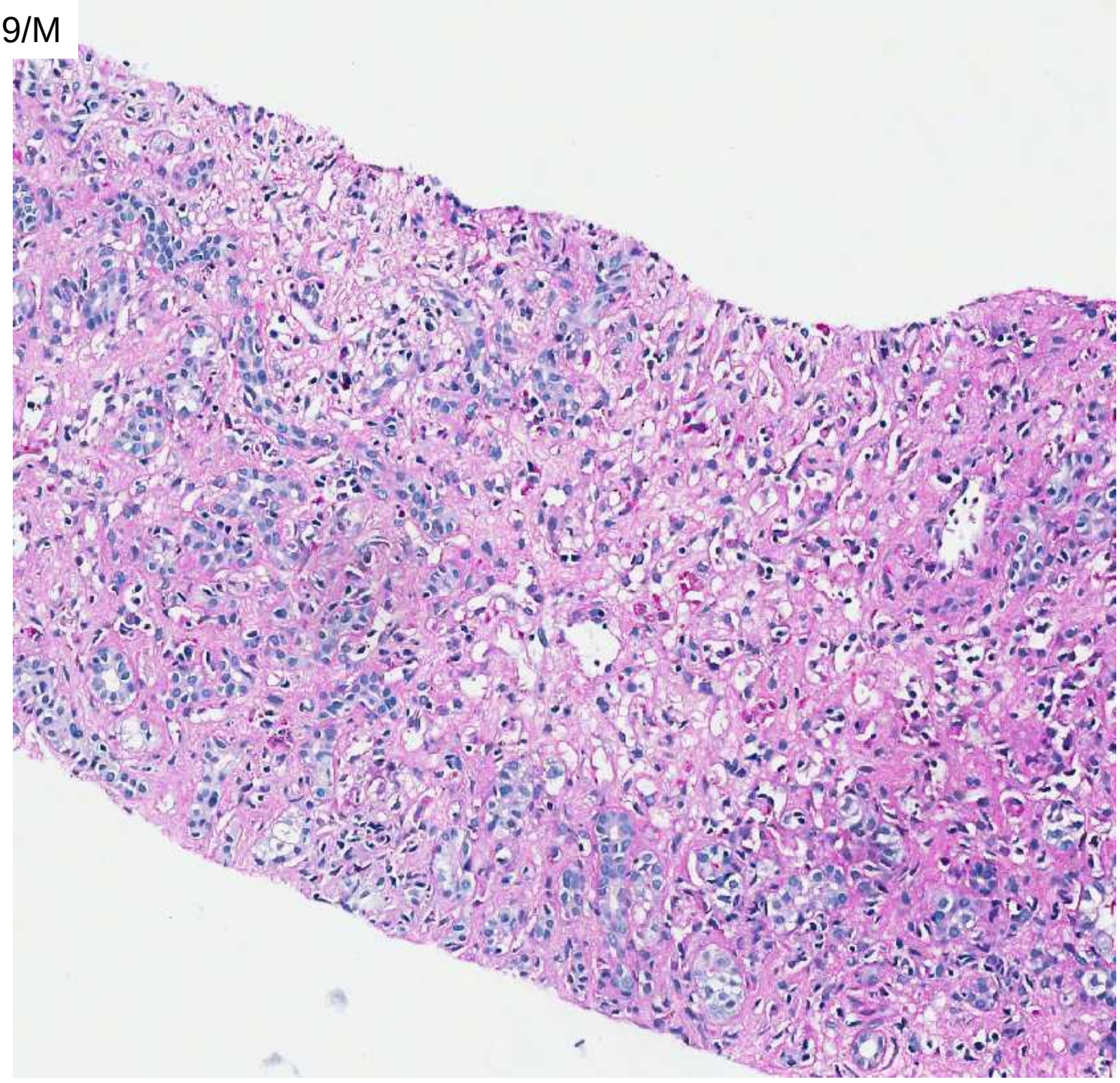

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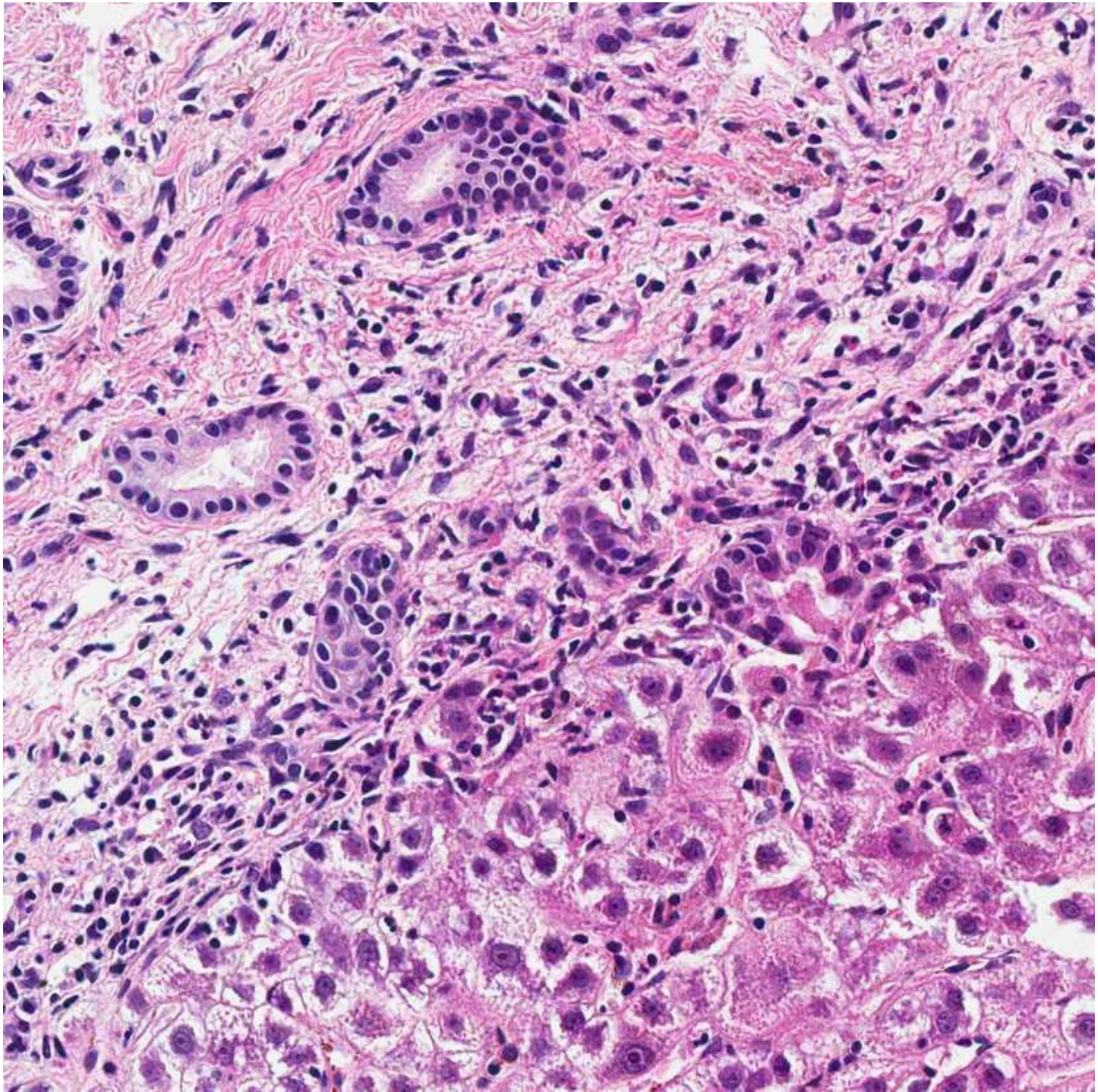

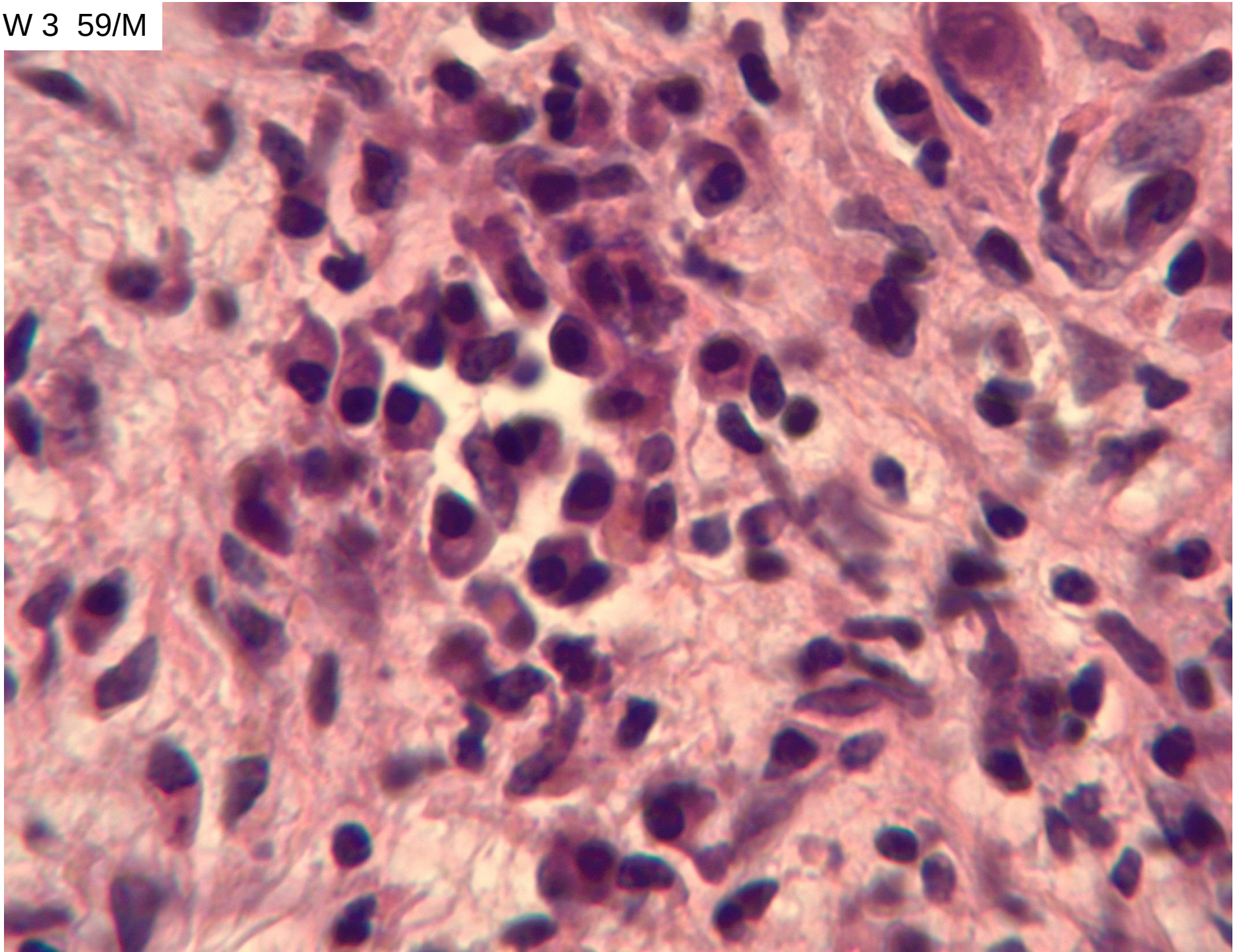
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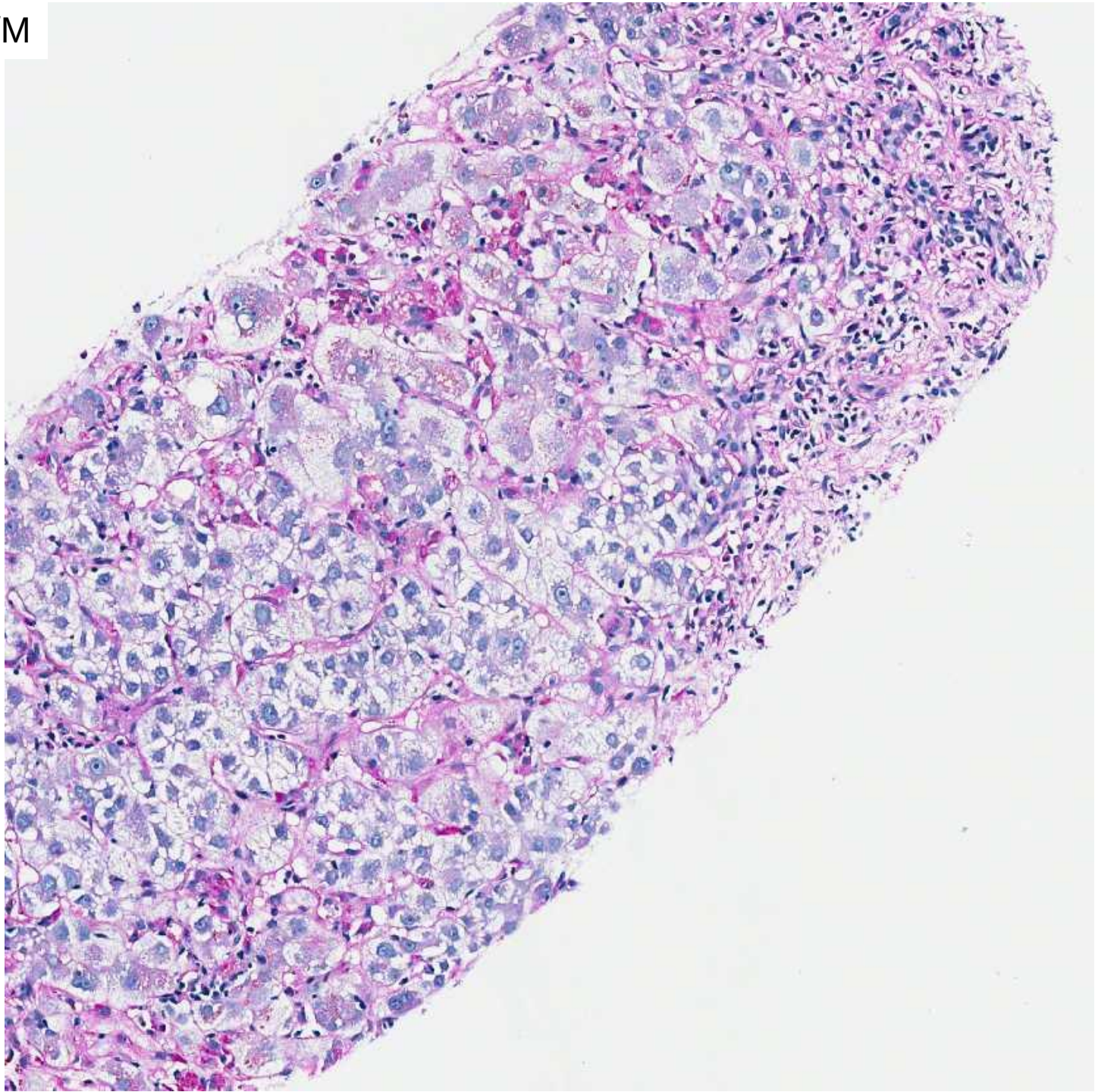

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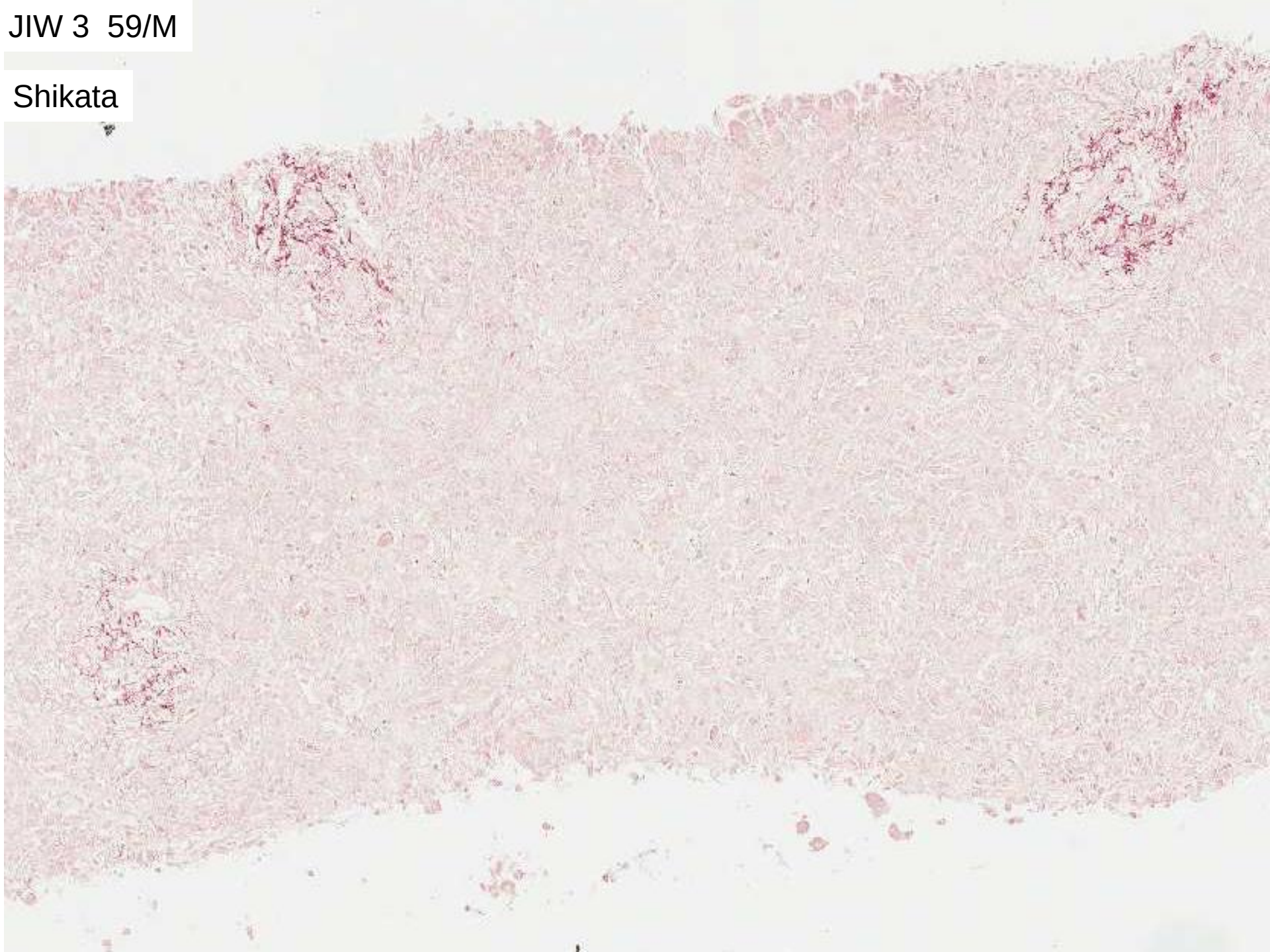

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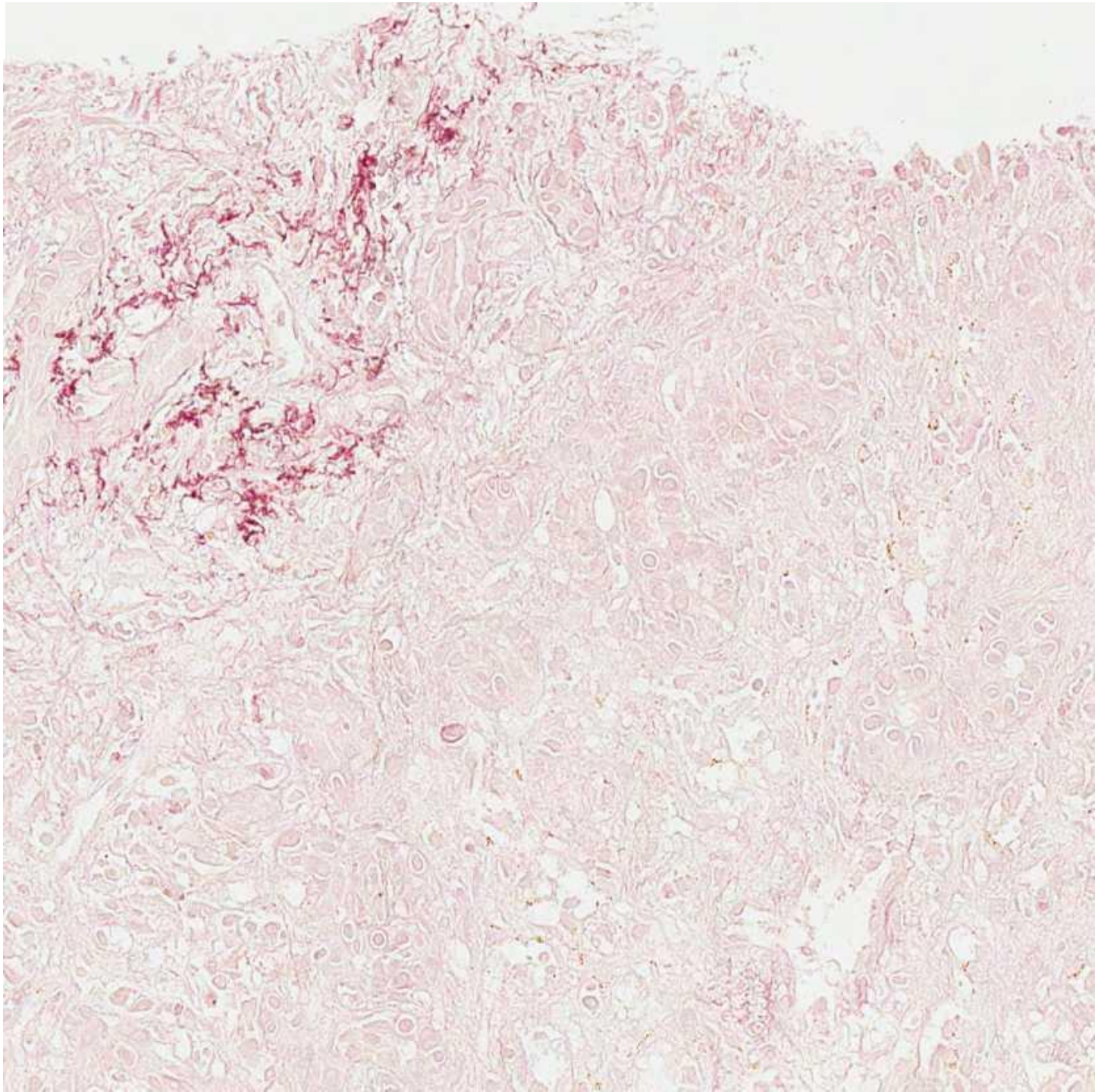


JIW 3 59/M

Two weeks history of jaundice. Coagulopathic, ALT >1000, bilirubin >500. Taken nitrofurantoin recently.

Diagnosis: severe acute hepatitis with cholestasis and confluent necrosis

Consistent with autoimmune hepatitis / nitrofurantoin DILI

ALT = 1205 day of biopsy, reduced to 142 1 month later.

- **Nitrofurantoin** is currently one of the most common causes of drug induced liver injury.
- Liver injury from nitrofurantoin can cause either an **acute or chronic** hepatitis-like syndrome.

- In some instances, **autoimmune features** are present, but these are more common with the chronic presentation of nitrofurantoin hepatotoxicity.

- The course and outcome of acute nitrofurantoin hepatotoxicity is variable, **severe forms with acute liver failure** can occur, and nitrofurantoin is regularly listed as one of the major causes of acute liver failure due to medications.

- The chronic form of nitrofurantoin hepatotoxicity is more common than the acute form and typically presents months to years after initiation of long term prophylactic therapy.

Drug-induced autoimmune hepatitis: clinical characteristics and prognosis

- Mayo clinic, 10 years, 24 (9%) of 261 patients with AIH
- 92% female
- Mainly nitrofurantoin (11) and minocycline (11)
- Long-term, median 24 and 12 months

- Similar autoantibodies, histology, steroid responsiveness to AIH that was not drug-induced

- Drug-induced had no relapse on withdrawing immunosuppression

Bjornsson E *et al*. Hepatology 2010;51;2040-2048

JIW 4 32/F

Malaise, high ALT, jaundice,

Liver biopsy 3 weeks earlier = severe hepatitis

Treated with steroids

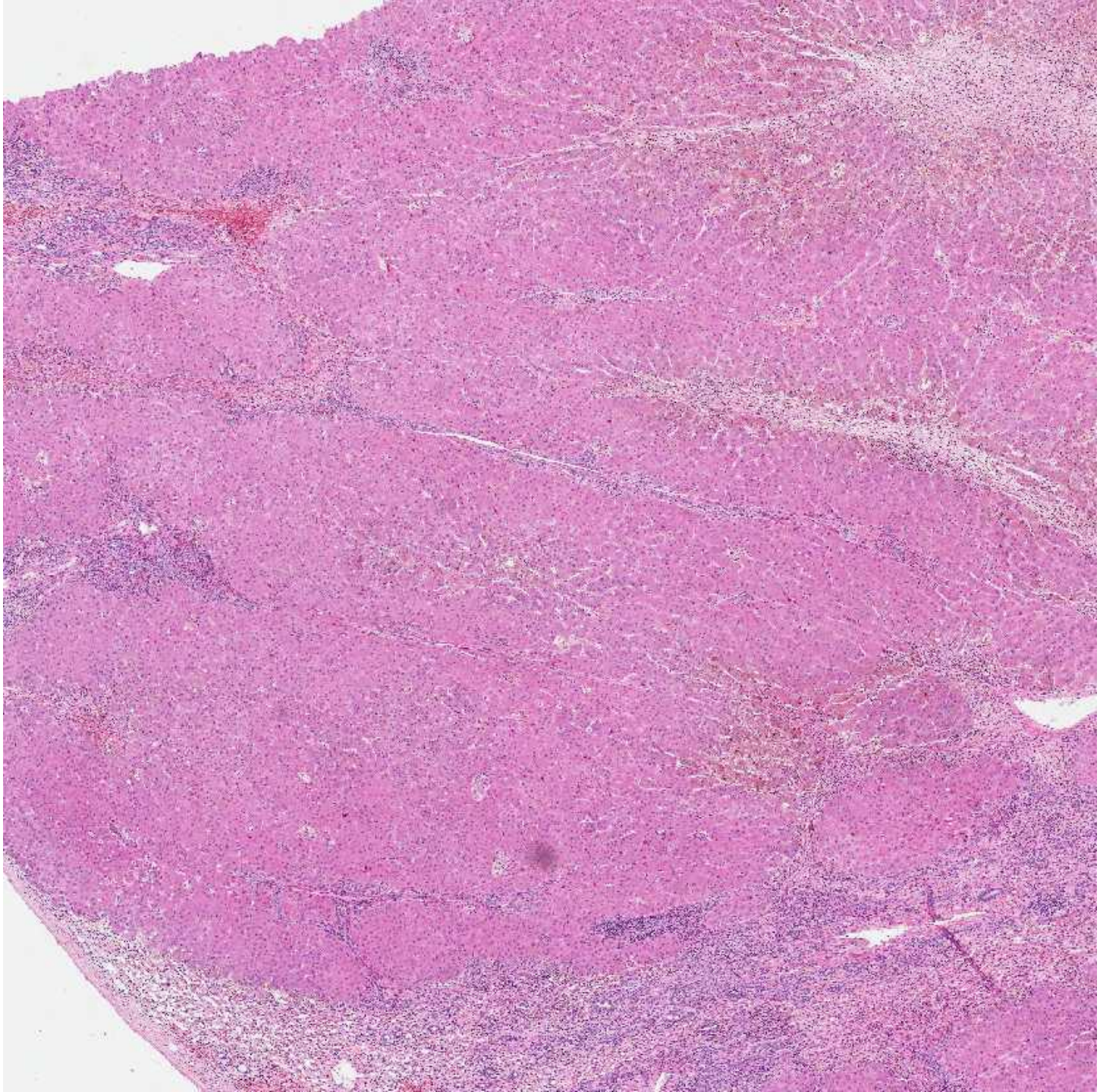
ALT decreasing, but coagulopathic and encephalopathic

Transplant - non A-E acute hepatitis

Explant liver – 860g

Map like necrosis

JIW 4 32/F



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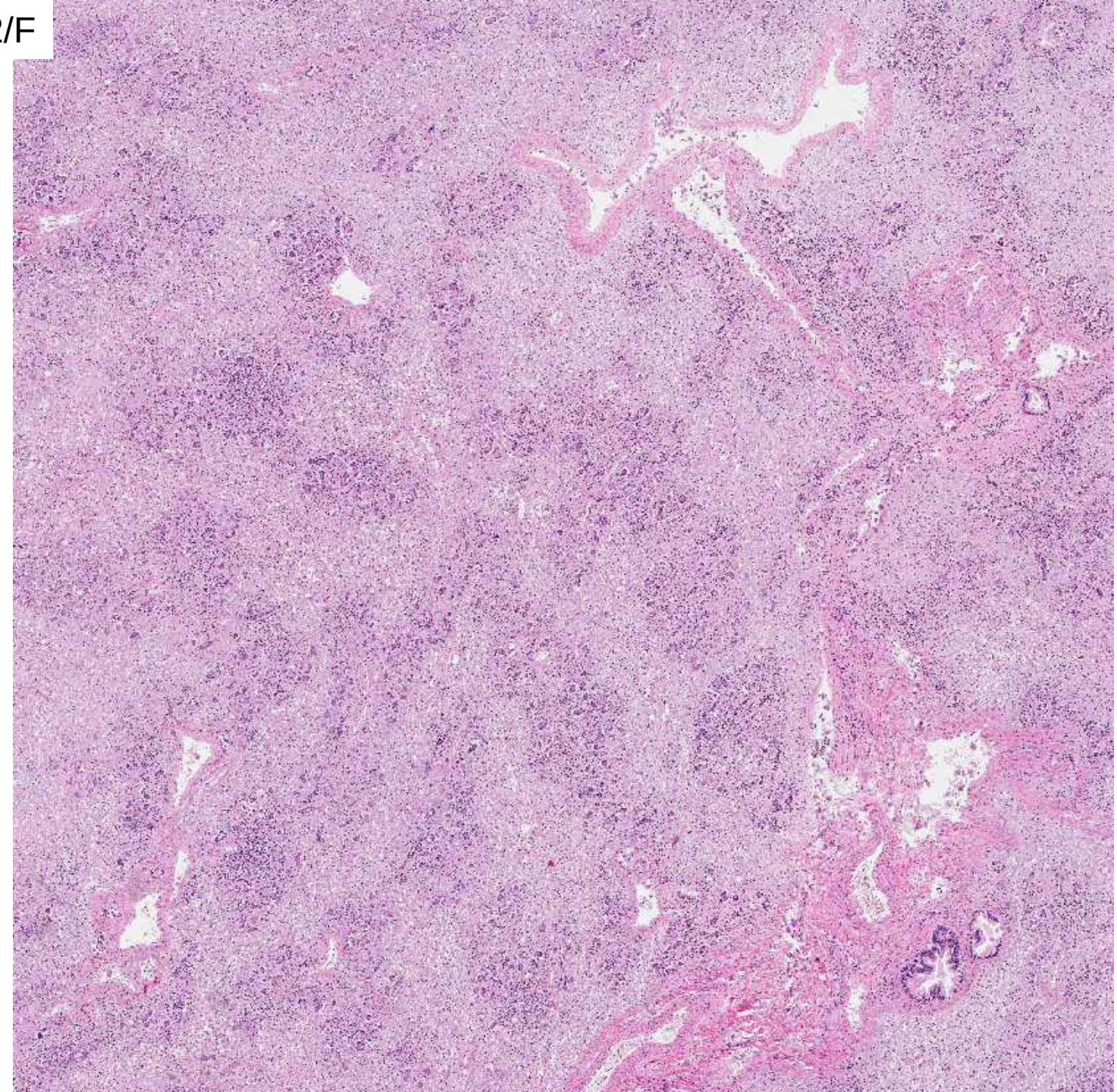

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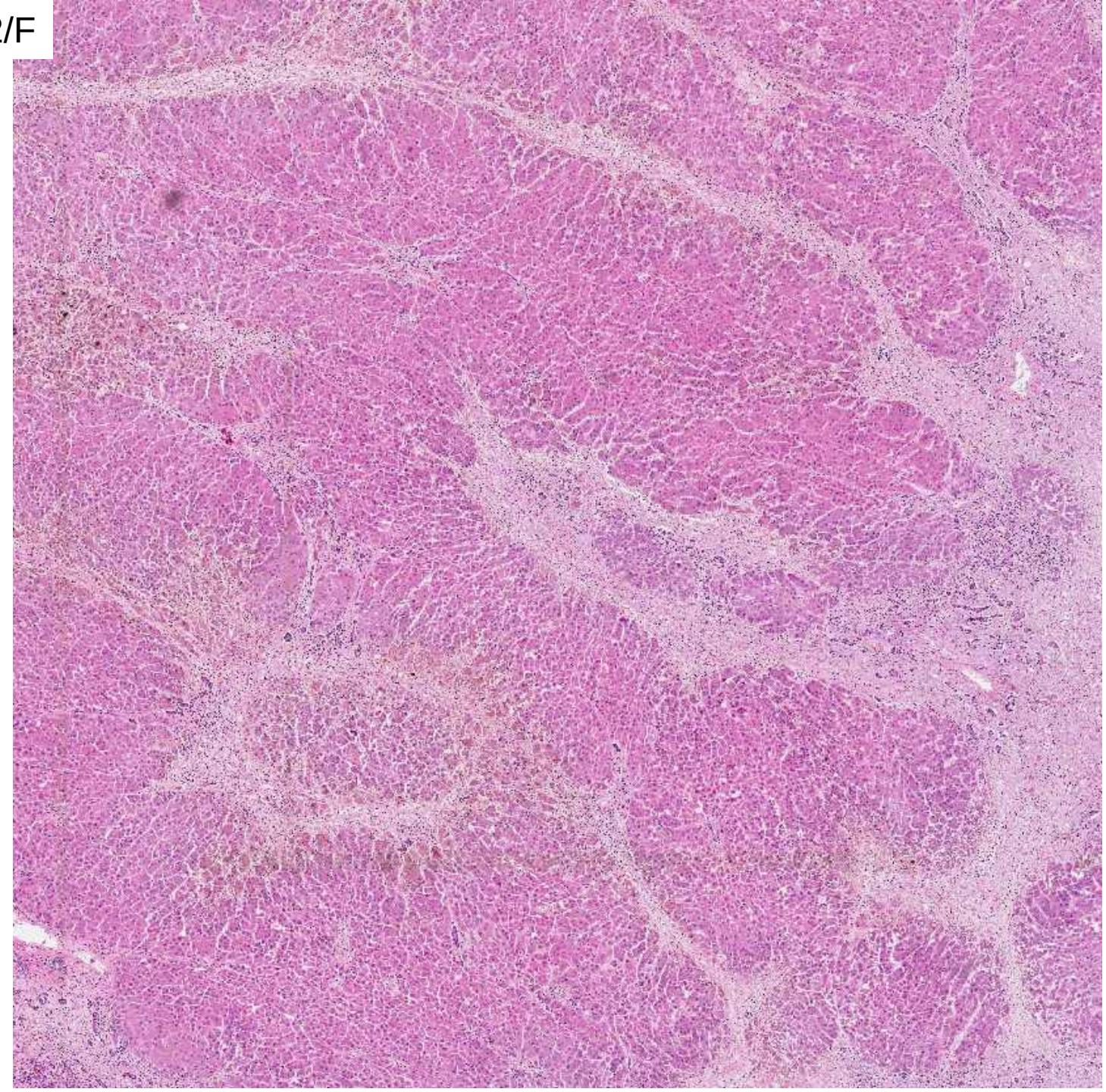

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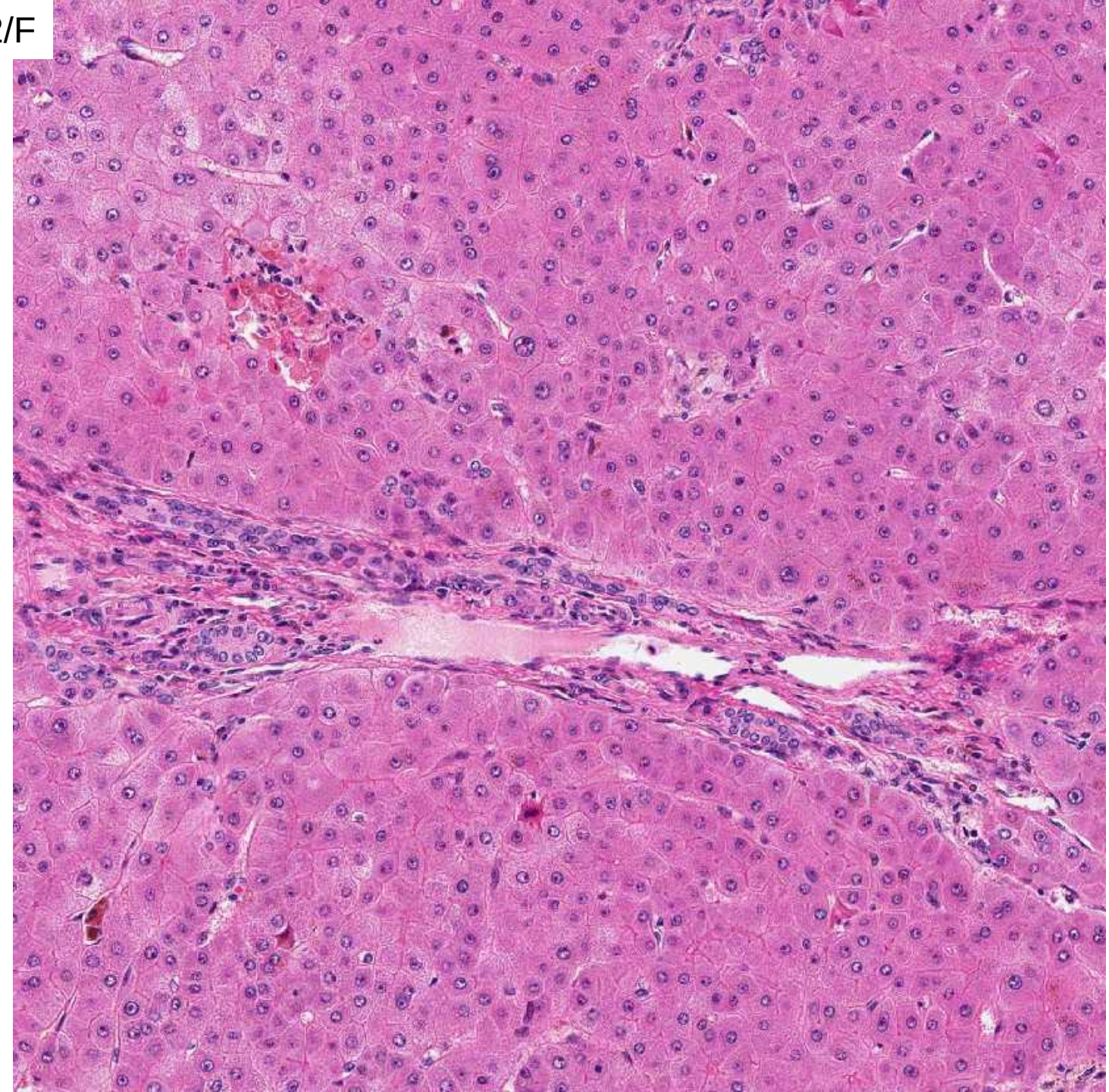

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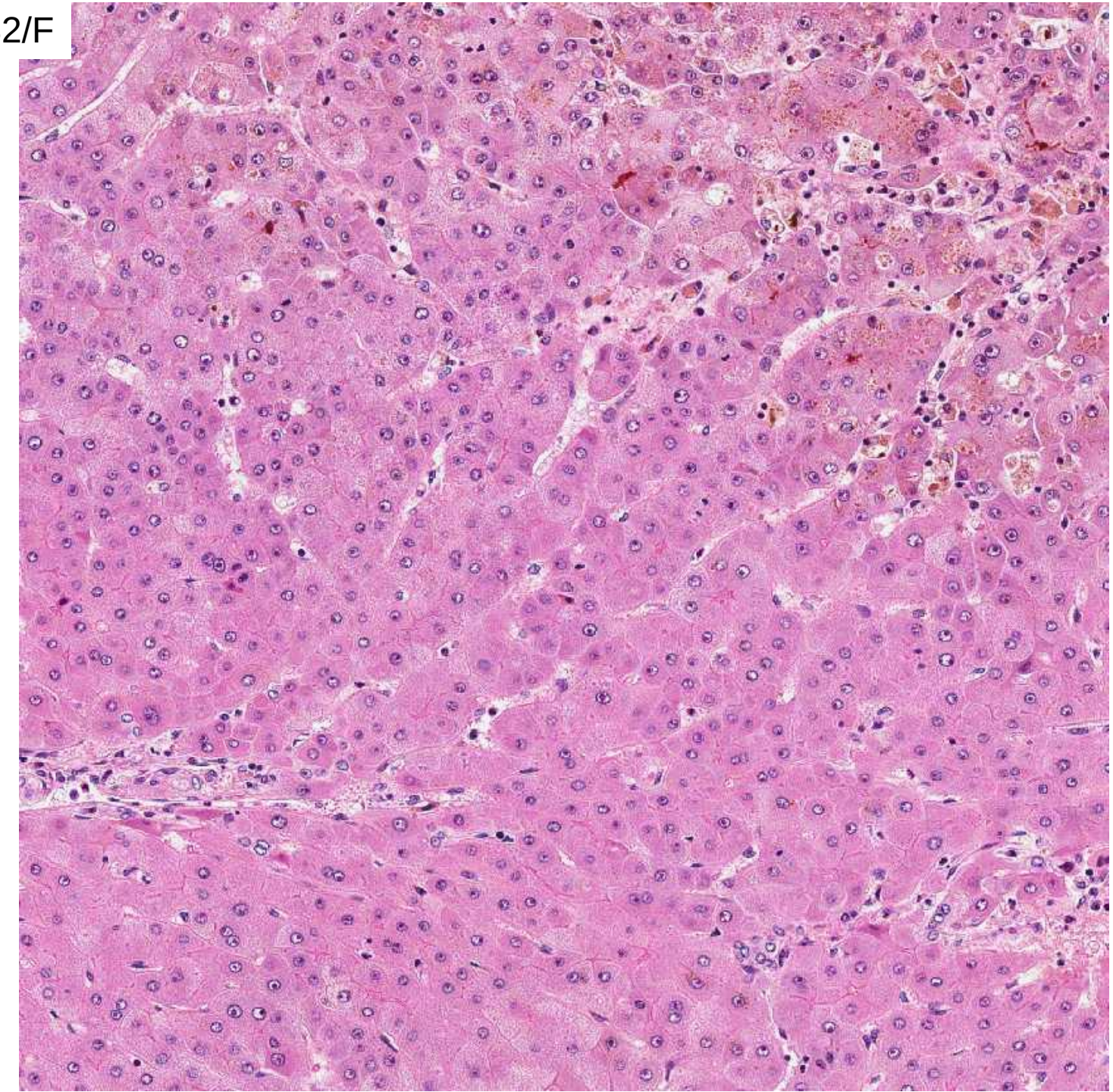

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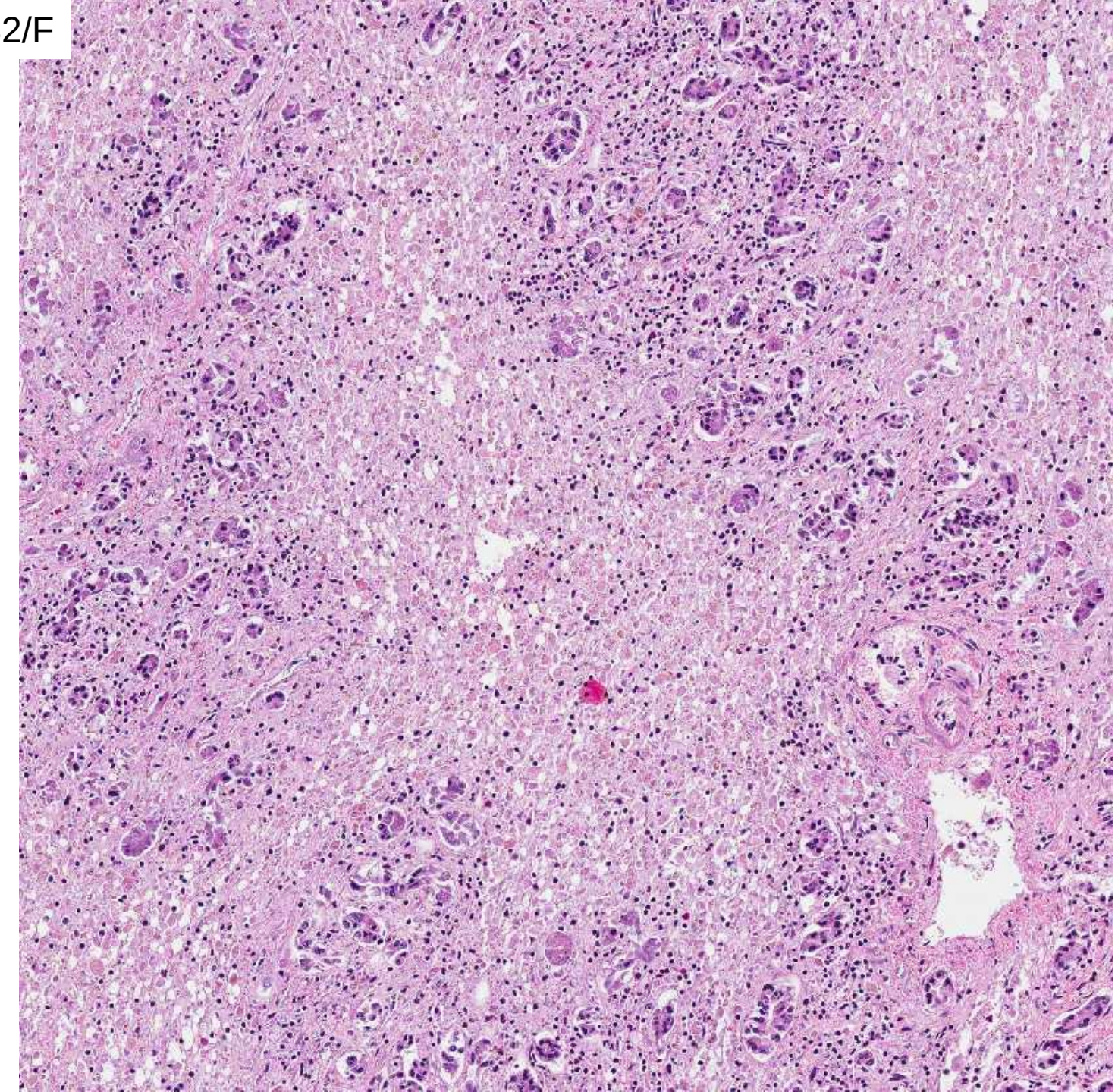

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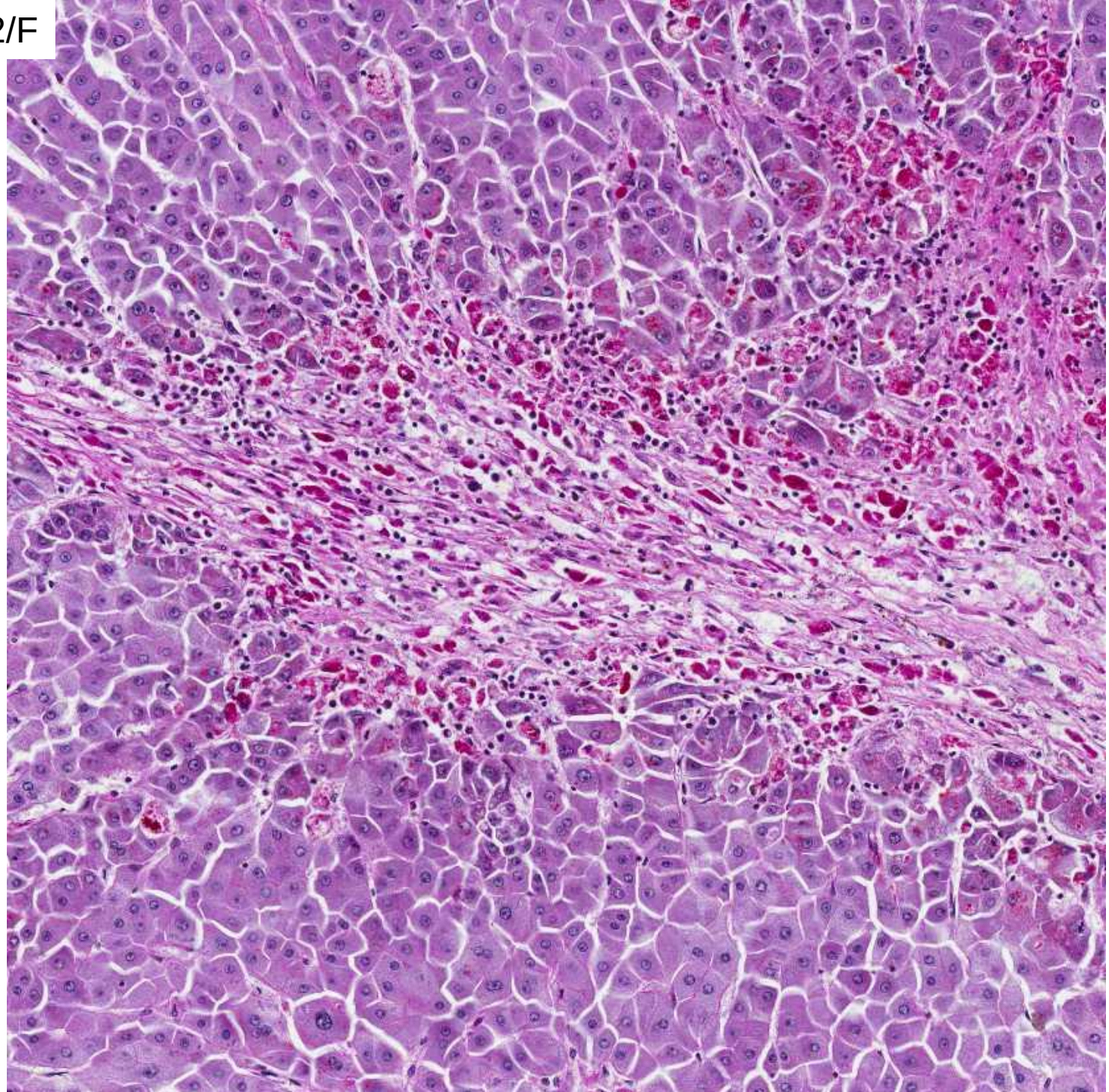

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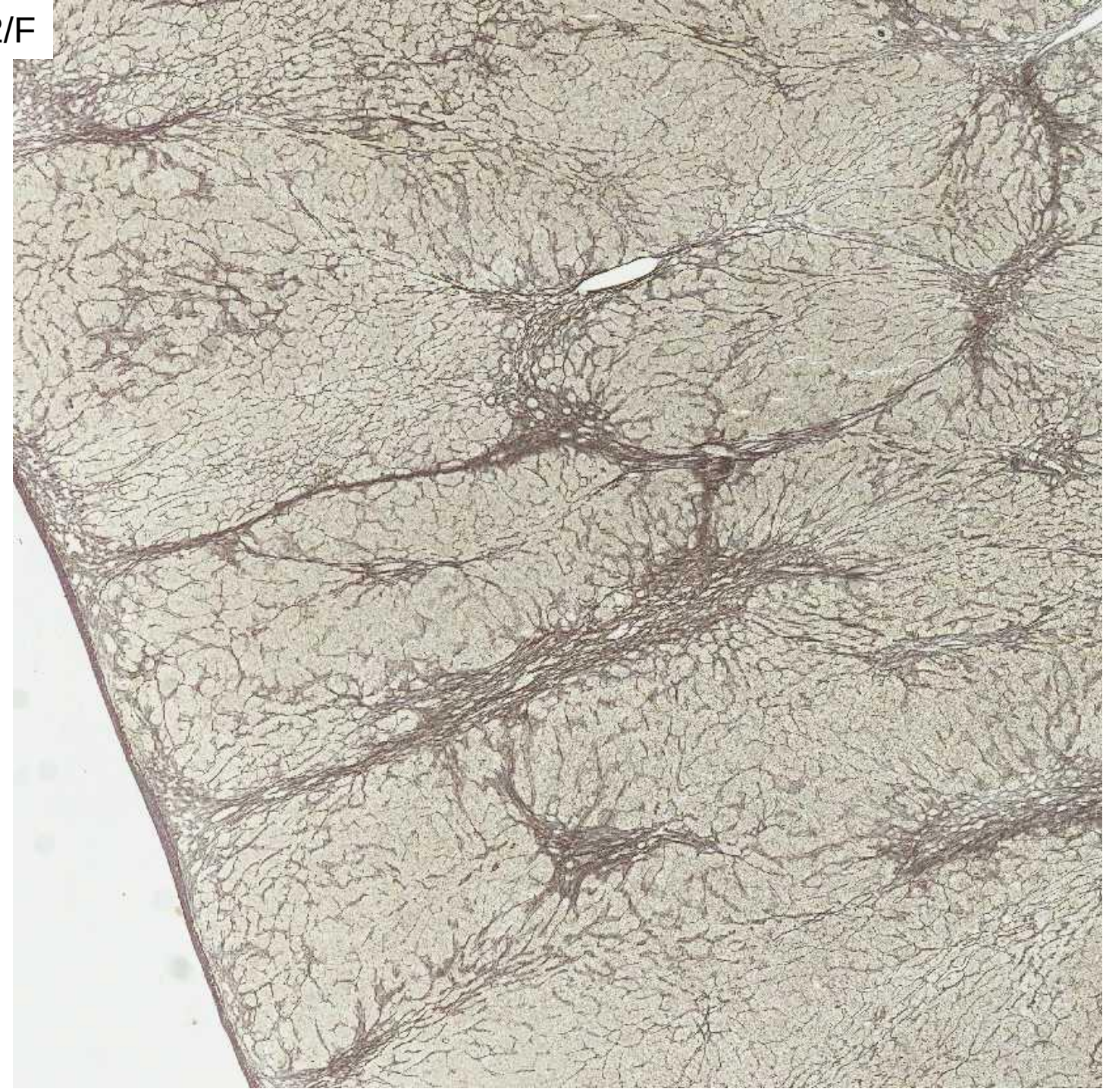

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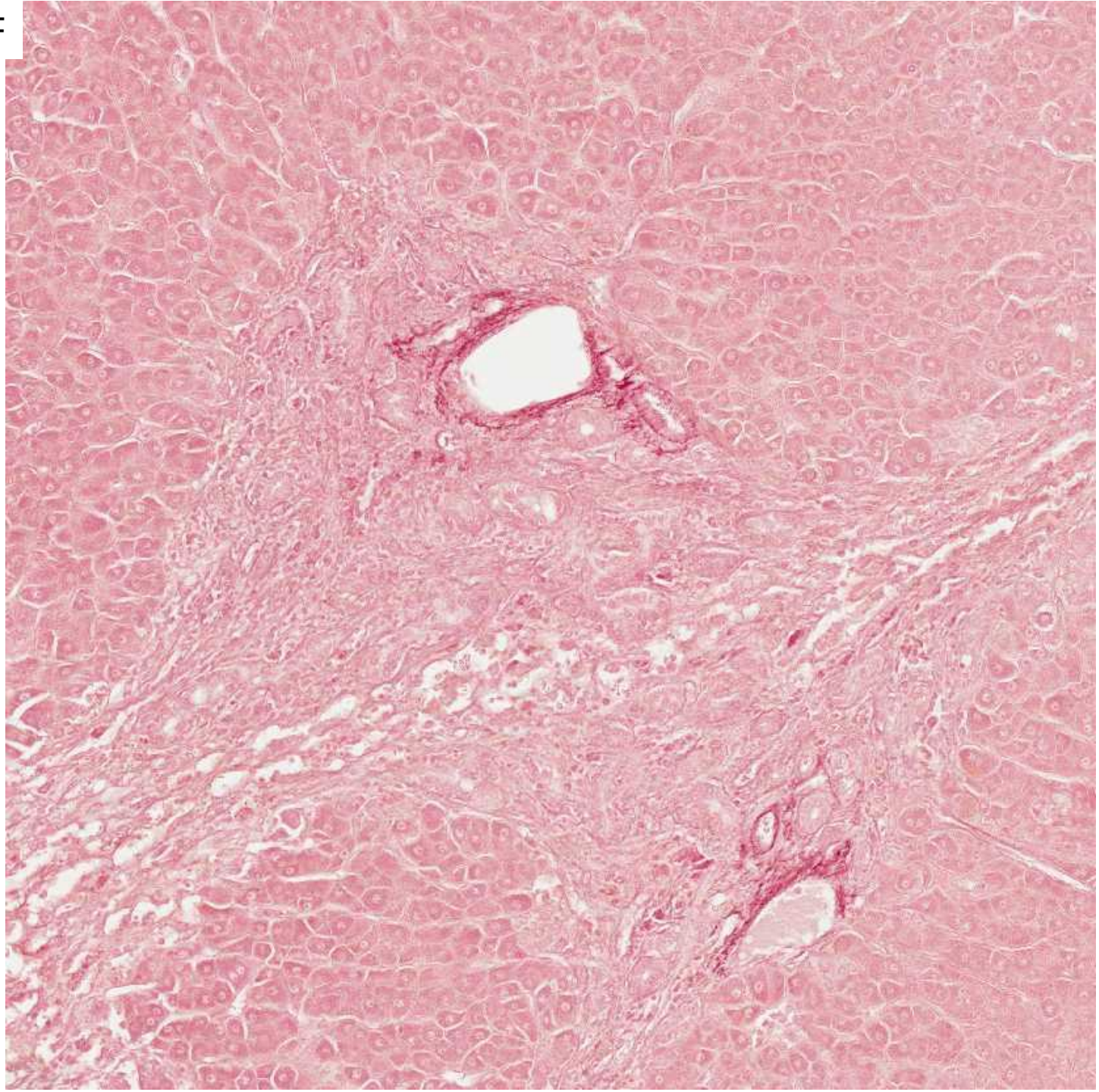

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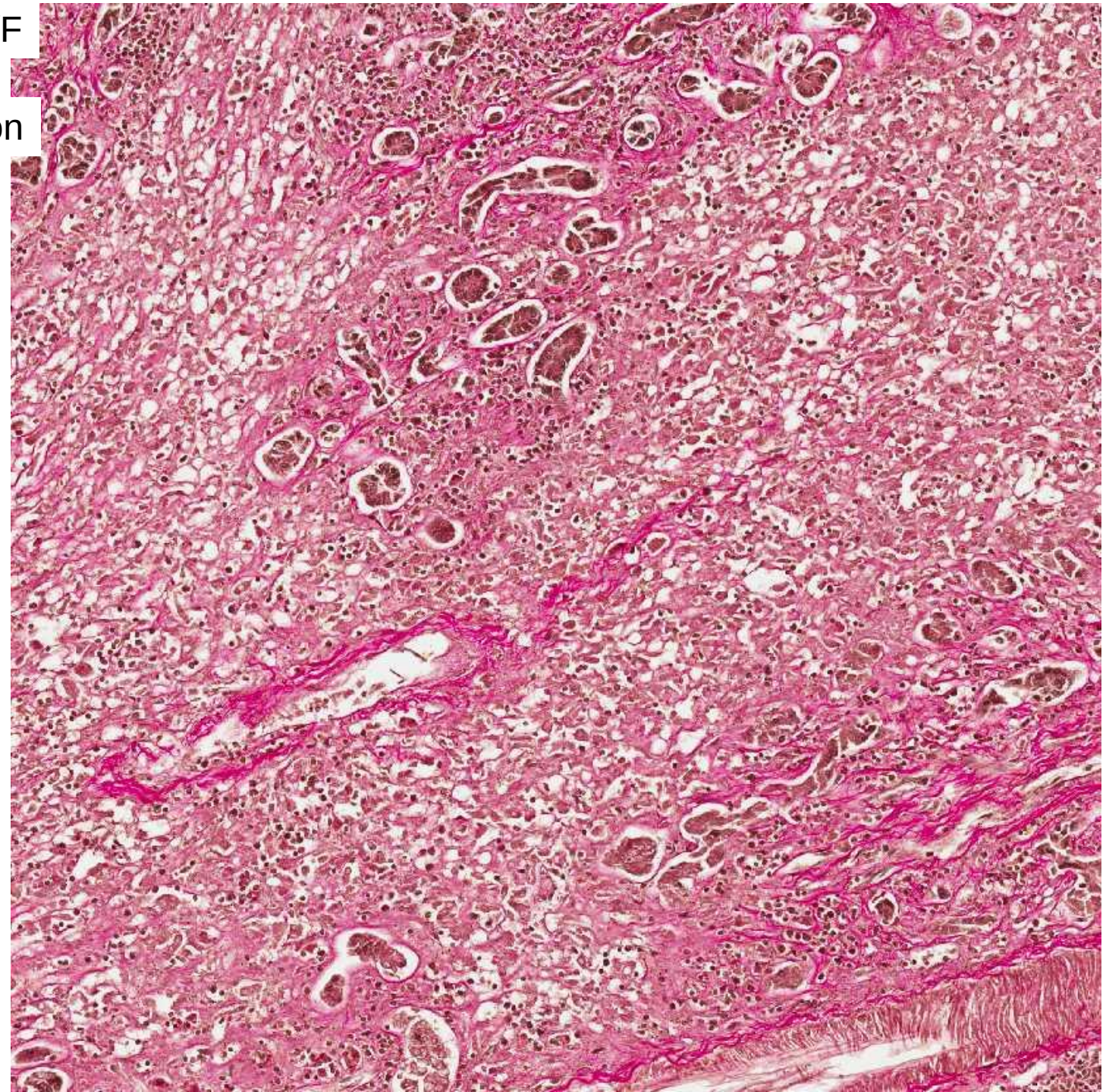

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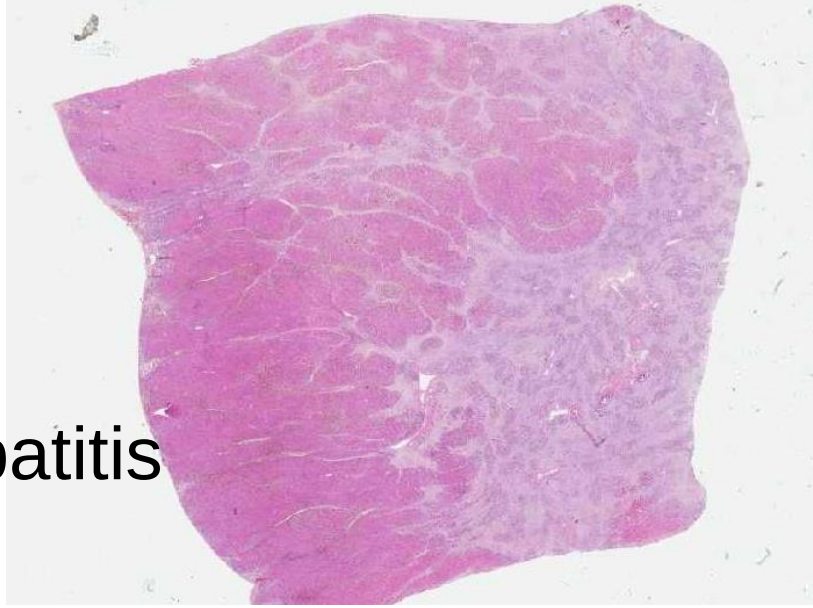


Transplant - non A-E acute hepatitis

Diagnosis: acute hepatitis with confluent multiacinar necrosis.

Compared with biopsy 3 weeks earlier (another hospital) - neither shows portal inflammation or plasma cells. No aetiology.

‘seronegative’ hepatitis, may be steroid responsive.

Urgent transplant if not.

UK Liver Transplants

NHS Blood and Transplant

Total liver transplants in 2017-18 = 998

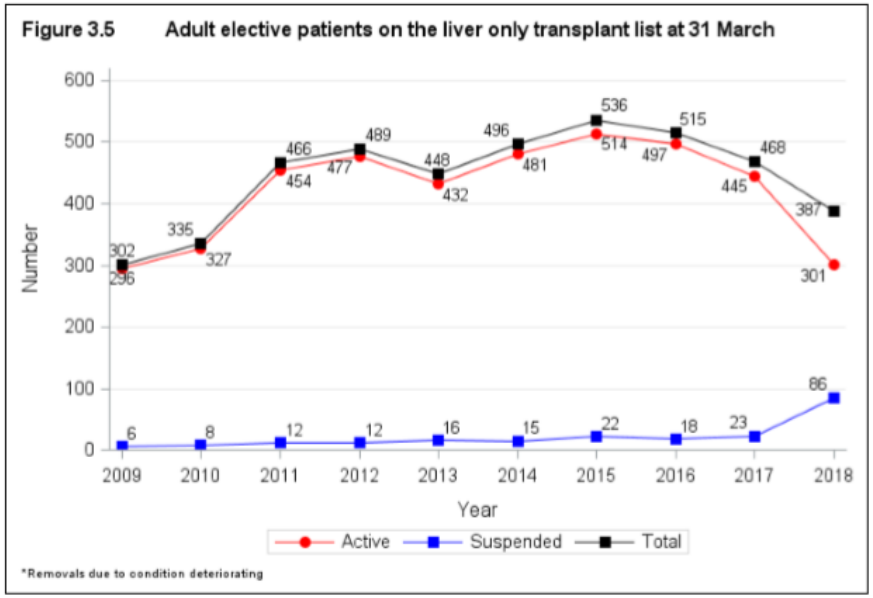
Elective: 754 adults, 61 children
Super-urgent:74 adults, 9 children
Overall – about 9% super-urgent

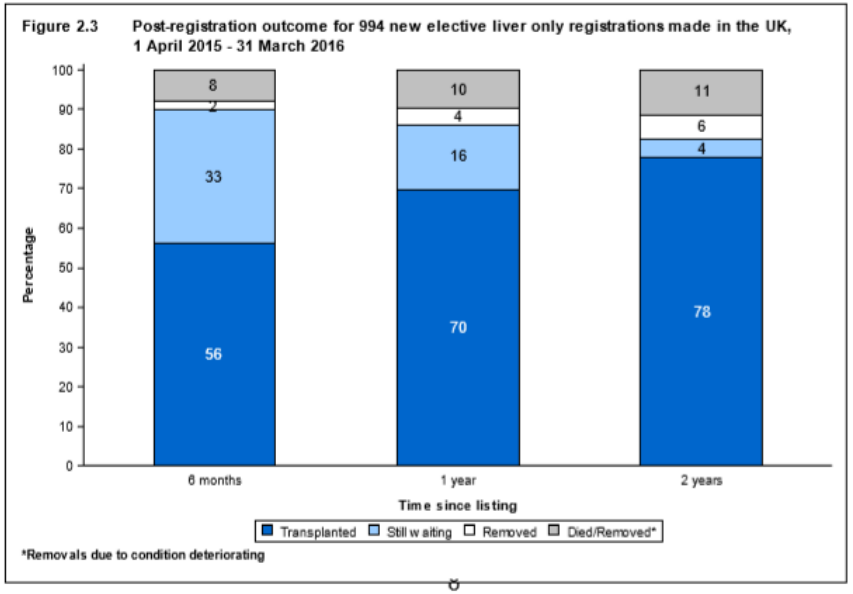
ANNUAL REPORT ON LIVER TRANSPLANTATION

REPORT FOR 2017/2018 (1 APRIL 2008 – 31 MARCH 2018)

PUBLISHED SEPTEMBER 2018

PRODUCED IN COLLABORATION WITH NHS ENGLAND





Explant livers

7 liver transplant centres in UK,

Insights into liver pathology

– especially 3d architecture in relation to needle biopsies – more of this later

Acute - confluent necrosis, bridging, variation

Chronic – fibrosis, cirrhosis,

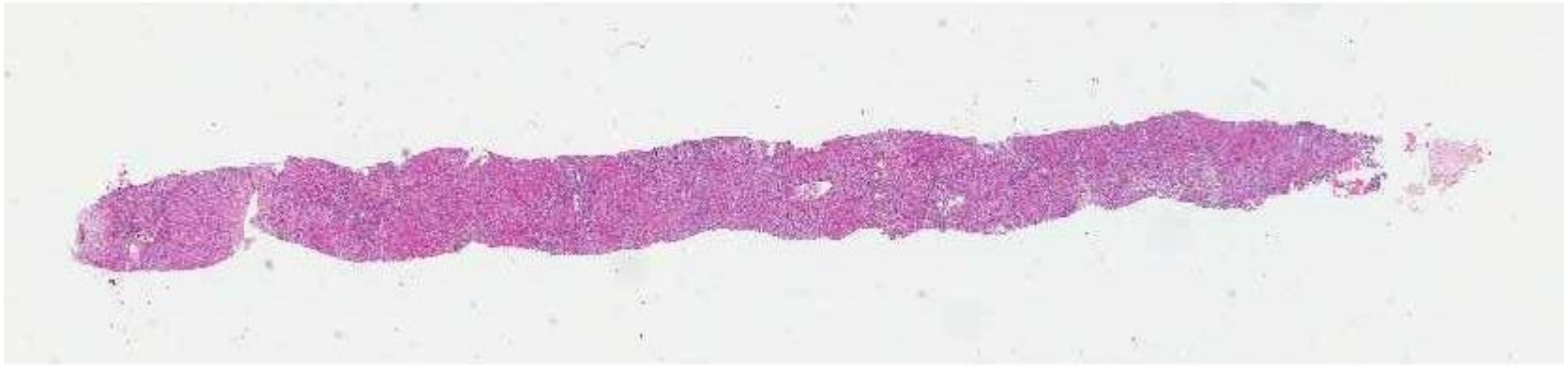
vascular and biliary may be heterogeneous,

fatty, viral hepatitis, autoimmune – more uniform

JIW 5 17/M

Deranged LFTs, raised ALT, SMA antibody positive.
? autoimmune hepatitis

Hepatologist – most likely to be EBV – but EBV -ve



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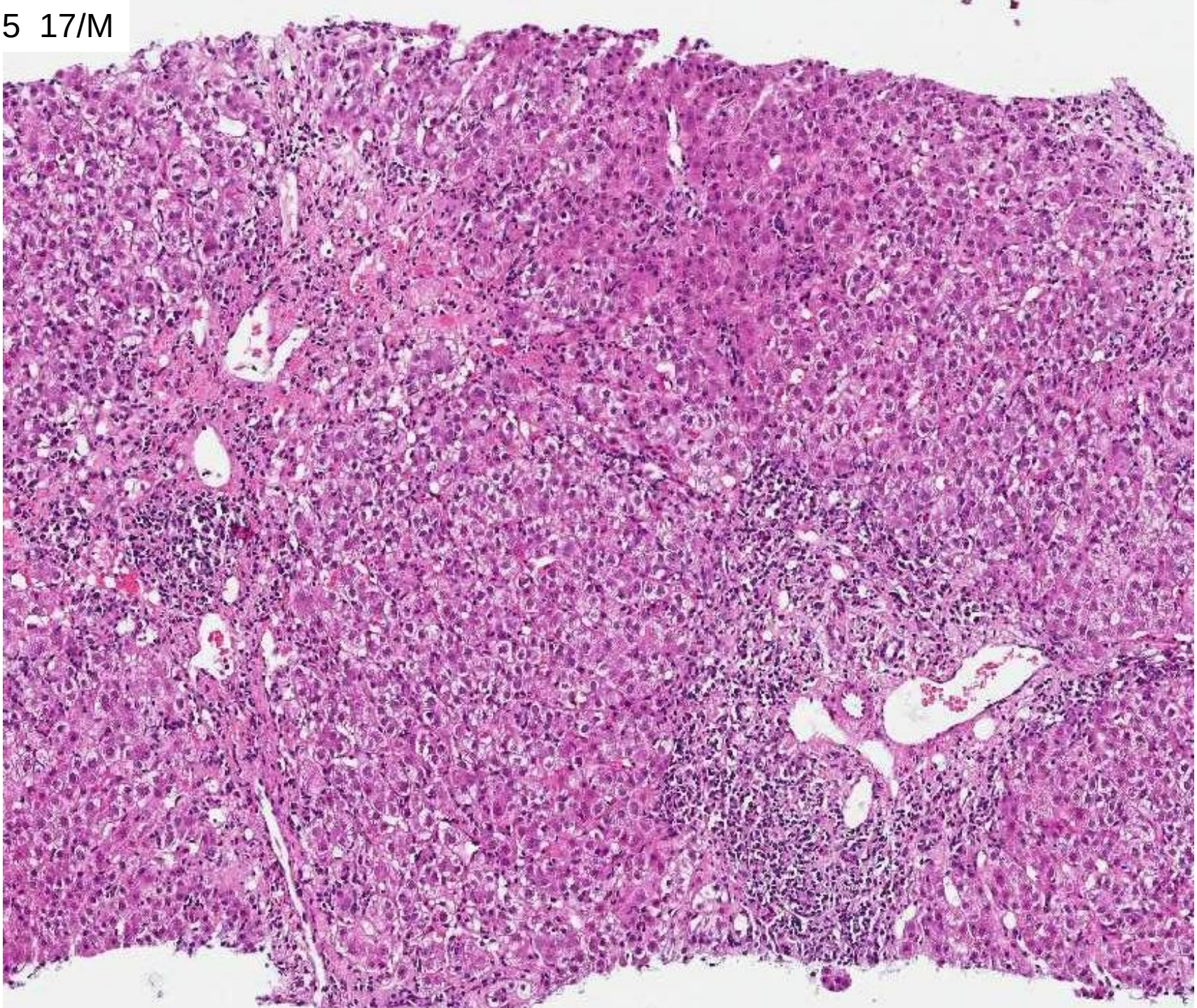

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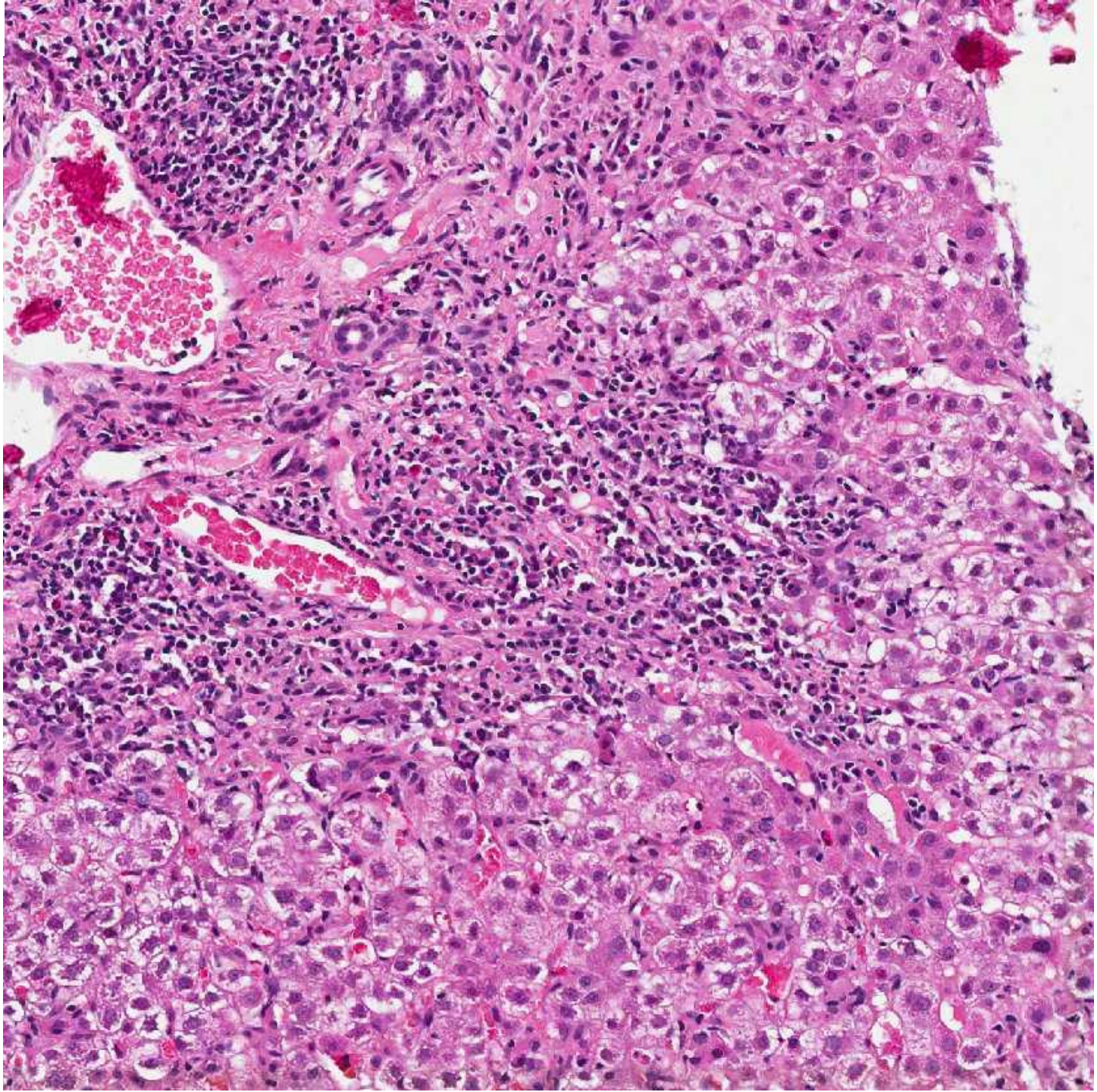

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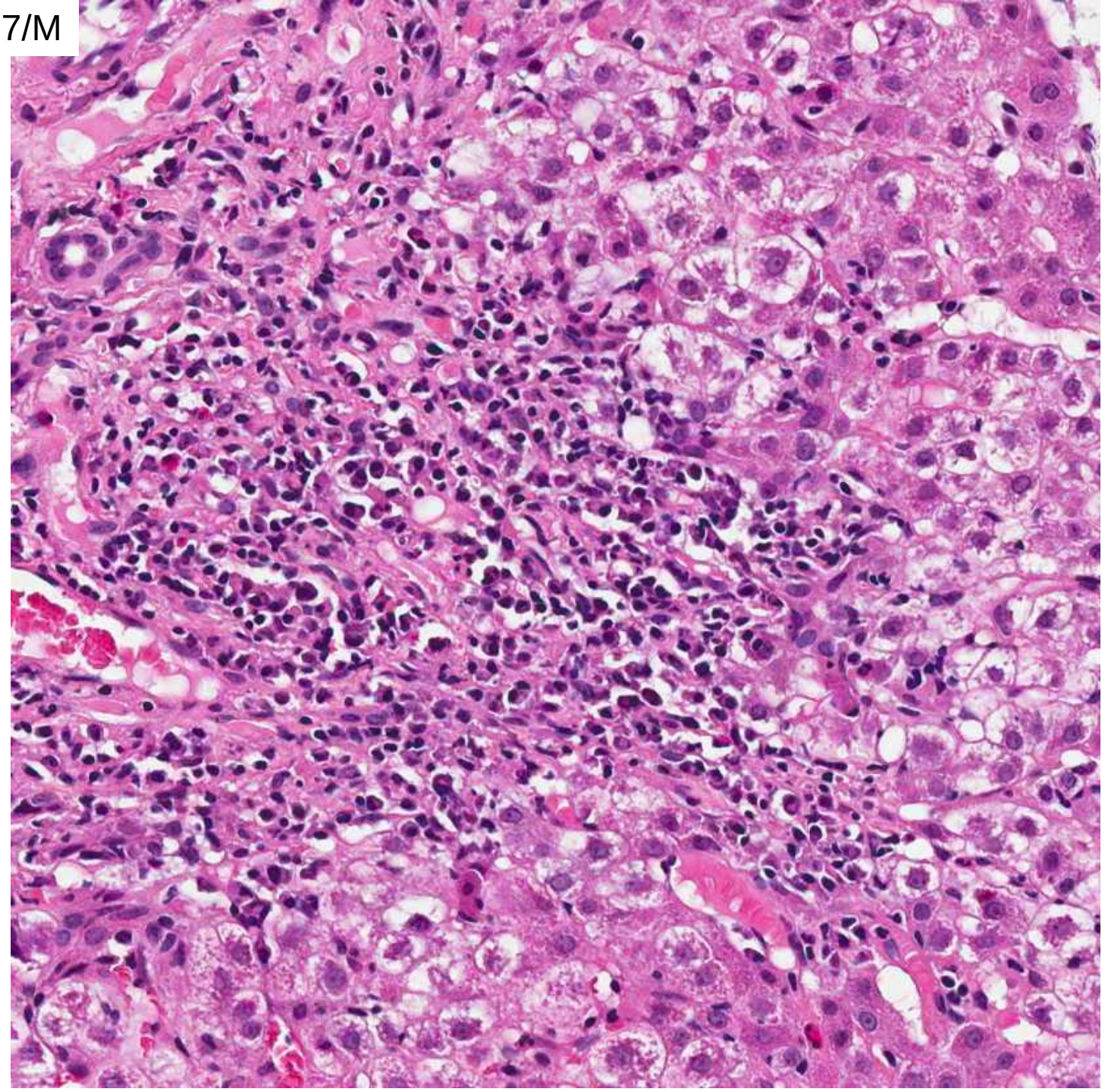

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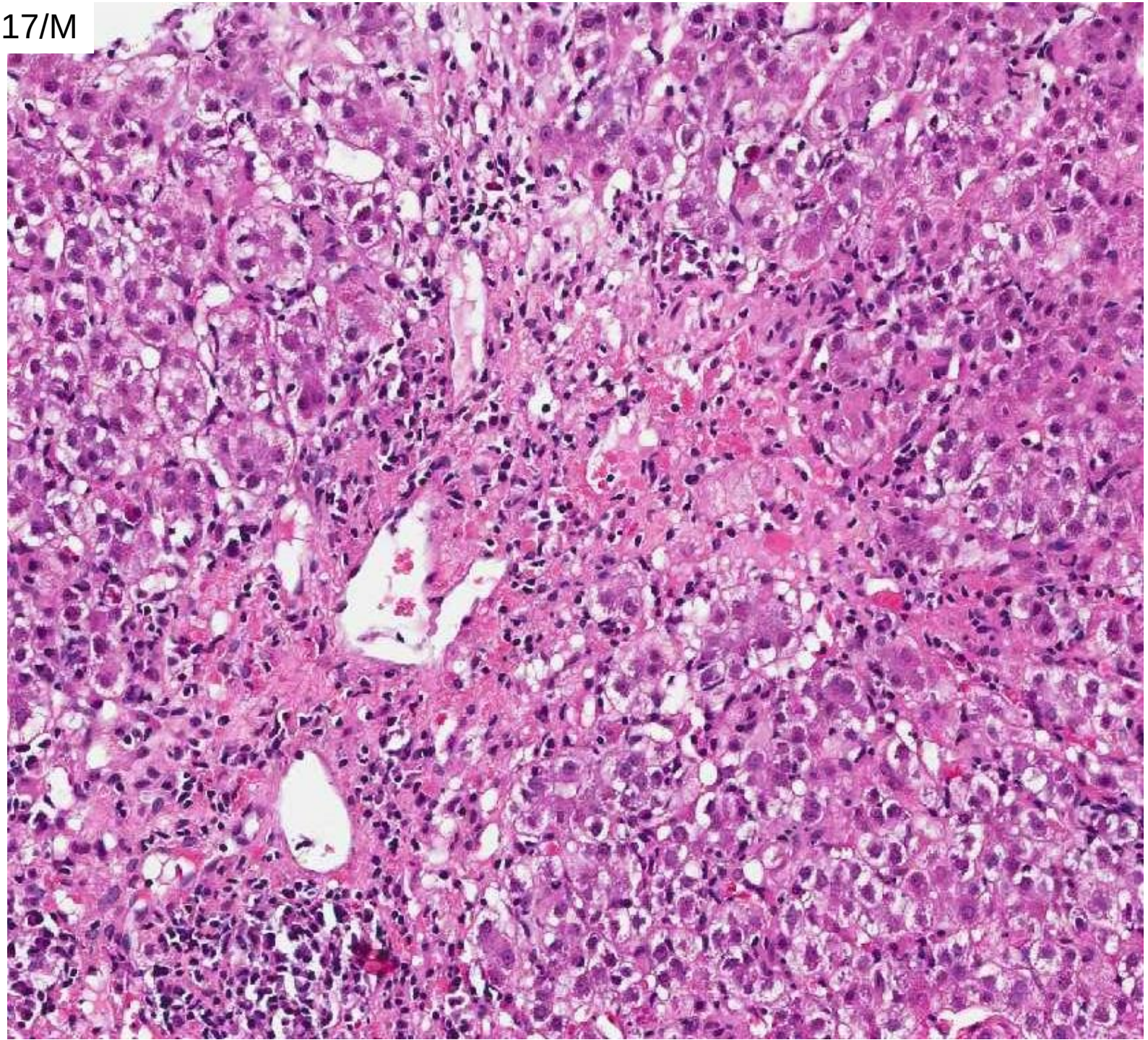

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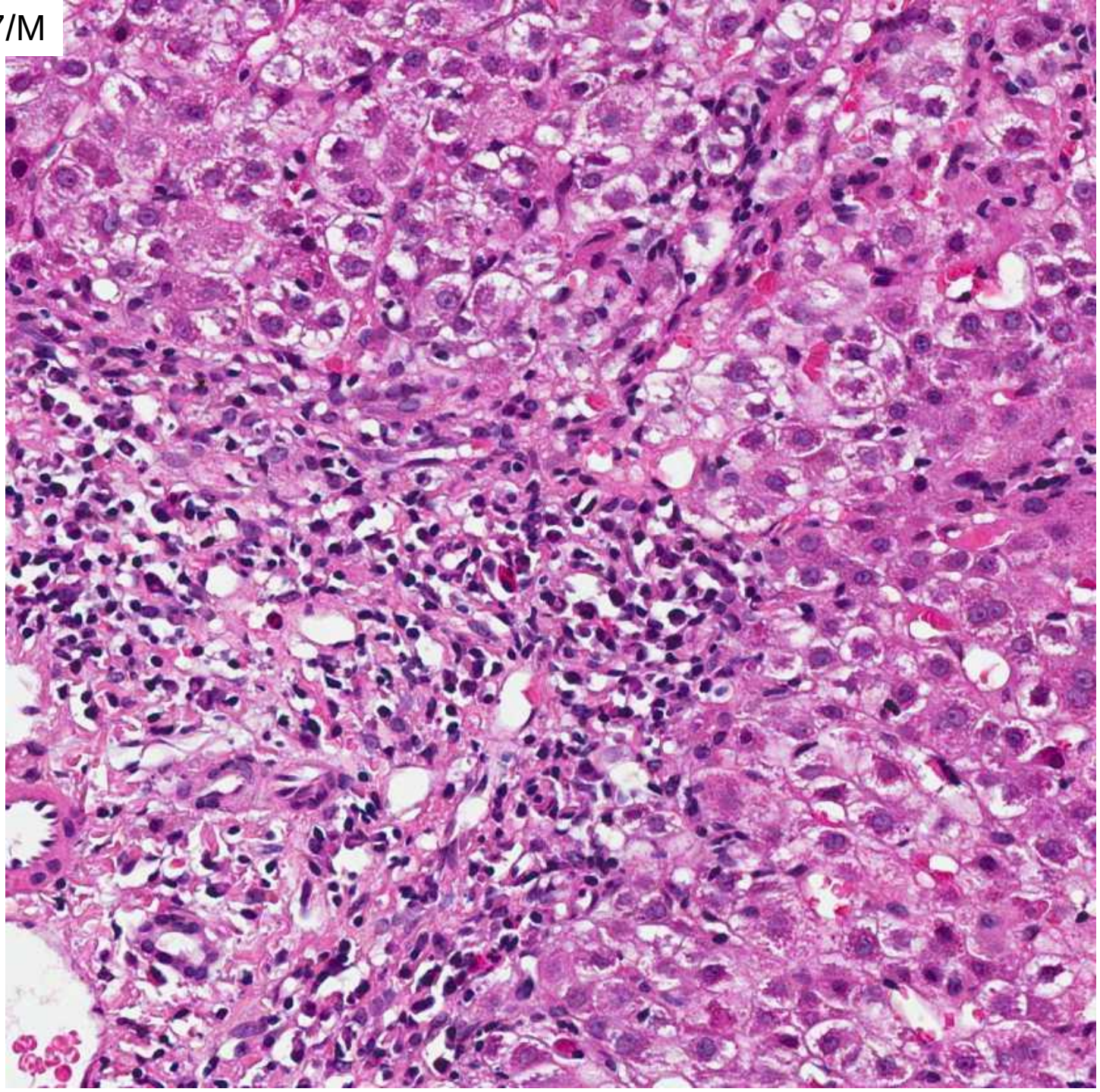

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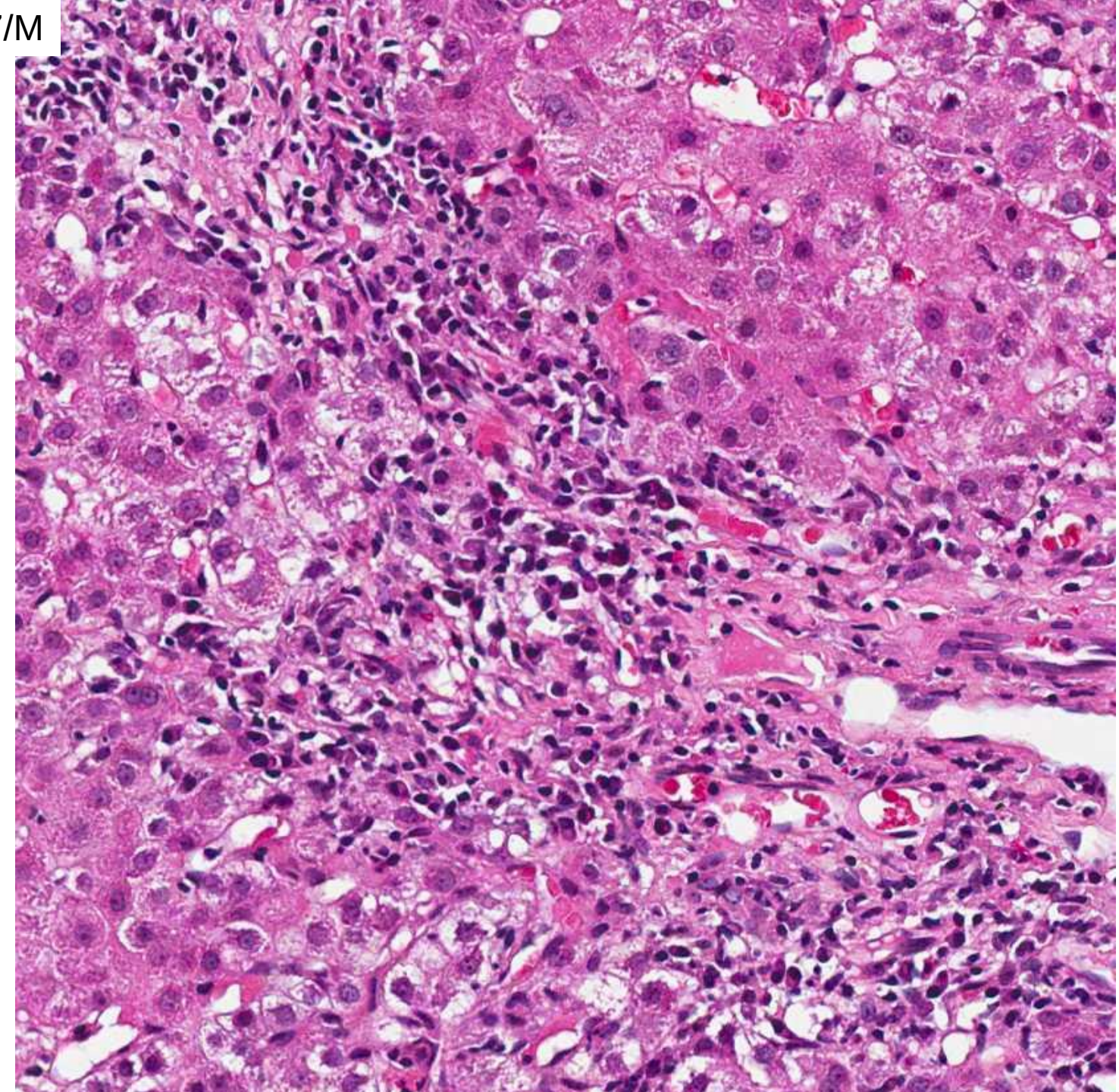

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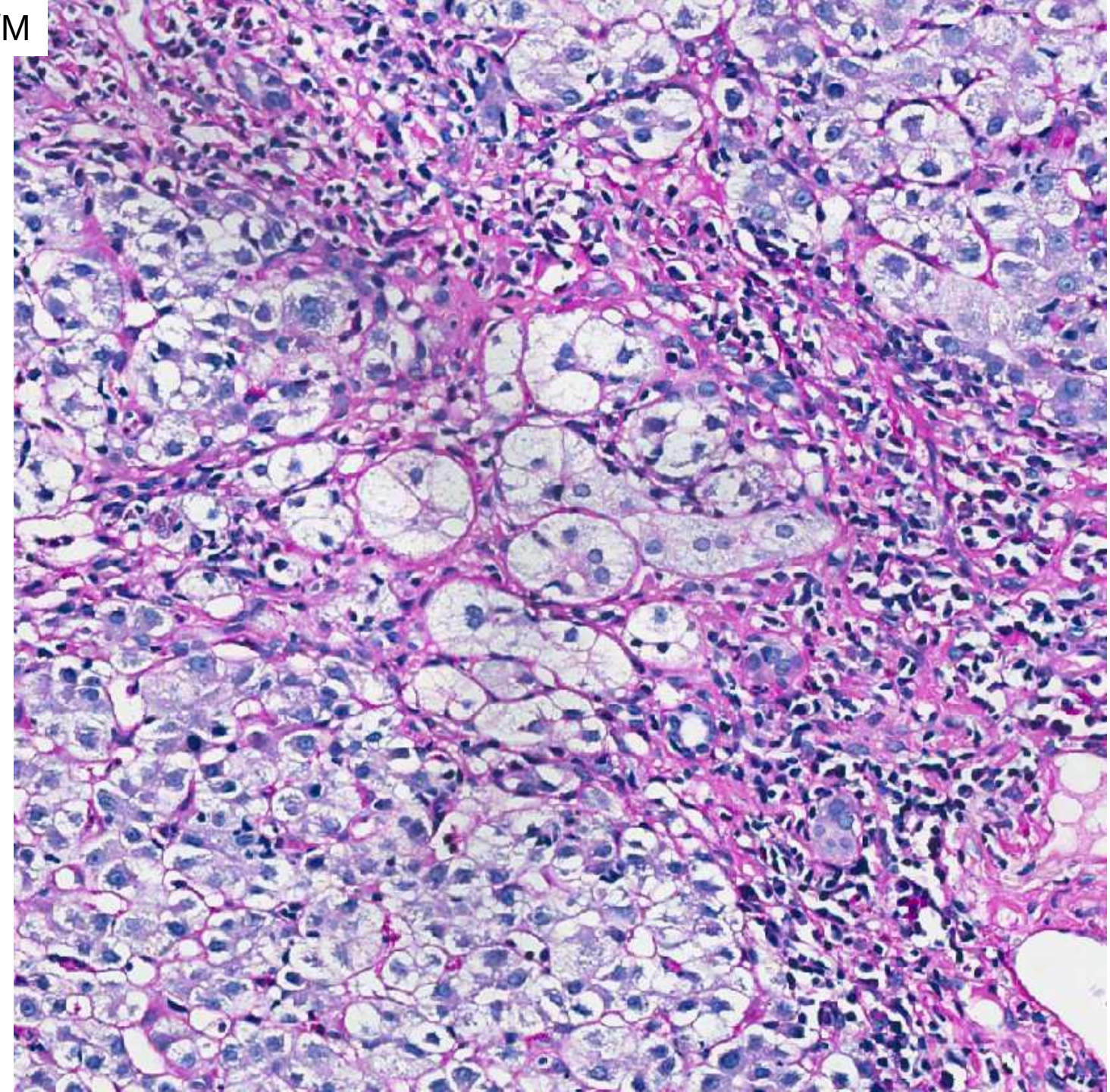

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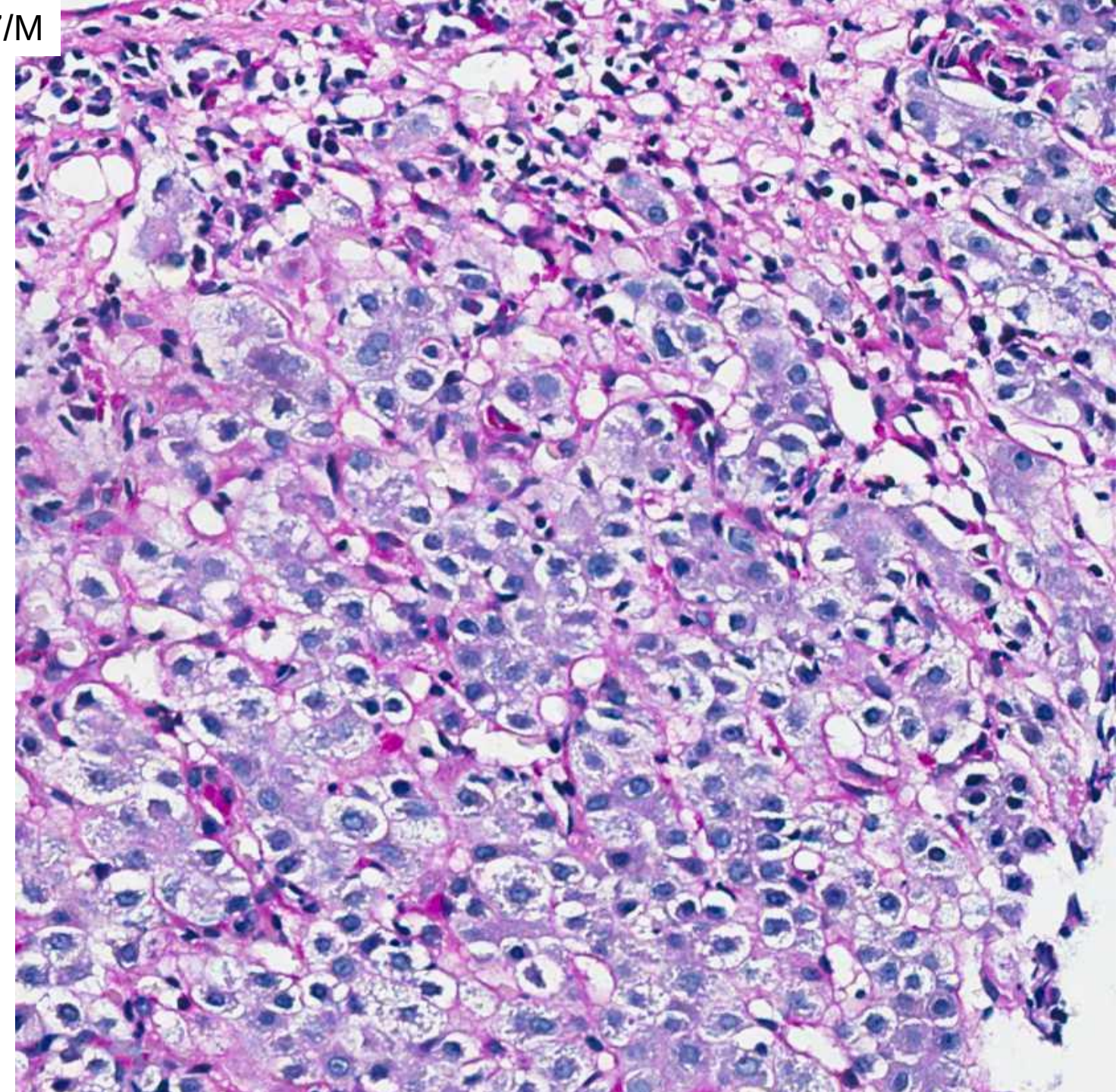
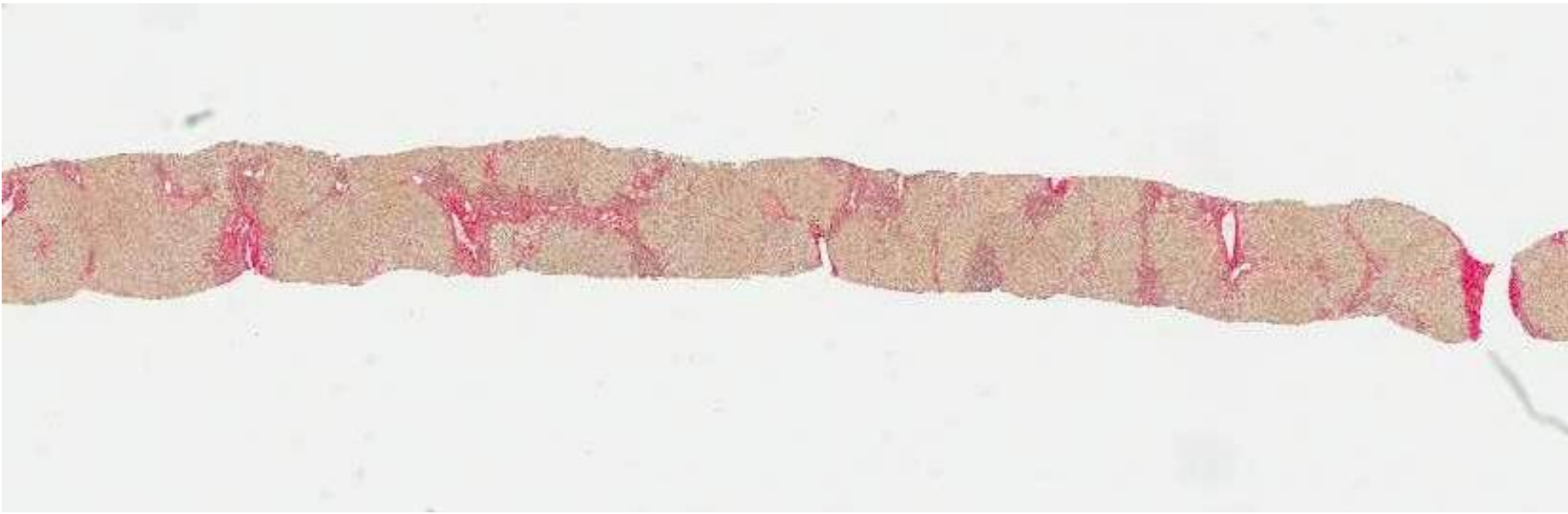


JIW 5 17/M

Sirius red



JIW 5 17/M

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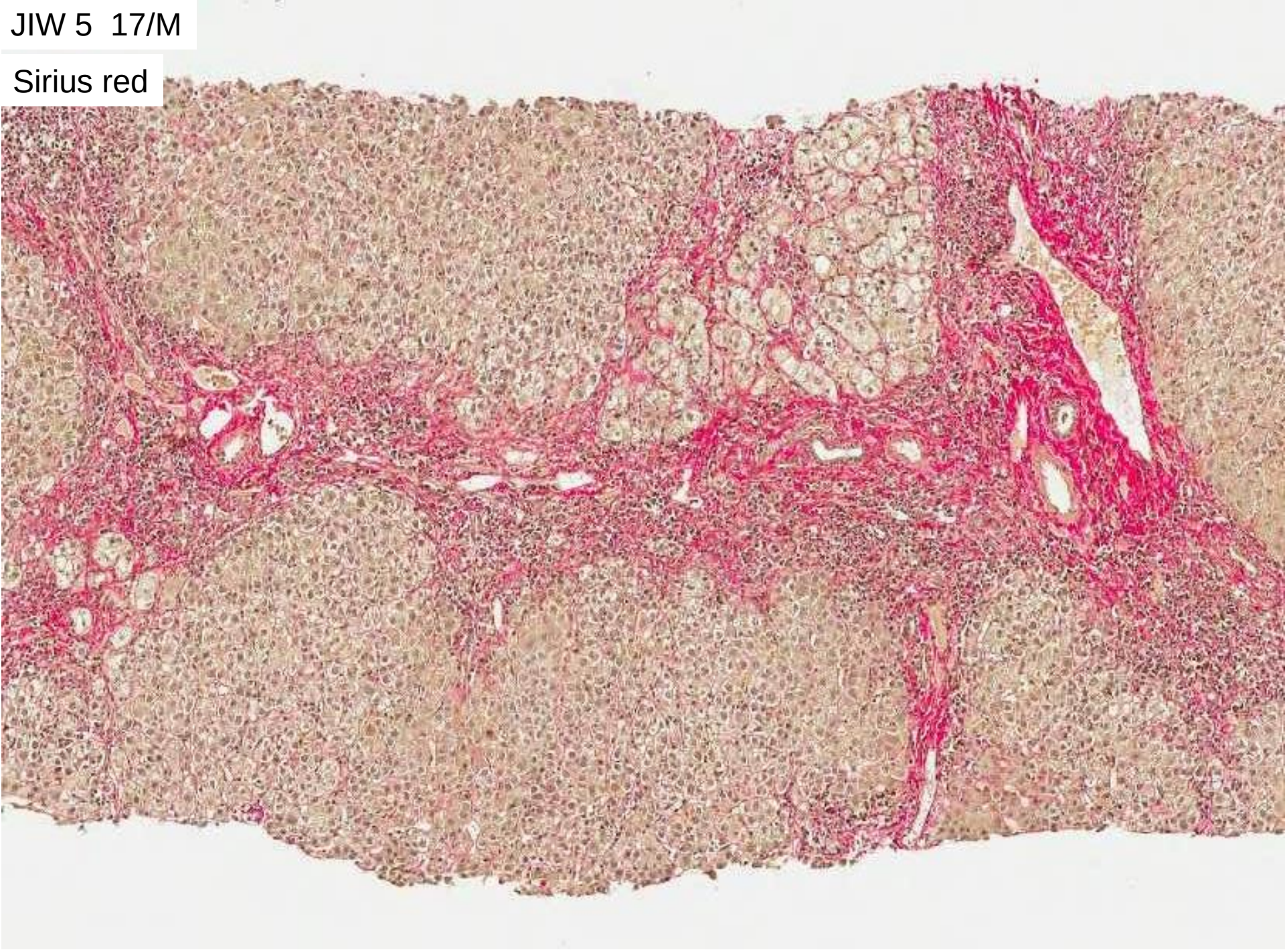
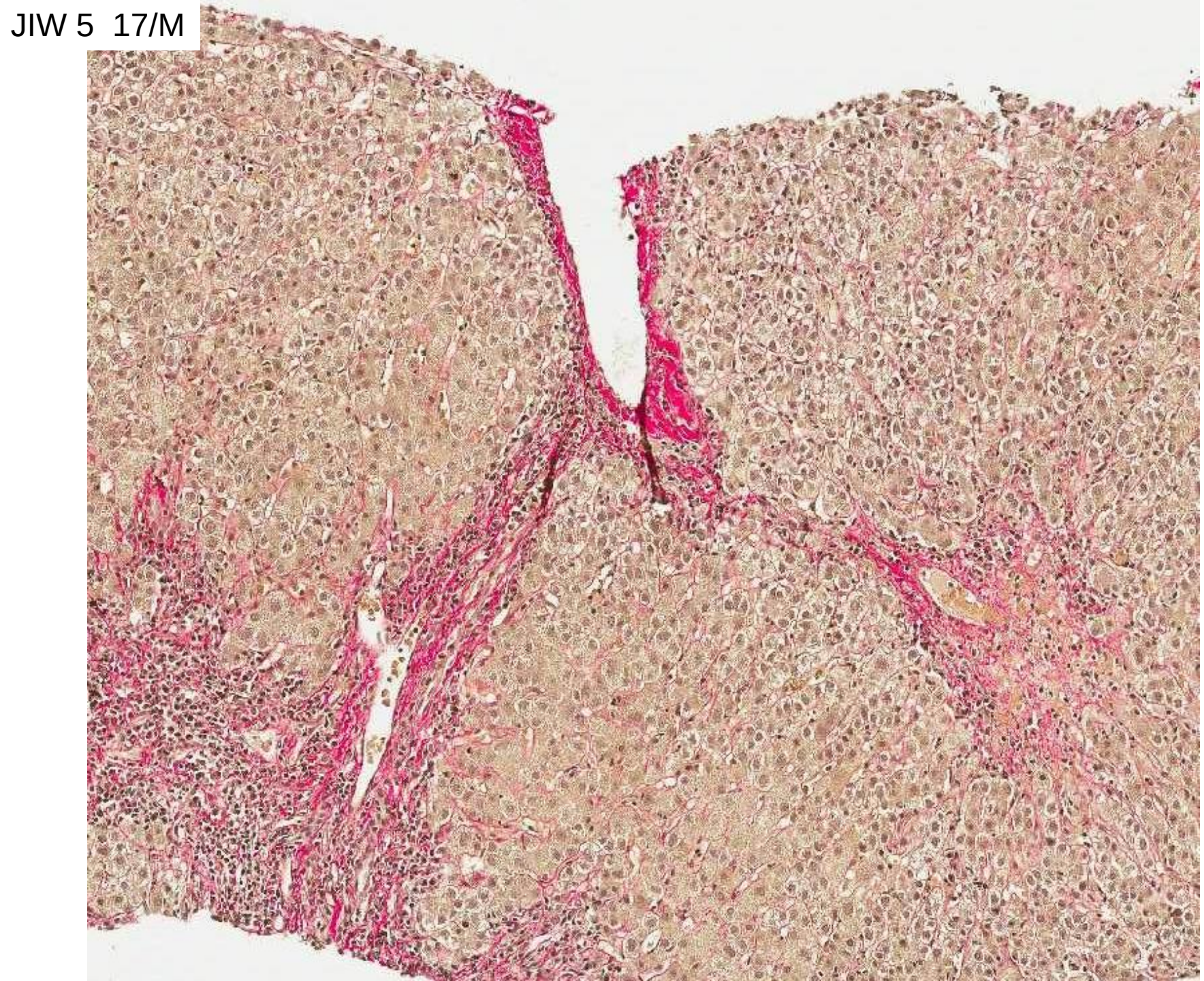



JIW 5 17/M

JIW 5 17/M

Deranged LFTs, raised ALT and SMA antibody positive.
? autoimmune hepatitis

Hepatologist – most likely to be EBV – but EBV –ve

Diagnosis: portal and lobular hepatitis with bridging necrosis. Plasma cell rich infiltrate, interface hepatitis.

Autoimmune hepatitis – recent onset.

Autoimmune Hepatitis - Acute Presentation

30-40% of cases present as acute hepatitis /acute liver failure

(Czaja & Freese 2002, Lohse 2011)

Increasing prevalence of AIH as a cause for acute liver failure (Fujiwara 2011)

? May reflect improved recognition

Autoantibodies unreliable in the diagnosis of acute AIH

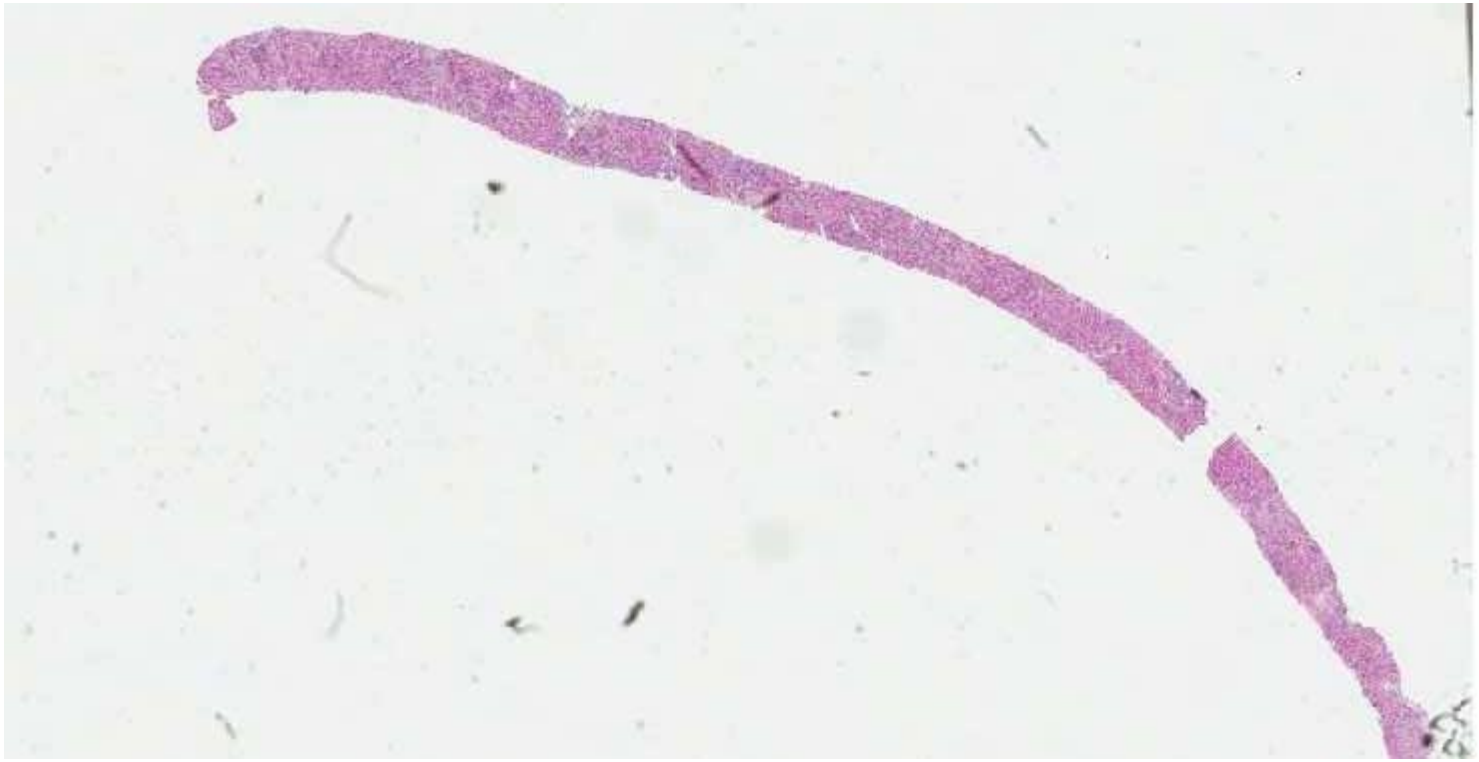
Autoantibodies and hypergammaglobulinaemia may not be present at the time of presentation with acute AIH (Lohse 2011)

Autoantibodies present in up to 40% of patients with other causes of acute liver failure - e.g viral or drug-induced (Bernal 2007)

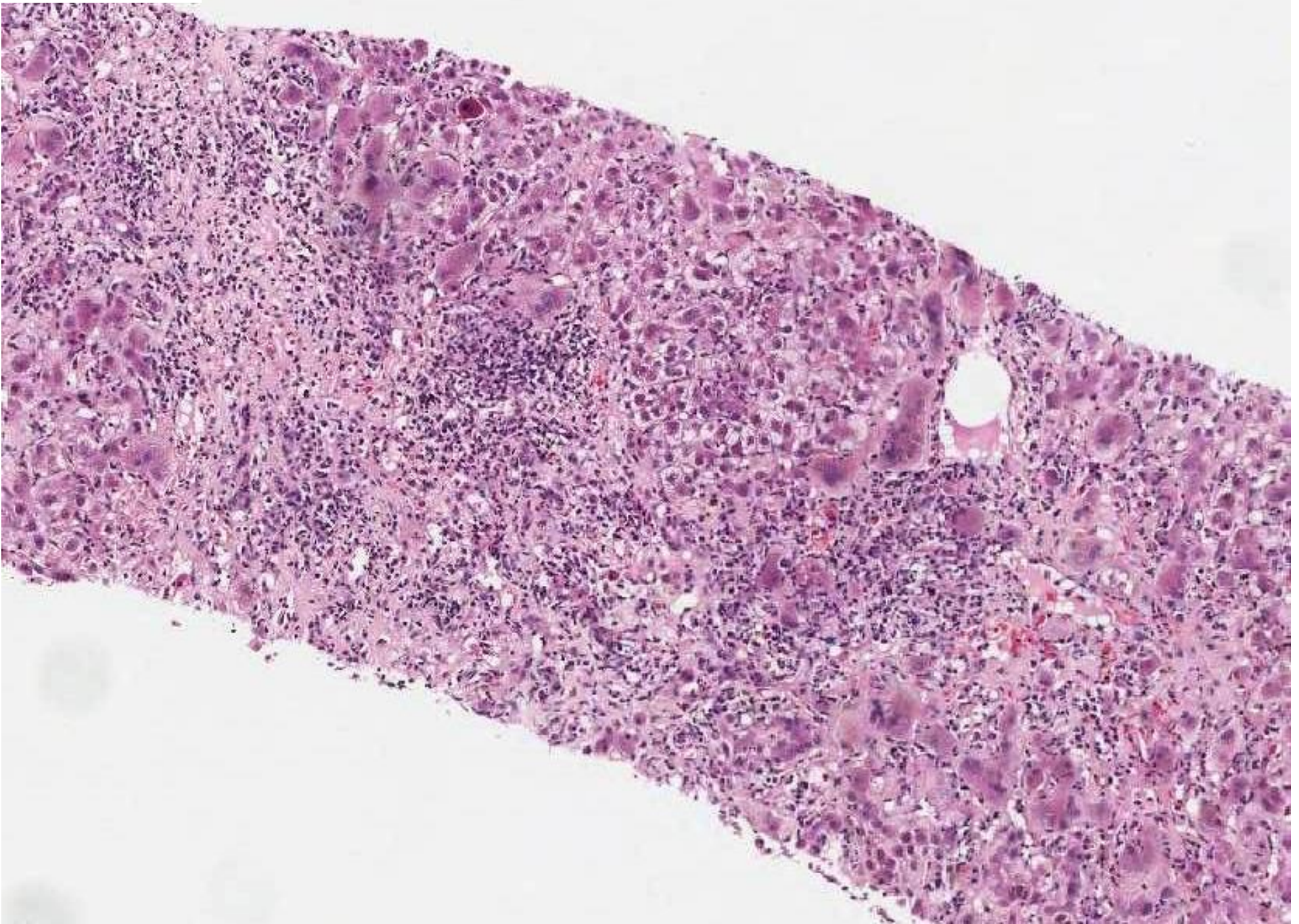
Tend to have – portal inflammation, plasma cells, follicles, centrilobular necrosis – but may have none of these.

JIW 6 45/M

Acute hepatitis. Positive autoantibodies,
? autoimmune hepatitis.



JIW 6 45/M



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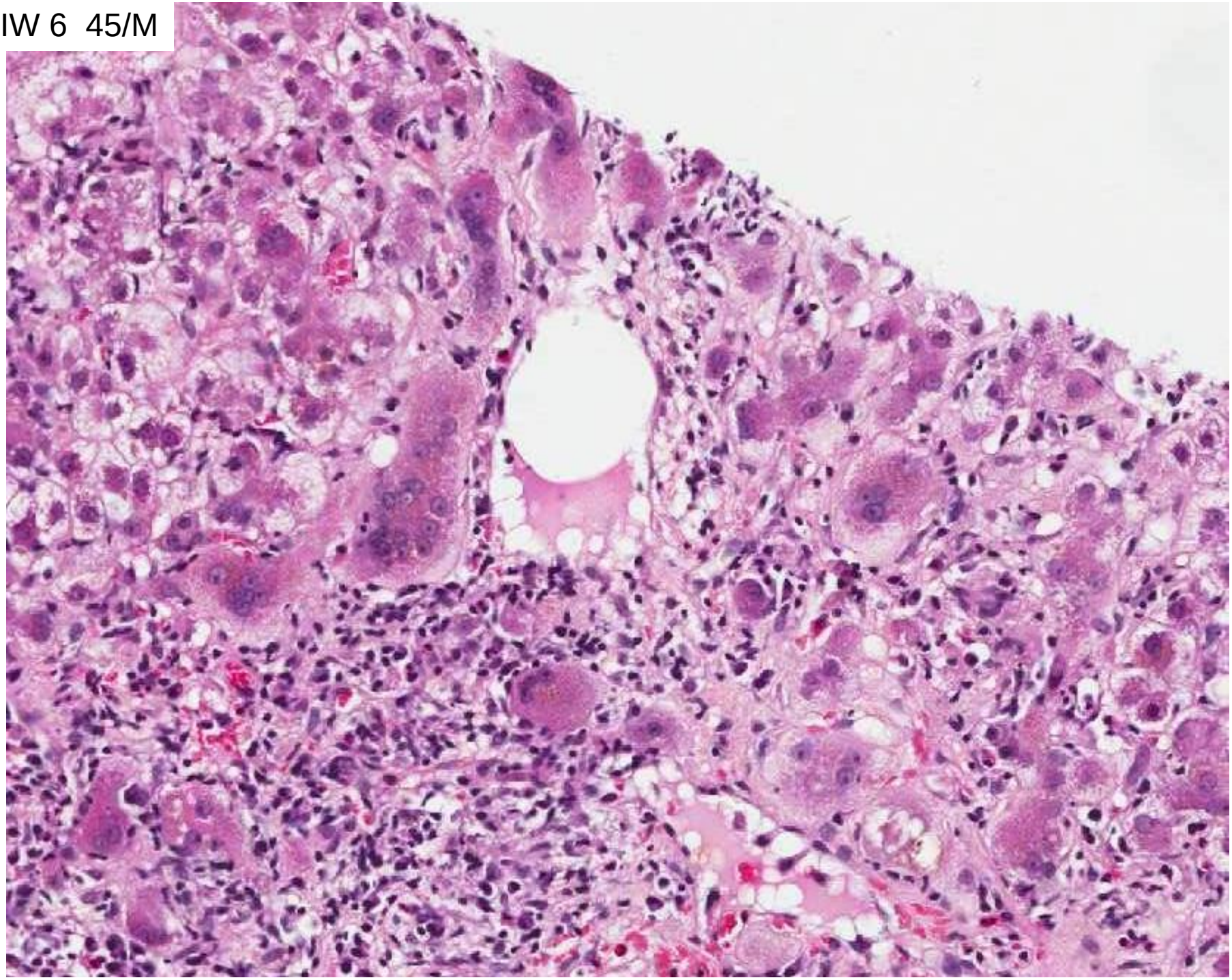

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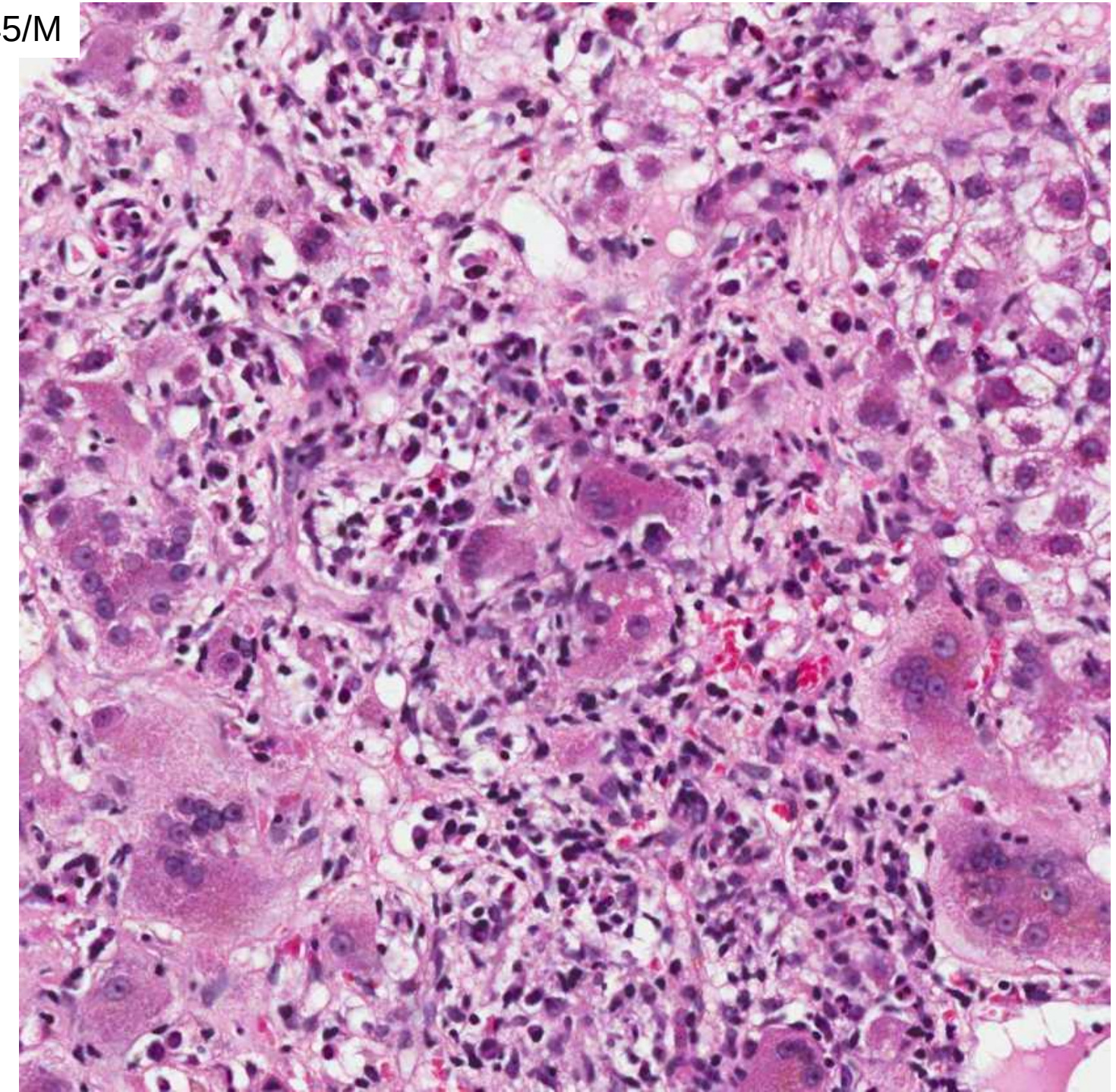


JIW 6 45/M

Acute hepatitis. Positive autoantibodies,
? autoimmune hepatitis.

Diagnosis: acute hepatitis with giant cell transformation (postinfantile giant cell hepatitis). Consistent with AIH.

Follow up – this biopsy is from 2003.

The patient has remained well, ALT mainly normal.

Repeat biopsy 9 years later, during flare of ALT
mild fibrosis, mild active chronic hepatitis

Post infantile giant cell hepatitis

Giant cell transformation common in neonatal liver disease of many causes

– immature biliary secretion enzymes.

Rare in adults – severe hepatitis, not any particular aetiology but 40% autoimmune, and those tend to do worse.

Immunohistochemistry – fusion of hepatocytes

(Ki67, CK7, CK19-ve)

JIW cases so far (1-6):

Examples of acute hepatitis

Range of severity – very mild to total necrosis

similar histology – lobular>portal inflammation

lobular disarray, acidophil bodies, Kupffer cells

+/- confluent necrosis (zonal, bridging, panacinar), collapse, giant cells, hepatitic rosettes

Cause – viral (don't usually biopsy, but same spectrum as others) incl E

autoimmune – some have PC and interface hepatitis

drugs – range of acute changes

non-specific, cholestatic,

eosinophils, autoimmune

don't know = 'seronegative' (or nonA-E)

= majority of severe cases

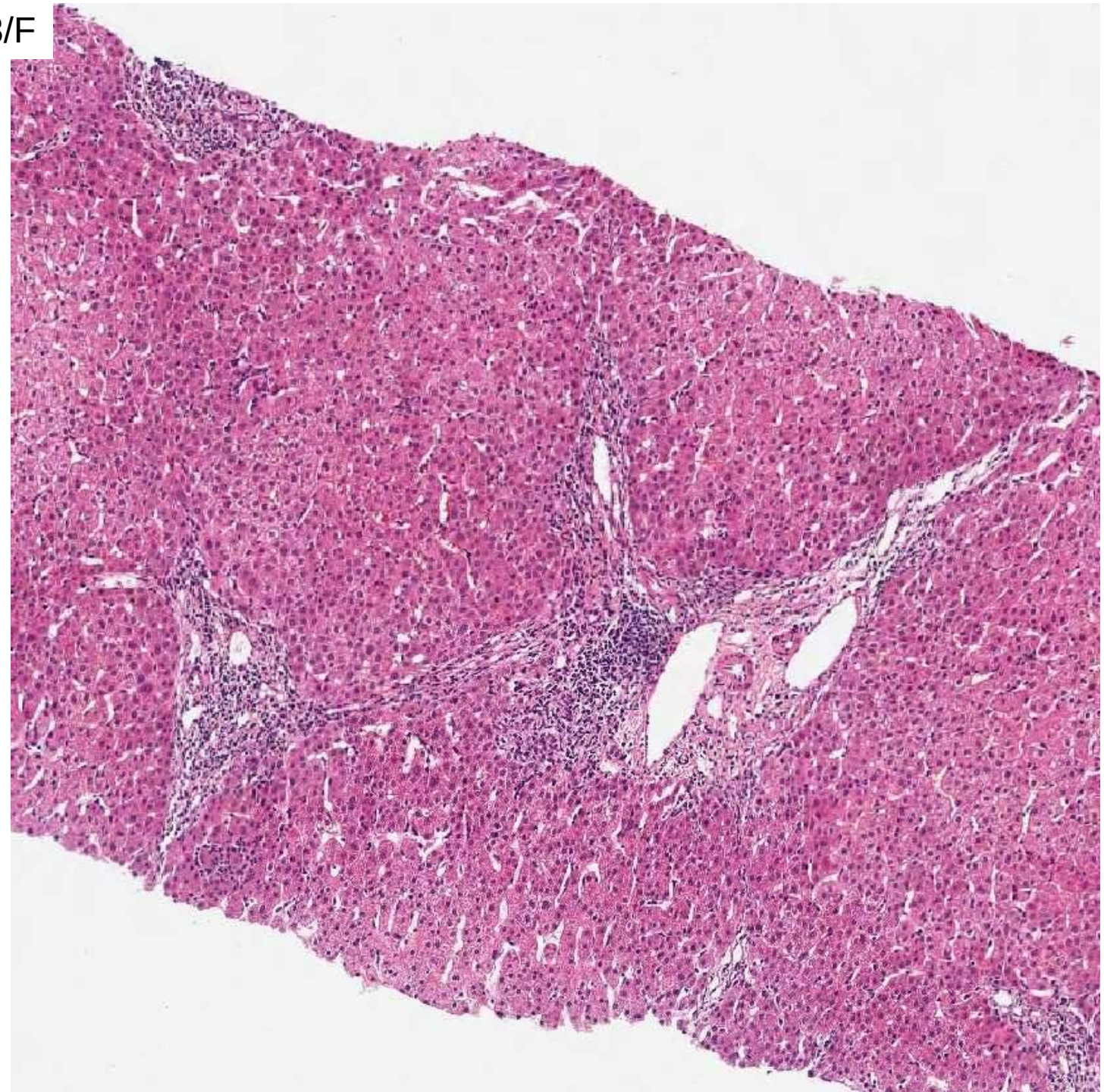
JIW 7 33/F

Raised IgG (27.6) and IgM(5.1). Positive AMA, LKM,
Persistently abnormal LFTs.

ultrasound scan - splenomegaly.

? AIH/PBC overlap.

JIW 7 33/F



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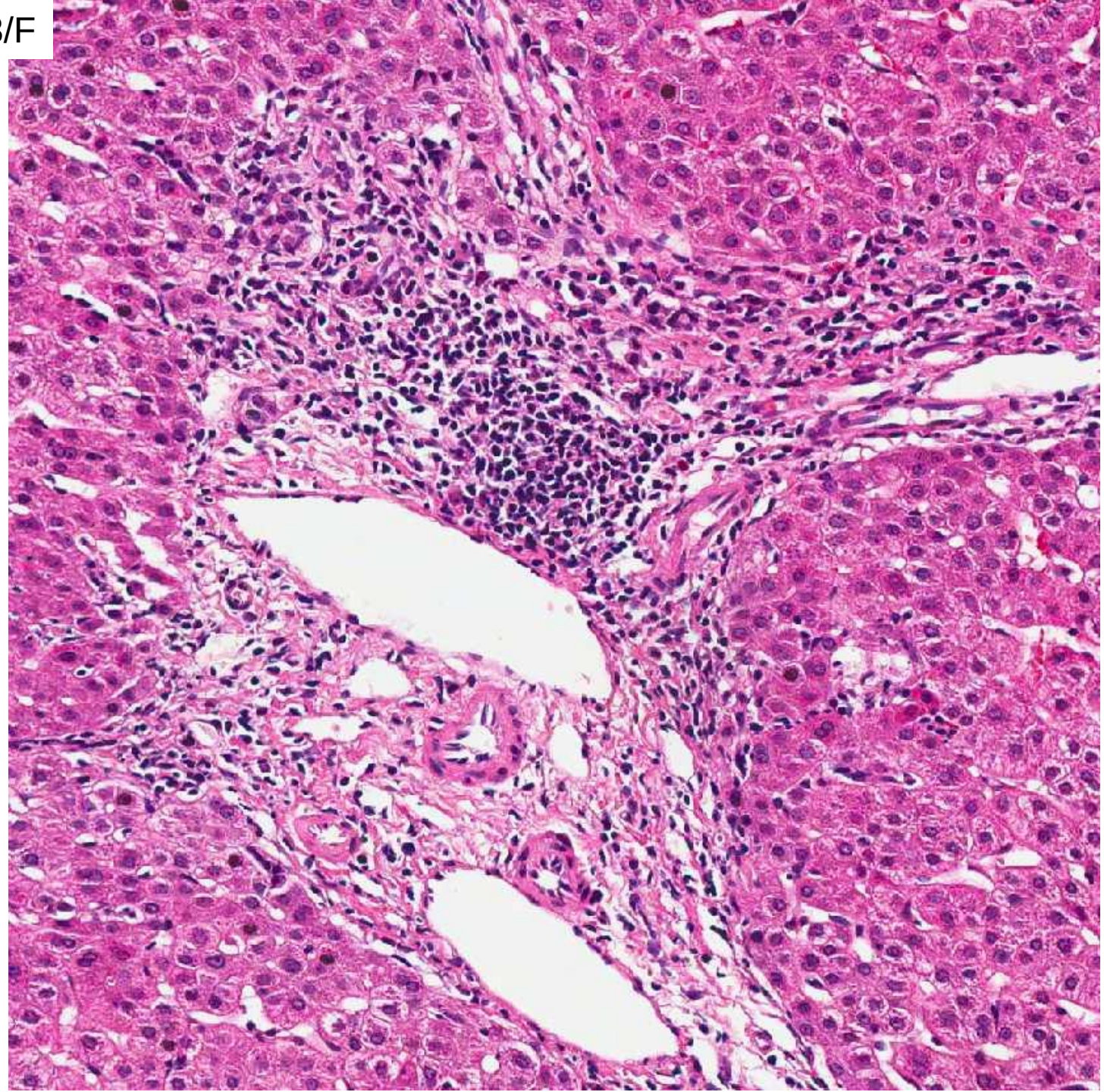

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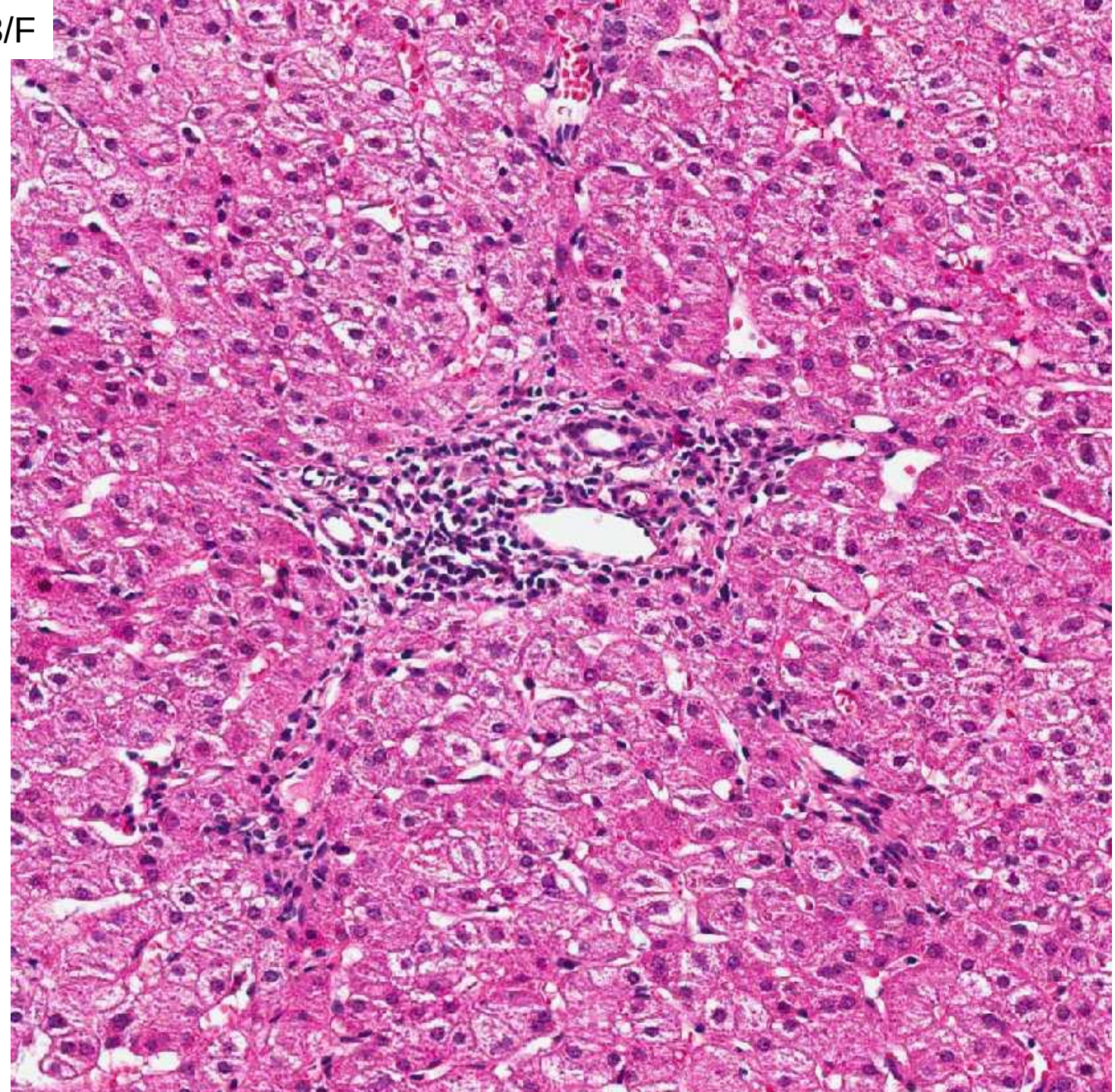

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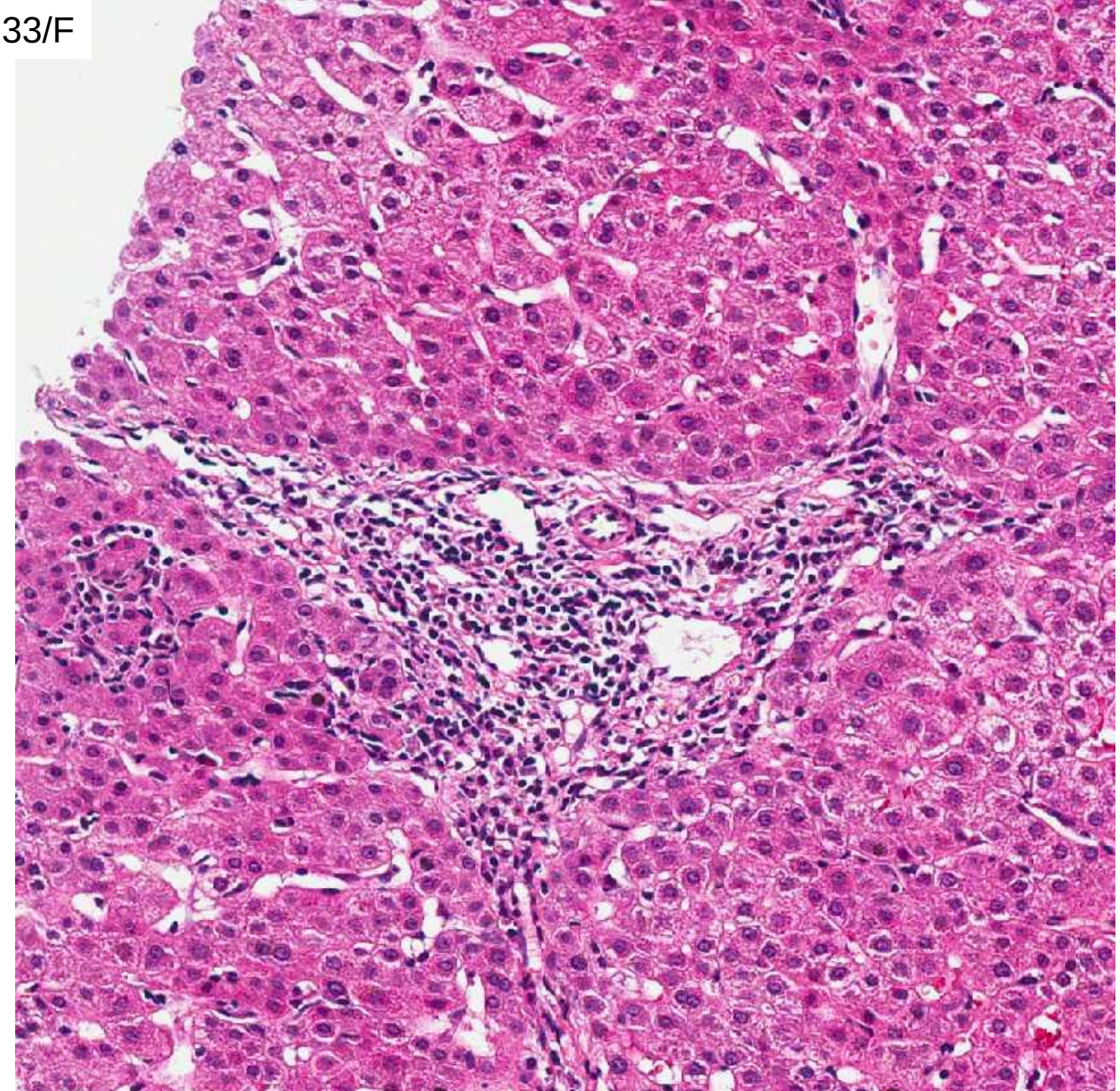

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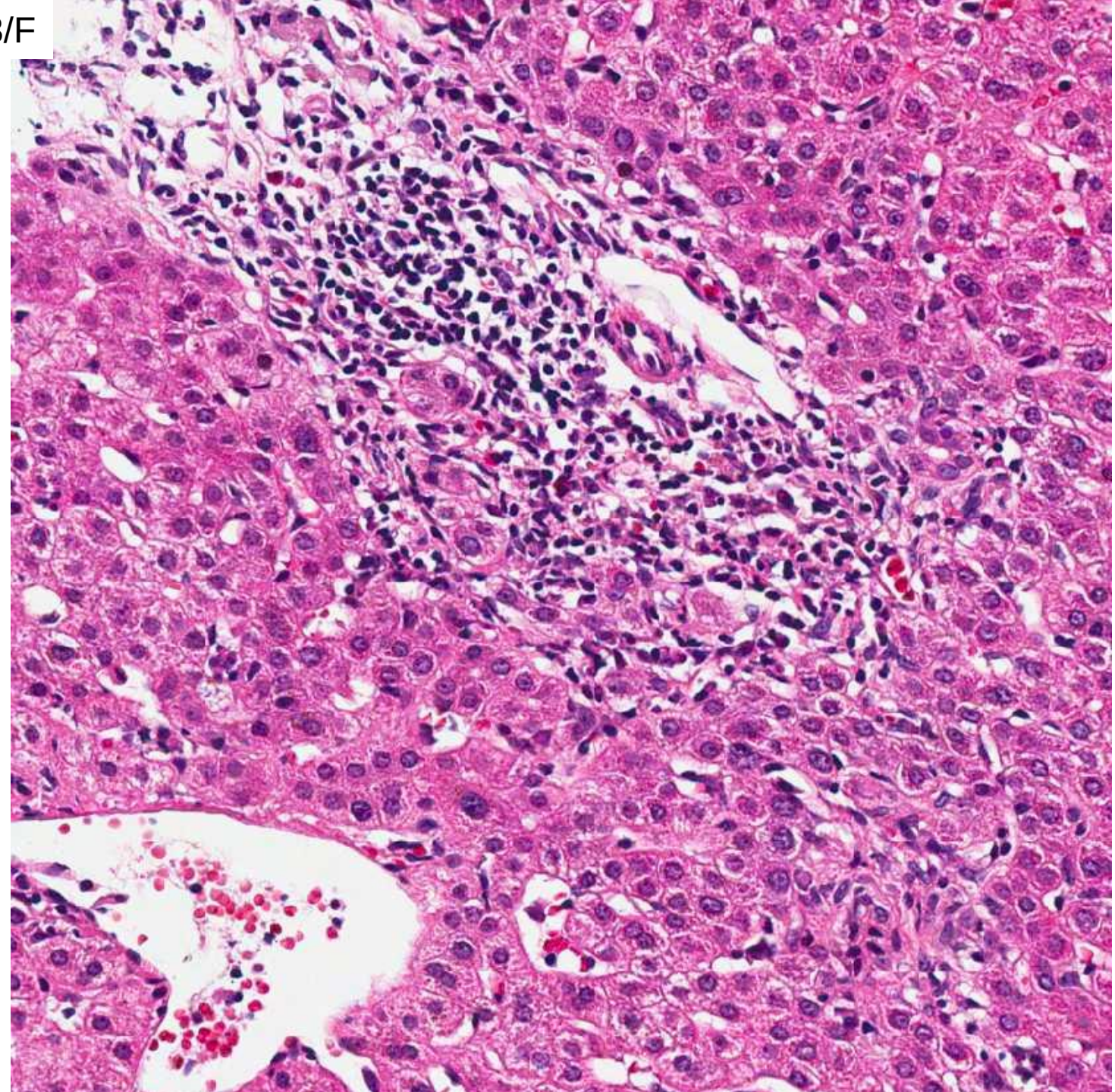

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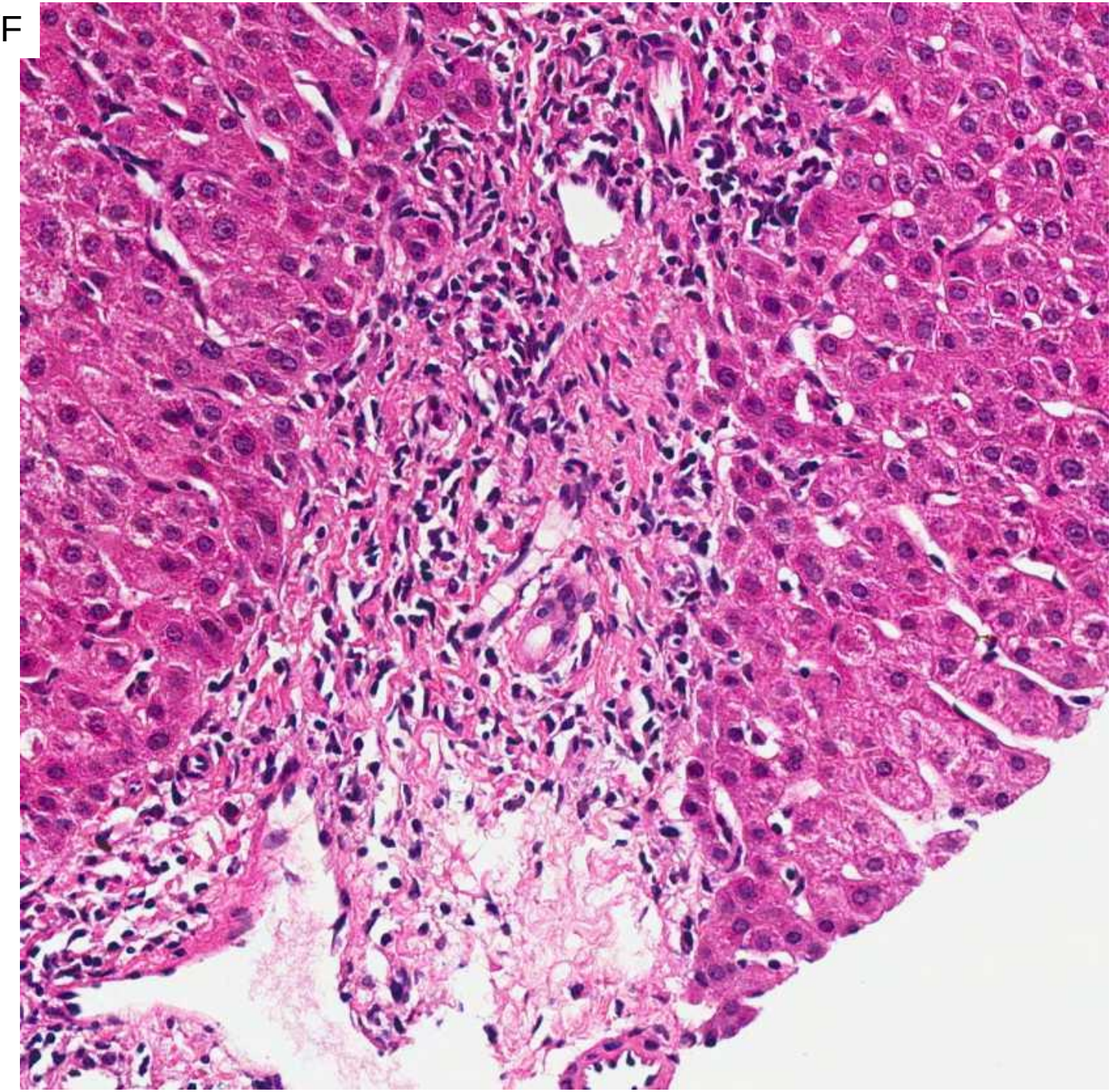

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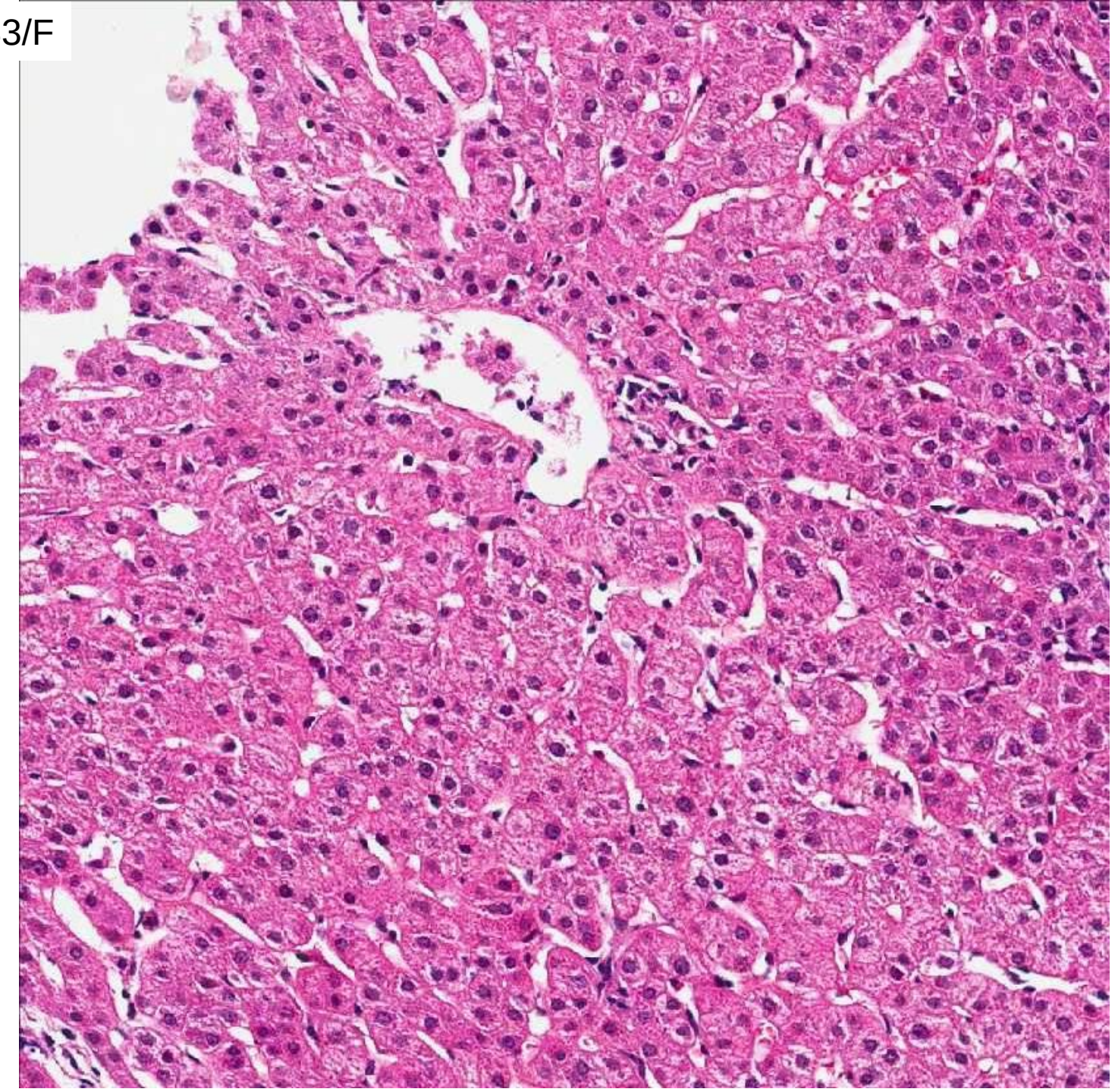

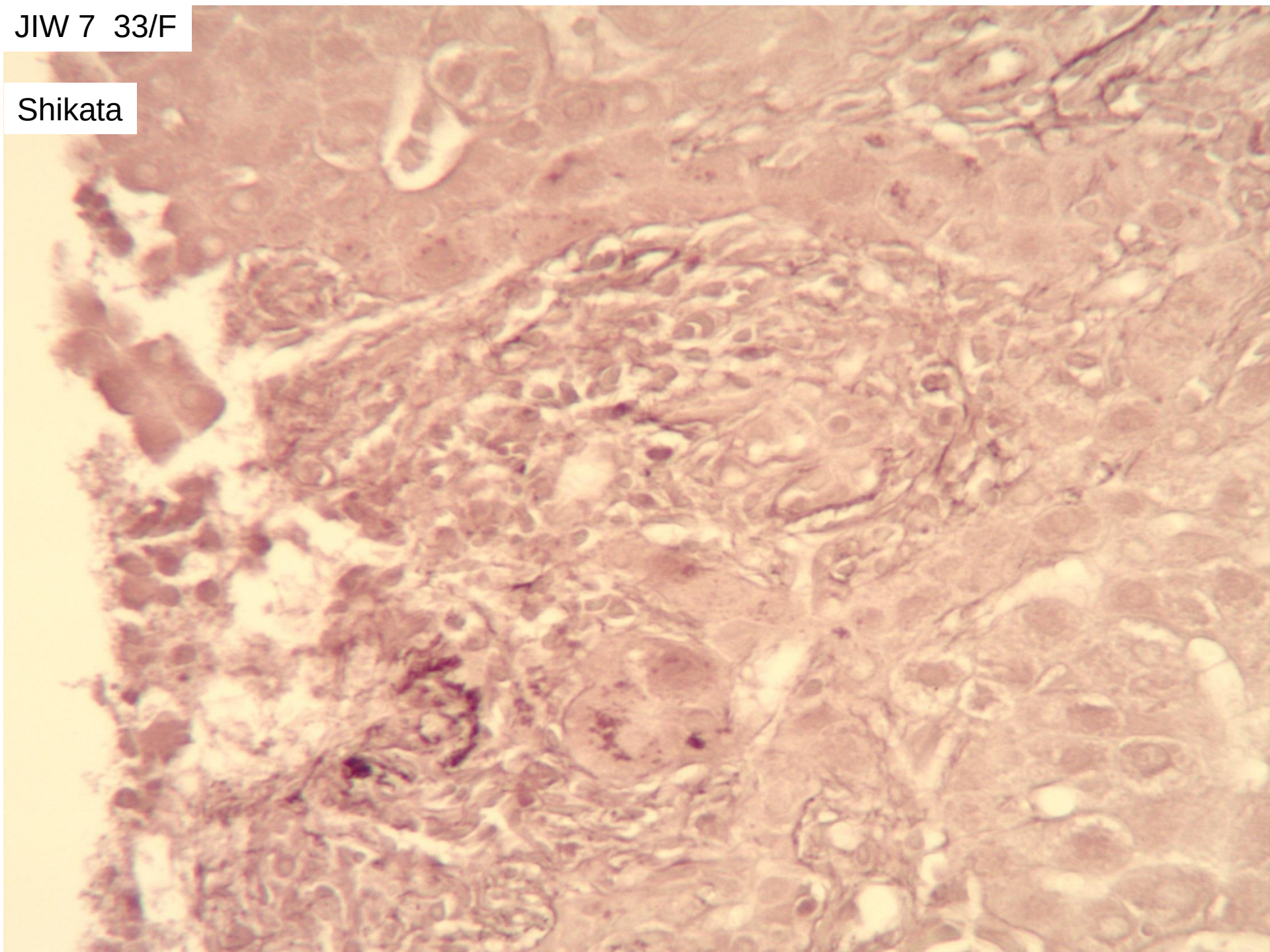
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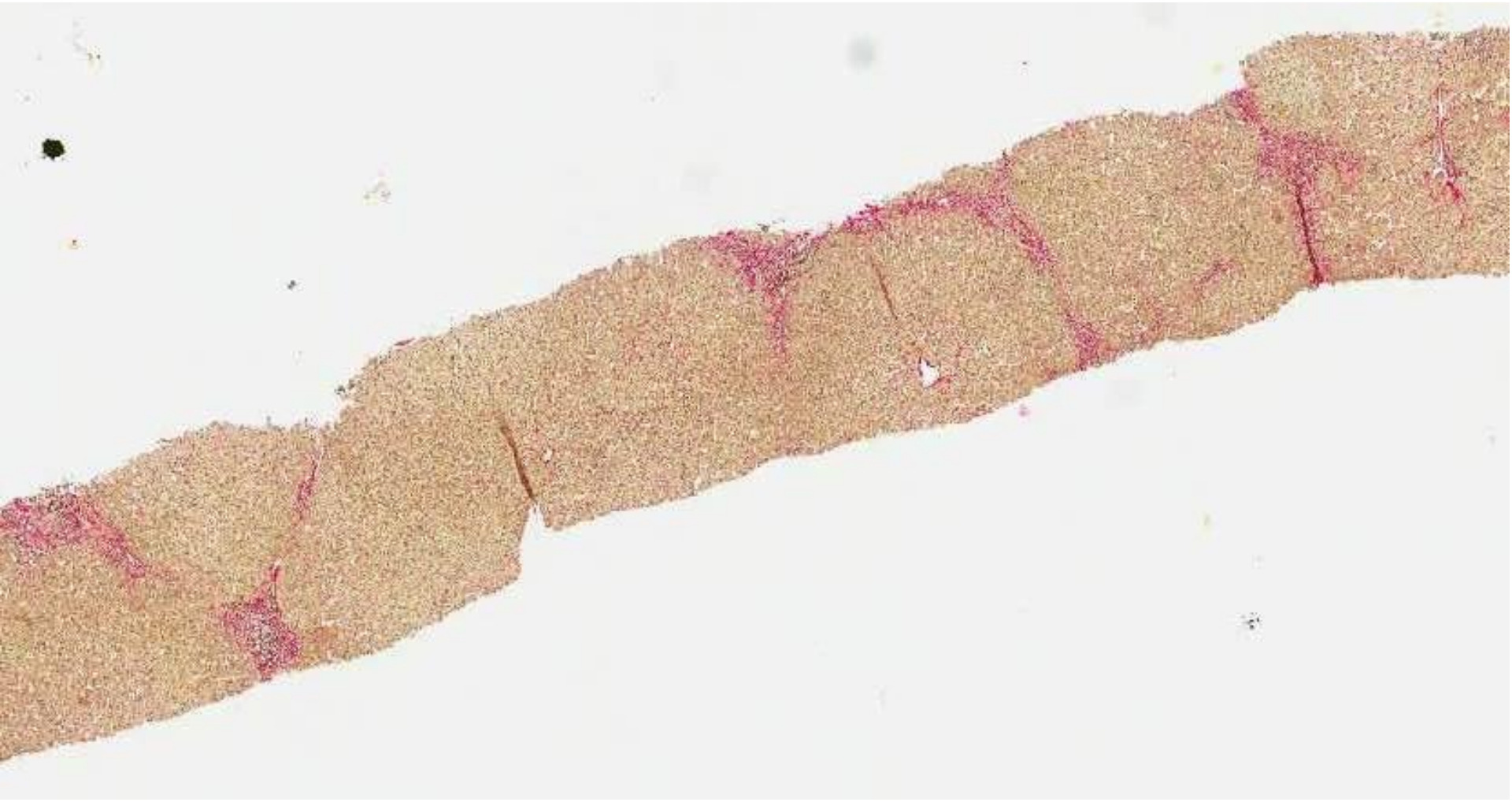
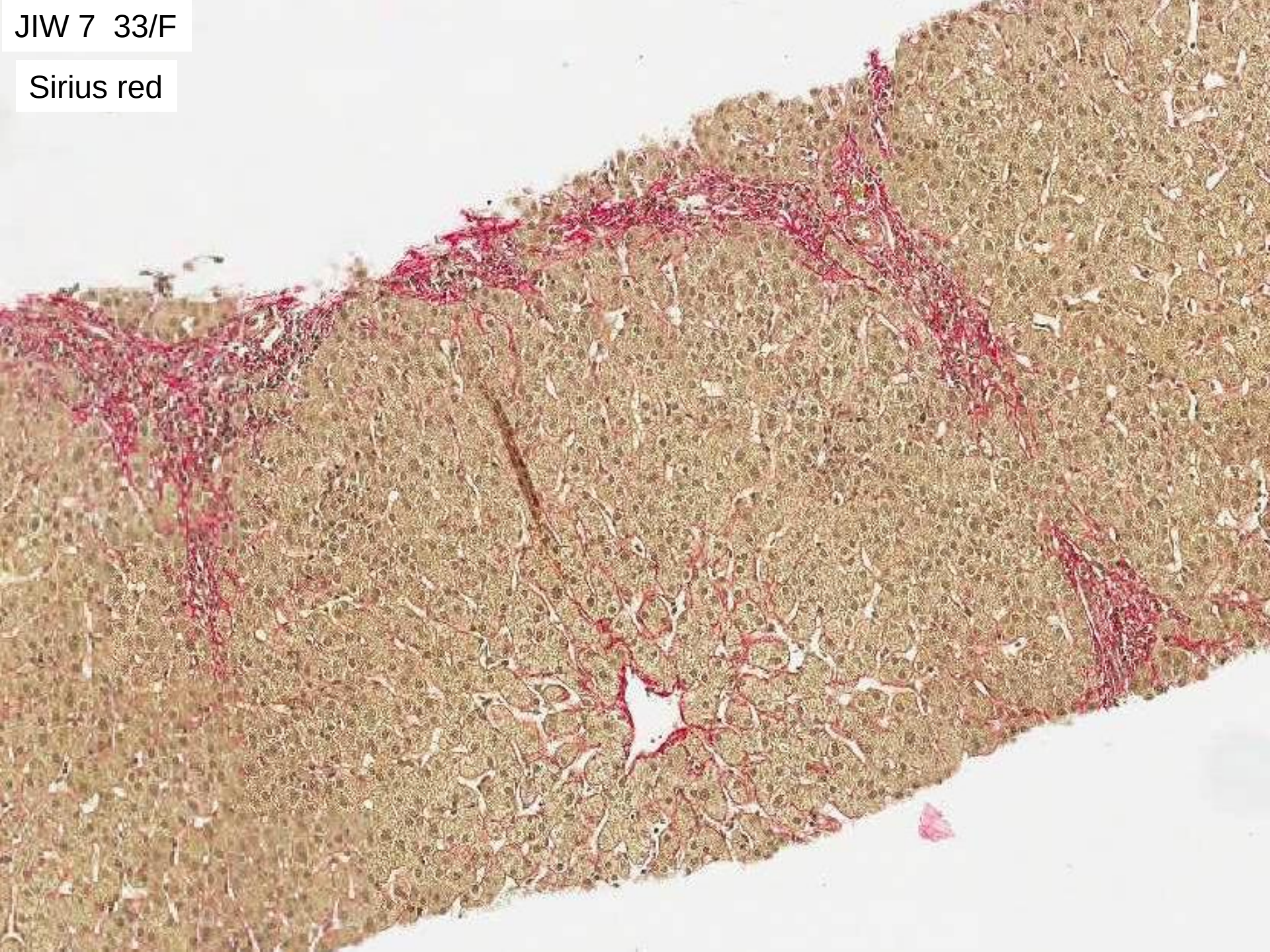
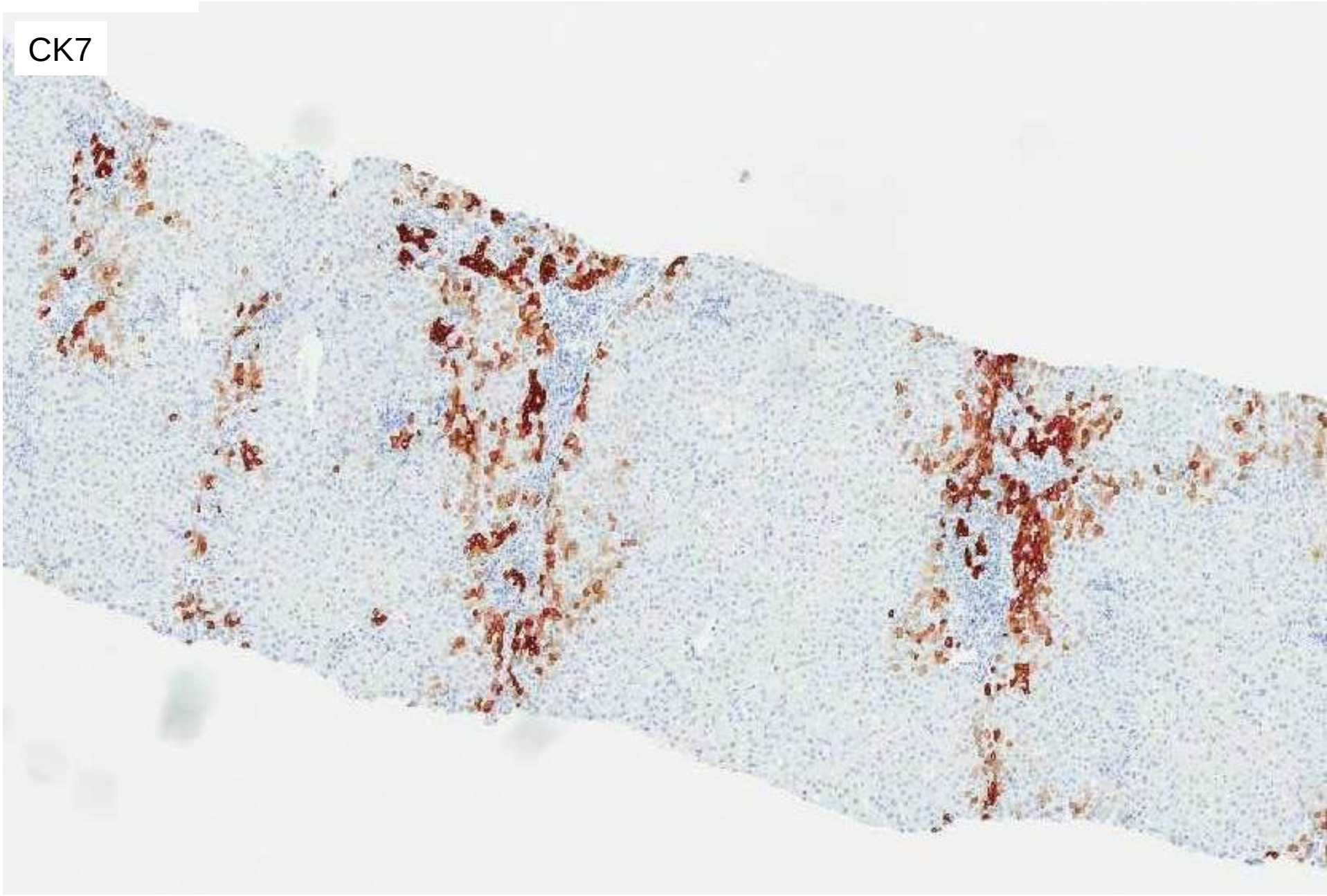
JIW 7 33/F

Sirius red



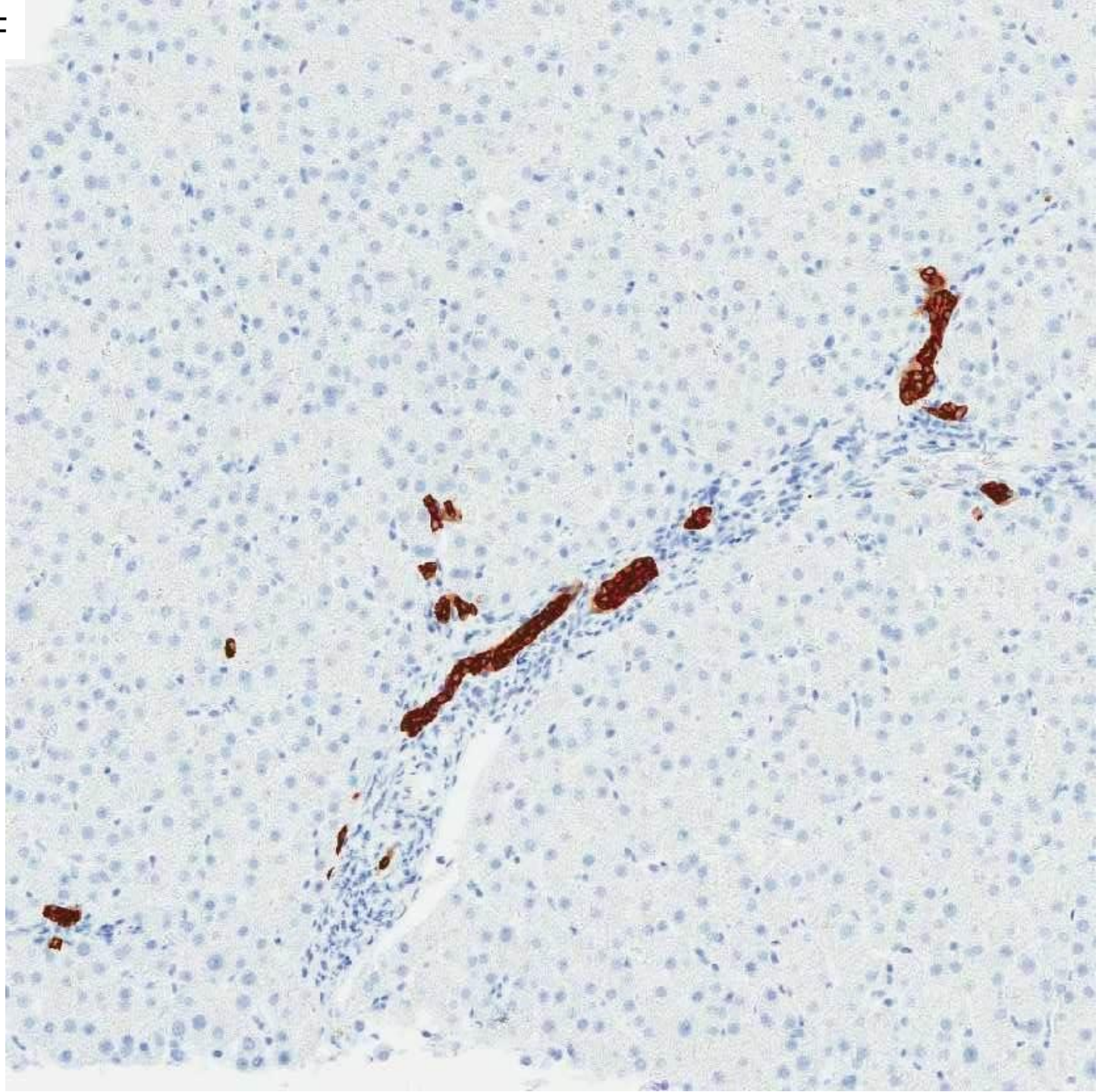

JIW 7 33/F
Sirius red

JIW 7 33/F



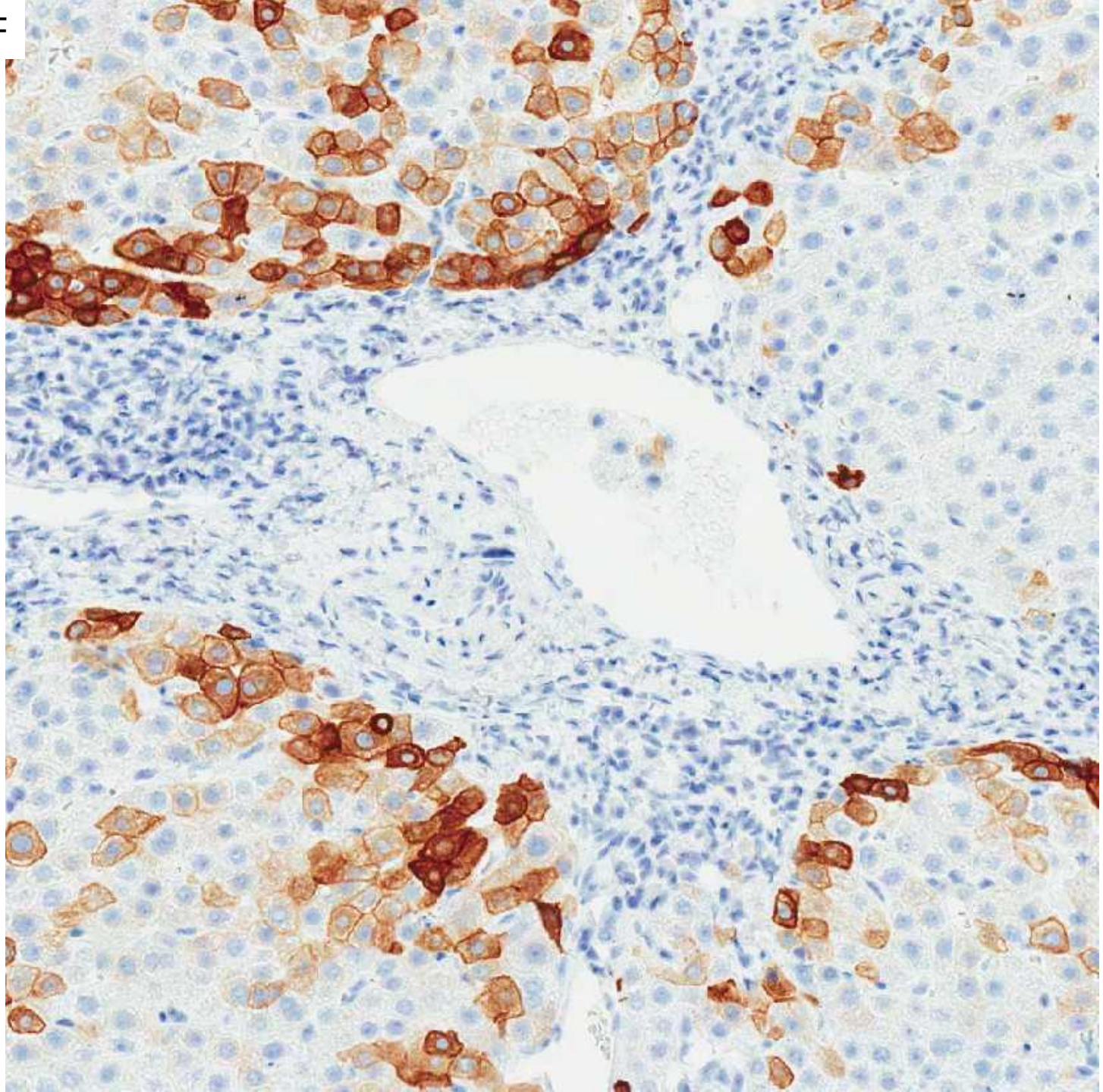
JIW 7 33/F

CK7



JIW 7 33/F

CK7



JIW 7 33/F

Raised IgG (27.6) and IgM(5.1). Positive AMA, LKM, Persistently abnormal LFTs. ultrasound scan - splenomegaly.

? AIH/PBC overlap.

Biopsy features:

Portal inflammation almost all tracts, interface hepatitis, although not conspicuous plasma cells

Ductopaenia – duct seen in 2/13 tracts

Although not ductular reaction.

Copper associated protein present, 1 portal tract.

Parenchymal mild necroinflammatory activity. No confluent necrosis.

CK7 – intermediate hepatobiliary cells. Confirms ductopenia.

Clinical context: ALT 160 (x4 ULN). Alk Phos 1743 (x5 ULN)

Both autoantibodies, both Immunoglobulins = full house for ‘overlap’

The overlap syndromes of autoimmune hepatitis

- Features of AIH mingled with those of PBC or PSC
- Respond poorly to conventional corticosteroid treatment
- PBC 7-13%
- PSC 8-17%
- (distinguish from patients with cholestatic disease and features of autoimmune hepatitis).
- Imprecise, heterogeneous and needs to be further studied.
- Categorise according to predominant features, not a separate disease.
- Treat with urso, and may need other imunosuppressants

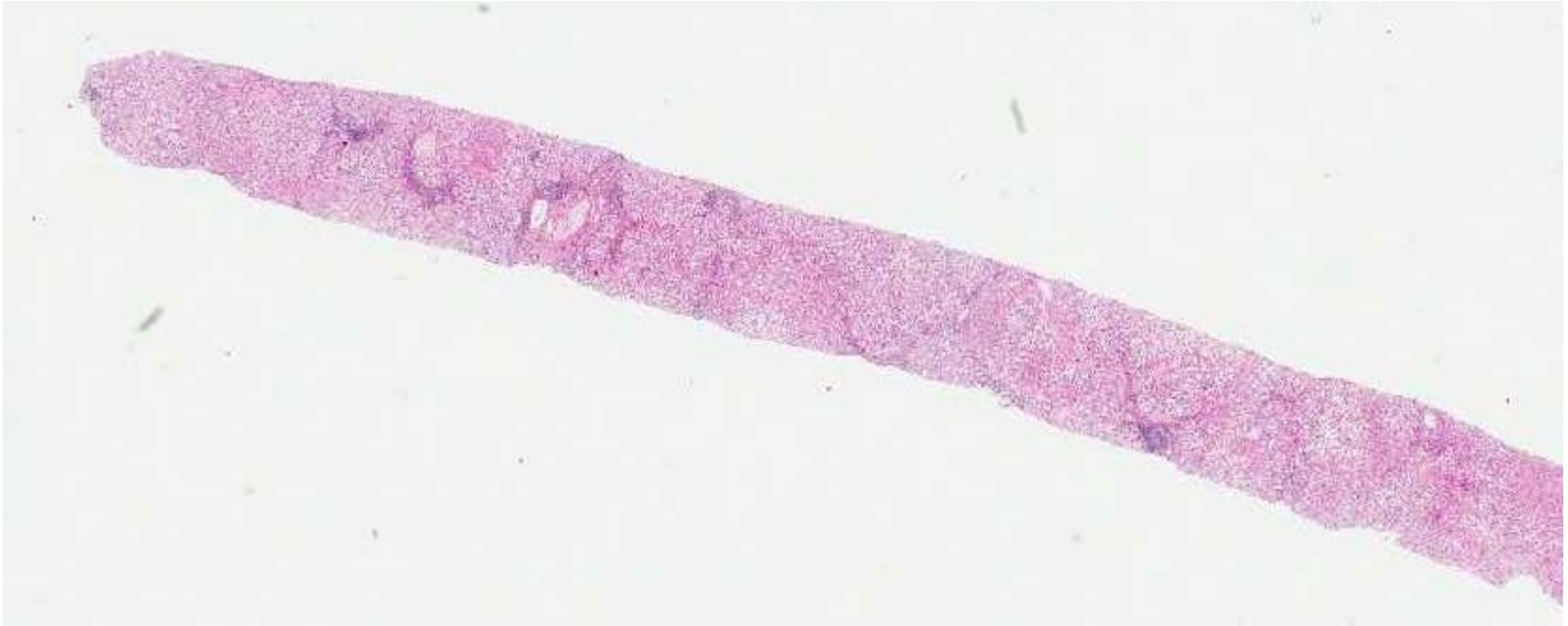
Czaja AJ Dig Dis Sci 2013;58(2)'326-343

JIW 8 48/M

Hepatitis C - previous biopsy.

Raised ALT. ? other cause.

Further information from server, genotype 3, ferritin 1405, ALT at time of biopsy 580.



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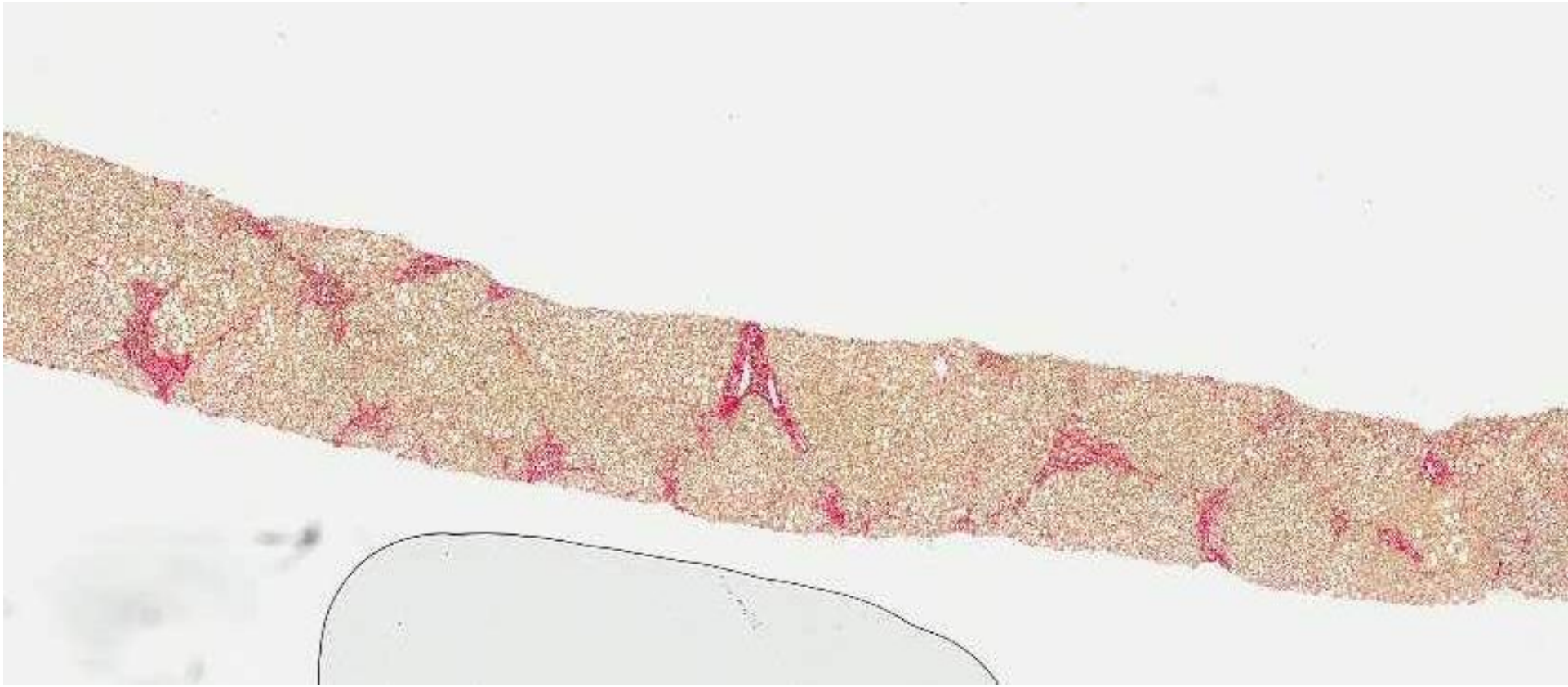

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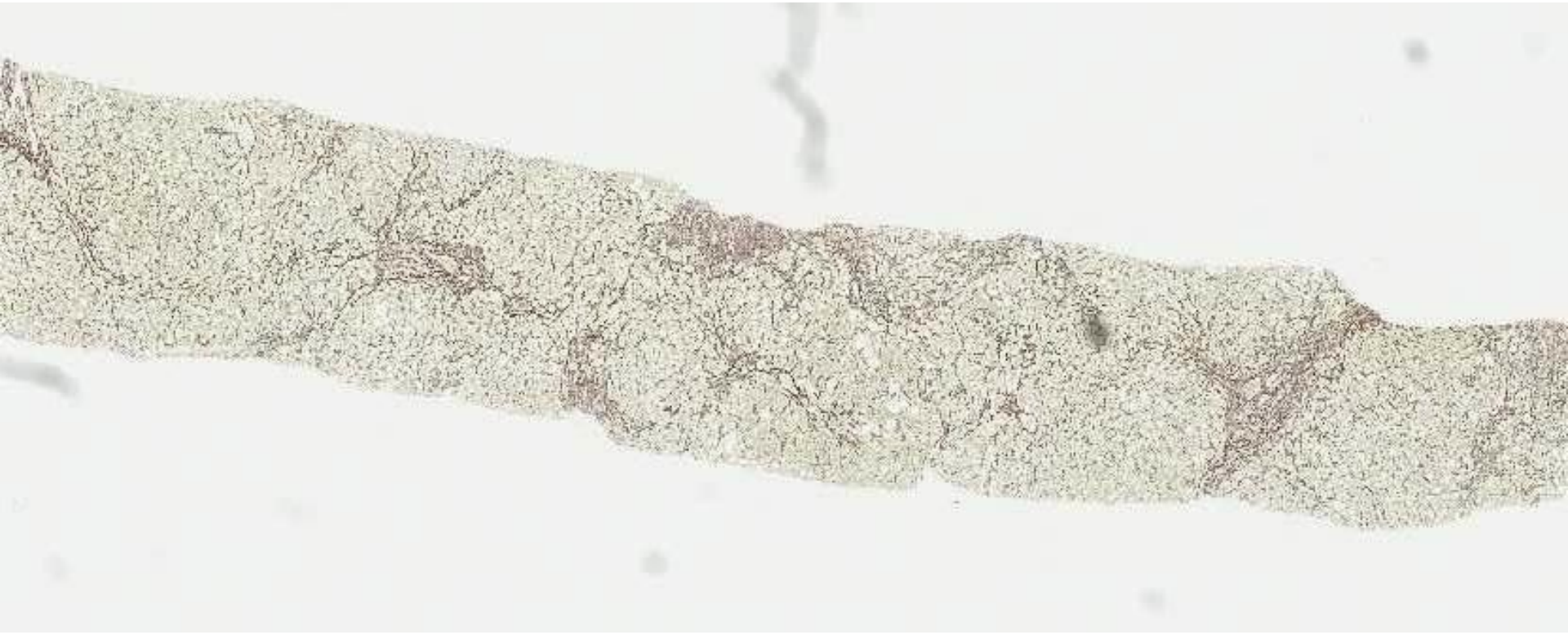

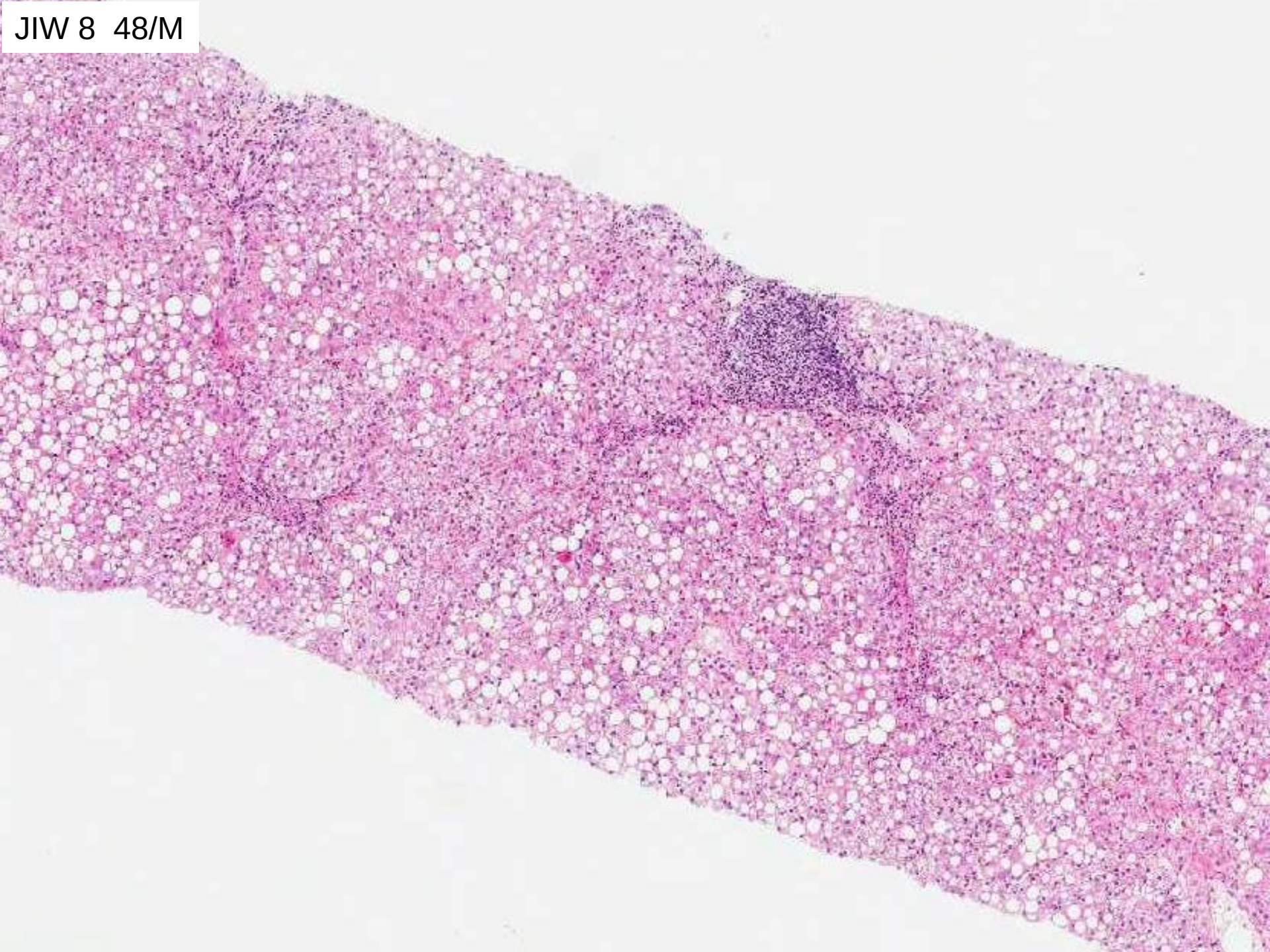
JIW 8 48/M

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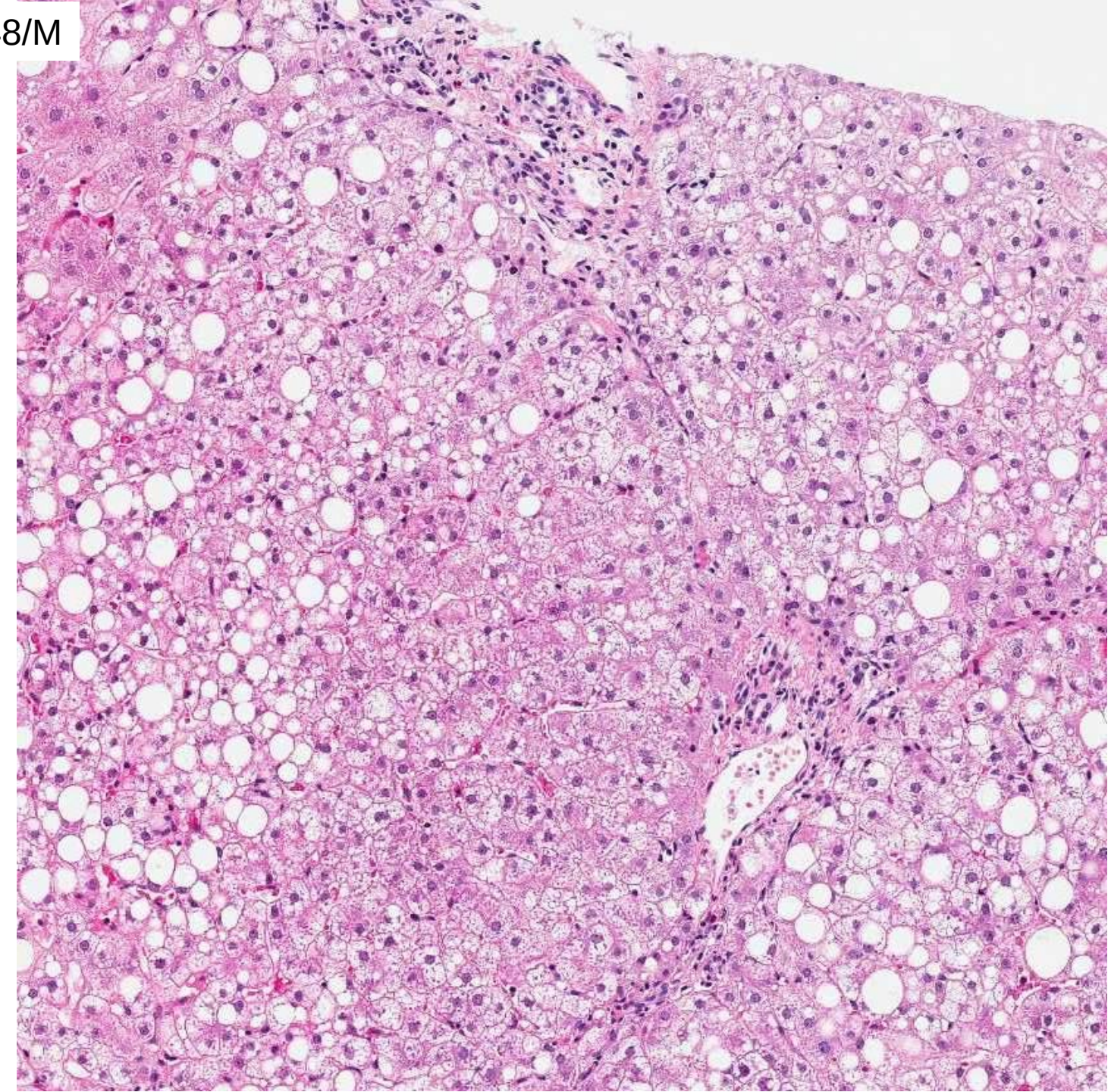

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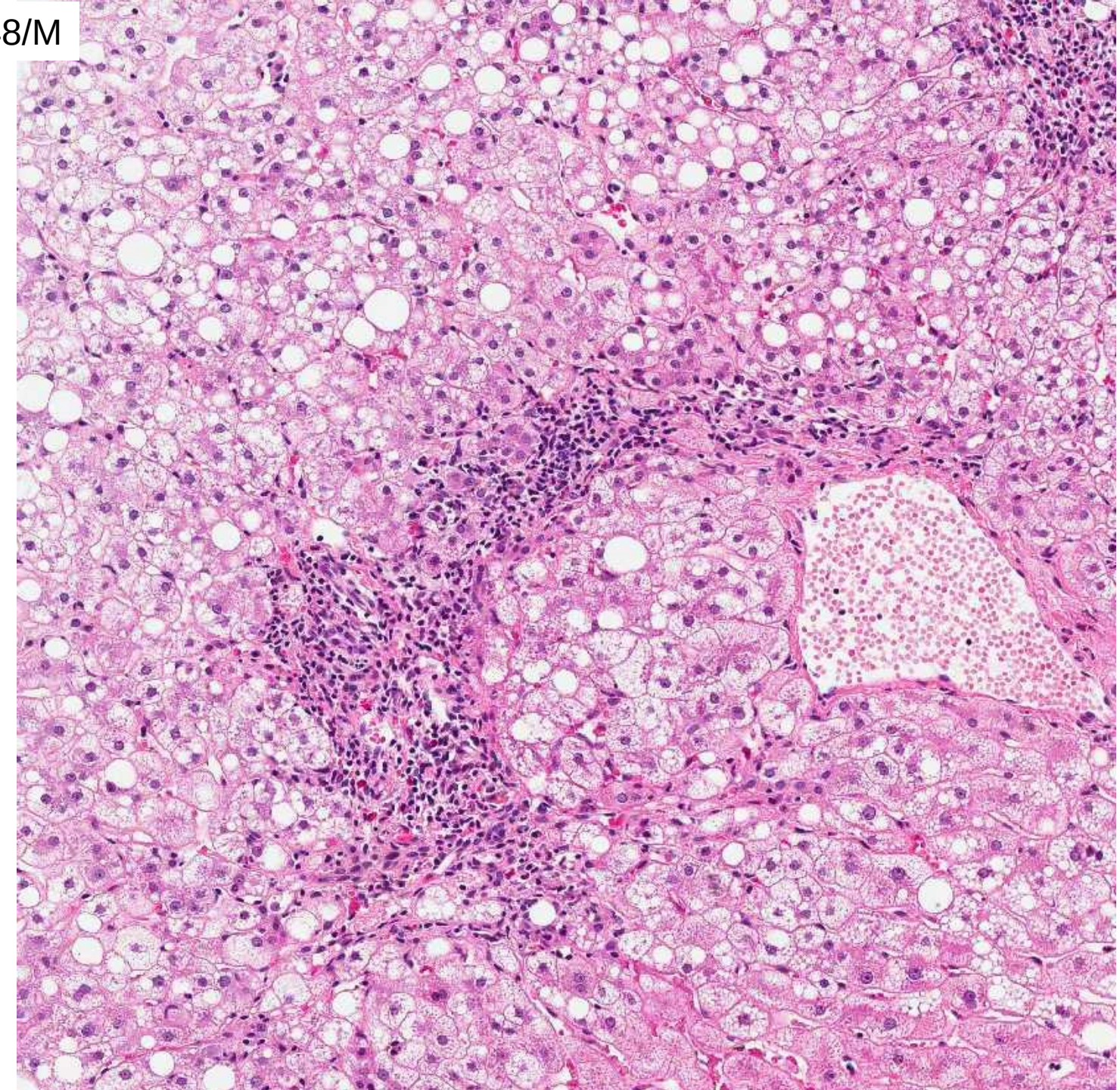

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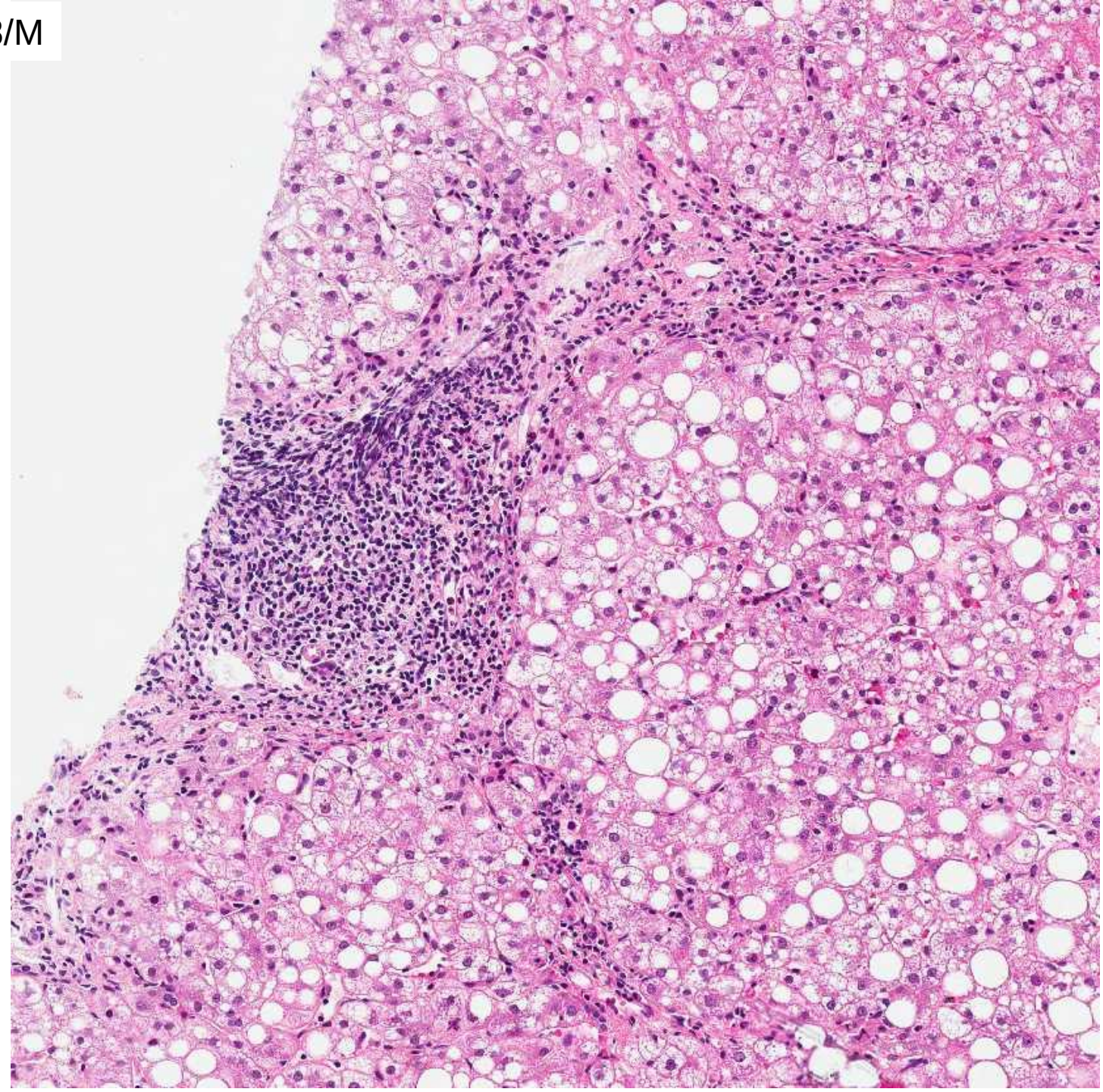

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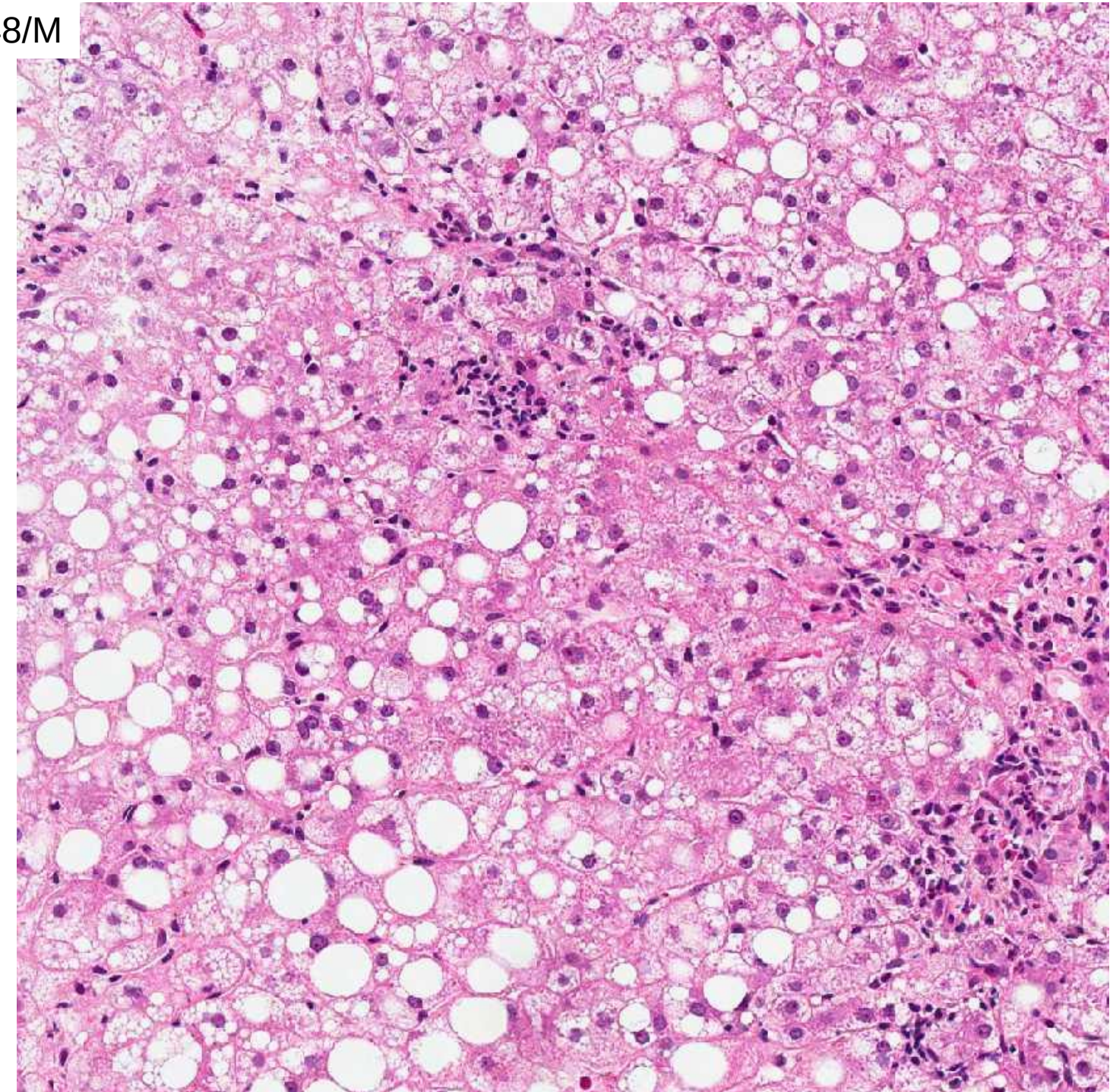

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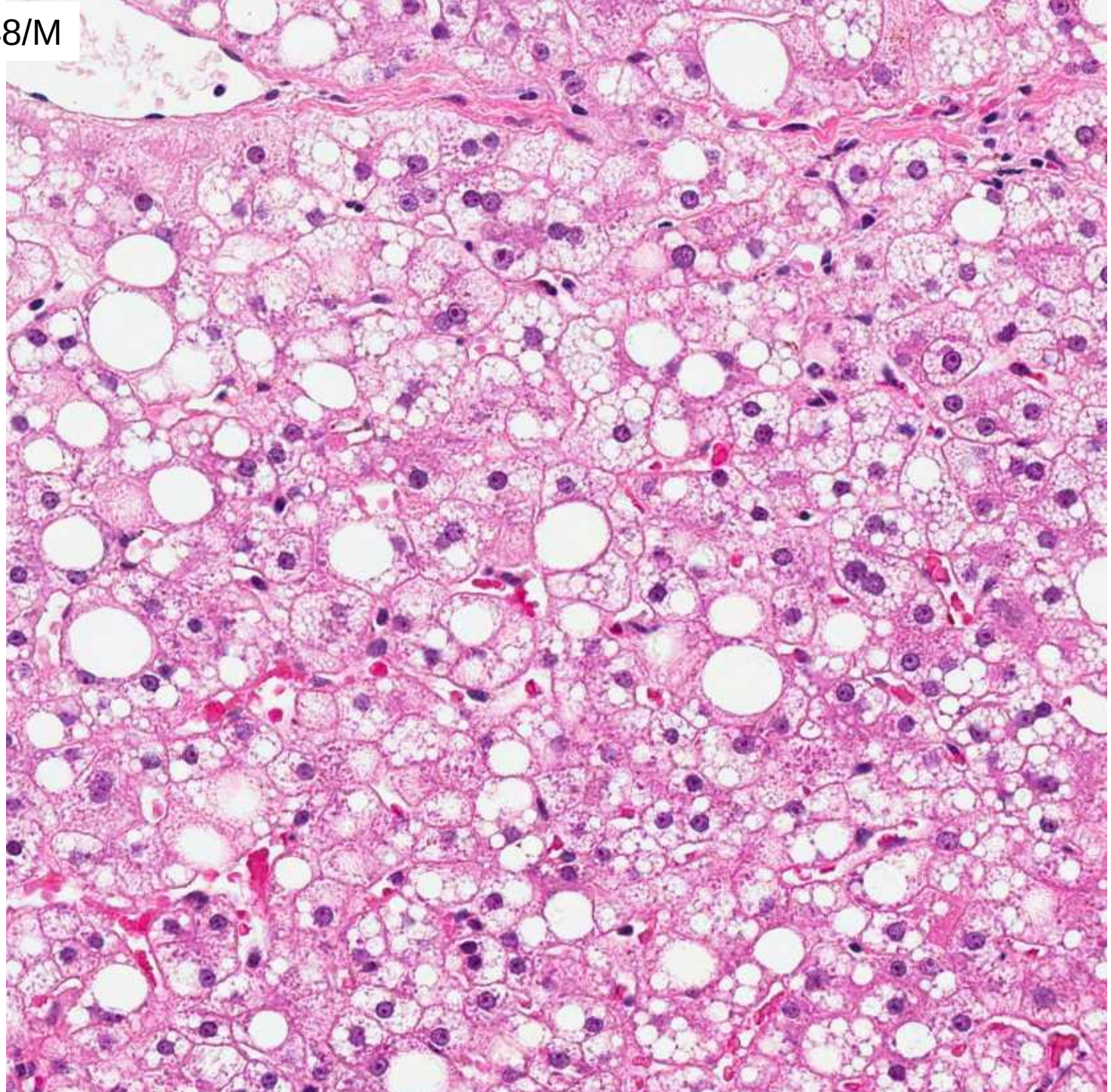

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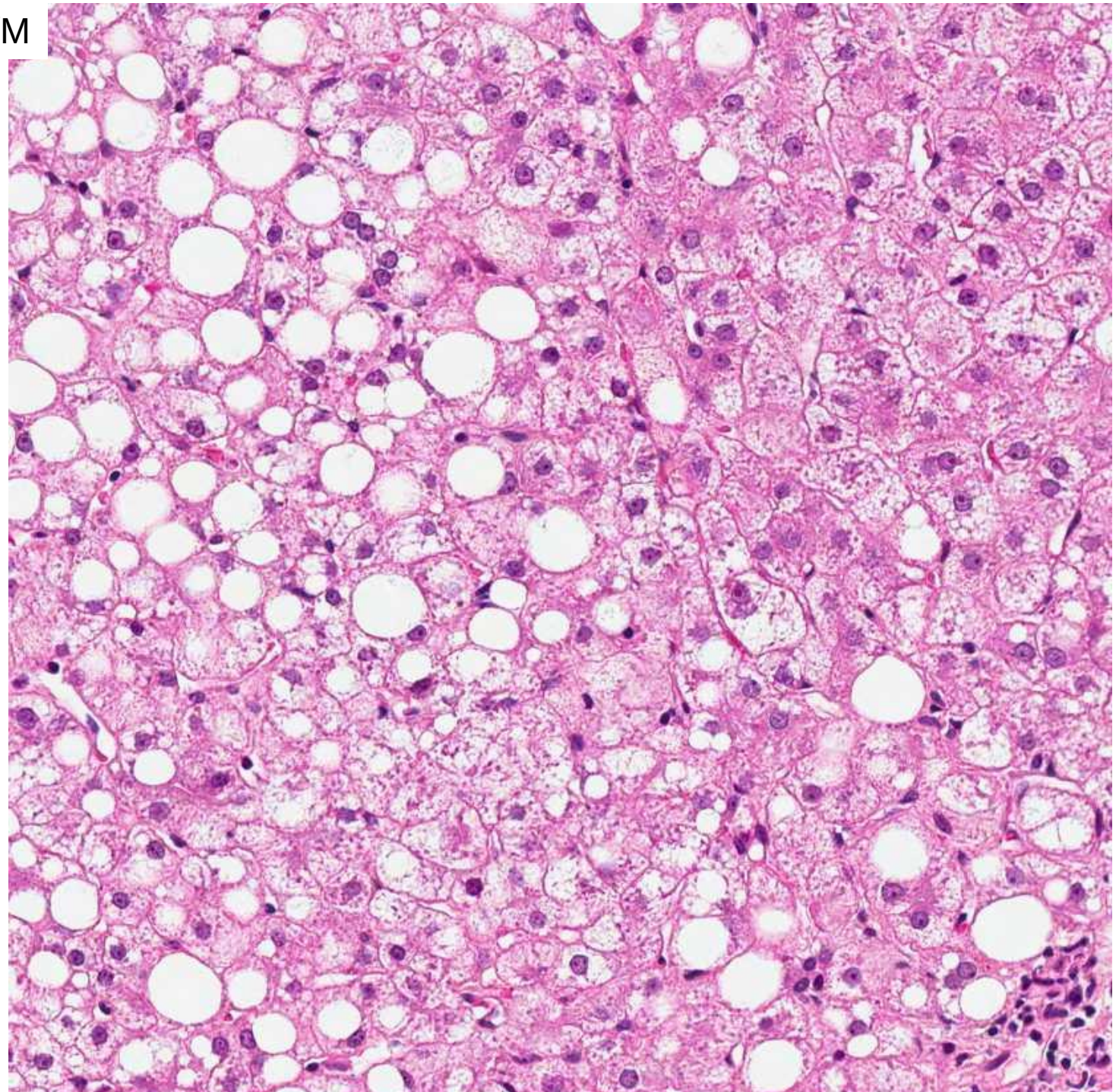

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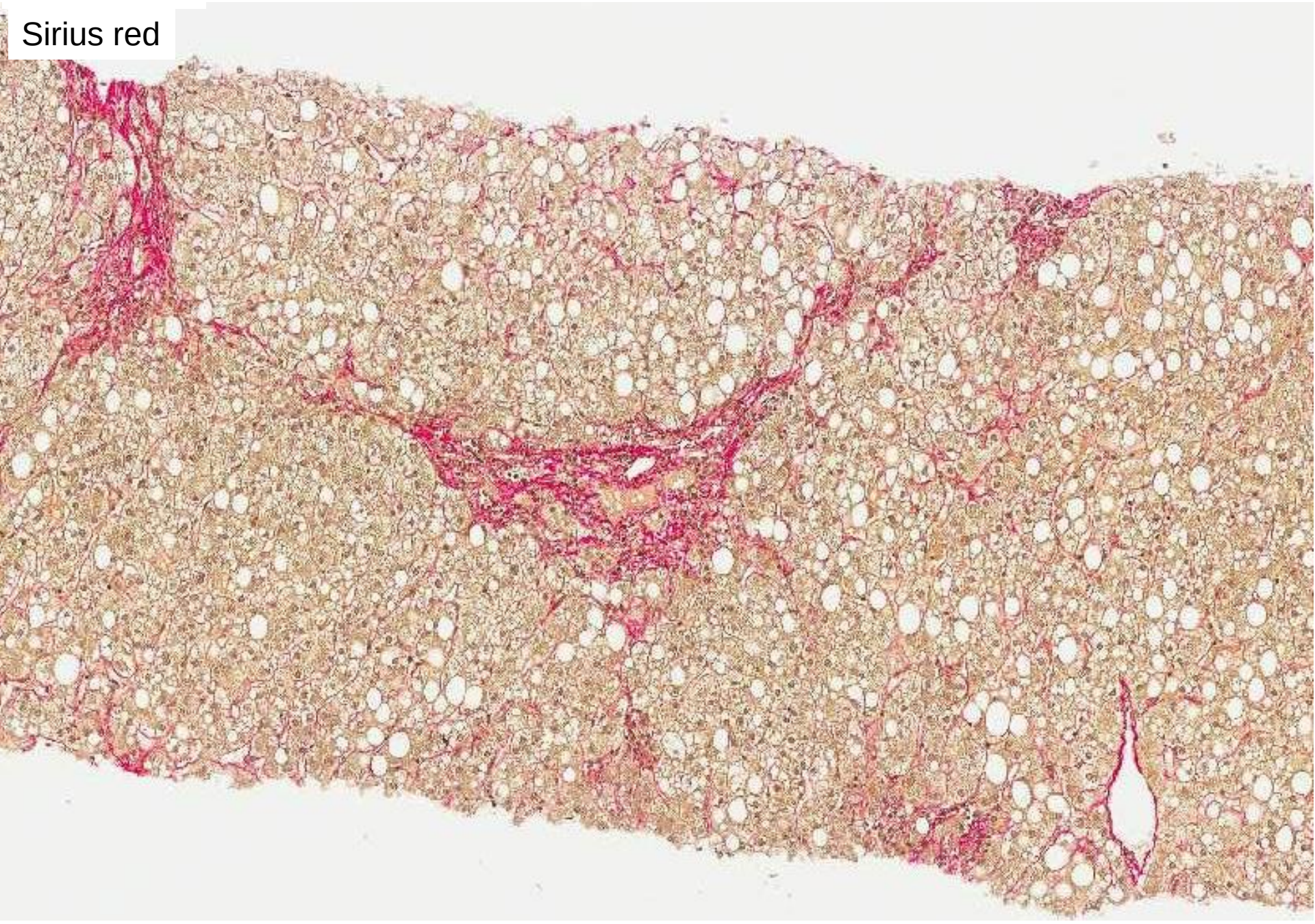

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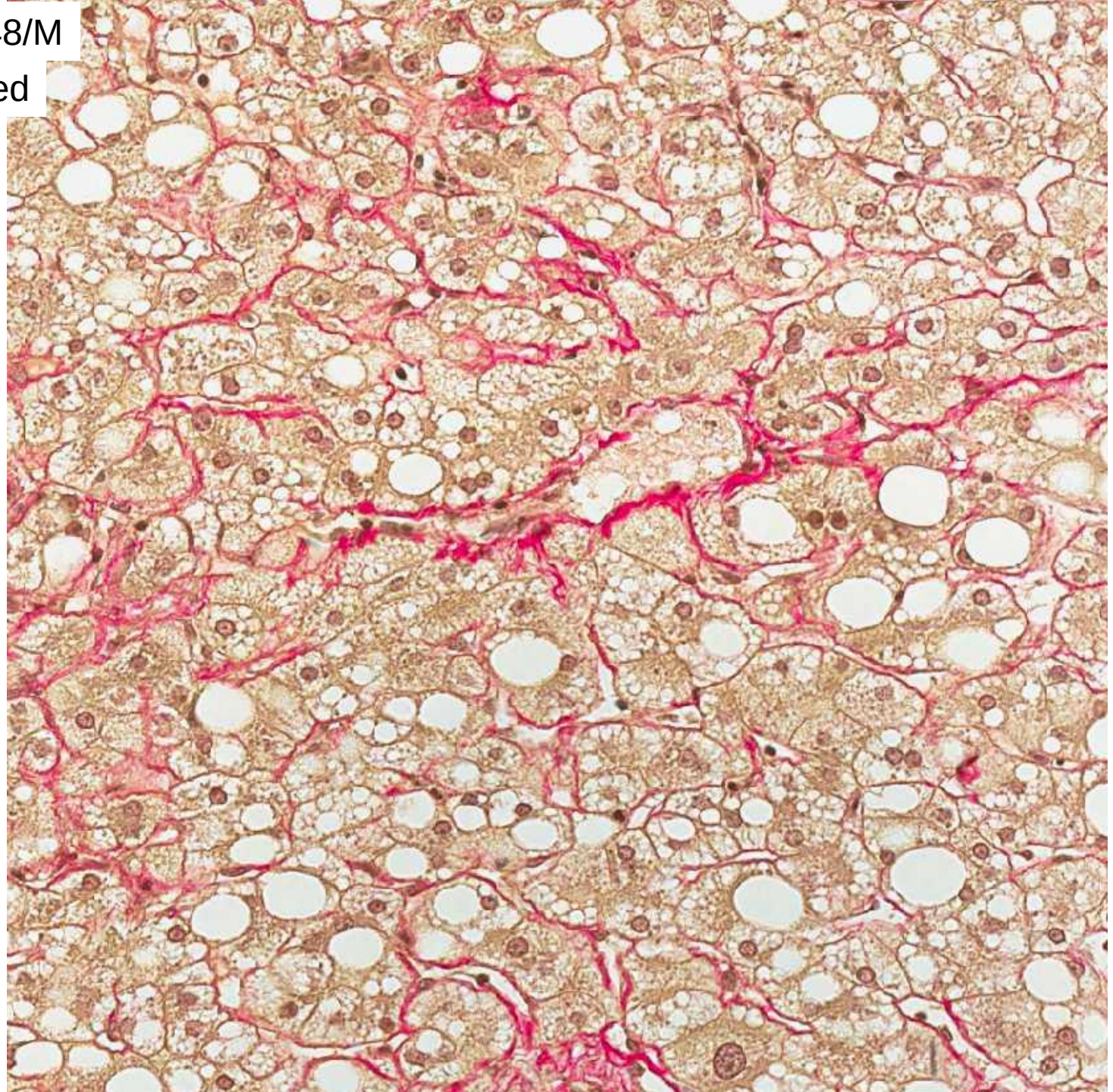
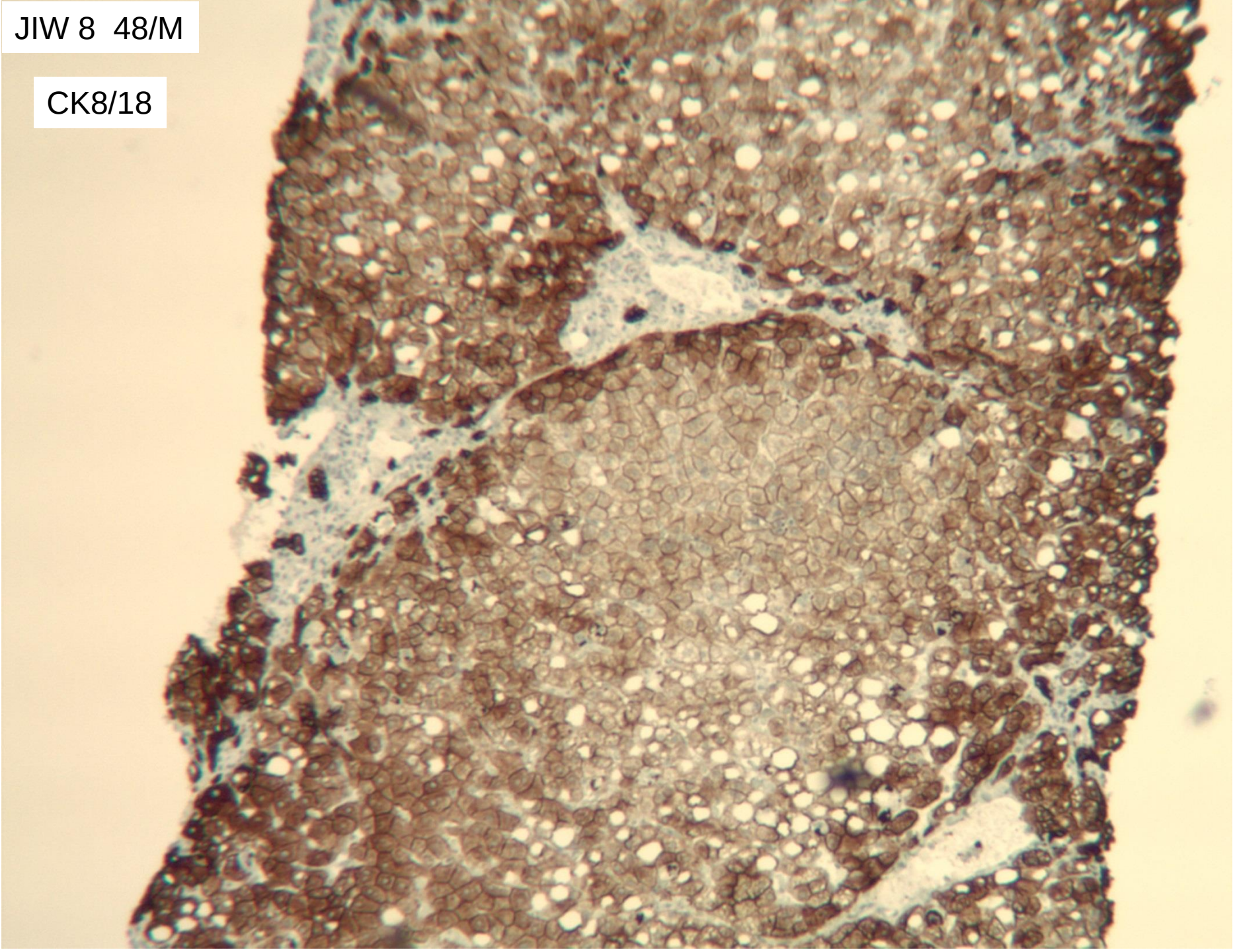
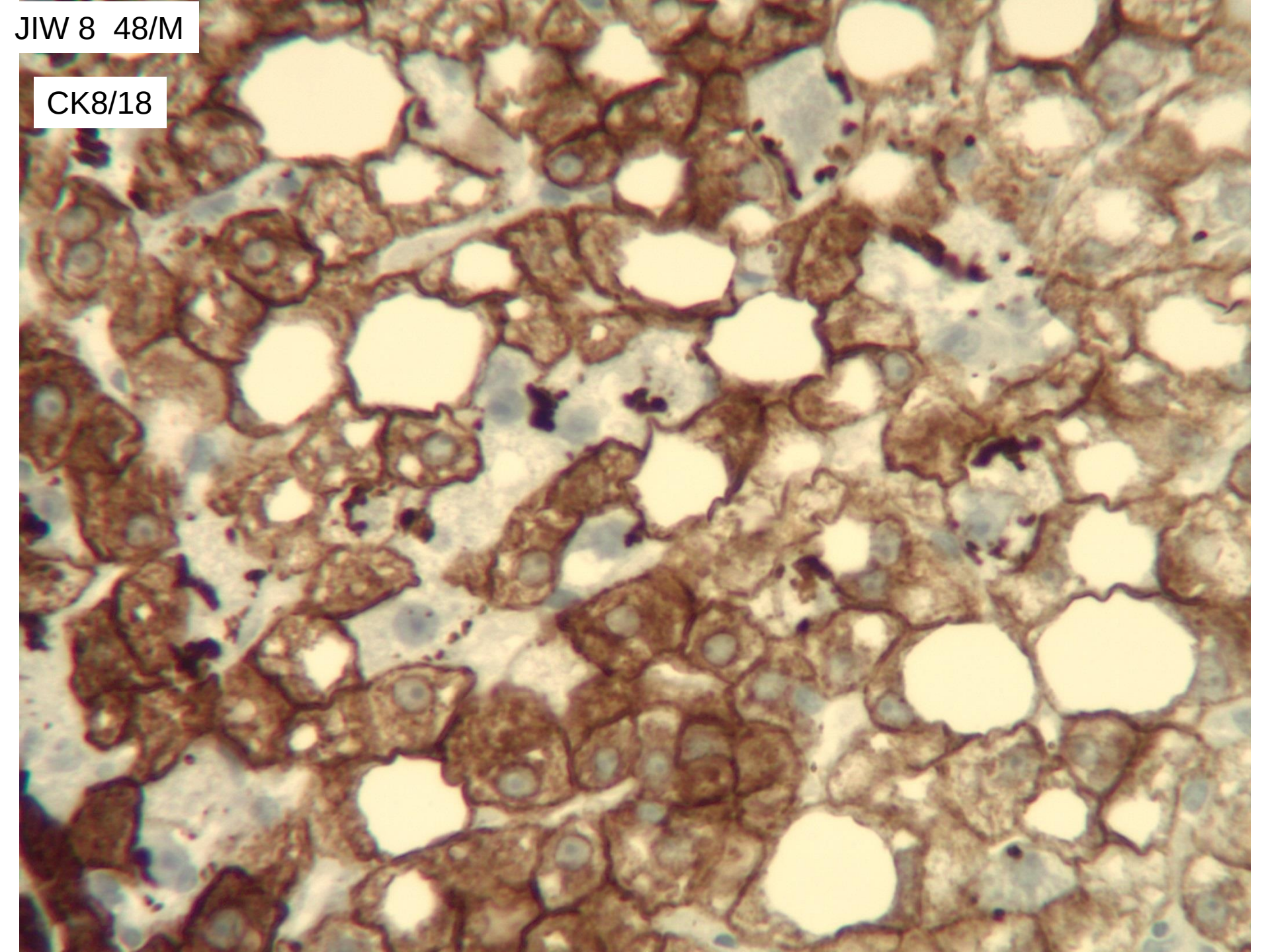



JIW 8 48/M
CK8/18


JIW 8 48/M
CK8/18

JIW 8 48/M

Hepatitis C - previous biopsy.

Raised ALT. ? other cause.

Further information from server, genotype 3, ferritin 1405, ALT at time of biopsy 580.

Diagnosis:

Features consistent with chronic hepatitis C,
stage 3 grade 5

(progression since previous biopsy 6 years ago)

Also moderate steatosis – genotype 3, therefore consistent with hepatitis C, although other cause (alcohol, metabolic syndrome) should be considered.

Steatosis in hepatitis C

- Due to direct effect of virus in genotype 3
- Due to interaction with host factors for NAFLD in other genotypes
- Actual steatohepatitis (ballooning and pericellular fibrosis) relatively rare (9%)
- Accelerates fibrosis, increases HCC risk, reduces response to treatment.

.Blonsky JJ and Harrison SA. Alim Pharm Ther 2008;27;855-865

Grade and stage in chronic viral hepatitis

In UK most clinicians like the Ishak score

Stage 0 (normal) to 6 (definite cirrhosis)

- 1,2 portal fibrosis (< or > half tracts)
- 3,4 bridging fibrosis
- 5 = bridging and nodularity
- 5 and 6 are late stage, and clinically considered to be cirrhosis

Grade – sum of portal (0-4), interface (0-4), lobular (0-4), confluent (0-6) Total 0-18

Subjective, non-linear, poorly reproducible.

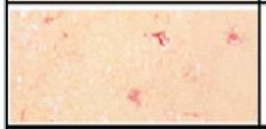
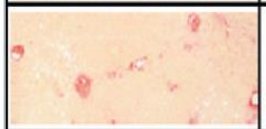
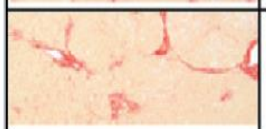
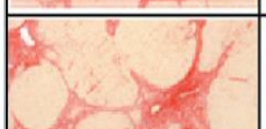
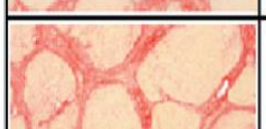
Intended for research not routine reporting.

Other systems simpler – Metavir, Batts & Ludwig, Scheuer

Or just describe what you see in words

What do we mean by “liver fibrosis”?

Differences between morphological appearance, description, stage scoring and liver fibrosis measurement

Appearance	Ishak stage: Categorical description	Ishak stage: Categorical assignment	Fibrosis measurement*
	No fibrosis (normal)	0	1.9%
	Fibrous expansion of some portal areas ± short fibrous septa	1	3.0%
	Fibrous expansion of most portal areas ± short fibrous septa	2	3.6%
	Fibrous expansion of most portal areas with occasional portal to portal (P-P) bridging	3	6.5%
	Fibrous expansion of portal areas with marked bridging (portal to portal (P-P) as well as portal to central (P-C))	4	13.7%
	Marked bridging (P-P and/or P-C), with occasional nodules (incomplete cirrhosis)	5	24.3%
	Cirrhosis, probable or definite	6	27.8%

Standish R et al. An appraisal of the histopathological assessment of liver fibrosis. Gut 55;569;2006

Importance of biopsy quality

Any assessment of grade/stage is unreliable if the biopsy is too small.

- What is big enough??

Tissue pathways for liver biopsies for the investigation of medical disease and for focal lesions

March 2014

How to describe biopsy quality?

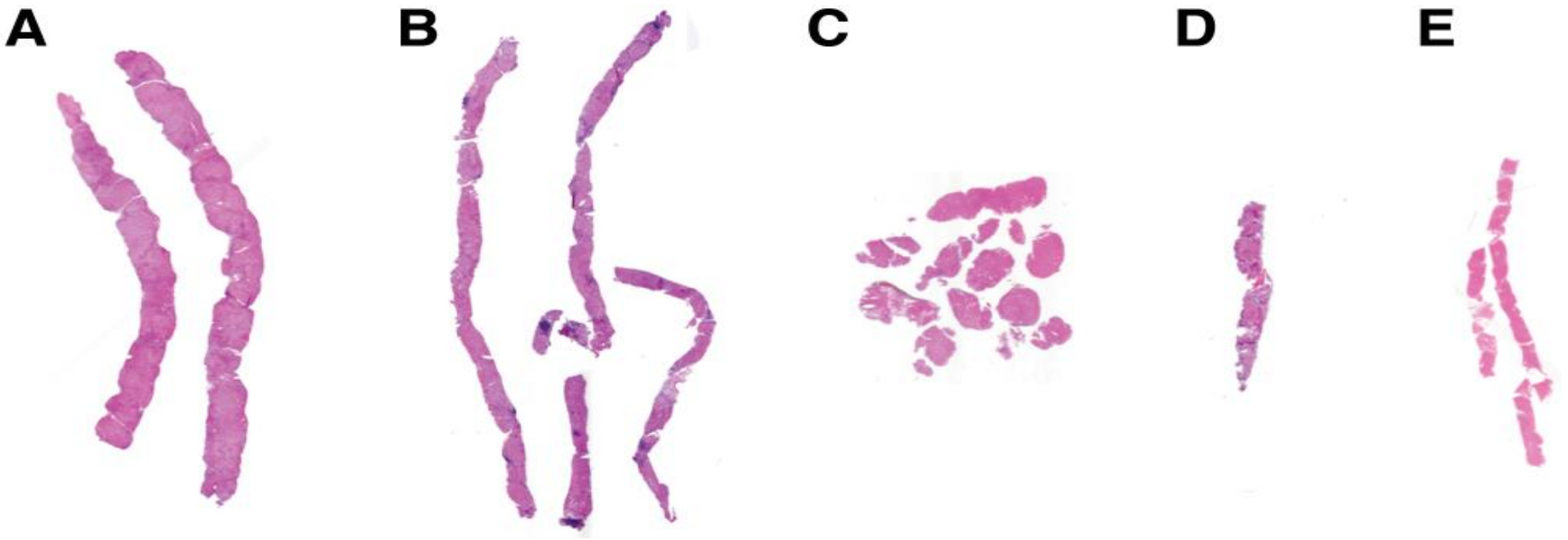
- Number of pieces
- Length, width,
- Number of portal tracts

AASLD POSITION PAPER:

Liver Biopsy

Don C. Rockey,1 Stephen H. Caldwell,2 Zachary D. Goodman,3 Rendon C. Nelson,4 and Alastair D. Smith5

This position paper has been approved by the AASLD and represents the position of the association.



A. 2 passes 16g needle, 2.7mm long

B. 3 passes, 18g needle, 4.8mm long

C. 16g suction 1.1cm total length

D. 1 pass 18g needle 0.5cm long

E. 2 passes 20g needle 1.5cm long

Impact of liver biopsy size on histological evaluation of chronic viral hepatitis: the smaller the sample, the milder the disease

Hep B&C; 161 biopsies ≥30mm x 1.4mm
Ishak score

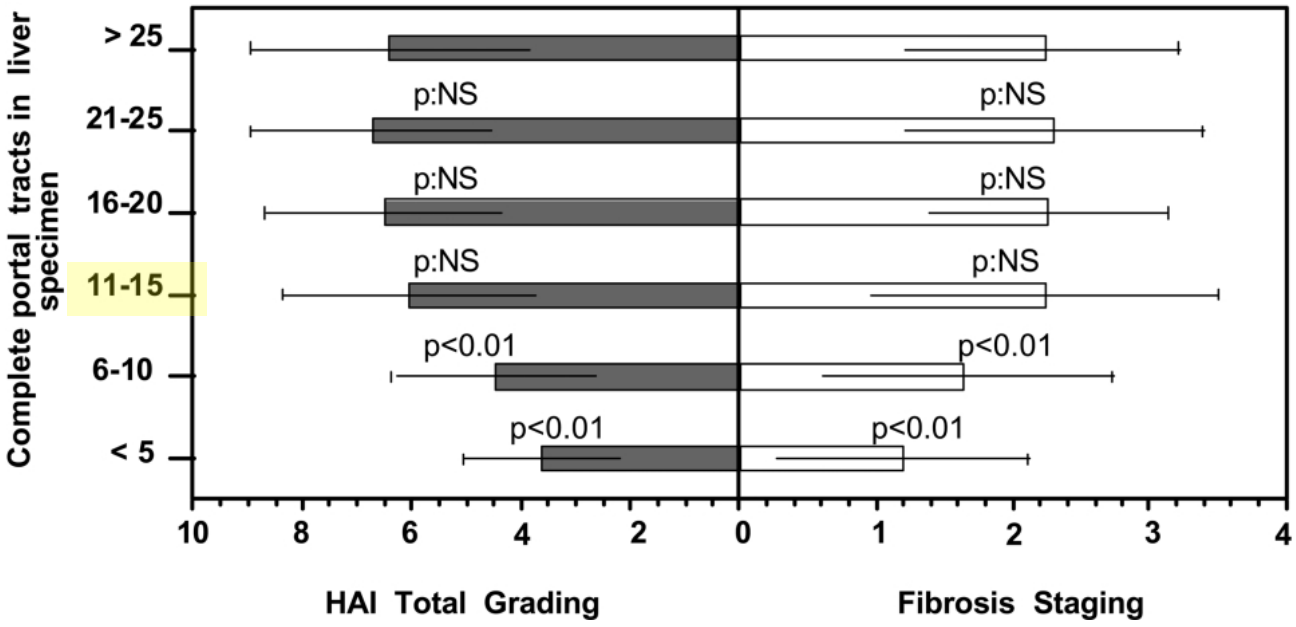
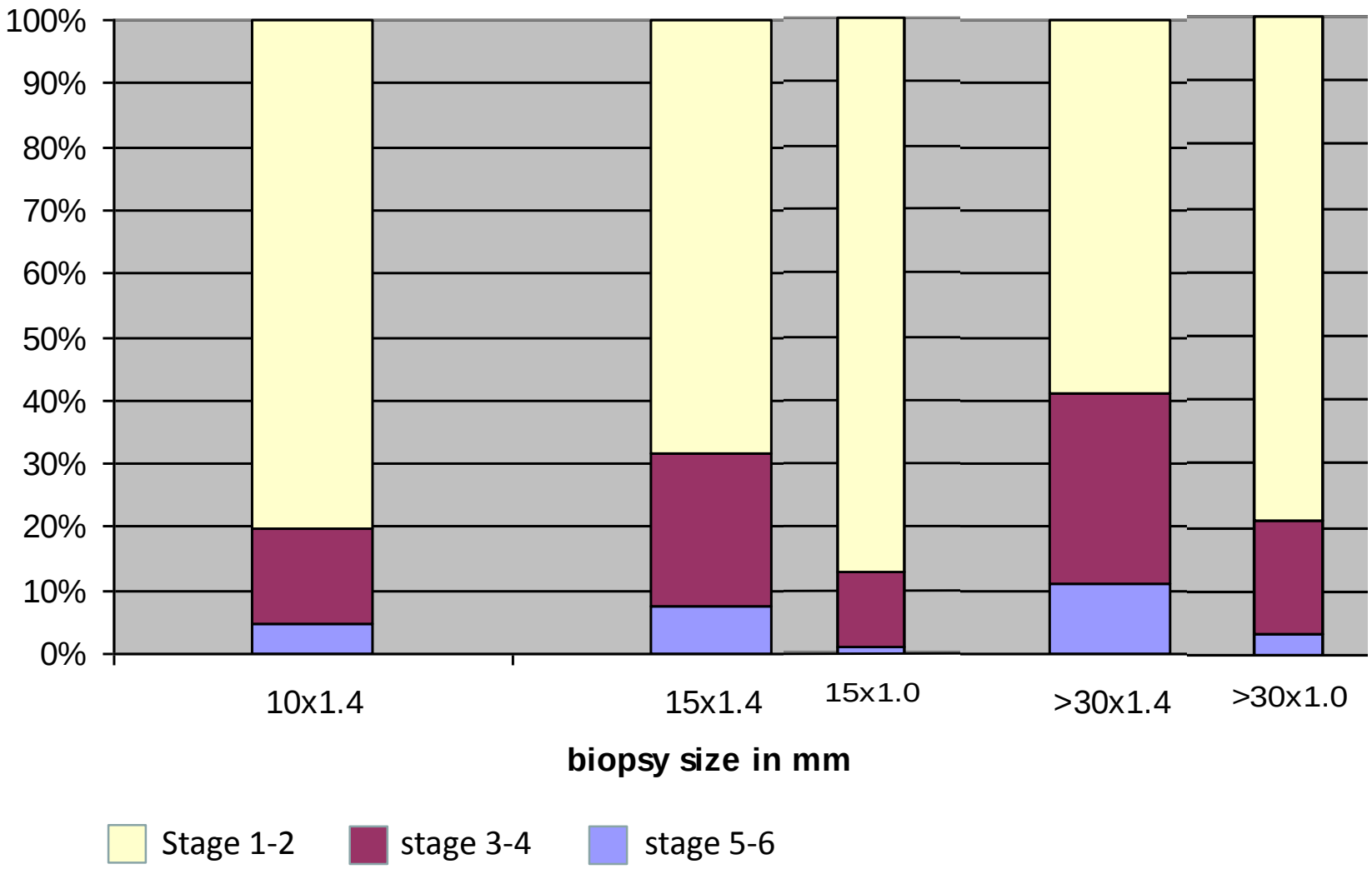


Fig. 1. Impact of the number of complete portal tracts on histological activity (HAI) grading and fibrosis staging.

Colloredo G, Guido M, Sonzogni A, Leandro G. J Hepatology 2003;39;239-244.

Effect of biopsy size on histological stage



*** Colloredo et al J Hepatol 2003;39;239-244*

Same magnification

2 passes, 18g needle

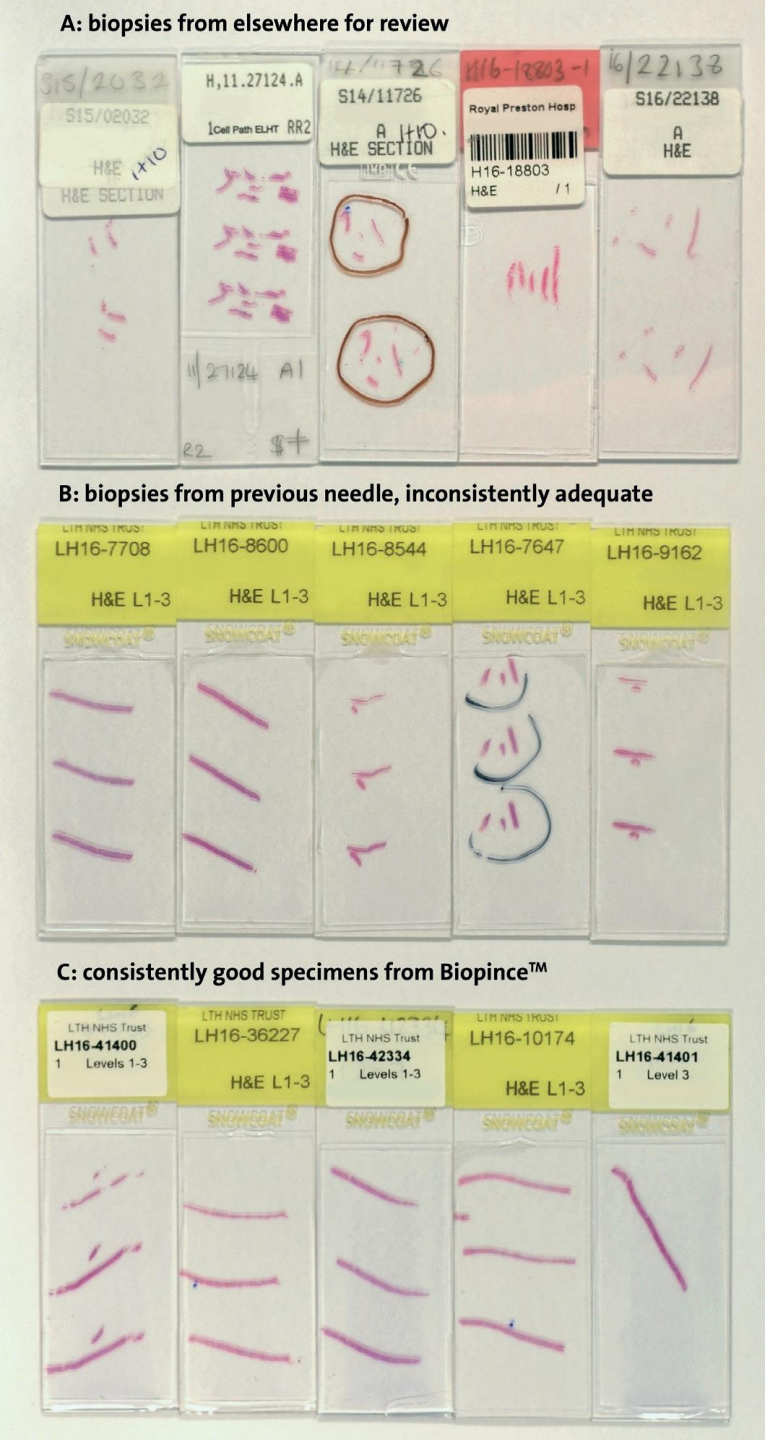
0.53mm

0.87mm

1 pass,
16g needle

≥6 portal tracts
In 90%

Palmer T *et al*. J Clin Path 2014



Liver biopsy adequacy and biopsy needle type

A good sample is an essential starting point for a good biopsy report.

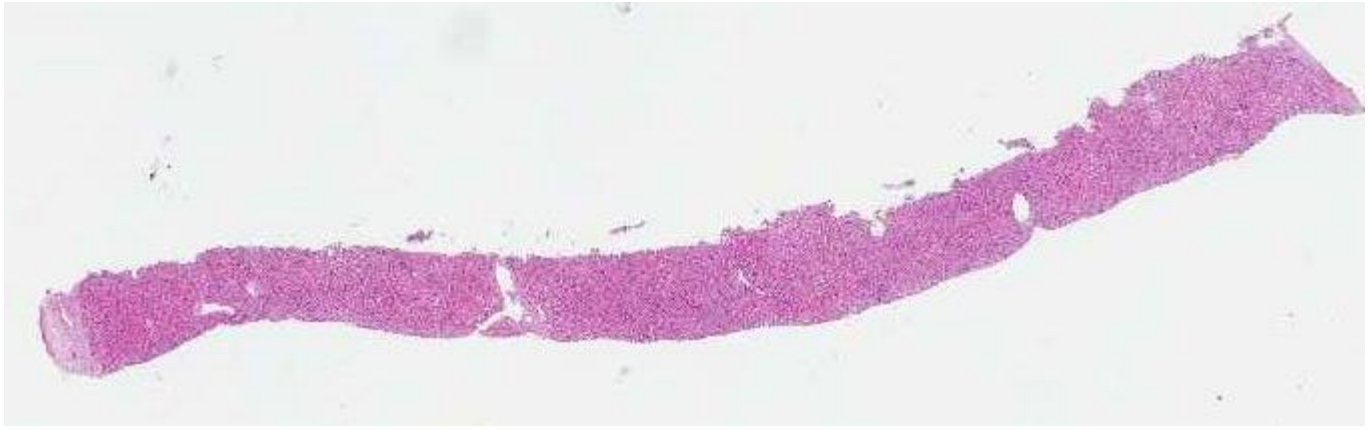
J Wyatt and S Hubscher.
Bulletin of the Royal College of Pathologists
January 2017;177;66-7.

Recommended 2cm core from at least a 16-G needle

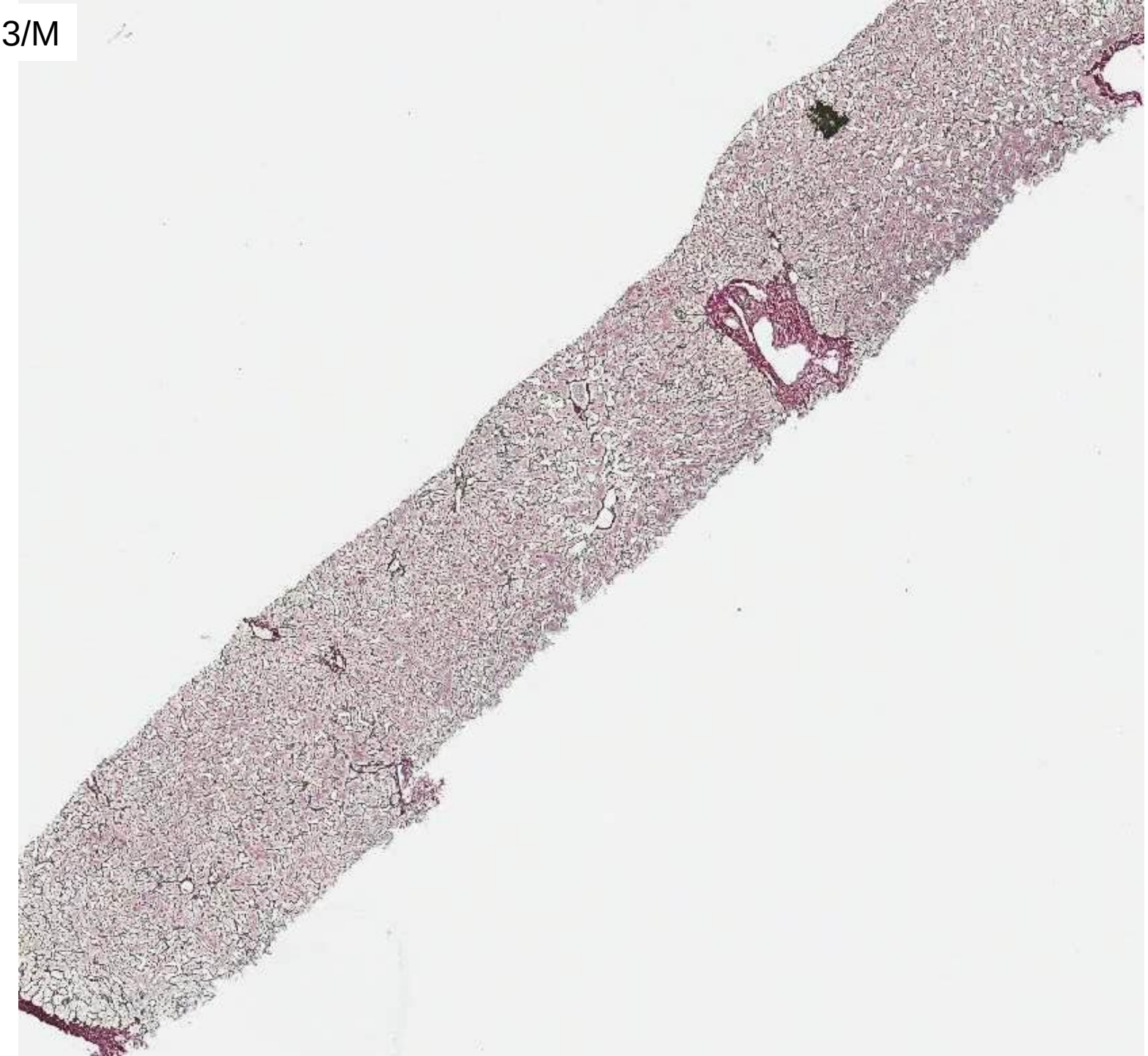
Kleiner DE and Bedossa P
Gastroenterology 2015;149;1305-1308

JIW 9 23/M

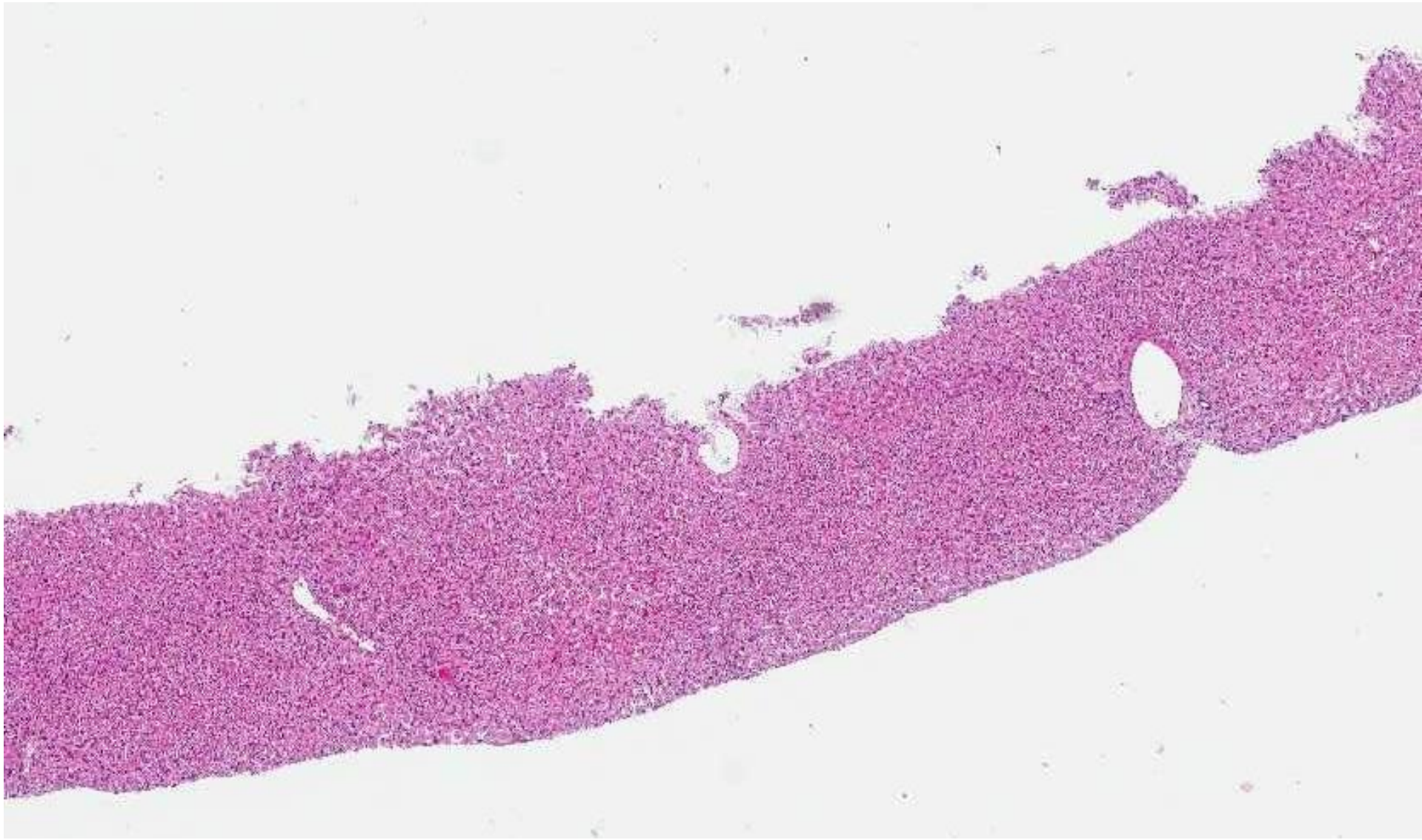
Chronic hepatitis B. Hepatitis B e-antigen negative, ALT fluctuating . Assess fibrosis.



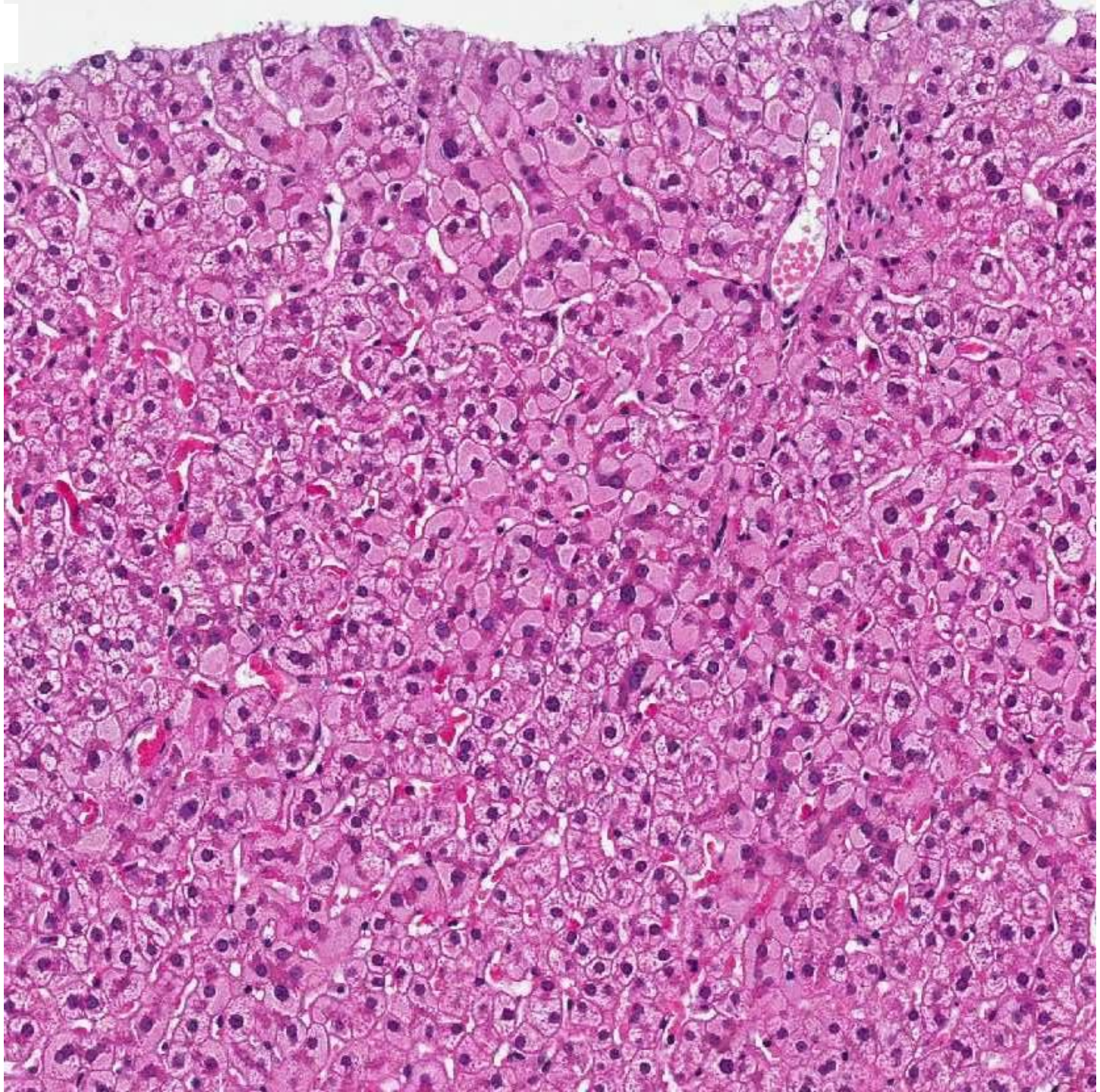
JIW 9 23/M



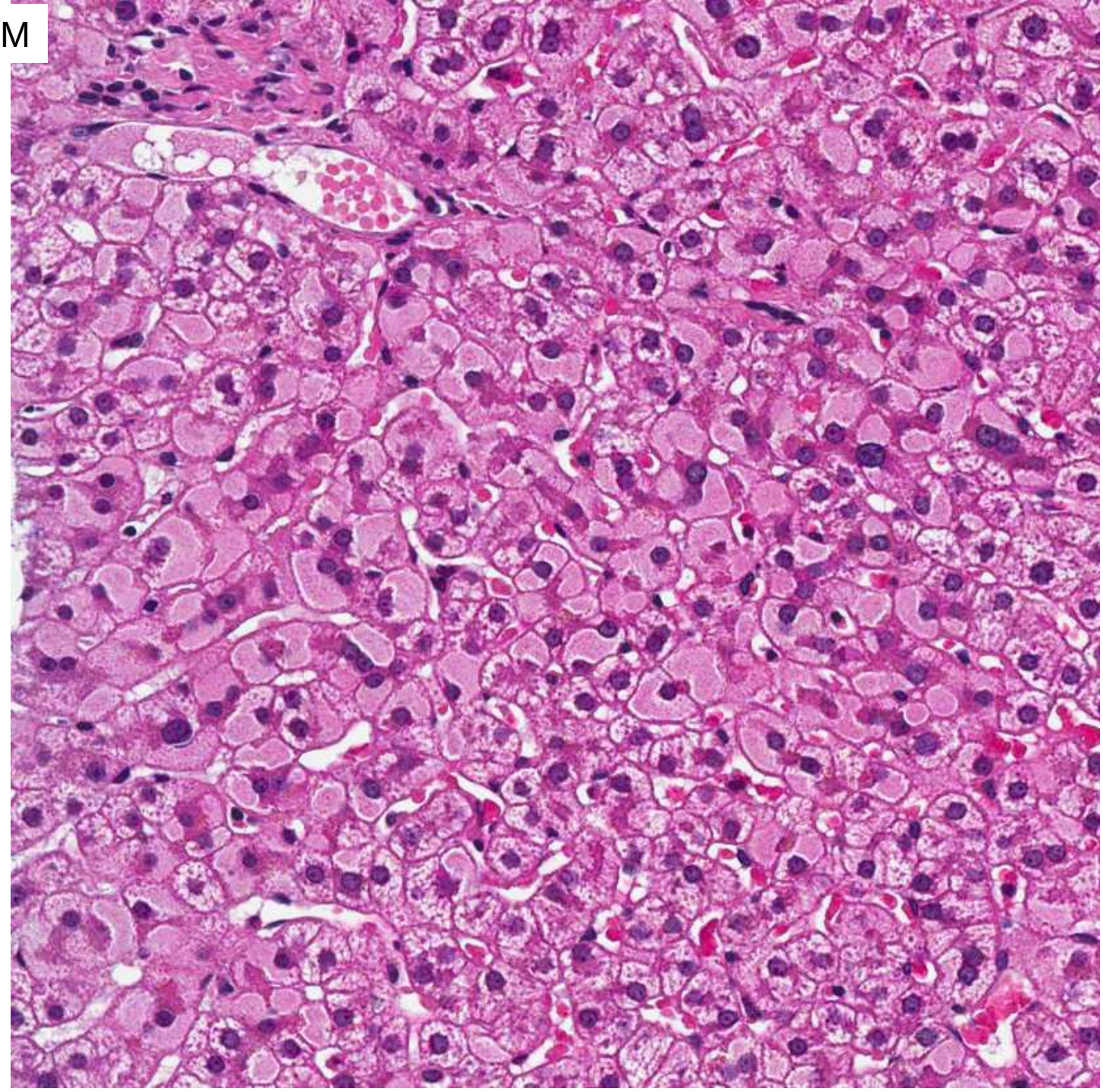
JIW 9 23/M



JIW 9 23/M

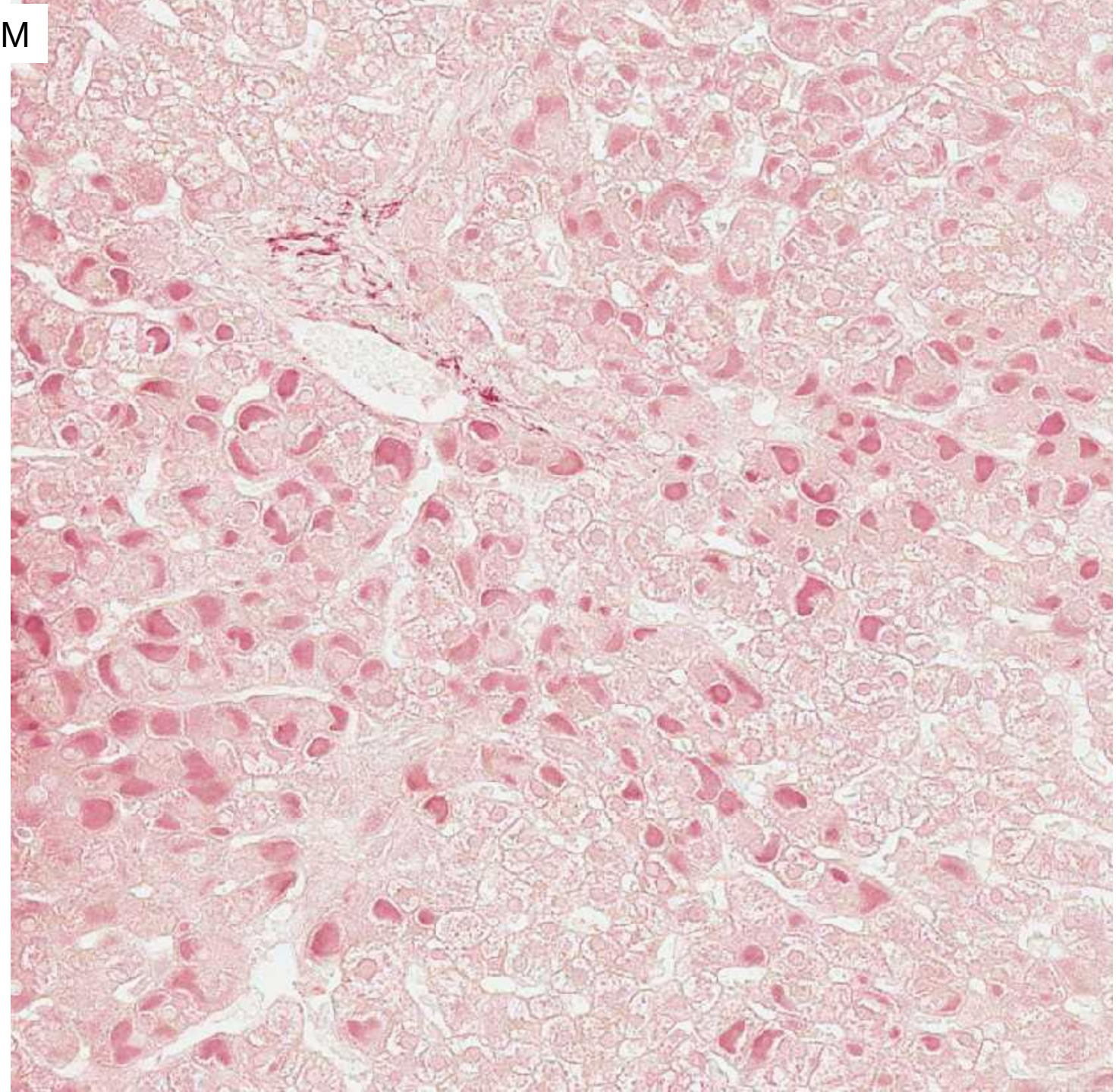


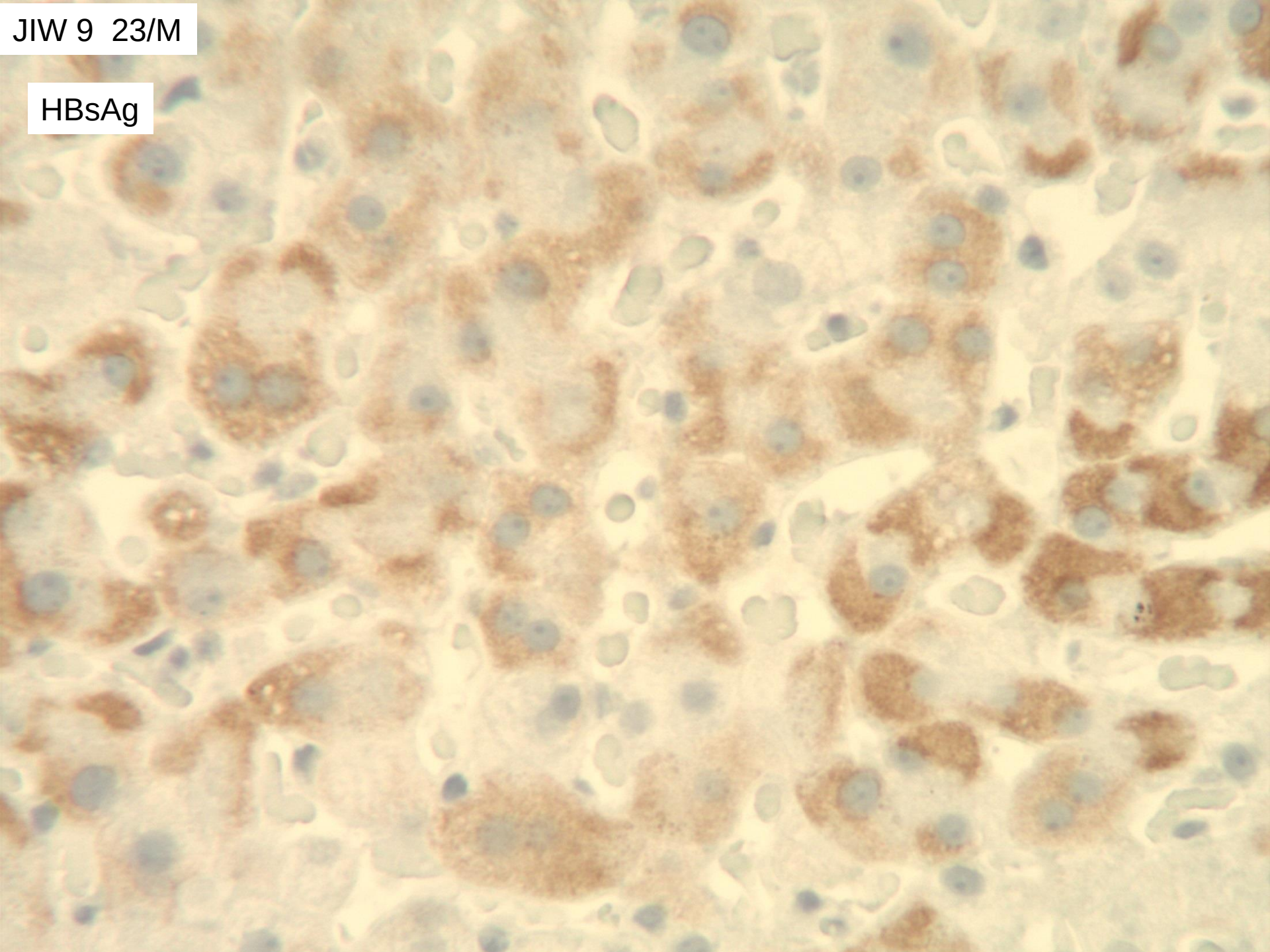
JIW 9 23/M

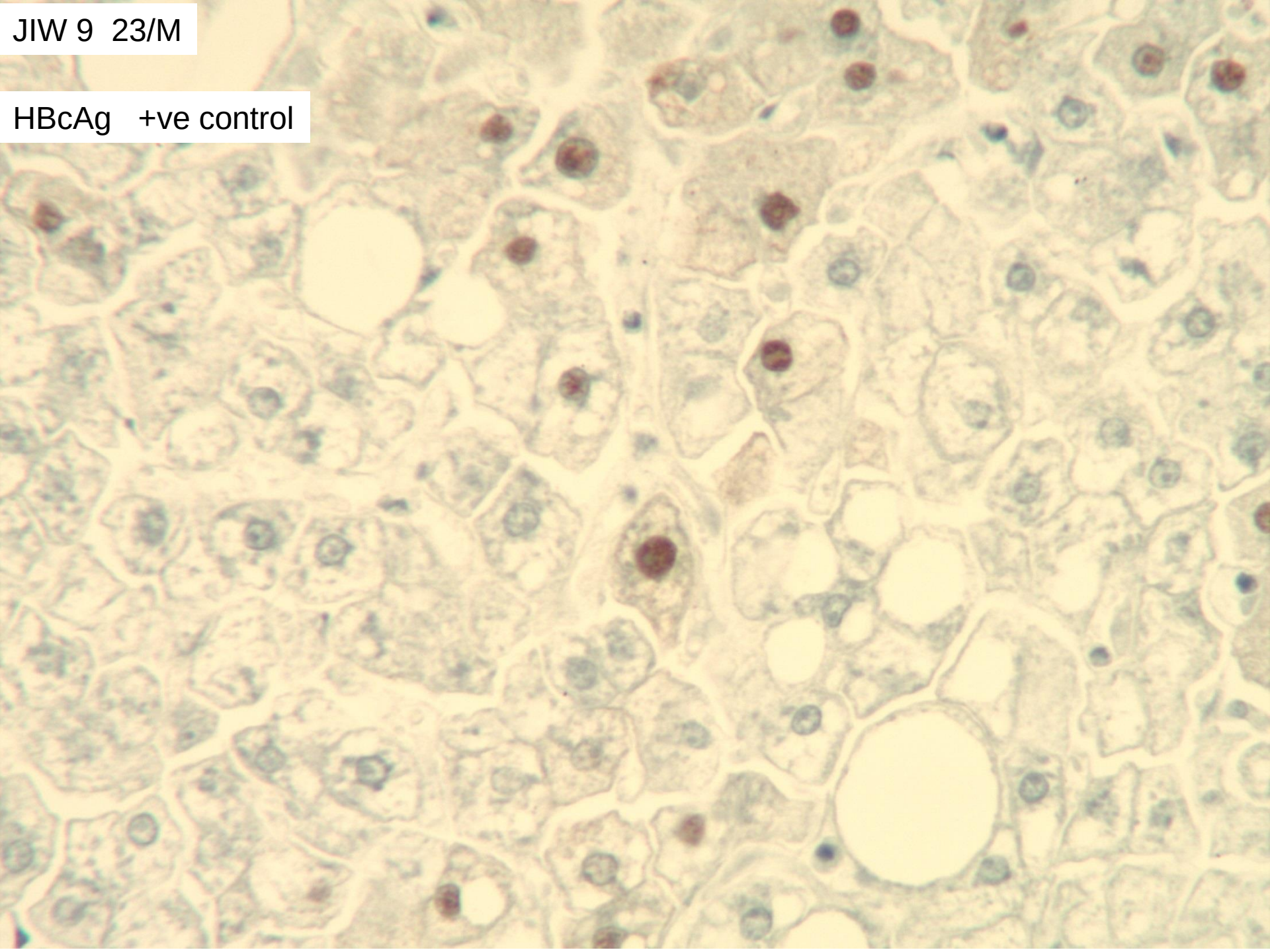


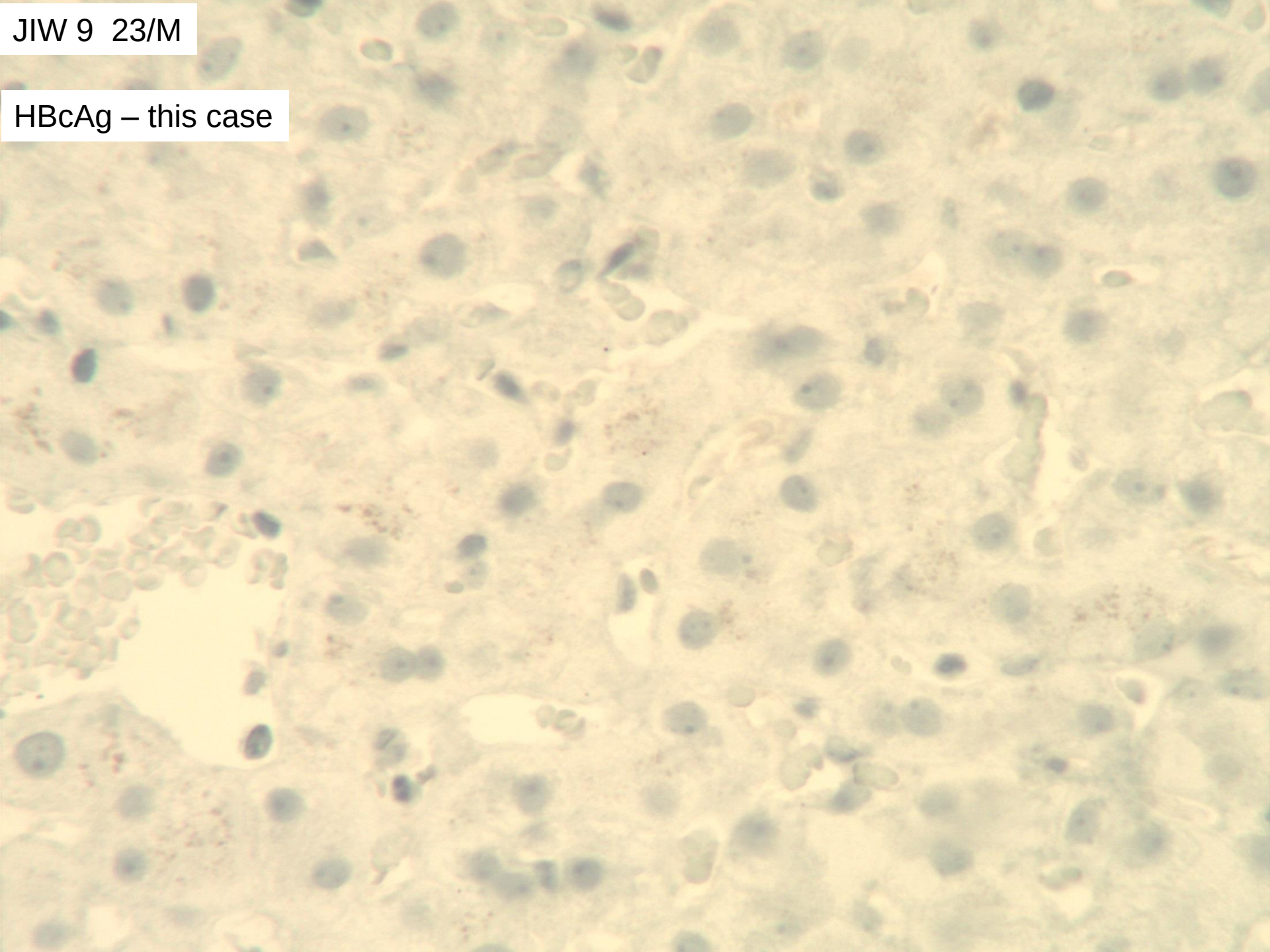
JIW 9 23/M

Shikata




JIW 9 23/M
HBsAg


JIW 9 23/M
HBcAg +ve control


JIW 9 23/M
HBcAg – this case

JIW 9 23/M

Chronic hepatitis B. Hepatitis B e-antigen negative, ALT fluctuating . Assess fibrosis.

Diagnosis:

Hepatitis B, Ishak stage 1 (at most), grade 0

Ground glass hepatocytes, but no inflammation currently.

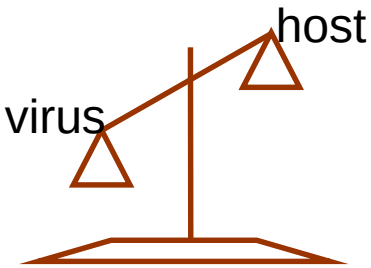
New nomenclature in chronic HBV

	HBeAg positive Chronic *infection*	HBeAg positive Chronic hepatitis	HBeAg negative Chronic *infection*	HBeAg negative Chronic hepatitis
HBsAg	High	High/Intermediate	Low	Intermediate
HBeAg	Positive	Positive	Negative	Negative
HBV DNA	>10E7 IU/mL	10E4-10E7 IU/mL	<2,000 IU/mL°°	>2,000 IU/mL
ALT	Normal	Elevated	Normal	Elevated*
Liver disease	None/minimal	Moderate/severe	None	Moderate/severe
Old terminology	Immune tolerant	Immune reactive HBeAg positive	Inactive carrier	HBeAg negative Chronic hepatitis

*Persisitently or intermittently

°° HBV-DNA levels can be between 2,000 and 20,000 IU/mL in some patients without sings of chronic hepatitis

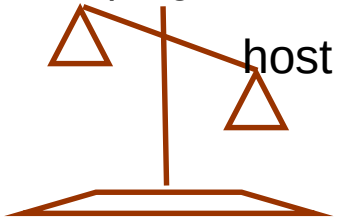
Phases of chronic hepatitis B each may last many years



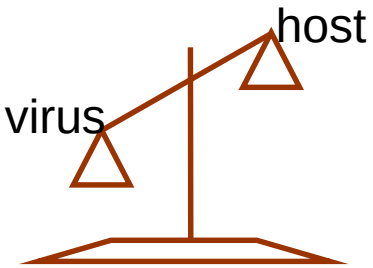
1. **HBeAg +ve chronic infection -** children
   - High replication, infectious, no liver damage
2. **HBeAg +ve chronic hepatitis**
   - Immune system begins to fight virus
     - liver damage results, cirrhosis 8-20% after 5 years

3. **HBeAg seroconversion 5-10% per year**
   - Flare of disease, get anti-HBeAb, good quality of life, low risk of disease progression = HBeAg-ve chronic infection

Most stay in this state



Phases of chronic hepatitis B each may last many years



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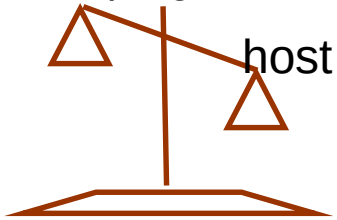
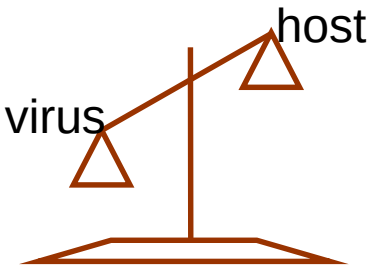


May then get

- **HBsAg seroconversion**
  - 0.5-2% per year in western countries. Rare in endemic countries.
  - Follows HBeAg seroconversion, represents resolution of chronic infection (although may be 'occult hepatitis B')

.

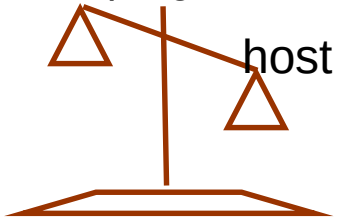
Phases of chronic hepatitis B each may last many years



1. **Immunotolerant phase -** children
   - High replication, infectious, no liver damage
2. **eAg +ve hepatitis B**
   - Immune system begins to fight virus
     - liver damage results, cirrhosis 8-20% after 5 years

3. **HBeAg seroconversion 5-10% per year**
   - Flare of disease, get anti-HBeAb, good quality of life, low risk of disease progression = Inactive HBsAg carrier state

Most stay in this state



May then get

HBsAg seroconversion

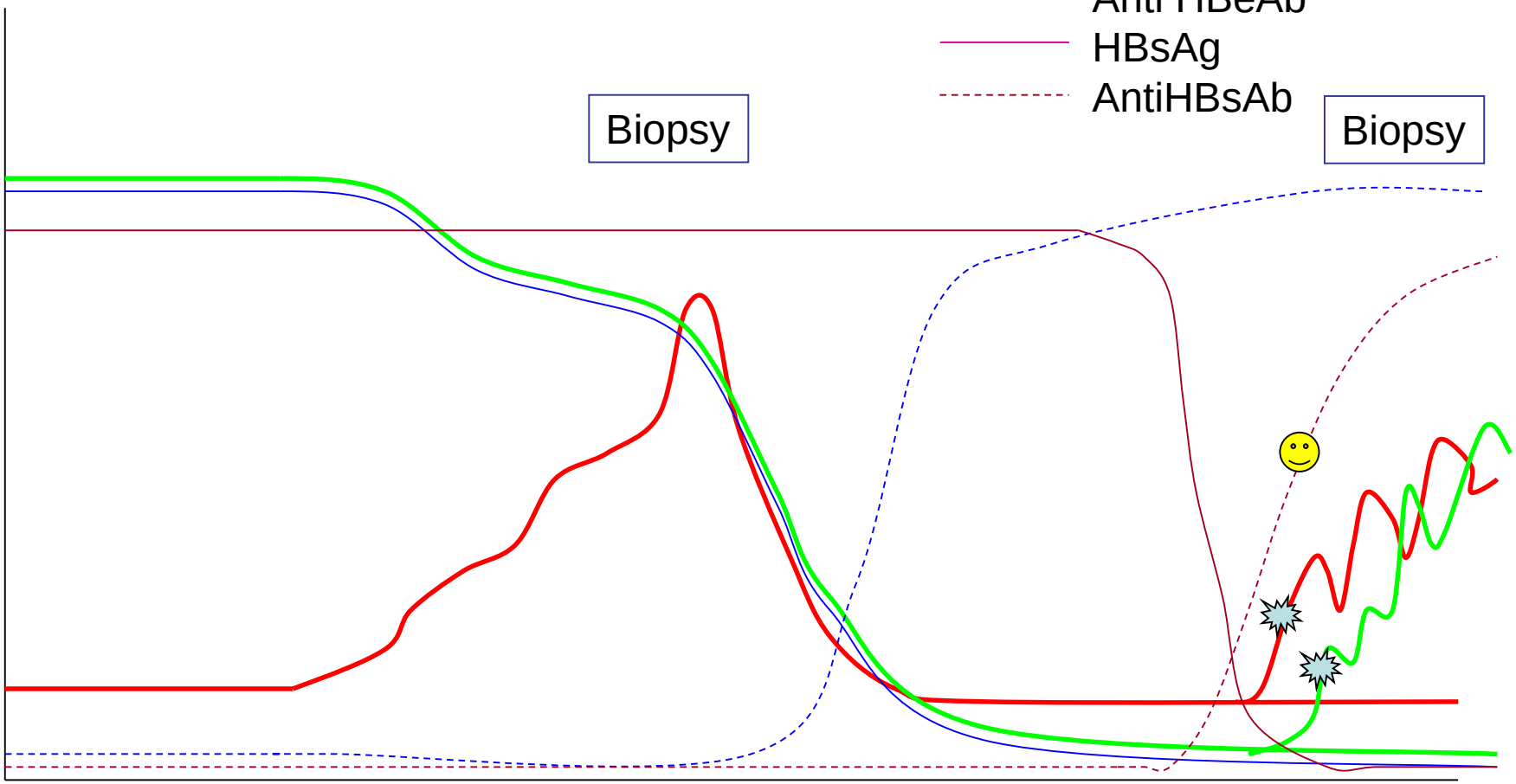
- 0.5-2% per year in western countries. Rare in endemic countries.
- Follows HBeAg seroconversion, represents resolution of chronic infection (although may be 'occult hepatitis B')

or

HBeAg –ve chronic hepatitis

- Original infection or by mutation, fluctuating course and poor prognosis. Can achieve lasting remission with treatment.
- Cirrhosis 8-10% per year.

Phases of chronic hepatitis B each may last many years

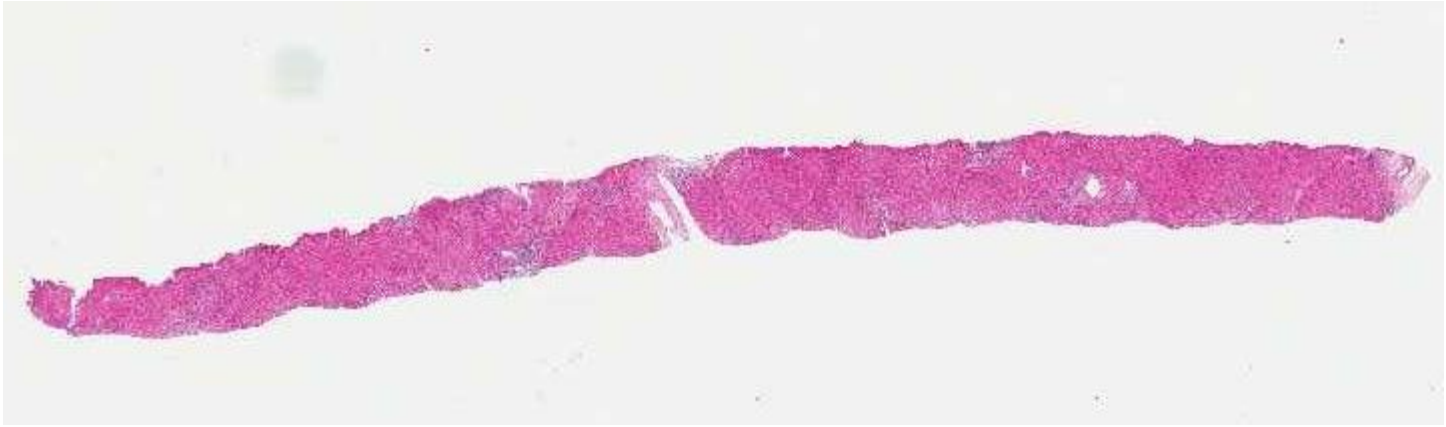


JIW 10 32/M

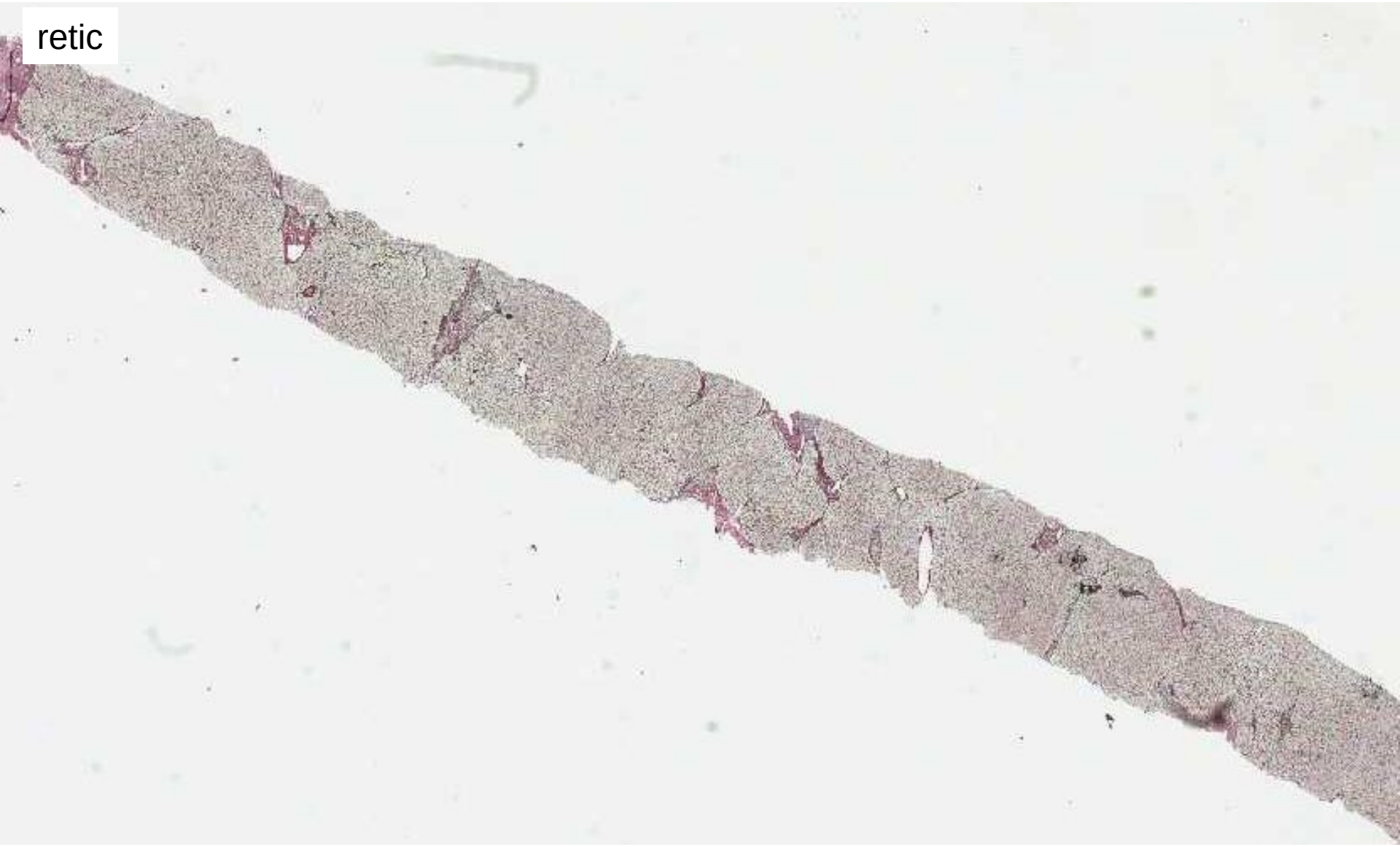
Known HBV positive. HBeAg +ve, HBsAg +ve

Last HBV PCR 3.8 x 10*5. ALT 50.

Fibroscan 10.1.

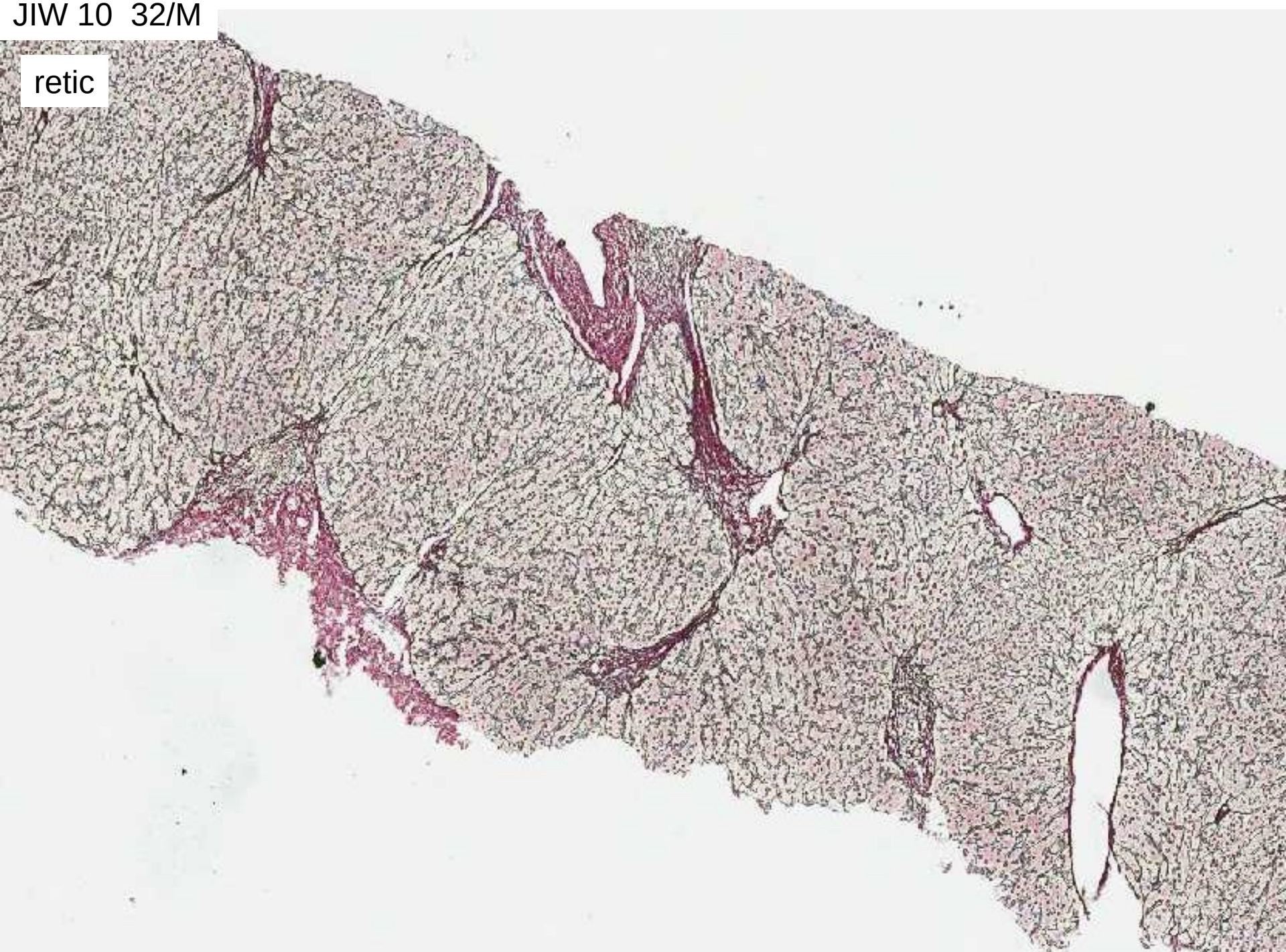


JIW 10 32/M



JIW 10 32/M

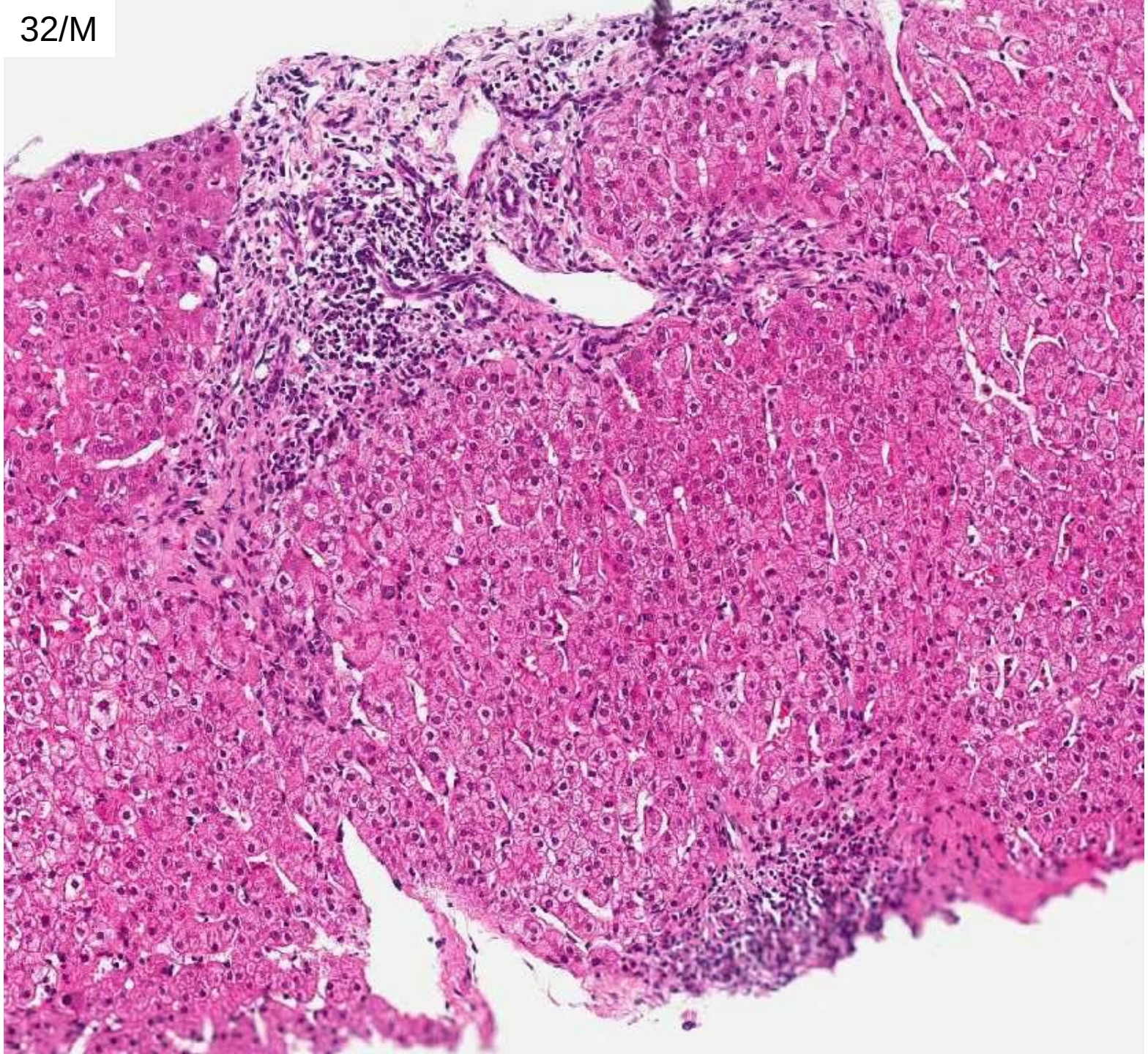
retic



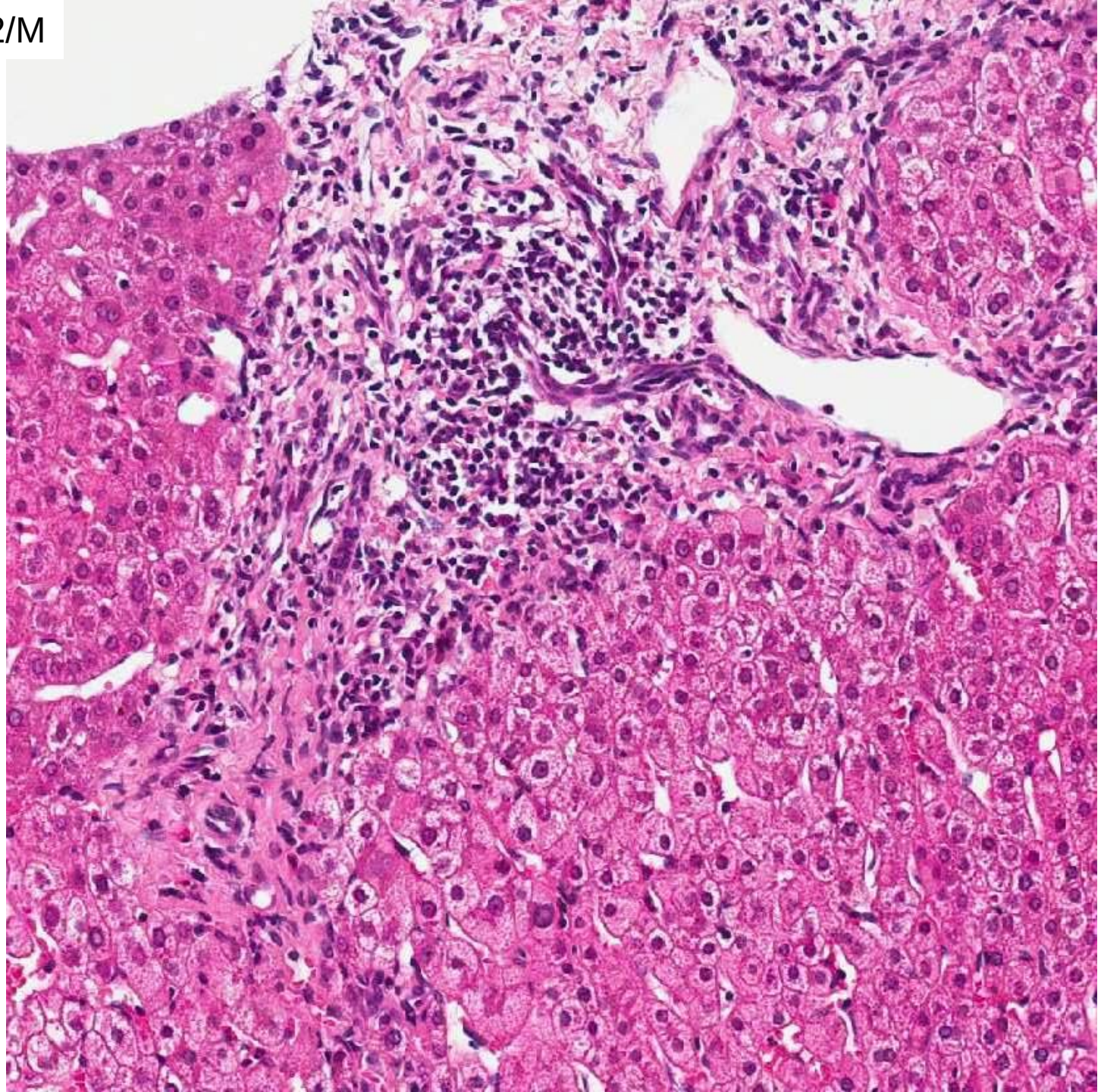
JIW 10 32/M

Sirius red

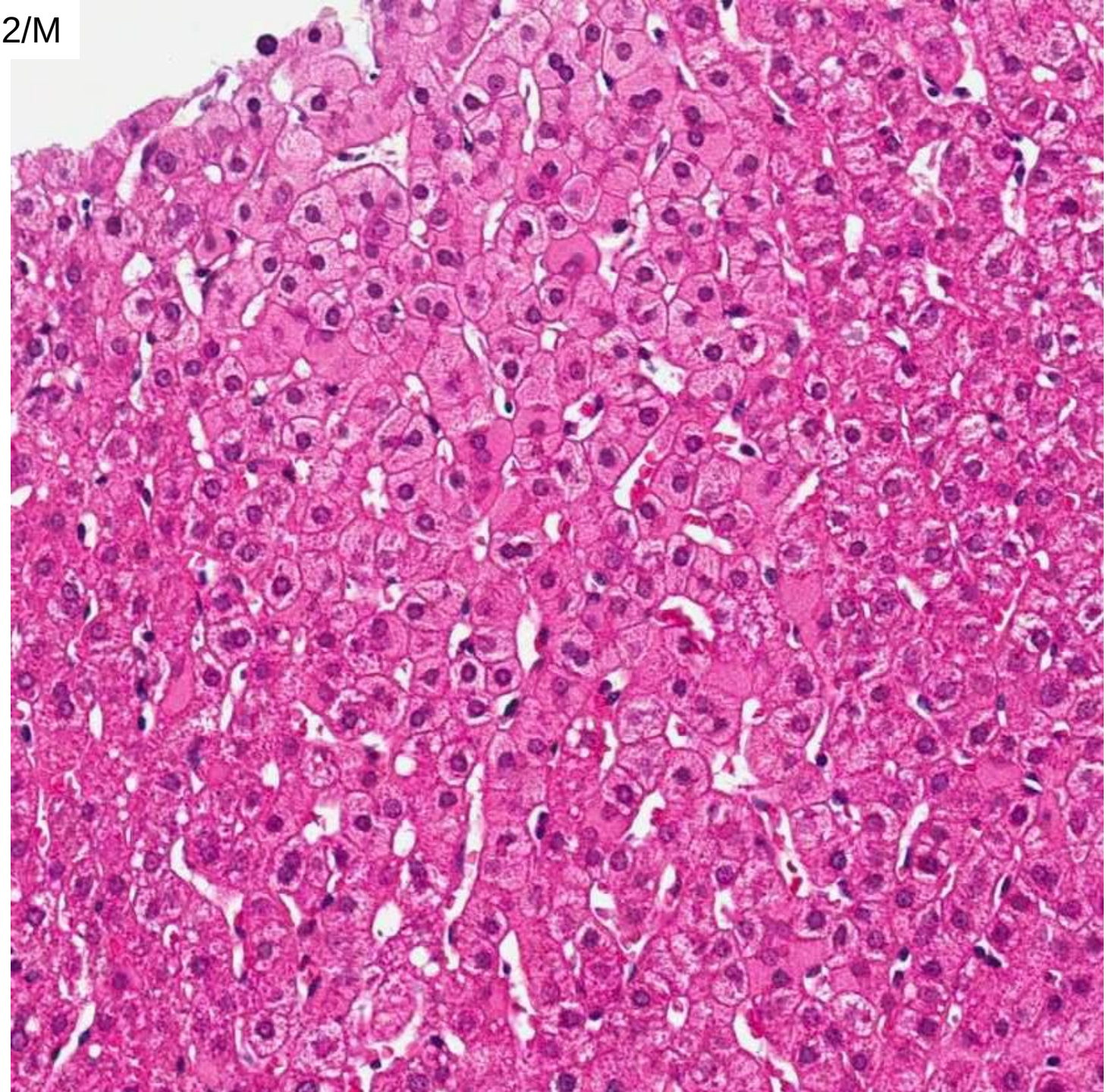
JIW 10 32/M



JIW 10 32/M

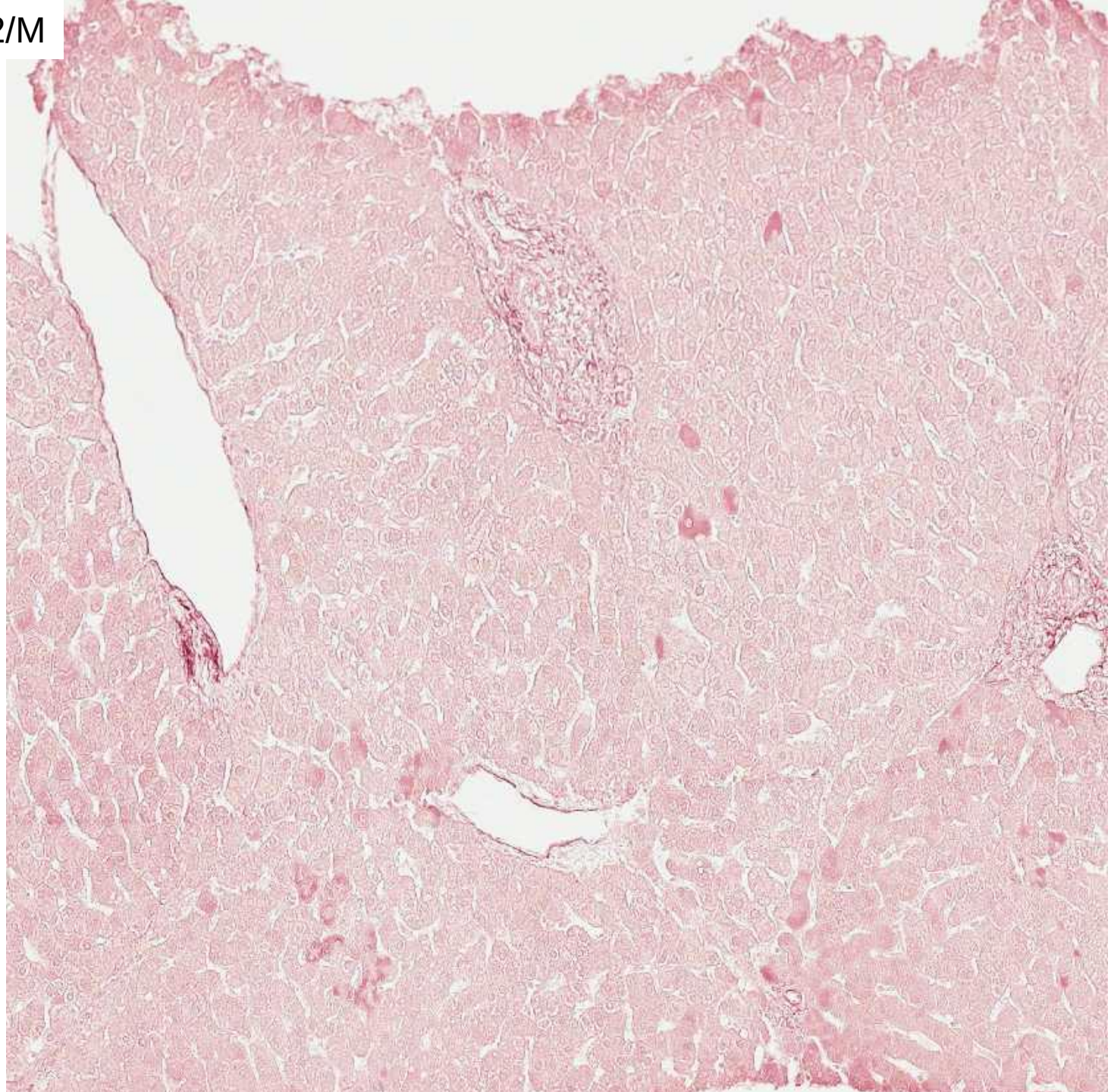


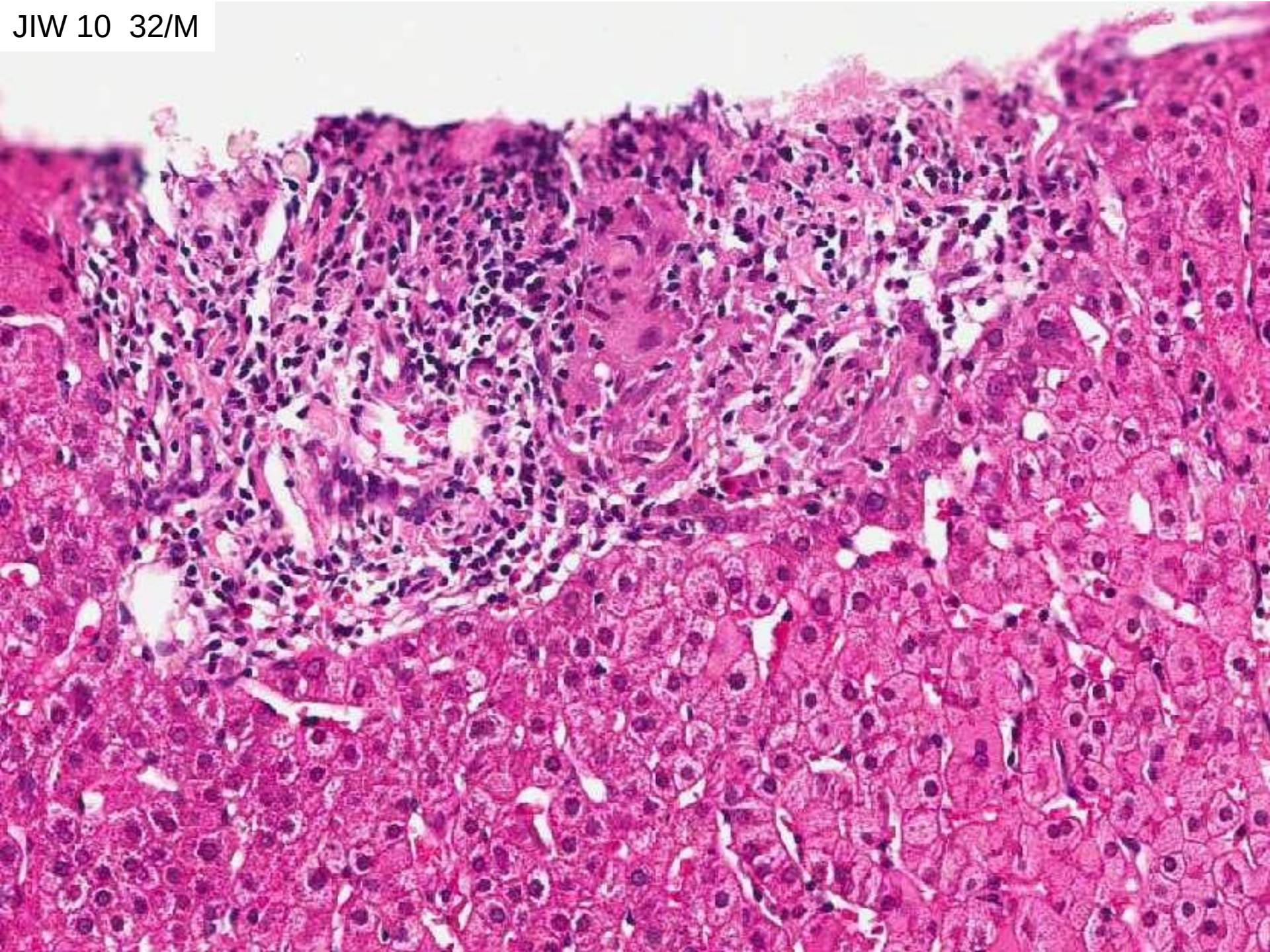
JIW 10 32/M



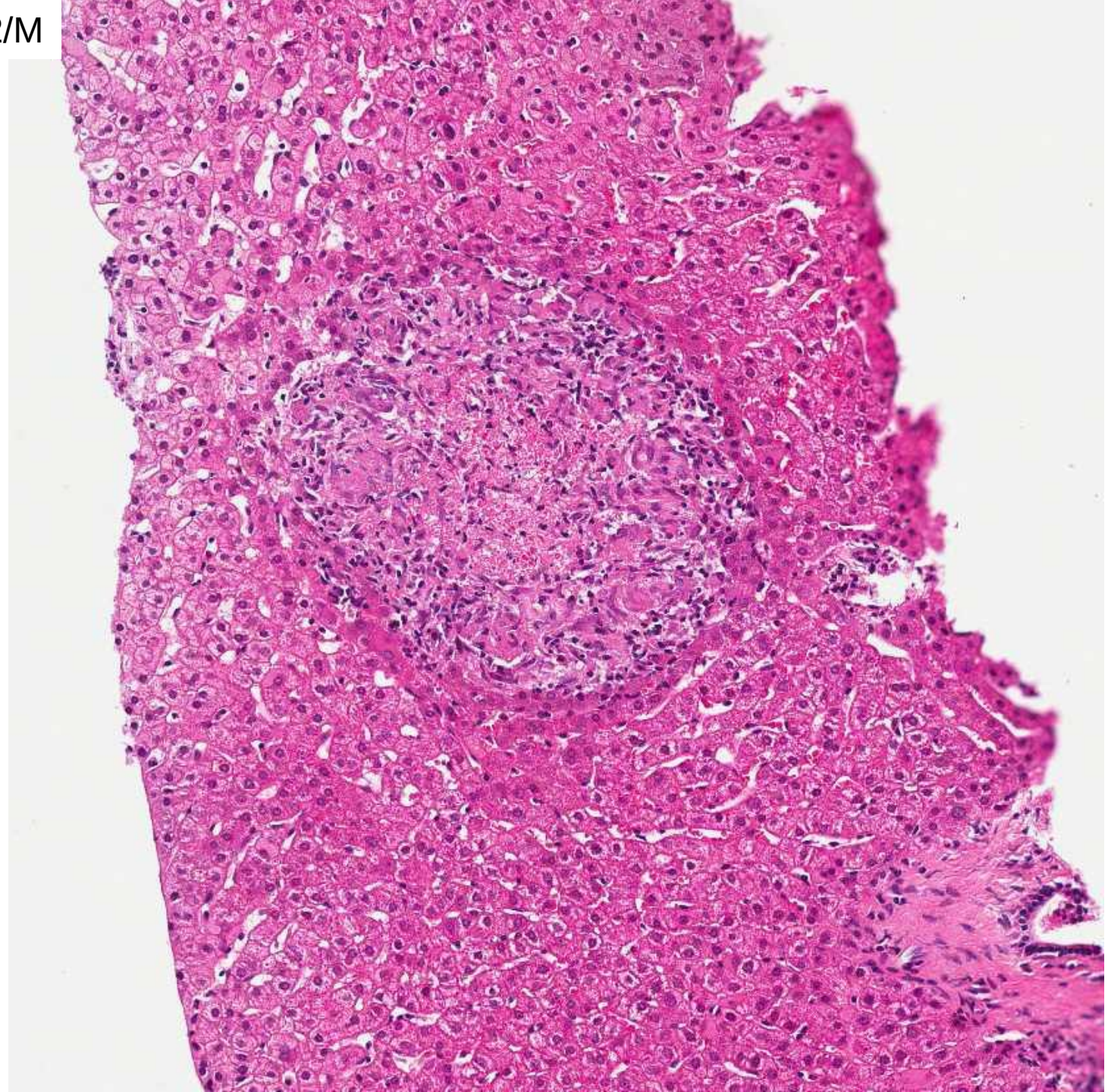
JIW 10 32/M

Shikata




JIW 10 32/M

JIW 10 32/M



JIW 10 32/M

Known HBV positive. HBeAg +ve, HBsAg +ve.
Last HBV PCR 3.8 x 10*5. ALT 50. Fibroscan 10.1.

Diagnosis: Chronic hepatitis B, Ishak stage 4, grade 5.
Also granulomas – exclude TB.

* Second diagnosis common in liver biopsies

Biopsies in chronic viral hepatitis

Changing indications

- Hepatitis C – only for diagnostic dilemma
- Hepatitis B – treatment depends on severity of disease
  - intermediate fibroscan
  - High ALT
  - High viral DNA

JIW cases so far (7-10)

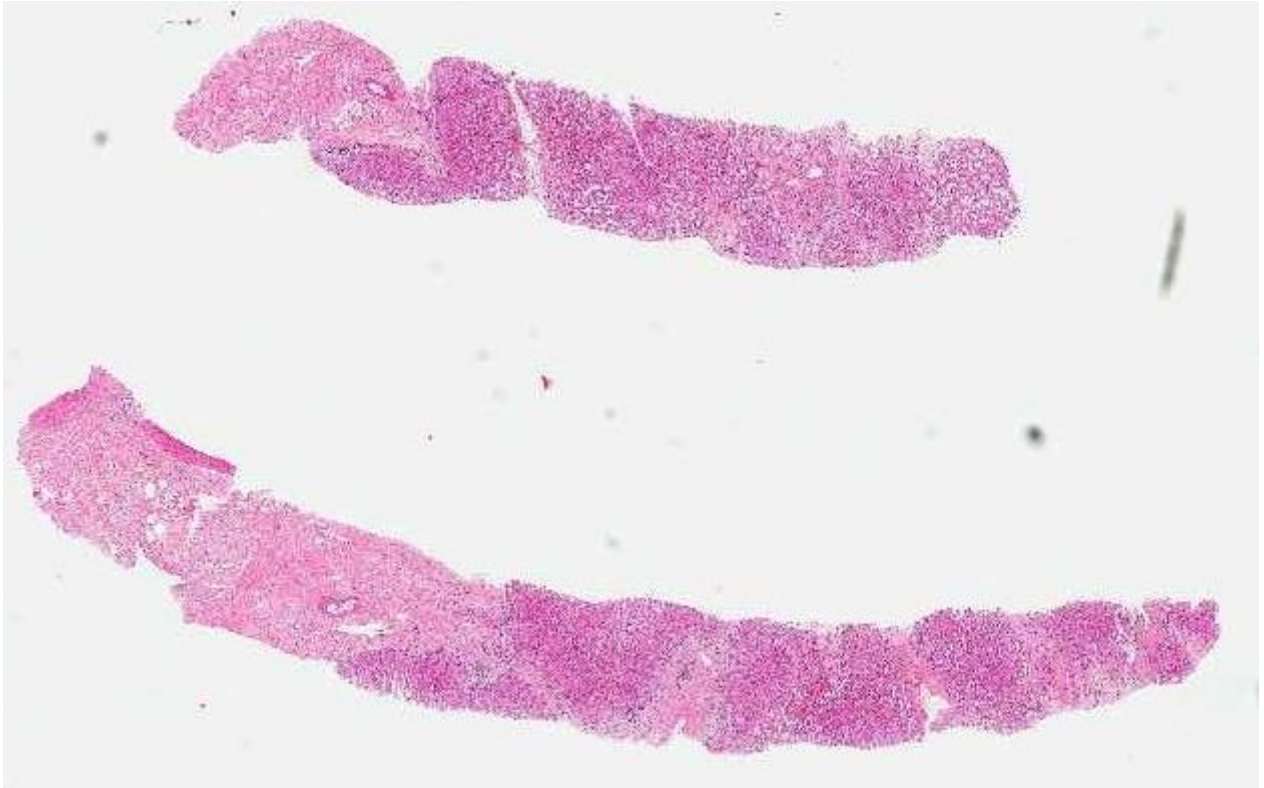
Chronic hepatitis – autoimmune, viral

How to report:

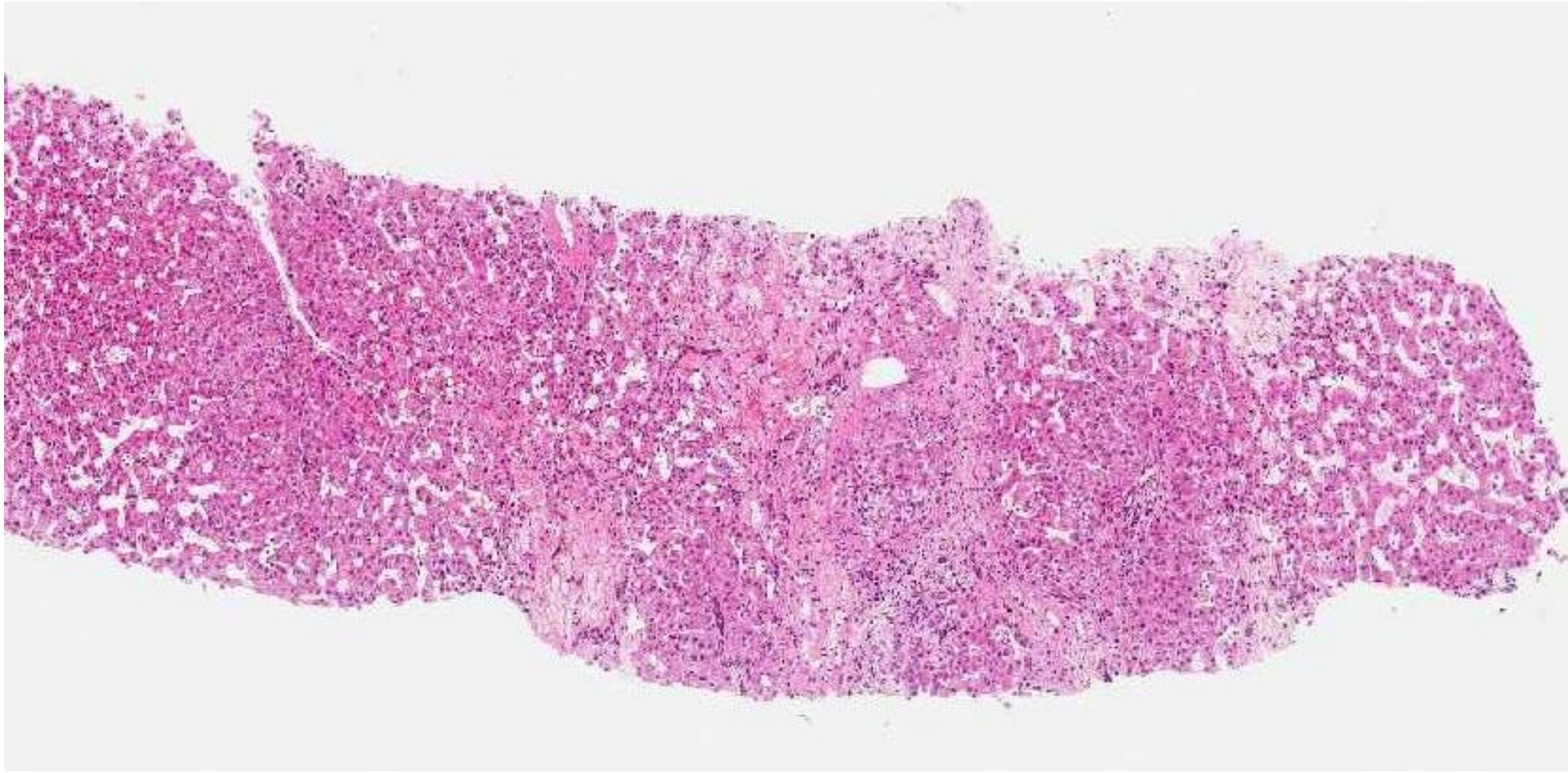
- Chronic hepatitis is a morphology, in need of a diagnosis (like ‘colitis’ v. ‘ulcerative colitis’)
- Need clinico-path correlation to make a complete diagnosis with an aetiology.
- Include severity – stage, grade, recognising limitations.
- And /or another diagnosis
- Rarely drugs

JIW 11 37/M

Alcohol-related liver cirrhosis (moderate drinker). Work up for liver transplant. Abstinent from alcohol?



JIW 11 37/M



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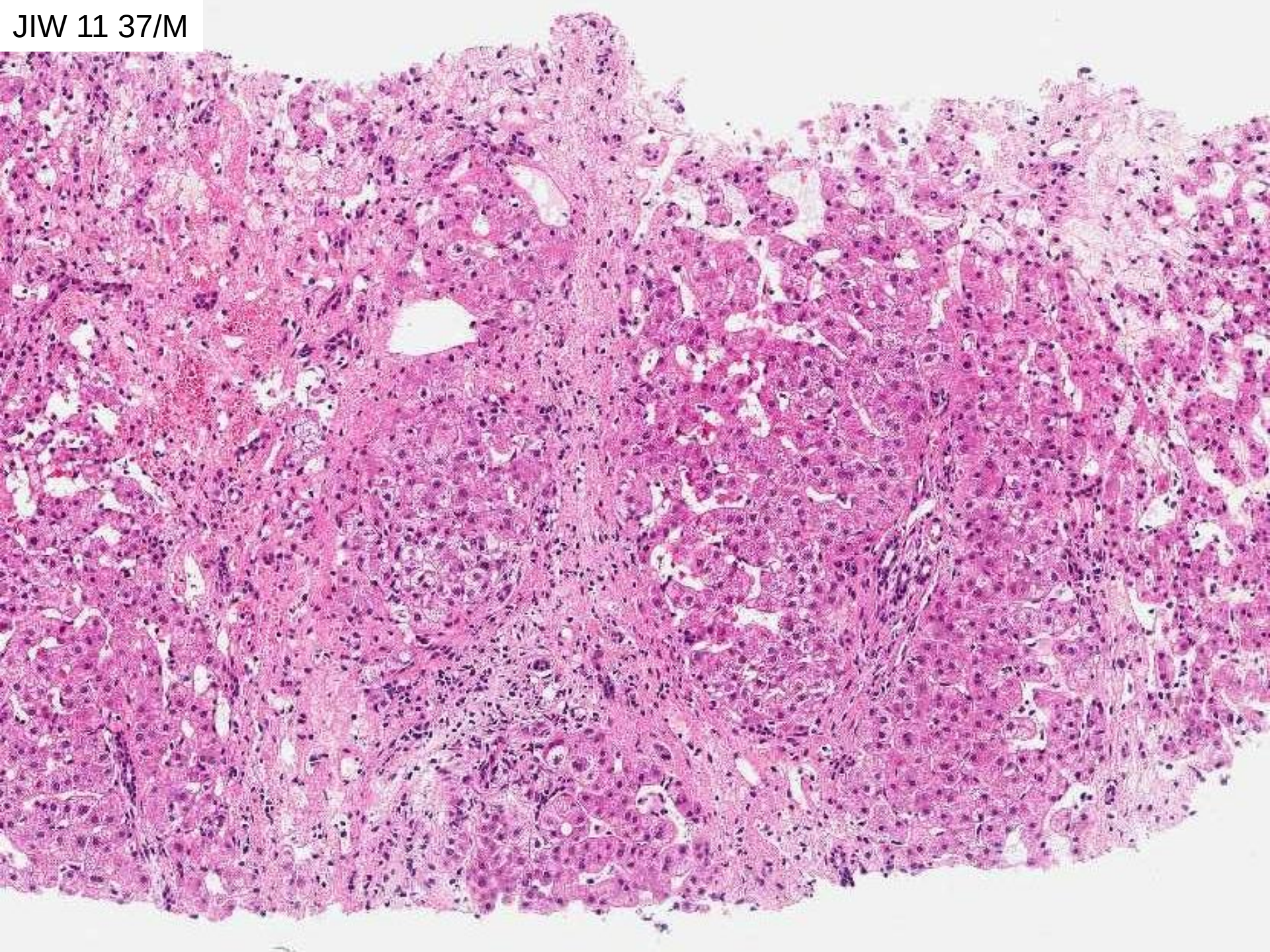

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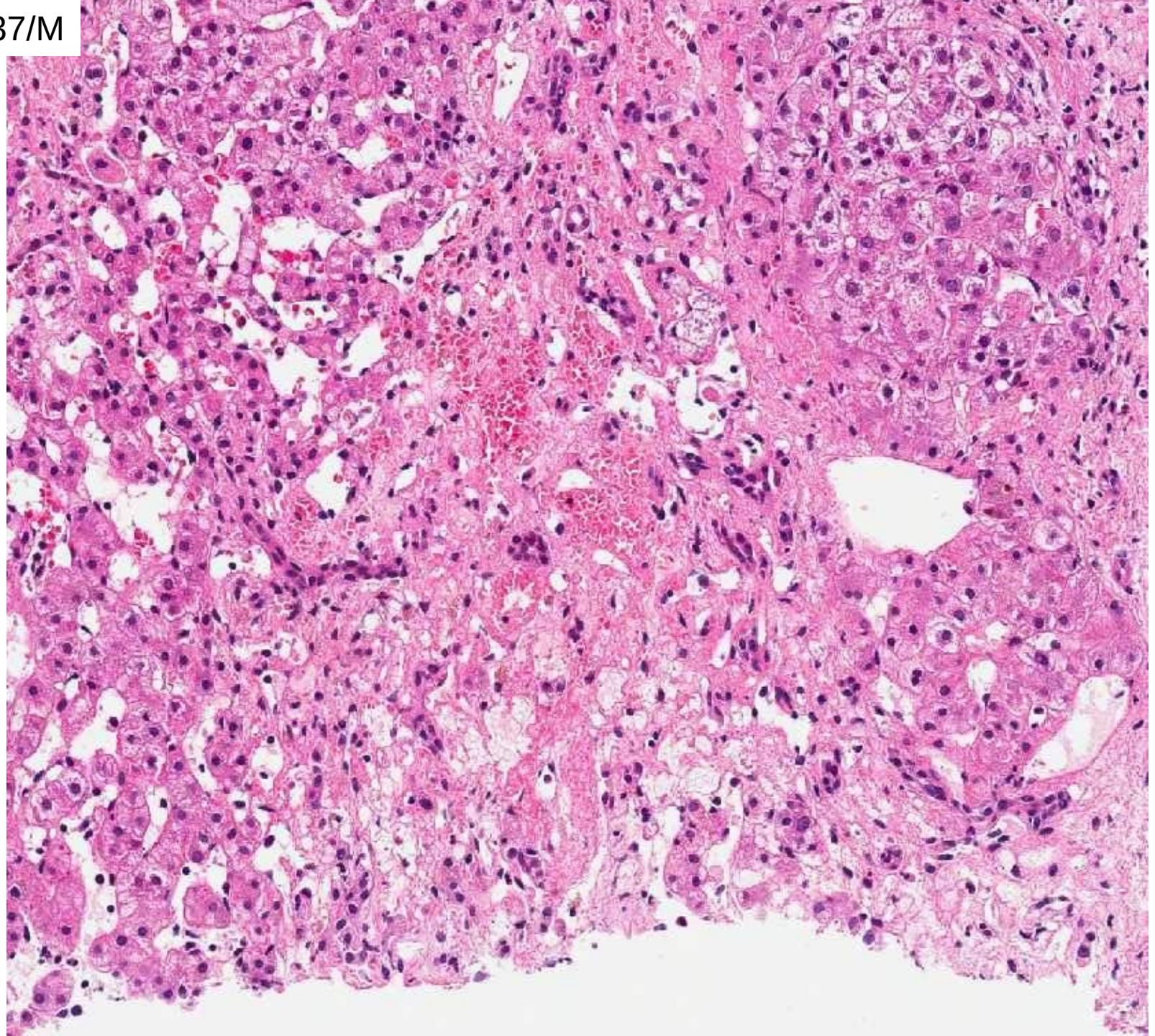

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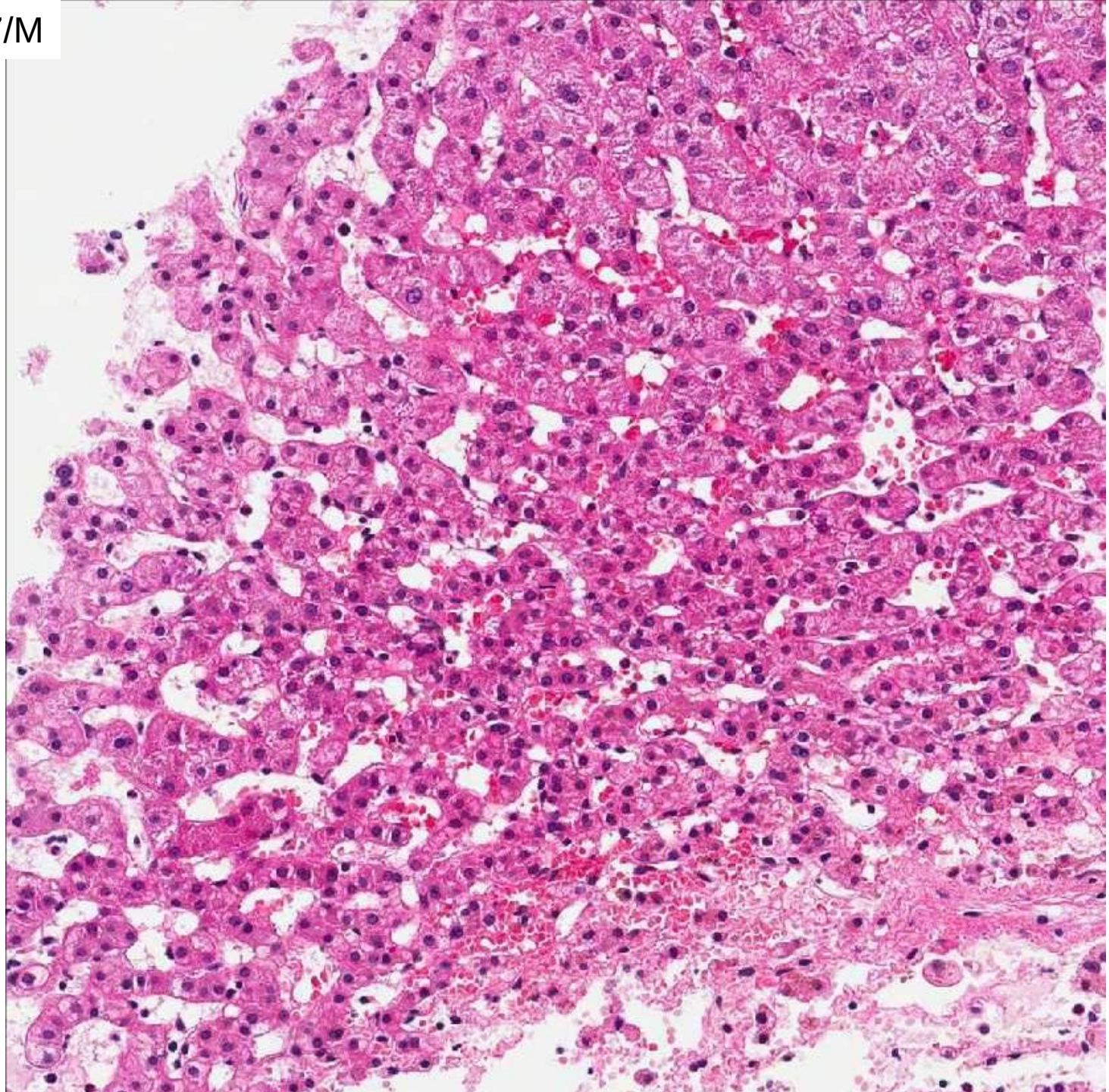

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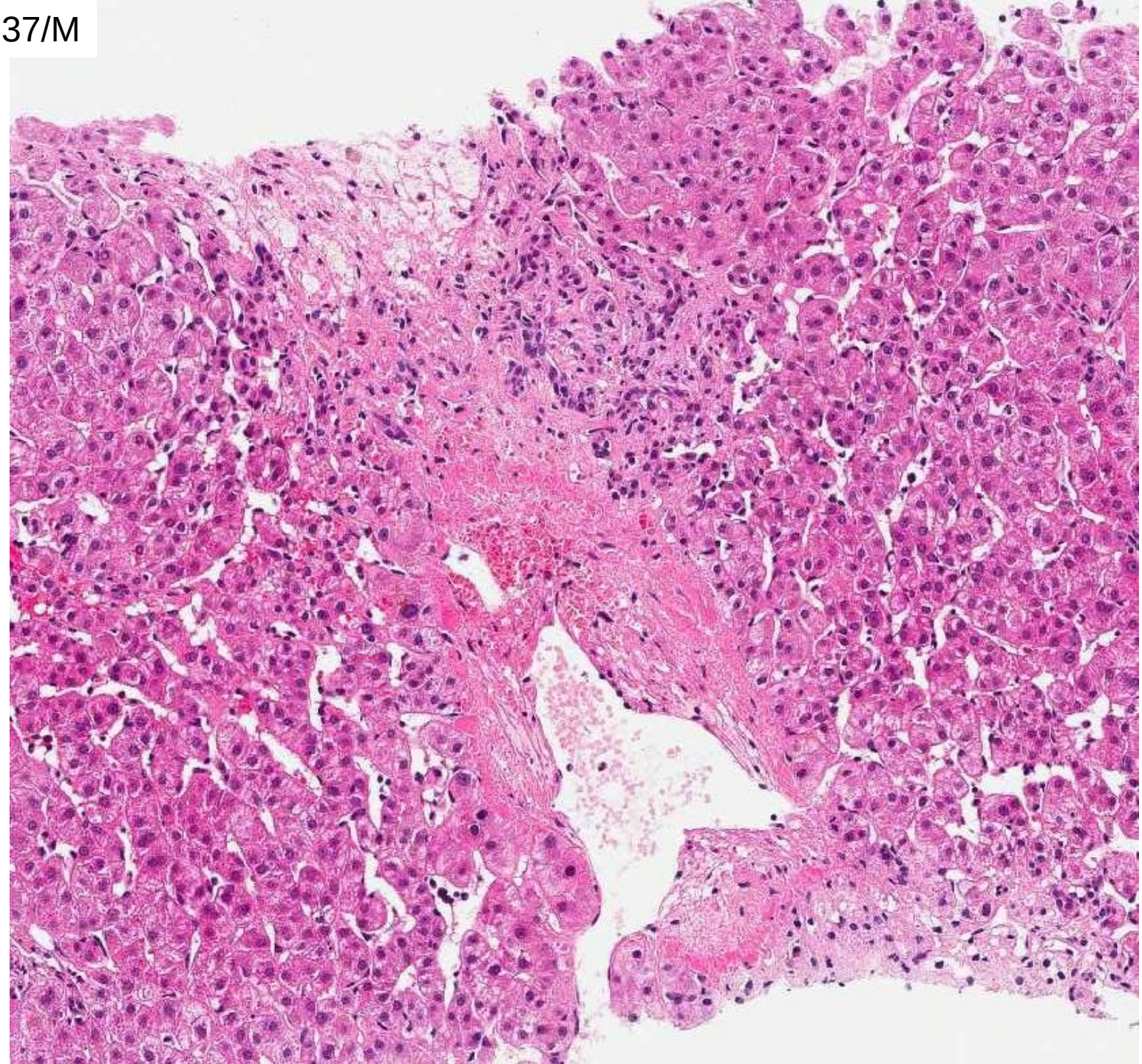

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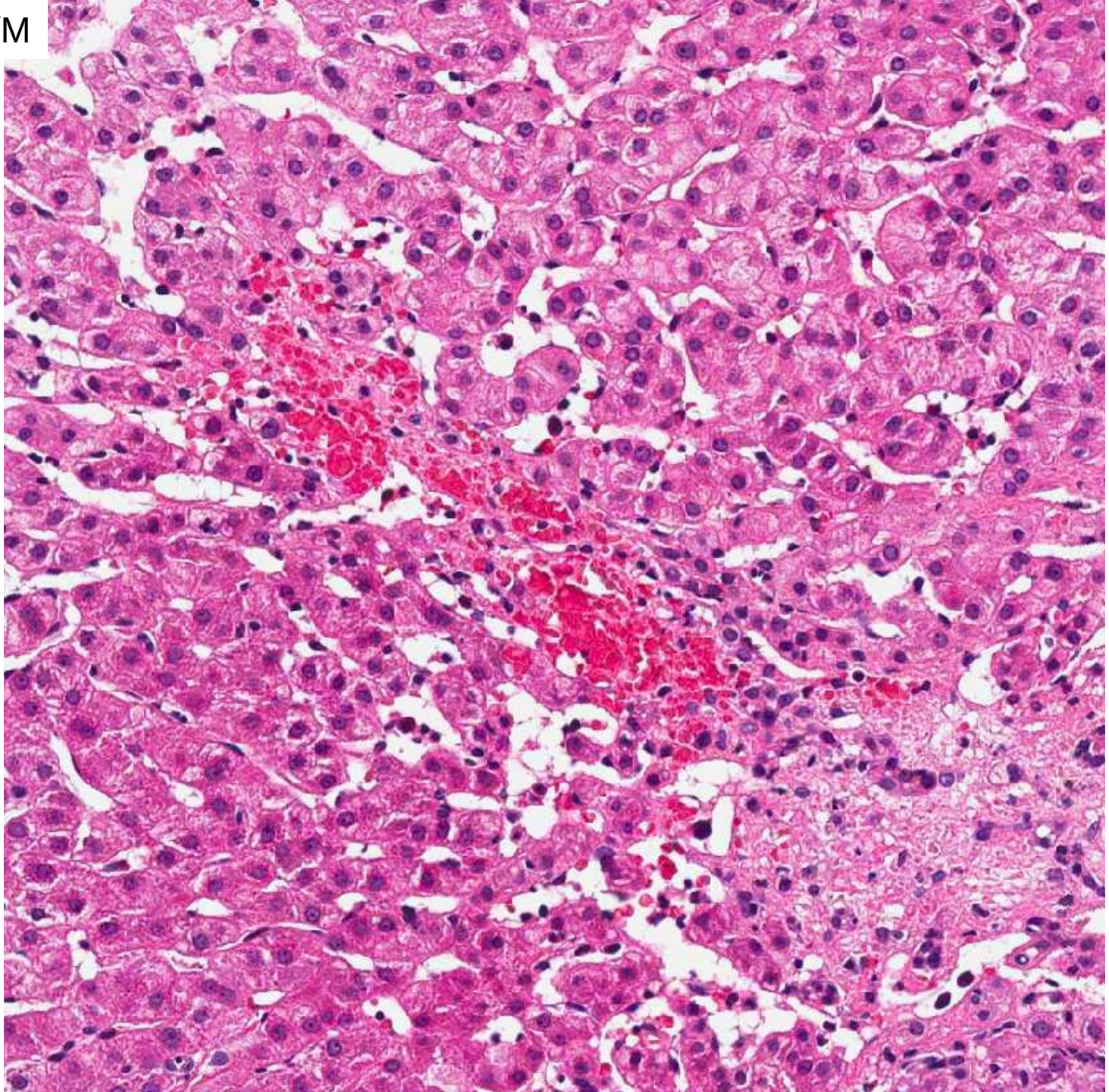
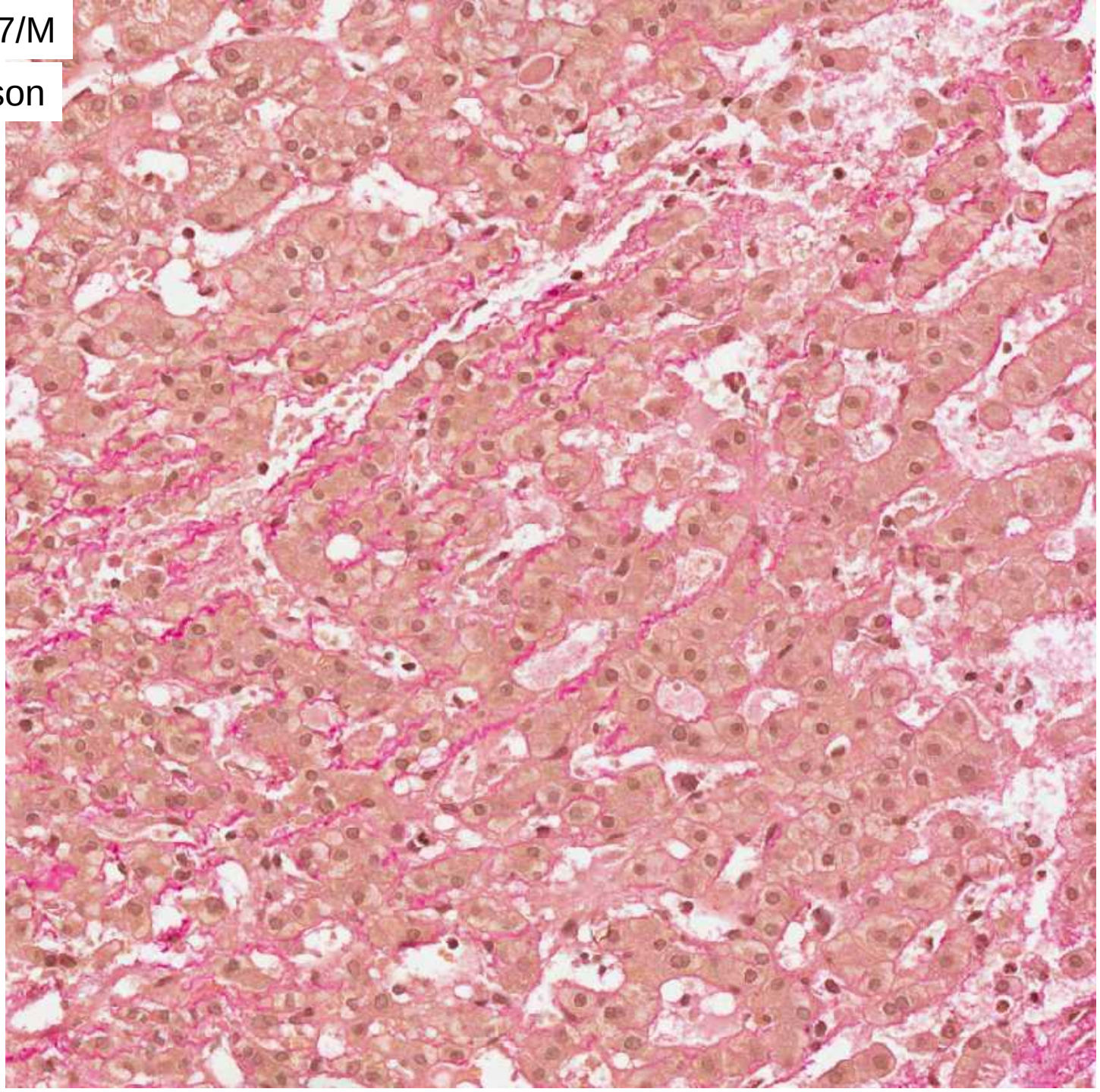


JIW 11 37/M

van Gieson



JIW 11 37/M

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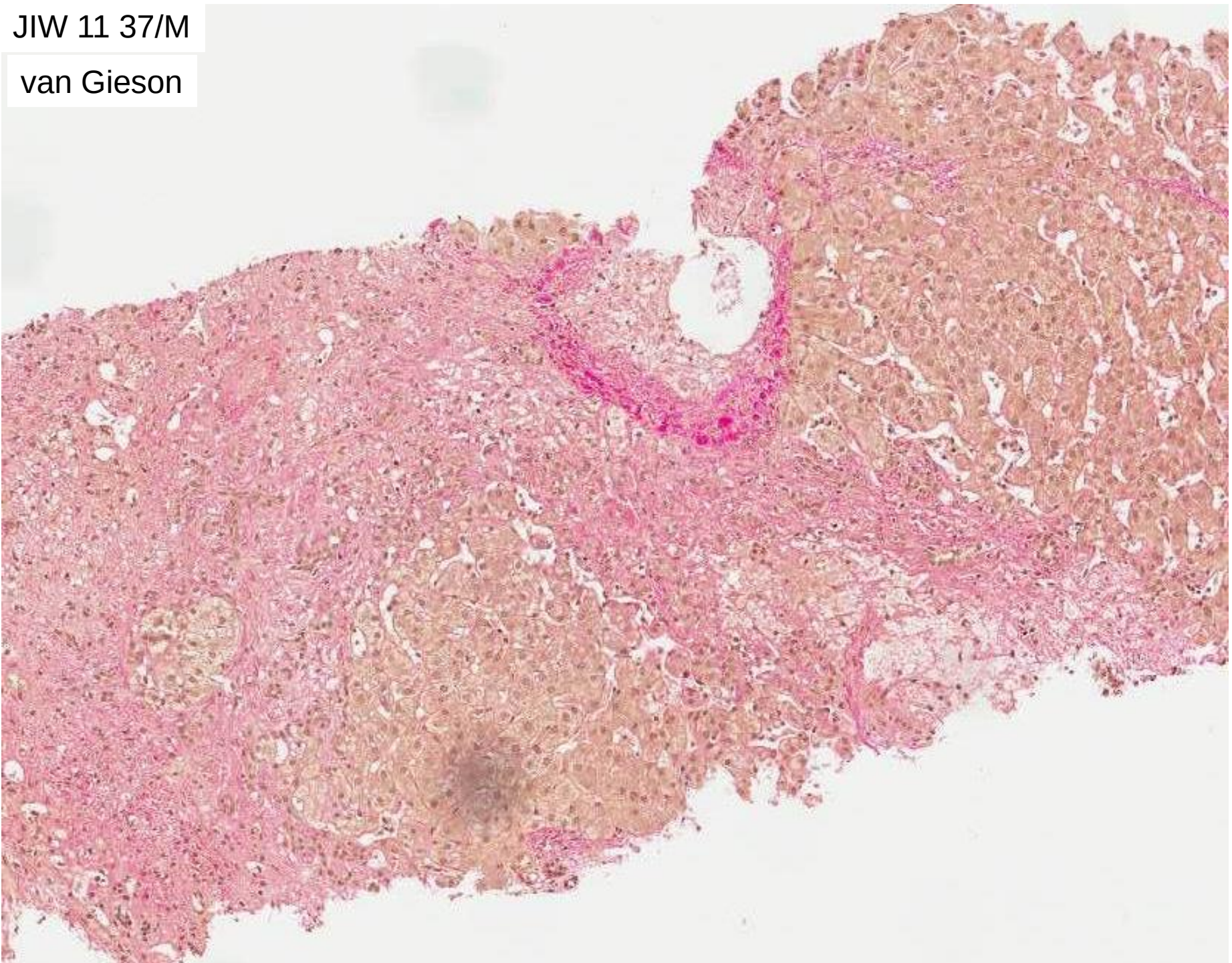


JIW 11 37/M

Alcohol-related liver cirrhosis (moderate drinker). Work up for liver transplant. Abstinent from alcohol?

Diagnosis:

"The biopsy confirms fibrosis and some nodular regeneration, although it is too small to determine whether there is cirrhosis.

The pattern of liver injury is much more suggestive of venous outflow obstruction (Budd Chiari or veno-occlusive disease) than alcoholic liver disease."

For discussion at CPC.

JIW 11 37/M

Alcohol-related liver cirrhosis (moderate drinker). Work up for liver transplant. Abstinent from alcohol?

<u>Final diagnoses:</u>

Budd Chiari Syndrome – thrombophilia with JAK2 mutation

All hepatic veins thrombosed, portal vein patent, IVC thrombosed. *(- so transplant not an option)*

Previous high alcohol intake but completely abstinent for 18/12

Previous ascites, controlled on diuretics

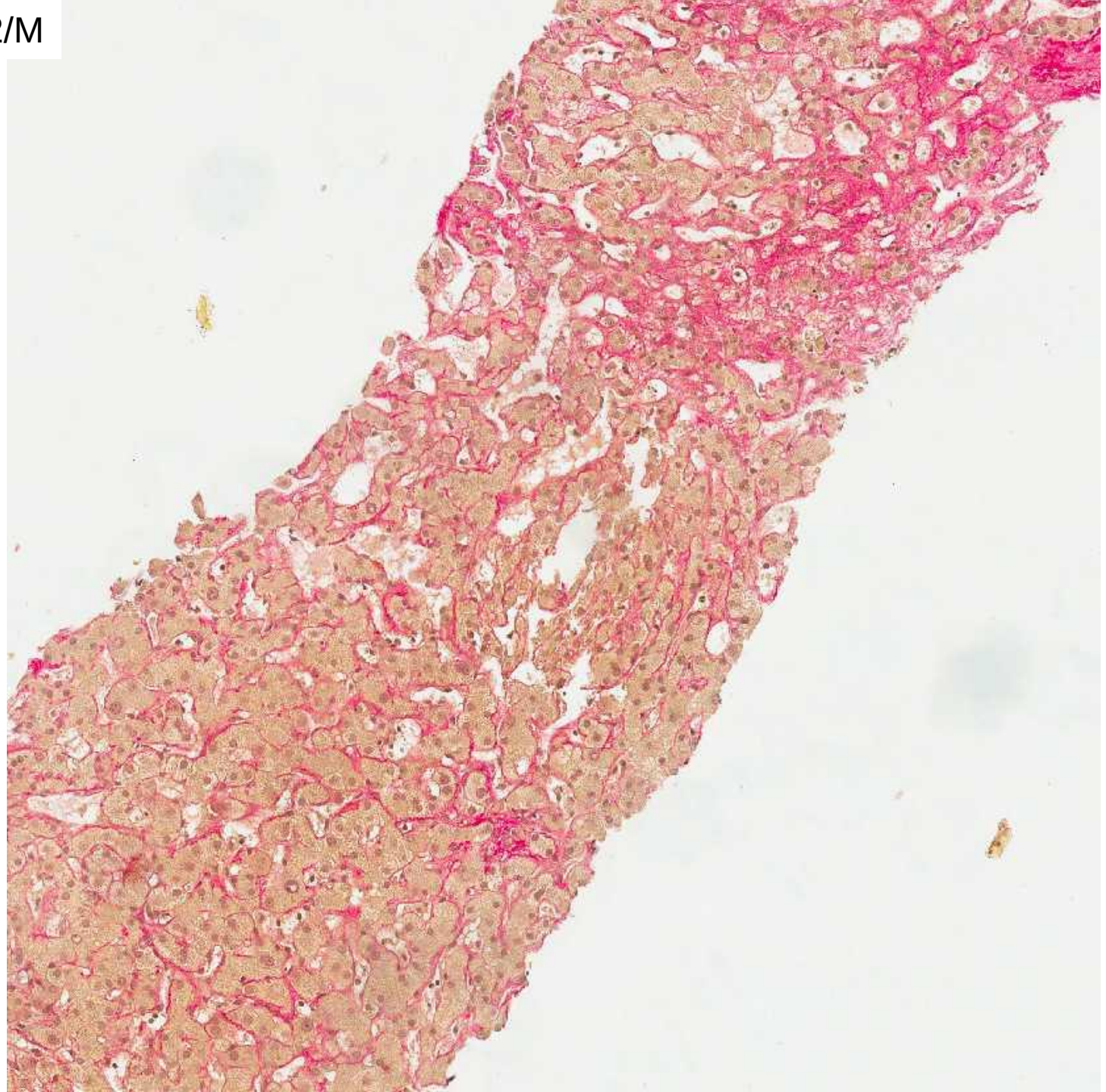
Anticoagulated with Warfarin, remains stable. 3 ½ years later

JIW 12 52/M

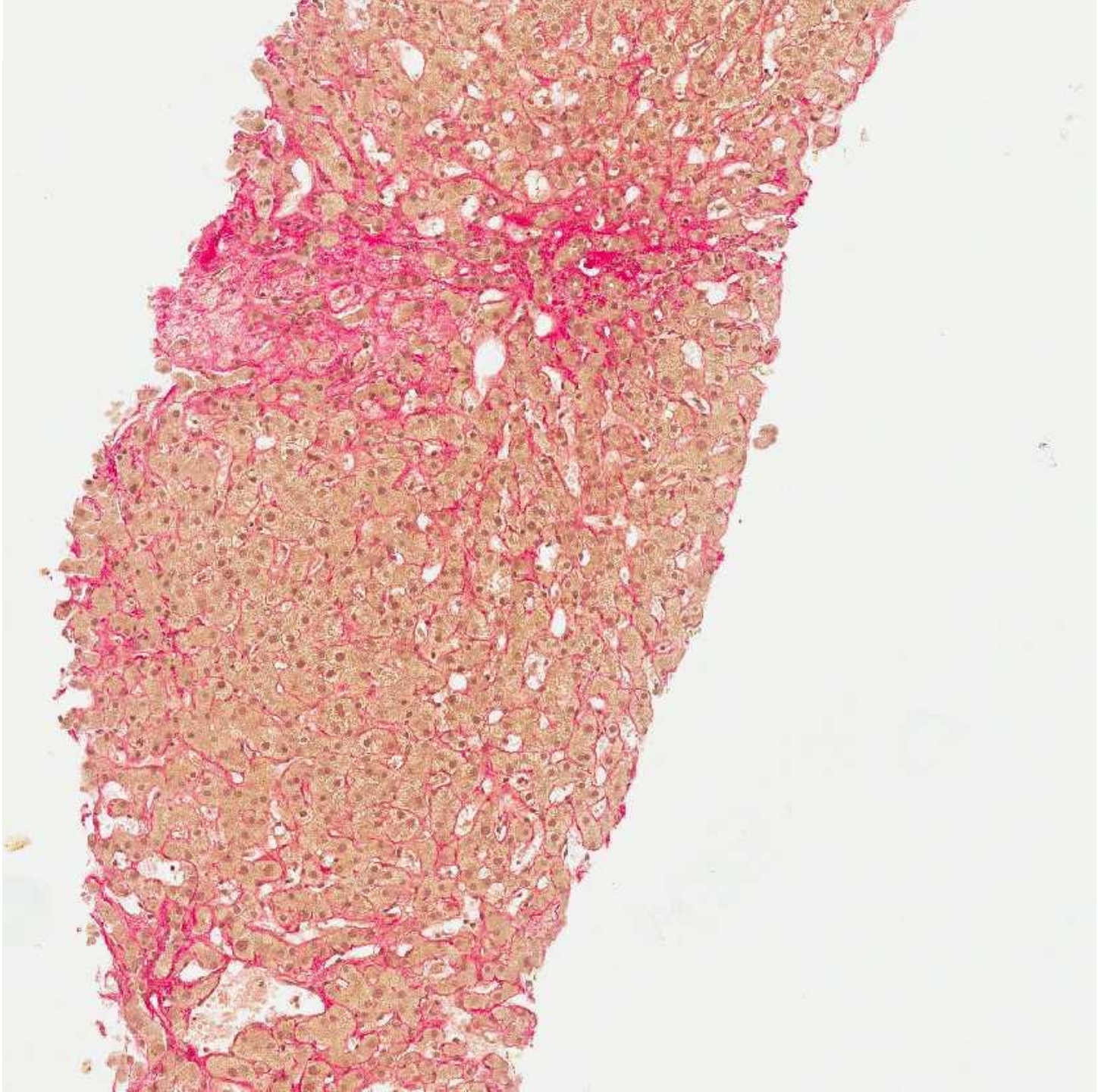
Transjugular liver biopsy. Abnormal LFTs, raised bilirubin 43, ALT 9, alk phos 381, ANA +ve, anti-DNA antibodies.
Hepatitis B and C serology negative.
Ultrasound scan - hepatomegaly, distended IVC.
Past history cardiomyopathy, IHD and previous cardiac arrest.

Clinical diagnosis intrinsic liver disease, ? cardiac related

JIW 12 52/M



JIW 12 52/M



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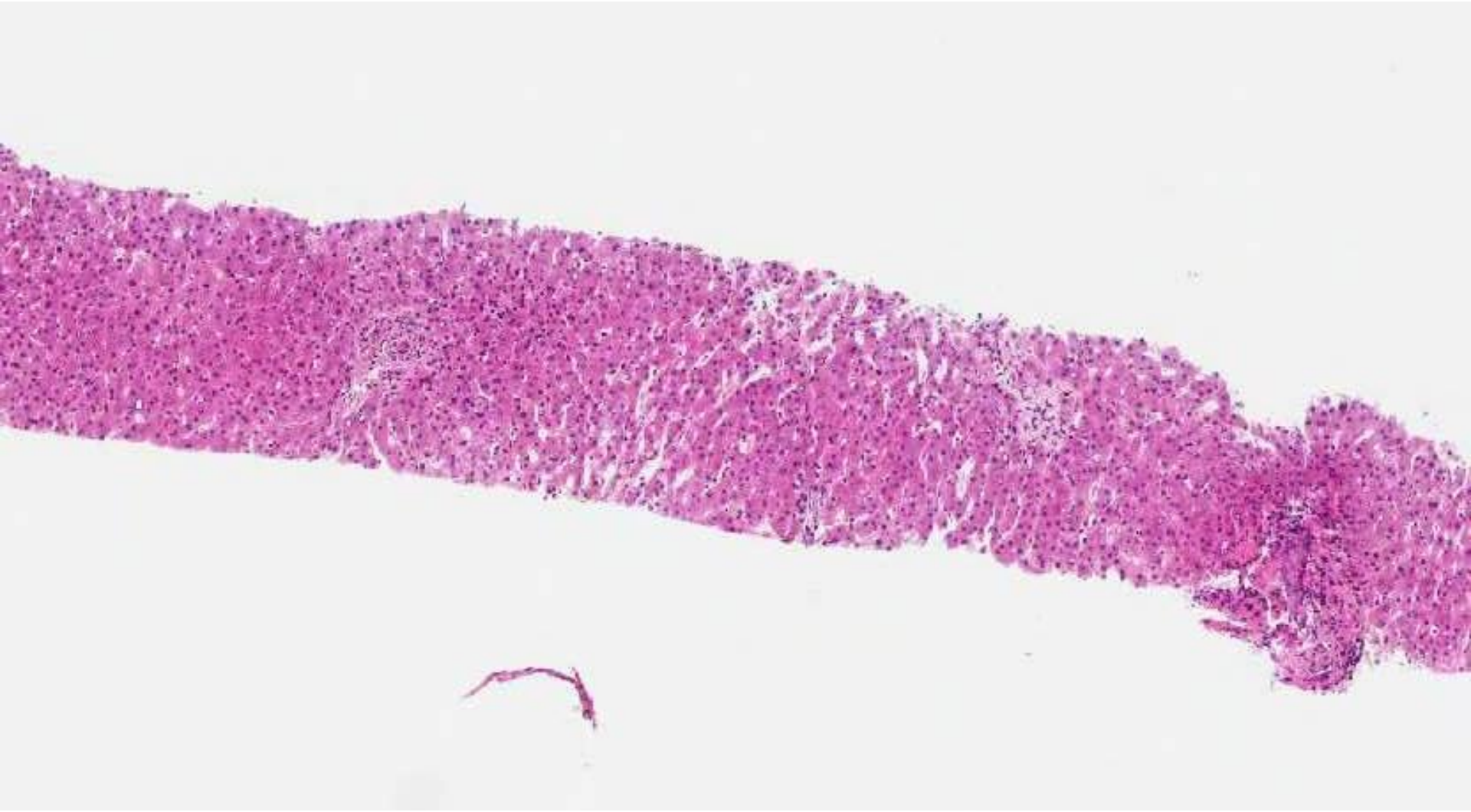

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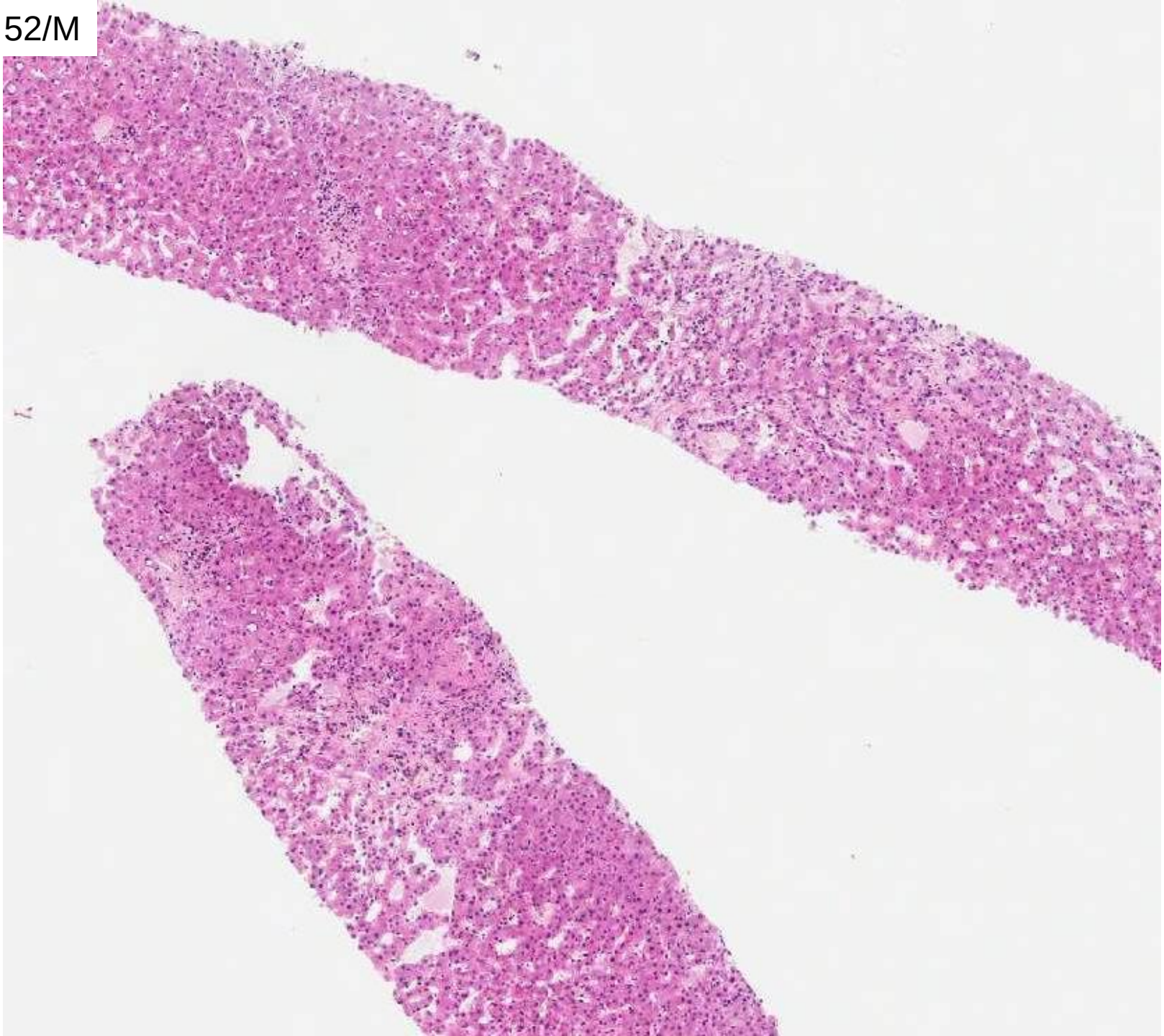
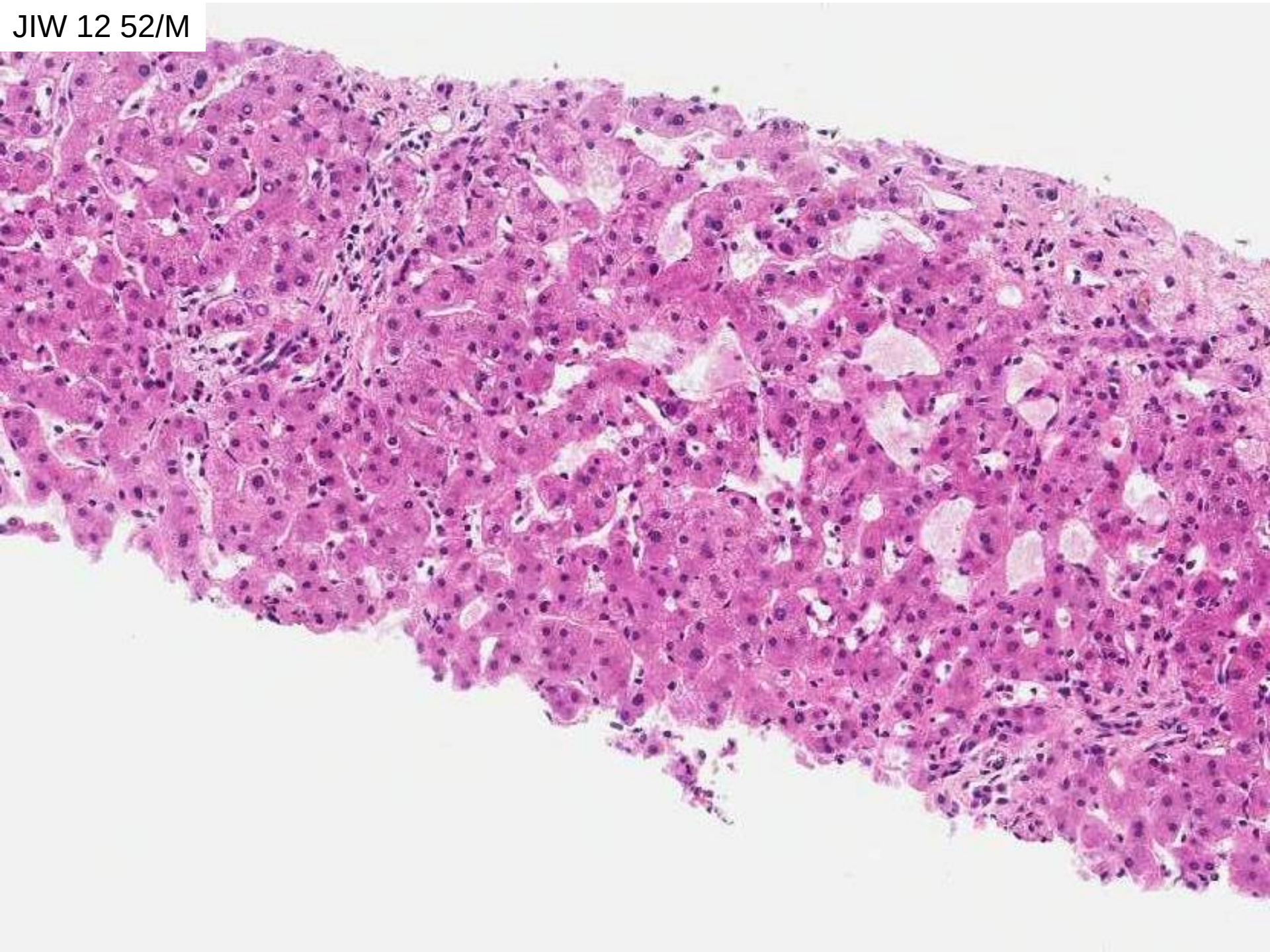
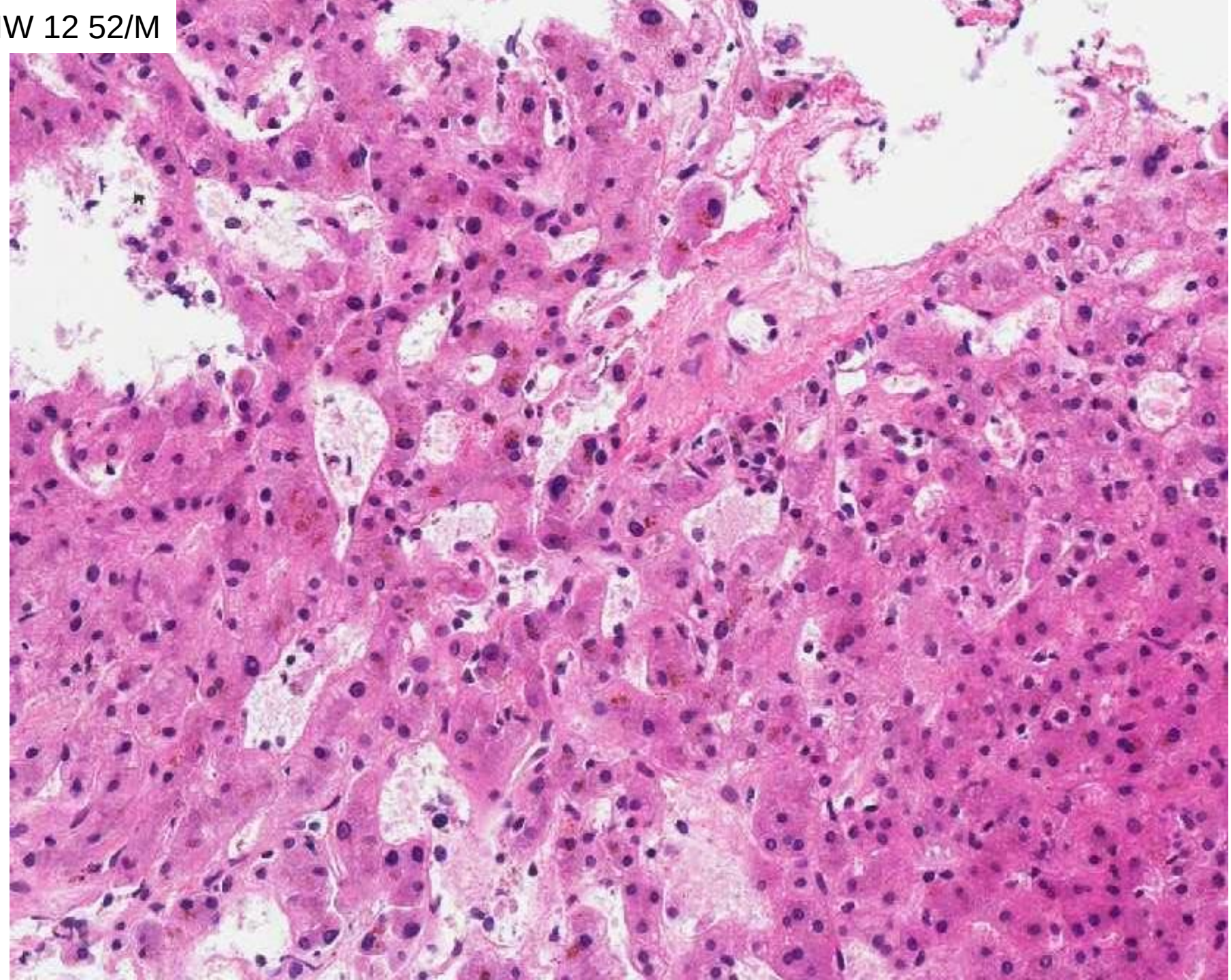



JIW 12 52/M

JIW 12 52/M



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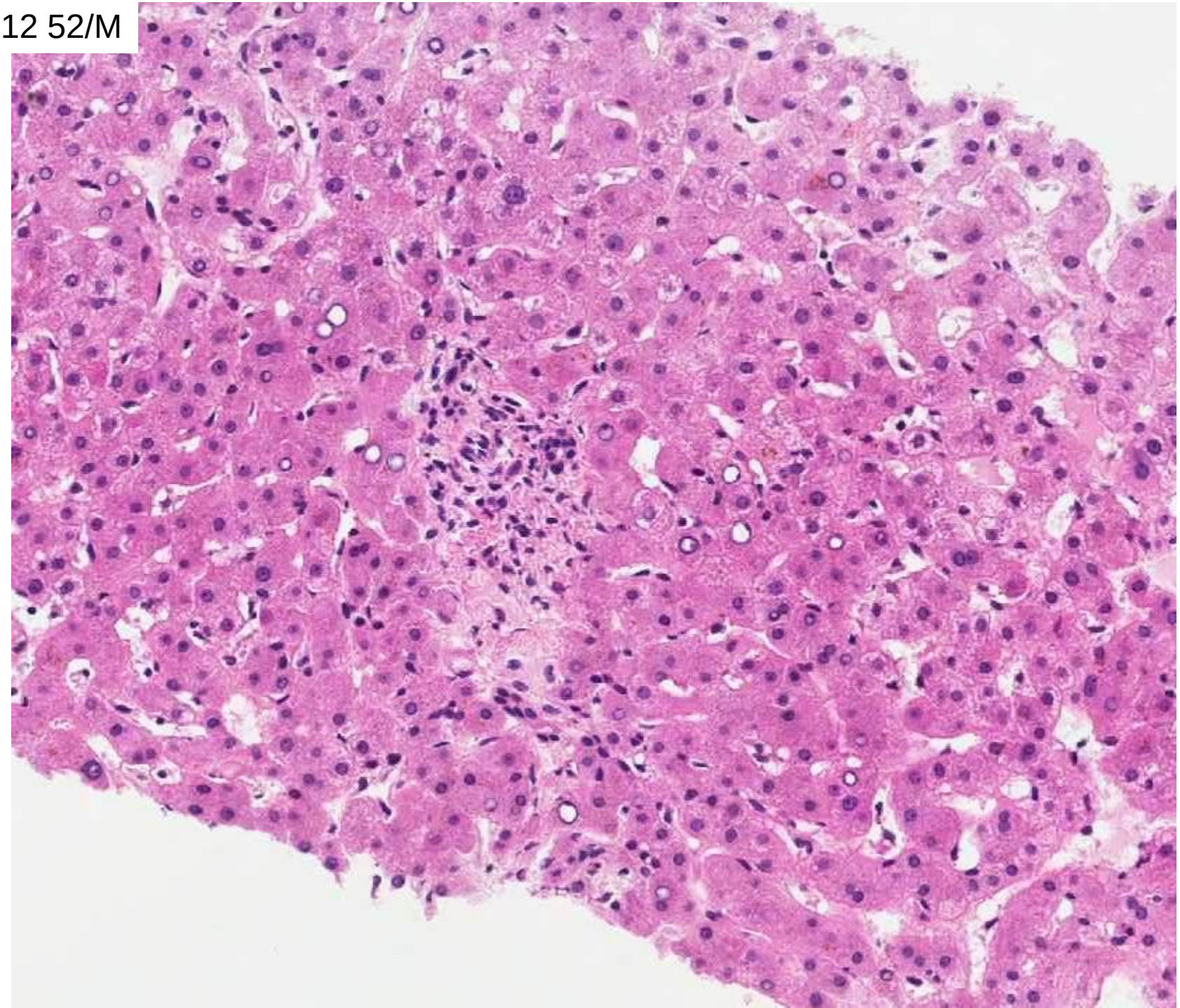

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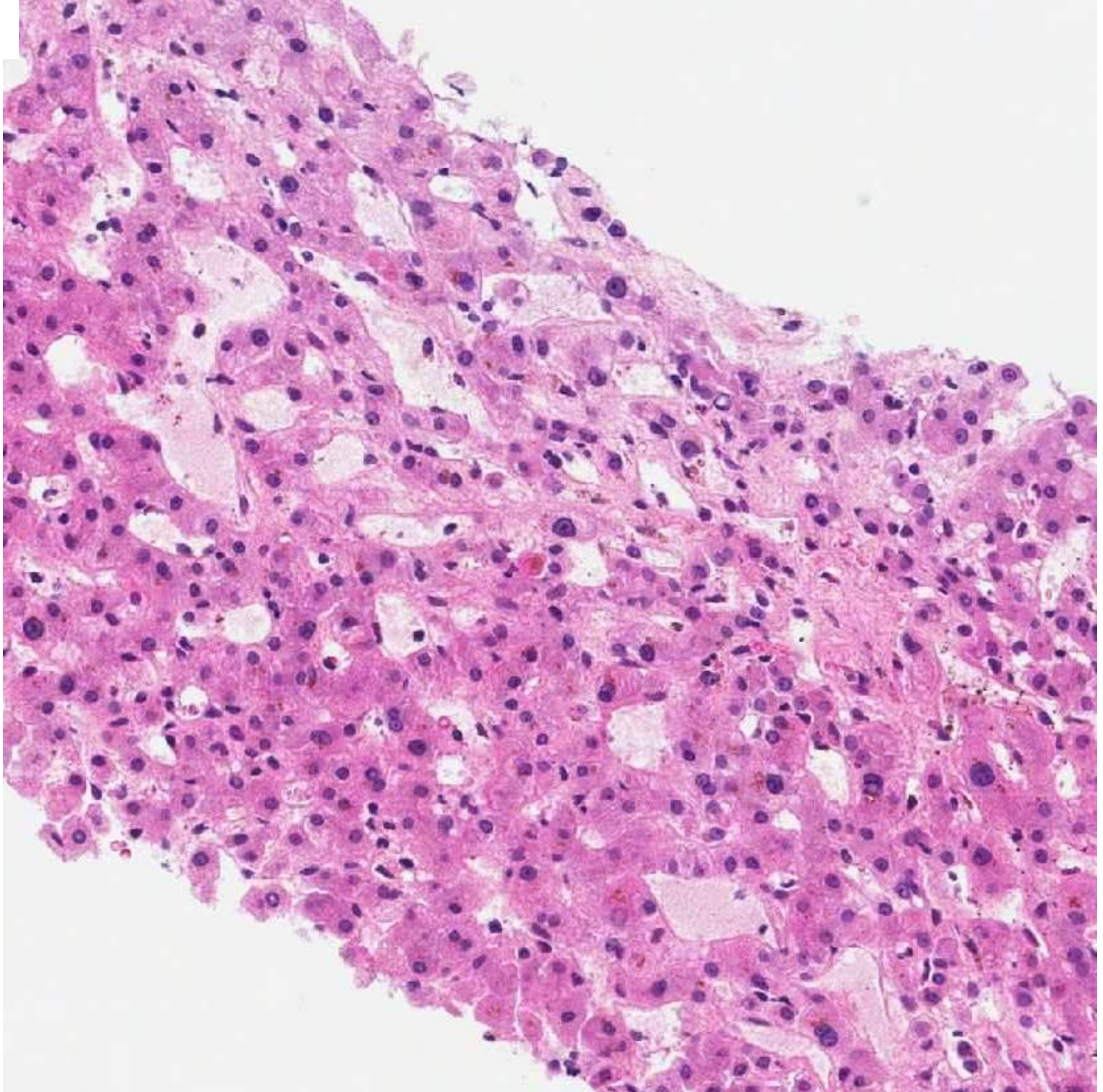


JIW 12 52/M

Transjugular liver biopsy. Abnormal LFTs, raised bilirubin 43, ALT 9, alk phos 381, ANA +ve, anti-DNA antibodies.
Hepatitis B and C serology negative.
Ultrasound scan - hepatomegaly, distended IVC.
Past history cardiomyopathy, IHD and previous cardiac arrest.

Clinical diagnosis intrinsic liver disease, ? cardiac related pathology.

Diagnosis: features suggest vascular disease, ? chronic venous outflow obstruction.

Pressure studies – raised CVP 27mmHg,

Same pressure in hepatic veins

Liver biopsy in vascular disease

Inflow obstruction - Non-cirrhotic portal hypertension
main portal vein thrombosis or obliterative portal venopathy

- nodular regenerative hyperplasia,
- inconspicuous portal veins,
- dilated periportal sinusoids

Outflow obstruction –

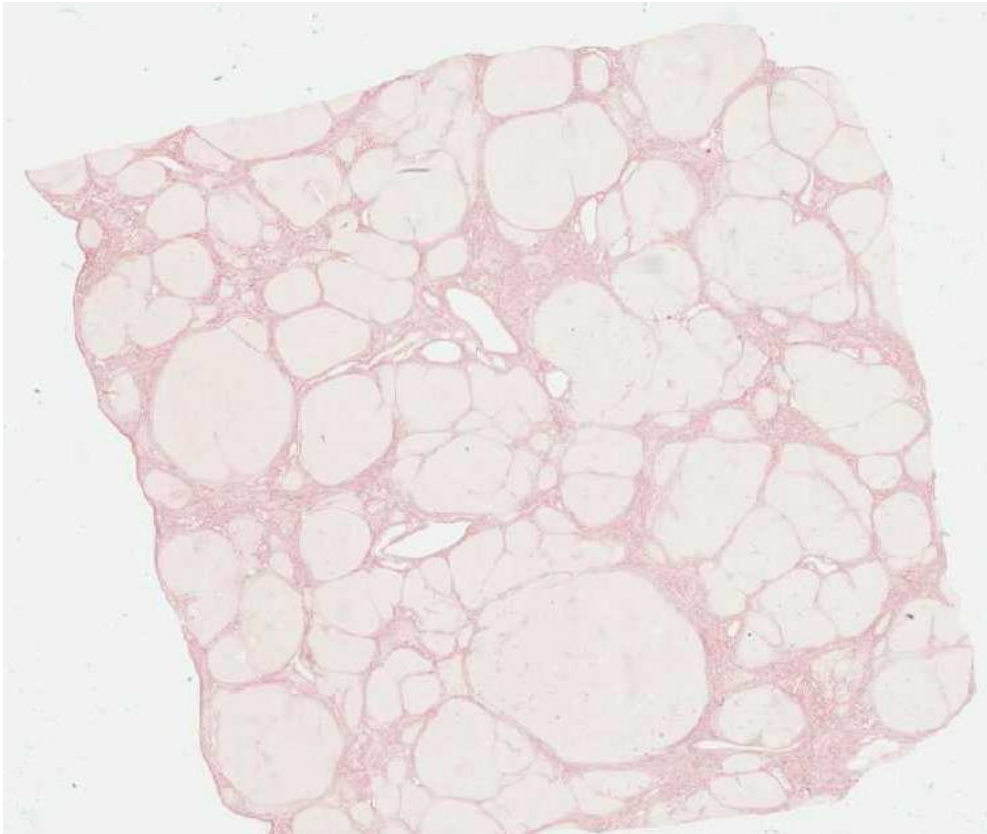
Main hepatic veins or within liver

– veno-occlusive disease or sinusoidal obstruction syndrome

- dilated sinusoids, red cell extravasation
- hepatocyte plate atrophy with sinusoidal fibrosis
- portal tracts normal

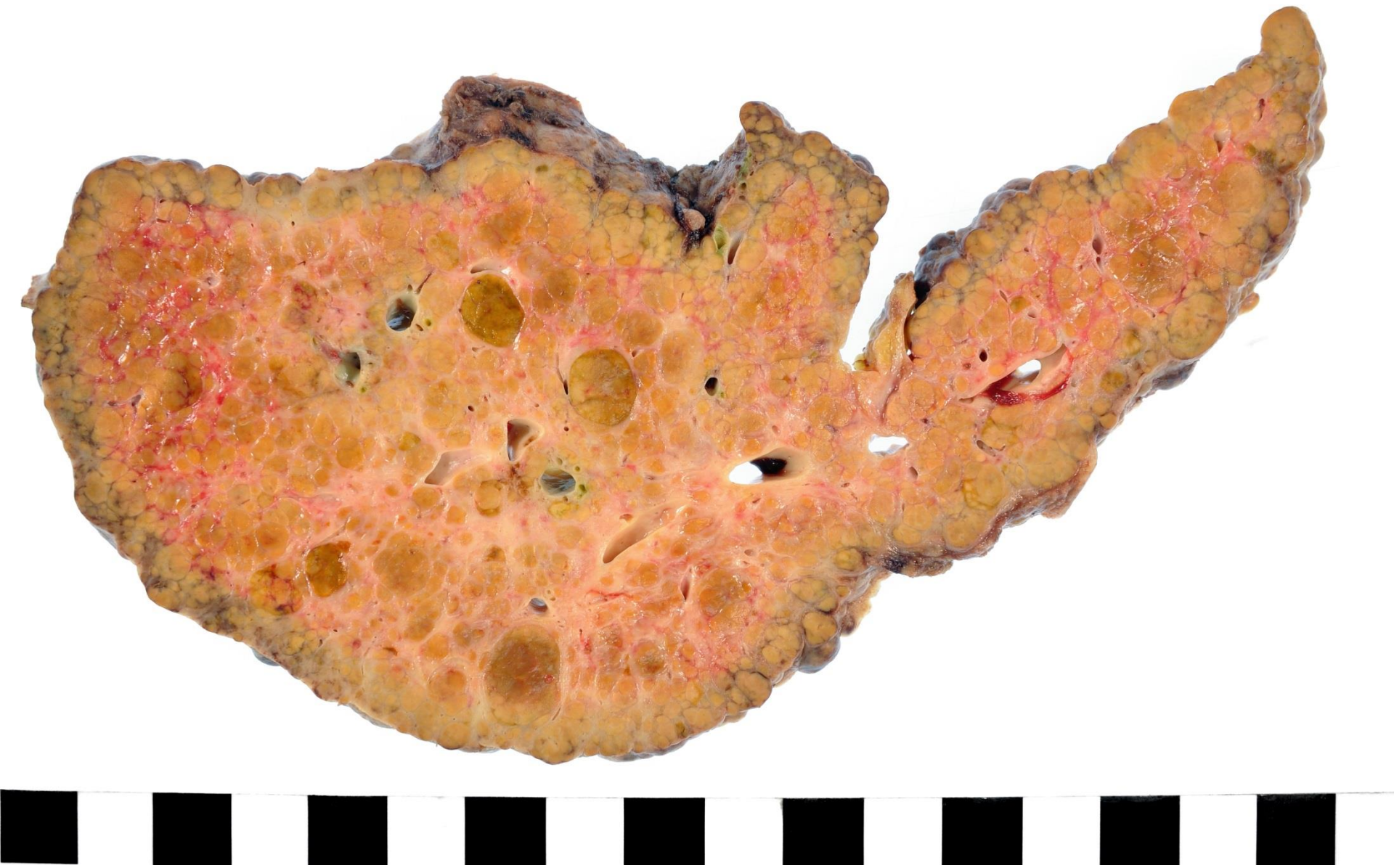
JIW 13 57/M

Liver transplant - cryptogenic cirrhosis



JIW 13 57/M

JIW 13 57/M



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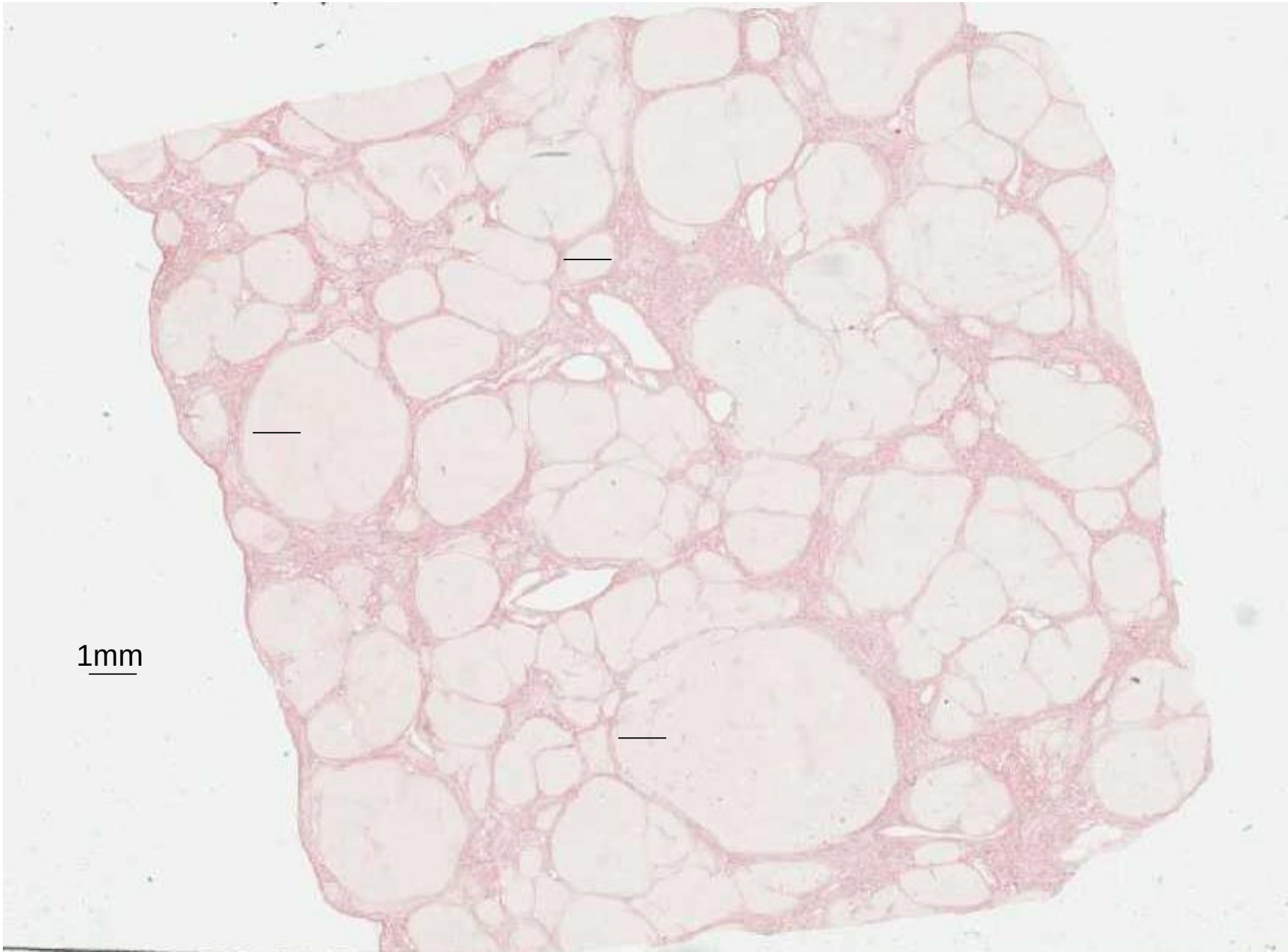


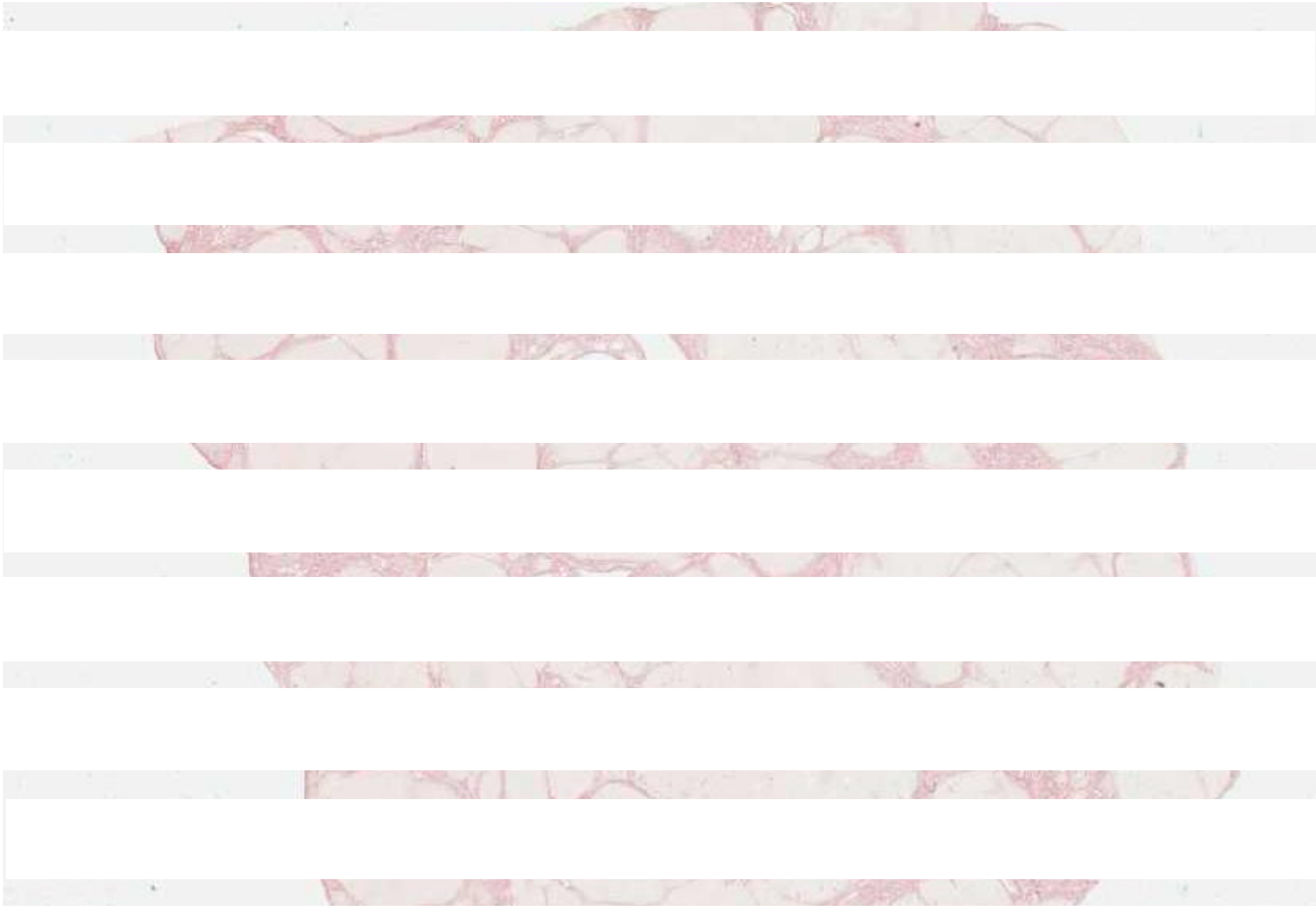
JIW 13 57/M

Strips left are 1 mm wide

JIW 13 57/M

JIW 13 57/M

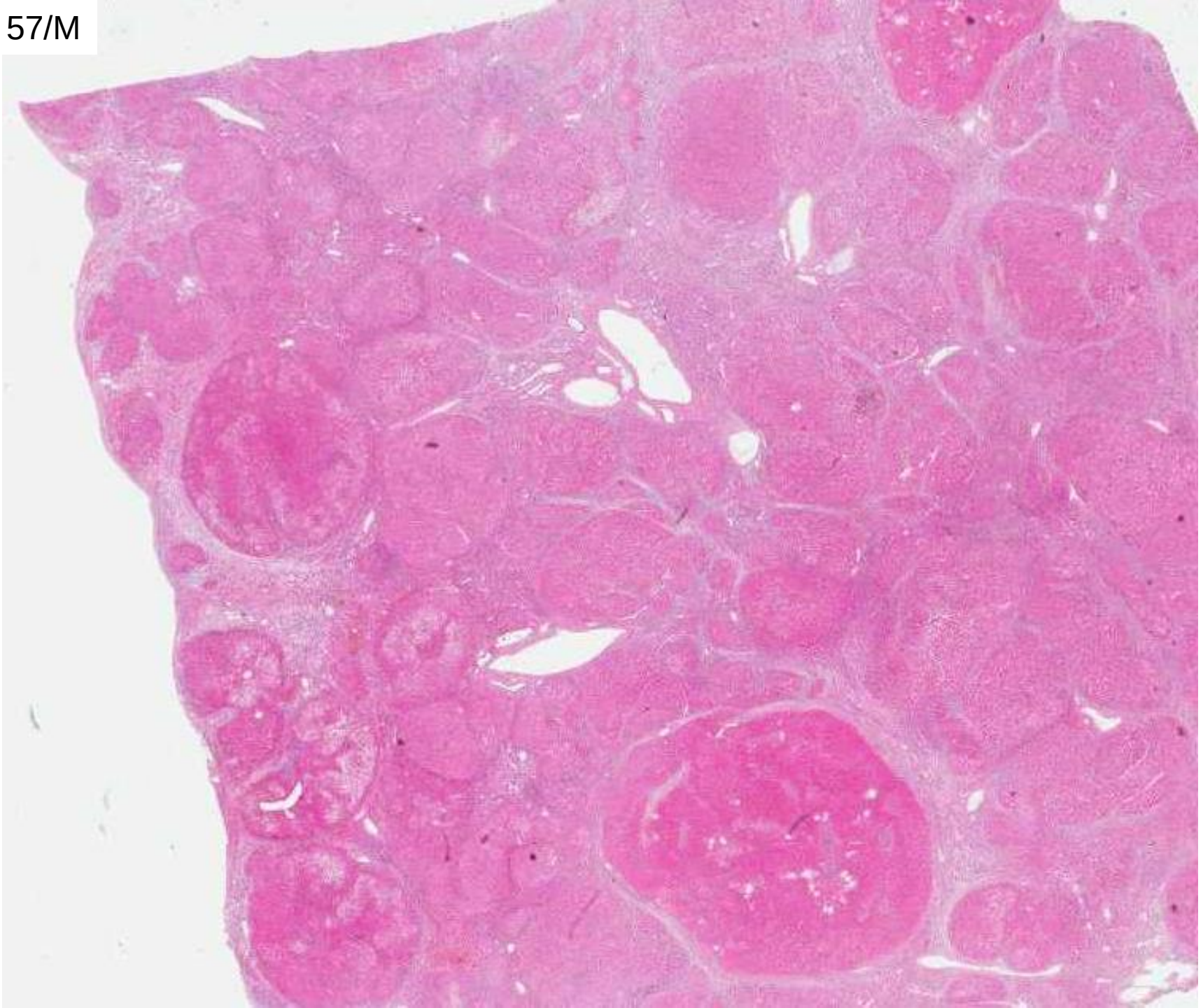
Strips left are 0.5 mm wide



JIW 13 57/M

Strips left are 0.5 mm wide

JIW 13 57/M



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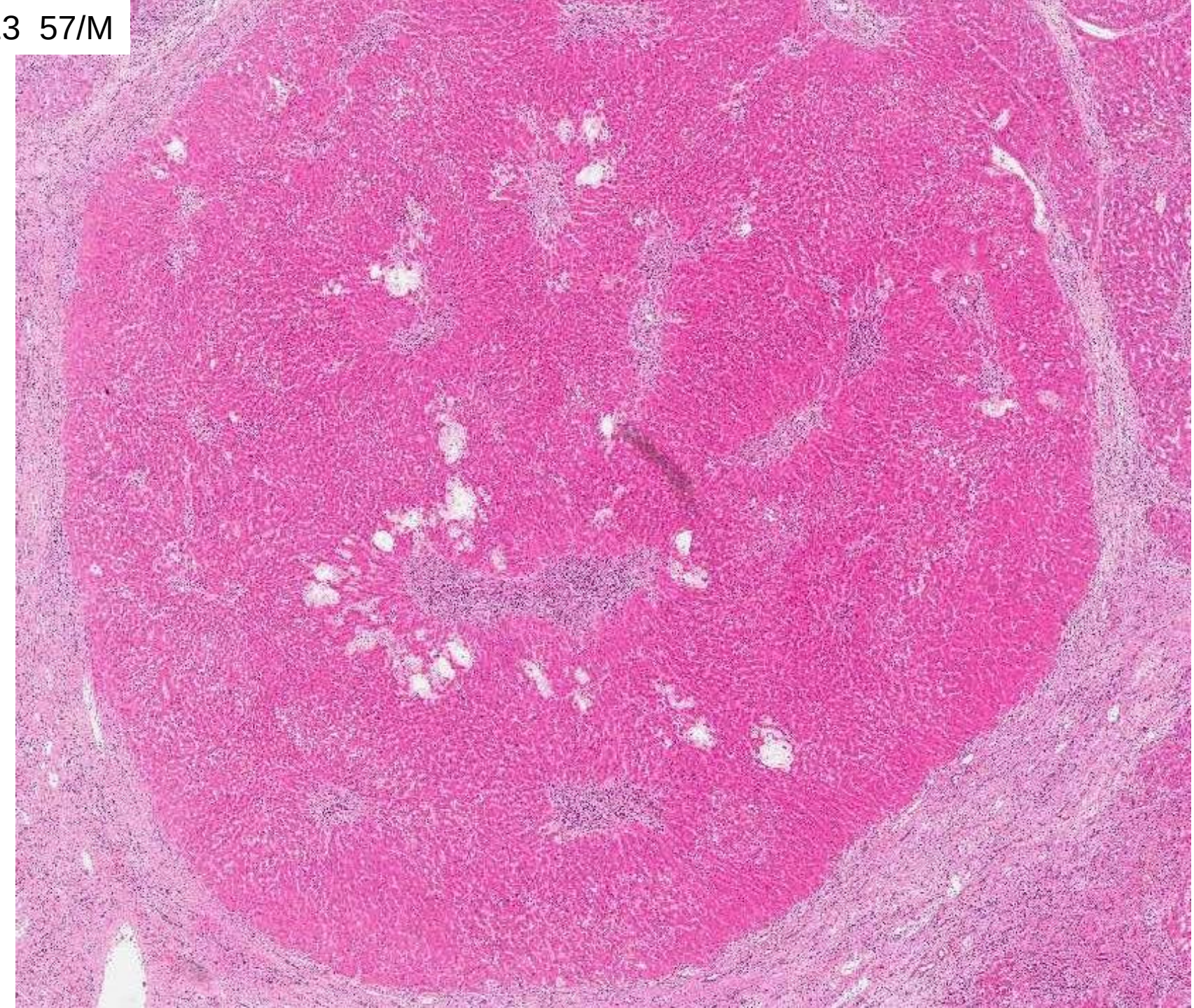

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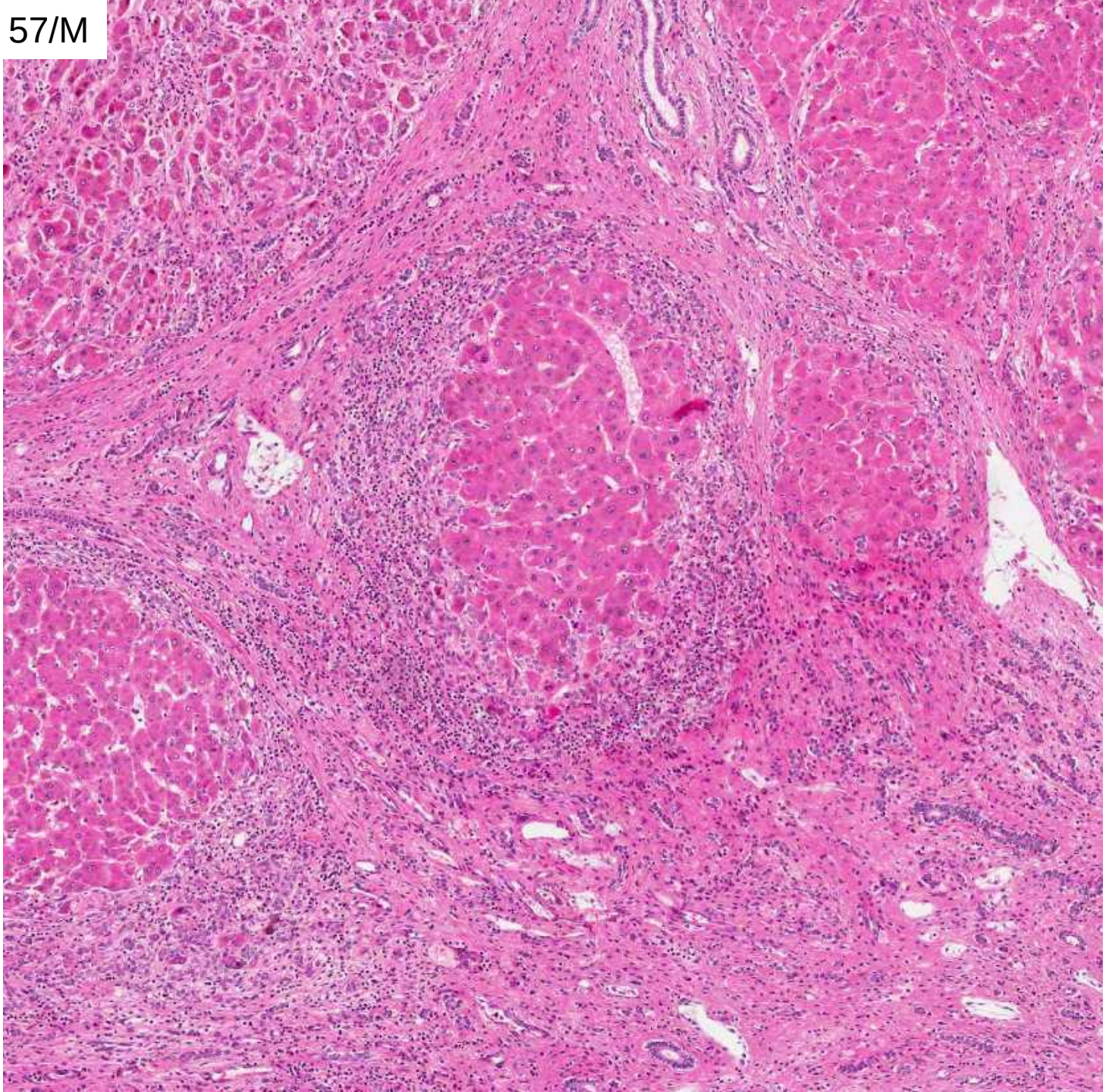

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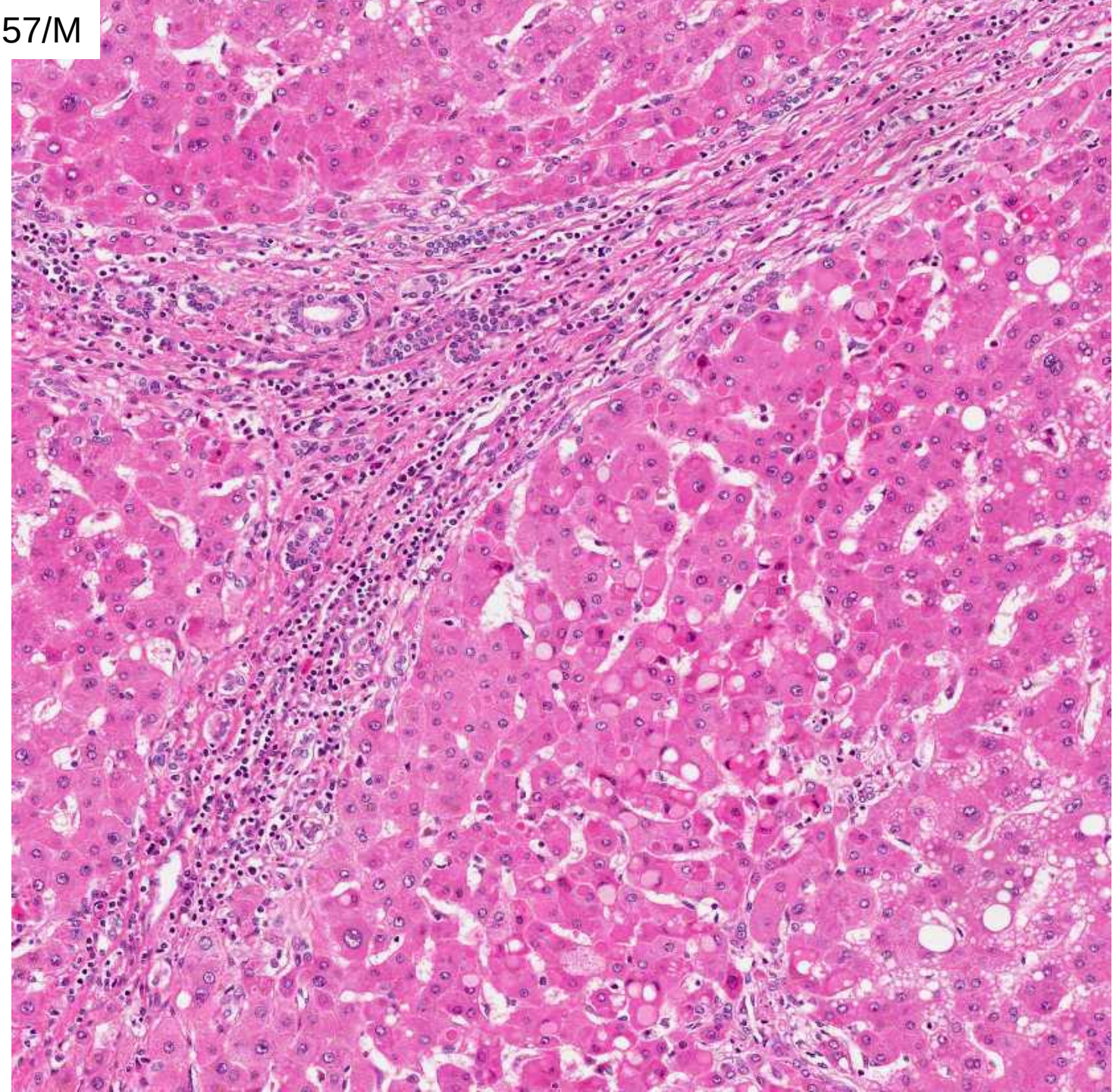

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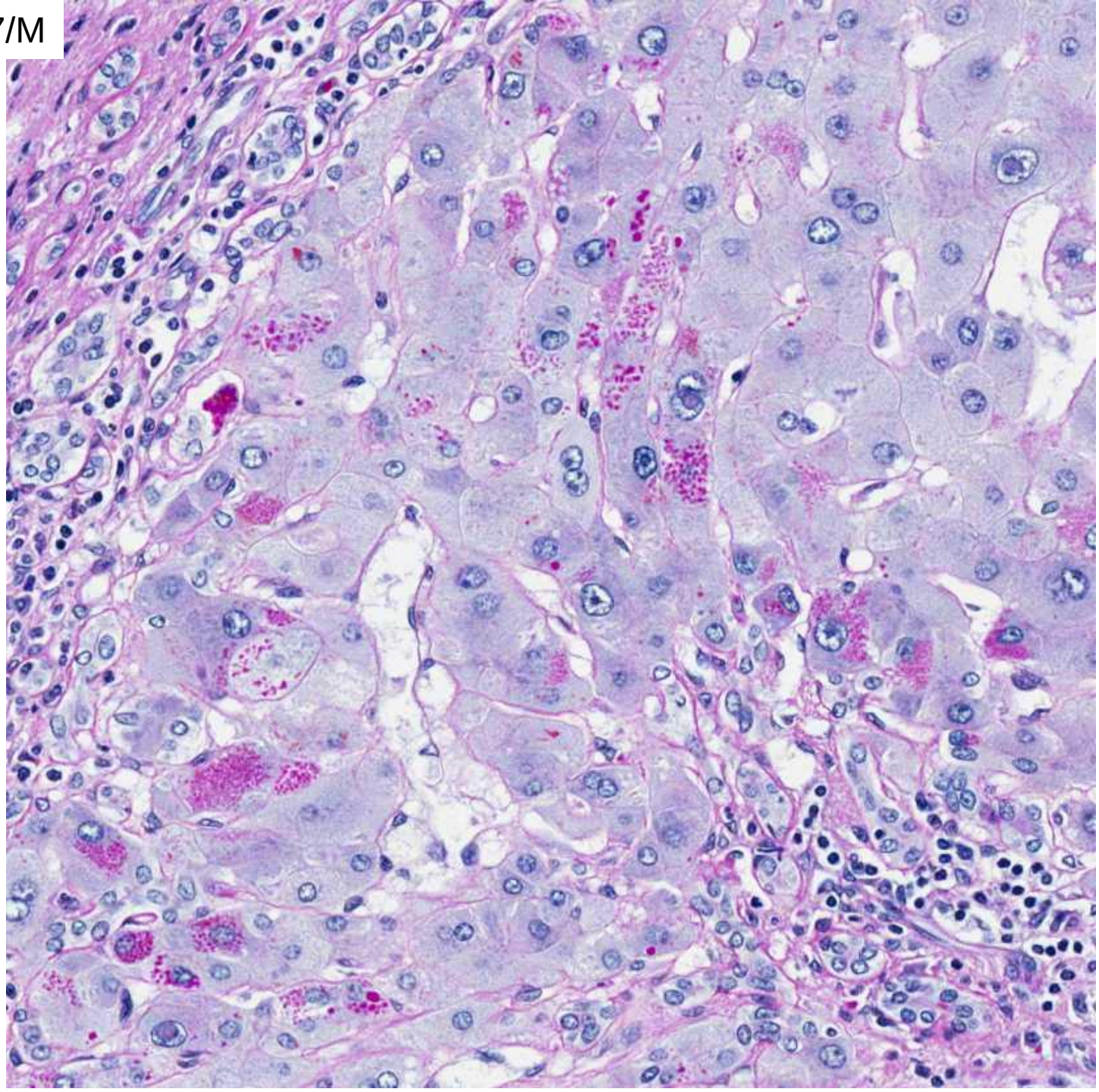


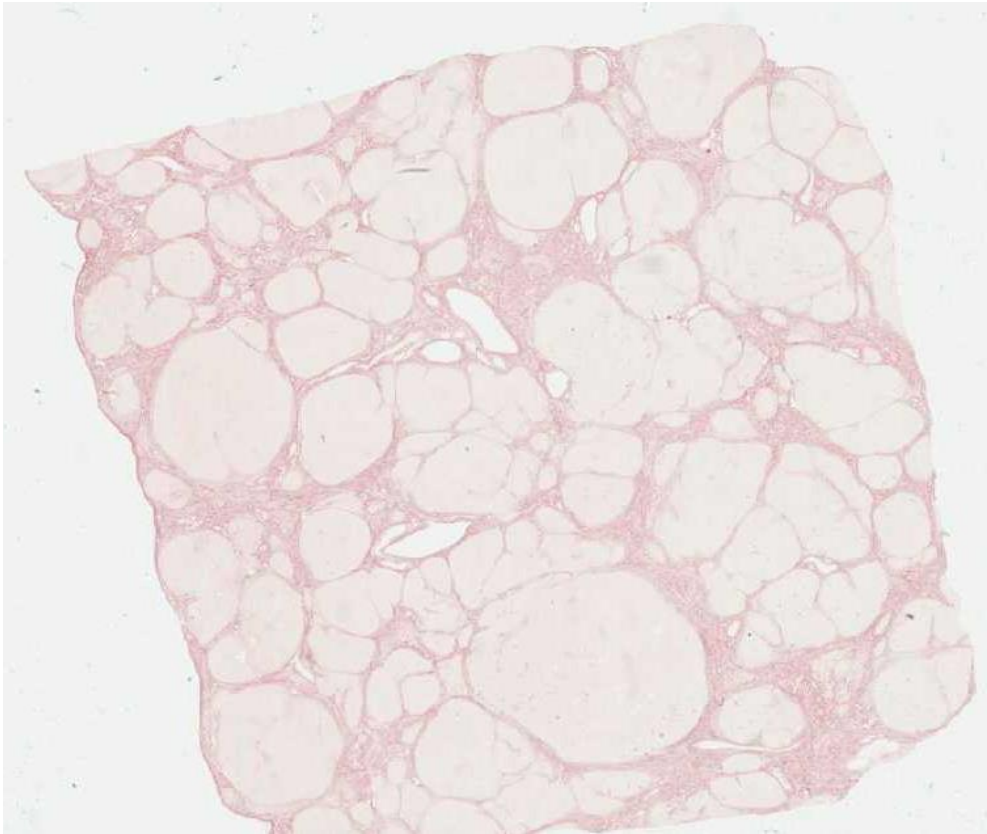
JIW 13 57/M

Liver transplant - cryptogenic cirrhosis

Explant histology = alpha 1 antitrypsin deficiency. No HCC

Imaging – hypovascular nodules, not HCC

Serum A1ATD low



Summary: JIW cases

Acute hepatitis (cases 1-6)

Chronic hepatitis (cases7-10)

include biopsy quality, stage & grade

Vascular disorders (cases 11,12)

Explant histology, acute and chronic disease (cases 3.13)

Most unrecognised diagnoses?

Biliary disease, acute hepatitis, vascular disease

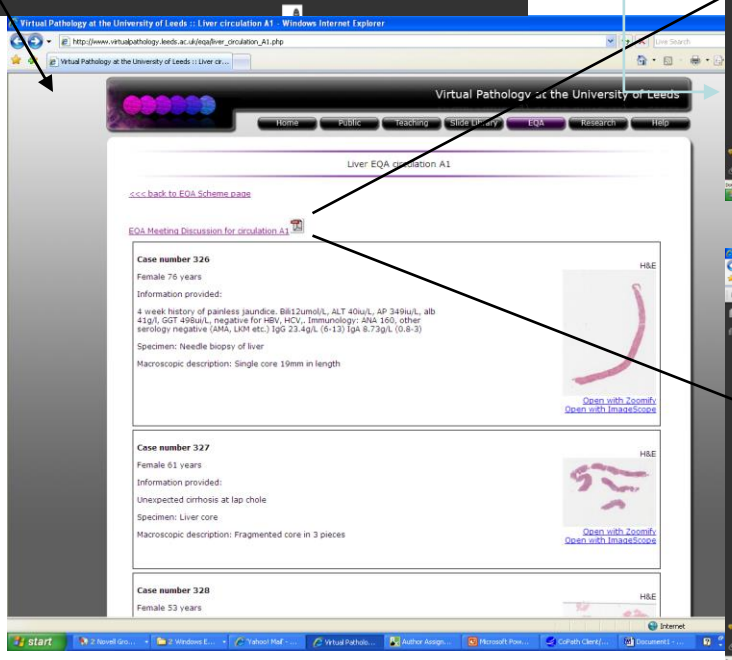
RCPath Tissue Pathways:

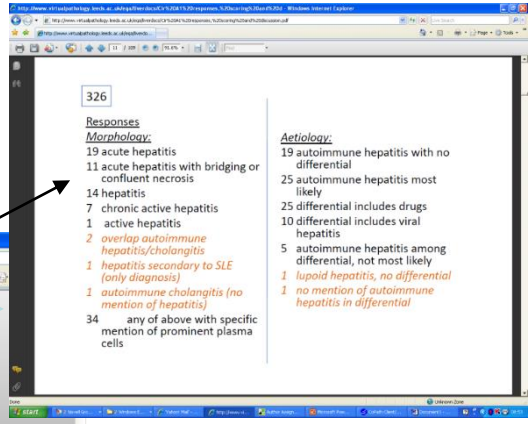
Tissue pathways for liver biopsies for the investigation of medical disease and for focal lesions

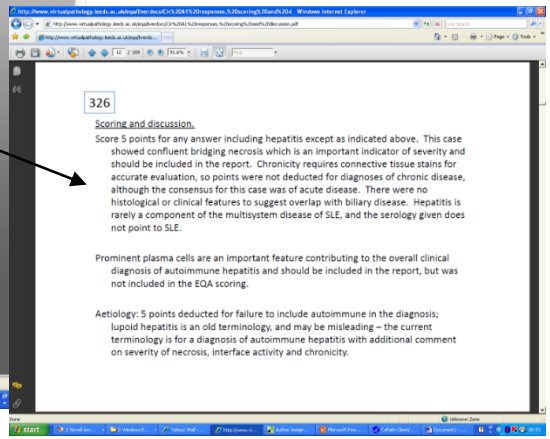
March 2014

Tables on – patterns of liver disease - acute and chronic
- special stains and immunos
- hepatocellular adenomas


virtualpathology.leeds.ac.uk/eqa/specialist/liver
Virtual Pathology at the University of Leeds
Home Public Slides EQA Teaching Research Clinical Trials Tissue Banking
UK Liver Pathology Group
The UK Liver Pathology Group (UKLPG) was formed in 2016 with the purpose:
To promote excellence in liver histopathology services in the UK and Ireland, across all levels of specialisation, through professional collaboration in education, quality assurance and research.
United Kingdom Liver Pathology Group
This year's CPD activities
Liver CPD archive (activities from 2006 with CPD resources available)
UK Liver Pathology EQA Scheme
Reference images for liver biopsy reporting
UKLPG - background and UKLPG committee meetings
UKLPG - membership + how to join UKLPG
Subcommittees
Liver transplant pathology
Paediatric liver pathology section
Other professional documents
Links to other sites
Site Map FAQ Terms and Conditions Privacy Statement About Us Contact


Virtual Pathology at the University of Leeds :: Liver circulation A1 - Windows Internet Explorer
Liver EQA circulation A1
<<< back to EQA Scheme page
EQA Meeting Discussion for circulation A1
Case number 326
Female 76 years
Information provided:
4 week history of painless jaundice. Bili12umol/L, ALT 40iu/L, AP 349iu/L, alb 41g/l, GGT 498iu/L, negative for HBV, HCV,. Immunology: ANA 160, other serology negative (AMA, LKM etc.) IgG 23.4g/L (6-13) IgA 8.73g/L (0.8-3)
Specimen: Needle biopsy of liver
Macroscopic description: Single core 19mm in length
H&E
Open with Zoomify
Open with ImageScope
Case number 327
Female 61 years
Information provided:
Unexpected cirrhosis at lap chole
Specimen: Liver core
Macroscopic description: Fragmented core in 3 pieces
Case number 328
Female 53 years


326
Responses
Morphology:
19 acute hepatitis
11 acute hepatitis with bridging or confluent necrosis
14 hepatitis
7 chronic active hepatitis
1 active hepatitis
2 overlap autoimmune hepatitis/cholangitis
1 hepatitis secondary to SLE (only diagnosis)
1 autoimmune cholangitis (no mention of hepatitis)
34 any of above with specific mention of prominent plasma cells
Aetiology:
19 autoimmune hepatitis with no differential
25 autoimmune hepatitis most likely
25 differential includes drugs
10 differential includes viral hepatitis
5 autoimmune hepatitis among differential, not most likely
1 lupoid hepatitis, no differential
1 no mention of autoimmune hepatitis in differential


326
Scoring and discussion.
Score 5 points for any answer including hepatitis except as indicated above. This case showed confluent bridging necrosis which is an important indicator of severity and should be included in the report. Chronicity requires connective tissue stains for accurate evaluation, so points were not deducted for diagnoses of chronic disease, although the consensus for this case was of acute disease. There were no histological or clinical features to suggest overlap with biliary disease. Hepatitis is rarely a component of the multisystem disease of SLE, and the serology given does not point to SLE.
Prominent plasma cells are an important feature contributing to the overall clinical diagnosis of autoimmune hepatitis and should be included in the report, but was not included in the EQA scoring.
Aetiology: 5 points deducted for failure to include autoimmune in the diagnosis; lupoid hepatitis is an old terminology, and may be misleading – the current terminology is for a diagnosis of autoimmune hepatitis with additional comment on severity of necrosis, interface activity and chronicity.

United Kingdom Liver Pathology Group

Liver pathology CPD on our website

http://www.virtualpathology.leeds.ac.uk/eqa/specialist/liver/

'Liver biopsy in the assessment of medical liver disease'
Course organiser: Stefan Hubscher,

and slide based workshop

April 4-5th. RCPath (10th time, 5th time)

Liver EQA website – Previous circulations available with results and discussion – since 2003, 388 cases

Annual BSG pathology meeting in November/December (2 days, liver and GI)

This year, in Cambridge, 7th November

Plus – web-based teaching materials for trainees