United Kingdom Liver Pathology Group

Liver histopathology EQA Scheme

Circulation LP Spring 2017

Liver EQA circulation LP

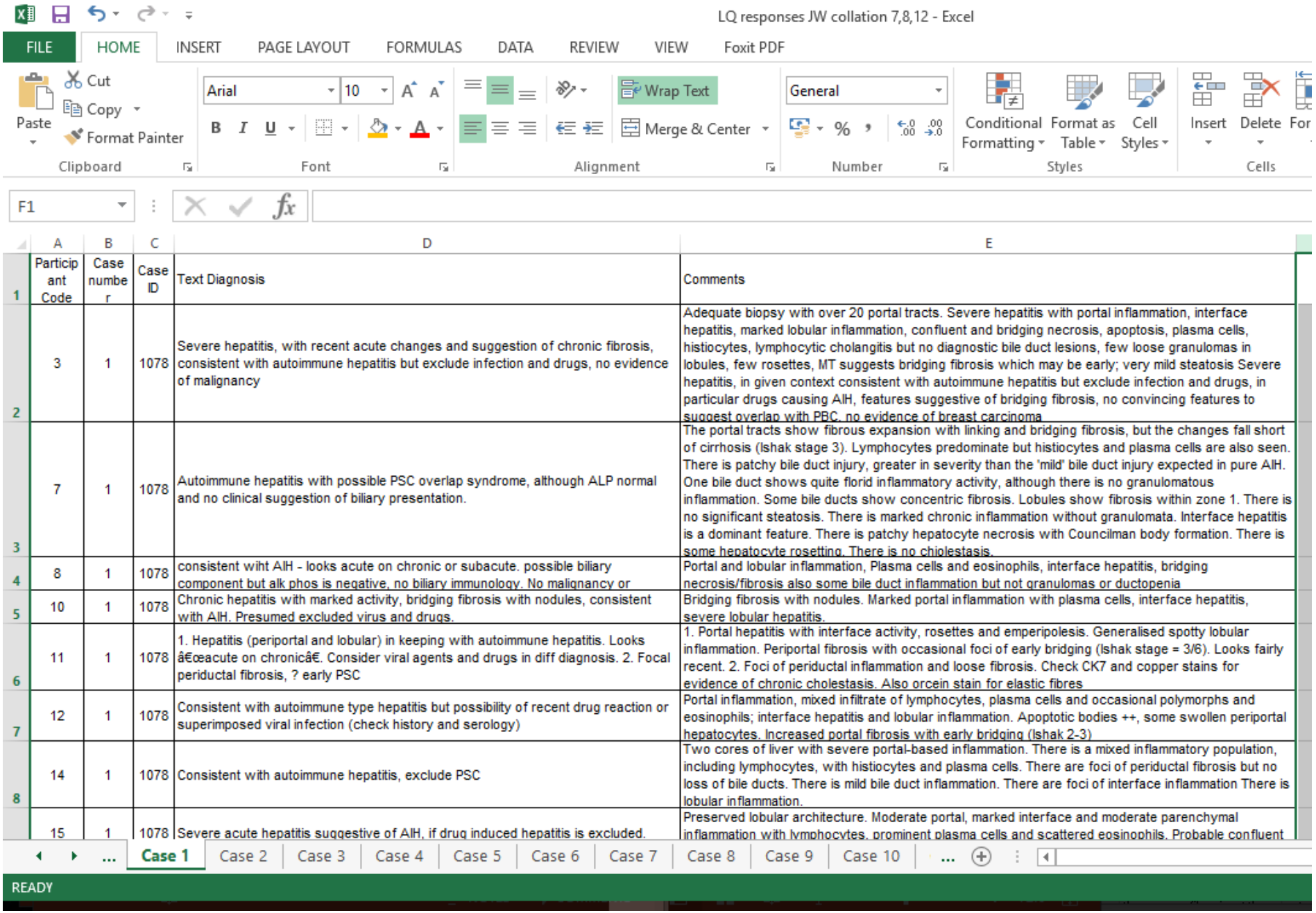
- Interpretive EQA schemes have primarily an educational purpose, also enable responses to be ranked – formative assessment, to see how our responses compare with our peers.

- 89 responses, so 80% consensus is 71. If 18 or more differ from the consensus diagnosis, then the case is not scored, but is often very educational.

- Liver EQA has developed over the years in a way that seeks to maximise the educational value of the slide circulations.

- Detailed list of diagnoses – so that you can see how yours compared with others - but makes for complicated slides.

- Impressive amount of work goes into writing the responses – aim to make it worthwhile.



LQ responses JW collation 7,8,12 - Excel

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	A	B	C	D	E
1	Participant Code	Case number	Case ID	Text Diagnosis	Comments
2	3	1	1078	Severe hepatitis, with recent acute changes and suggestion of chronic fibrosis, consistent with autoimmune hepatitis but exclude infection and drugs, no evidence of malignancy	Adequate biopsy with over 20 portal tracts. Severe hepatitis with portal inflammation, interface hepatitis, marked lobular inflammation, confluent and bridging necrosis, apoptosis, plasma cells, histiocytes, lymphocytic cholangitis but no diagnostic bile duct lesions, few loose granulomas in lobules, few rosettes, MT suggests bridging fibrosis which may be early; very mild steatosis Severe hepatitis, in given context consistent with autoimmune hepatitis but exclude infection and drugs, in particular drugs causing AIH, features suggestive of bridging fibrosis, no convincing features to suggest overlap with PBC, no evidence of breast carcinoma
3	7	1	1078	Autoimmune hepatitis with possible PSC overlap syndrome, although ALP normal and no clinical suggestion of biliary presentation.	The portal tracts show fibrous expansion with linking and bridging fibrosis, but the changes fall short of cirrhosis (Ishak stage 3). Lymphocytes predominate but histiocytes and plasma cells are also seen. There is patchy bile duct injury, greater in severity than the 'mild' bile duct injury expected in pure AIH. One bile duct shows quite florid inflammatory activity, although there is no granulomatous inflammation. Some bile ducts show concentric fibrosis. Lobules show fibrosis within zone 1. There is no significant steatosis. There is marked chronic inflammation without granulomata. Interface hepatitis is a dominant feature. There is patchy hepatocyte necrosis with Councilman body formation. There is some hepatocyte rosetting. There is no cholestasis.
4	8	1	1078	consistent wiht AIH - looks acute on chronic or subacute. possible biliary component but alk phos is negative, no biliary immunology. No malignancy or	Portal and lobular inflammation, Plasma cells and eosinophils, interface hepatitis, bridging necrosis/fibrosis also some bile duct inflammation but not granulomas or ductopenia
5	10	1	1078	Chronic hepatitis with marked activity, bridging fibrosis with nodules, consistent with AIH. Presumed excluded virus and drugs.	Bridging fibrosis with nodules. Marked portal inflammation with plasma cells, interface hepatitis, severe lobular hepatitis.
6	11	1	1078	1. Hepatitis (periportal and lobular) in keeping with autoimmune hepatitis. Looks â€œacute on chronicâ€. Consider viral agents and drugs in diff diagnosis. 2. Focal periductal fibrosis, ? early PSC	1. Portal hepatitis with interface activity, rosettes and emperipolesis. Generalised spotty lobular inflammation. Periportal fibrosis with occasional foci of early bridging (Ishak stage = 3/6). Looks fairly recent. 2. Foci of periductal inflammation and loose fibrosis. Check CK7 and copper stains for evidence of chronic cholestasis. Also orcein stain for elastic fibres
7	12	1	1078	Consistent with autoimmune type hepatitis but possibility of recent drug reaction or superimposed viral infection (check history and serology)	Portal inflammation, mixed infiltrate of lymphocytes, plasma cells and occasional polymorphs and eosinophils; interface hepatitis and lobular inflammation. Apoptotic bodies ++, some swollen periportal hepatocytes. Increased portal fibrosis with early bridging (Ishak 2-3)
8	14	1	1078	Consistent with autoimmune hepatitis, exclude PSC	Two cores of liver with severe portal-based inflammation. There is a mixed inflammatory population, including lymphocytes, with histiocytes and plasma cells. There are foci of periductal fibrosis but no loss of bile ducts. There is mild bile duct inflammation. There are foci of interface inflammation There is lobular inflammation.
	15	1	1078	Severe acute hepatitis suggestive of AIH, if drug induced hepatitis is excluded.	Preserved lobular architecture. Moderate portal, marked interface and moderate parenchymal inflammation with lymphocytes, prominent plasma cells and scattered eosinophils. Probable confluent

... Case 1 Case 2 Case 3 Case 4 Case 5 Case 6 Case 7 Case 8 Case 9 Case 10 ...

READY

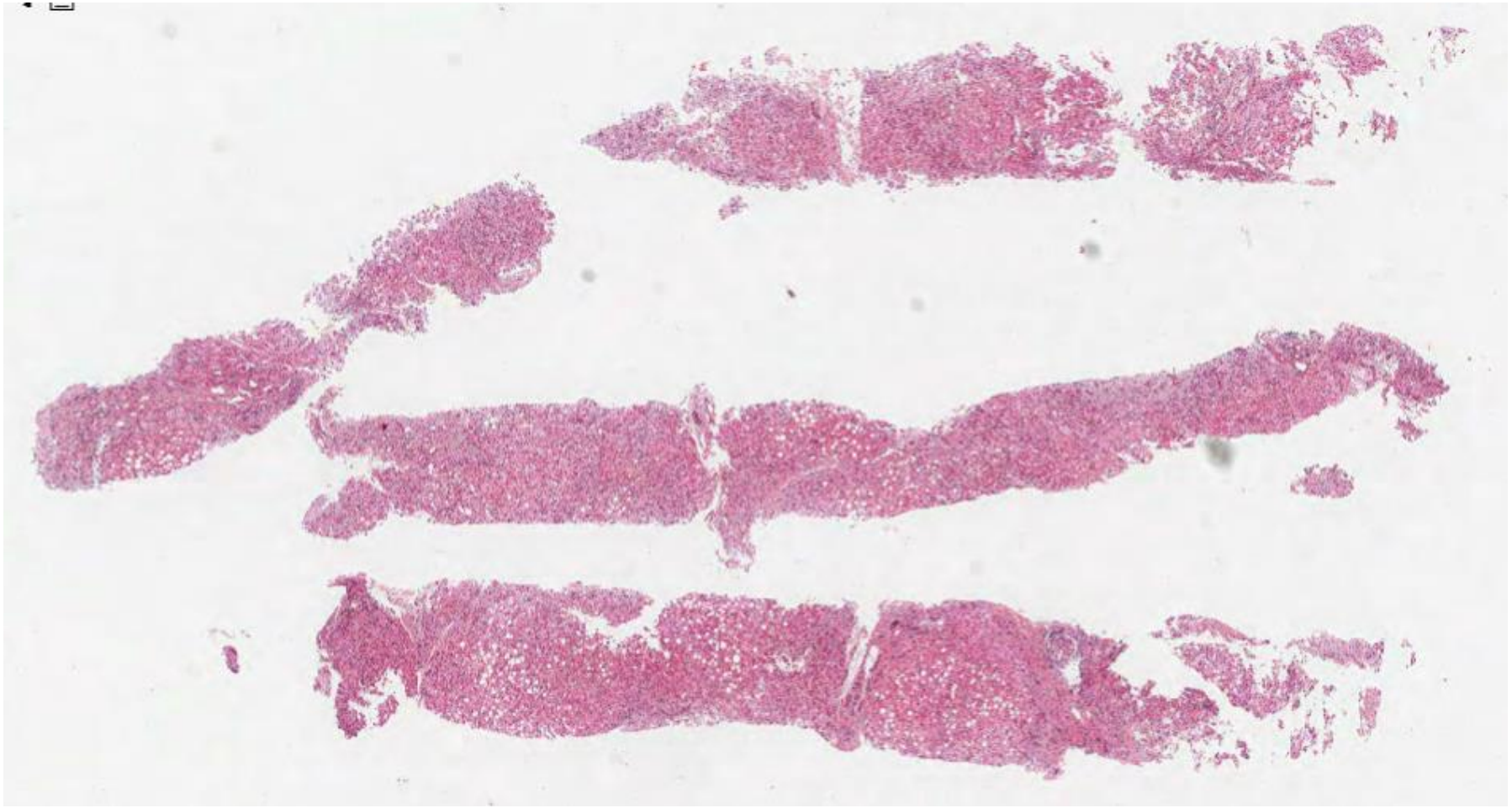
Liver EQA circulation LP

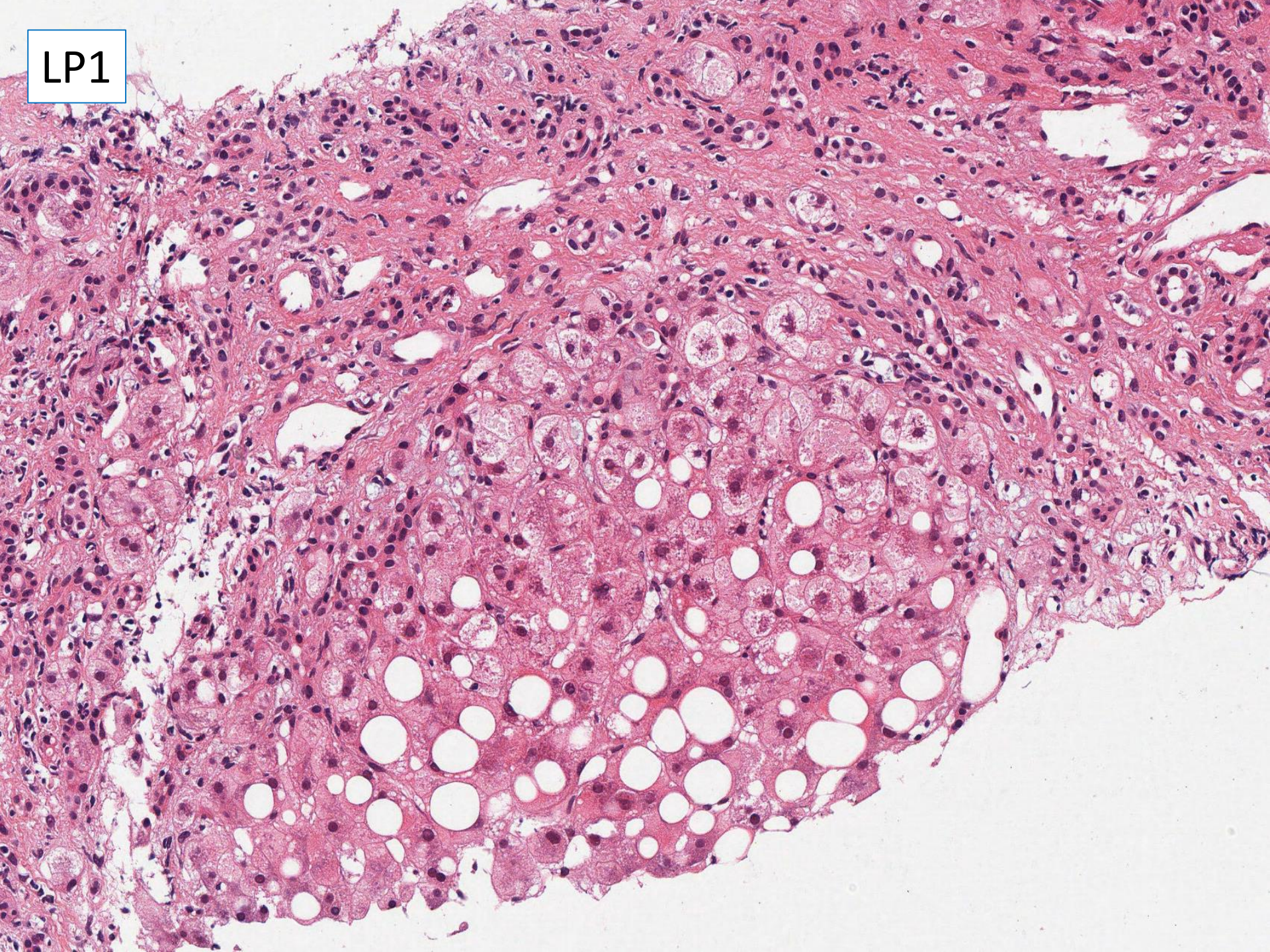
How to present the responses?

- Responses collated by JW, and summary sent to all EQA members for comments via surveymonkey,
- Both morphology and aetiology are important aspects of the report.
- 11 comments received – all cases considered suitable for scoring except LP 5 and 12. Reply to specific questions.
- The results presented here are the agreed scoring after discussion at the meeting.
- Masterclass presentations – DILI- Philip Kaye and AML – Ali Winstanley.
- MCQ version for non-EQA members – 5 responses..

Case LP1 57F

? liver cirrhosis; ascites. LKM1 antibodies AMA neg; ANA neg; ASM neg mild elevation of IgM viral screen neg (HCV,HBV,HIV).

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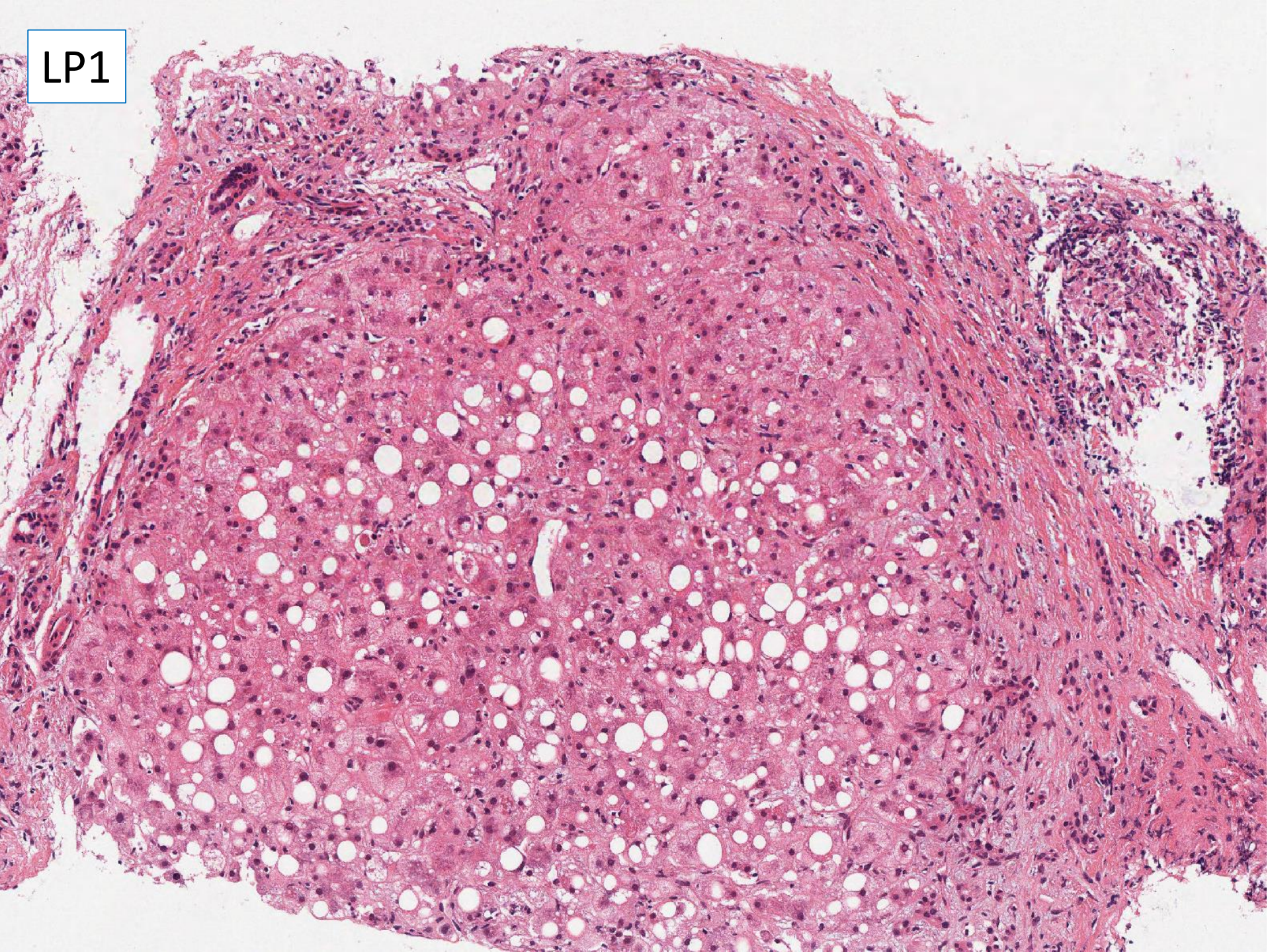
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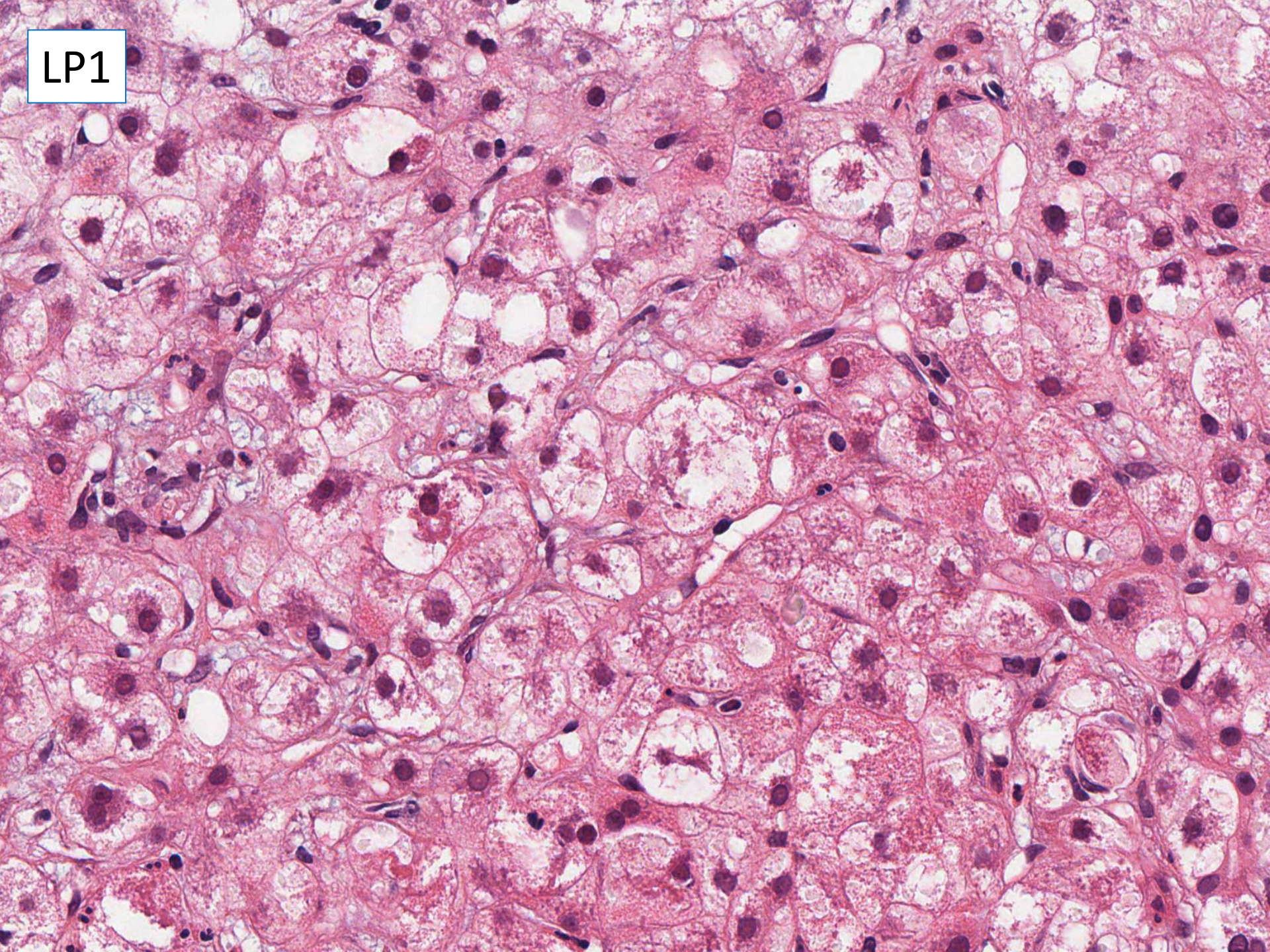
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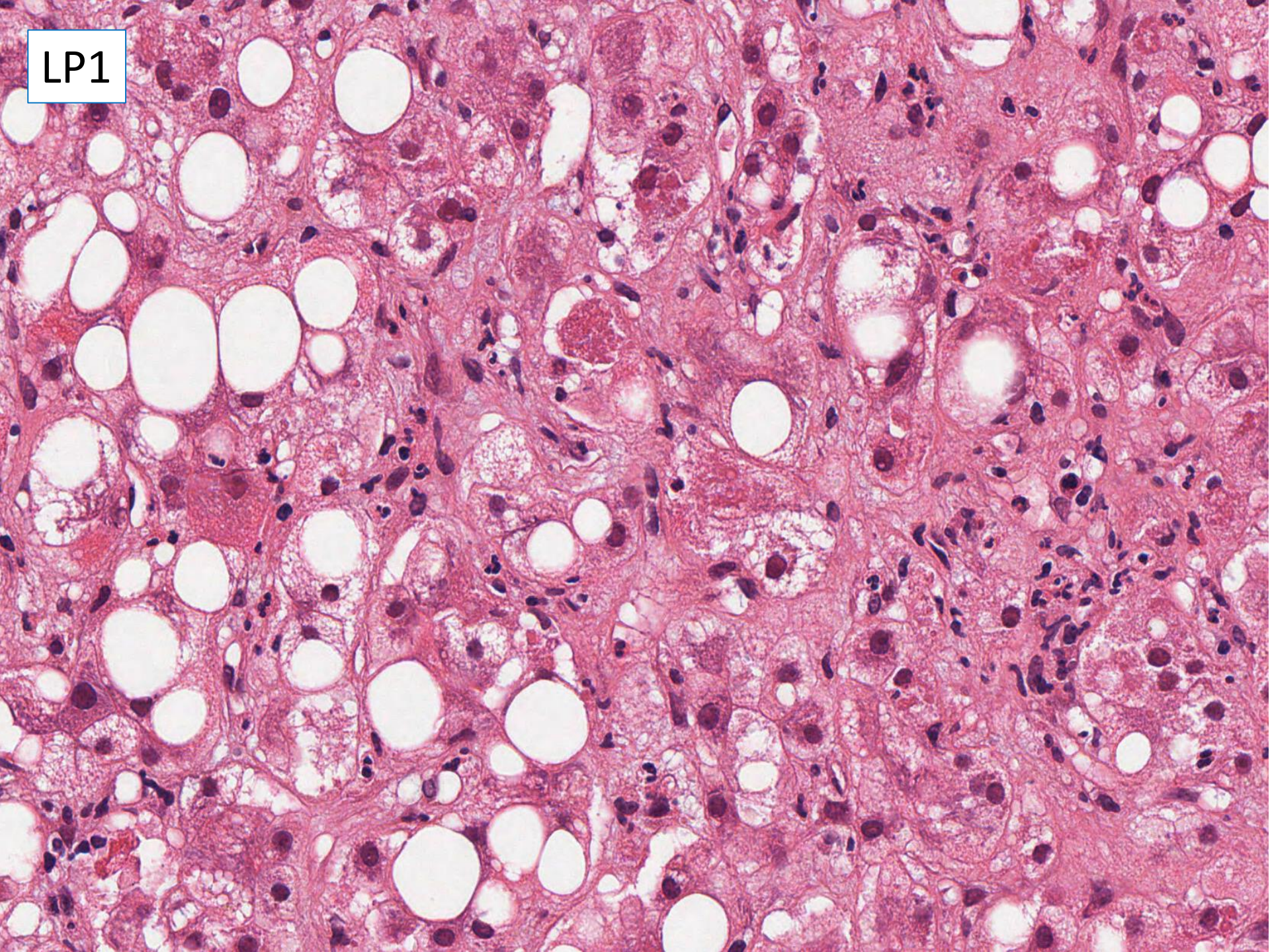
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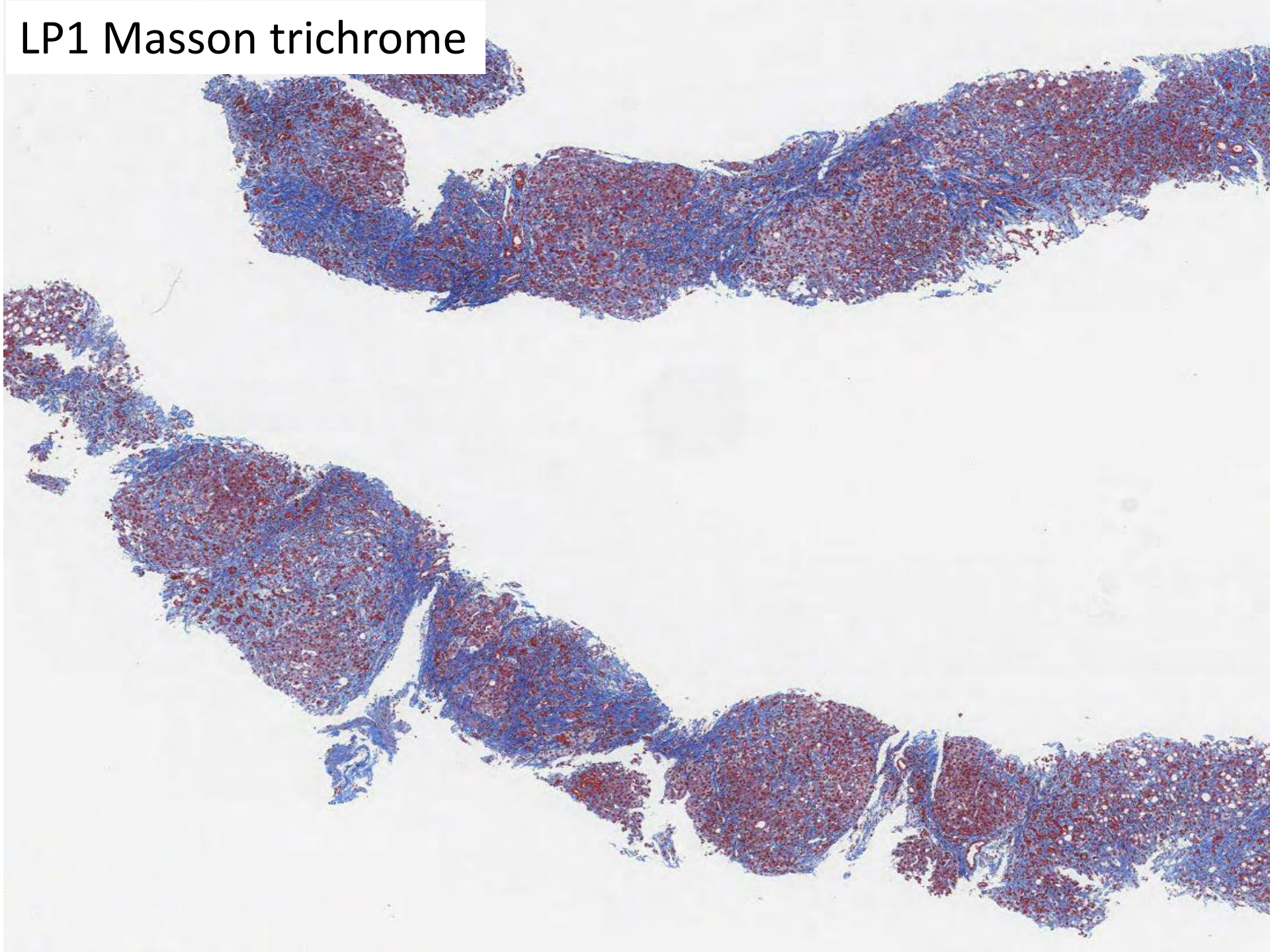
LP1 Masson trichrome



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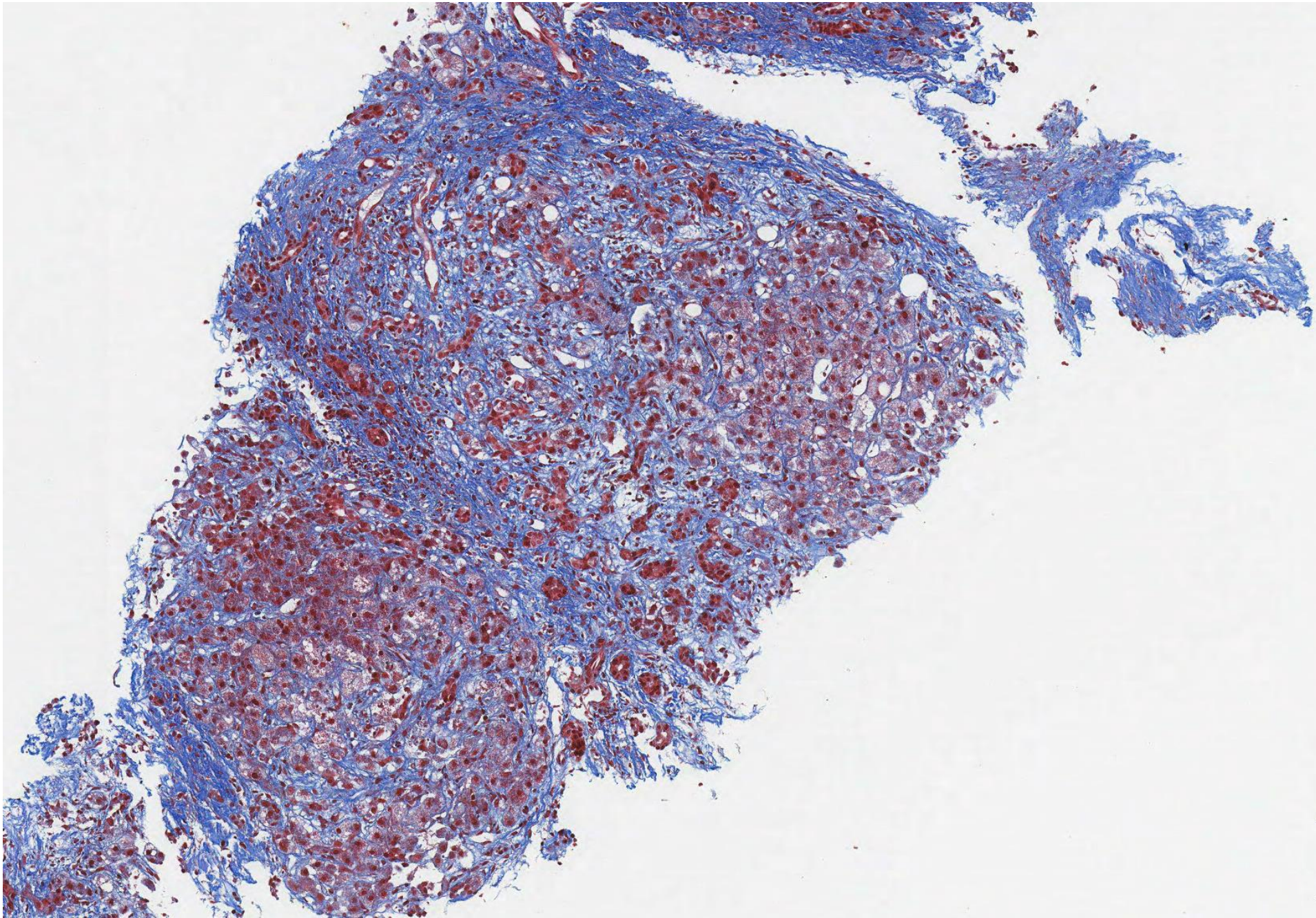
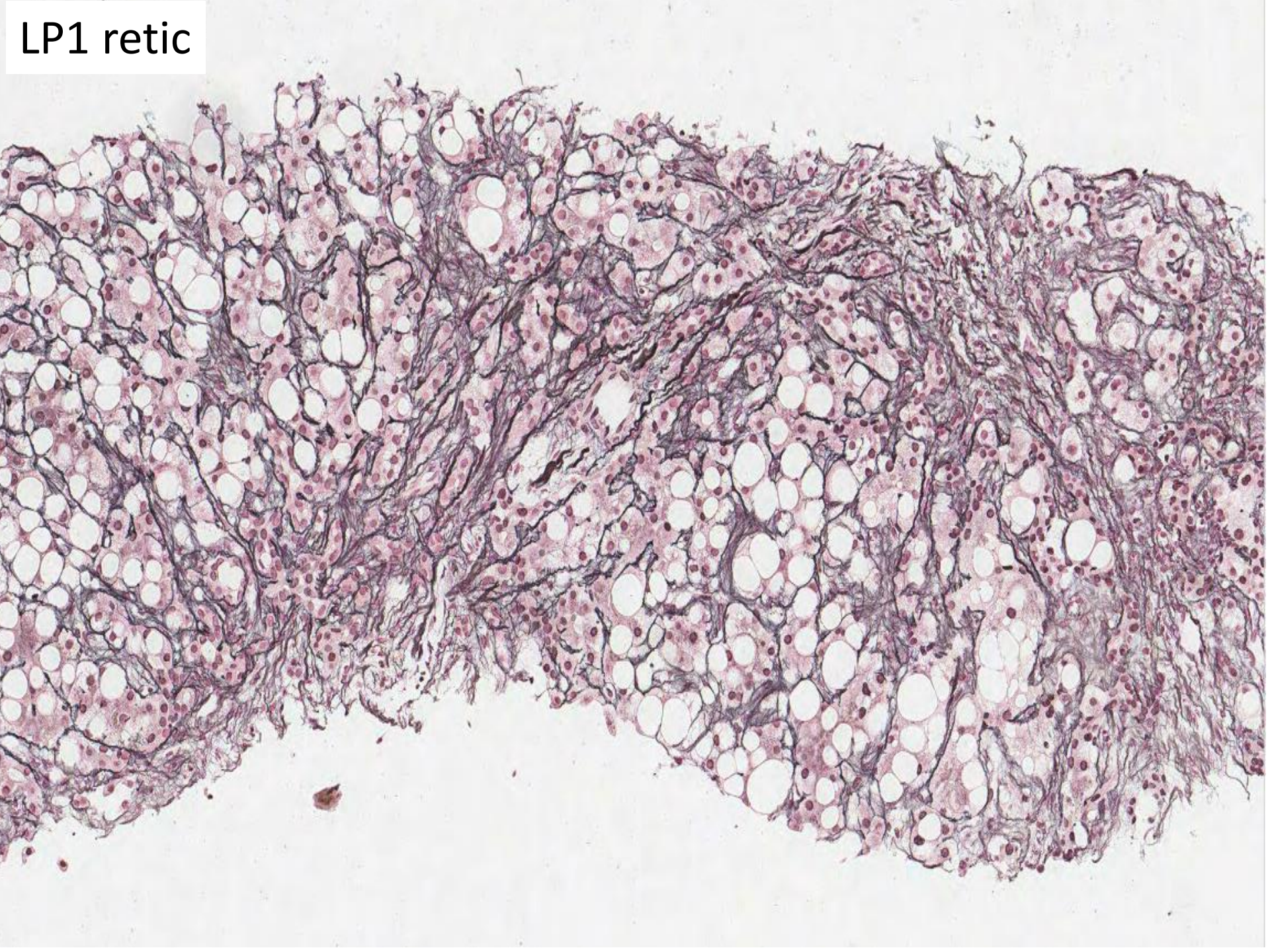


LP1 retic



Case LP1 57F

? liver cirrhosis; ascites. LKM1 antibodies AMA neg; ANA neg; ASM neg mild elevation of IgM viral screen neg (HCV,HBV,HIV).

Stage	
Pericellular bridging fibrosis	1
Description – not mentioned/confirmed cirrhosis	2
advanced fibrosis	2
Cirrhosis	84
Pattern of liver disease	
Steatosis	6
Steatohepatitis or fatty liver hepatitis	72
Steatohepatitis features mentioned, but 'steatohepatitis' not used	8
Not likely/no features of AIH	23
AIH	5
AIH possible if alcohol excluded	3
Alcohol	13
Alcohol favoured over NAFLD	14
Alcohol or non-alcoholic	44
No cause of fatty liver disease mentioned	14
'burnt out AIH'	1
'consistent with treated AIH'	1

Consensus complete responses would include –

cirrhosis/advanced stage fibrosis, with steatohepatitis as the dominant process – histology favours ALD over NAFLD. There are not histological features of AIH.

Suggested scoring: for 10 points include cirrhosis/advanced stage fibrosis and steatohepatitis as the dominant process with alcohol as potential aetiology

Case LP1 57F

? liver cirrhosis; ascites. LKM1 antibodies AMA neg; ANA neg; ASM neg mild elevation of IgM viral screen neg (HCV,HBV,HIV).

Agreed scoring:

For full marks – clear indication that this is cirrhosis/late stage fibrosis; otherwise lose 5 marks.

Steatohepatitis is present. Lose 5 marks for steatosis, or a description including e.g. 'ballooning' and 'Mallory Denk bodies' but not using the word 'steatohepatitis' or abbreviation ASH/NASH. Pathologists should not assume that clinicians are sufficiently familiar with histological features of steatohepatitis to make that diagnosis from their description.

Lose 5 marks if autoimmune hepatitis is the only aetiological factor mentioned.
Marks were not deducted if no cause for fatty liver was mentioned, since there was insufficient consensus for scoring this aspect of the response.
In this case, the high degree of pericellular fibrosis, and prominence of Mallory Denk bodies with neutrophil satellitosis suggests this is likely to be alcohol related steatohepatitis.

There was discussion around including alcohol related liver disease in the diagnosis if no history of alcohol is given. The pathologist should suggest it as a possible/likely aetiology, which can be useful for clinicians in eliciting the history which may otherwise be unforthcoming.

Case LP1 57F

? liver cirrhosis; ascites. LKM1 antibodies AMA neg; ANA neg; ASM neg mild elevation of IgM viral screen neg (HCV,HBV,HIV).

A Cirrhosis, steatosis, non-alcoholic fatty liver disease

B Cirrhosis, consistent with ‘burnt out’ autoimmune hepatitis

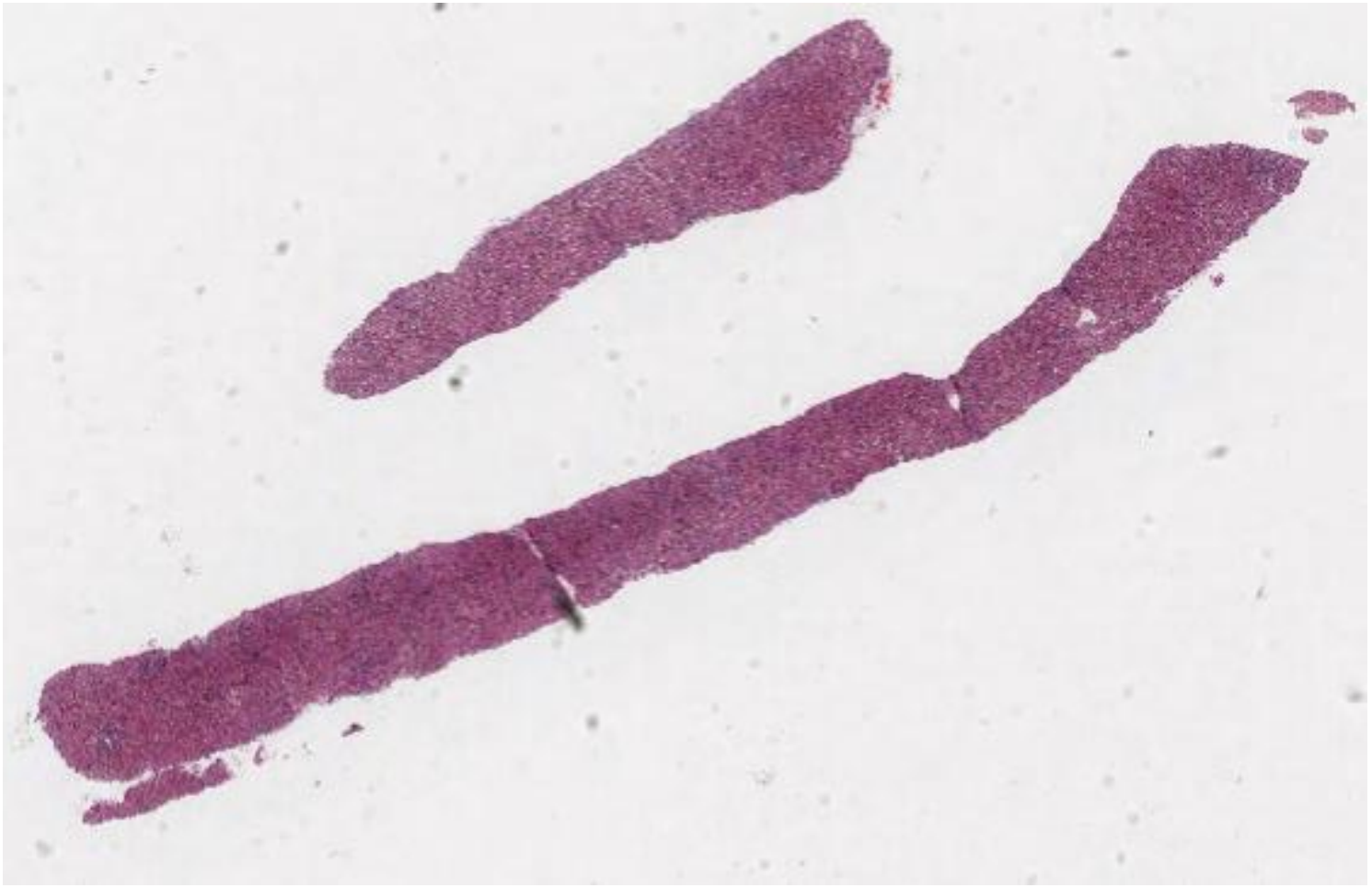
C Bridging fibrosis, steatohepatitis

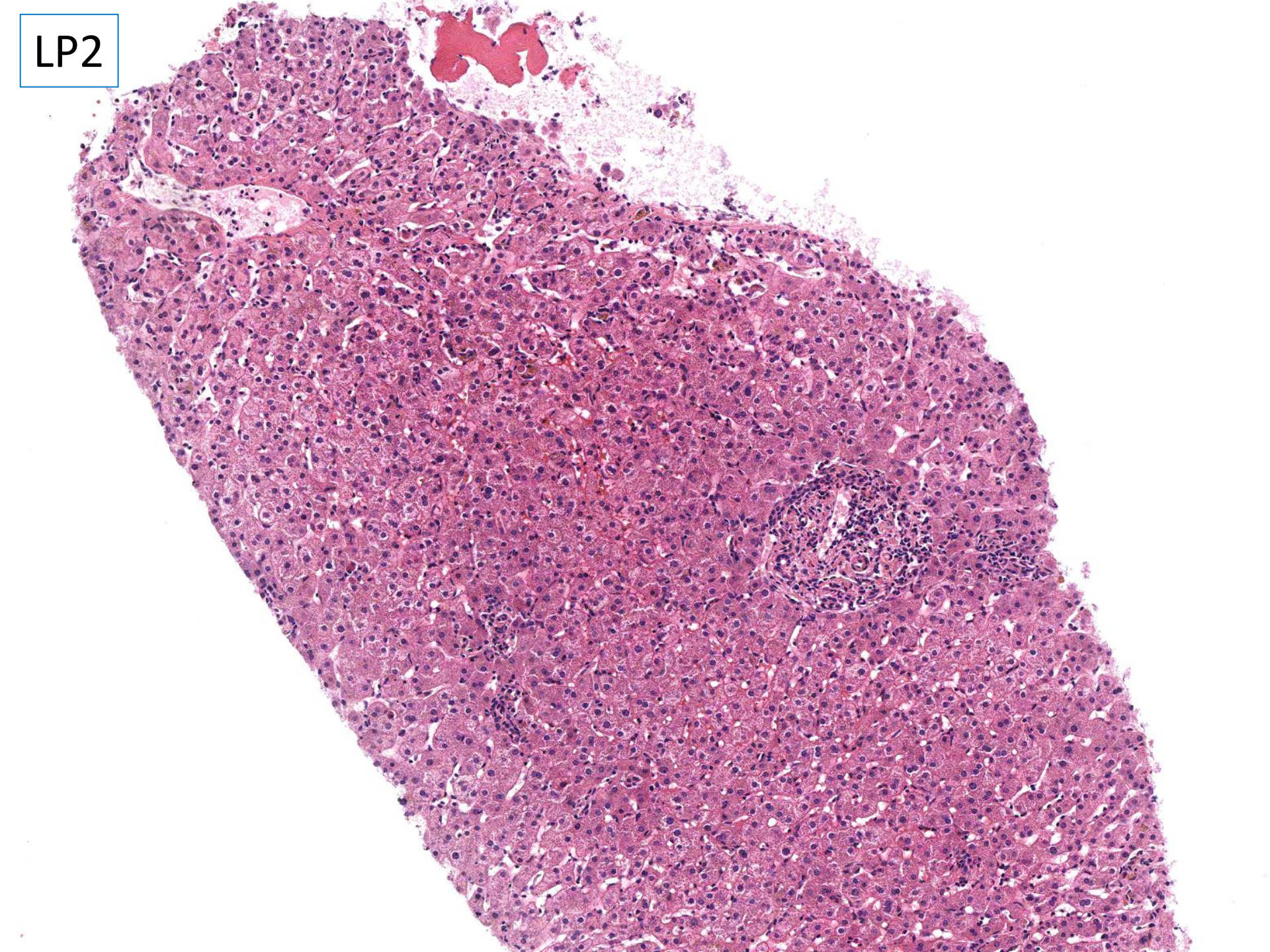
D Cirrhosis, steatohepatitis, probably alcohol related liver disease

E Cirrhosis, autoimmune hepatitis

Case LP2 50F

Very raised ALT. DILI v AIH Urgent histology. Recently started Etanercept for rheumatoid arthritis. Concurrent use of Isoniazid for latent TB control. no other medication. Some viral symptoms 1 month ago. Subsequent spike in ALT 1700, with normal function of liver ? DILI, ? AIH.

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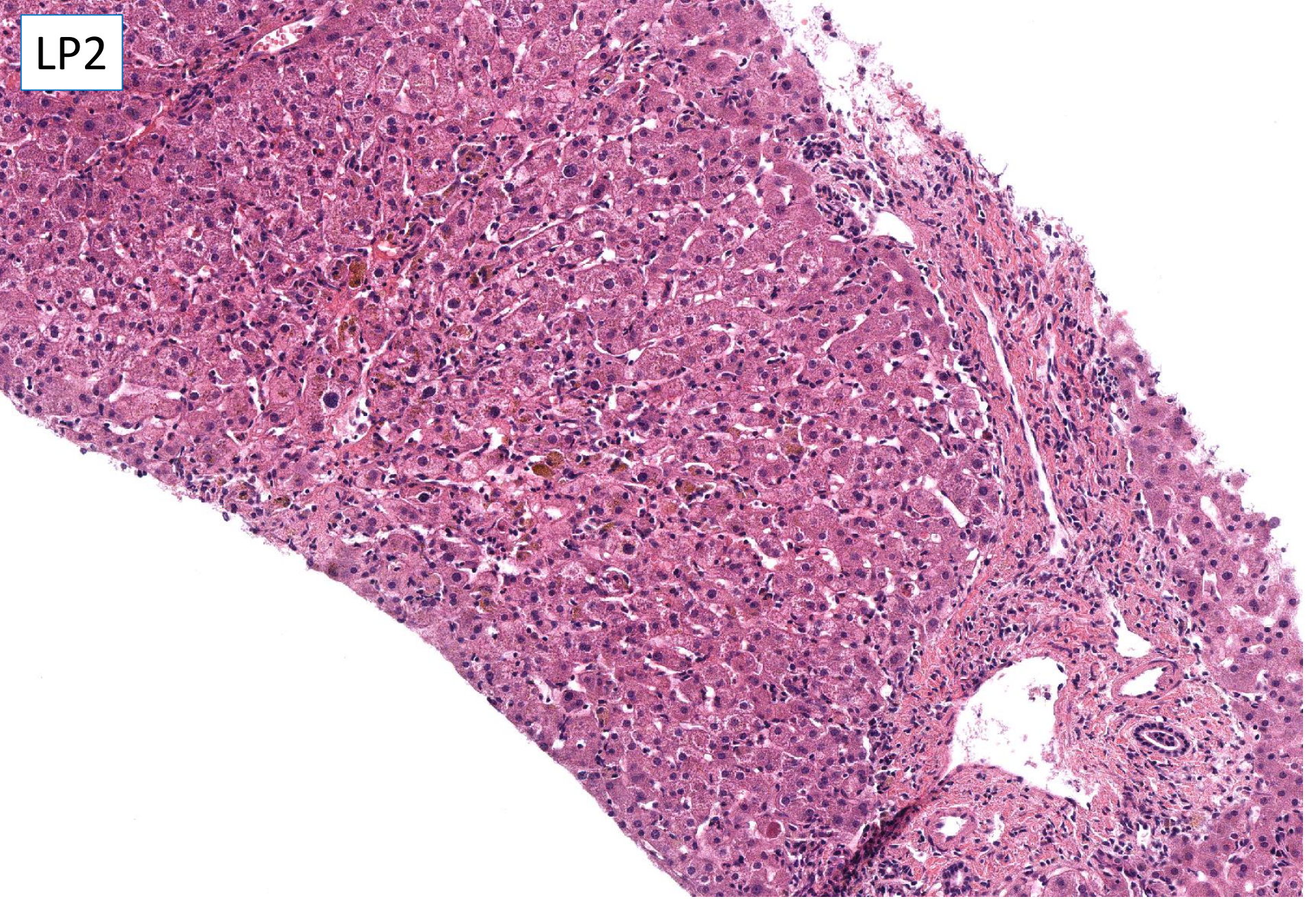
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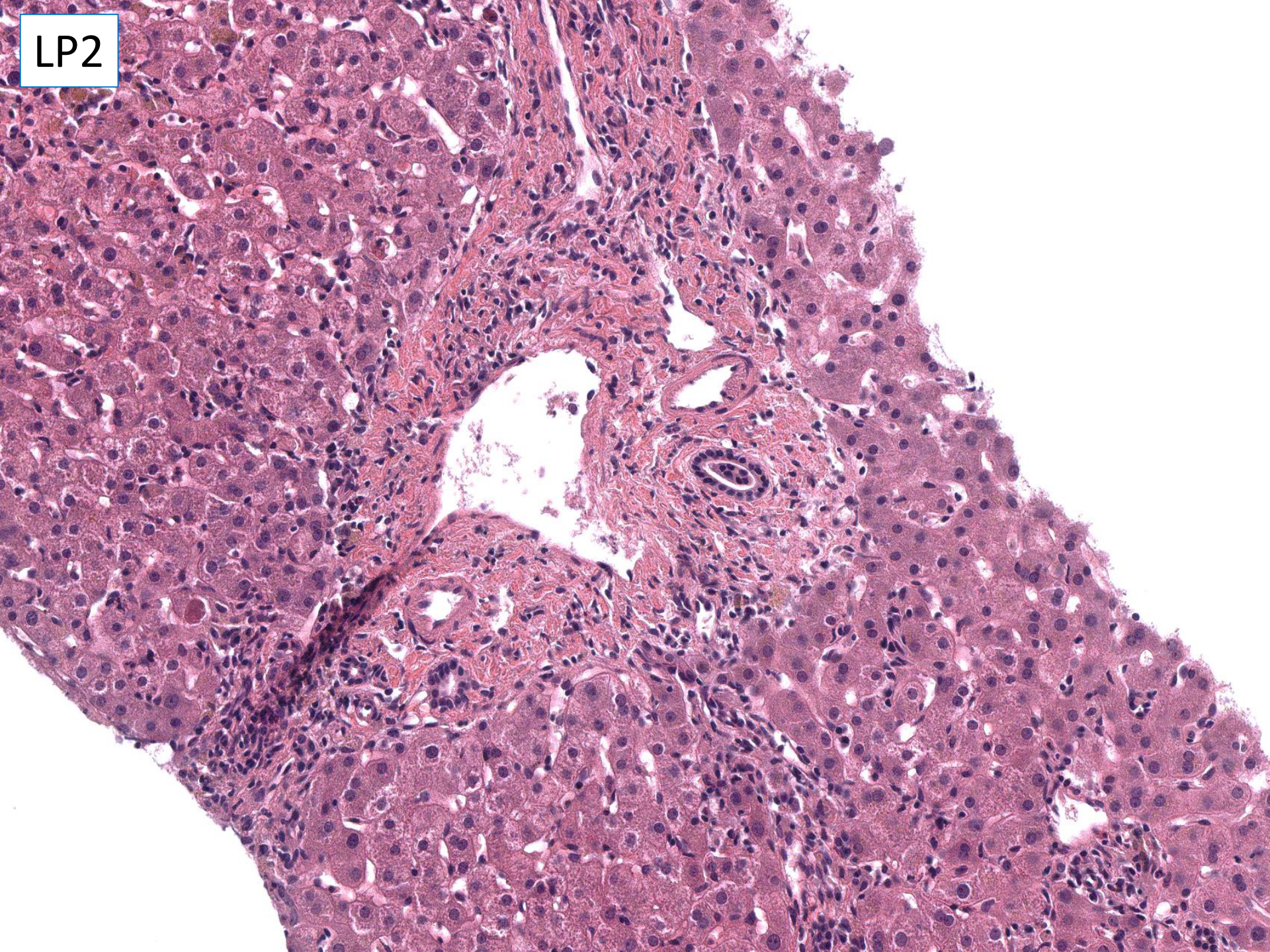
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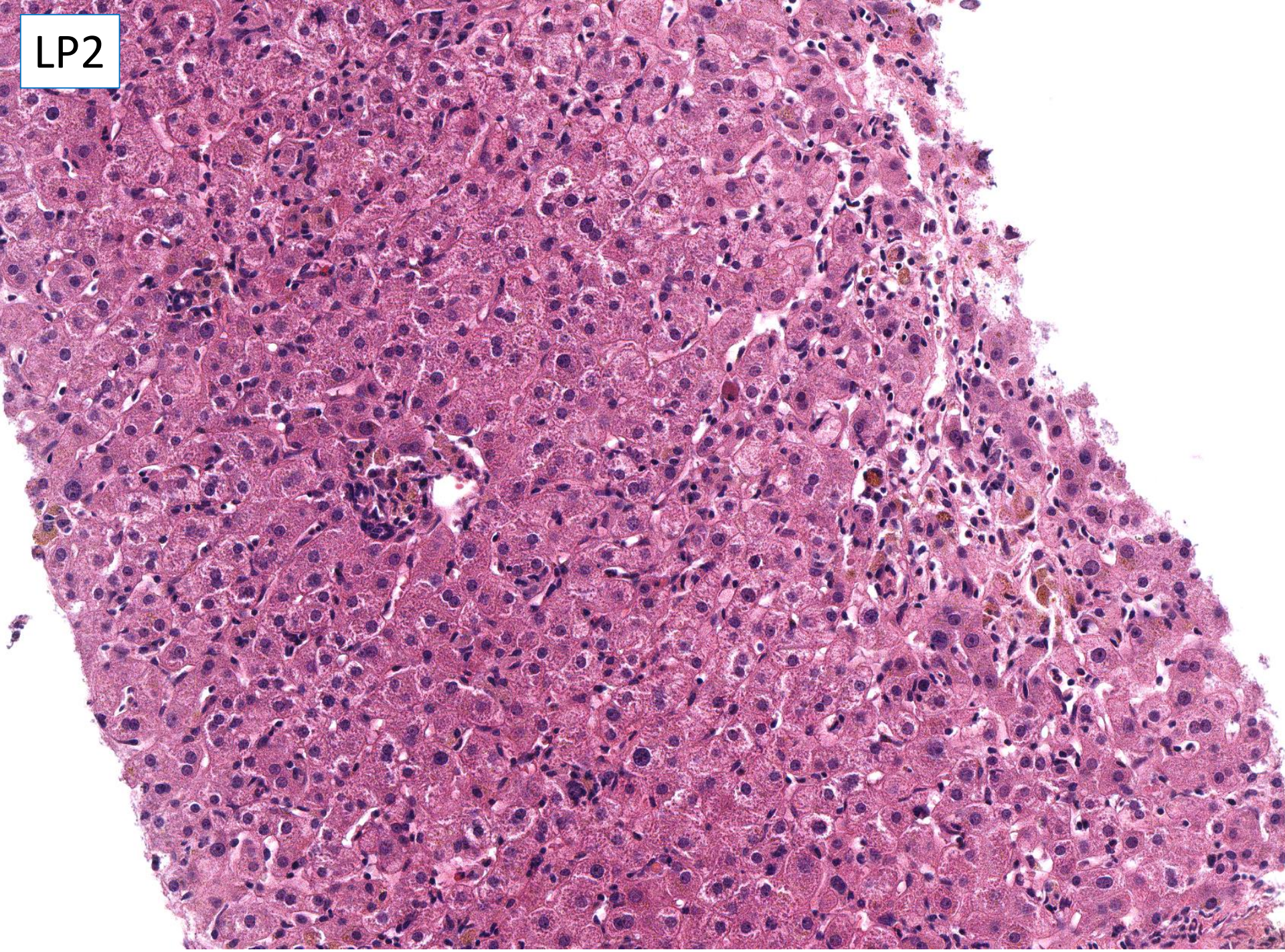
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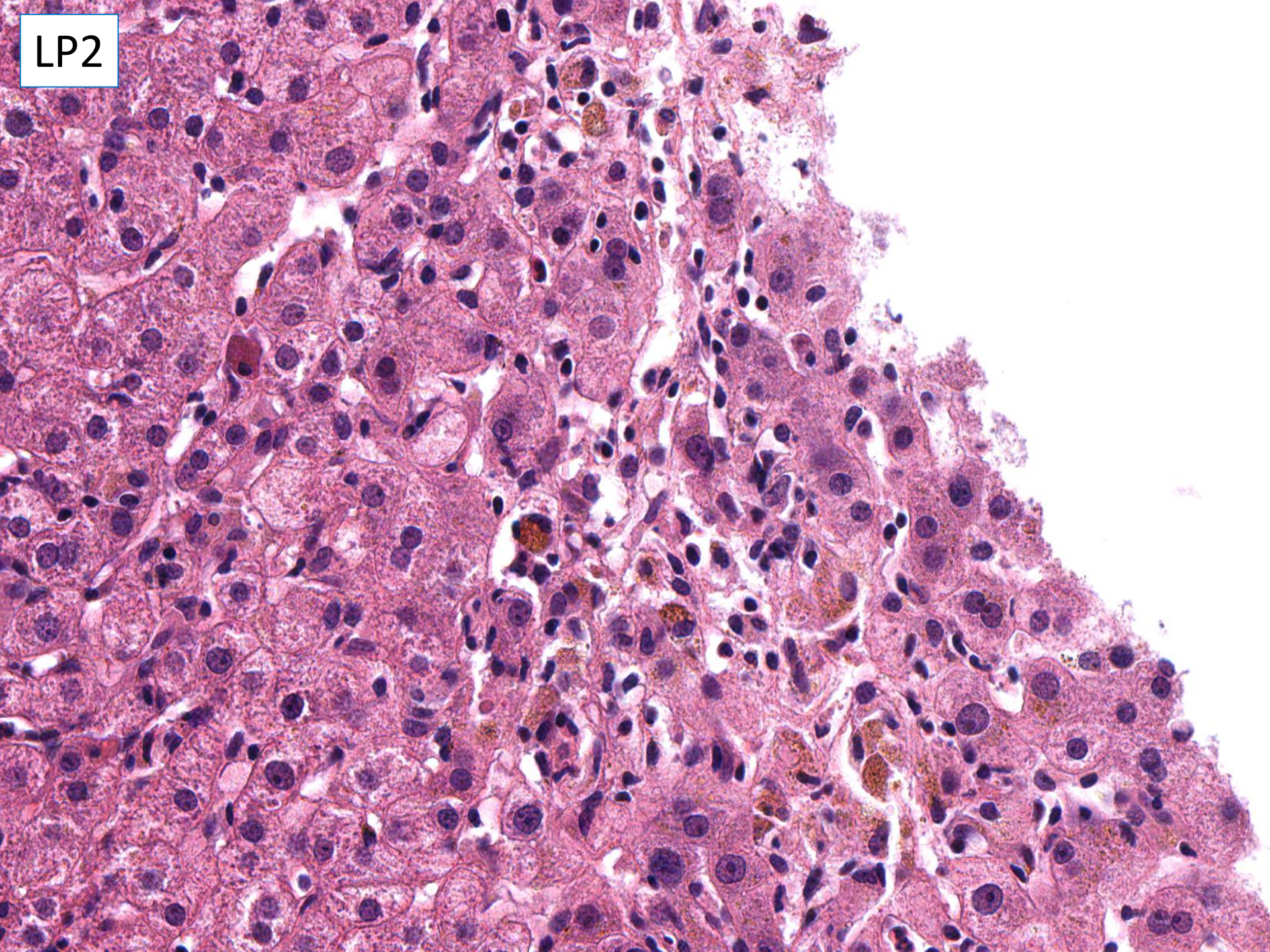
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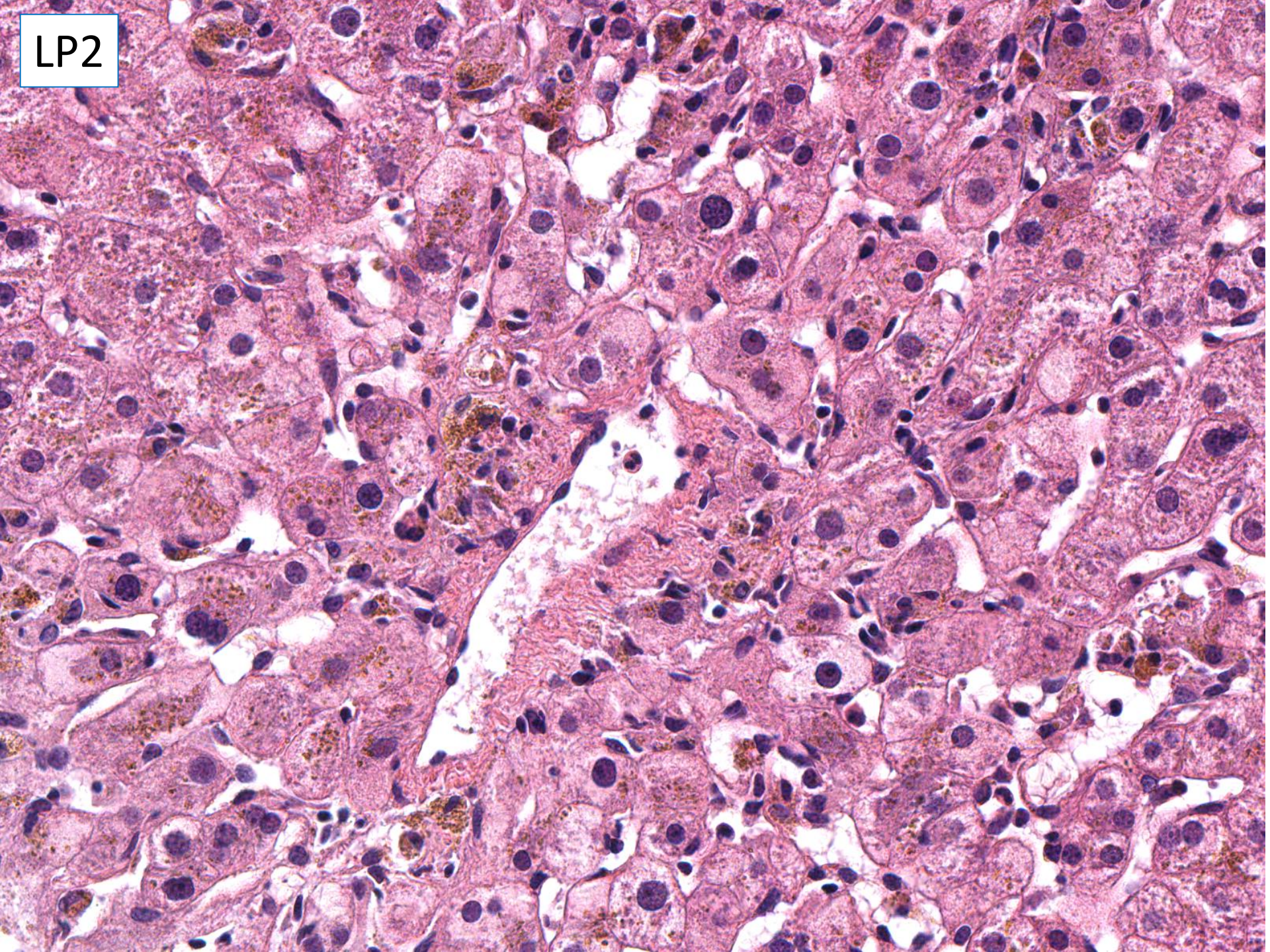
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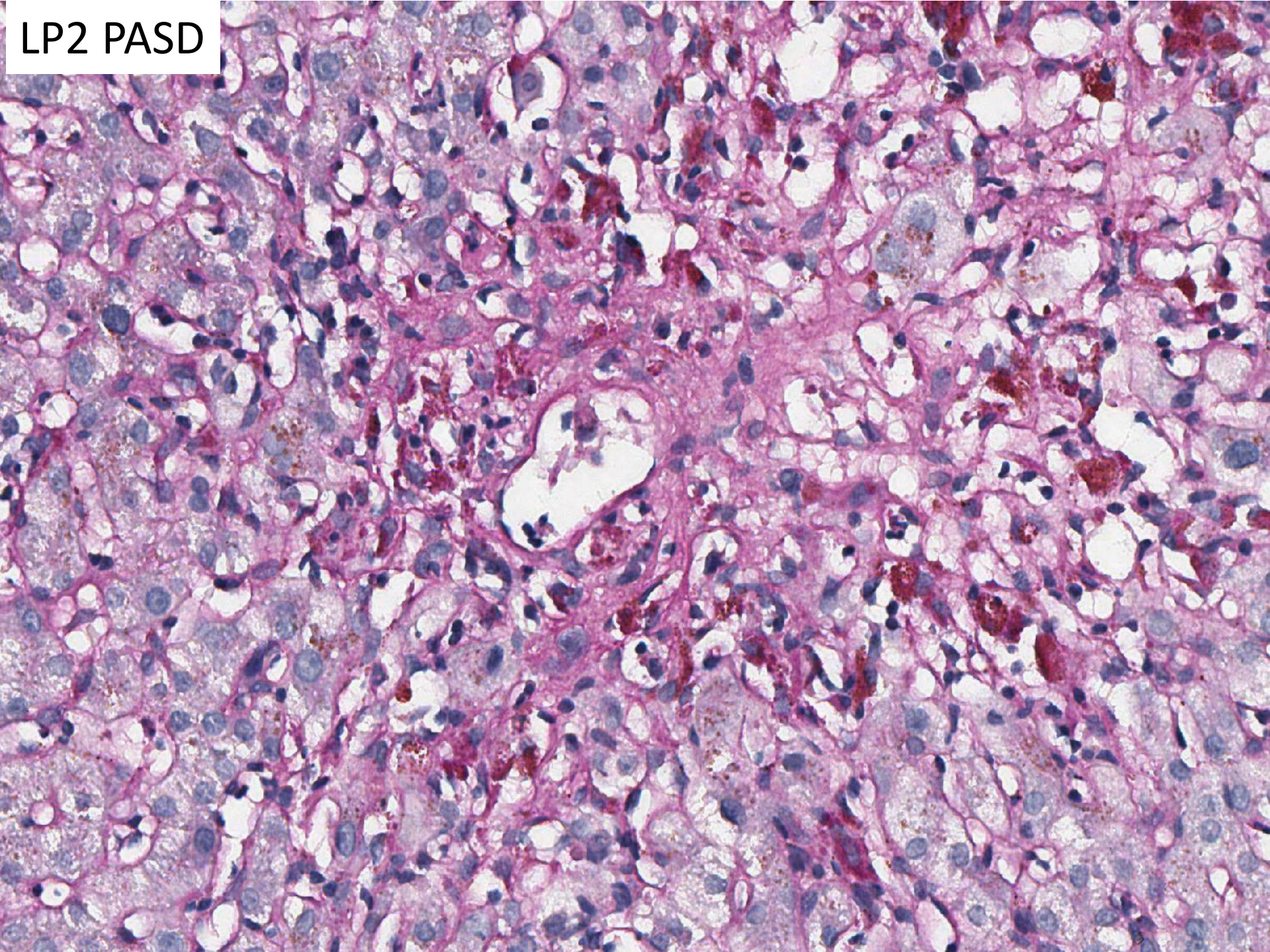
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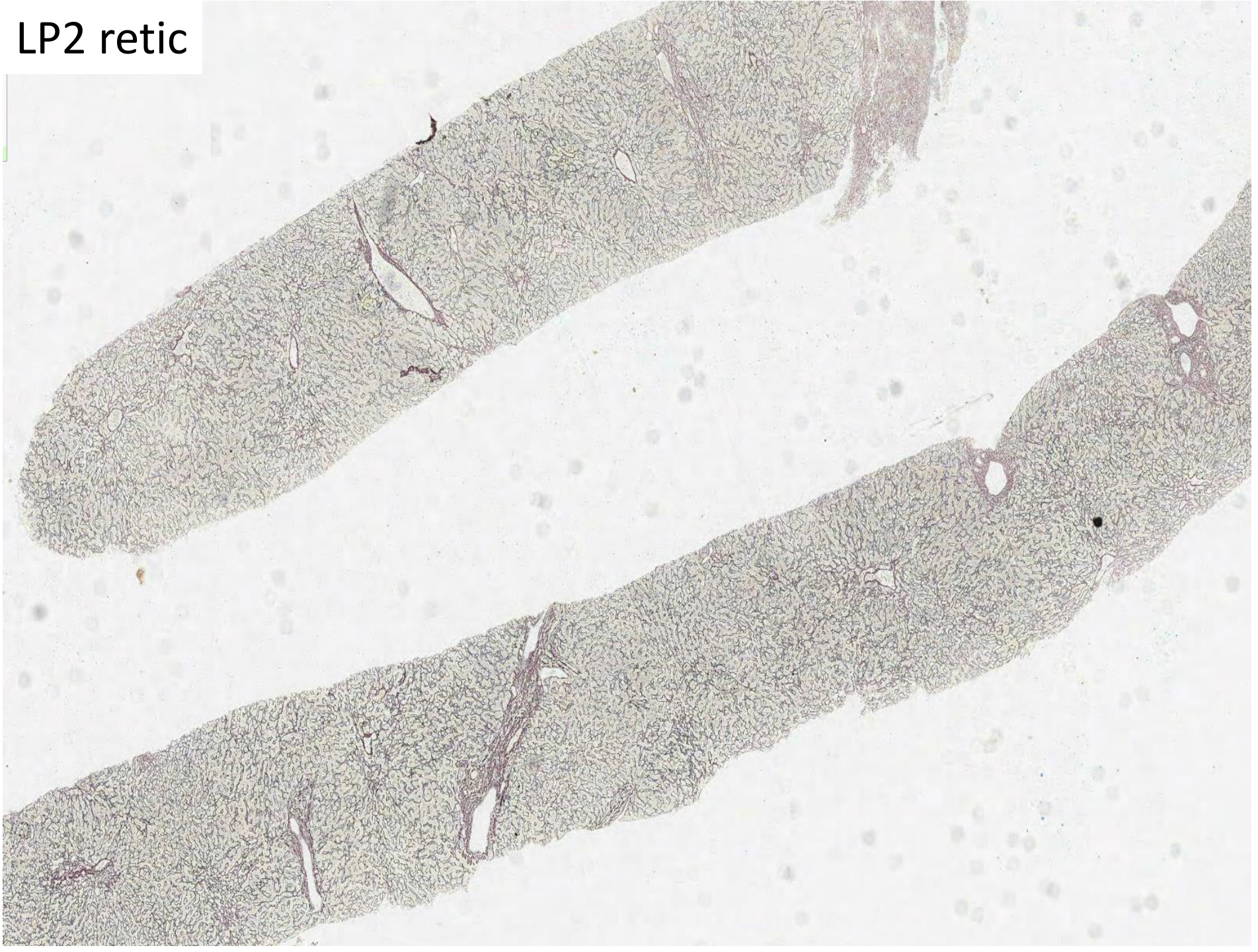
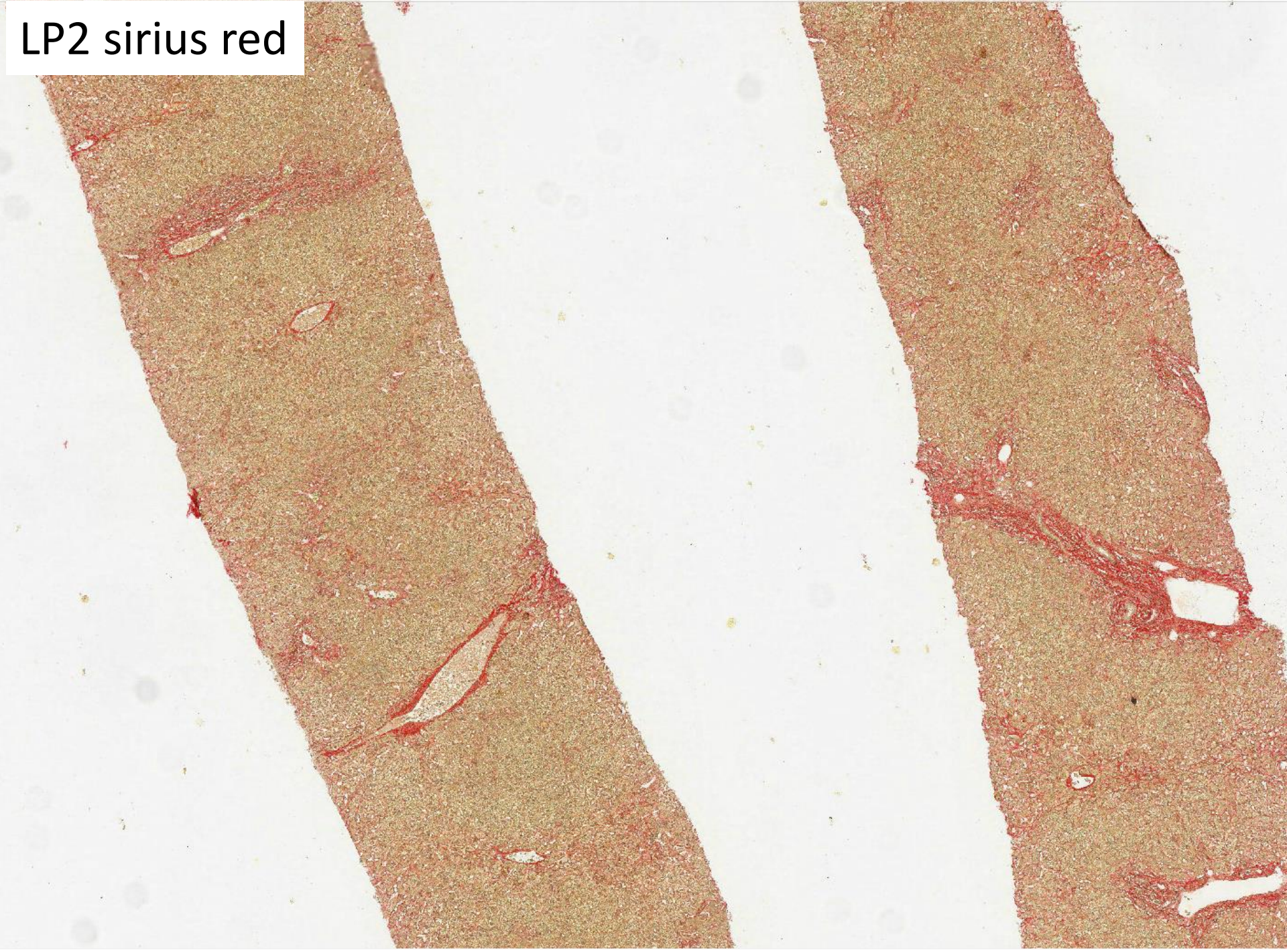
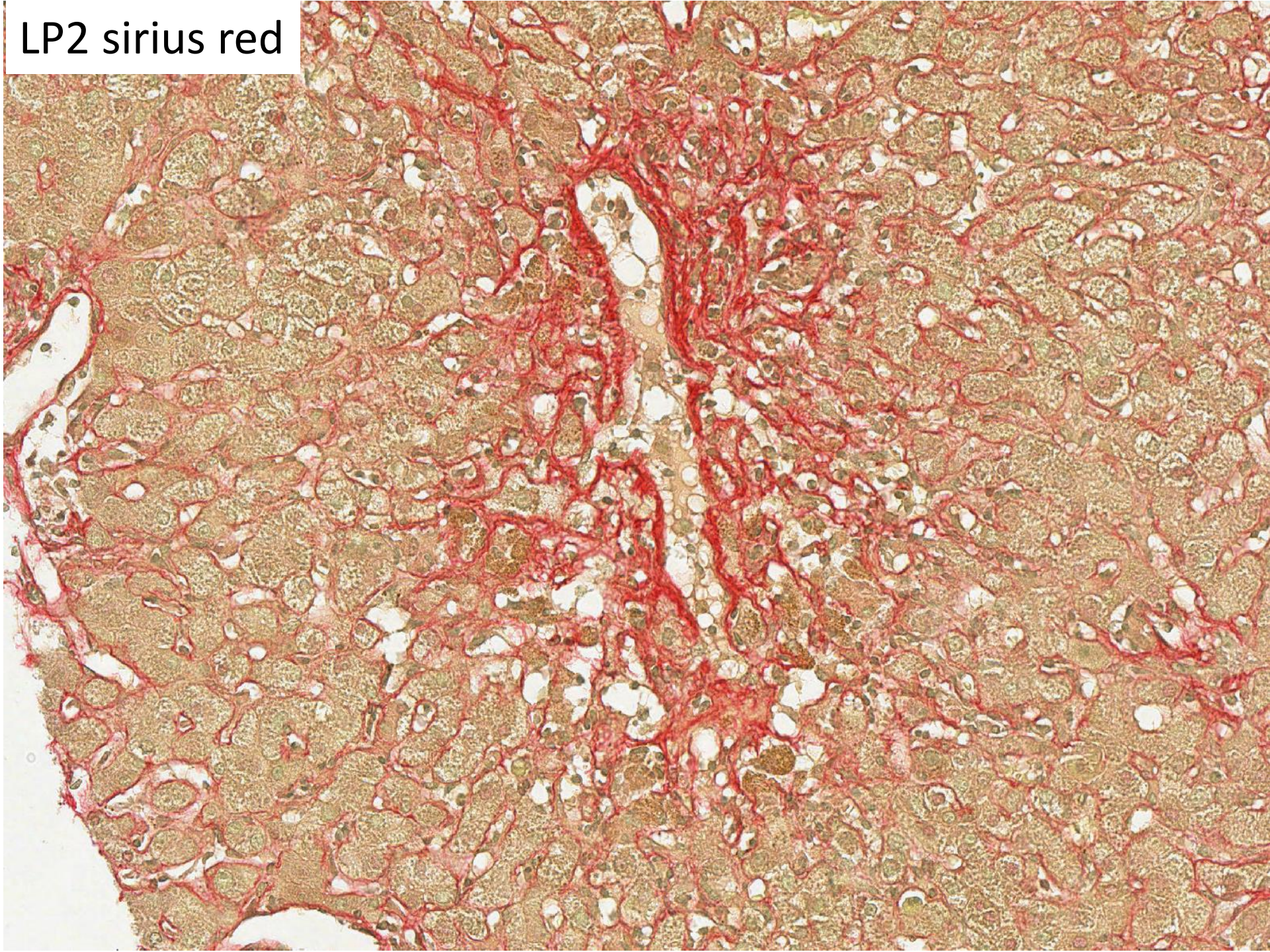
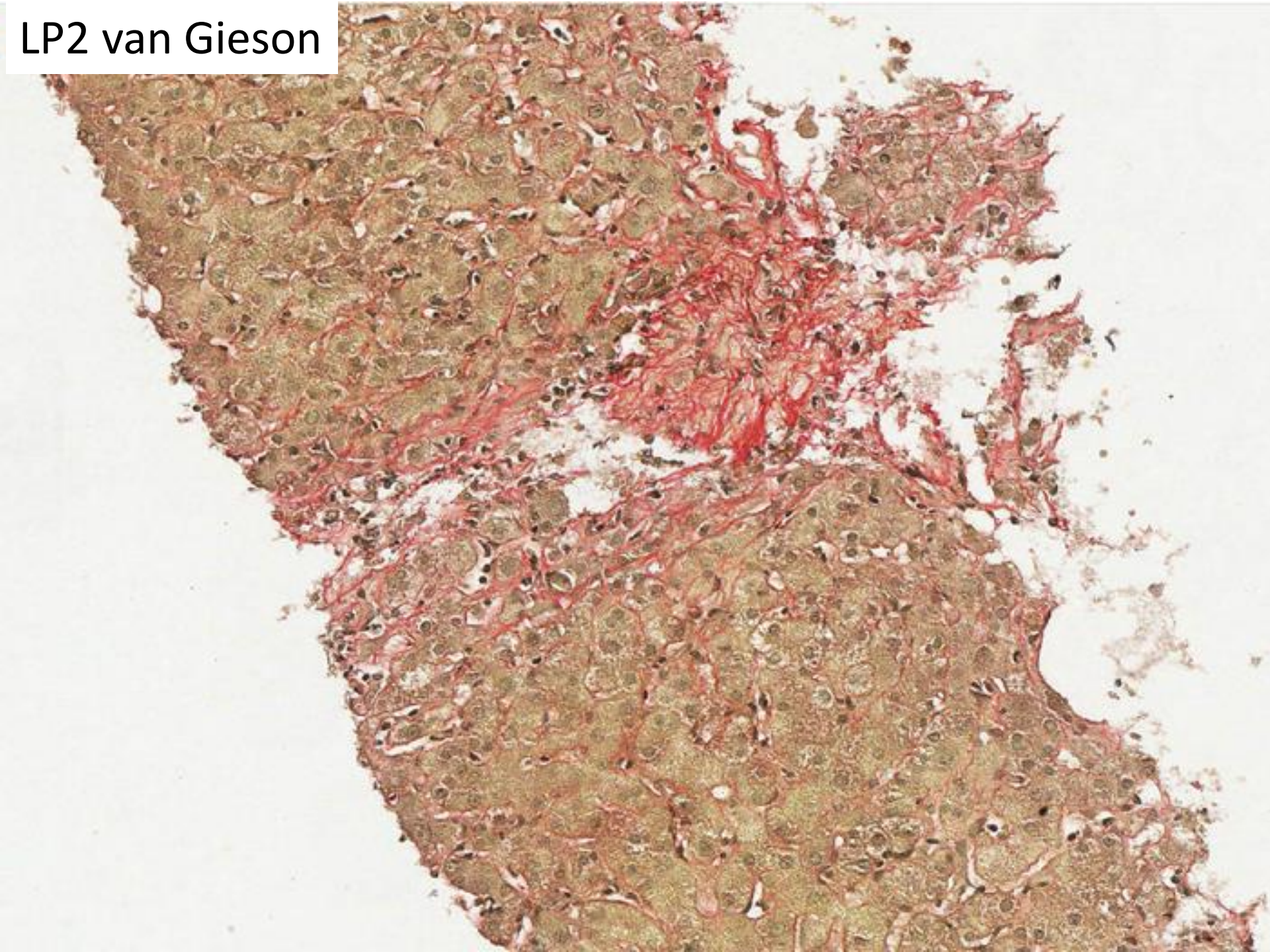



LP2 sirius red


LP2 sirius red

LP2 van Gieson



Case LP2 50F

Very raised ALT. DILI v AIH Urgent histology. Recently started Etanercept for rheumatoid arthritis. Concurrent use of Isoniazid for latent TB control. no other medication. Some viral symptoms 1 month ago. Subsequent spike in ALT 1700, with normal function of liver ? DILI, ? AIH.

Hepatitis – of which	77
Cholestatic	35
Zonal necrosis	18
Submassive necrosis	1
Chronic hepatitis	3
Acute hepatitis on background of chronic hepatitis	2
Descriptive report, 'hepatitis' not mentioned	4
'regenerative process ongoing with mild inflammatory changes persisting	1
Main cause:	
Drug induced liver injury (+/- differential of AIH, viral)	83
Autoimmune pattern, may be enteracept	4
'drug induced chronic active hepatitis'	1
AIH, drugs not mentioned	1
Acute on chronic hepatitis ? reactivation of hepatitis B – drugs not mentioned	1

Consensus complete response would include:
recent acute cholestatic hepatitis, likely to be drug induced liver injury.
+/- differential diagnosis includes viral and autoimmune hepatitis
and comment that enteracept reaction may have autoimmune features.

Case LP2 50F

Very raised ALT. DILI v AIH Urgent histology. Recently started Etanercept for rheumatoid arthritis. Concurrent use of Isoniazid for latent TB control. no other medication. Some viral symptoms 1 month ago. Subsequent spike in ALT 1700, with normal function of liver ? DILI, ? AIH.

Hepatitis – of which	77	From survey:		
Cholestatic	35	10	5	0
Zonal necrosis	18			
Submassive necrosis	1			
Chronic hepatitis	3	0	2	7
Acute hepatitis on background of chronic hepatitis	2	0	7	3
Descriptive report, 'hepatitis' not mentioned	4	0	3	7
'regenerative process ongoing with mild inflammatory changes persisting	1	0	2	8
Main cause:				
Drug induced liver injury (+/- differential of AIH, viral)	83			
Autoimmune pattern, may be enteracept	4	3	4	3
'drug induced chronic active hepatitis'	1			
AIH, drugs not mentioned	1			
Acute on chronic hepatitis ? reactivation of hepatitis B – drugs not mentioned	1			

Case LP2 50F

Very raised ALT. DILI v AIH Urgent histology. Recently started Etanercept for rheumatoid arthritis. Concurrent use of Isoniazid for latent TB control. no other medication. Some viral symptoms 1 month ago. Subsequent spike in ALT 1700, with normal function of liver ? DILI, ? AIH.

Agreed scoring:

For full marks – acute hepatitis, and drug induced liver injury as a cause, with or without a differential.

Score no marks for a descriptive report if the word 'hepatitis' is not mentioned, or a diagnosis of chronic hepatitis. Lose 5 marks for acute on chronic hepatitis, or 'regenerative process ongoing with mild inflammatory changes'

Score no marks if there is no mention of drug induced liver injury as a possible cause, and 5 marks if the pattern is stated to be autoimmune.

Comments: Avoid 'chronic active hepatitis' – this is a historic term, and ambiguous, referring either to a specific disease, or a morphological description. We should use ' chronic hepatitis' (if appropriate – not this case) and then add a comment about activity.

Although many responses described cholestasis, it was probably not present in this case – the pigment is in Kupffer cells. The bilirubin was not raised. ALT normalised within a month of stopping both drugs.

Autoantibodies can be seen in any acute liver injury, and both etanercept and isoniazid can be associated with autoantibodies, without necessarily having morphological features of autoimmune hepatitis.

Case LP2 50F

Very raised ALT. DILI v AIH Urgent histology. Recently started Etanercept for rheumatoid arthritis. Concurrent use of Isoniazid for latent TB control. no other medication. Some viral symptoms 1 month ago. Subsequent spike in ALT 1700, with normal function of liver ? DILI, ? AIH.

A Submassive necrosis

B Drug induced chronic hepatitis

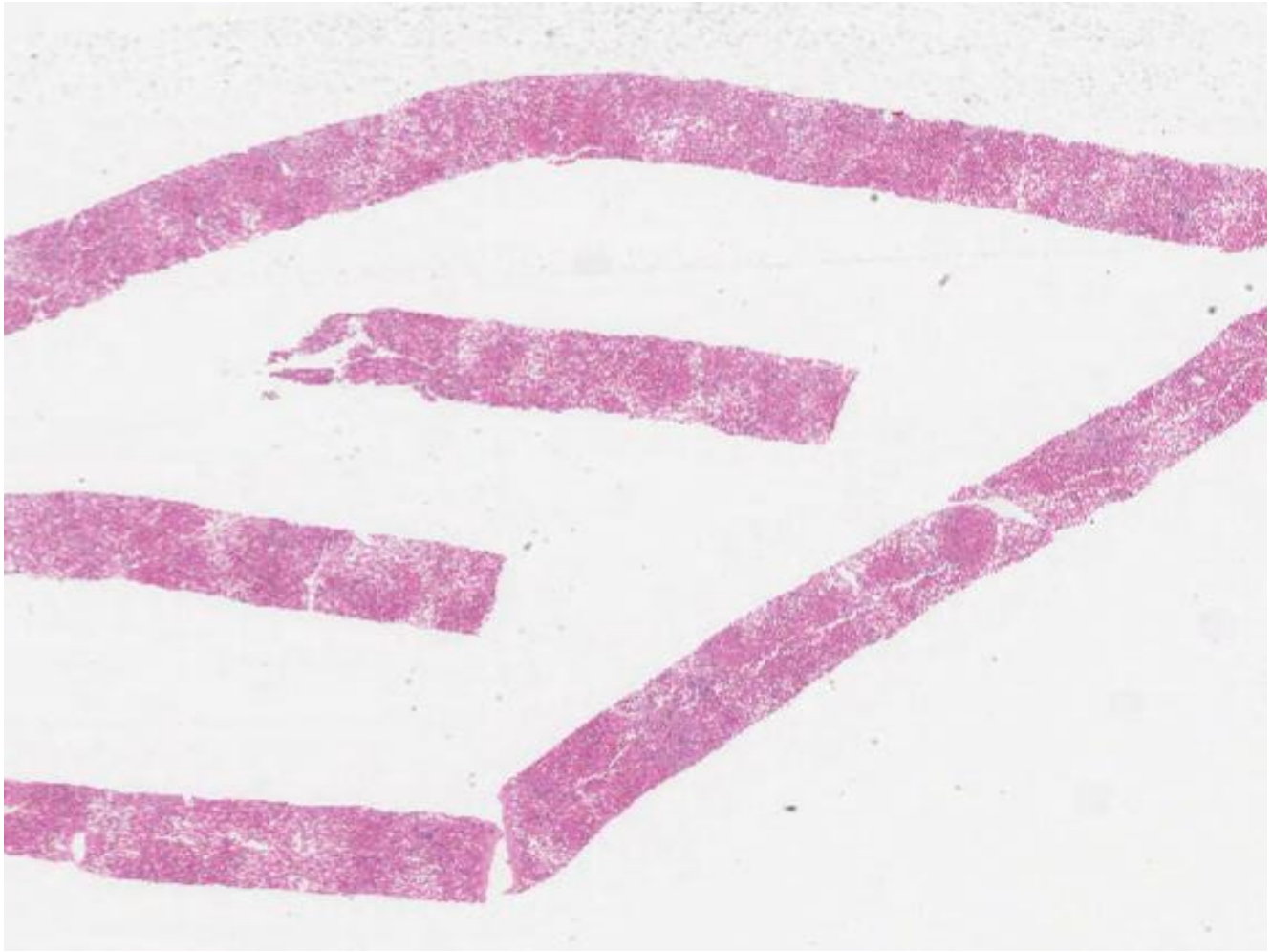
C Regenerative process ongoing with mild inflammatory changes persisting, ? drug induced

D Autoimmune hepatitis, may be drug related

E Cholestatic hepatitis, likely drug induced liver injury

Case LP3 62M

Heavy alcohol consumption. Risk factors for NAFLD??



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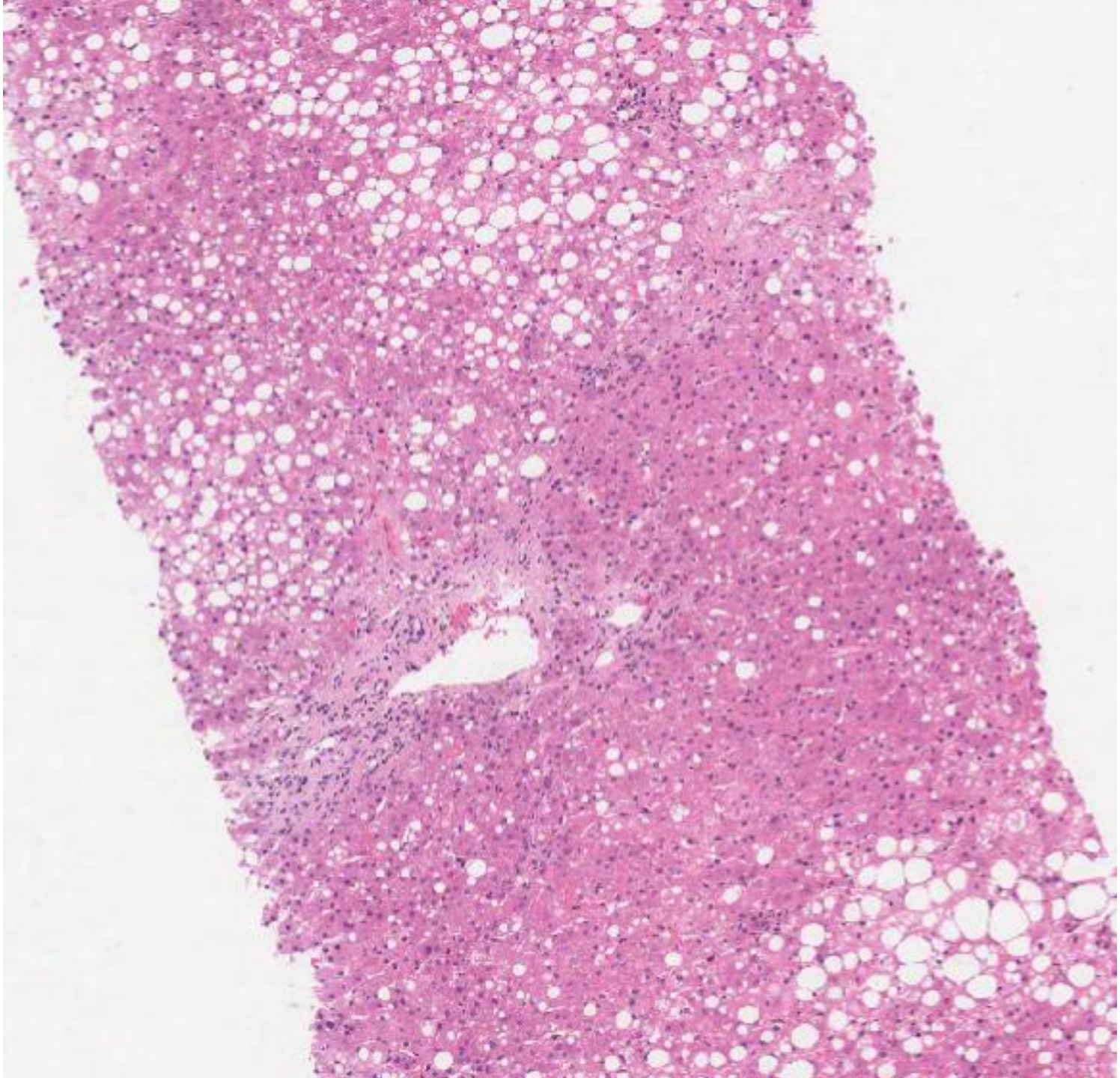

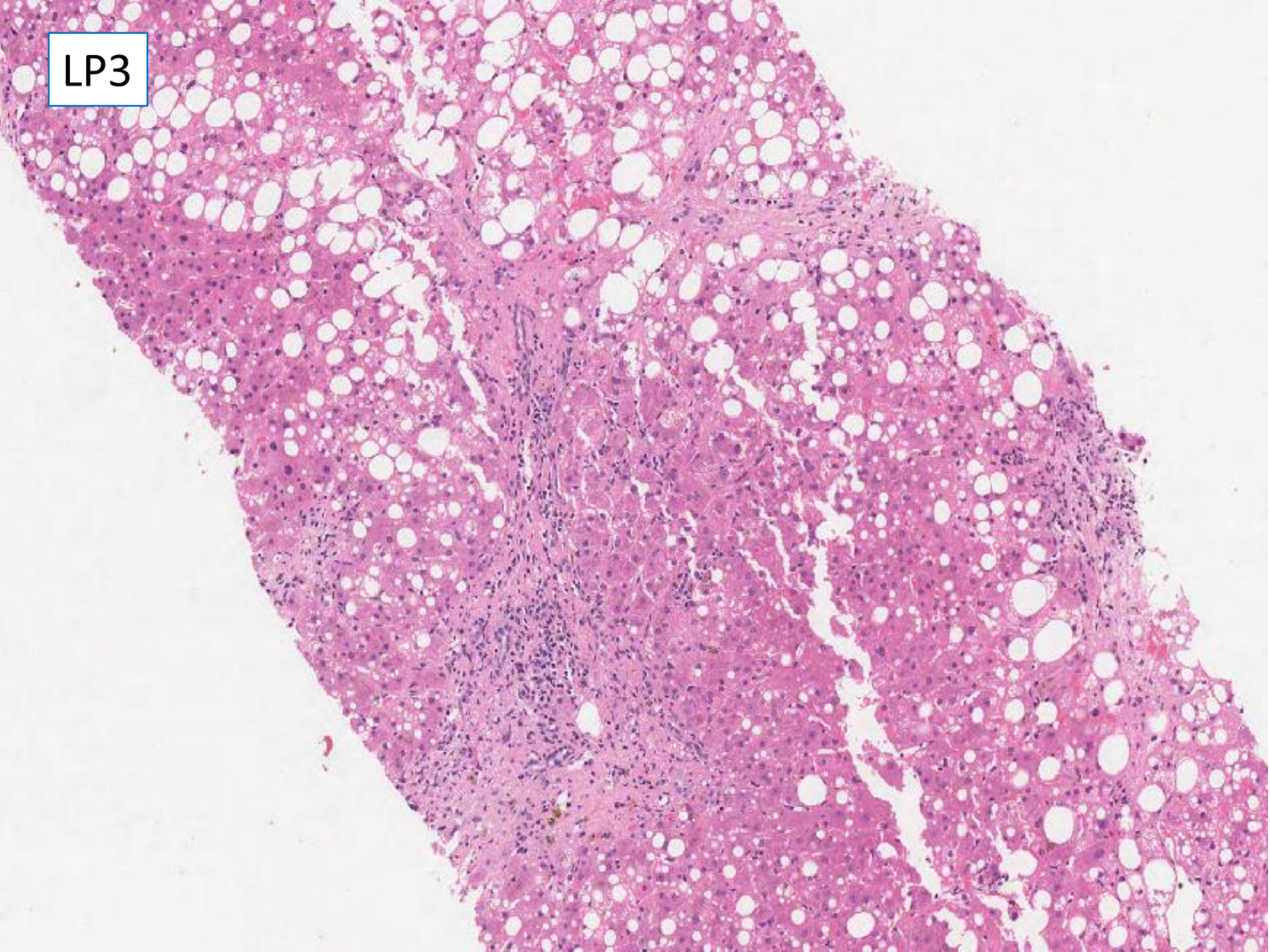
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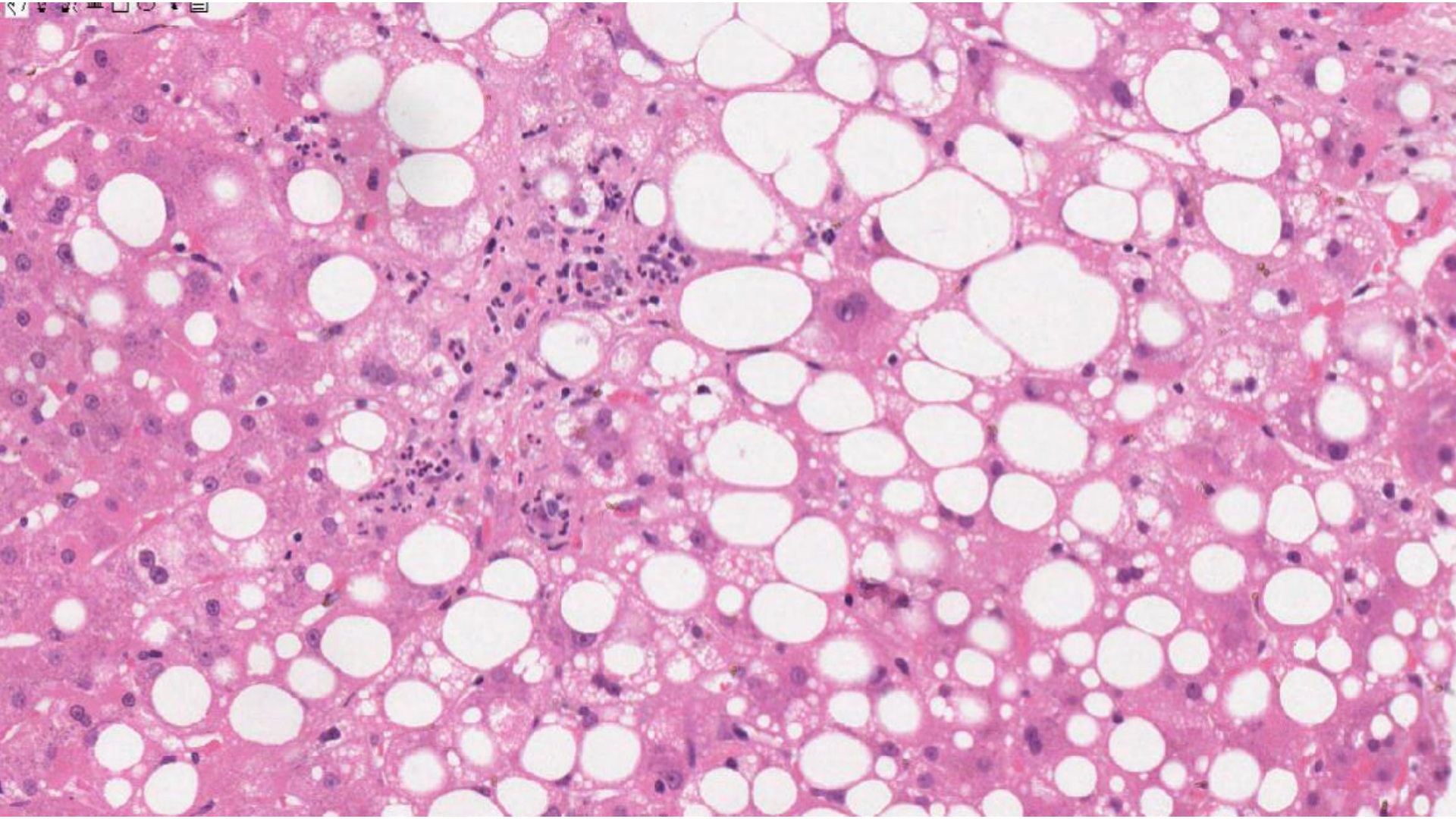

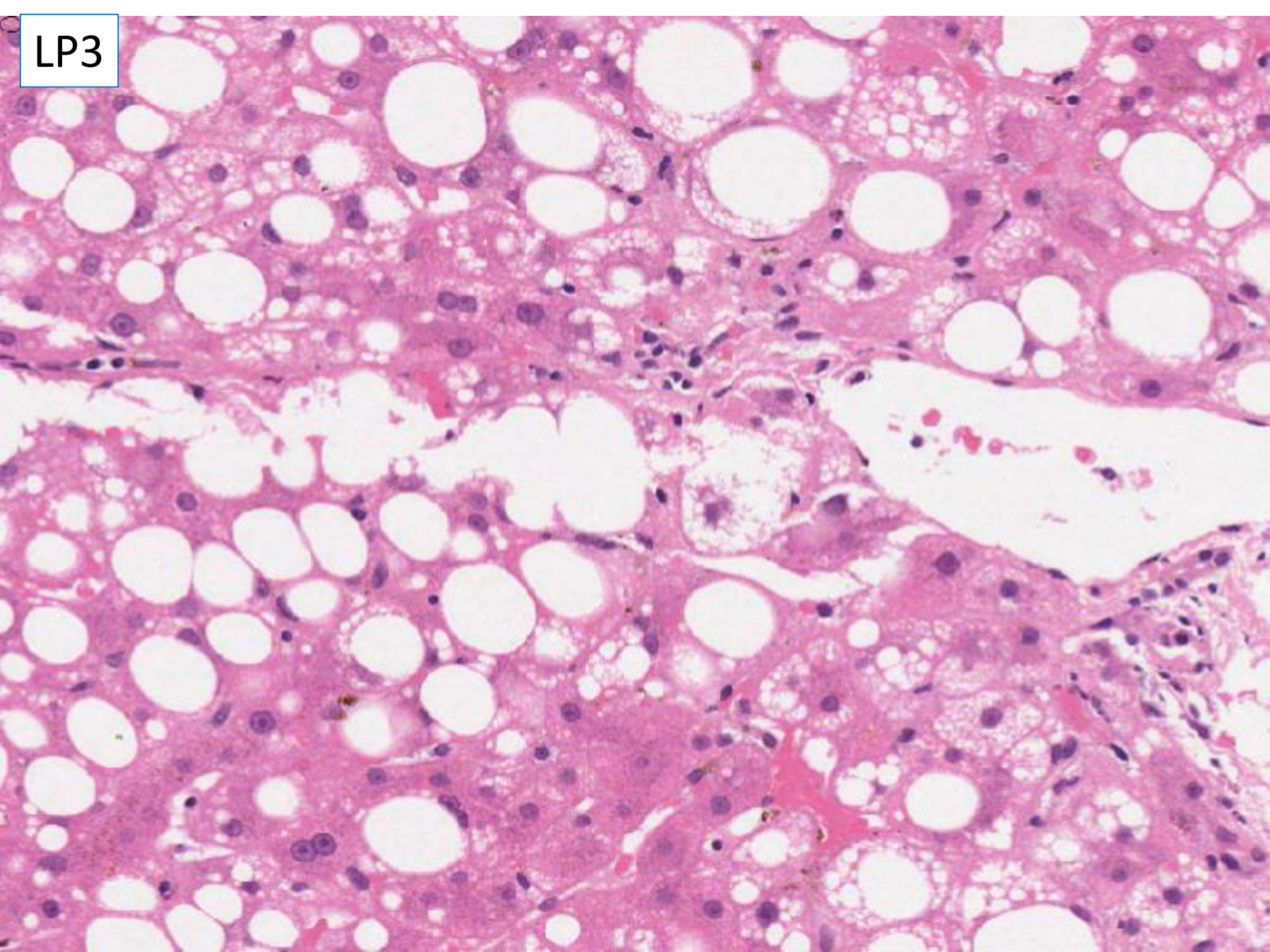
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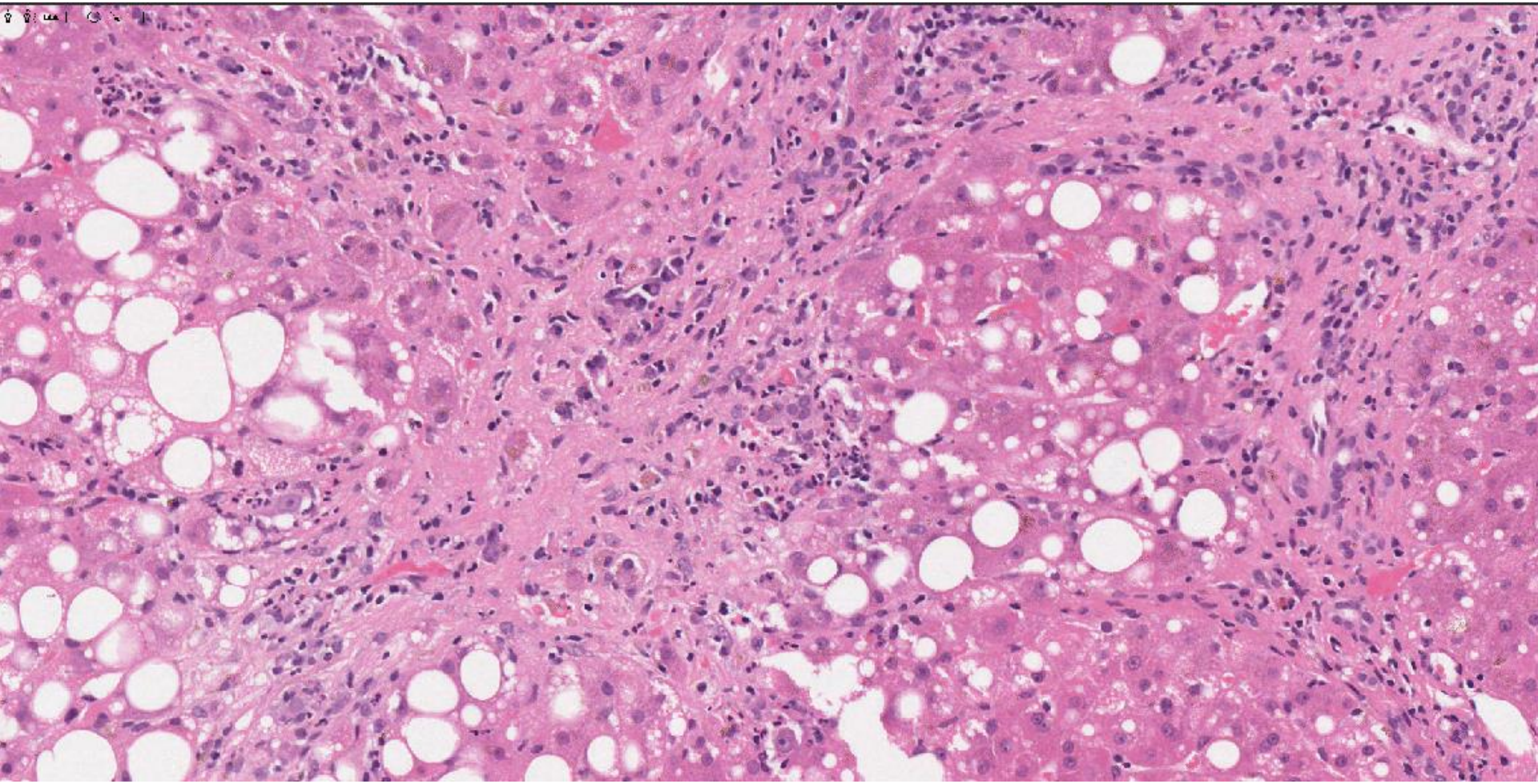

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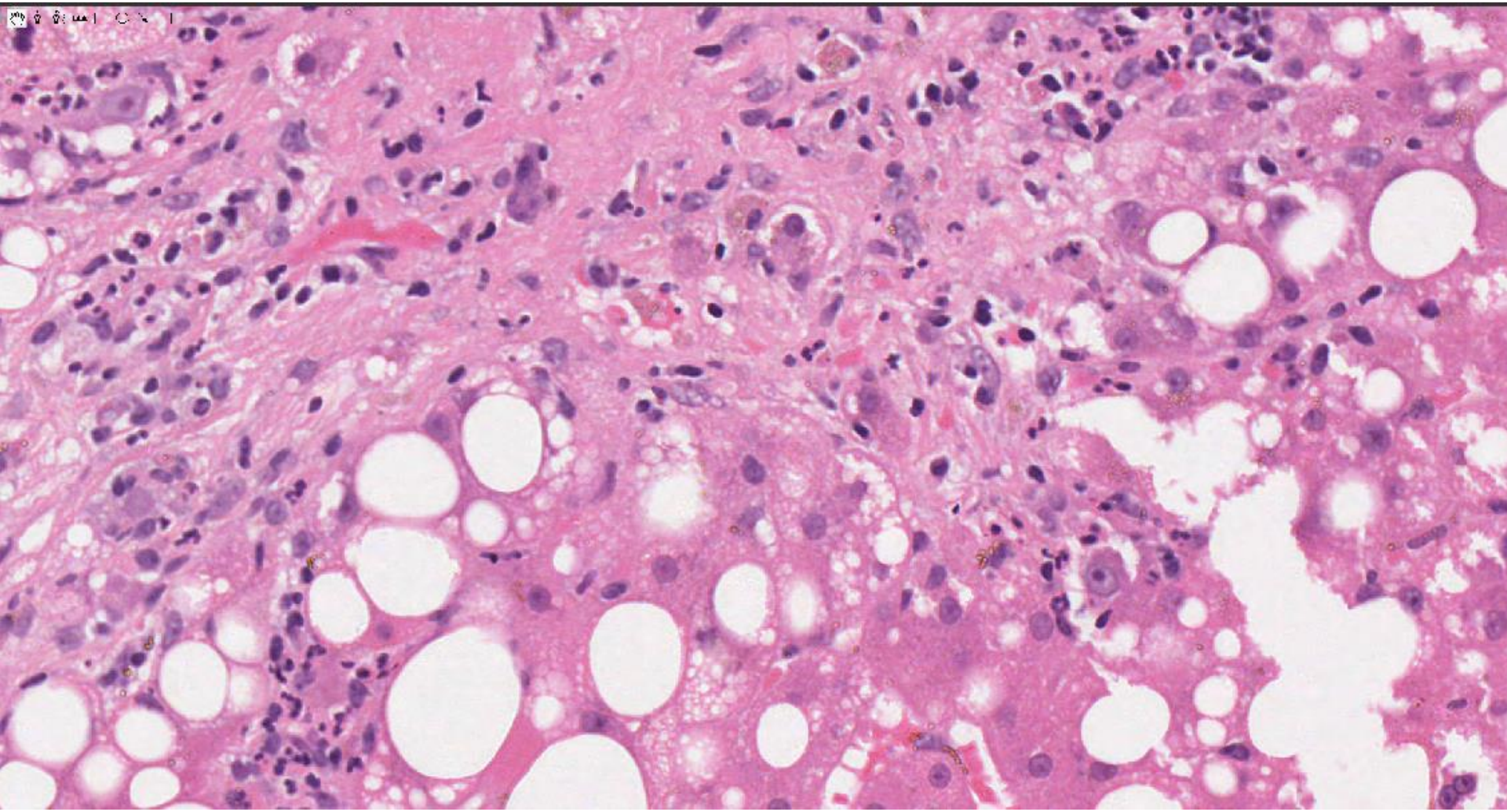


Case LP3 62M

Heavy alcohol consumption. Risk factors for NAFLD??

Stage	
Bridging fibrosis	47
Portal +/- central fibrosis	8
Mild fibrosis	1
Moderate fibrosis	7
Central sclerosing hyaline necrosis	12
Early cirrhosis	1
Needs collagen stains to assess fibrosis	46
No mention of fibrosis stage nor the need for stains	5
Pattern of liver disease	
Steatohepatitis or fatty liver hepatitis	80
Description of features, steatohepatitis not stated	2
'alcoholic hepatitis'	3
Steatosis and polymorphs	1
Aetiology	
Alcohol (definite, only or favoured)	68
Favour NASH > ASH	1
Alcohol and/or non-alcoholic - neither favoured	13
Alcohol not mentioned	6
"Steatosis, with inflammation and probable fibrosis" (alcohol not mentioned)	1
Iron present/ dysmetabolic iron - several, not separately collated - ? a masterclass topic	

Consensus complete response would include:

either a comment on fibrosis, or that special stains are needed to assess fibrosis.

A clear statement of steatohepatitis, or 'alcoholic hepatitis' or 'fatty liver hepatitis' and include alcohol as a potential cause +/- other metabolic cause.

Case LP3 62M

Heavy alcohol consumption. Risk factors for NAFLD??

Agreed scoring:

For full marks – either a comment on fibrosis stage, or that connective tissue stains are needed to assess this, and a diagnosis of steatohepatitis or synonym fatty liver hepatitis or 'alcoholic hepatitis'.

Lose 5 marks for description of the features of steatohepatitis without using the word, and if no mention of fibrosis or need for stains.

Also lose 5 marks if no mention that alcohol is likely to be the cause of steatohepatitis in this case – the history of heavy alcohol consumption is given. Therefore score 0 for ' steatosis with inflammation and probable fibrosis (alcohol not mentioned).

Comment: on discussion - the report should include the word 'steatohepatitis' not just a description of the features. There should be harmonisation of terminology like this – the report should be able to be understood by clinicians without being required to know the significance of histological features.

Case LP3 62M

Heavy alcohol consumption. Risk factors for NAFLD??

A Steatosis with inflammation and probable fibrosis

B Steatohepatitis, consistent with alcohol, bridging fibrosis

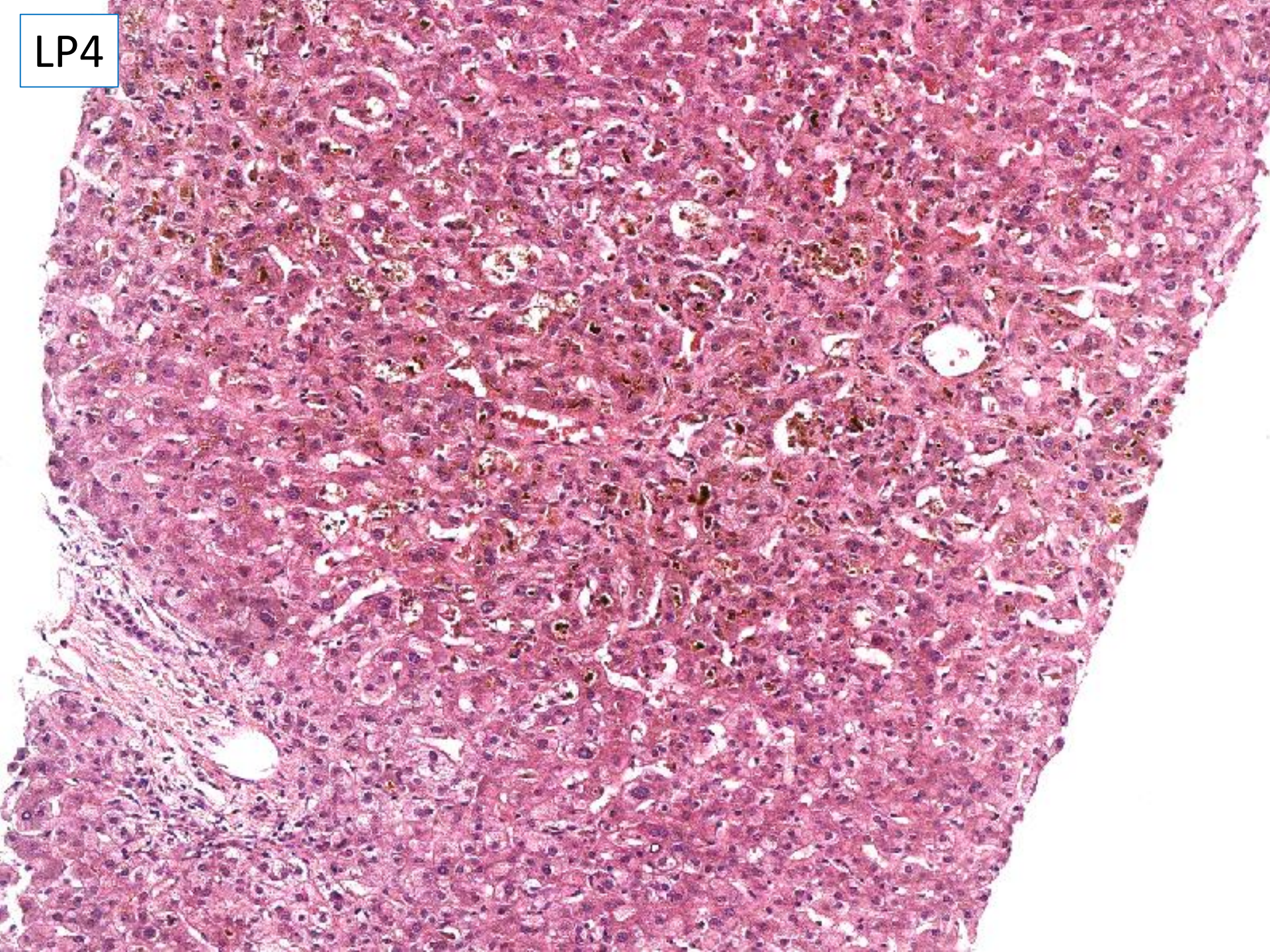
C Fatty change with ballooning and pericellular fibrosis,

D Alcoholic hepatitis

E Cholestatic hepatitis, bridging fibrosis, consistent with alcohol

Case LP4 50M

Fractured right middle finger, given co-amoxiclav.
Deranged LFTs Negative NILS. ? drug induced liver injury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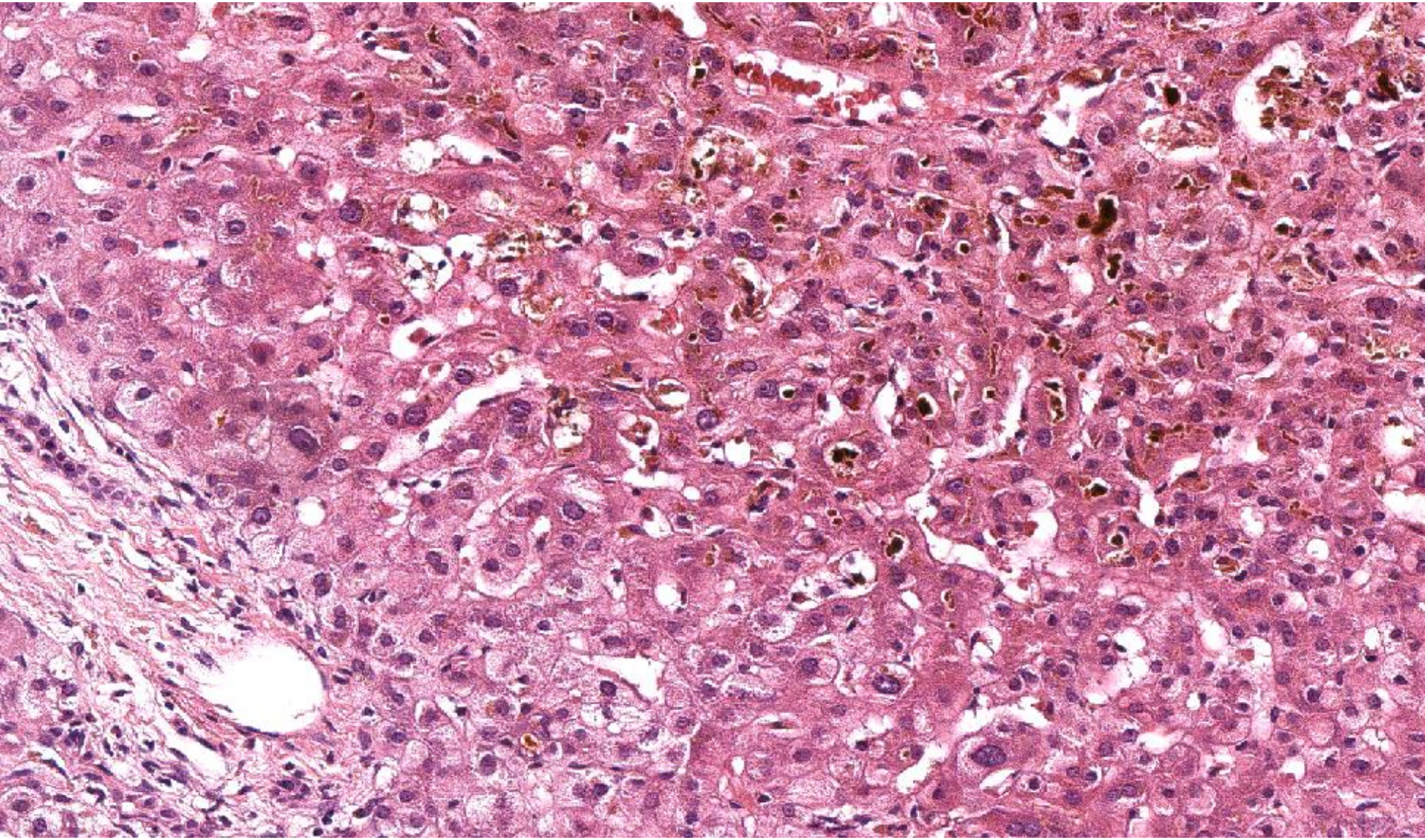
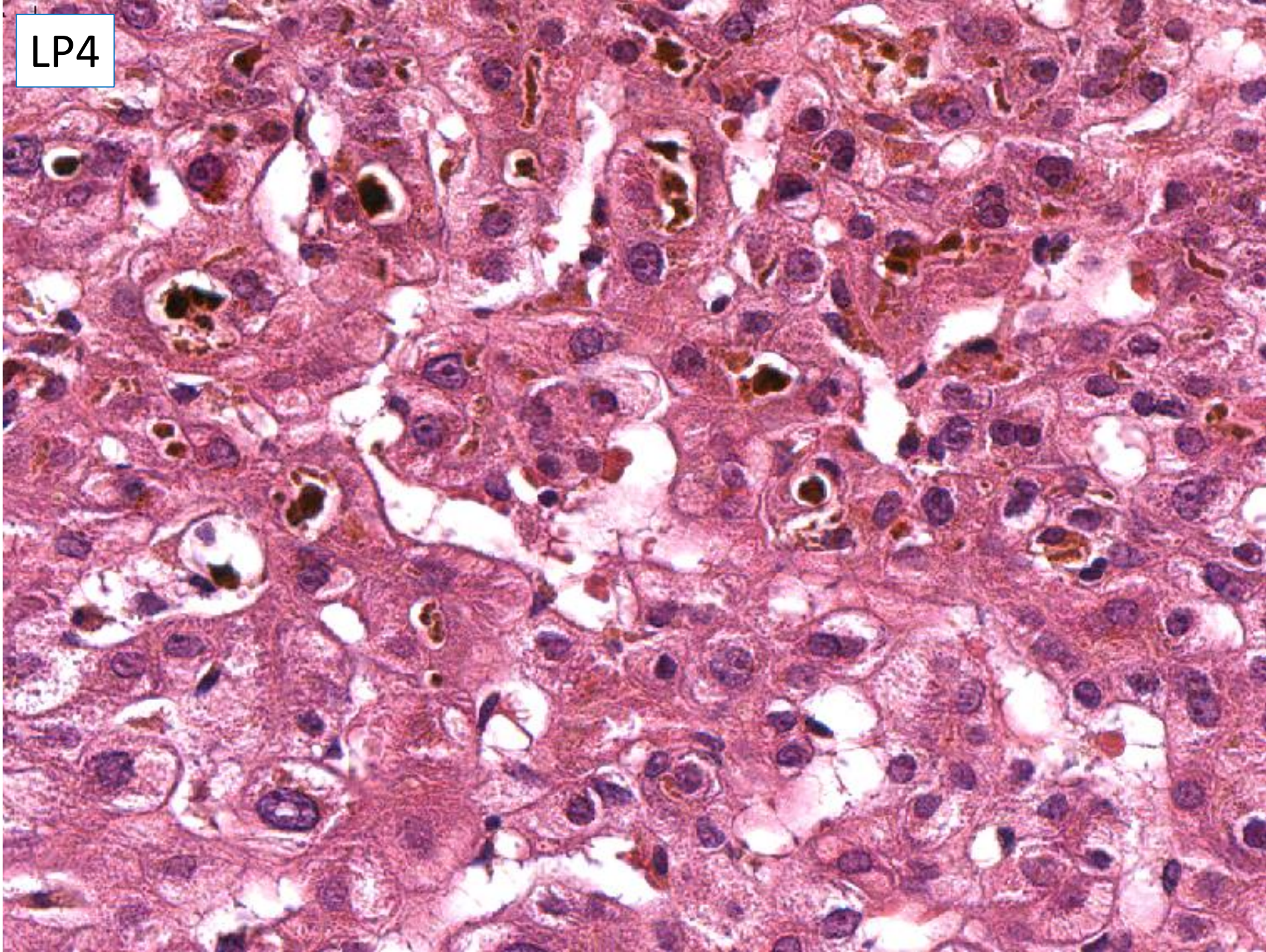
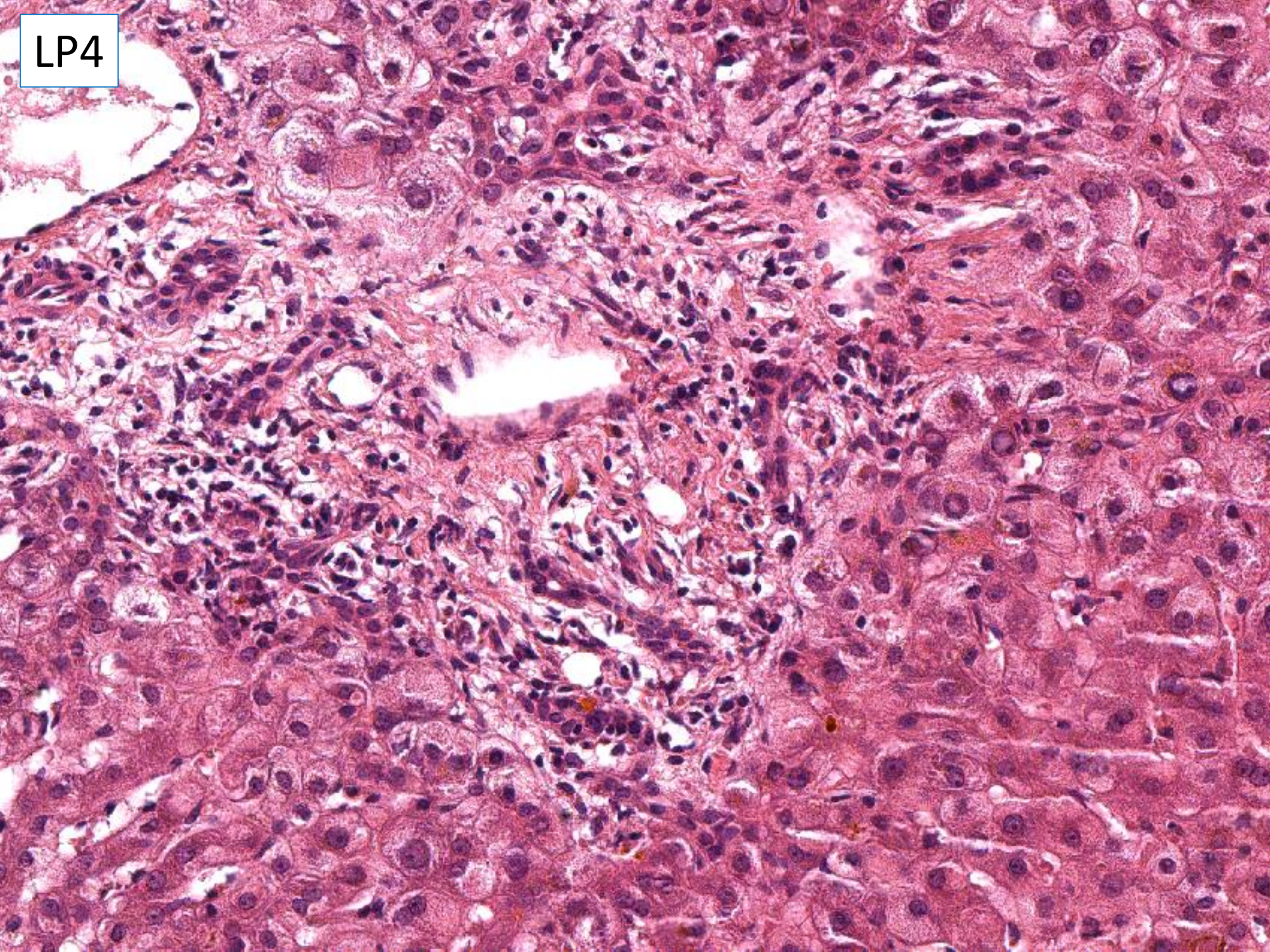
LP4




LP4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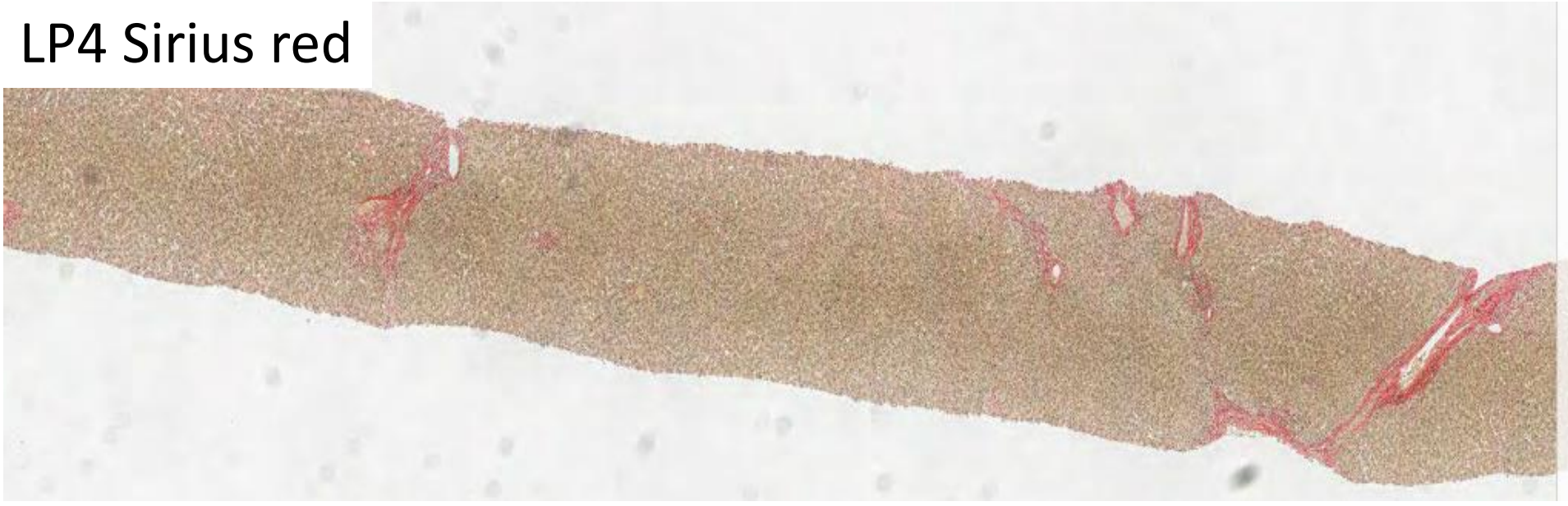
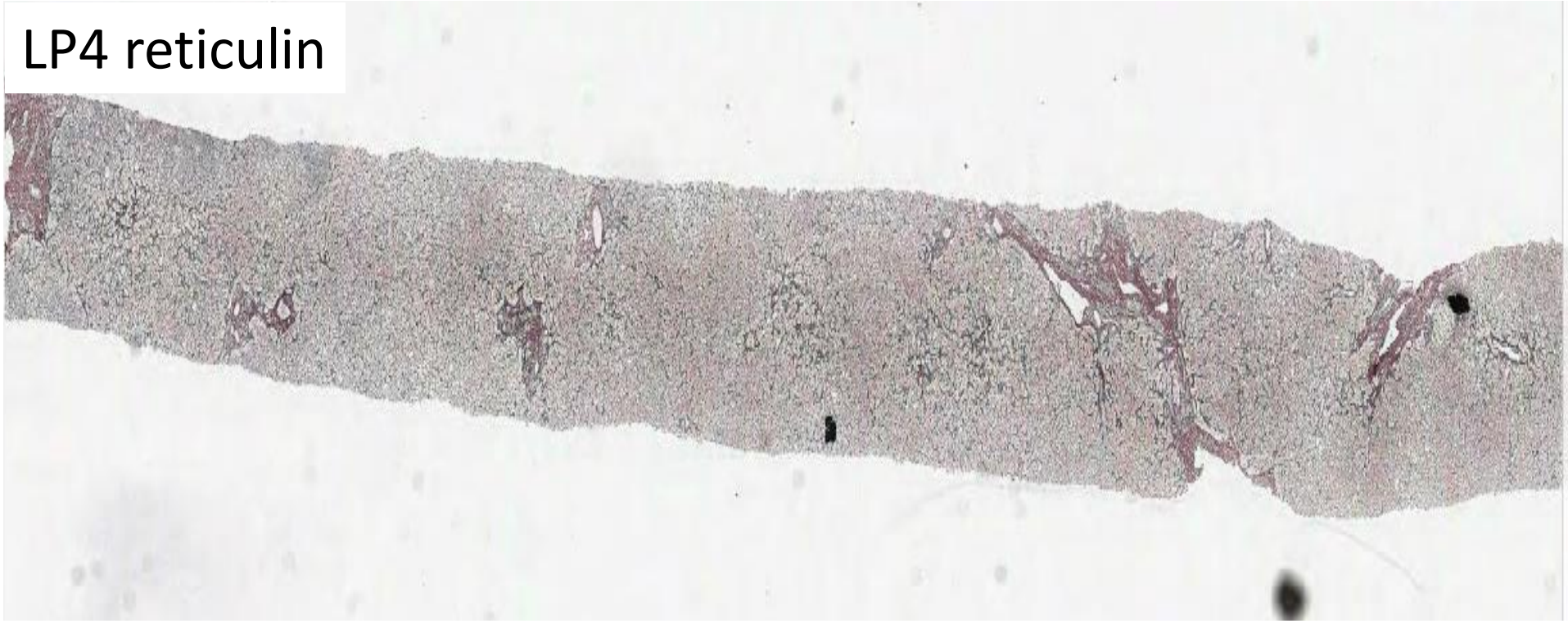
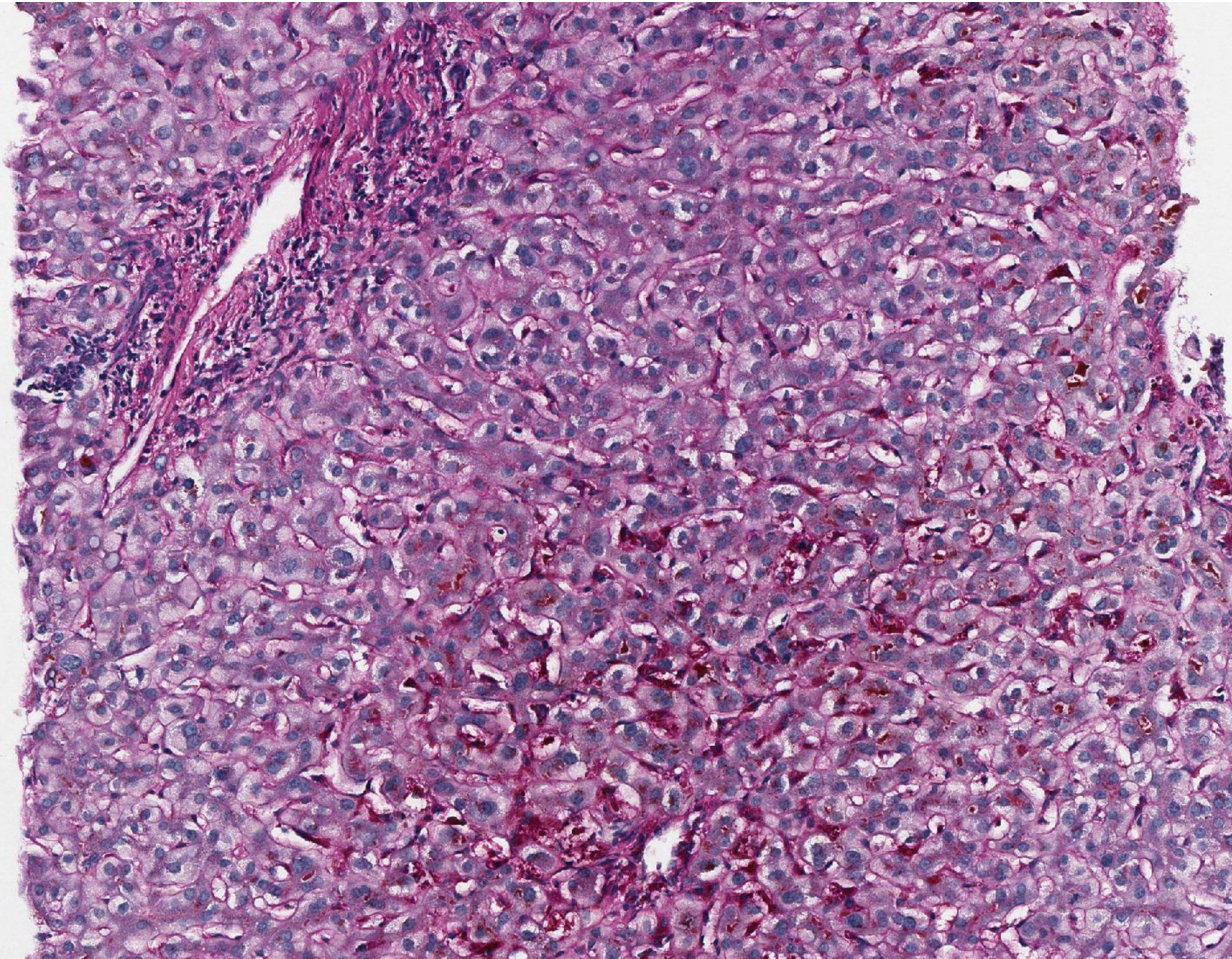
LP4 Sirius red



LP4 reticulin





Case LP4 50M

Fractured right middle finger, given co-amoxiclav.
Deranged LFTs Negative NILS. ? drug induced liver injury

Cholestasis (bland)	56
Cholestatic hepatitis	33
Aetiology:	
Consistent with DILI	88
"acute hepatitis, favour LBDO" - drug not mentioned	1
Main diagnosis is DILI but suggests imaging to exclude LBDO (included in above)	9
"Mild chronic hepatitis with acute cholestatic changes - DILI Ishak stage 3" (separated because implies chronic disease)	1
Fibrosis and cholangiolitis/ductular reaction - mentioned by several but not collated.	

Consensus complete diagnosis –
acute cholestatic disease (cholestasis/cholestatic hepatitis),

most likely due to DILI.

Comment - use of Ishak score in context other than chronic hepatitis - deduct points?

Survey results: 10/5/0 = 2/5/3

Case LP4 50M

Fractured right middle finger, given co-amoxiclav.
Deranged LFTs Negative NILS. ? drug induced liver injury

Agreed scoring:
For full marks need cholestatic liver injury – either bland cholestasis or cholestatic hepatitis,
And that this is likely to be due to drug induced liver injury.

Score 0 marks for 'acute hepatitis, favour LBDO' with drug not mentioned.

Score 5 marks for chronic hepatitis, with Ishak stage 3, since this was not a chronic hepatitis.

Discussion: Does the terminology bland cholestasis v cholestatic hepatitis matter? Not much, although some drugs e.g. oestrogen, androgen characteristically cause bland cholestasis, while cholestatic hepatitis is more characteristic of antibiotics. It is rare to have no cholestasis at all in acute hepatitis, but relatively prominent cholestasis should always be a prompt to consider DILI.
Follow up – in this case, LFTs returned to normal after stopping the drug, although this took over a year. Ductular reaction may be an indication of a more protracted course of jaundice.

Most people thought Ishak should not be used except for chronic hepatitis, and perhaps only then in the context of research – descriptive terminology for fibrosis may be preferred. In this case, there is no indication of chronic hepatitis, and so using Ishak would be misleading. There was also a discussion on scoring in fatty liver disease (CRN) and PBC – in general, pathologists prefer to use descriptive terms, but clinicians can put pressure to use numerical scores.

Case LP4 50M

Fractured right middle finger, given co-amoxiclav. Deranged LFTs Negative NILS. ? drug induced liver injury

A Acute cholestatic hepatitis, most likely drug induced liver injury

B Cholestasis, probable large bile duct obstruction, needs imaging

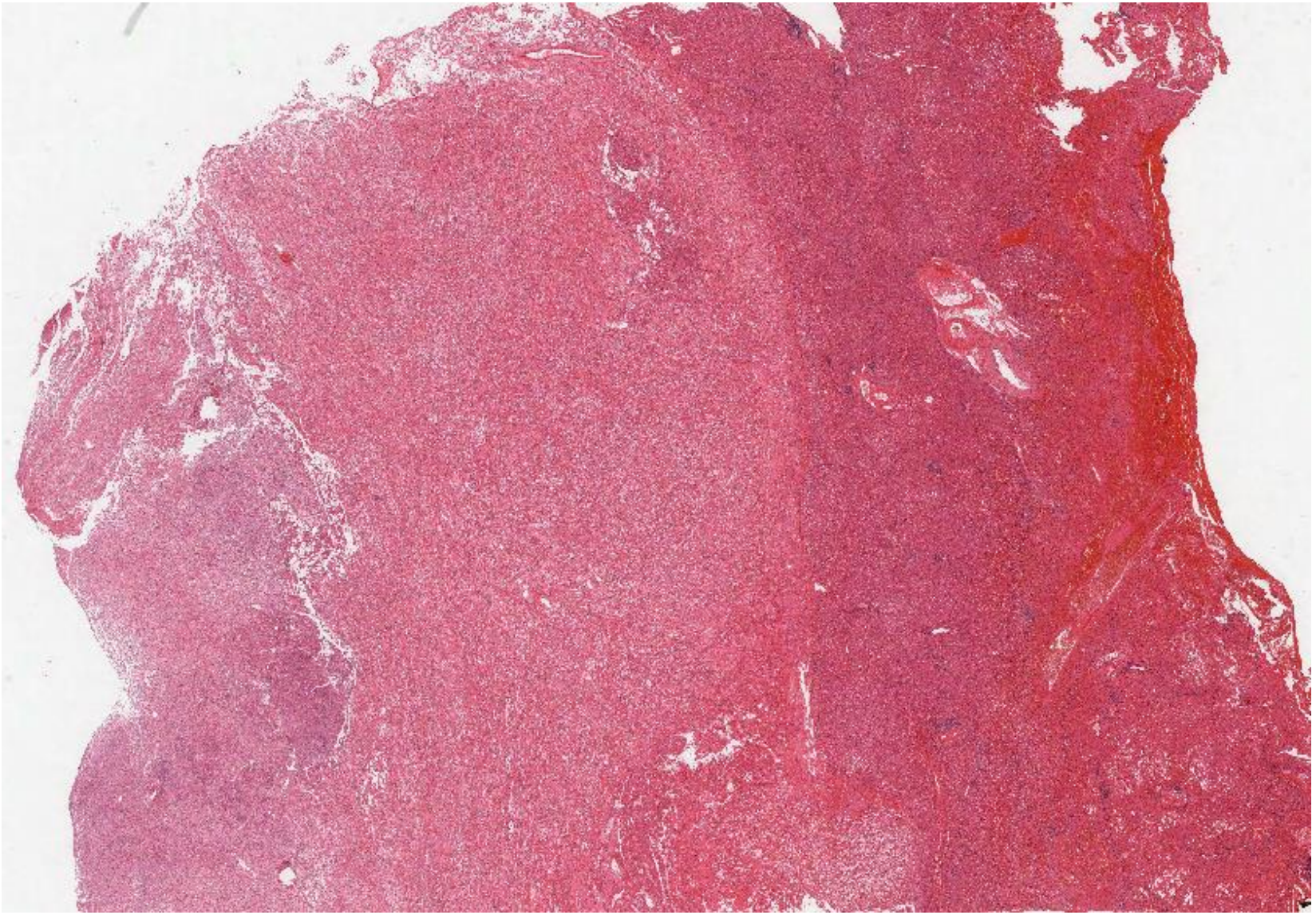
C Mild chronic hepatitis, with cholestasis, bridging fibrosis, drug induced

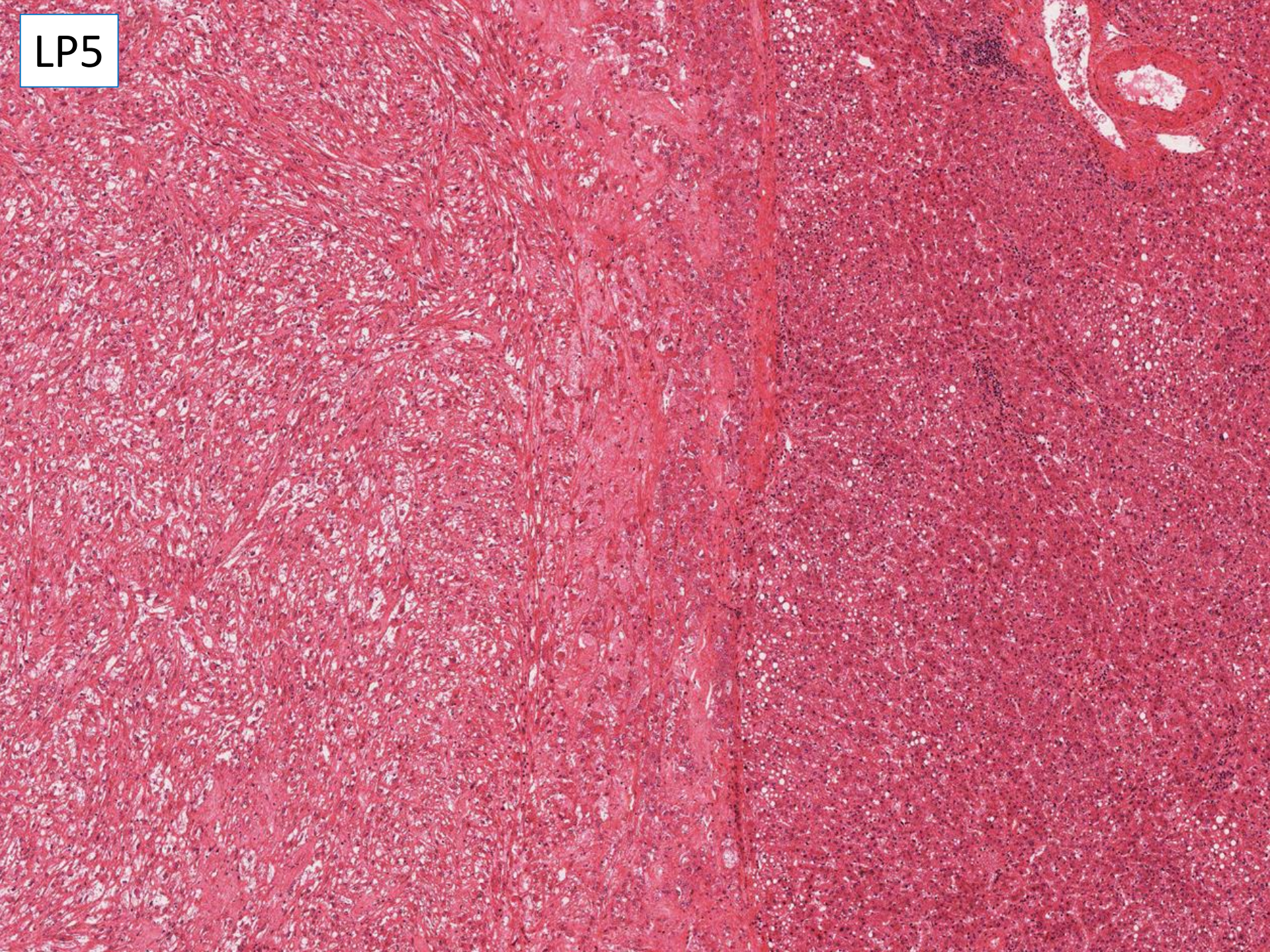
D Fibrosis and cholangitis, ? PSC

E Bland cholestasis, suspect inborn error e.g. BRIC

Case LP5 65F

Left Hepatectomy ? HCC Left Liver lobe weighing 238gm measuring 15.5x8x4.5cm. slicing shows a variegated tumour nodule 6.3cm dia

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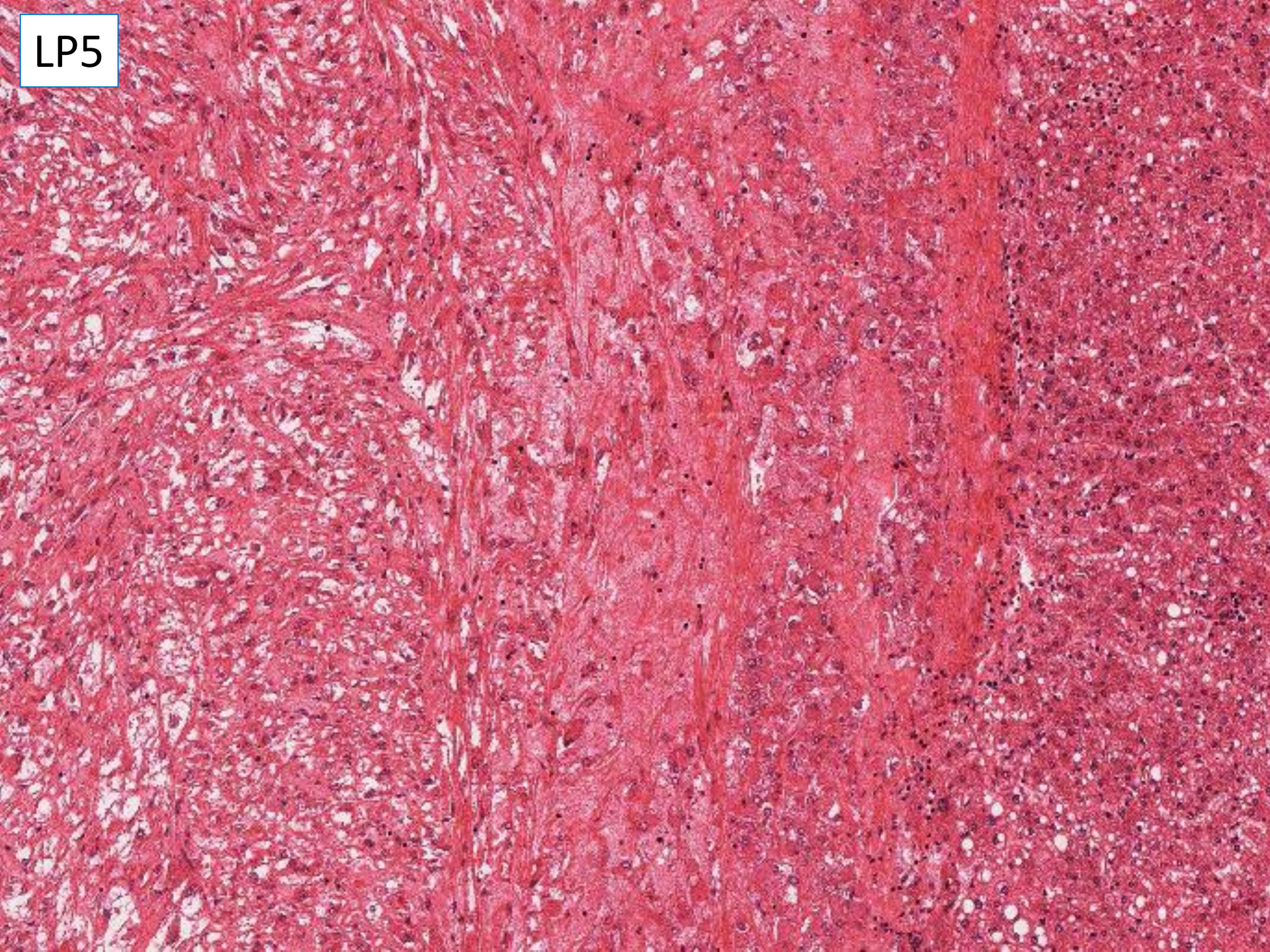
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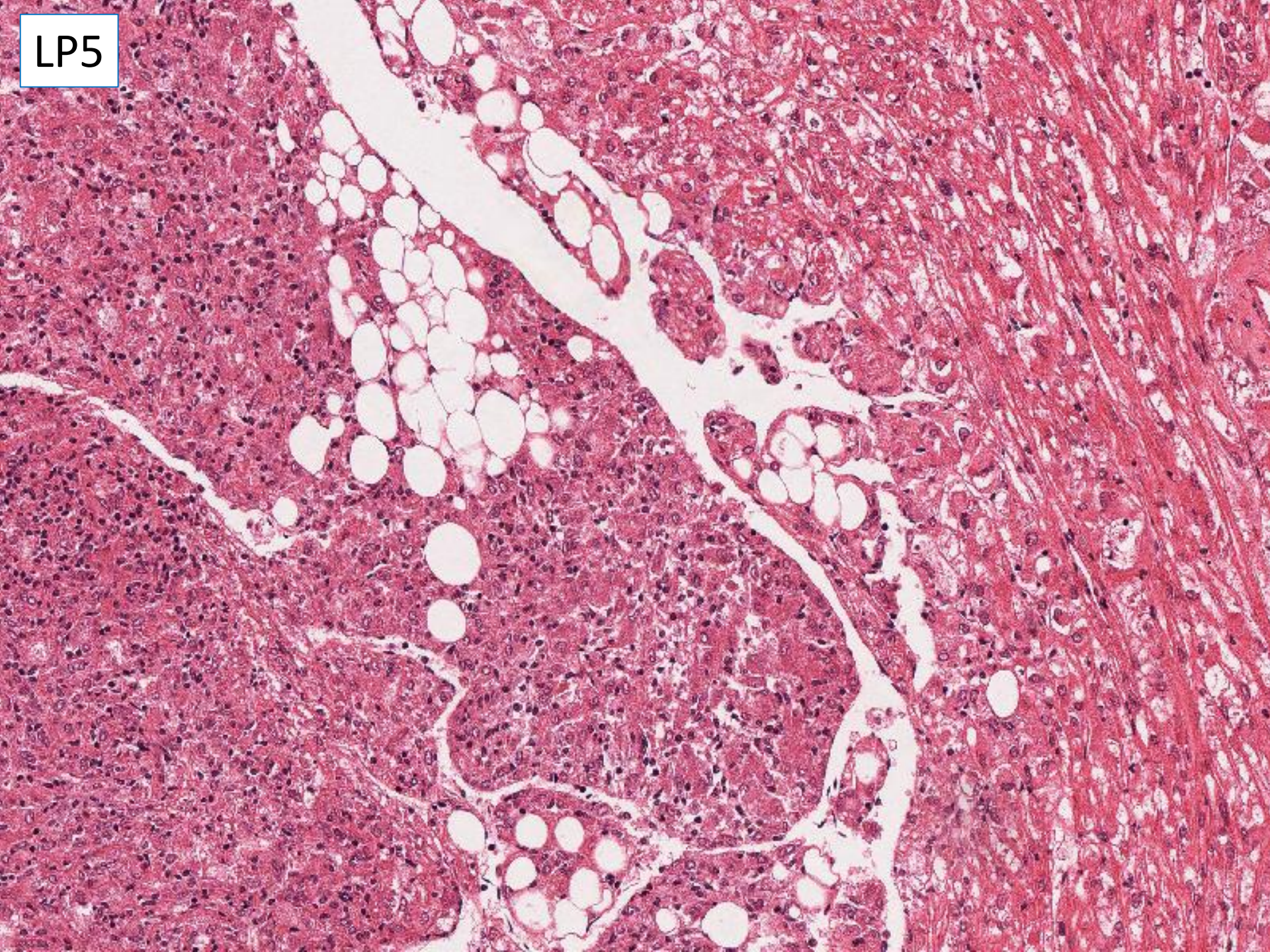
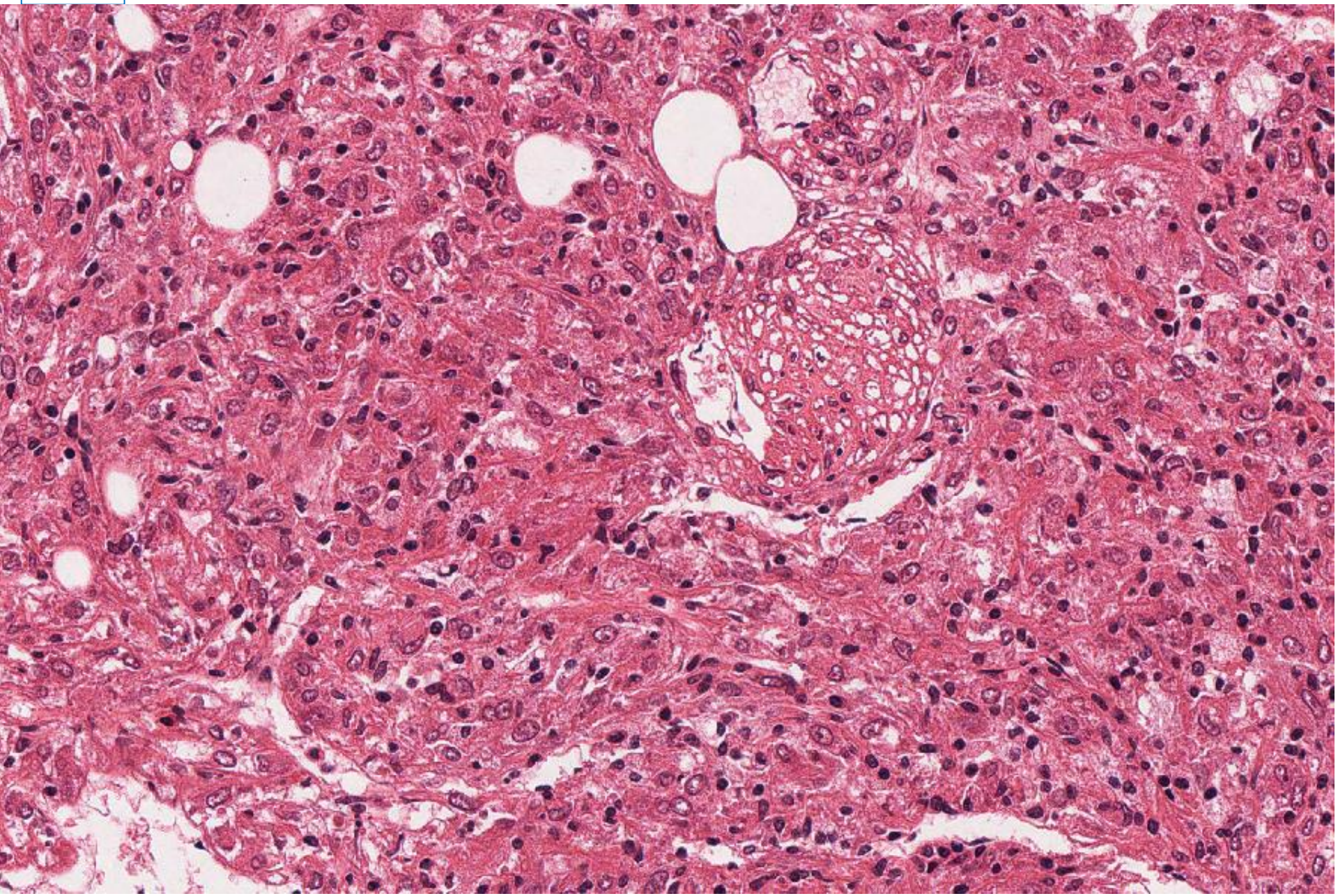
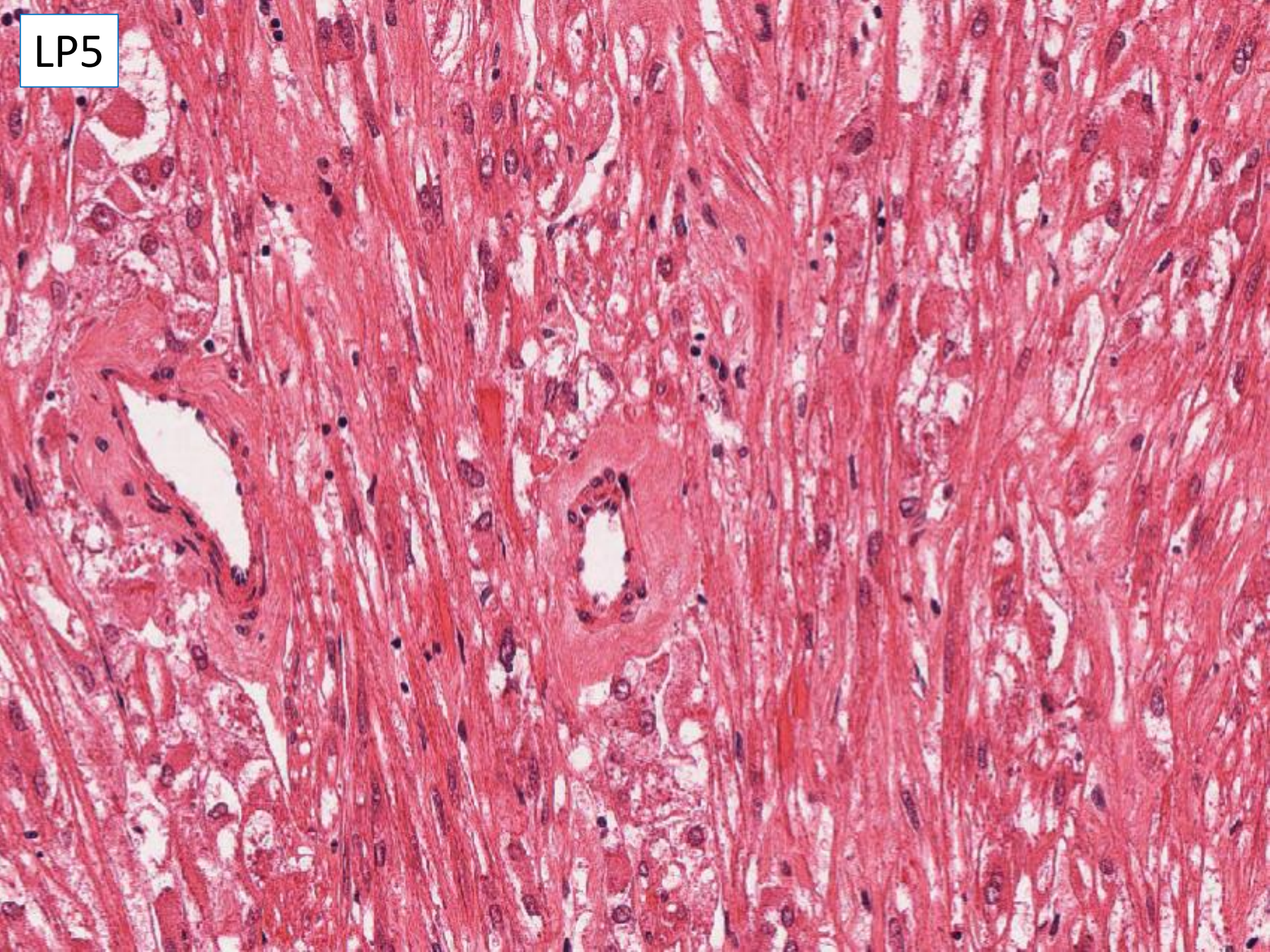

LP5

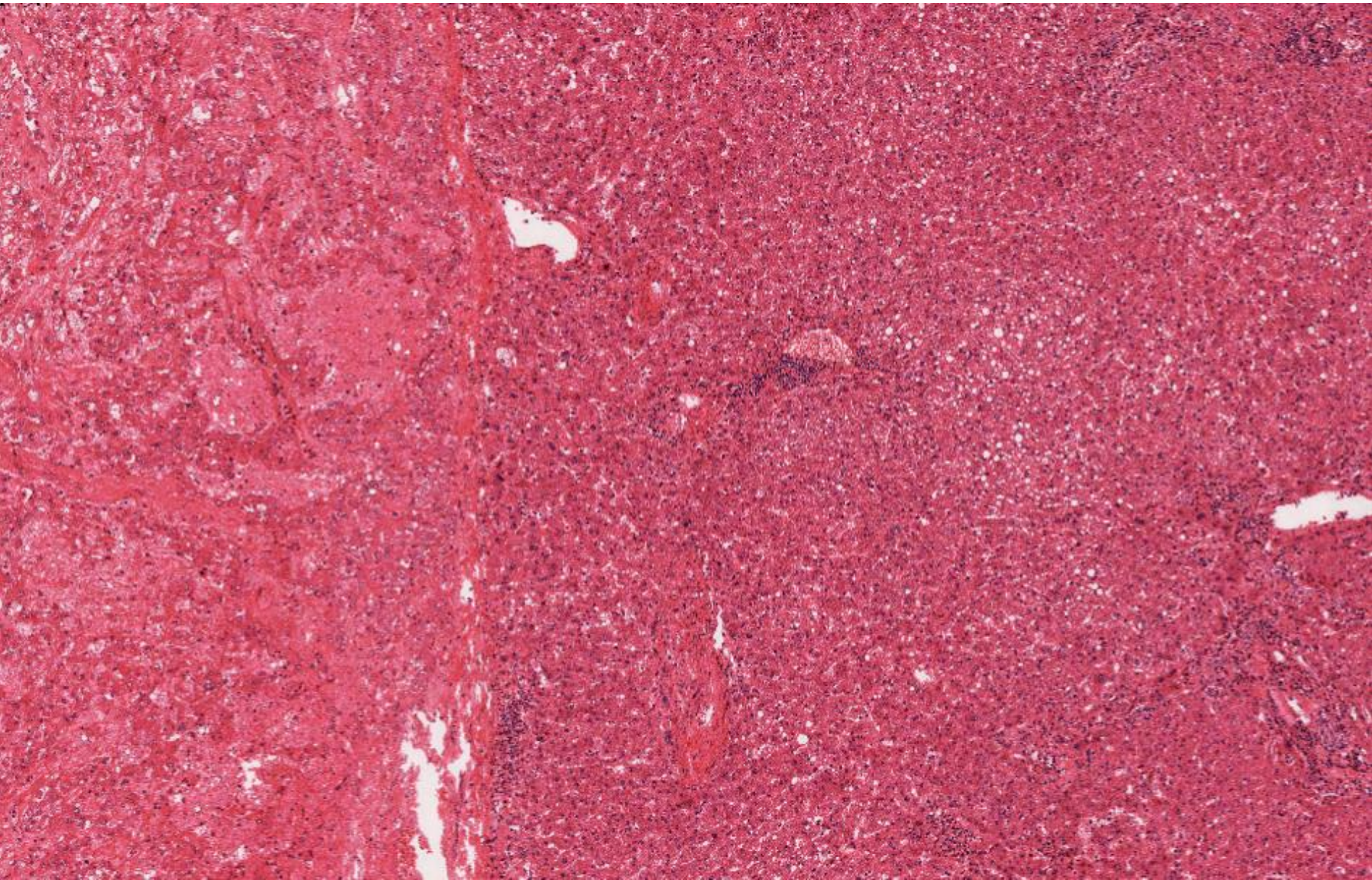
LP5




LP5

LP5

Edge of lesion, background liver



Case LP5 65F

Left Hepatectomy ? HCC Left Liver lobe weighing 238gm measuring 15.5x8x4.5cm. slicing shows a variegated tumour nodule 6.3cm dia

Angiomyolipoma	47
- of which required IHC confirmation	39
HCC, no IHC mentioned	19
(of which 6 suggested FLC, 8 sarcomatous)	
Favour HCC, for IHC to confirm	10
Differential diagnosis HCC v AML, for IHC	2
Kaposi sarcoma - for IHC	1
Malignant tumour, needs IHC	8
Not report without IHC - ? inflammatory myofibroblastic / infl. pseudotumour	1

Consensus response: angiomyolipoma,
but insufficient agreement, no suitable for scoring.

Case LP5 65F

Left Hepatectomy ? HCC Left Liver lobe weighing 238gm measuring 15.5x8x4.5cm. slicing shows a variegated tumour nodule 6.3cm dia

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Malignant tumour, needs IHC	8
Not report without IHC - ? inflammatory myofibroblastic / infl. pseudotumour	1

Consensus response:
angiomyolipoma,
but insufficient agreement, no suitable for scoring.

Comments: It was asked whether cases like this should be included without immunohistochemistry – and considered that they should – the point here is to suspect this is not a hepatocellular lesion and request immunos in the first place.

Also the question of including resection specimens which may be unfamiliar to members not receiving resections. This has been previously discussed – EQA members voted to include resection specimens, but with a maximum of 4 per EQA circulation.

Case LP5 65F

Left Hepatectomy ? HCC Left Liver lobe weighing 238gm measuring 15.5x8x4.5cm. slicing shows a variegated tumour nodule 6.3cm dia

A Hepatocellular carcinoma - sarcomatous

B Angiomyolipoma

C Kaposi sarcoma

D Fibrolamellar type of HCC

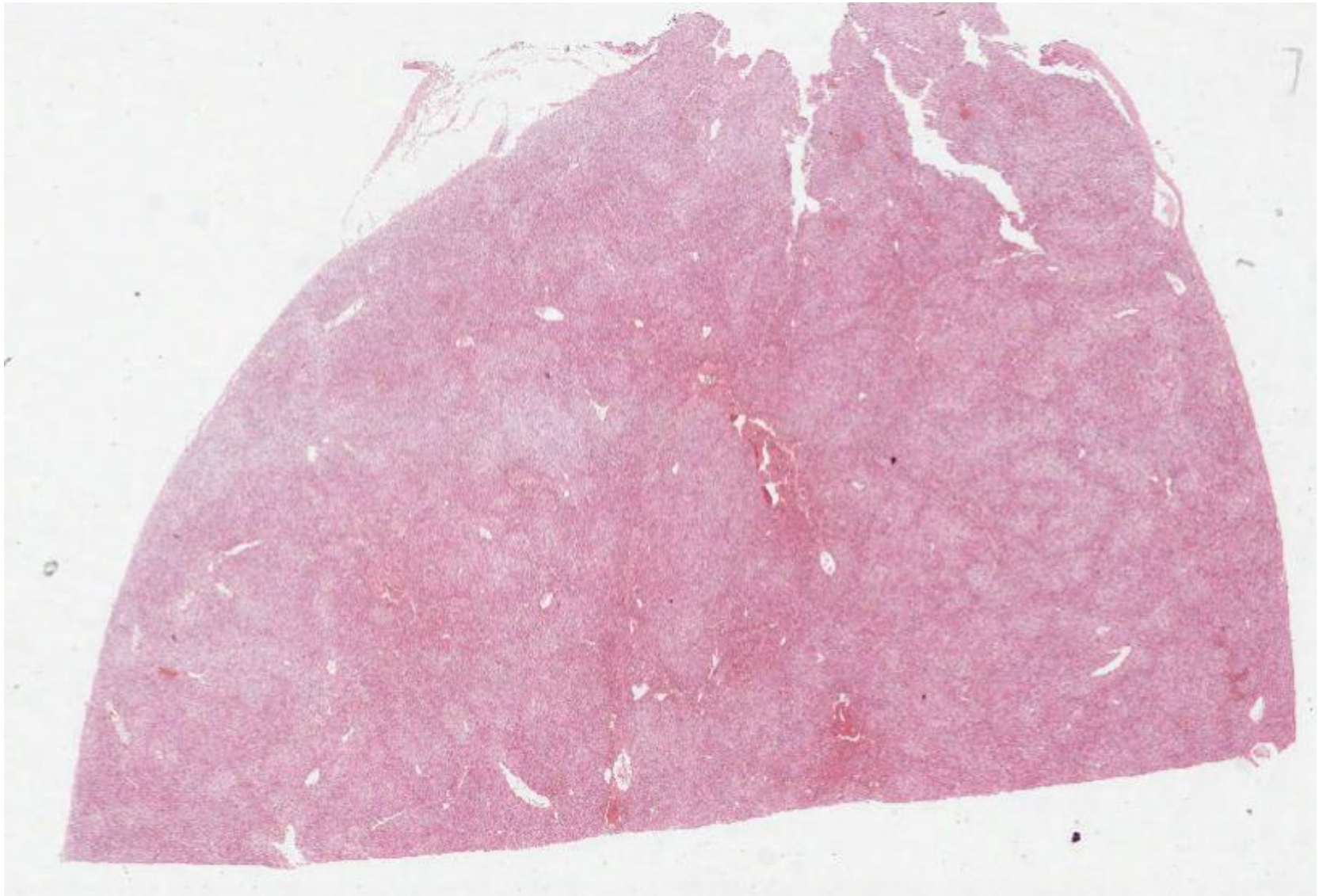
E Malignant tumour ? what, needs immunos

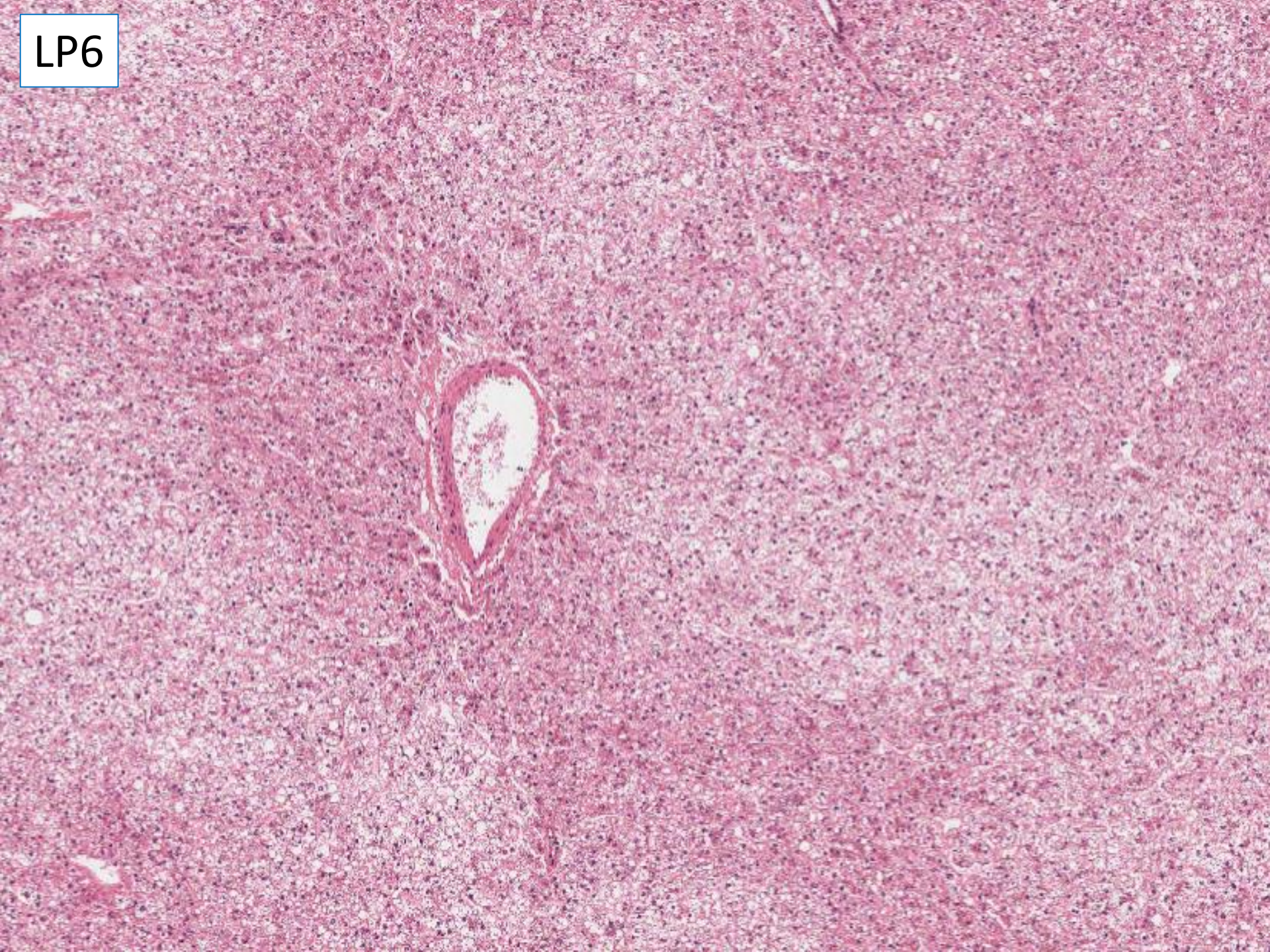
Masterclass slides: angiomyolipoma. Ali Winstanley

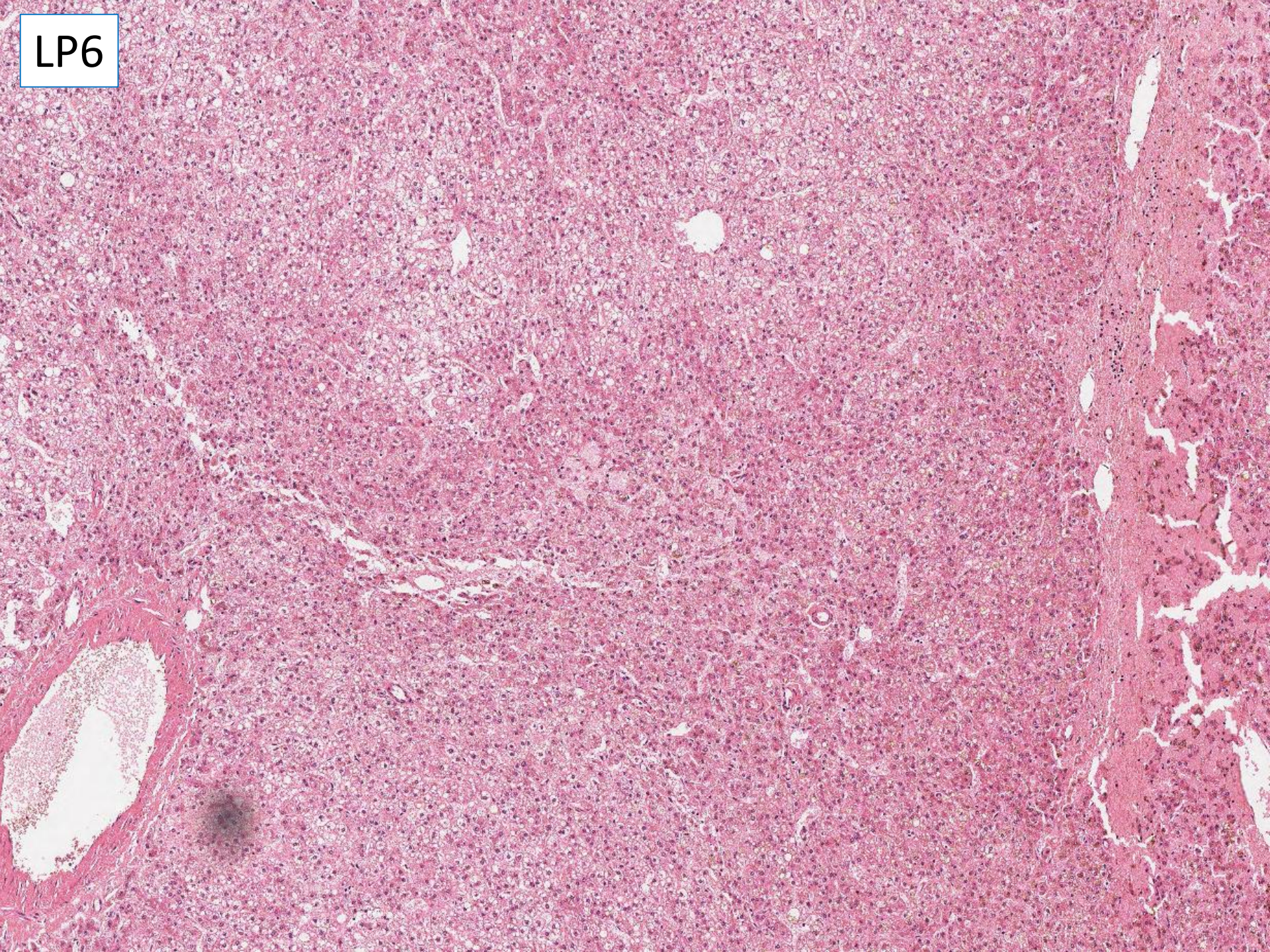
- at the end, after case LP12

Case LP6. 31F

Incidental finding right upper quadrant. Wedge resection.
Pedunculated nodule measuring 55mm max




LP6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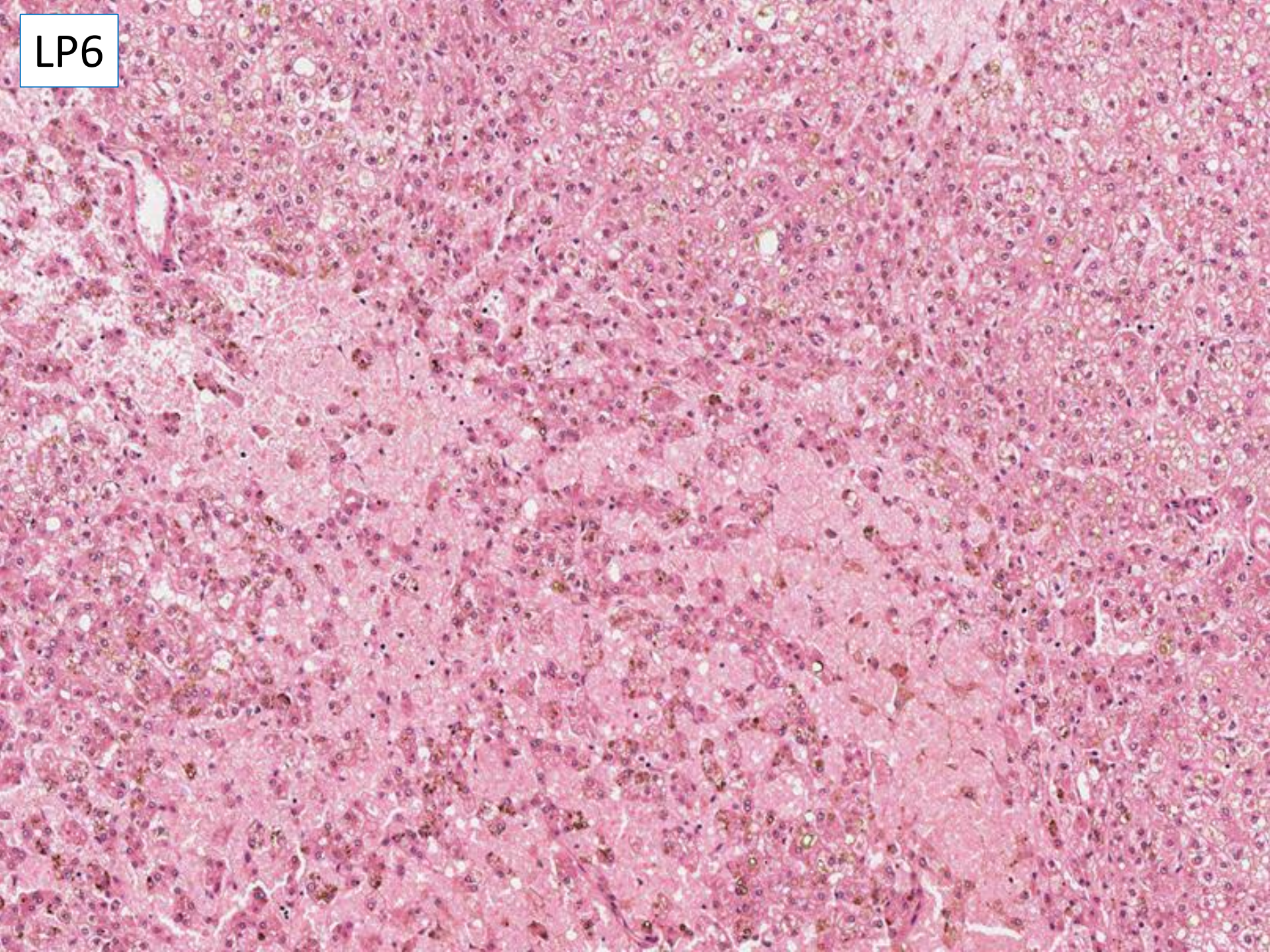
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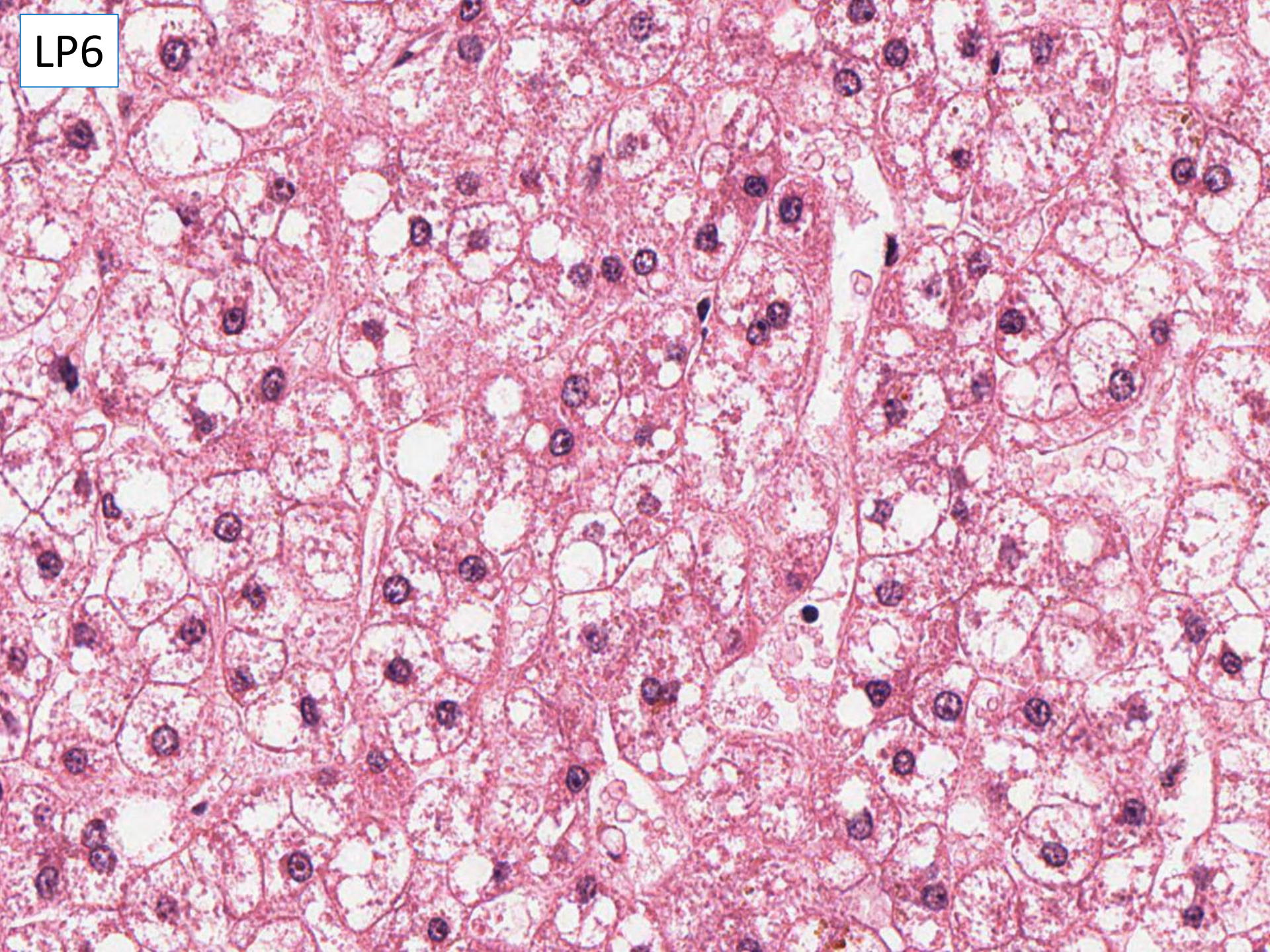

LP6

Case LP6. 31F

Incidental finding right upper quadrant. Wedge resection.

Pedunculated nodule measuring 55mm max

Hepatocellular adenoma (HCA) NOS	48
Of which - 27 no IHC, 21 needs IHC	
HCA with suggested subtype	18
Of which – inflammatory = 8, telangiectatic = 1, steatotic = 7, steatotic or telangiectatic = 2	
Liver cell adenoma (LCA)	9
Focal nodular hyperplasia (FNH)	2
Well differentiated hepatocellular lesion, HCA v HCC, favour HCA	8
Focal nodular hyperplasia v liver cell adenoma	1
HCA v nodular regenerative hyperplasia v macroregenerative nodule	1
'the appearances are of a hepatic adenoma / hepatoma'	1

Consensus complete diagnosis:
hepatocellular adenoma (current terminology, favoured over liver cell adenoma) with recognition that these can be further characterised – based on immunohistochemistry +/- a suggestion of type based on morphology.

Case LP6. 31F

Incidental finding right upper quadrant. Wedge resection.
Pedunculated nodule measuring 55mm max

Agreed Scoring:

For full marks – a diagnosis of hepatocellular adenoma (preferred terminology) as definite or preferred diagnosis, or liver cell adenoma.

Score 0 for focal nodular hyperplasia, or a differential with nodular regenerative hyperplasia (a diffuse abnormality, not a focal lesion).

'Hepatoma' should not be used – this is an outdated term for hepatocellular carcinoma.

Hepatocellular adenoma is now subdivided based on morphology and immunohistochemistry – those results are not available in this case, which was an old case, diagnosed before immunohistochemistry was available.

Discussion: The terminology 'well differentiated hepatocellular lesion' should be used only for HCA where immunohistochemistry fails to identify the subtype of adenoma, and/or with atypia where there is real uncertainty between hepatocellular adenoma and well differentiated HCC. These are particularly seen in patients with an underlying vascular abnormality (e.g. Budd Chiari) or with a history of androgen exposure.

Terminologies such as 'atypical adenoma' or 'hepatocellular lesion of uncertain malignant potential (HUMP) are in use for such lesions, which are rare.

Case LP6. 31F

Incidental finding right upper quadrant. Wedge resection. Pedunculated nodule measuring 55mm max

A Liver cell adenoma

B Focal nodular hyperplasia

C Well differentiated HCC

D Hepatocellular adenoma, telangiectatic type

E Hepatocellular adenoma, needs immunos to subtype

Case LP6. 31F

Incidental finding right upper quadrant. Wedge resection.
Pedunculated nodule measuring 55mm max

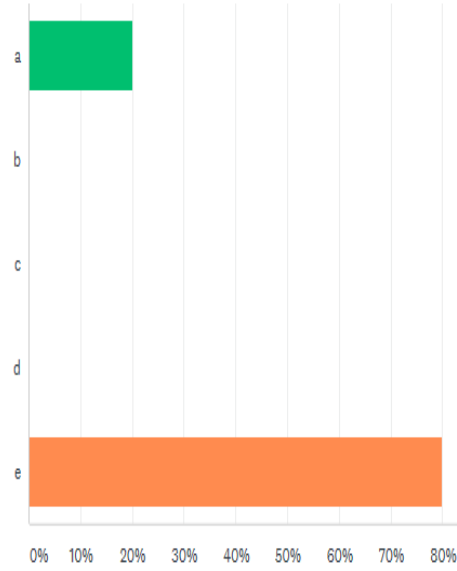
A Liver cell adenoma

B Focal nodular hyperplasia

C Well differentiated HCC

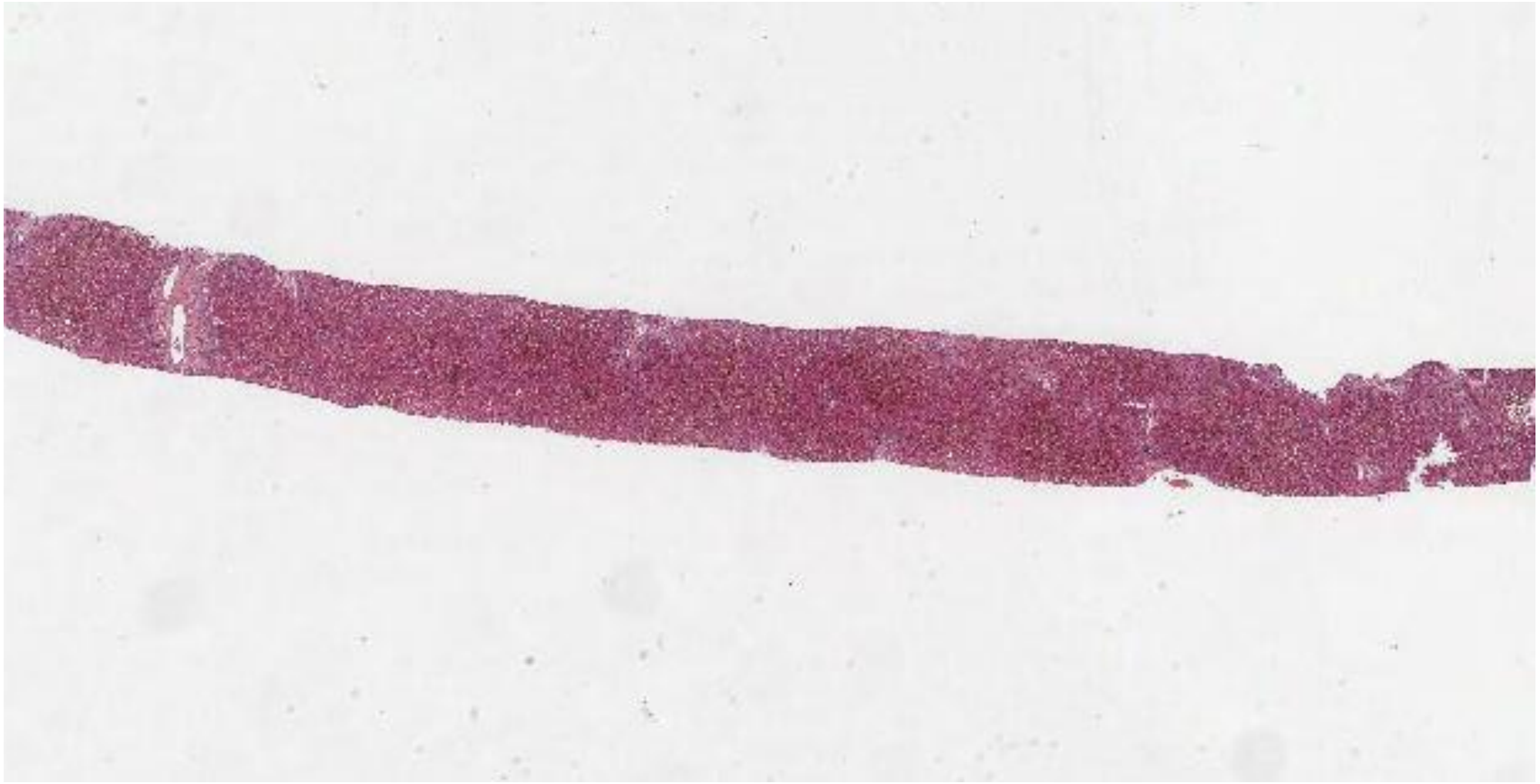
D Hepatocellular adenoma, telangiectatic type

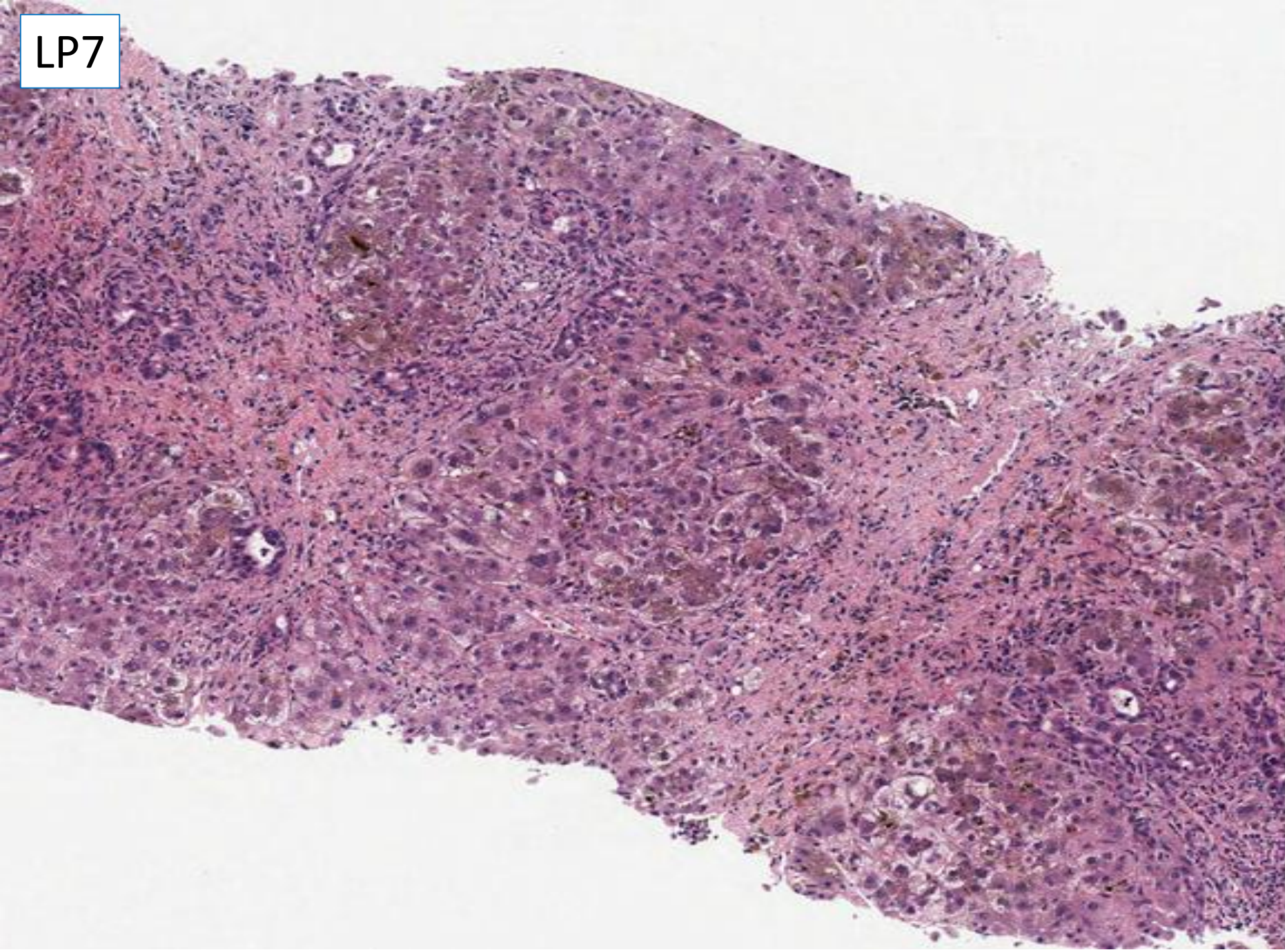
E Hepatocellular adenoma, needs immunos to sub



Case LP7 61M

Paracetamol overdose - liver failure.

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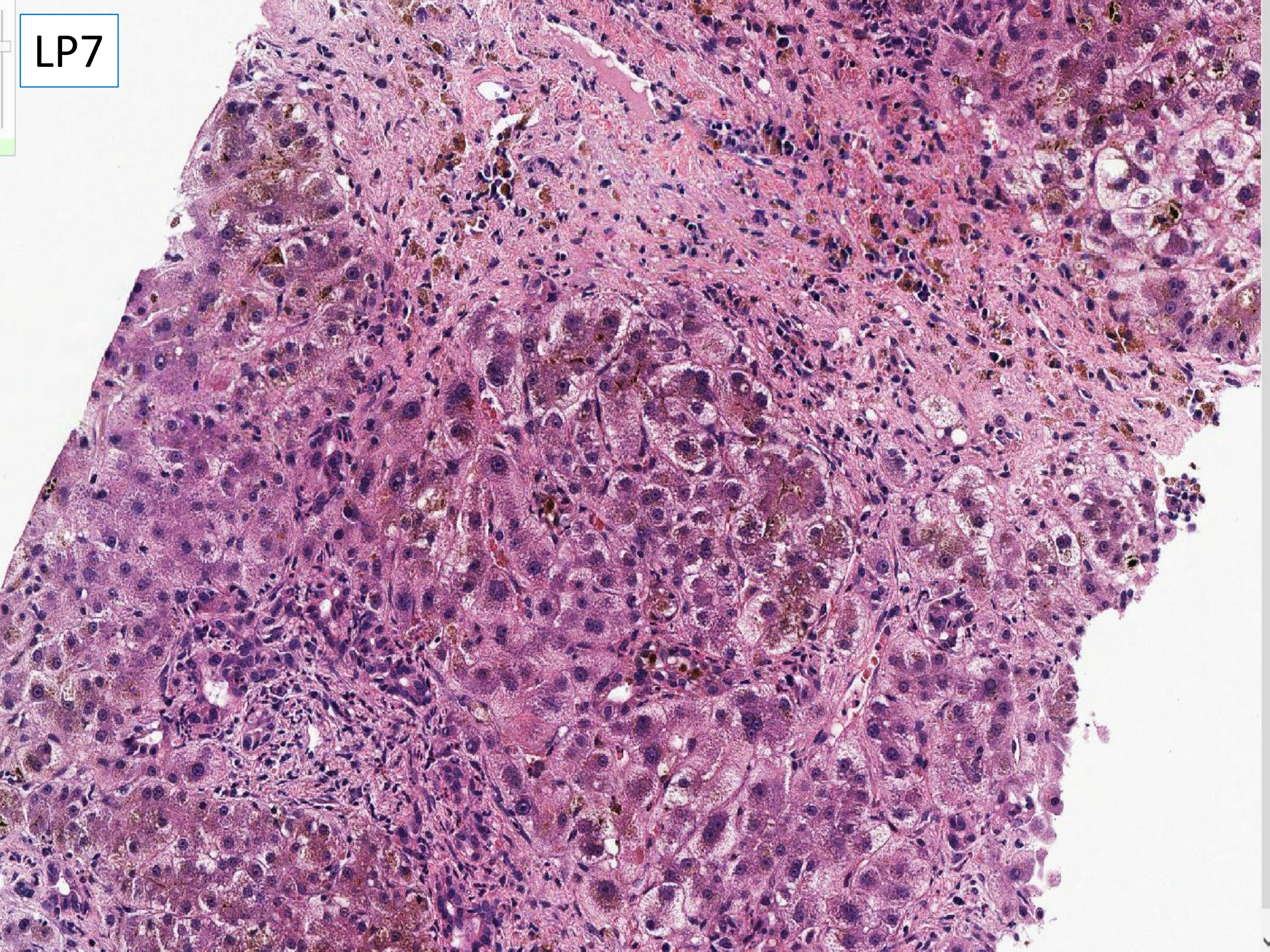
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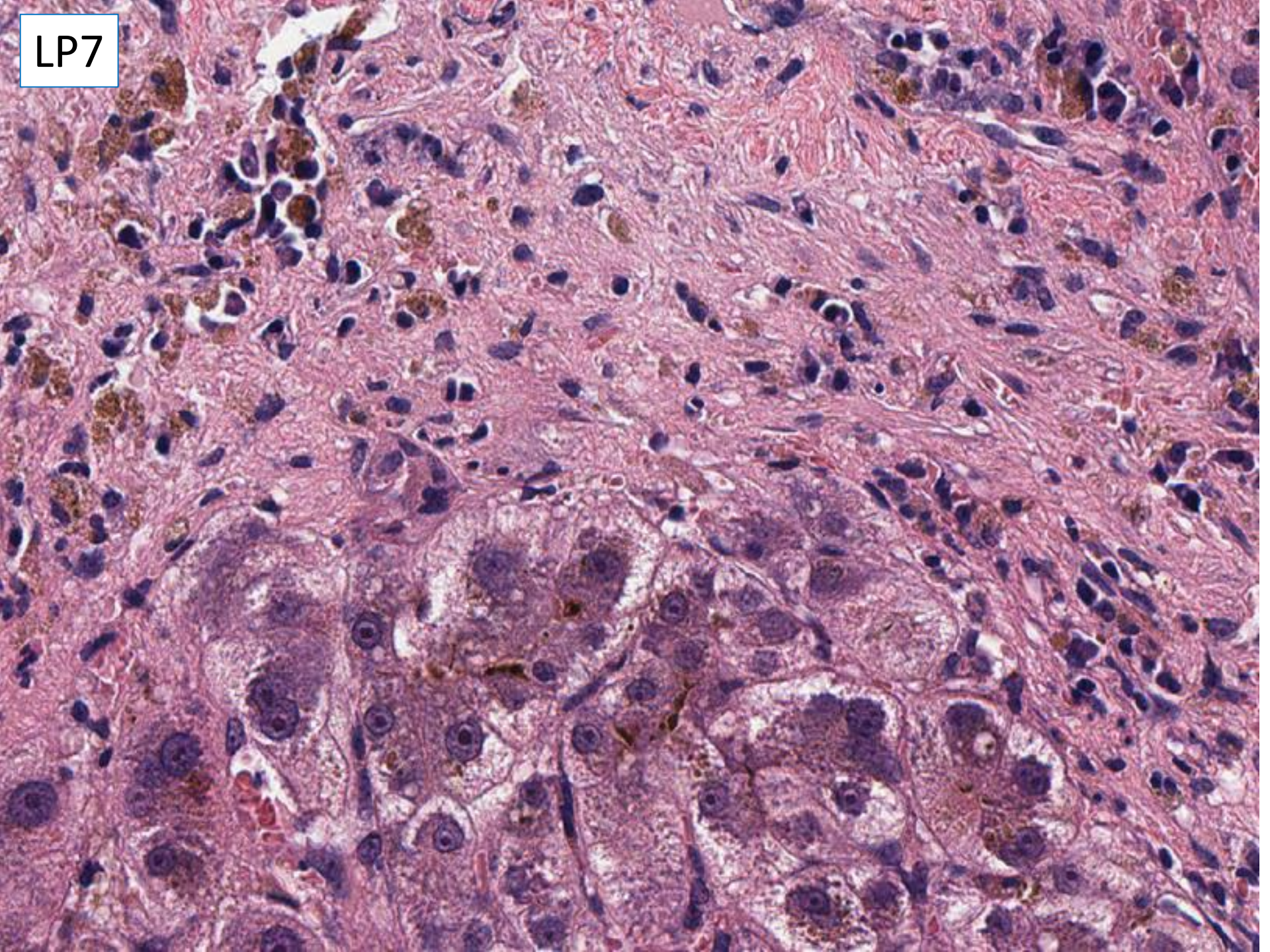
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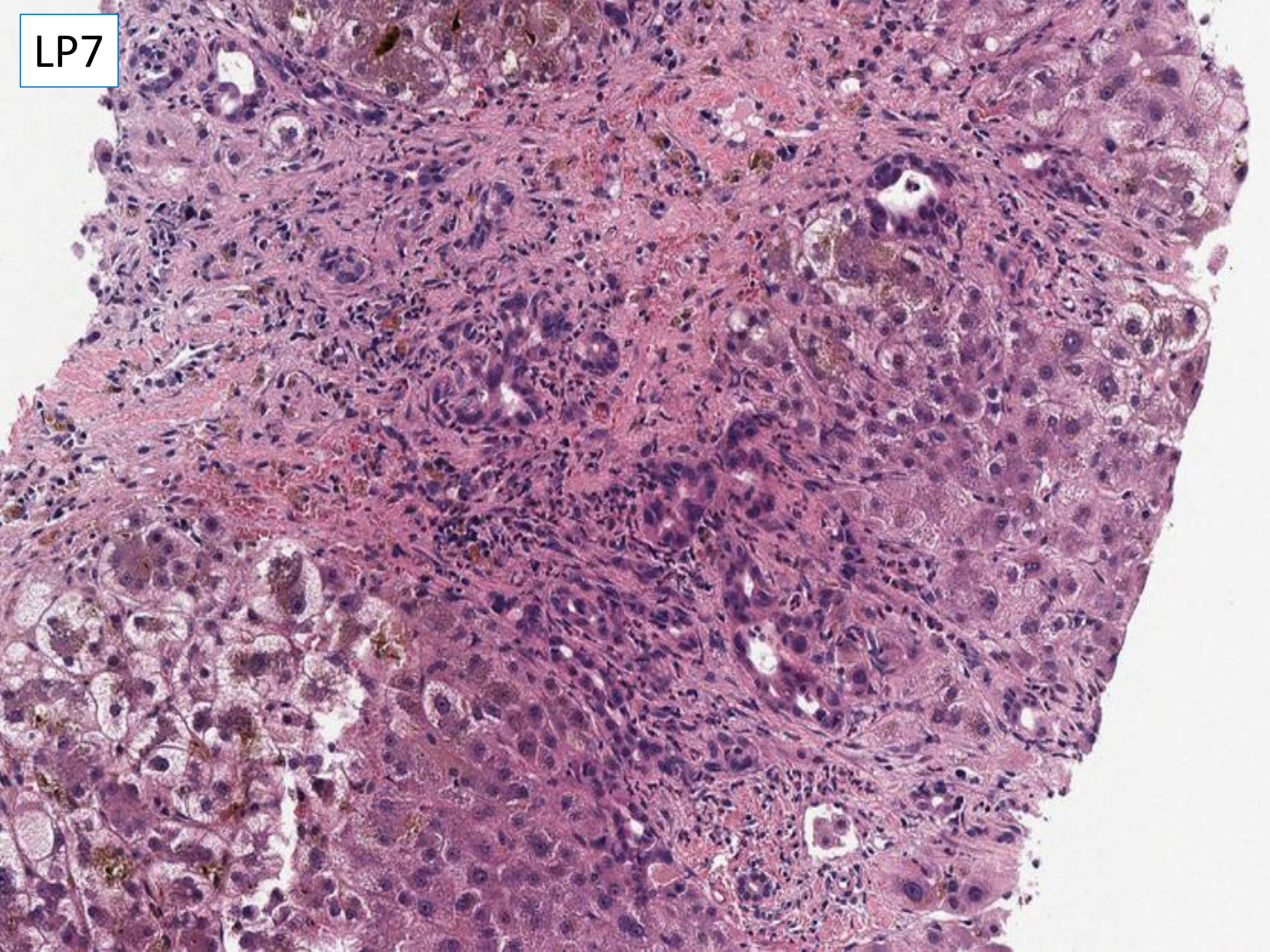
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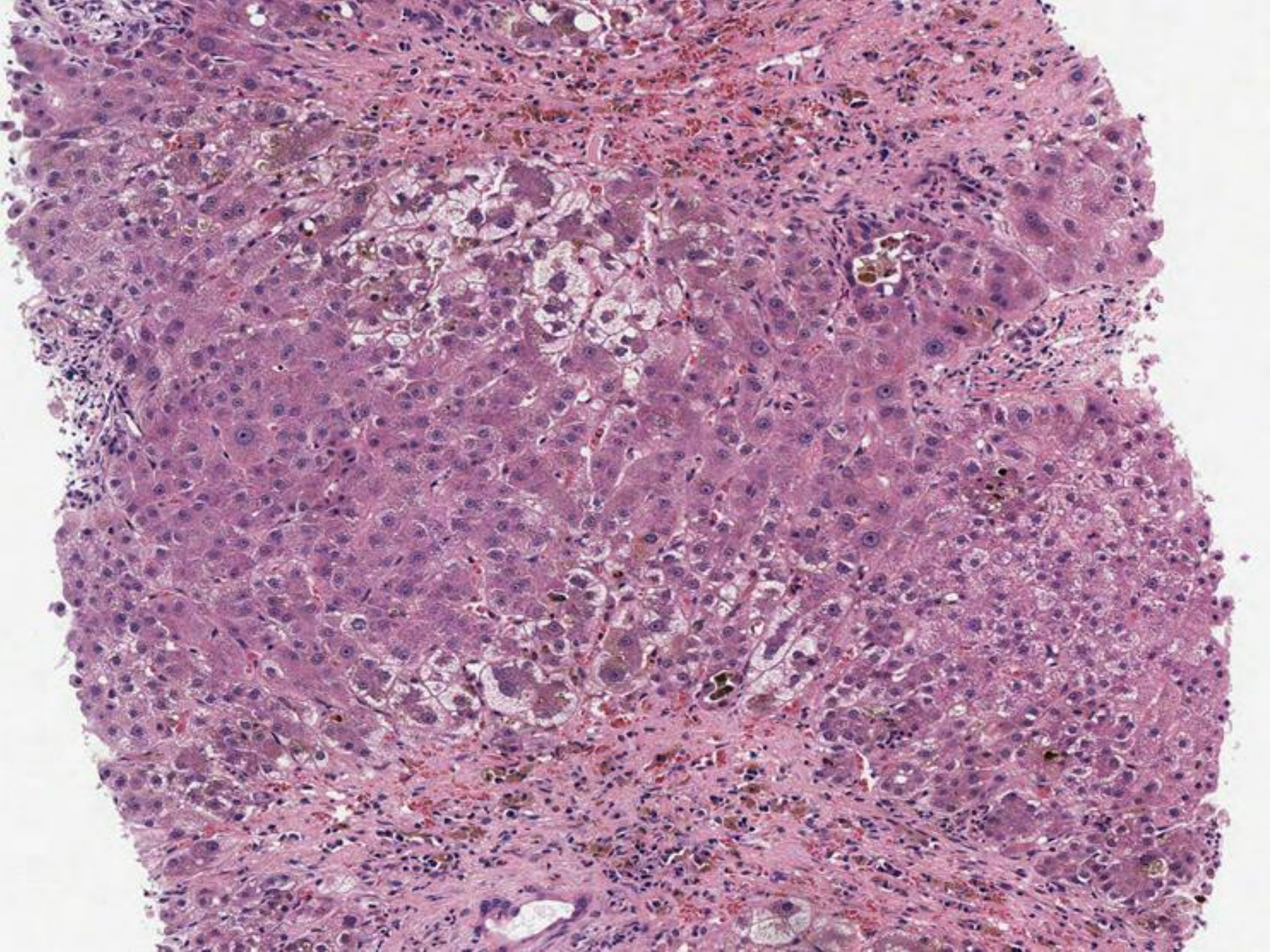

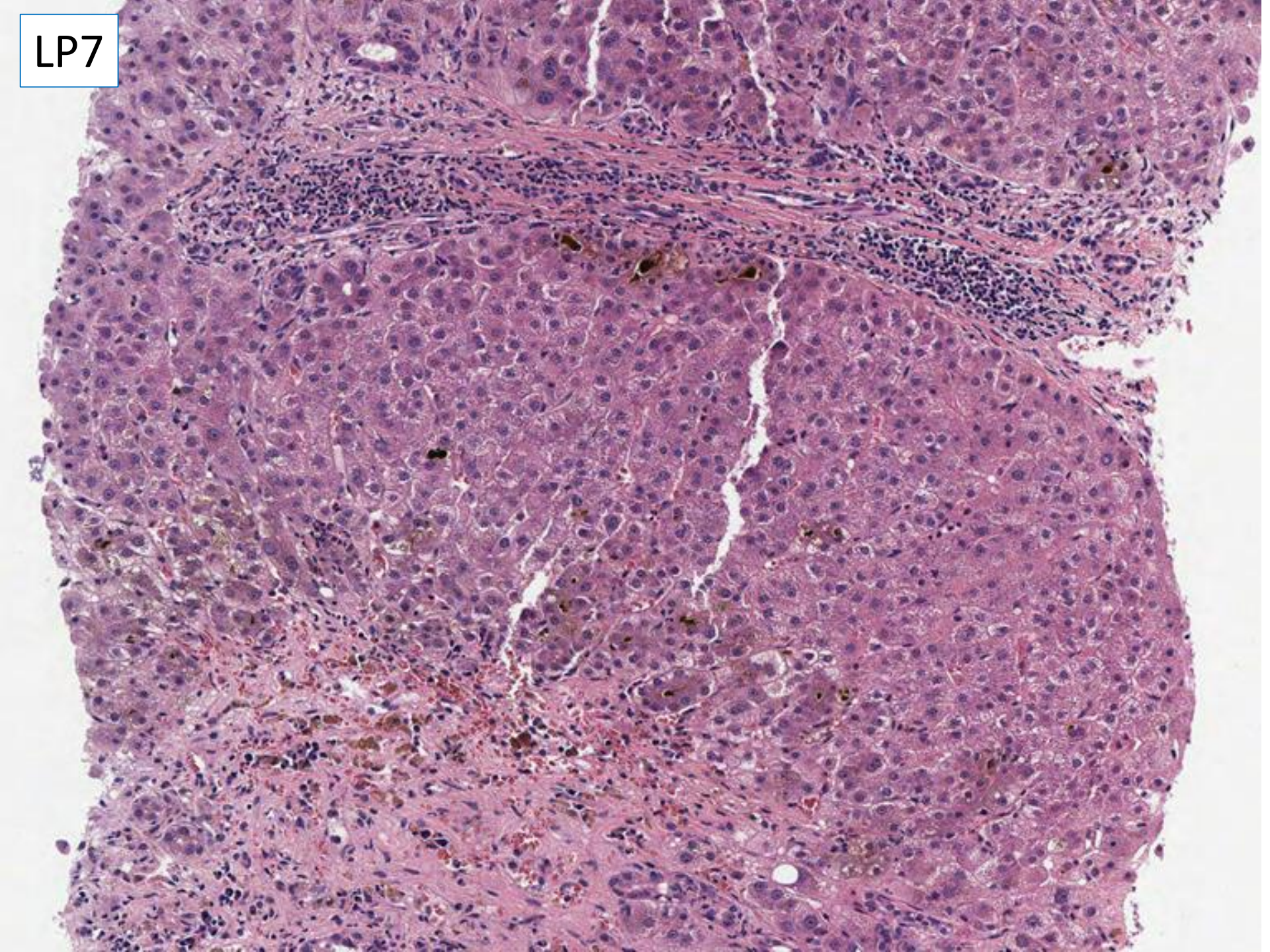
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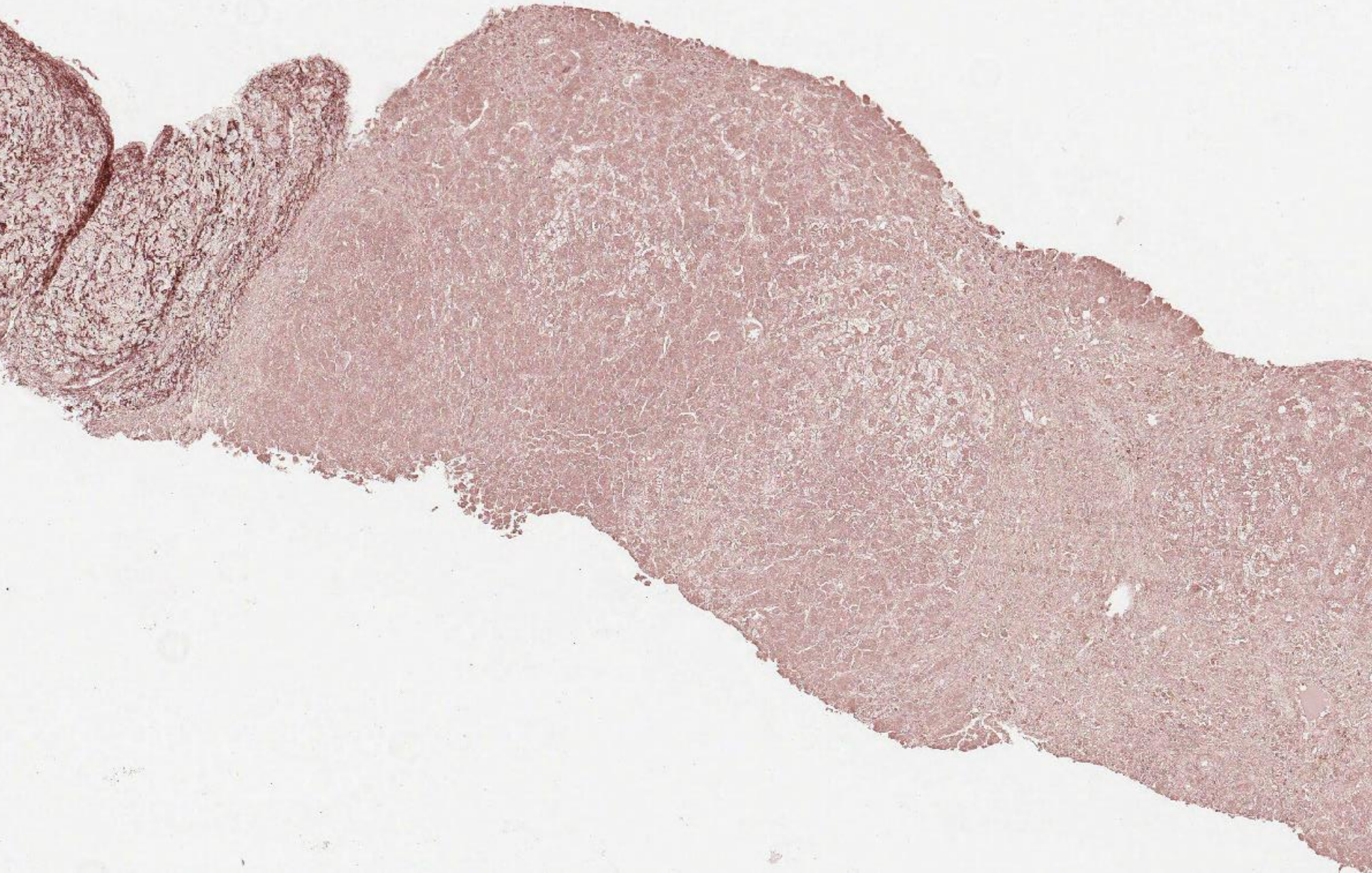
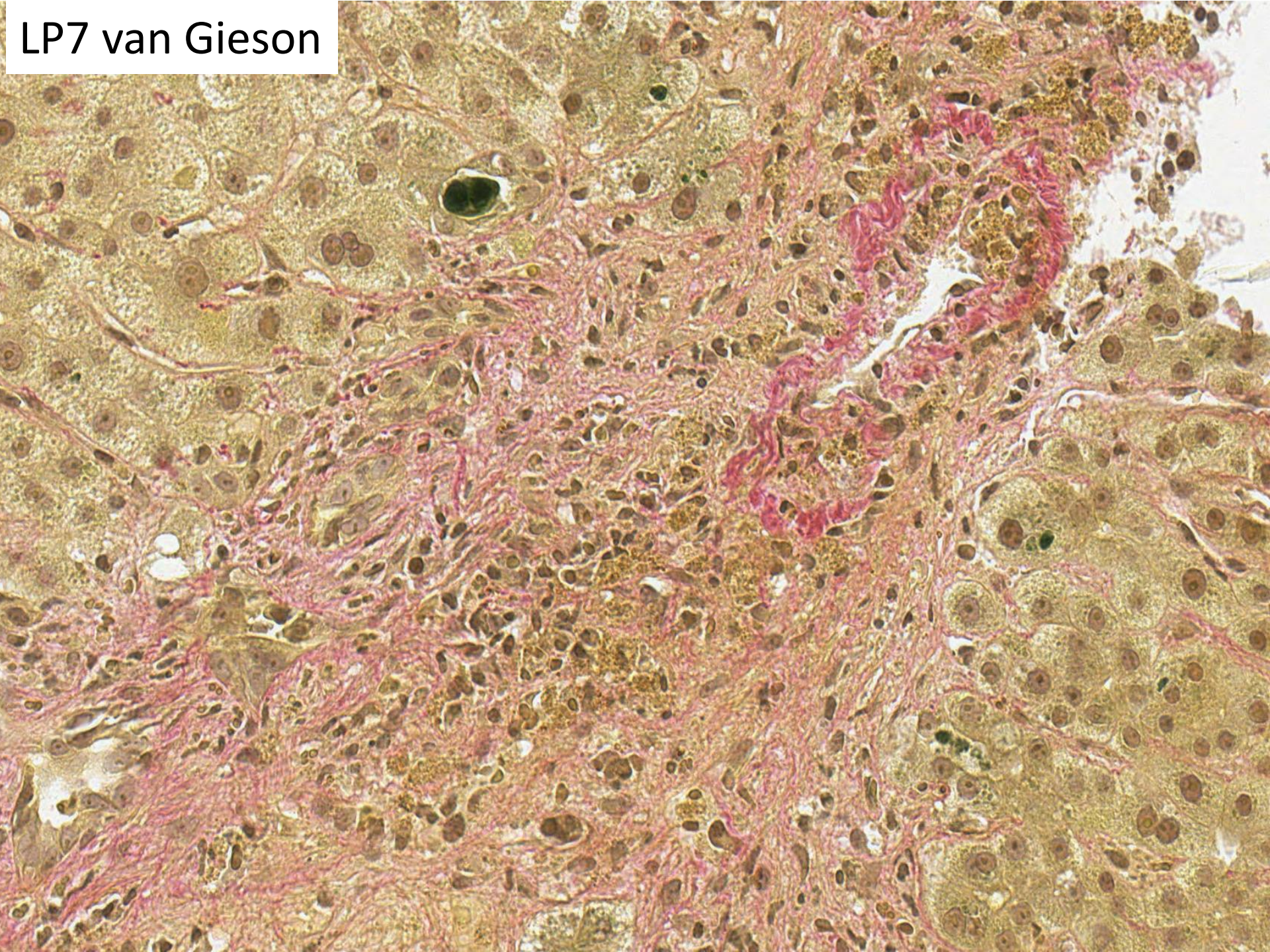
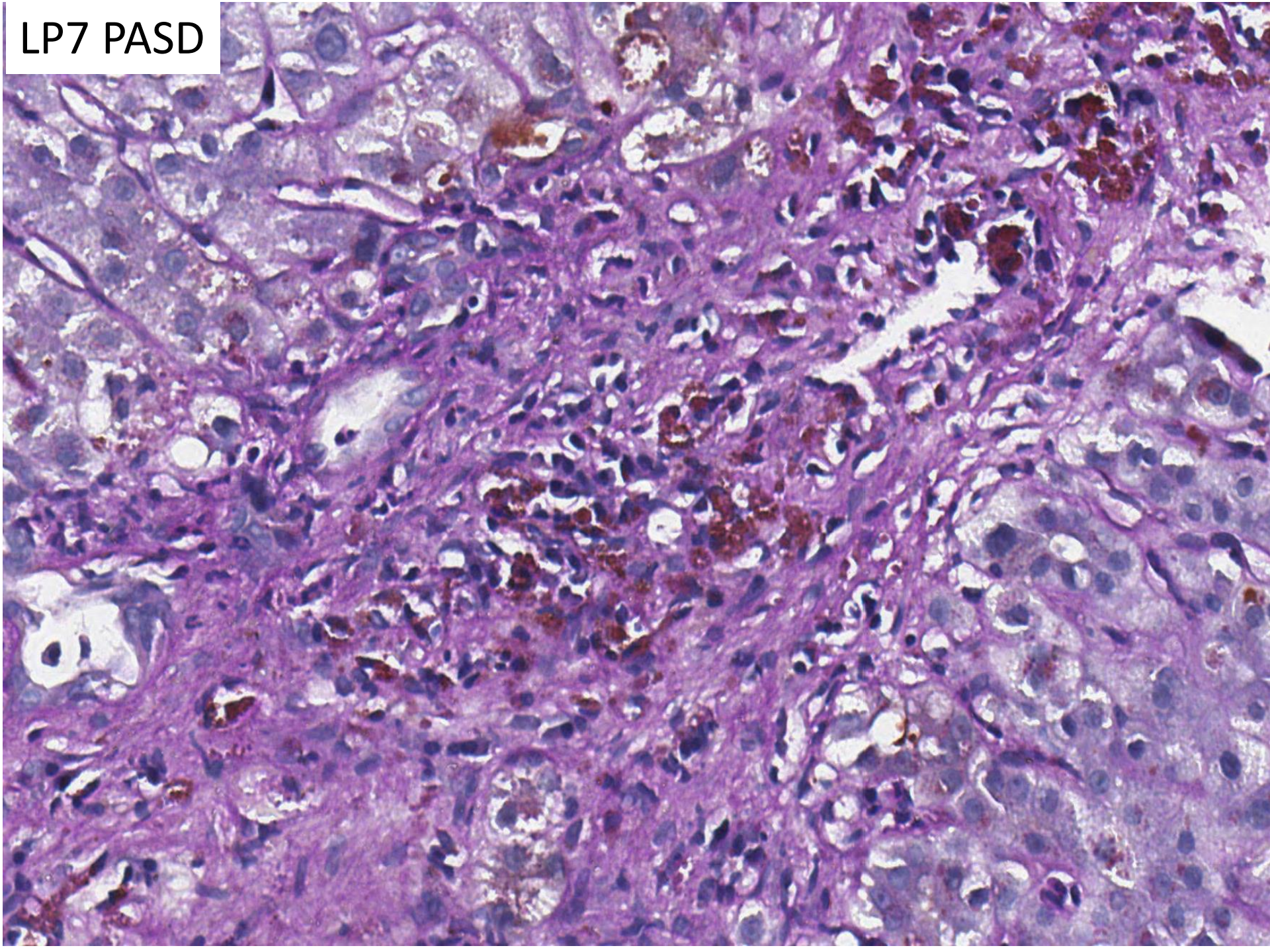
LP7 Shikata



LP7 van Gieson




LP7 PASD

Case LP7 61M

Paracetamol overdose - liver failure.

cholestasis	78
Zonal necrosis	55
No necrosis	1
Cholestatic hepatitis	9
Aetiology:	
Drug induced liver injury (DILI) – paracetamol NOS	49
DILI – paracetamol – delayed effects	18
Drugs not mentioned	3
Drug induced liver injury – paracetamol not mentioned	7
Not typical of paracetamol – various alternatives suggested, or need to exclude other diagnoses	12
c/w paracetamol but pre-existing chronic liver disease/cirrhosis	8
Not paracetamol - ? biliary disease,	3
Not paracetamol - ? autoimmune hepatitis	1
'acute severe hepatitis ? drugs/virus/AIH', with Ishak score	2

Consensus complete diagnosis includes - cholestasis and previous necrosis
– attributable to paracetamol toxicity, suggesting time frame of a few weeks (delayed effects).

Difficult case to score – may be unsuitable for scoring. There was insufficient clinical information relating to the time frame of paracetamol overdose to biopsy.

Could include if response indicates that the changes are attributable to paracetamol toxicity rather than a different cause.

Case LP7 61M

Paracetamol overdose - liver failure.

		Survey result:		
		10	5	0
cholestasis	78			
Zonal necrosis	55			
No necrosis	1	0	1	7
Cholestatic hepatitis	9			
Aetiology:				
Drug induced liver injury (DILI) – paracetamol NOS	49			
DILI – paracetamol – delayed effects	18			
Drugs not mentioned	3	0	0	9
Drug induced liver injury – paracetamol not mentioned	7	0	9	0
Not typical of paracetamol – various alternatives suggested, or need to exclude other diagnoses	12			
c/w paracetamol but pre-existing chronic liver disease/cirrhosis	8			
Not paracetamol - ? biliary disease,	3	0	0	8
Not paracetamol - ? autoimmune hepatitis	1	0	1	8
'acute severe hepatitis ? drugs/virus/AIH', with Ishak score	2	1	5	3

Could include if response indicates that the changes are attributable to paracetamol toxicity rather than a different cause. Suitable for scoring: yes 8/10

Case LP7 61M

Paracetamol overdose - liver failure.

Agreed scoring:

On a show of hands, this case was considered suitable for scoring.

For full marks – include necrosis and that the liver injury is attributable to paracetamol.

Score 0 for responses that state there is no necrosis, and those which don't include any mention of drugs as a cause of the liver injury, or which specifically indicate the features are not attributable to paracetamol.

Score 5 points for drug induced liver injury but not mentioning paracetamol, and for the responses 'acute severe hepatitis, ? Drugs/virus/AIH' with Ishak score.

Discussion: in practice, this case would not be reported without additional clinical information, and therefore inclusion in an EQA is artificial. Nevertheless members voted to include this case for scoring.

Further history – this biopsy was taken about 4 weeks after a staggered paracetamol overdose. It is unusual to take a liver biopsy at this time – in view of the slow recovery, the clinicians wanted to determine whether there had been previous chronic liver disease, or whether the liver injury was all a consequence of paracetamol toxicity.

Case LP7 61M

Paracetamol overdose - liver failure.

A Cholestatic hepatitis ? viral

B Acute severe hepatitis ? drug/virus/AIH

C previous necrosis, cholestasis, consistent with previous paracetamol toxicity

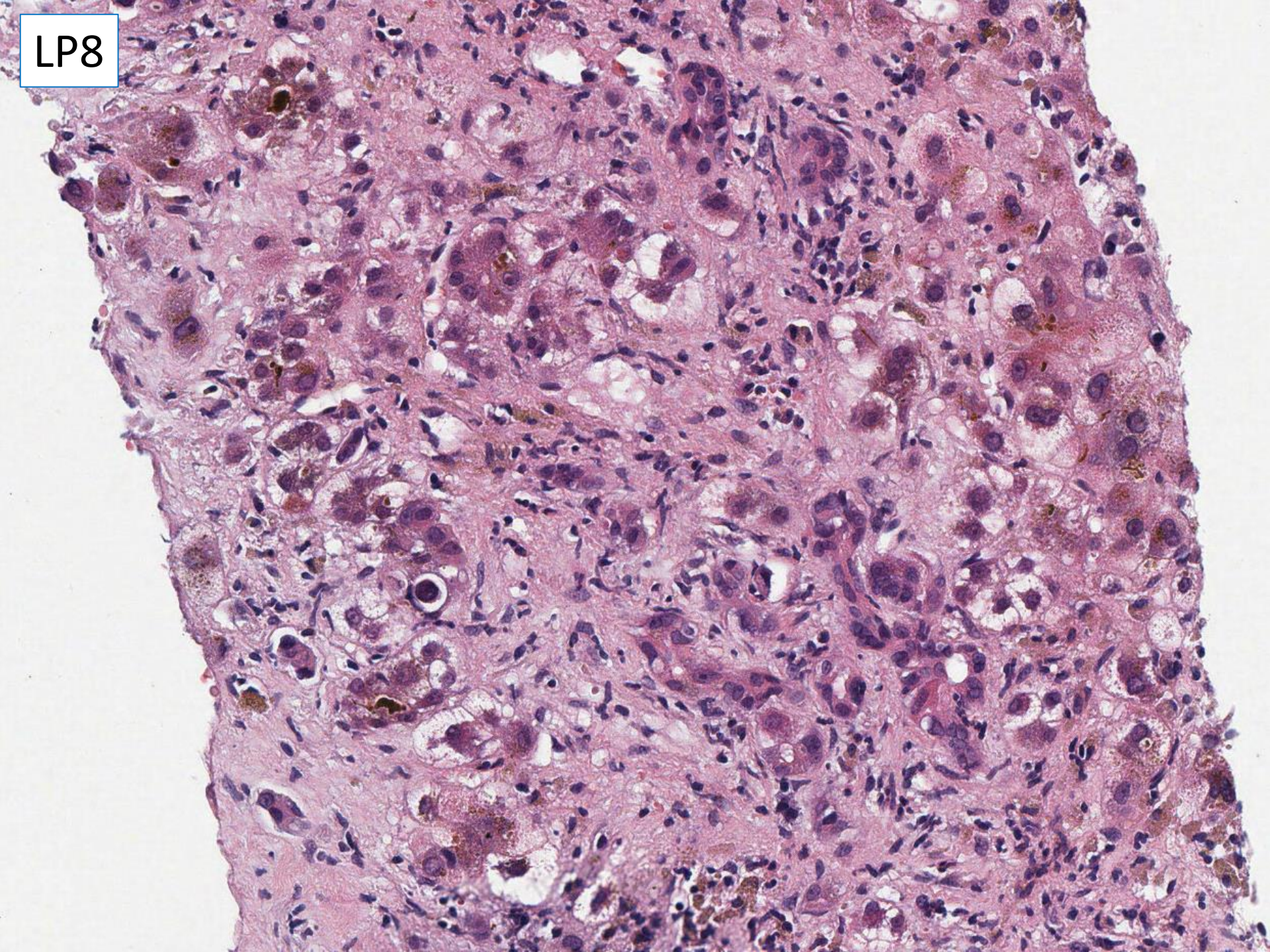
D Not typical of paracetamol, ? large bile duct obstruction

E Autoimmune hepatitis/biliary overlap

Case LP8 49F

jaundice for 3 weeks, no known history of liver disease. raised calcium, cause unclear. CT/MRI suggests possible chronic liver disease with acute element, however, subacute. bilirubin 180, ALP 819, ALT 59. ?chronic liver disease ?aetiology ?subacute hepatitis. liver aetiology screen negative


LP8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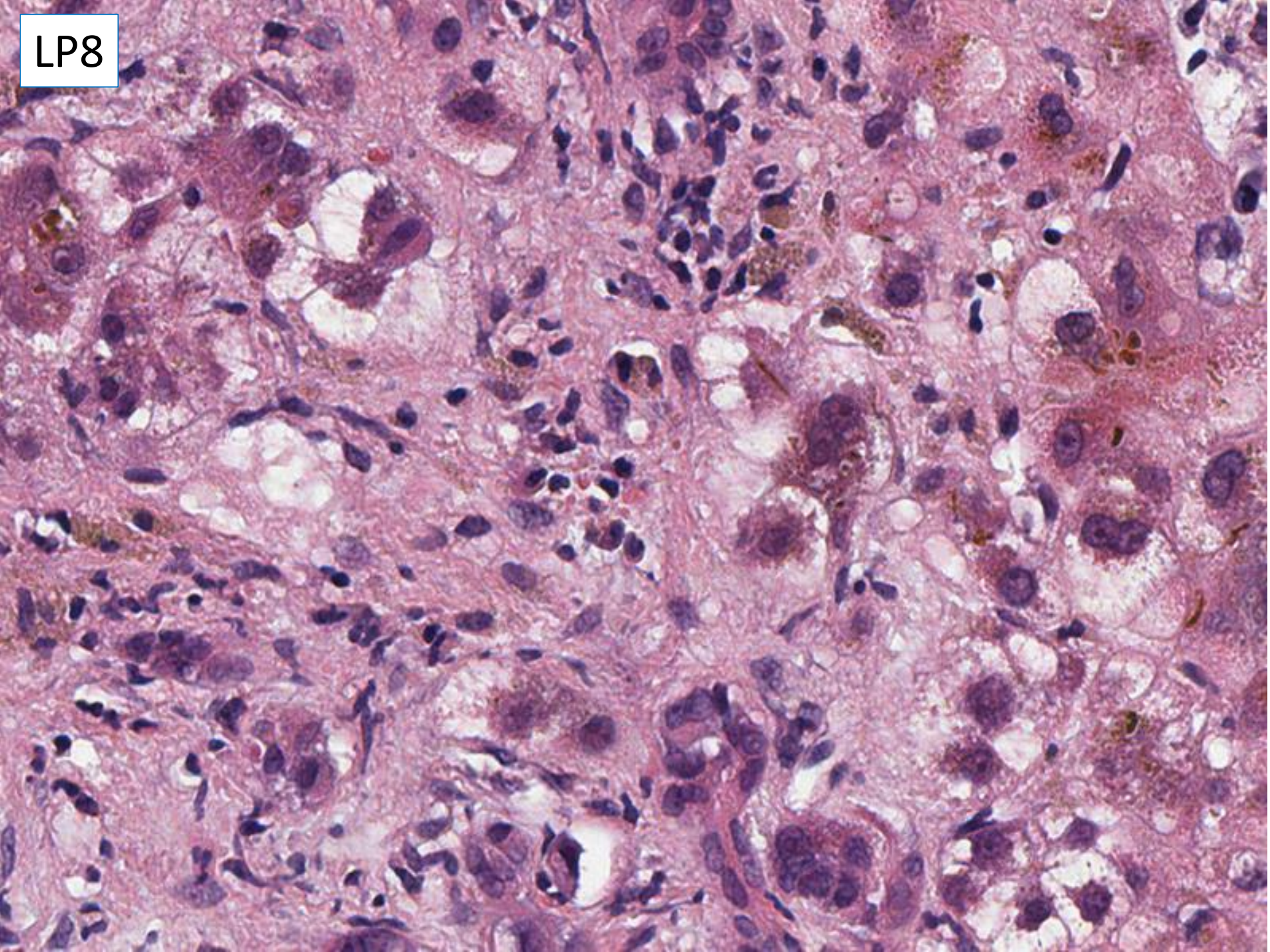
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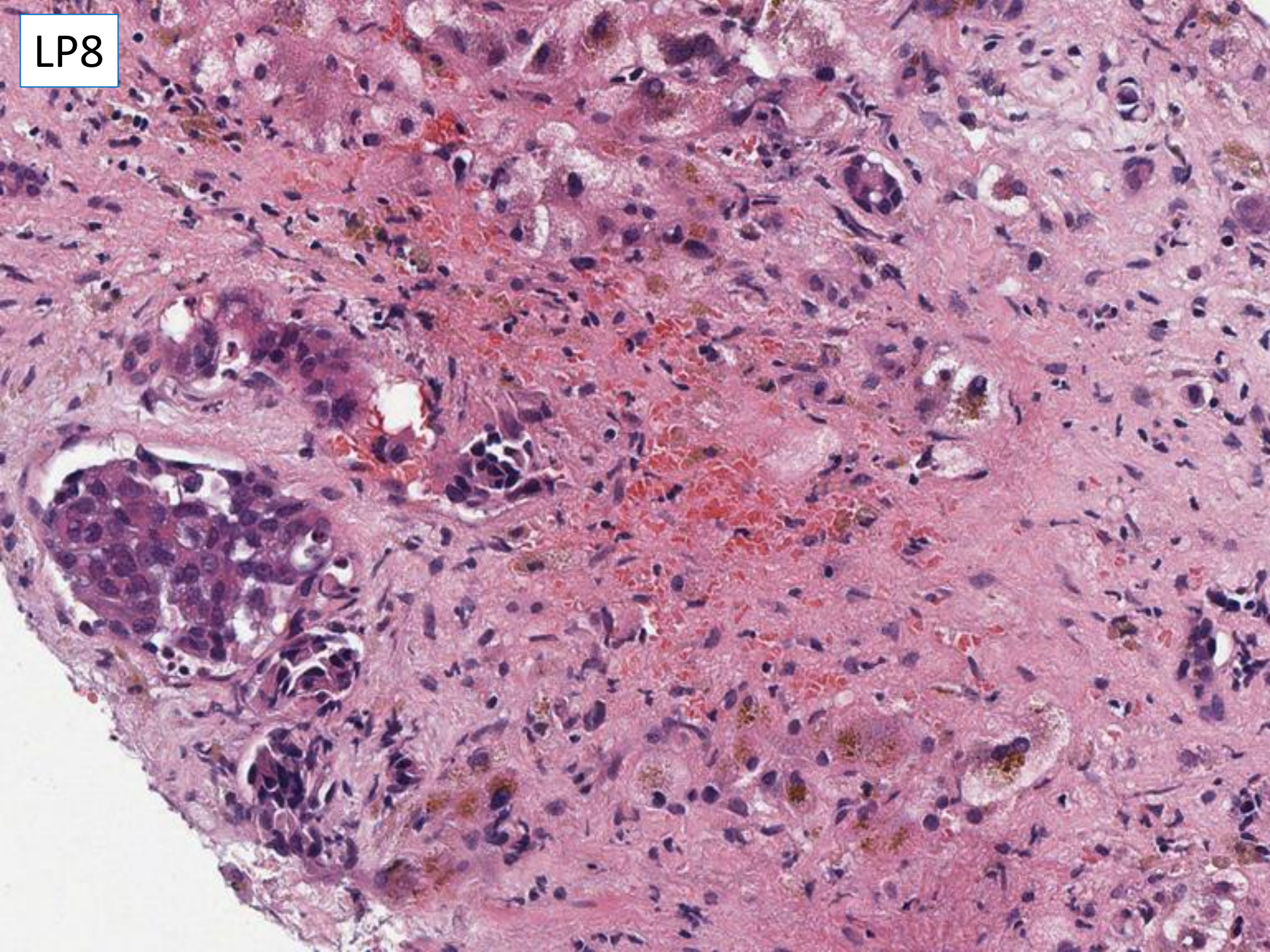
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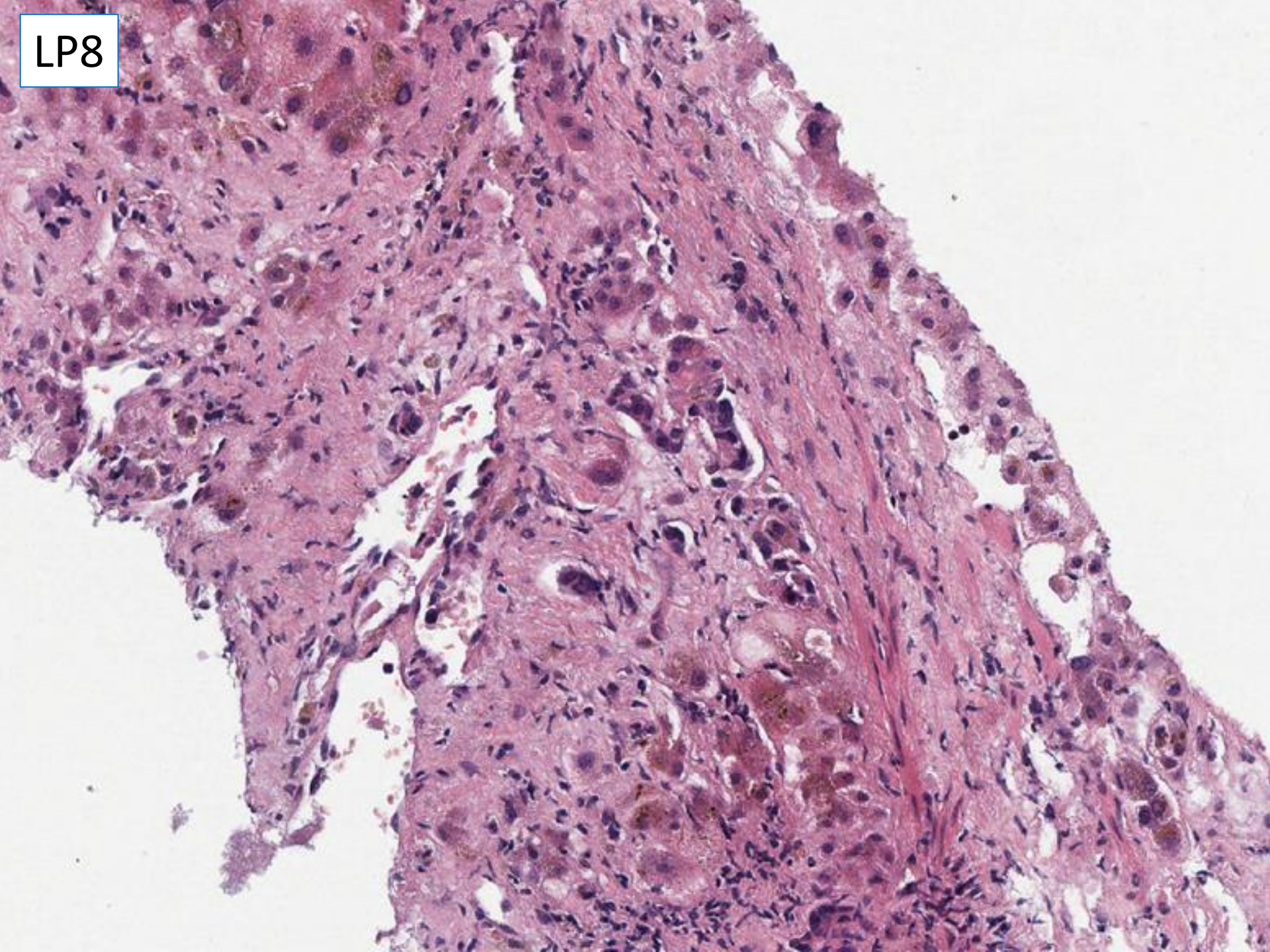
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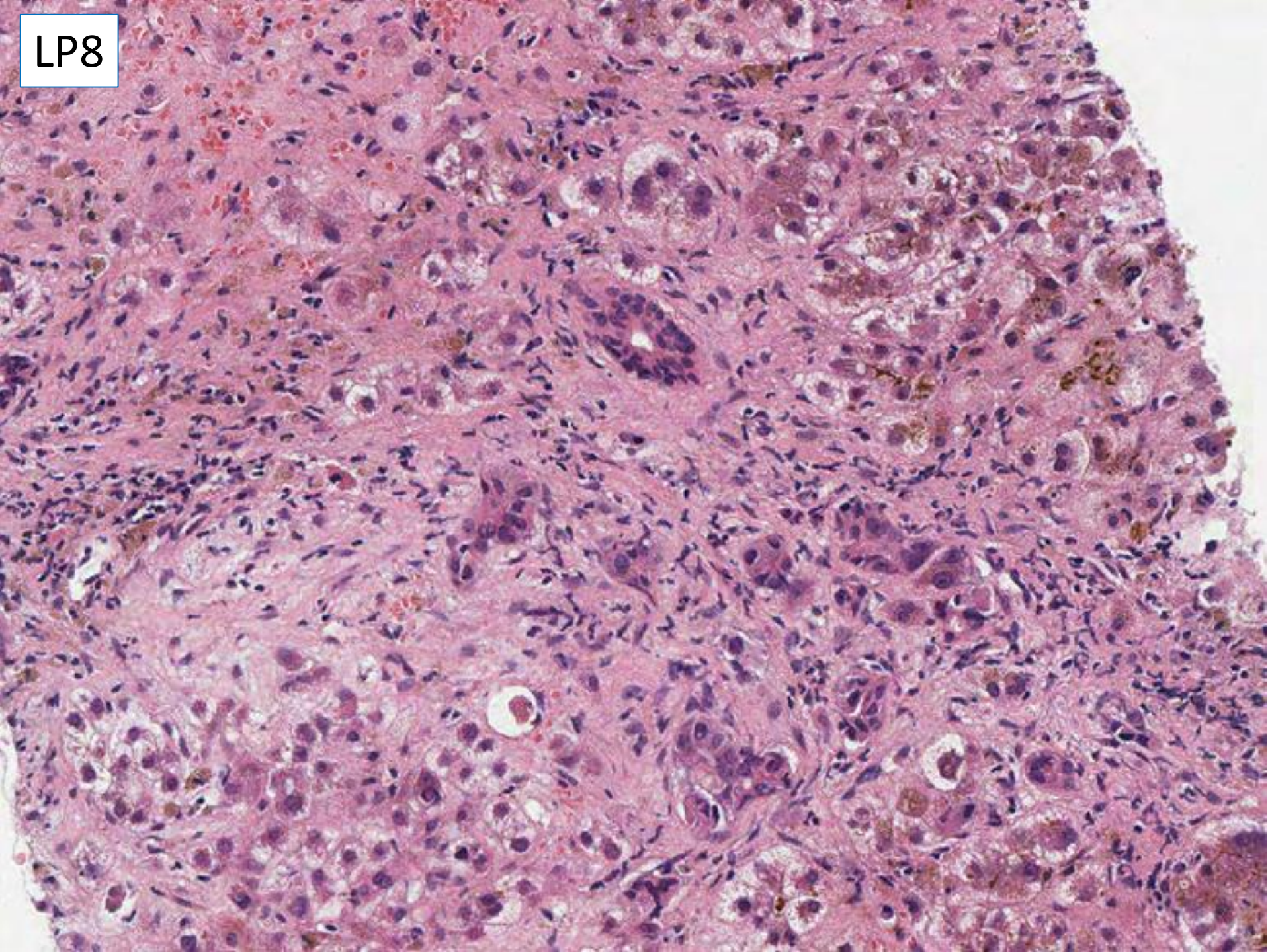
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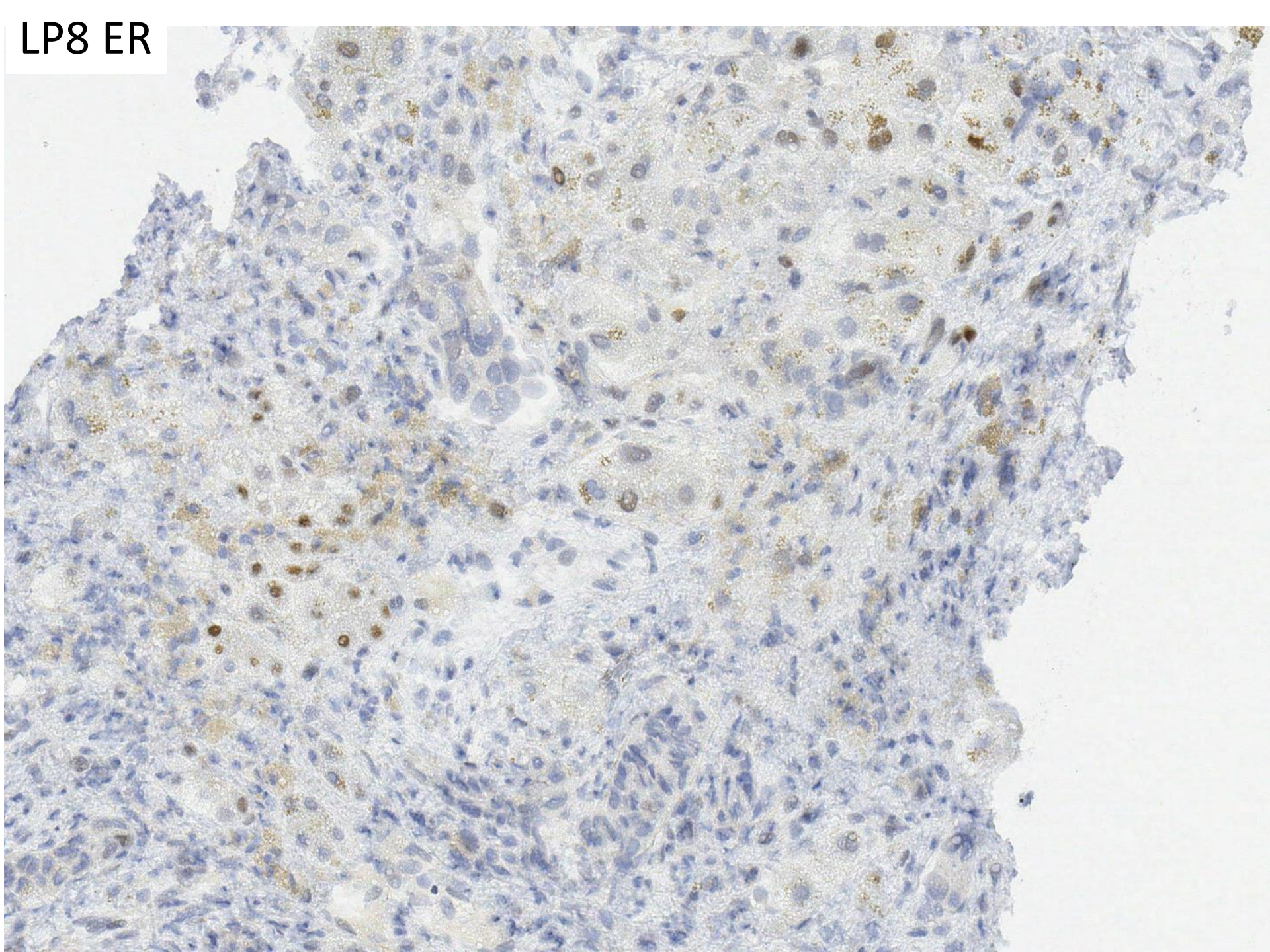
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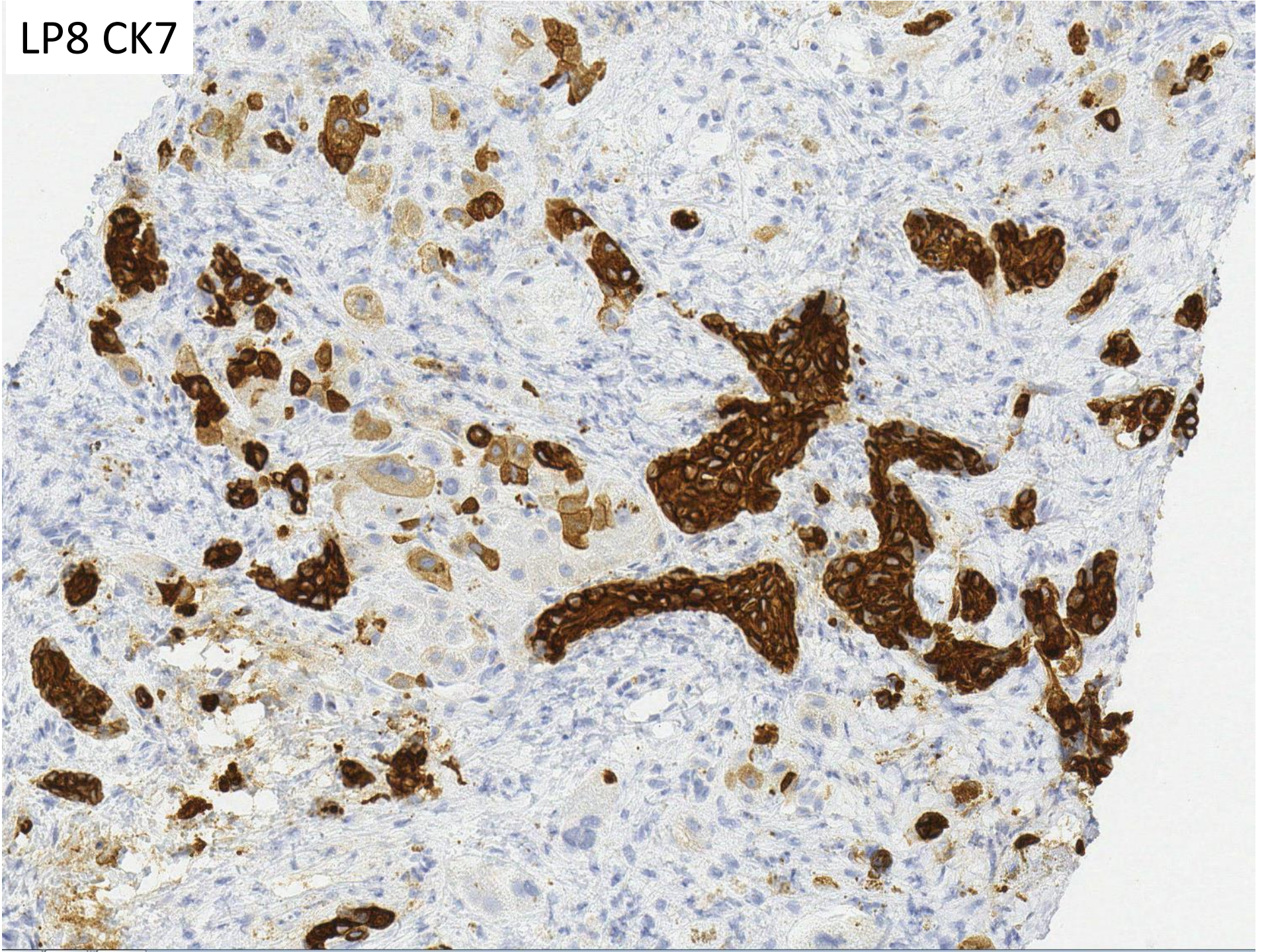
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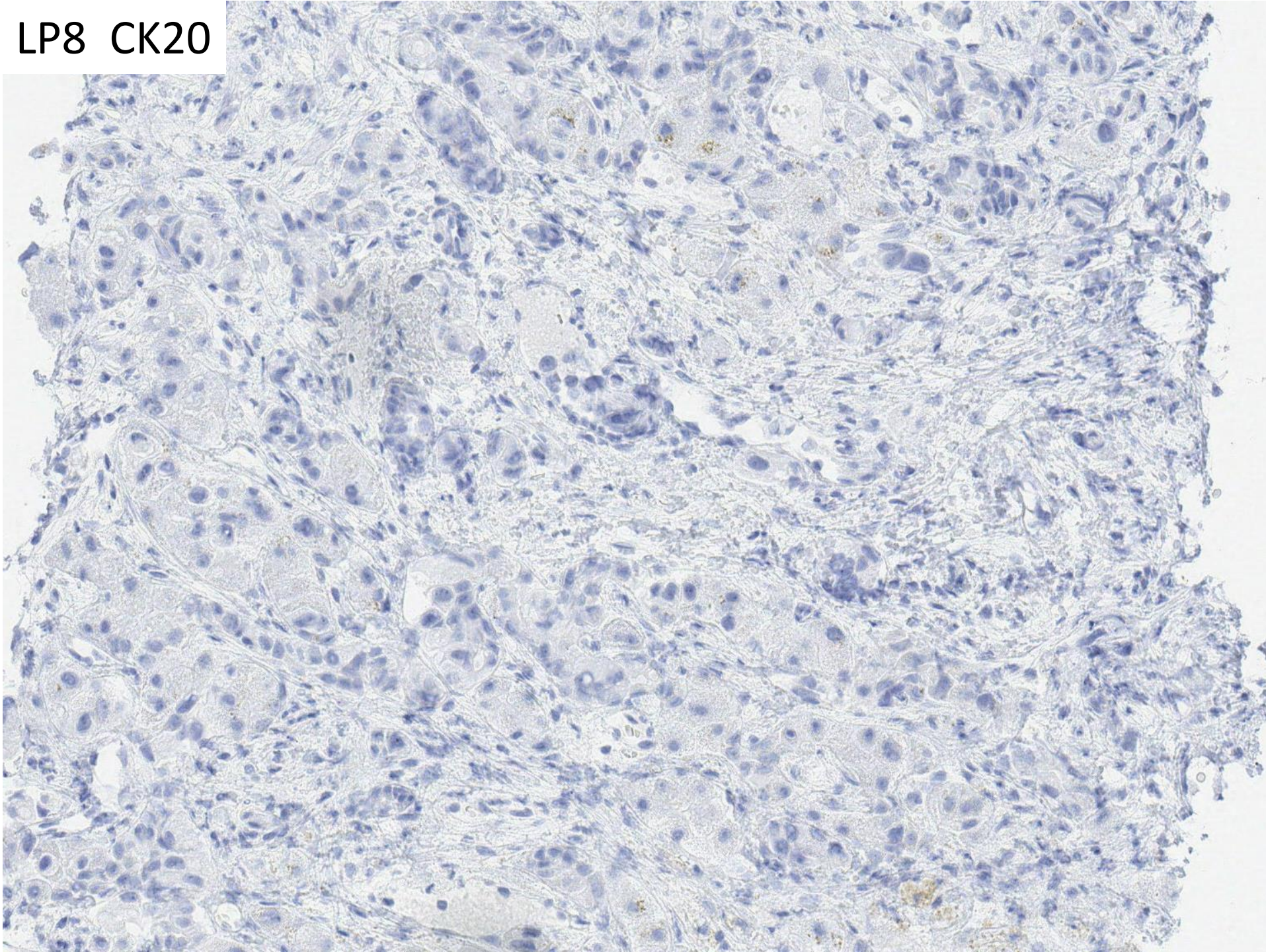
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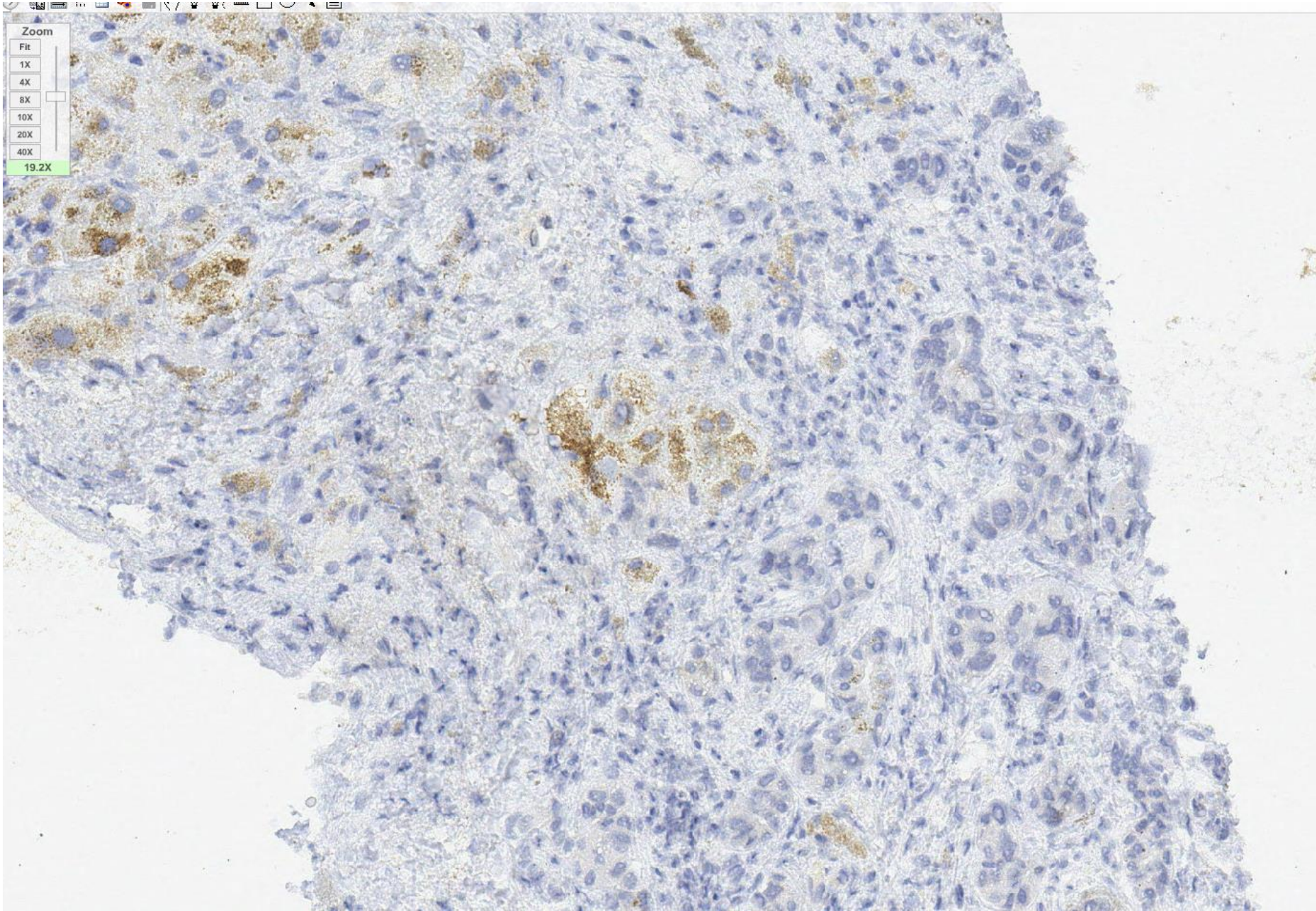
LP8 TTF



Case LP8 49F

jaundice for 3 weeks, no known history of liver disease. raised calcium, cause unclear. CT/MRI suggests possible chronic liver disease with acute element, however, subacute. bilirubin 180, ALP 819, ALT 59. ?chronic liver disease ?aetiology ?subacute hepatitis. liver aetiology screen negative

Carcinoma/adenocarcinoma	83
Of which: Adenocarcinoma, primary or metastatic	25
Metastatic carcinoma	9
Metastatic adenocarcinoma	21
Metastatic adenocarcinoma - probably breast	19
Carcinoma, ? cholangiocarcinoma (met not mentioned)	8
Angiosarcoma	1
No mention of malignancy in response	5
Of which - recent acute hepatitis with necrosis	3
- longstanding LBDO	1
- chronic active hepatitis with fibrosis and biliary	1
Background liver disease as well as malignancy	23
Background liver changes are attributed to malignant infiltration	9

Consensus complete diagnosis – adenocarcinoma, may be primary or metastatic.

It is unclear whether fibrosis is due to the malignant infiltration or underlying chronic liver disease.

Case LP8 49F

jaundice for 3 weeks, no known history of liver disease. raised calcium, cause unclear.
CT/MRI suggests possible chronic liver disease with acute element, however, subacute.
bilirubin 180, ALP 819, ALT 59. ?chronic liver disease ?aetiology ?subacute hepatitis.
liver aetiology screen negative

<u>Agreed scoring:</u>

For full marks, include carcinoma/adenocarcinoma. On a show of hands, these responses are all accepted, whether they include primary cholangiocarcinoma, metastatic malignancy, or either.

Score 0 marks for responses which didn't recognise the presence of malignancy, and for angiosarcoma.

Case LP8 49F

jaundice for 3 weeks, no known history of liver disease. raised calcium, cause unclear. CT/MRI suggests possible chronic liver disease with acute element, however, subacute. bilirubin 180, ALP 819, ALT 59. ?chronic liver disease ?aetiology ?subacute hepatitis. liver aetiology screen negative.

A Recent acute hepatitis with necrosis

B Longstanding large bile duct obstruction

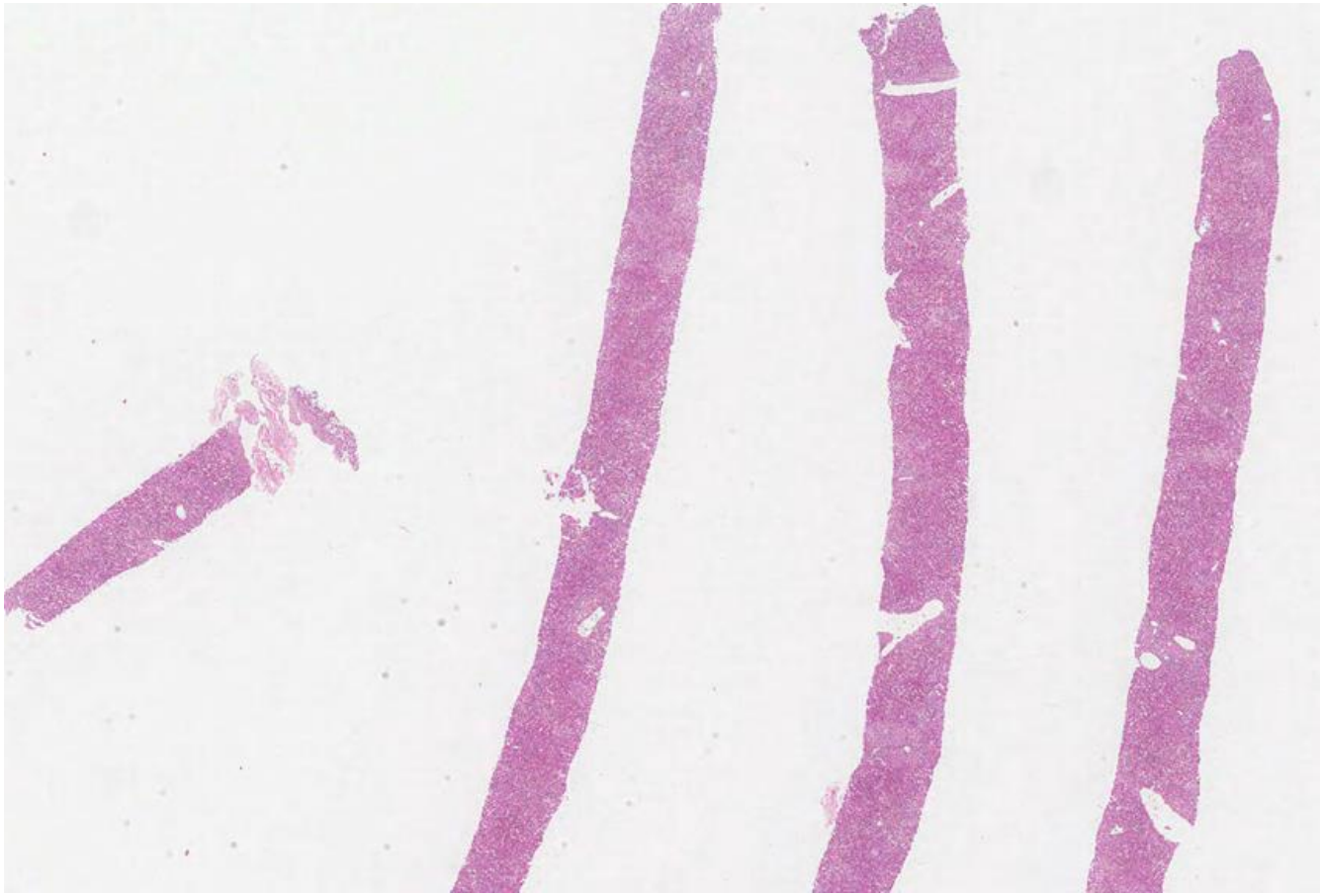
C Adenocarcinoma, primary or metastatic

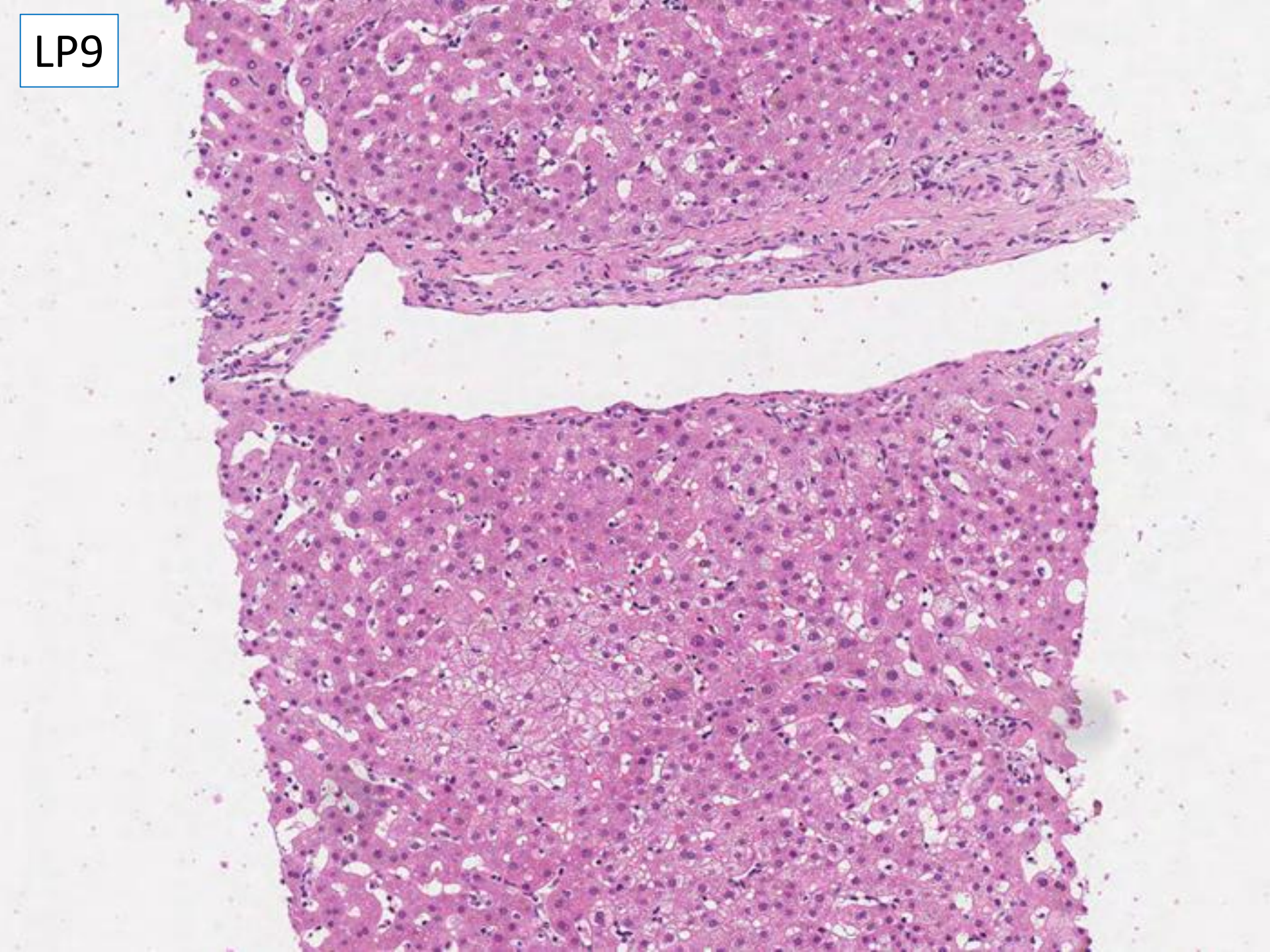
D Cholangiocarcinoma

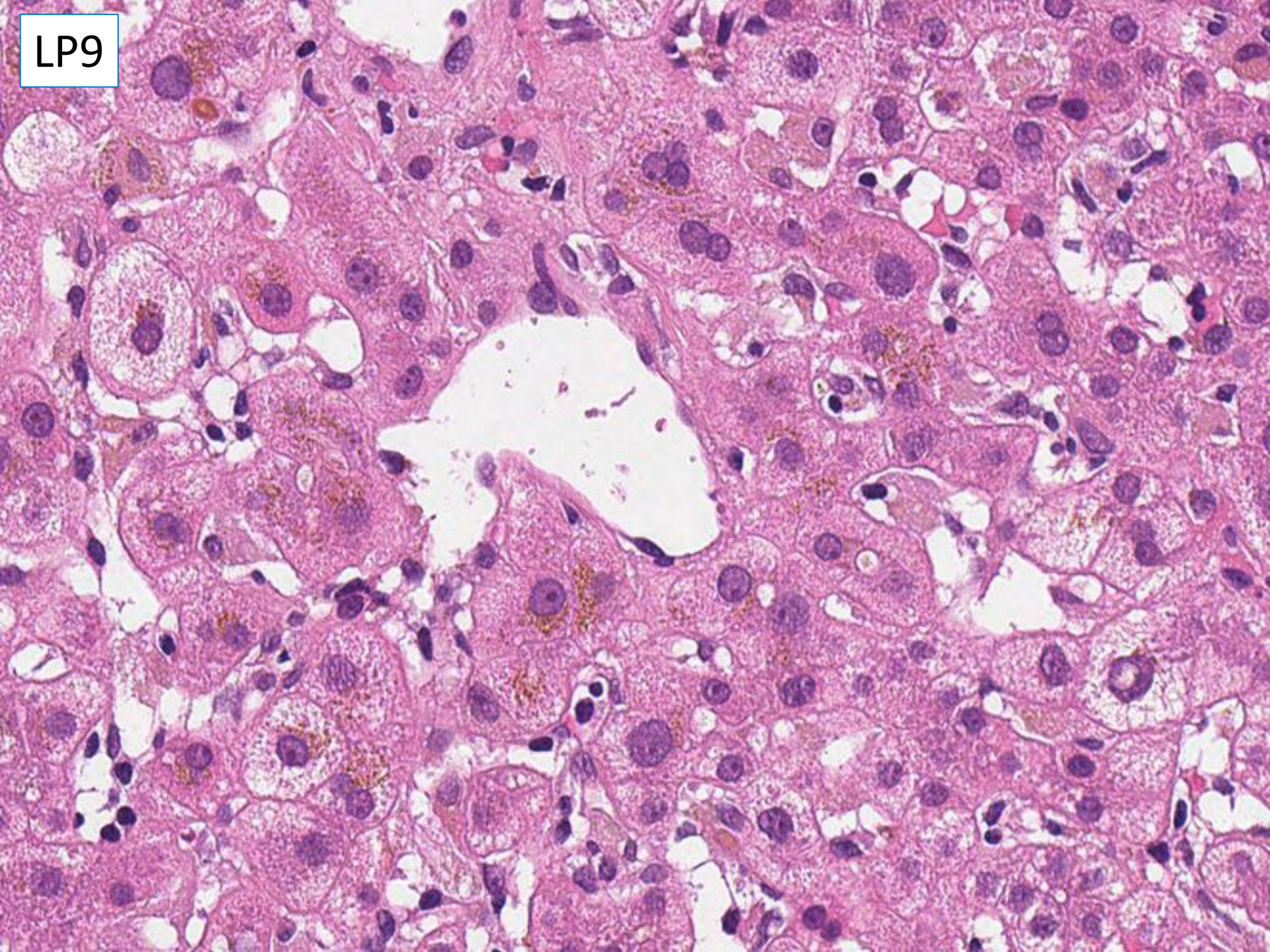
E angiosarcoma

Case LP9 52F

Jaundice x 1 month. History or clarithromycin over 1 month ago. Drug stopped. Liver function tests now improving. Viral screen negative (HCV,HBV,HIV, EBV). ALT 308; Alkaline phosphatase 144; MRCP normal.




LP9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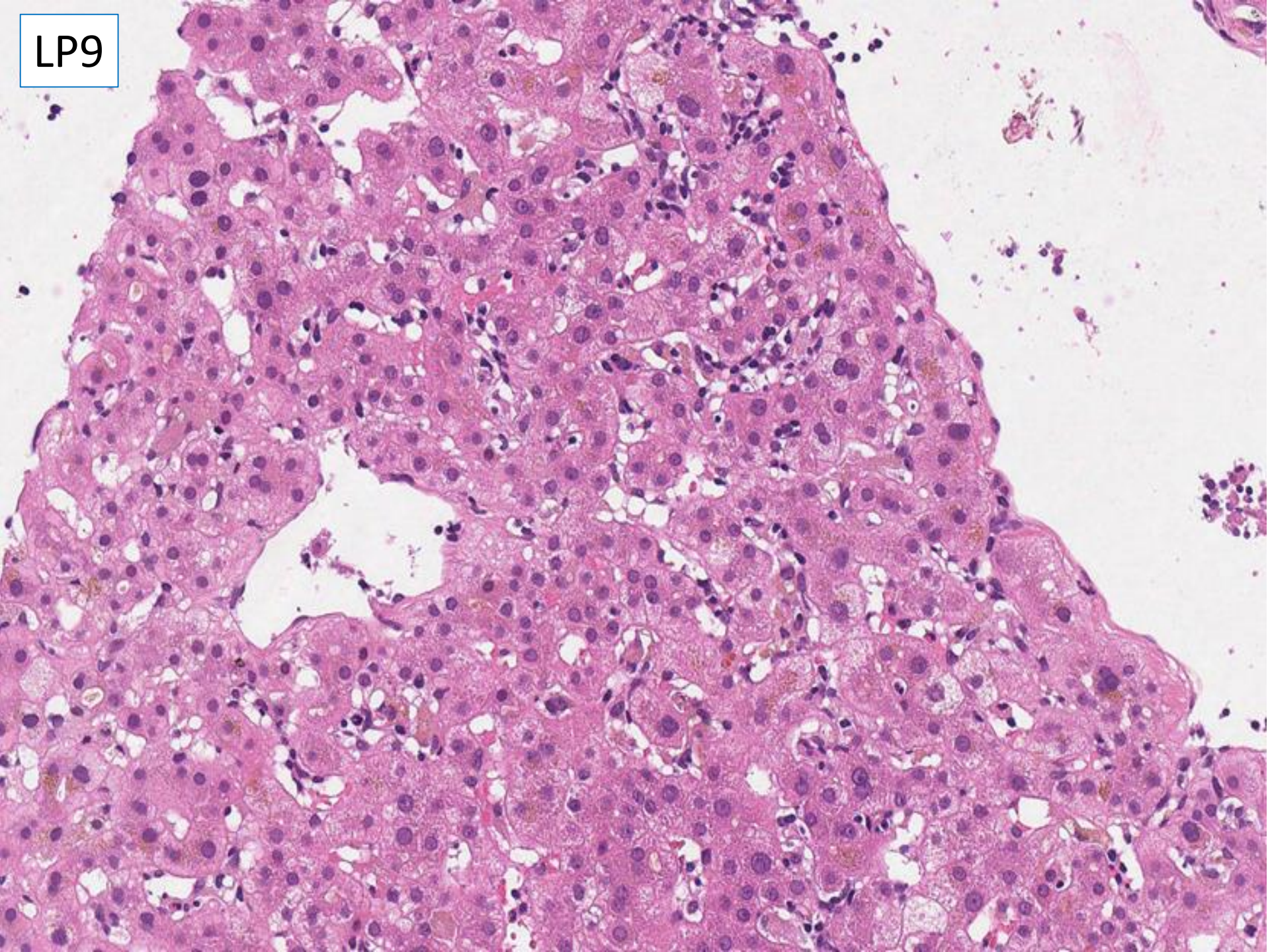
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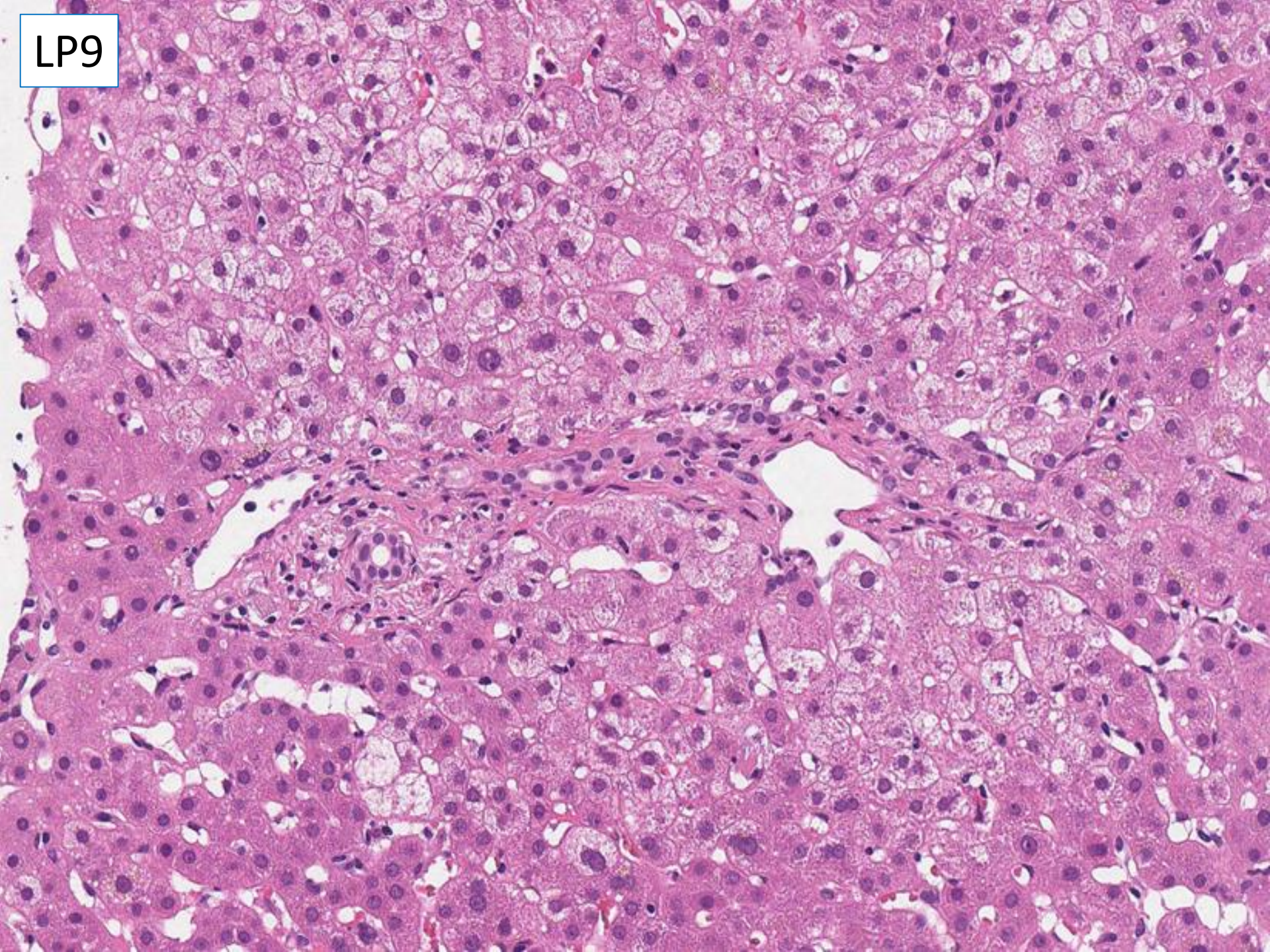
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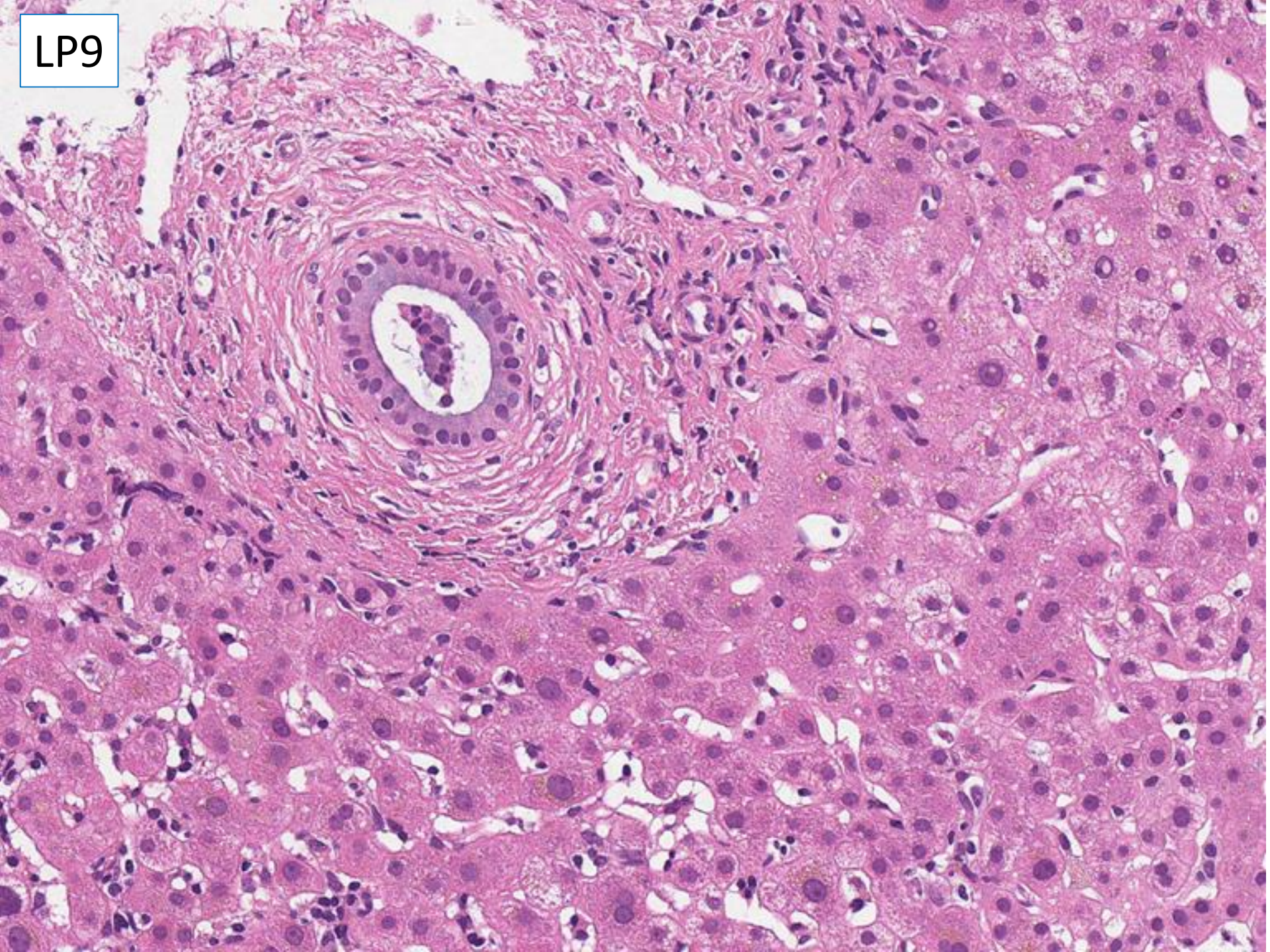
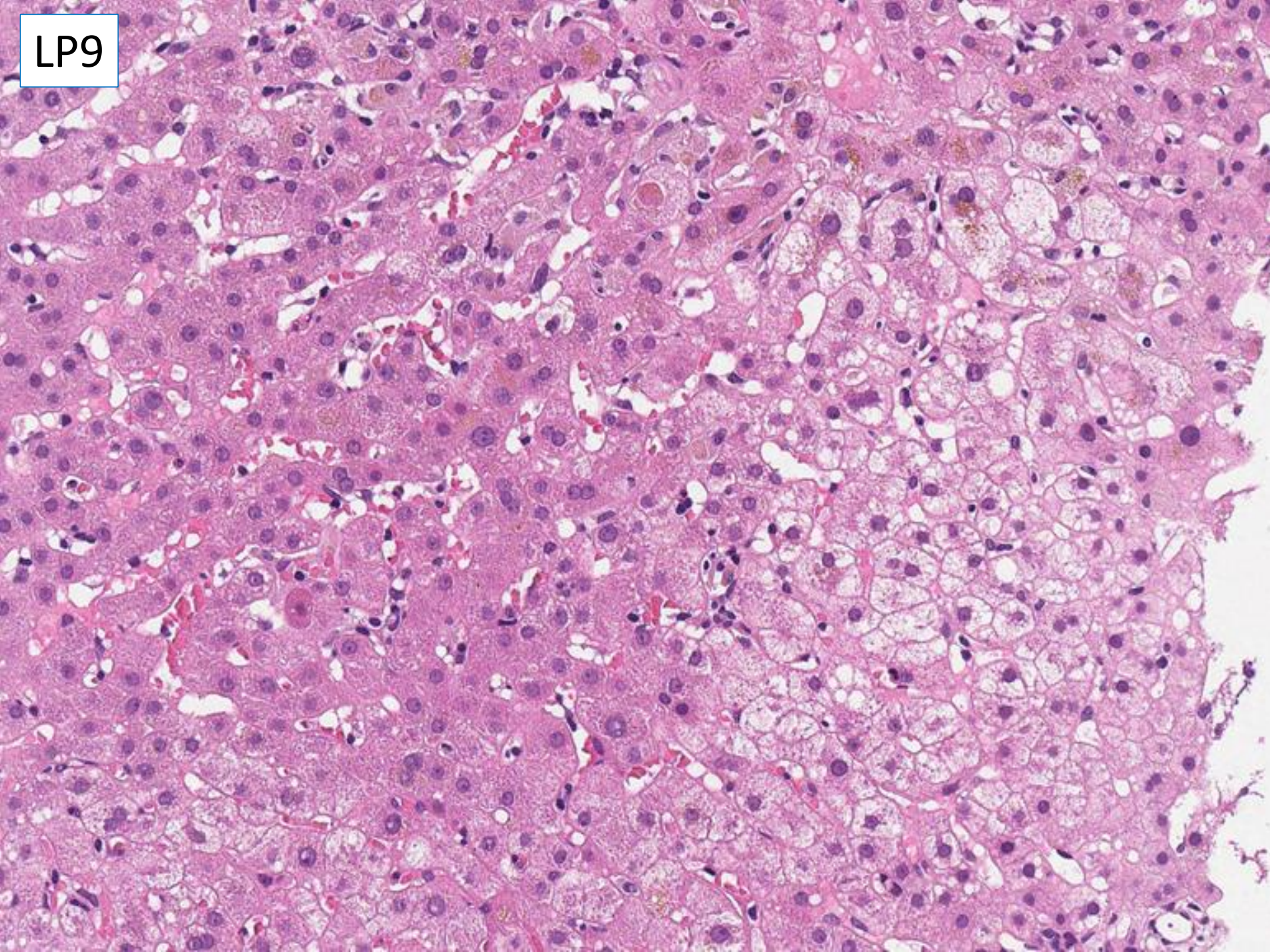
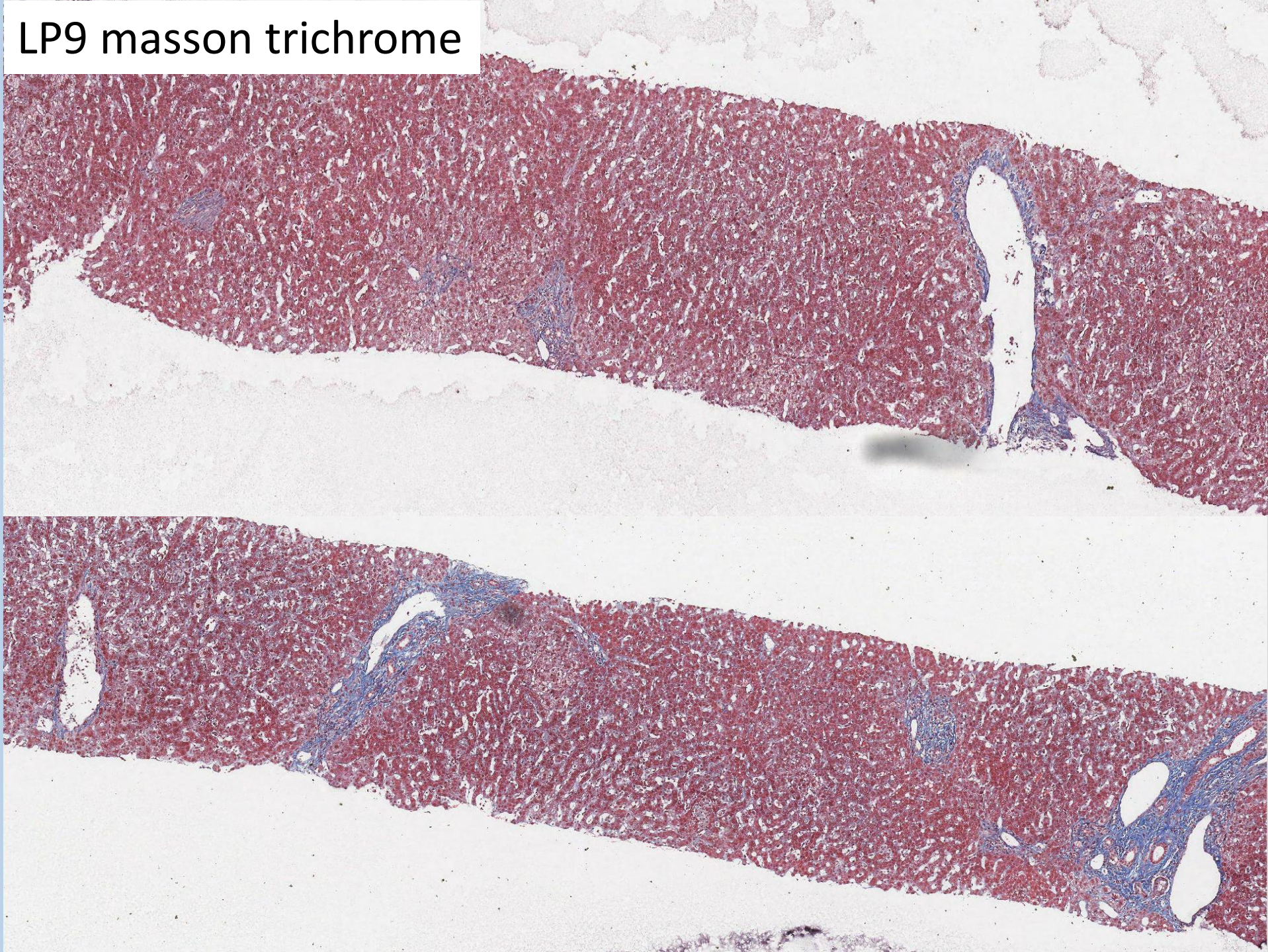
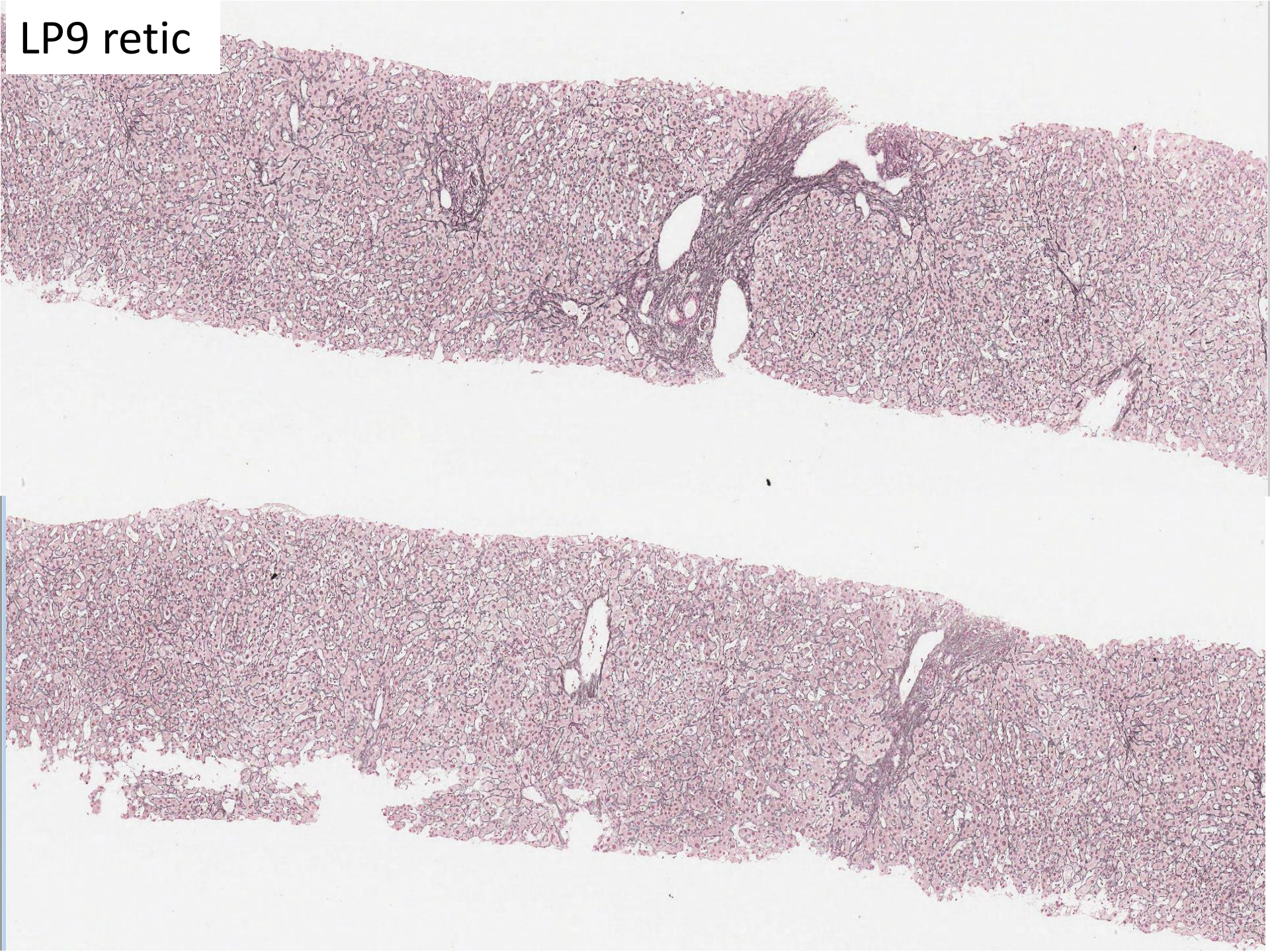

LP9


LP9

LP9 masson trichrome




LP9 retic

Case LP9 52F

Jaundice x 1 month. History or clarithromycin over 1 month ago. Drug stopped.
Liver function tests now improving. Viral screen negative (HCV,HBV,HIV, EBV).
ALT 308; Alkaline phosphatase 144; MRCP normal.

Cholestatic hepatitis	33
Hepatitis	35
Cholestasis	2
Recovery from acute injury	13
Steatohepatitis with cholestasis	1
Alcoholic hepatitis	1
Chronic hepatitis/ chronic biliary disease	4
Aetiology:	
DILI – clarithromycin	32
DILI – no named drug	43
Drug favoured over viral hepatitis (hepatitis E or EBV)	5
Drugs not mentioned	3
Several commented on many sinusoidal lymphocytes ? EBV, excl lymphoma (2)	
Several commented on periductal fibrosis, possibly PSC as well.	

Consensus complete diagnosis: cholestatic liver injury, consistent with clarithromycin induced.
No evidence of underlying chronic liver disease.

These were very descriptive responses which I would classify as inflammatory/resolving/ cholestatic in 83.
There was a minority favouring fatty liver disease or chronic hepatitis.

How to score 'drugs not mentioned? – survey result 10/5/0 = 0/2/9

Case LP9 52F

Jaundice x 1 month. History or clarithromycin over 1 month ago. Drug stopped.
Liver function tests now improving. Viral screen negative (HCV,HBV,HIV, EBV).
ALT 308; Alkaline phosphatase 144; MRCP normal.

Agreed scoring:

For full marks, include hepatitis/cholestasis/resolving injury as the morphological description, and that this is attributable to drug induced liver injury.

Score 0 marks if drugs not mentioned.

Score 5 marks for steatohepatitis, alcoholic h epatitis, or chronic hepatitis / chronic biliary disease.

Follow up information – there is no additional information relating to the possibilities mentioned of PSC, or a cause for increased sinusoidal lymphocytes.

Case LP9 52F

Jaundice x 1 month. History or clarithromycin over 1 month ago. Drug stopped. Liver function tests now improving. Viral screen negative (HCV,HBV,HIV, EBV). ALT 308; Alkaline phosphatase 144; MRCP normal.

A Cholestatic hepatitis, exclude hepatitis E

B Cholestatic hepatitis, consistent with drug induced liver injury

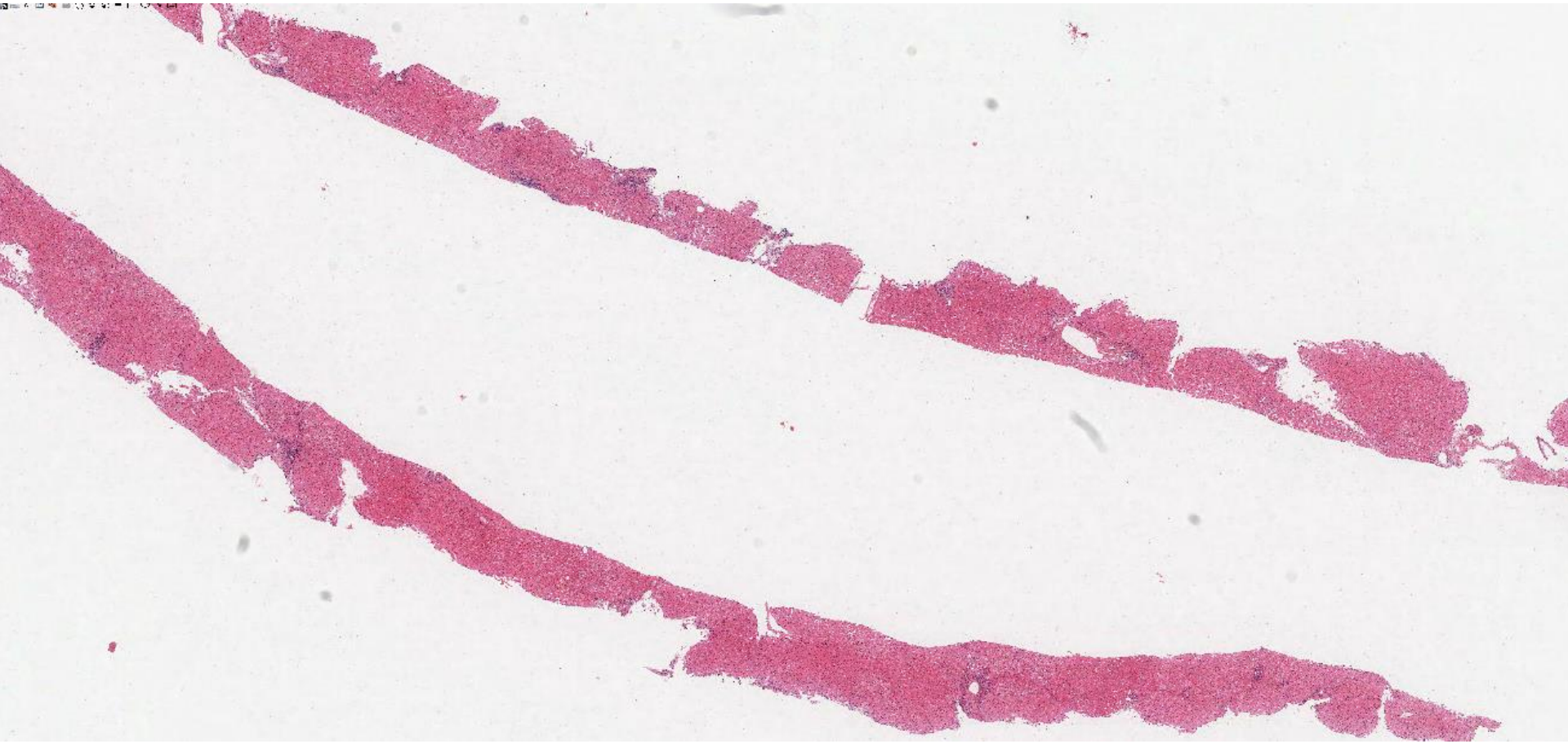
C Hepatitis with sinusoidal lymphocytes, ? EBV

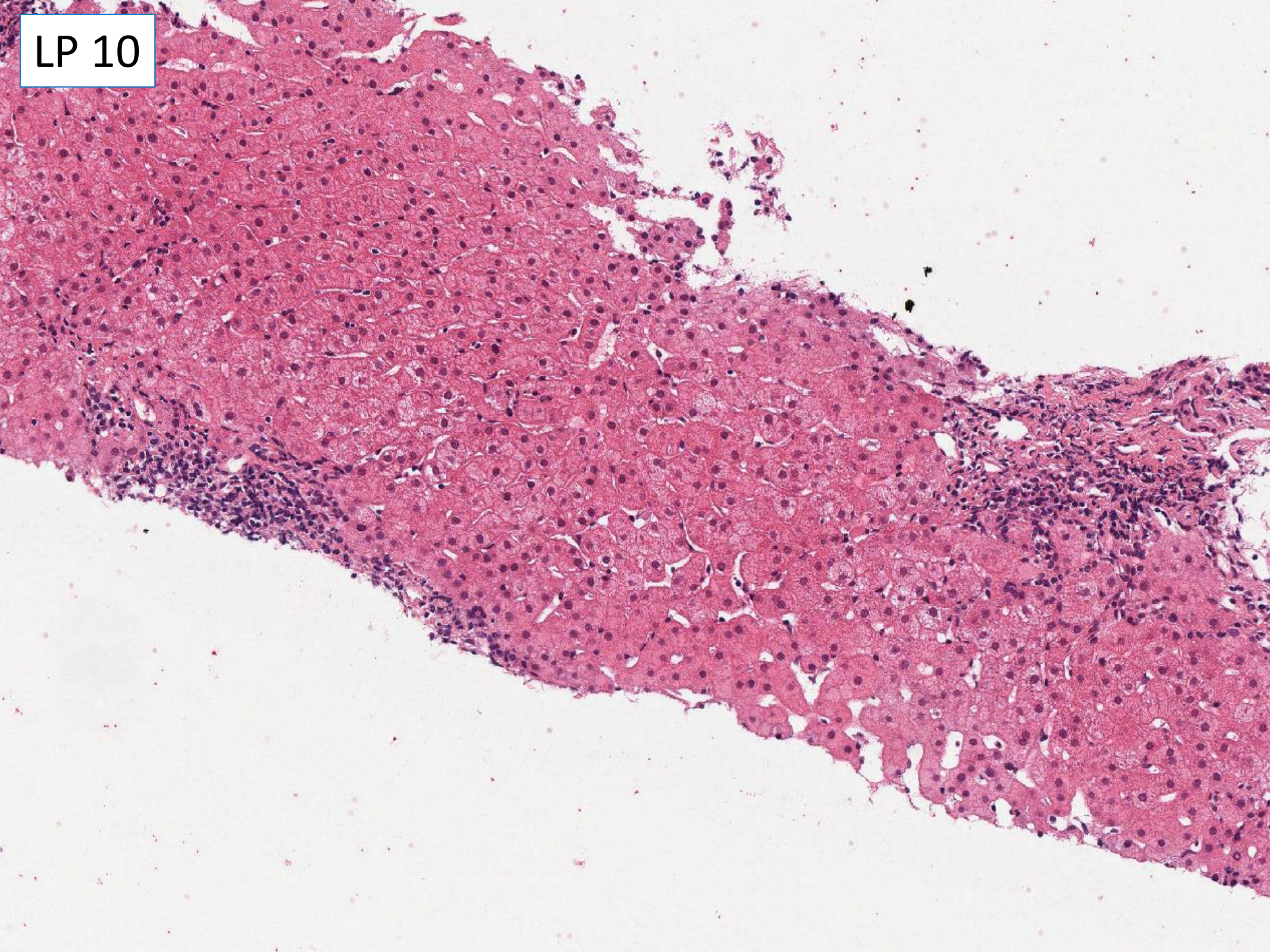
D Cholestasis with periductal fibrosis – PSC

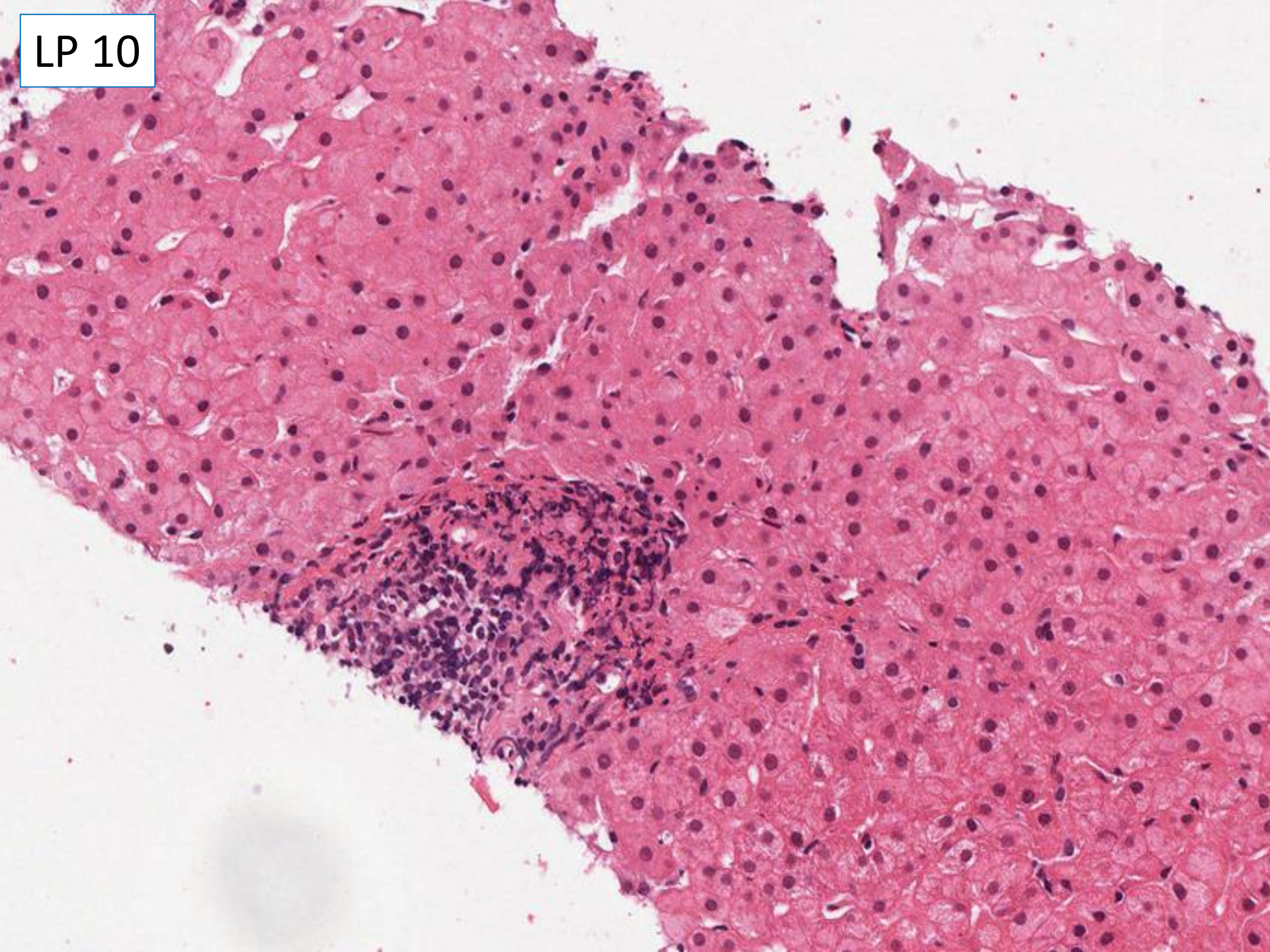
E Steatohepatitis with cholestasis, suggestive of alcohol related liver disease

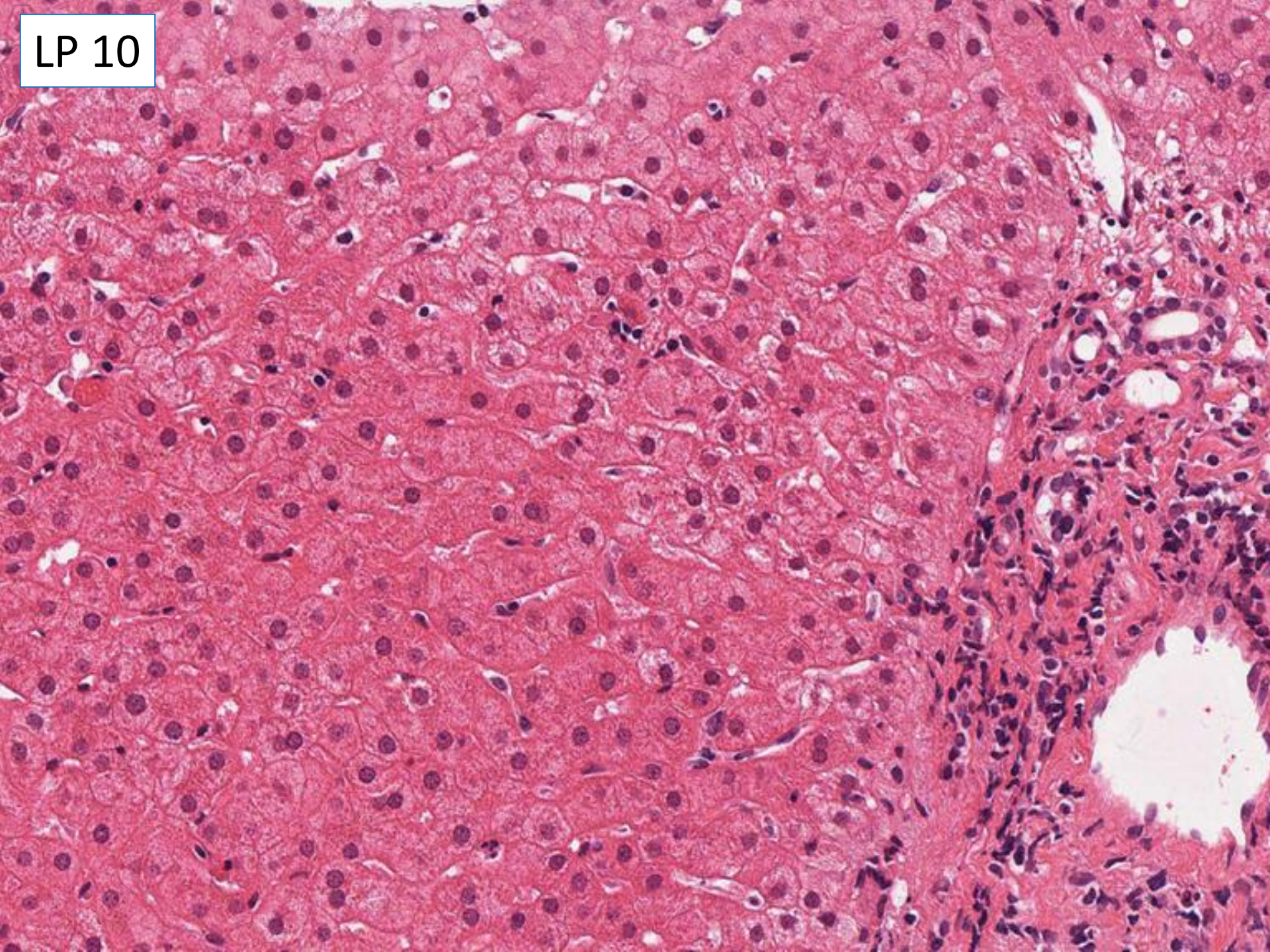
Case LP10 37M

Known HCV and HIV positive. For assessment of disease activity.

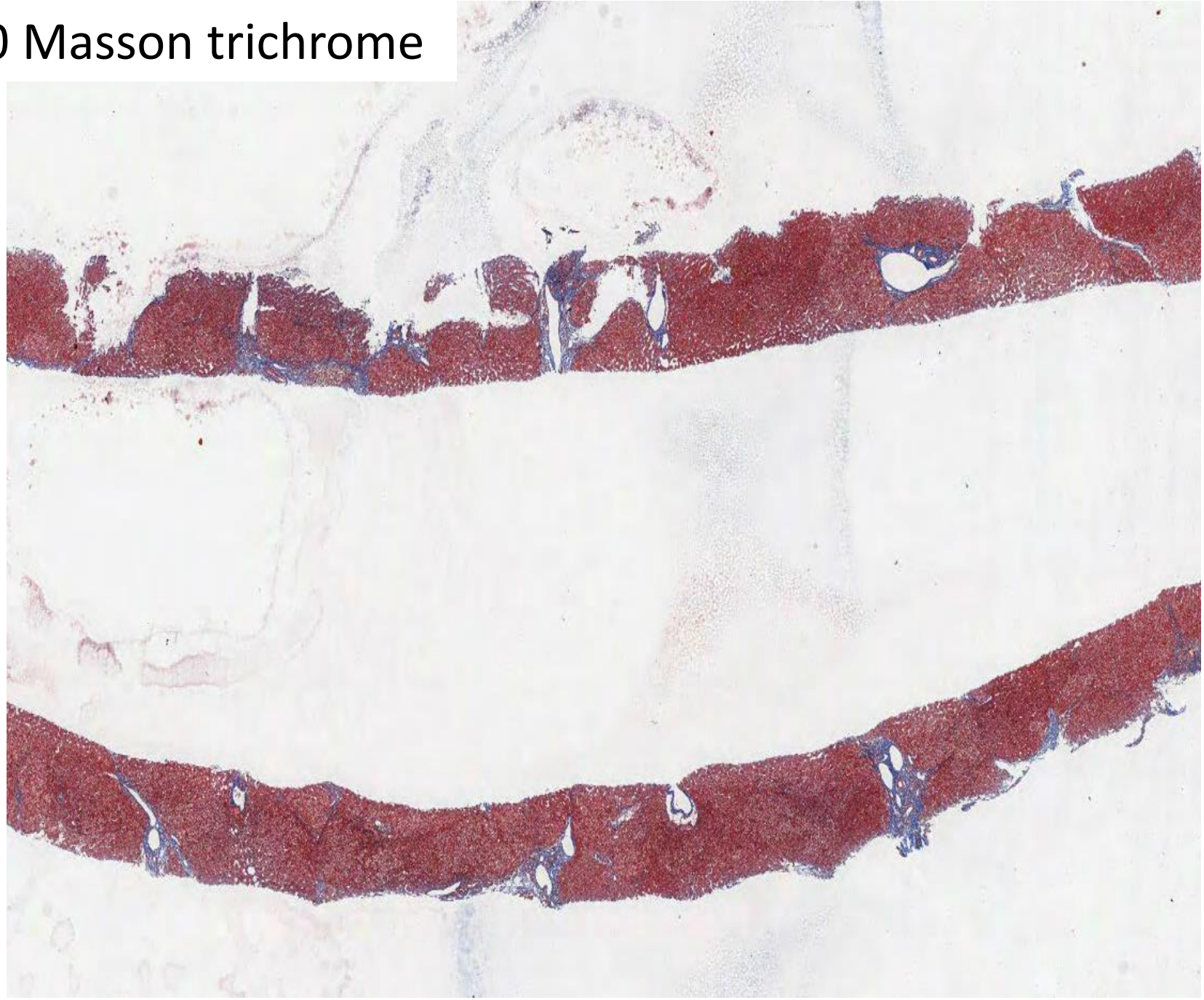



LP 10

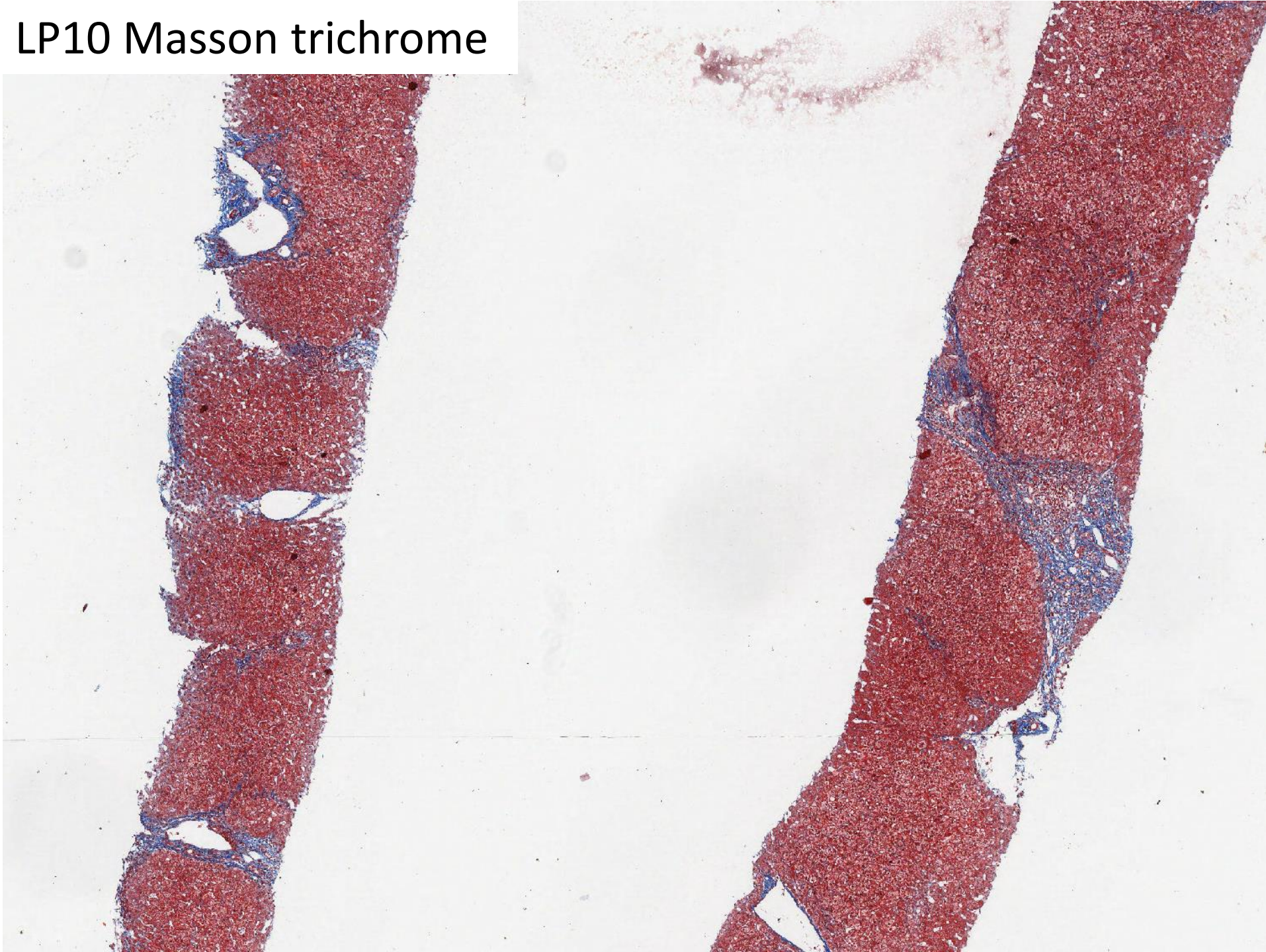

LP 10


LP 10

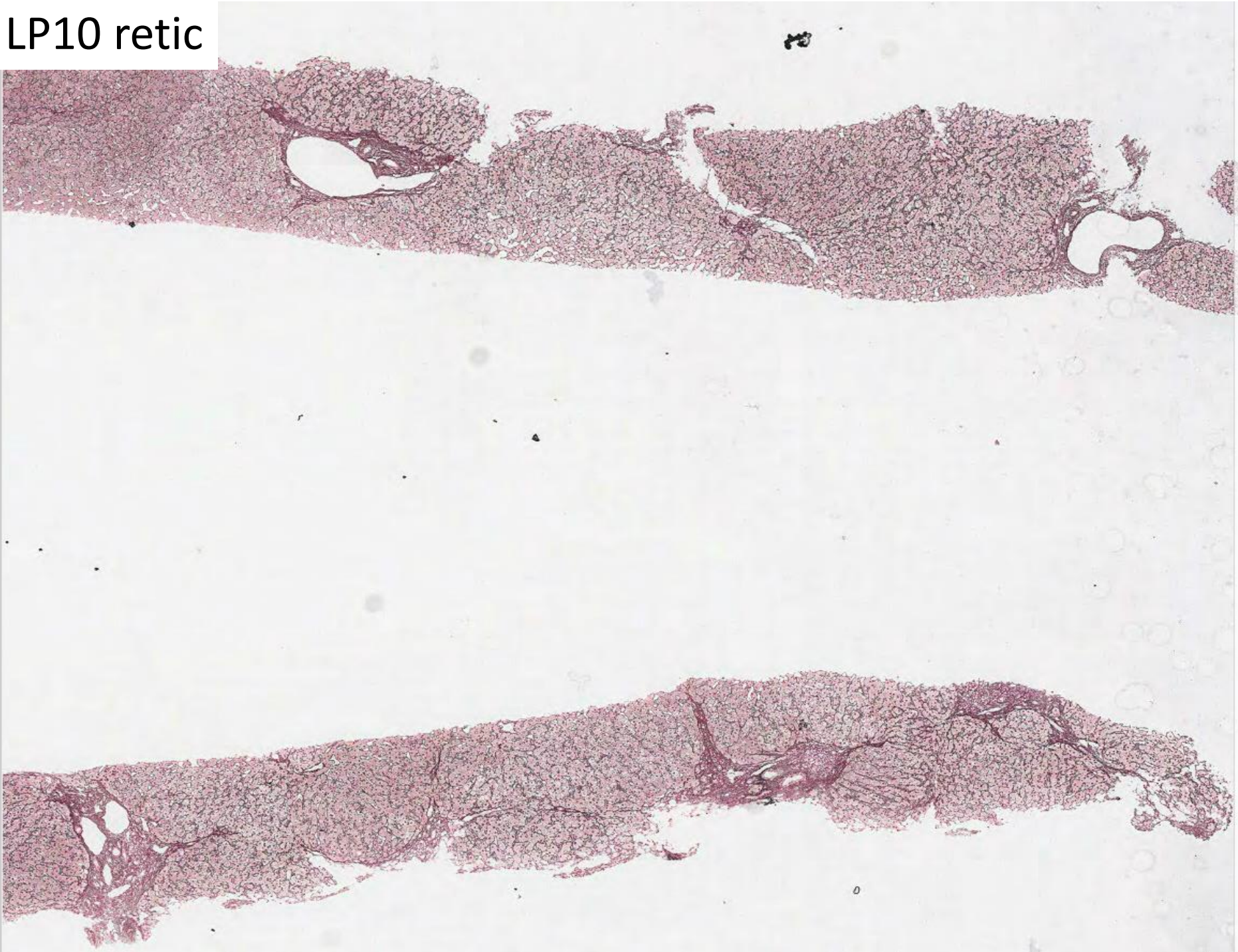
LP10 Masson trichrome



LP10 Masson trichrome



LP10 retic



Case LP10 37M

Known HCV and HIV positive. For assessment of disease activity.

Hepatitis C	86
'viral hepatitis' - Hepatitis C not mentioned	2
HBV and HCV	1
Response includes fibrosis stage as text and/or numerical score	89
Response includes grade as text and/or numerical score	88
Additional comment on effect of HIV	26
Several commented on ground glass/induced hepatocytes, and /or would do additional stains for opportunistic infections.	

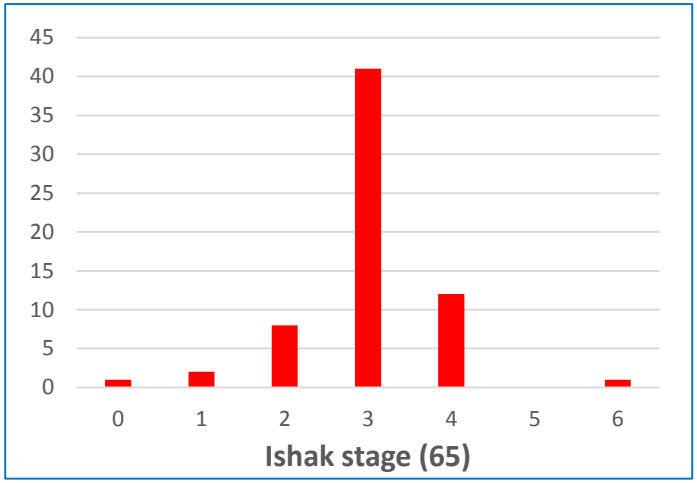
Consensus complete diagnosis -
chronic hepatitis consistent with hepatitis C, with bridging fibrosis (Ishak stage 3) and a comment on grade/severity.

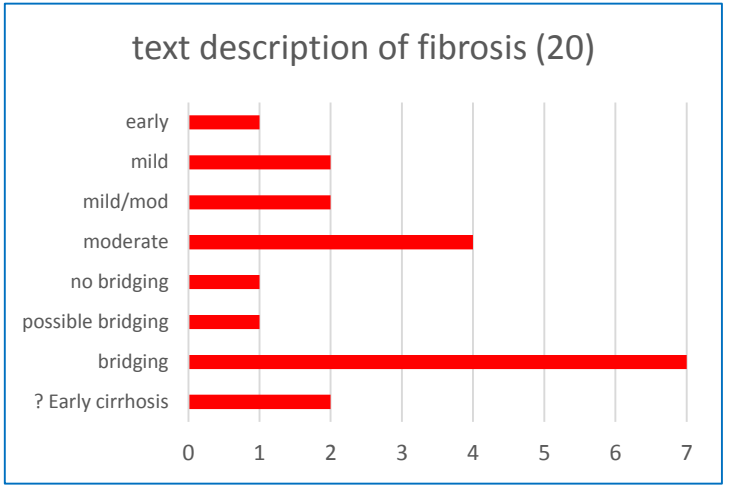
Agreed scoring: for full marks – include mention of hepatitis C and comment on fibrosis stage. Results of stage and grade to follow, included for information, not scored.

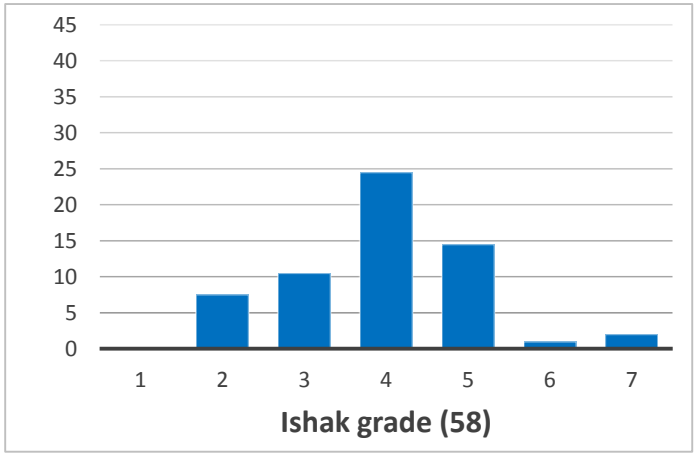
Case LP10 37M

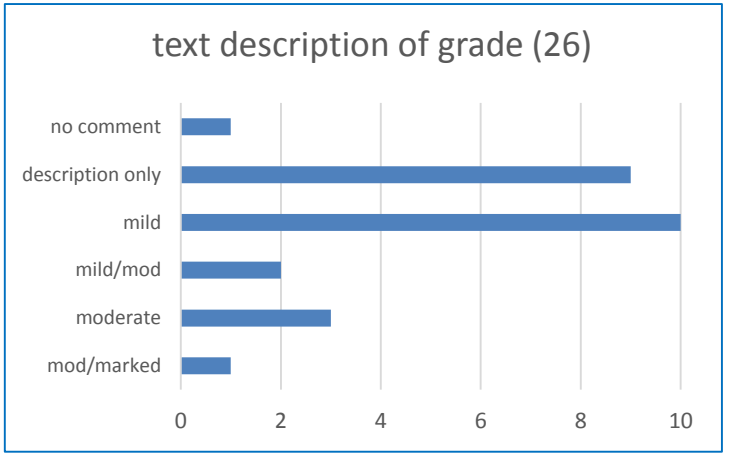
Known HCV and HIV positive. For assessment of disease activity.

Consensus complete diagnosis -
chronic hepatitis consistent with hepatitis C, with bridging fibrosis (Ishak stage 3)
and a comment on grade/severity.





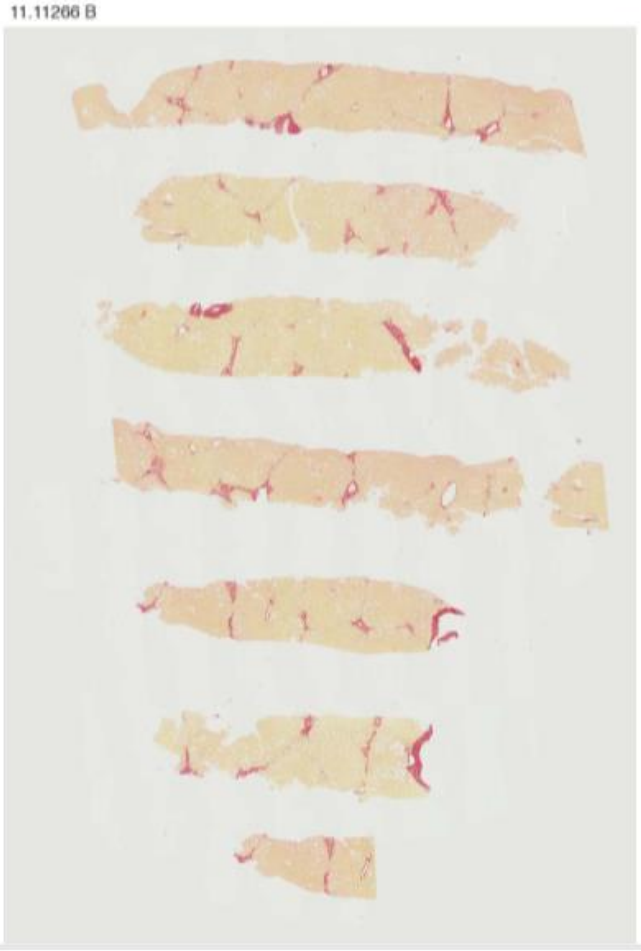




http://www.virtualpathology.leeds.ac.uk/eqa/specialist/liver/liverdocs/2017/Fibrosis%20stage%20reference%20images.v%20June.pdf

Early/bridging

Bridging



Case LP10 37M

Known HCV and HIV positive. For assessment of disease activity.

A Chronic hepatitis C, early cirrhosis

B Chronic hepatitis B and C, bridging fibrosis

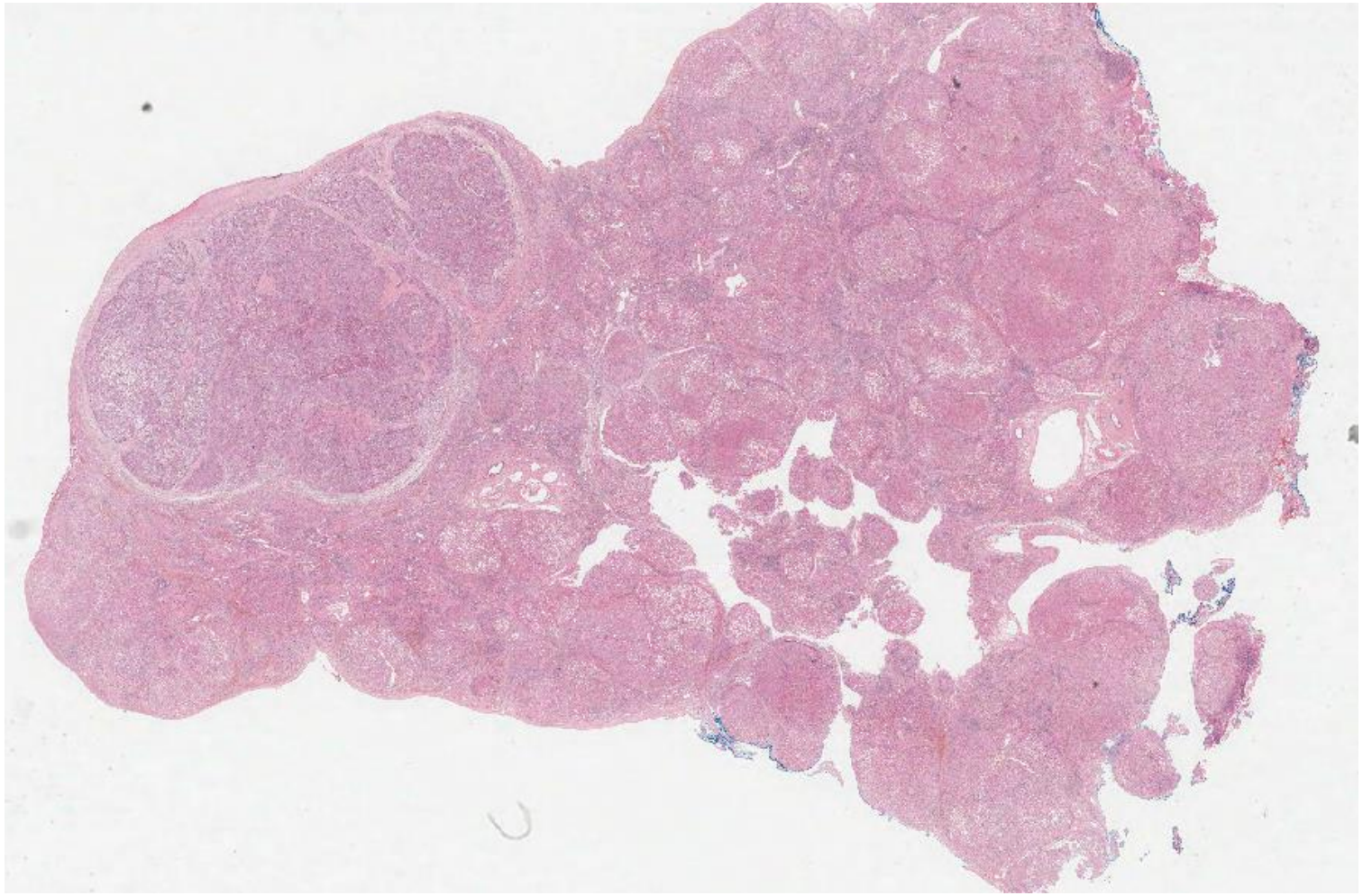
C Chronic hepatitis C, early fibrosis

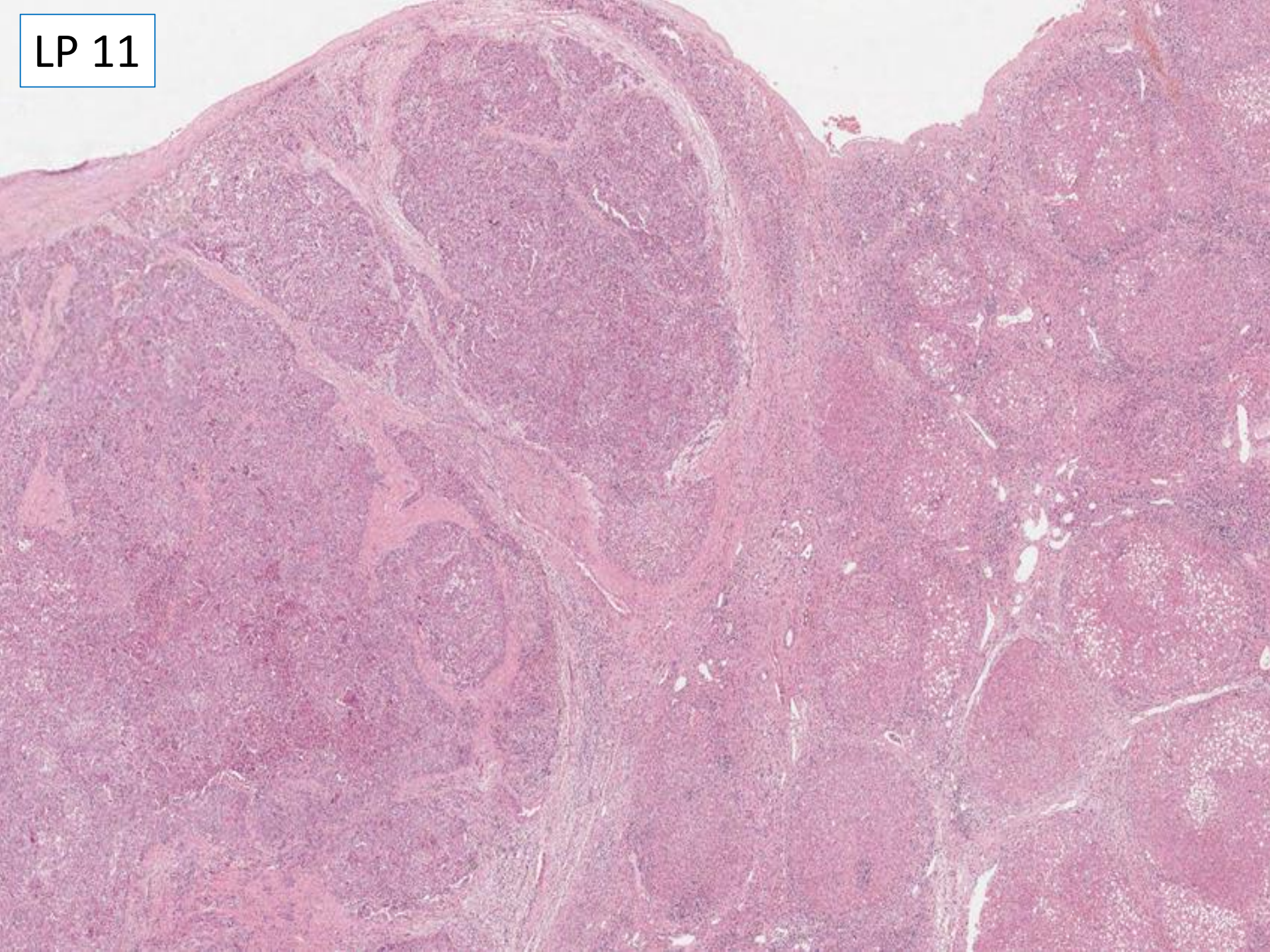
D Chronic hepatitis C, bridging fibrosis

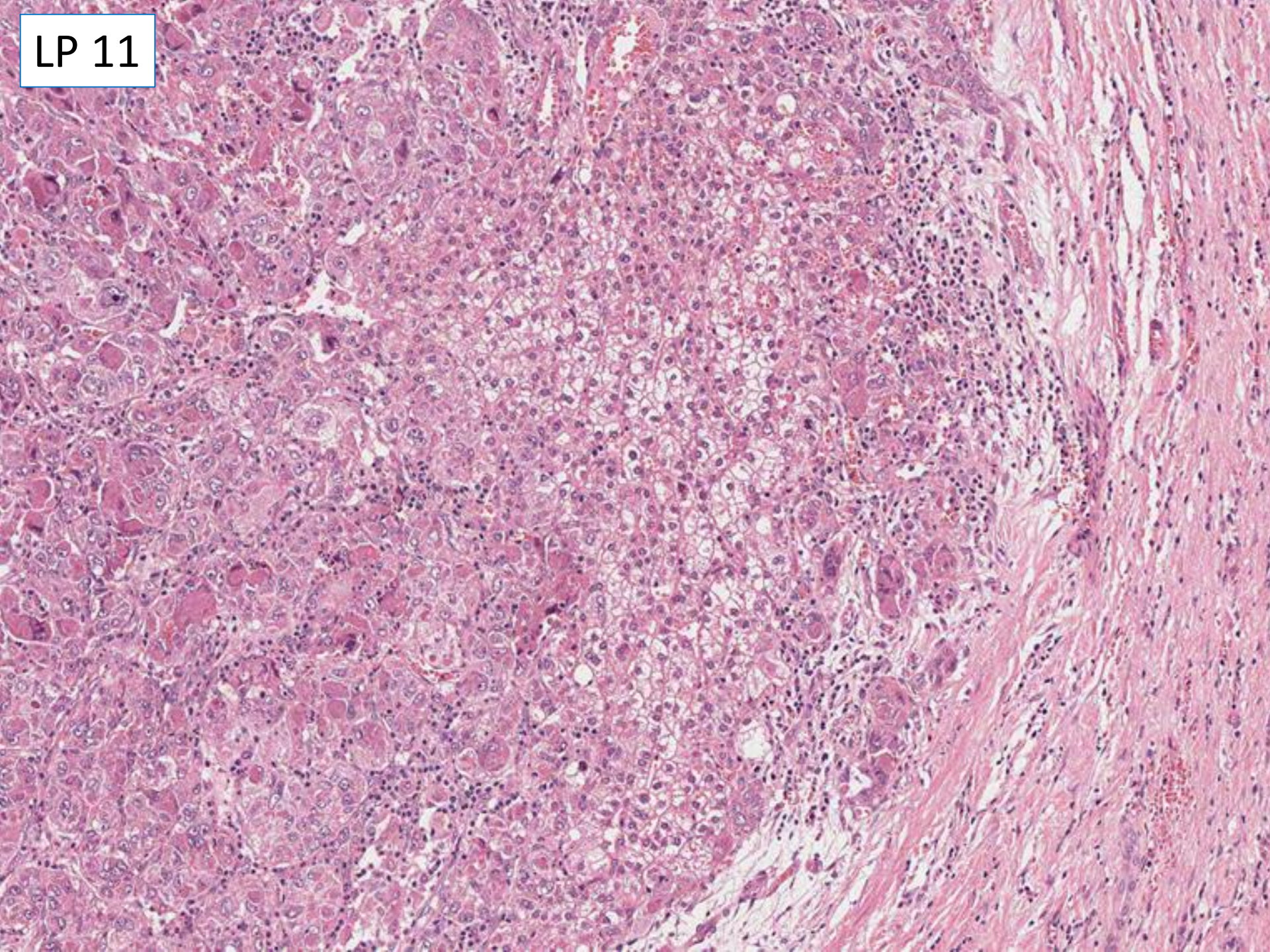
E Changes due to HIV and hepatitis C

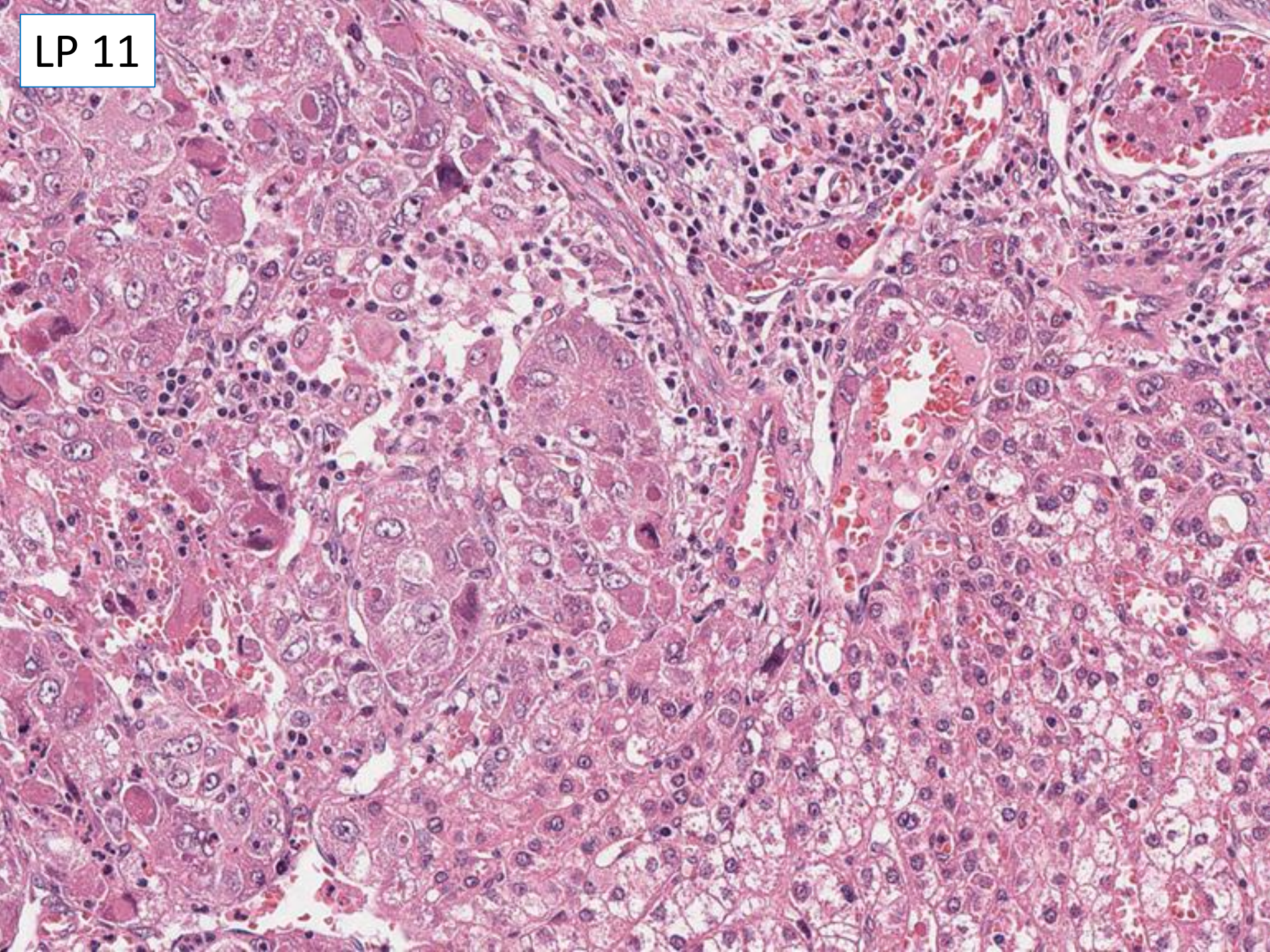
Case LP11 59M

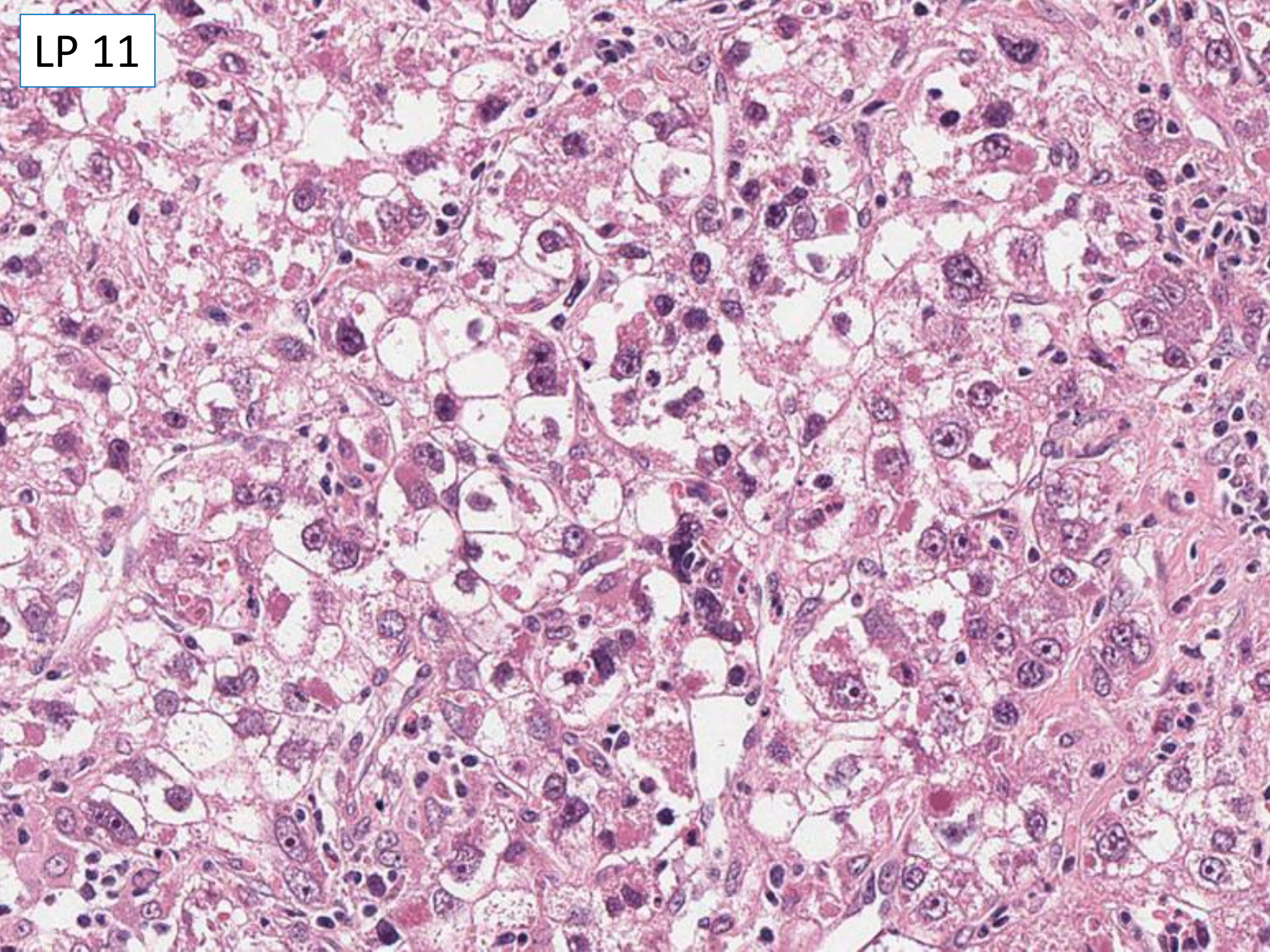
Known HCV infection. Wedge resection of liver with a subcapsular cream lesion 13 mm in maximum dimensions. HSA positive with canalicular pattern of staining with CD13 and pCEA.




LP 11


LP 11


LP 11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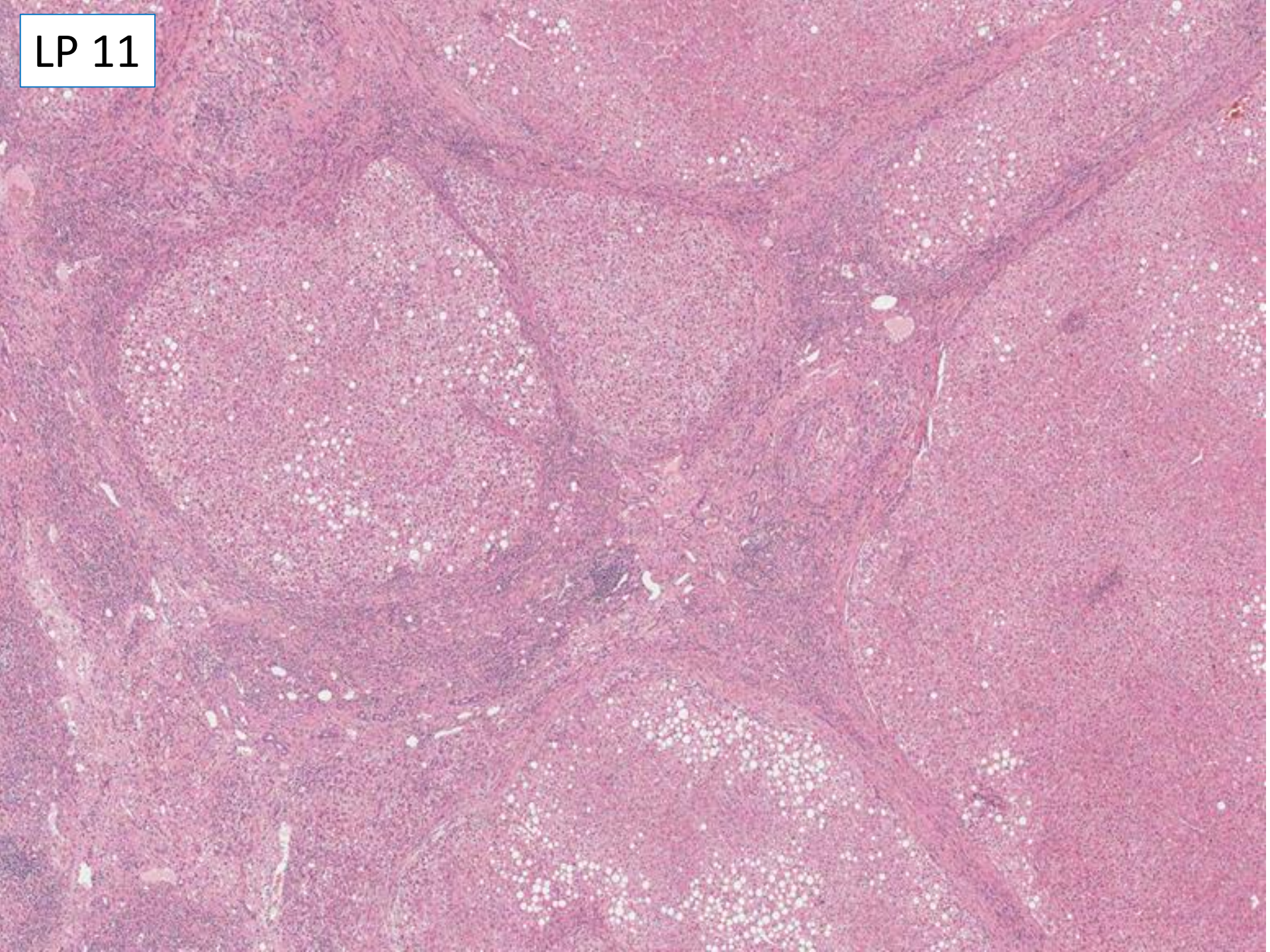
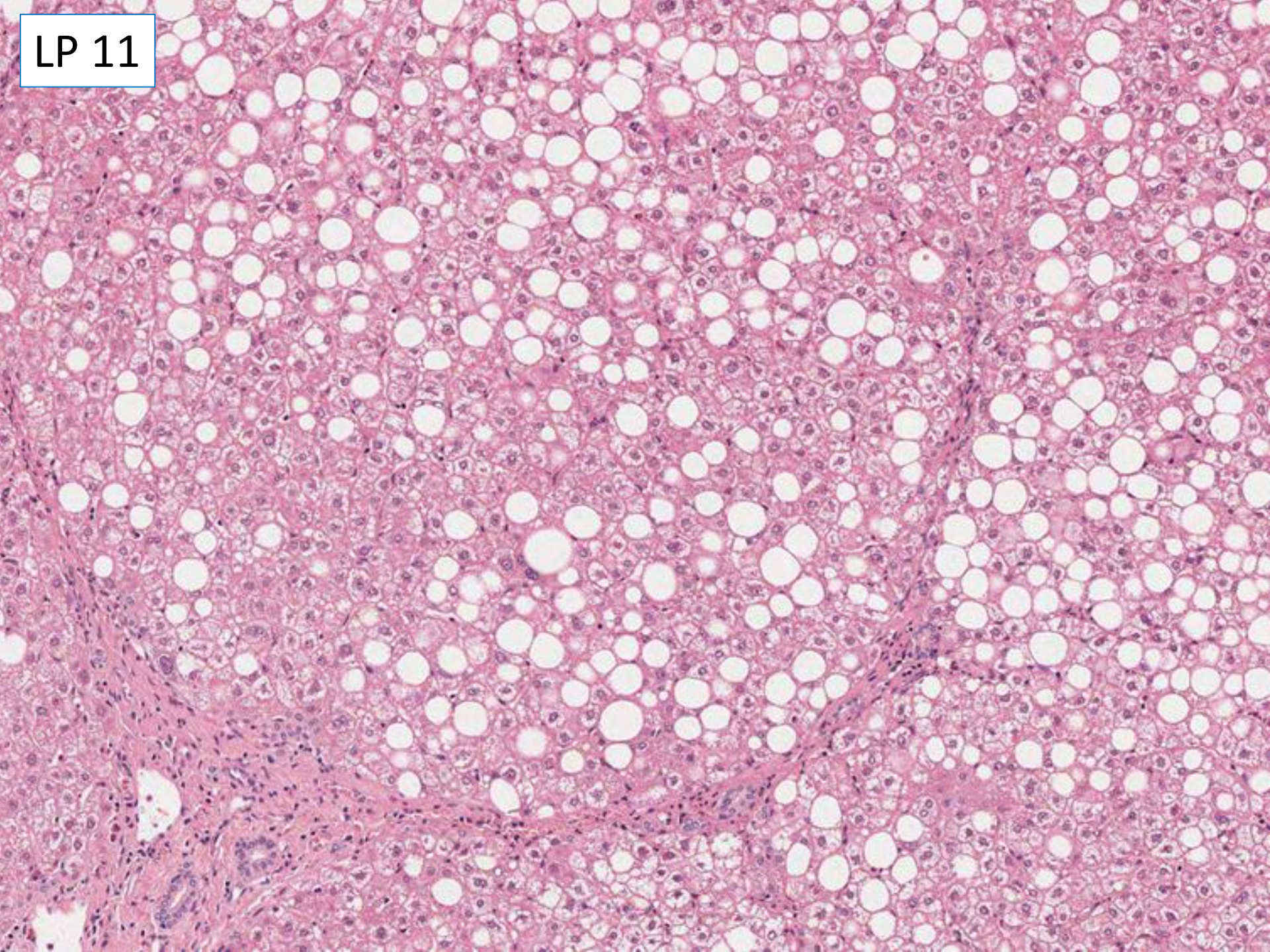
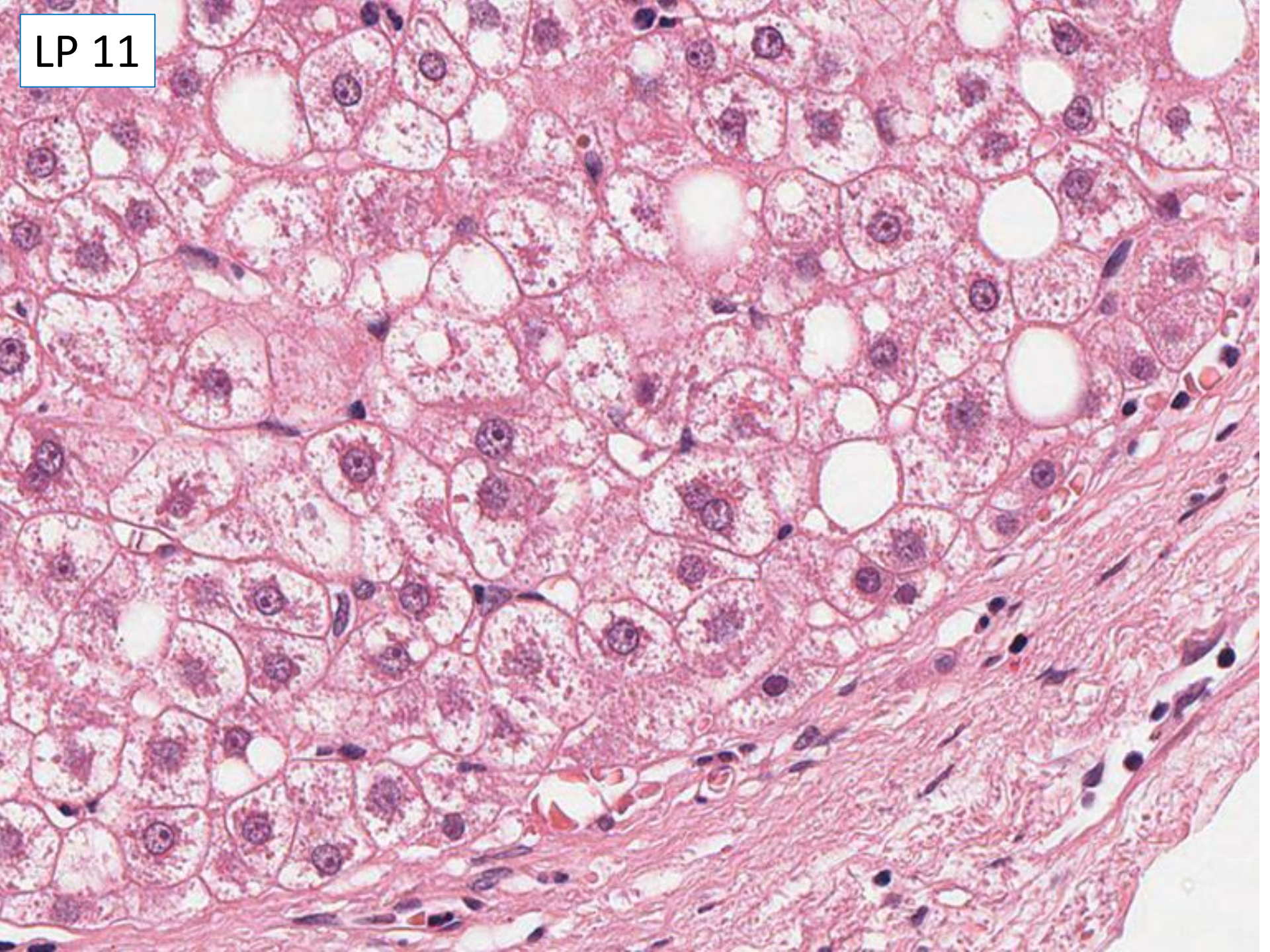

LP 11


LP 11


LP 11

Case LP11 59M

Known HCV infection. Wedge resection of liver with a subcapsular cream lesion 13 mm in maximum dimensions. HSA positive with canalicular pattern of staining with CD13 and pCEA.

Hepatocellular Carcinoma	89
Of which: HCC NOS	44
Well differentiated	1
Moderately differentiated	16
Poorly differentiated	16
Grade 2	1
Grade 3	2
High grade	4
Edmondson grade 3	1
Background liver not mentioned	2
Background cirrhosis	83
Advanced fibrosis	2
Consistent with HCV (several mentioned additional steatohepatitis)	58
Other cause (steatohepatitis or AIH), HCV not mentioned	3
No cause mentioned	23
Hepatitis B	1

Consensus complete diagnosis –

HCC on a background of cirrhosis consistent with hepatitis C.

How to score hepatitis B?
Survey results:
10/5/0 = 1/8/3

Agreed scoring:
for full marks include HCC and background cirrhosis. Lose 5 marks for hepatitis B and for background liver not mentioned.

Case LP11 59M

Known HCV infection. Wedge resection of liver with a subcapsular cream lesion 13 mm in maximum dimensions. HSA positive with canalicular pattern of staining with CD13 and pCEA.

A Cirrhosis, hepatitis B, probable HCC

B Cirrhosis, dysplastic nodule, needs reticulin

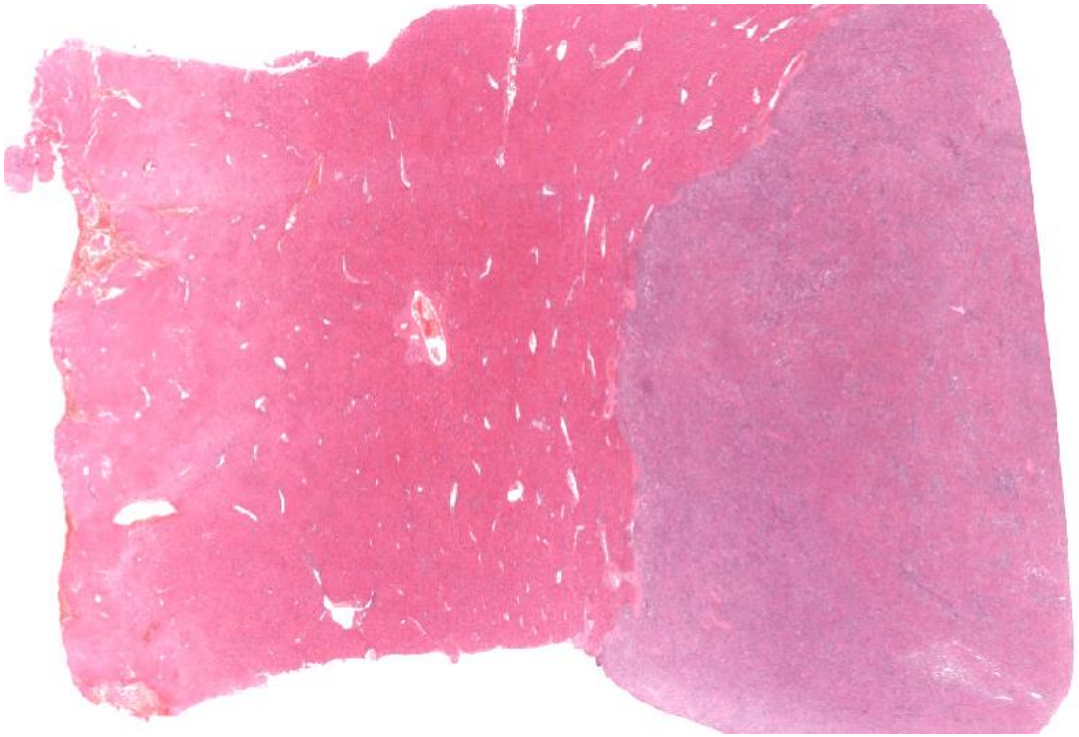
C HCC, cirrhosis, autoimmune hepatitis

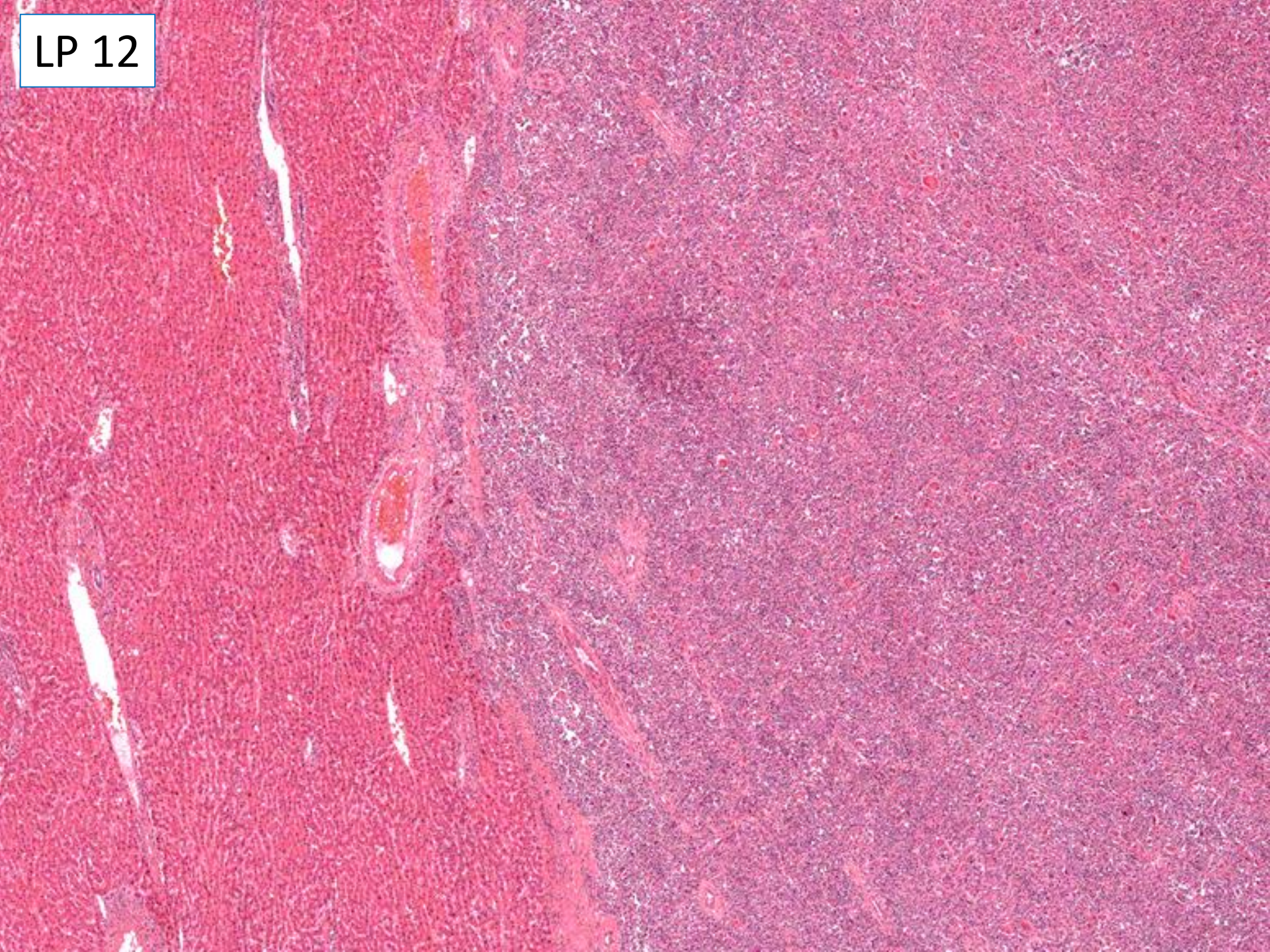
D HCC, cirrhosis, consistent with hepatitis C

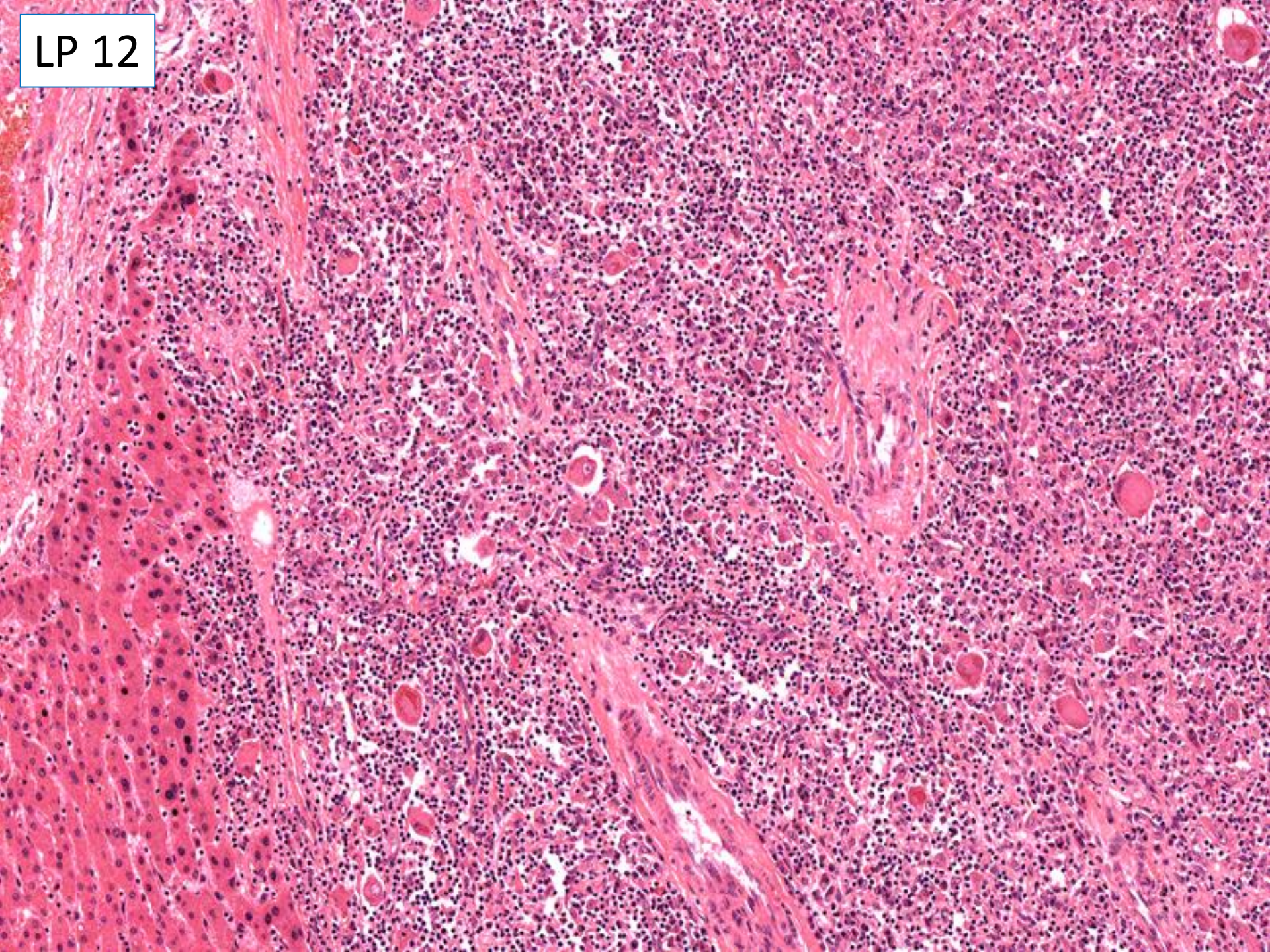
E HCC, cirrhosis, steatohepatitis

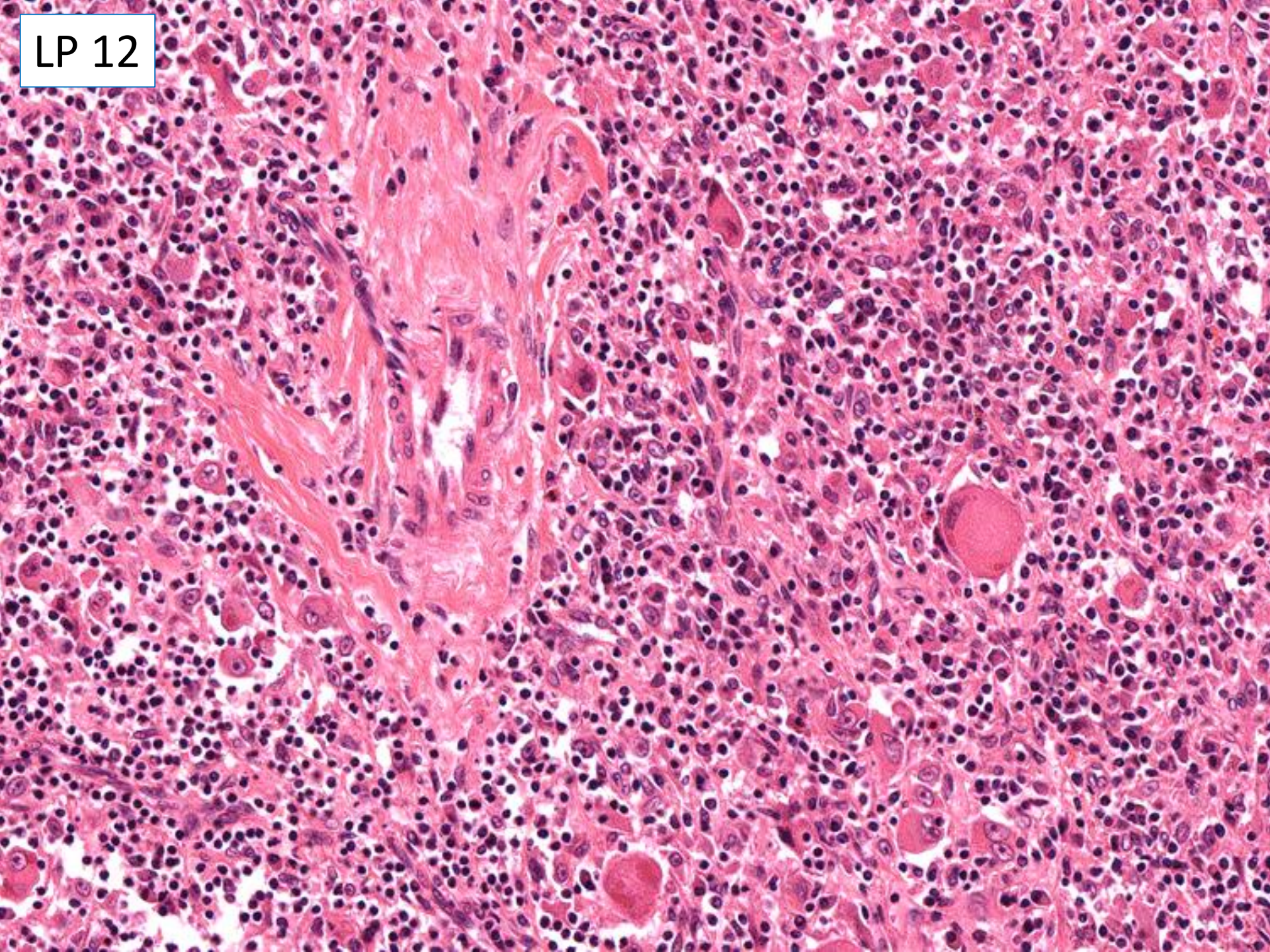
Case LP12 70M

Bladder resection previously for TCC. Now liver lesion ? met.
Segment 6 resection.
Liver with a well circumscribed partially cystic mass with a gelatinous and haemorrhagic cut surface nodule measuring 80 x 70 mm.
Patchy cytoplasmic positivity for HMB45. Negative for pancytokeratin, Desmin and SMA.




LP 12


LP 12


LP 12

Case LP12 70M

Bladder resection previously for TCC. Now liver lesion ? met. Segment 6 resection.
Liver with a well circumscribed partially cystic mass with a gelatinous and haemorrhagic cut surface nodule measuring 80 x 70 mm.
Patchy cytoplasmic positivity for HMB45. Negative for pancytokeratin, Desmin and SMA.

Angiomyolipoma (AML) most likely	20
AML unequivocal	14
Metastatic melanoma most likely	33
Neoplasm ? what, needs more IHC	15
Inflammatory pseudotumour/plasma cell granuloma	1
Extramedullary plasmacytoma	1
Inflammation due to TCC treatment	1
'tumour that is not typical of PEComa'	1
Differential granulomatous reaction to TCC treatment v AML v MM	1
Differential metastatic sarcomatoid TCC or benign inflammatory lesion	1

Consensus complete response – AML. Some mention inflammatory type of AML

Agreed scoring – not suitable for scoring. Educational case.

Case LP12 70M

Bladder resection previously for TCC. Now liver lesion ? met.

Segment 6 resection. Liver with a well circumscribed partially cystic mass with a gelatinous and haemorrhagic cut surface nodule measuring 80 x 70 mm.

Patchy cytoplasmic positivity for HMB45.
Negative for pancytokeratin, Desmin and SMA.

A Angiomyolipoma

B Metastatic malignant melanoma

C Inflammatory pseudotumour

D Metastatic sarcomatoid TCC

E Inflammation due to TCC treatment

The end