

# Liver EQA discussion LW 24.6.21.

Introduction – LW pilot of drop down menus – Rachel Brown

Cases 1-3 Paul Kelly

Cases 4-6 Rachel Brown

Cases 7-9 Rosa Miguel

Cases 10 – 12 Judy Wyatt

# Introduction

Thanks! 95 out of 116 participated.

New things:

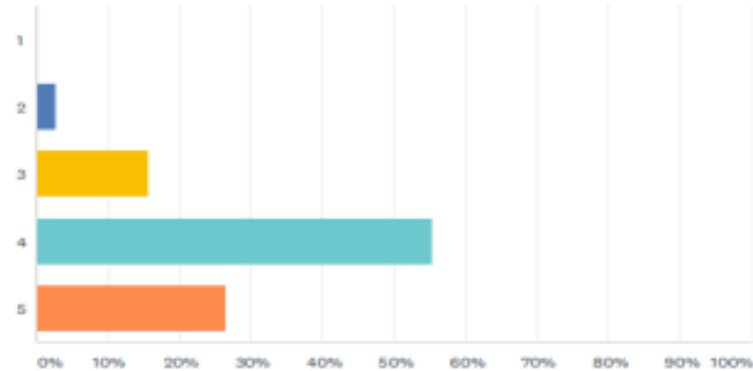
1. One virtual meeting per year and one as part of the annual November update day.
2. Digital slides.
3. Dropdown menus for responses.

How was it as participants? – survey responses (38)

# All responders (38) participated

Q2 The new drop down list formatThis is much easier for collation, and largely eliminates the subjective assessment of responses. How straightforward did you find it? - on a scale of 1 (really difficult) to 5 (very straightforward)

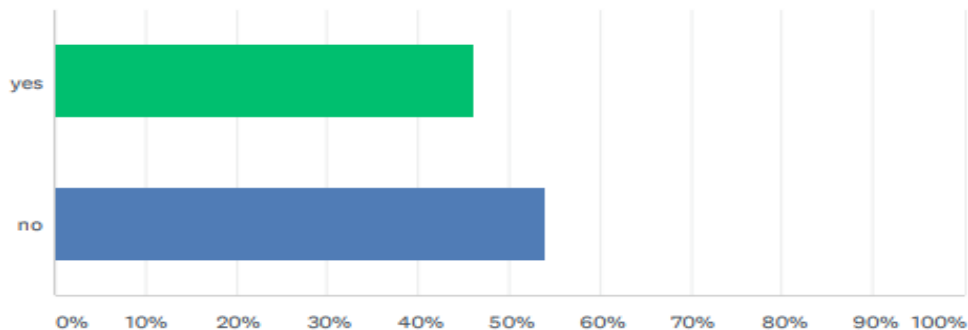
Answered: 38 Skipped: 0



ANSWER CHOICES	RESPONSES	
1	0.00%	0
2	2.63%	1
3	15.79%	6
4	55.26%	21
5	26.32%	10
TOTAL		38

Q3 Did you refer to the guidance provided for using the drop down menus? (From the liver EQA website - "This is the pilot EQA round for drop down menus. Guidance about using drop down menus is available here ")

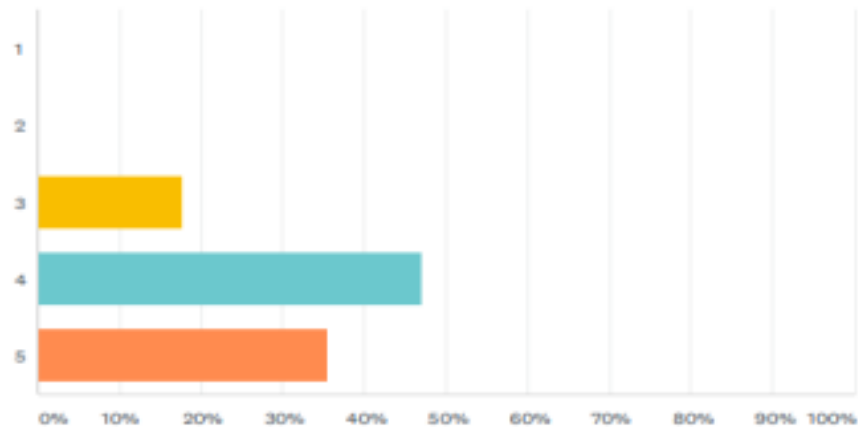
Answered: 37 Skipped: 1



ANSWER CHOICES	RESPONSES	
yes	45.95%	17
no	54.05%	20
TOTAL		37

Q4 If yes - was this guidance clear and comprehensive? (scale of 1 = impossible to understand to 5 = perfectly clear)

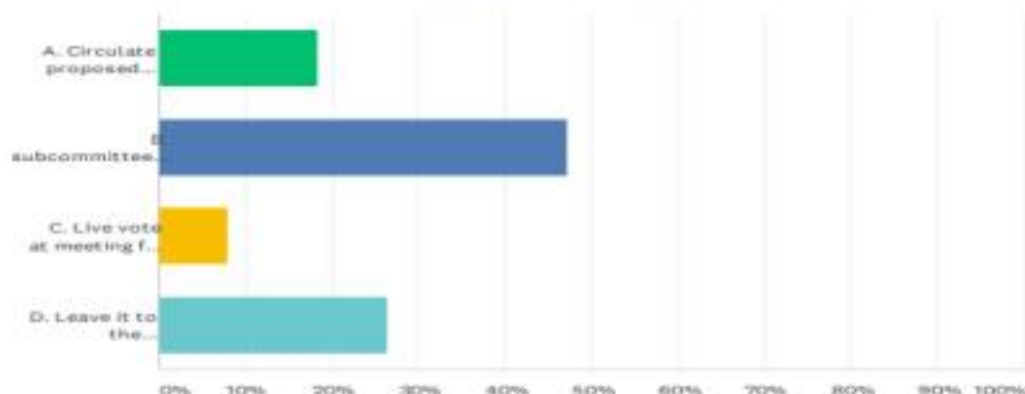
Answered: 17 Skipped: 21



ANSWER CHOICES	RESPONSES	
1	0.00%	0
2	0.00%	0
3	17.65%	3
4	47.06%	8
5	35.29%	6
TOTAL		17

**Q5** ScoringIt is a principle of EQA schemes that the scoring should be agreed by a quorate meeting of members rather than a small number of individuals. However this is really difficult in practice. If criteria are decided in advance of the meeting it leaves more time in the meeting itself for educational discussion rather than taking up time collecting votes. We have done this in different ways in the past - please indicate which you think we should adopt:

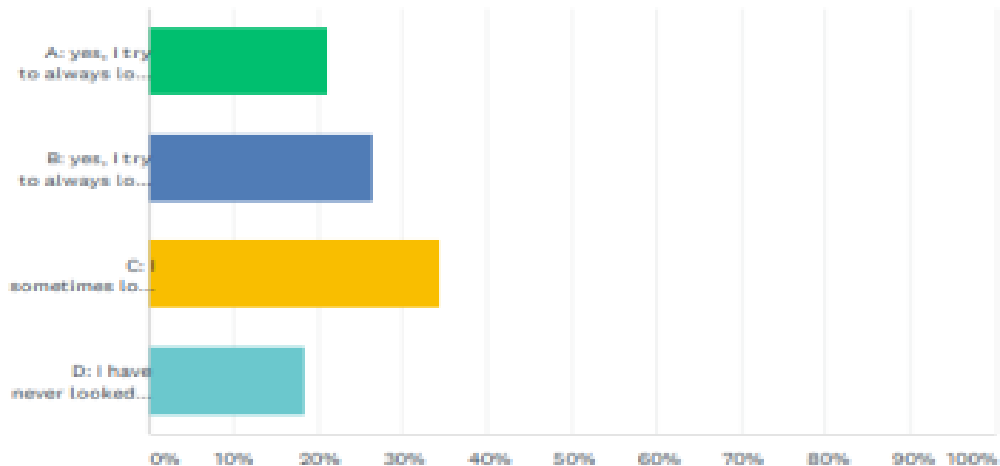
Answered: 38 Skipped: 0



ANSWER CHOICES	RESPONSES	
A. Circulate proposed scoring in advance of the meeting, collect comments prior to the meeting on surveymonkey	18.42%	7
B. subcommittee proposes principles for scoring, live vote at meeting where these may be contentious, then the agreed principles used to review response and determine score (what we're doing this time).	47.37%	18
C. Live vote at meeting for any response that may not score full marks	7.89%	3
D. Leave it to the subcommittee to mark responses, providing transparent criteria; no voting in meeting just educational discussion	26.32%	10
<b>TOTAL</b>		<b>38</b>

## Q6 When we have circulated proposed scoring for previous circulations in advance of the meeting have you looked at this?

Answered: 38 Skipped: 0



ANSWER CHOICES	RESPONSES	
A: yes, I try to always look before the meeting and send comments on proposals via surveymonkey	21.05%	8
B: yes, I try to always look before the meeting but have not sent comments	26.32%	10
C: I sometimes look before the meeting	34.21%	13
D: I have never looked at the circulated proposed scoring before the meeting.	18.42%	7
<b>TOTAL</b>		<b>38</b>

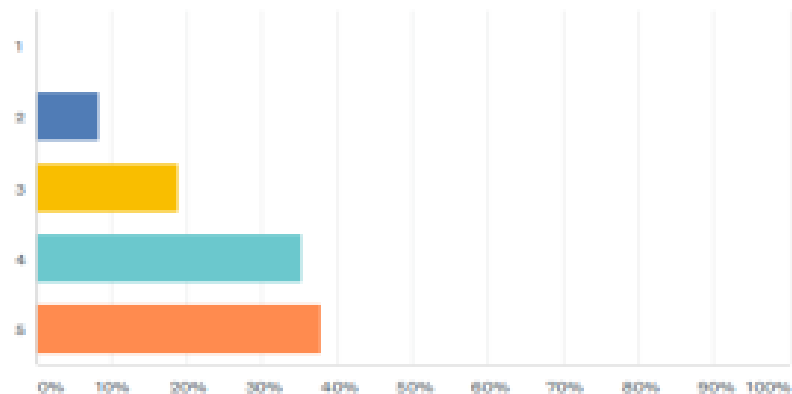
Q7 Do you feel this is adequate consultation of the membership to then avoid the need for frequent voting in the meeting?

Answered: 29 Skipped: 9

- In areas where the panel is unsure and % doesn't help voting a good use of time
- I like the subcommittee doing the scoring and then contentious areas discussed and points adjusted as per group consensus.
- If it is left to outside the meeting, as most members will not engage in the decisions; 1 ) their views will not be known 2) they themselves will lose the learning that comes from engaging in the difficult decisions
- This seems the best compromise, although pre-circulation of the suggested scoring is appreciated and allows contemplation and preparation for discussion.

Q8 We are in the process of changing to digital slides only. While this is still not routine diagnostic practice for most of us, it is now becoming the format of choice for EQA schemes. There are clear advantages in ensuring all participants see the same material, being able to include small biopsies, and efficiency of EQA organisation. This time there was an opportunity to request a box of glass slides - only 2 members did so. Were you able to view the slides digitally relatively easily?- on a scale of 1 (not possible) to 5 (no problems)

Answered: 37 Skipped: 1



ANSWER CHOICES	RESPONSES	
1	0.00%	0
2	8.11%	3
3	18.92%	7
4	35.14%	13
5	37.84%	14
TOTAL		37

# Digital slides

- Slower to look at them
- Several attempts needed
- sometimes difficult to load
- Early mornings or at home
- Time slots?
- Clean slides
- Fewer specials

Q9 Any insights from other EQAs that you take part in?

Answered: 17 Skipped: 21

Many schemes digital

Q10 Any other changes you would like to suggest?

Answered: 10 Skipped: 28

Liver – ‘concavity of spoons not sharpness of knives’

Appropriateness of dropdowns

As collators – much easier! Actually not different to what was happening before, we were manually having to define and separate responses into very similar categories now presented as menus.



Case number	Pathology	Tumour 1	Tumour 2	Text Diagnosis	consensus score
12	154	-No tumour/lesion present		venoocclusive disease	1
12	228	Other (please specify in Comments)		?segmental atrophy	1
12	18	focal nodular hyperplasia	hepatocellular adenoma NOS	Liver has features of both FNH and adenoma. Stain for Glutamine synthetase and for Beta catenin, SAA and LPDP.	5
12	53	hepatocellular adenoma NOS		I think adenoma rather than FNH.	5
12	66	hepatocellular adenoma NOS		'Telangiectatic FNH'	5
12	3	focal nodular hyperplasia		Focal nodular hyperplasia with multiple large abnormal vessels - some septa, but not diffusely nodular throughout, would be Glutamine synthetase for confirmation, as difficult background liver tissue	
12	7	focal nodular hyperplasia			
12	8	focal nodular hyperplasia			
12	11	focal nodular hyperplasia			
12	12	focal nodular hyperplasia		This looks like FNH; would do some connective tissue stain	
12	15	focal nodular hyperplasia			
12	16	focal nodular hyperplasia			
12	24	focal nodular hyperplasia			
12	22	focal nodular hyperplasia			
12	24	focal nodular hyperplasia		would like IHC against adenoma panel	
12	25	focal nodular hyperplasia		Beta and Glutamine synthetase to confirm (will have normal perivascular spaces in background)	
12	28	focal nodular hyperplasia			
12	31	focal nodular hyperplasia			
12	33	focal nodular hyperplasia			
12	34	focal nodular hyperplasia		focal nodular hyperplasia	
12	35	focal nodular hyperplasia	focal nodular hyperplasia		
12	37	focal nodular hyperplasia			
12	38	focal nodular hyperplasia			
12	48	focal nodular hyperplasia			
12	44	focal nodular hyperplasia			
12	55	focal nodular hyperplasia		Diagnosed Focal Nodular Hyperplasia (FNH)	
12	57	focal nodular hyperplasia		Other (please specify in Comments)	
12	58	focal nodular hyperplasia			
12	64	focal nodular hyperplasia		DIFFERENTIAL OF IHCW would like some special stains and IHC.	
12	65	focal nodular hyperplasia			
12	67	focal nodular hyperplasia			
12	74	focal nodular hyperplasia			
12	72	focal nodular hyperplasia			
12	75	focal nodular hyperplasia			
12	76	focal nodular hyperplasia			
12	77	focal nodular hyperplasia			
12	84	focal nodular hyperplasia			
12	82	focal nodular hyperplasia		FNH	
12	83	focal nodular hyperplasia		Liver is FNH. Looks prominent scar and bile ductular prol	3
12	85	focal nodular hyperplasia	focal nodular hyperplasia	FNH with vascular scar	7
12	88	focal nodular hyperplasia		Macrolicly and nodular scar and dividing fibrous septa with des	8
12	38	focal nodular hyperplasia		nodules. Consistent with focal nodular hyperplasia	11
12	35	focal nodular hyperplasia			
12	33	-No tumour/lesion present	focal nodular hyperplasia		
12	188	focal nodular hyperplasia			This looks like FNH; would do some connective tissue
12	181	focal nodular hyperplasia			
12	183	focal nodular hyperplasia		Young female single node containing irregular vascular area	16
12	143	focal nodular hyperplasia			
12	128	focal nodular hyperplasia			
12	126	focal nodular hyperplasia		No background liver present for assessment.	22
12	123	focal nodular hyperplasia			
12	158	focal nodular hyperplasia	-No tumour/lesion present		24
12	151	focal nodular hyperplasia			
12	157	focal nodular hyperplasia			
12	153	focal nodular hyperplasia			

Example of drop-down menu:  
 From Case 12: responses from EQALite, excel spread sheet, conditional formatting to identify and analyse non-consensus responses.

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12	33	focal nodular hyperplasia			
12	34	focal nodular hyperplasia		focal nodular hyperplasia	
12	35	focal nodular hyperplasia	focal nodular hyperplasia		
12	37	focal nodular hyperplasia			
12	38	focal nodular hyperplasia			
12	48	focal nodular hyperplasia			
12	44	focal nodular hyperplasia			
12	55	focal nodular hyperplasia		Diagnosed Focal Nodular Hyperplasia (FNH)	
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12	76	focal nodular hyperplasia			
12	77	focal nodular hyperplasia			
12	84	focal nodular hyperplasia			
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12	83	focal nodular hyperplasia		Liver is FNH. Looks prominent scar and bile ductular prol	3
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12	88	focal nodular hyperplasia		Macrolicly and nodular scar and dividing fibrous septa with des	8
12	38	focal nodular hyperplasia		nodules. Consistent with focal nodular hyperplasia	11
12	35	focal nodular hyperplasia			
12	33	-No tumour/lesion present	focal nodular hyperplasia		
12	188	focal nodular hyperplasia			This looks like FNH; would do some connective tissue
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12	123	focal nodular hyperplasia			
12	158	focal nodular hyperplasia	-No tumour/lesion present		24
12	151	focal nodular hyperplasia			
12	157	focal nodular hyperplasia			
12	153	focal nodular hyperplasia			

# EQAlite response form with drop down menus –

1. tumour, non-lesional: 2. pattern of injury; 3. architecture/stage;
4. favoured diagnosis; comments (used in scoring)

## Your Diagnosis

1. Please select either 'No tumour/lesion present' or choose the best option for the lesion you think is present, you may choose two options if two lesions are present (BOTH need to be present this is NOT to give a differential diagnosis).

- No tumour/lesion present

\*\*\* Please Select \*\*\*

2. Non-lesional assessment (includes background liver, if sufficiently represented, in a section of a lesion). Please select the best option for the pattern of injury (see RCPATH tissue pathways appendix C). Use any available special stains. You may choose two options if two patterns are present (BOTH need to be present this is NOT to give a differential diagnosis).

steatohepatitis

\*\*\* Please Select \*\*\*

3. Architecture/Stage as RCPATH tissue pathway. If there is a connective tissue stain this is expected to be completed. You may still offer a stage on an H&E if you wish/feel it is appropriate. Include background liver in a section with a lesion.

fibrosis with bridging between vascular structures

4. Favoured diagnosis, take account of available clinical information. Tumour diagnosis will have been given in section 1, if applicable use this for background diagnosis. You may choose more than one if two diagnoses are suggested (BOTH need to be present this is NOT to give a differential diagnosis).

fatty liver disease - either alcohol or non-alcohol

\*\*\* Please Select \*\*\*

Comments (maximum 200 characters) relevant to the diagnosis that will be read by the collators and **can be used in the scoring**. You may record brief, essential information not covered by the menu options.

NASH CRN steatosis 1 inflammation 3 ballooning 2 = 6/8 fibrosis 3/4.

Personal notes - to use as your own aide memoire - **the contents of this will not be used for scoring**.

- Today; aim to share what data looks like and how we propose to use it to create scoring criteria the membership is comfortable with. Wont be used for ranking/identification of lowest 2%. Will still count for CPD.
- Our instructions to you – seems from responses it was not clear that if there is only one pattern or diagnosis just need to use one box. Impression that the menus might be ‘forcing’ a second option to be filled in. Might have written something more nuanced...
- Process illustrated by examples today.

# EQA aims

- Artificial exercise
- Good for ticking appraisal/revalidation boxes
- Self reflection
- Educational
- Report, not harmful, and ideally useful ! to the patient that any hepatologist anywhere in the country understands
- **Please send cases! 3 x H&E plus relevant specials**

# Circulation LW

- Number of responses = 95 / 116 current members (82%)
- Number needed to achieve 80% consensus = 76
- Members offered the option of a box of glass slides on request – only 2 boxes were requested.

**LW1**

# LW1

Female 61 years

Abnormal liver function; fatty on ultrasound Additional from lb computer system- patient wheelchair bound with MS; Anti smooth muscle antibody positive; other autoantibodies negative; no record of viral screen; no history of alcohol ; no drug history available.

Specimen: Liver biopsy.

Macroscopic description: 3 cores.

Immunohistochemistry: Massons Trichrome and retic provided.

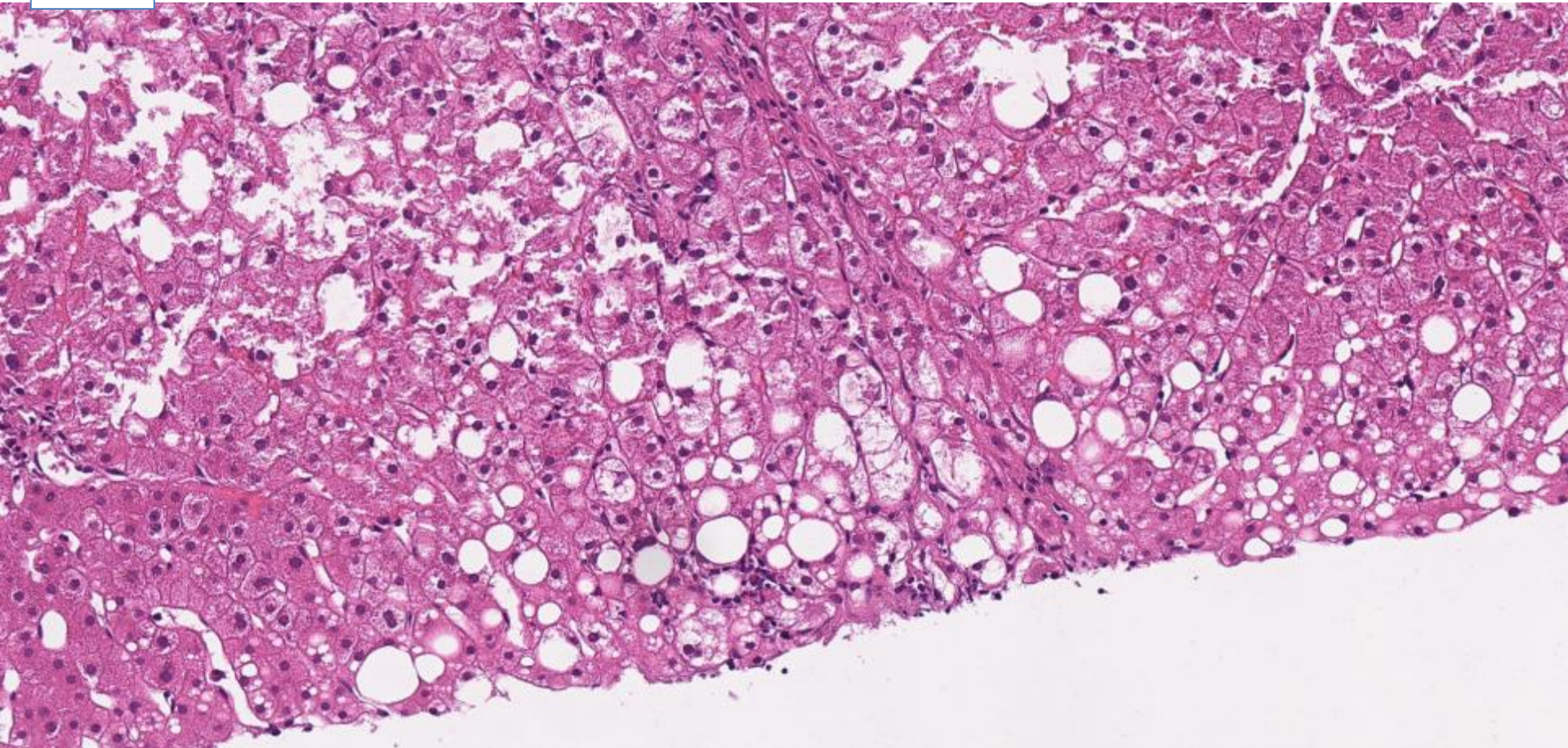
LW1



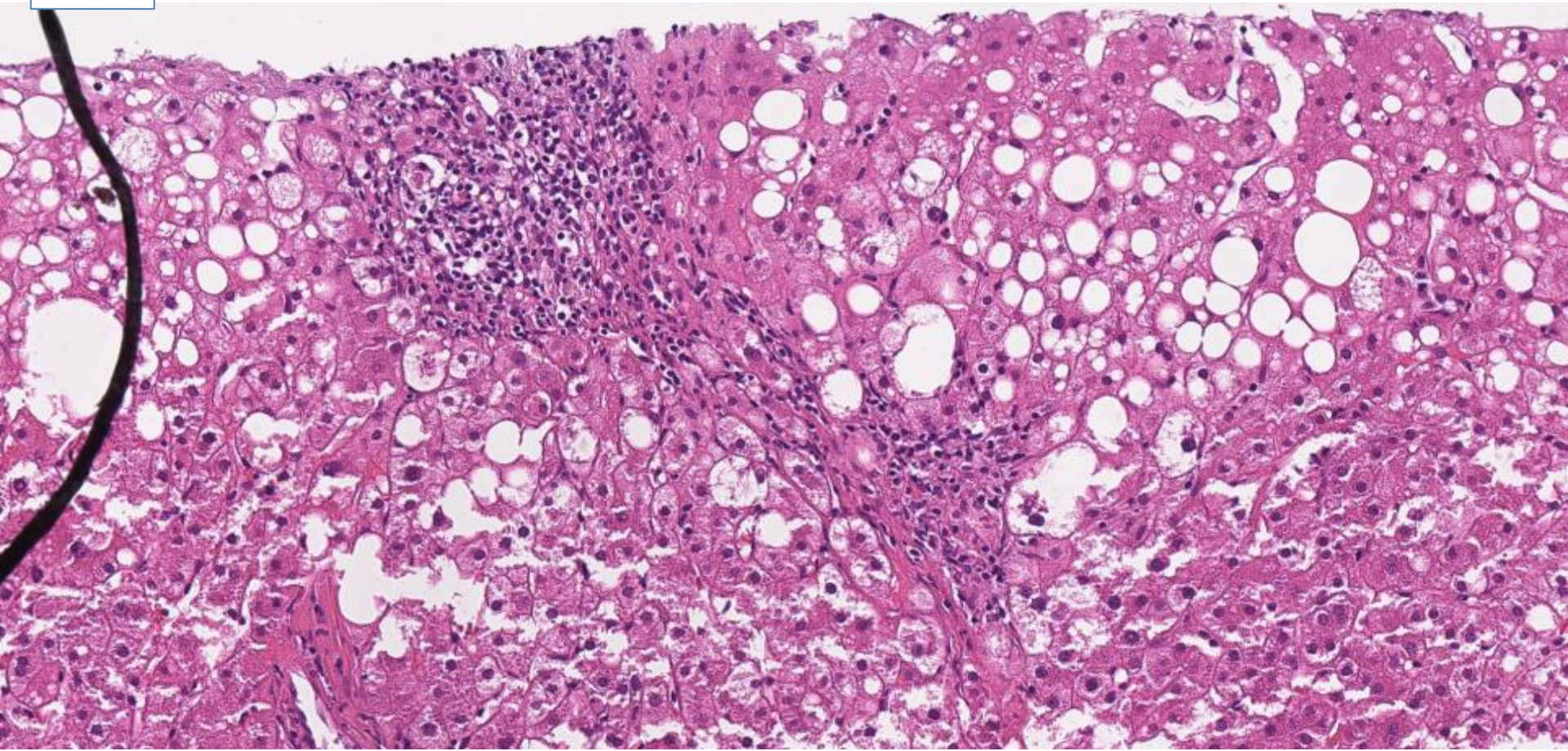
LW1



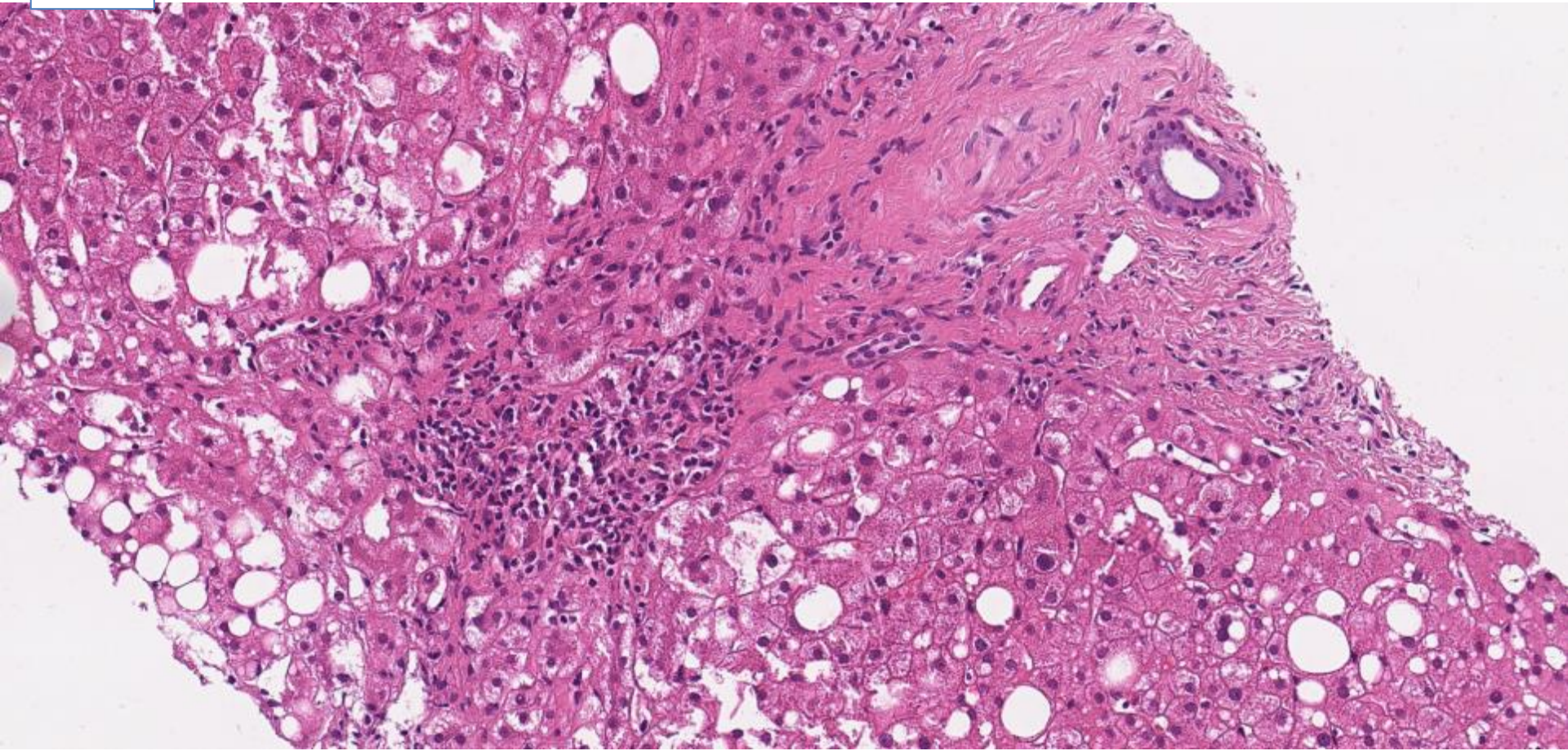
LW1



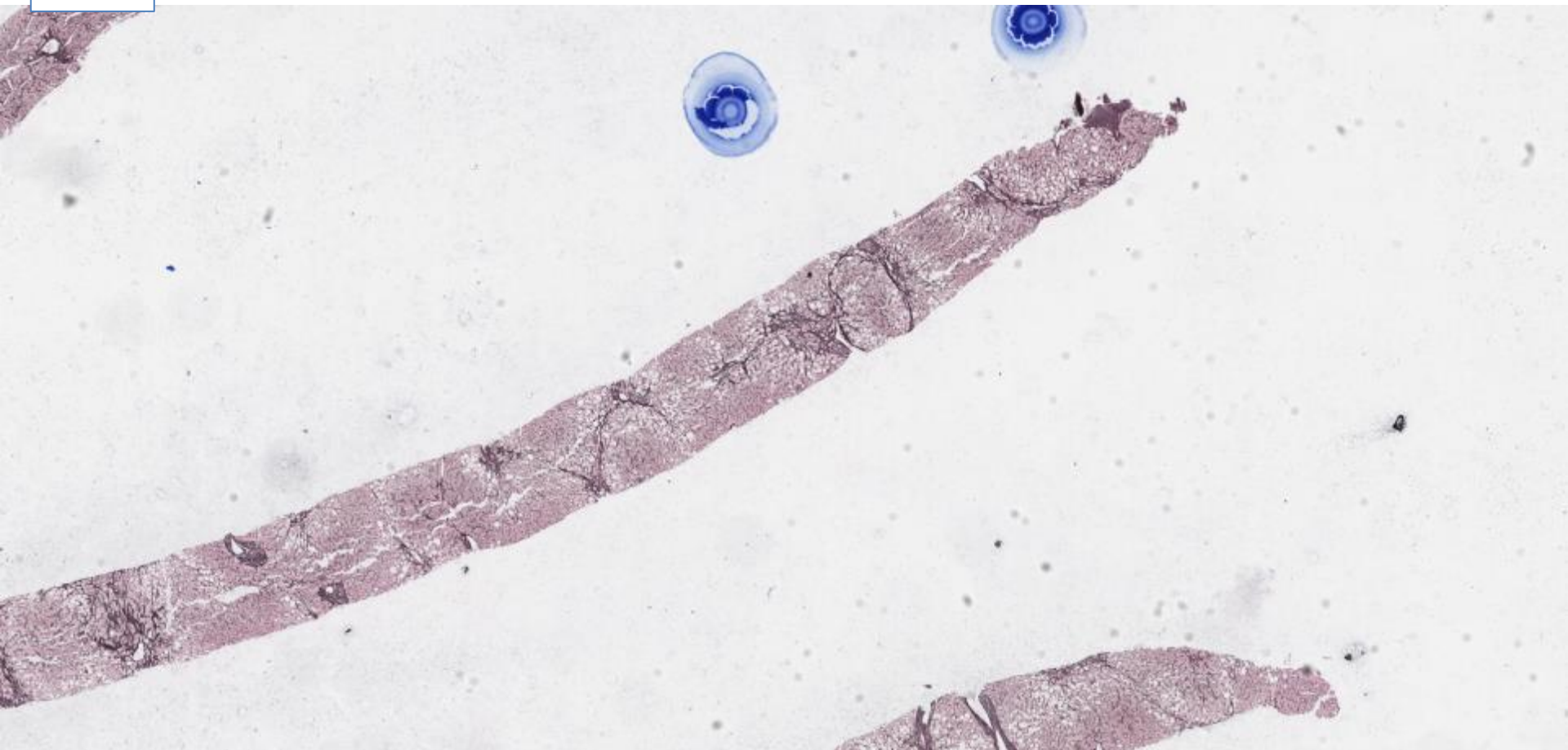
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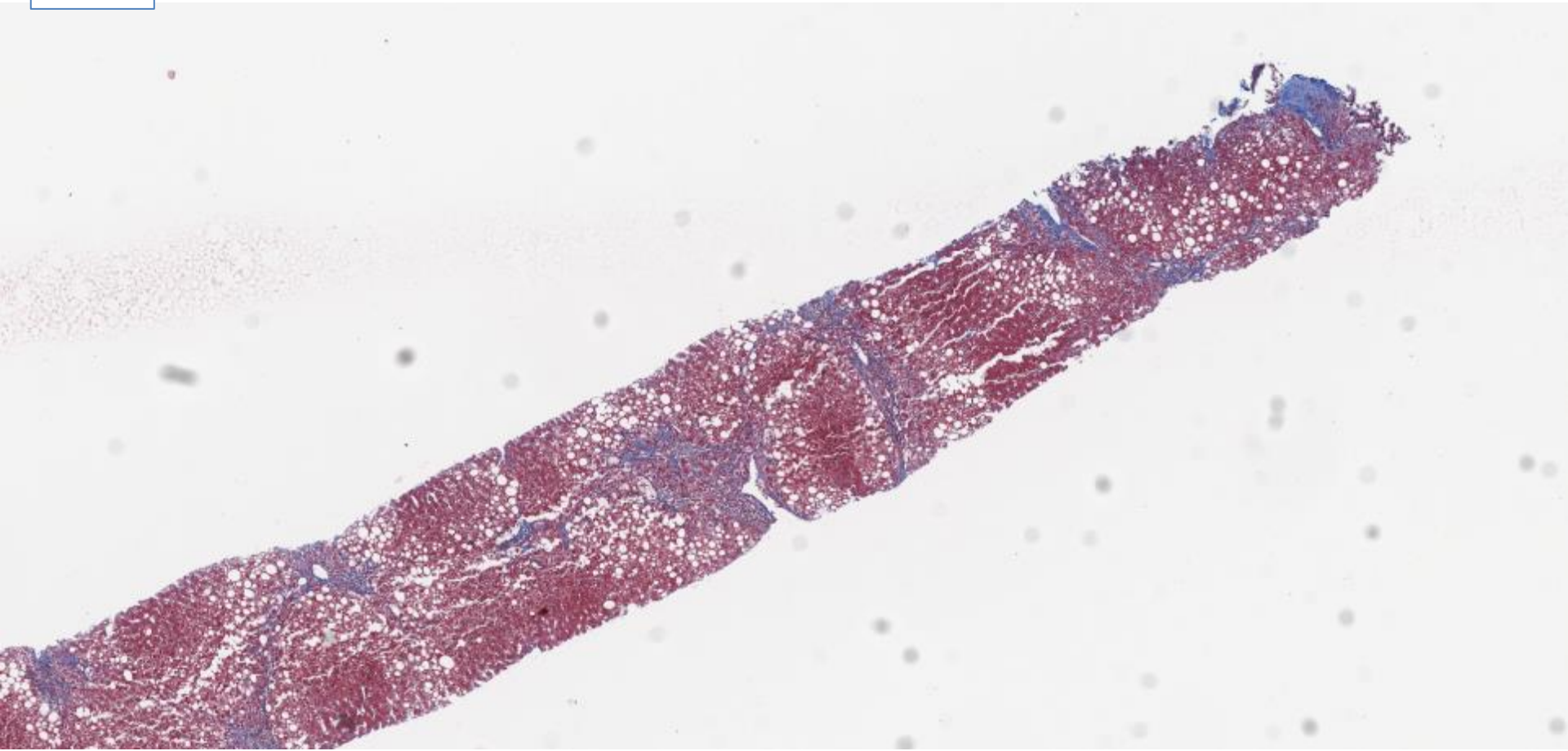
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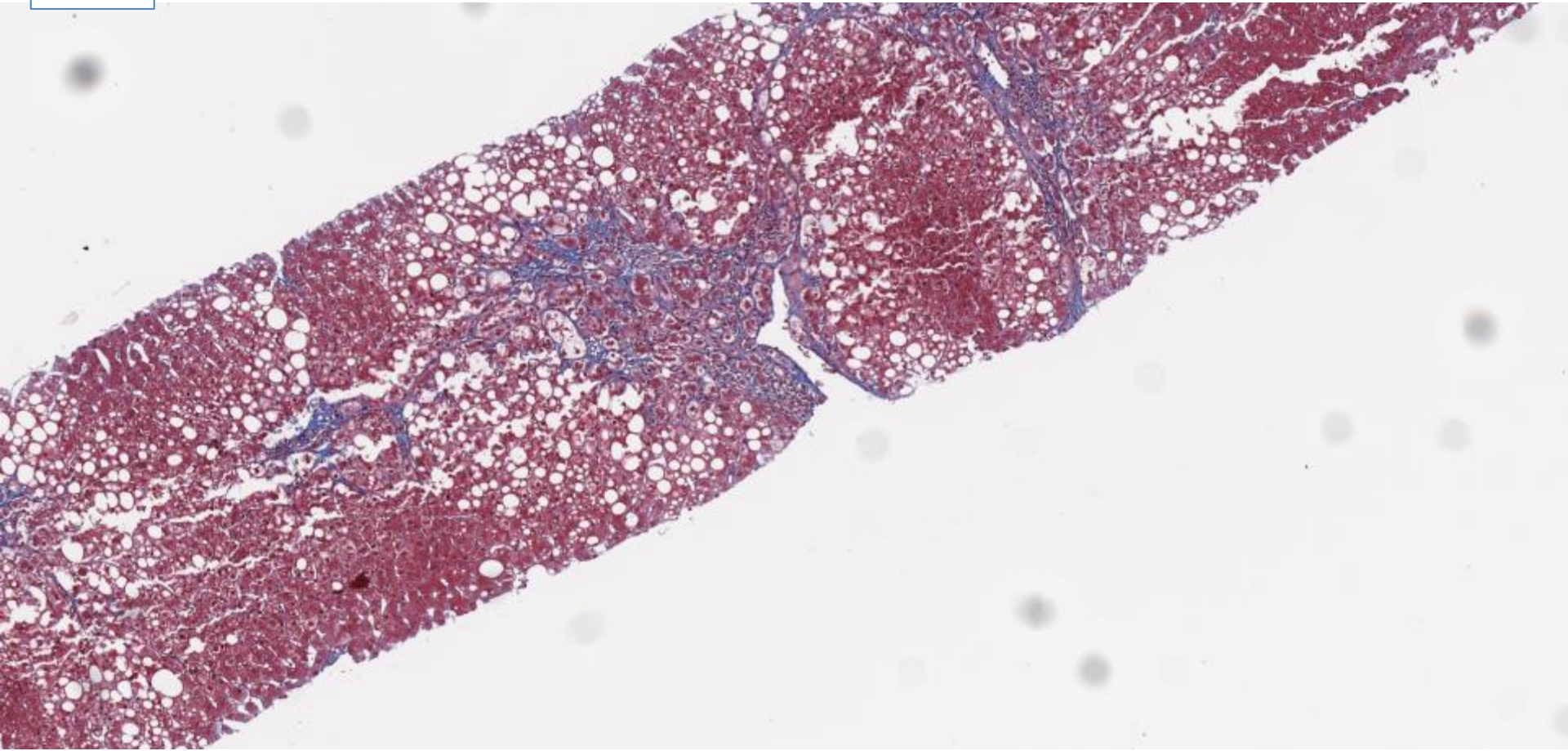
LW1



LW1



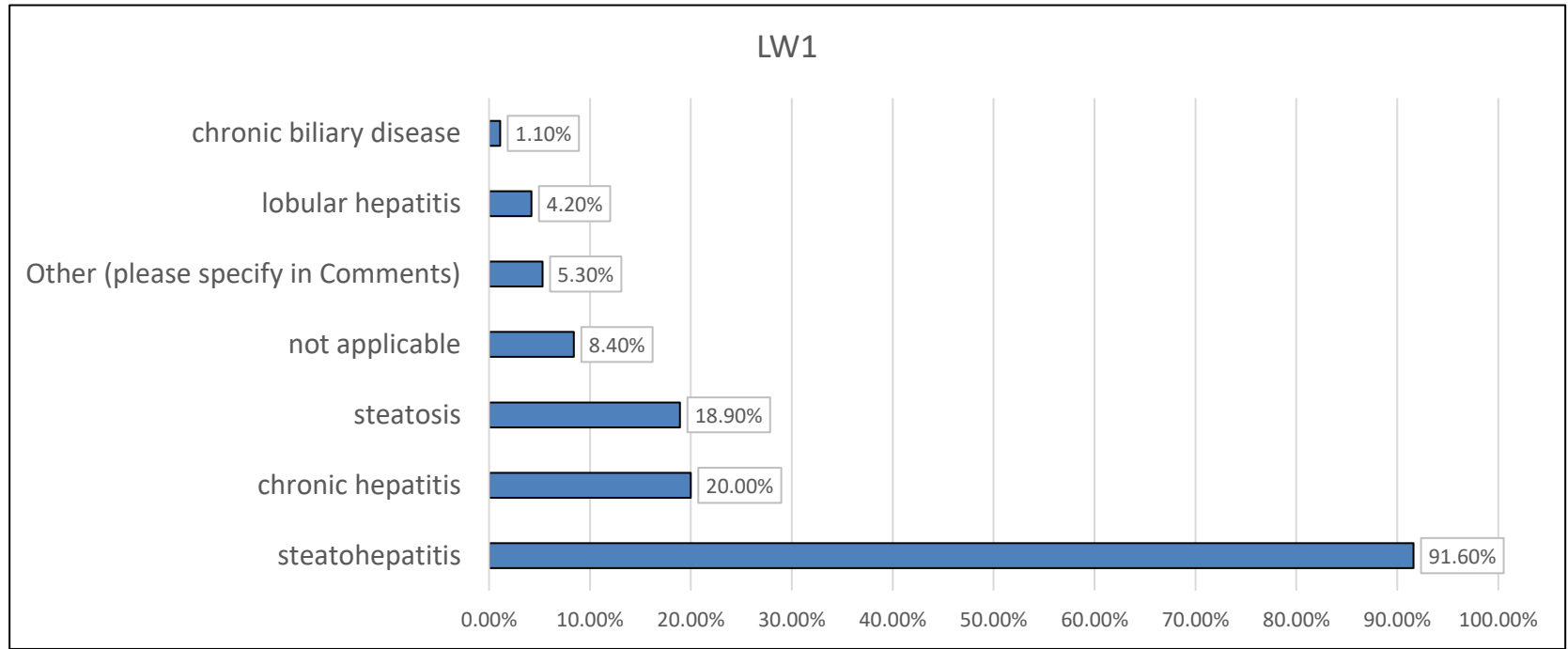
LW1



# Staging

Stages:	Popularity:
<b>fibrosis with bridging between vascular structures</b>	75.8%
<b>advanced fibrosis with bridging and nodularity/cirrhosis</b>	22.1%
<b>Other (please specify in Comments)</b>	1.1%
<b>mild/early fibrosis without bridging</b>	1.1%

~ 98% bridging or worse:  
consensus achieved



87 participants documented steatohepatitis (SH)

78: SH as Pattern 1

9 : SH as Pattern 2 (Pattern 1 = steatosis (n = 6); chronic hepatitis (n = 2); chronic biliary disease (n = 1))

19 participants documented chronic hepatitis (n = 6 as pattern 1, n = 13 as pattern 2)

Pattern 1:	Pattern 2:	Count:	
steatohepatitis		43	
steatohepatitis	chronic hepatitis	13	
steatohepatitis	not applicable	8	
steatosis	steatohepatitis	6	
steatohepatitis	steatosis	6	
steatohepatitis	Other (please specify in Comments)	4	
chronic hepatitis	steatosis	3	D = Viral hepatitis
steatohepatitis	lobular hepatitis	2	
chronic hepatitis	steatohepatitis	2	
steatohepatitis	steatohepatitis	2	D = FLD; SH in comment
steatosis	lobular hepatitis	1	D = AIH
chronic hepatitis		1	SH not clear from comment
steatosis	Other (please specify in Comments)	1	
chronic biliary disease	steatohepatitis	1	D = AIH/FLD
lobular hepatitis	lobular hepatitis	1	
steatosis		1	

Pattern 1:	Pattern 2:	Count:	
<p>&gt;80% of participants stated SH            BUT            by default includes significant minority that indicated second, concurrent pattern e.g. chronic hepatitis</p>			
chronic hepatitis	steatosis	3	
<b>steatohepatitis</b>	lobular hepatitis	2	
<b>chronic hepatitis</b>	<b>steatohepatitis</b>	2	
<b>steatohepatitis</b>	<b>steatohepatitis</b>	2	D = FLD; SH in comment
<b>steatosis</b>	lobular hepatitis	1	AIH in diagnosis
<b>chronic hepatitis</b>		1	SH not clear from comment
<b>steatosis</b>	Other (please specify in Comments)	1	
<b>chronic biliary disease</b>	<b>steatohepatitis</b>	1	AIH/FLD as diagnosis
<b>lobular hepatitis</b>	lobular hepatitis	1	
<b>steatosis</b>		1	

Diagnostic categories:	Popularity:
fatty liver disease - non-alcohol related fatty liver disease	64.2%
fatty liver disease - either alcohol or non-alcohol	31.6%
autoimmune hepatitis	20.0%
Other (please enter alternative diagnosis in comments box)	2.1%
chronic viral hepatitis (hepatotropic viruses - please specify in comments box)	1.1%
- histologically indeterminate for cause	1.1%
Diagnosis Combination:	Count:
fatty liver disease - non-alcohol related fatty liver disease	44
fatty liver disease - either alcohol or non-alcohol	25
autoimmune hepatitis, fatty liver disease - non-alcohol related fatty liver disease	14
autoimmune hepatitis, fatty liver disease - either alcohol or non-alcohol	4
[No selections made]	2
fatty liver disease - non-alcohol related fatty liver disease, Other (please enter alternative diagnosis in comments box)	2
- histologically indeterminate for cause	1
autoimmune hepatitis	1
chronic viral hepatitis (hepatotropic viruses - please specify in comments box)	1
fatty liver disease - either alcohol or non-alcohol, fatty liver disease - non-alcohol related fatty liver disease	1

~76%

21%

Diagnostic categories:	Popularity:
fatty liver disease - non-alcohol related fatty liver disease	64.2%
fatty liver disease - either alcohol or non-alcohol	31.6%

No consensus for responses stating a **single** diagnostic category **in isolation** but “FLD” OR “FLD + AIH” is > 80%

fatty liver disease - non-alcohol related fatty liver disease	44	} 21 %
fatty liver disease - either alcohol or non-alcohol	25	
autoimmune hepatitis, fatty liver disease - non-alcohol related fatty liver disease	14	
autoimmune hepatitis, fatty liver disease - either alcohol or non-alcohol	4	
[No selections made]	2	
fatty liver disease - non-alcohol related fatty liver disease, Other (please enter alternative diagnosis in comments box)	2	
- histologically indeterminate for cause	1	
autoimmune hepatitis	1	
chronic viral hepatitis (hepatotropic viruses - please specify in comments box)	1	
fatty liver disease - either alcohol or non-alcohol, fatty liver disease - non-alcohol related fatty liver disease	1	

# Summary

- >80% responses: “at least bridging fibrosis”
- >80 % responses: steatohepatitis (pattern 1 or 2)
  - *Includes participants that stated steatohepatitis and an additional pattern e.g. chronic hepatitis etc.*
- No consensus for fatty liver disease in isolation as diagnosis
  - i.e. no outright consensus for “SH and FLD, and bridging fibrosis”
- **“SH, FLD and at least bridging fibrosis” combined with “SH, FLD and AIH and bridging fibrosis” reaches consensus**

# Consensus complete response (if accepted)

- Steatohepatitis (SH); fatty liver disease, non-alcohol related +/- alcohol related. At least bridging fibrosis. 10 marks.
  - FLD and AIH AND SH included as a pattern, and at least bridging fibrosis 10 marks
- 
- Lose 5 marks
    - Steatosis but not steatohepatitis
    - Chronic biliary disease (as well as steatohepatitis)
    - A single cause other than FLD/steatohepatitis
    - Less than bridging fibrosis
  - Lose 10 marks
    - If more than one above from lose 5 marks categories

- Is this case acceptable for scoring as presented?
  - Consensus requires diagnostic and pattern combinations to achieve necessary 80% threshold
- Yes or no? – **vote at the meeting - yes**

# Discussion points

**Original diagnosis: steatohepatitis with significant fibrosis/some incomplete nodules/probable cirrhosis**

How much portal/lobular inflammation is allowed in FLD?

How to report biopsies with potential AIH and FLD?

## Discussion at the meeting

Some portal inflammation is common in NASH, especially with advancing fibrosis. We should be very cautious about diagnosing AIH as well as NASH, SMA is not uncommon in NASH.

Perivenular inflammation and fibrosis – can also develop ducts and arteries so start to look very similar to portal tracts – may account for some of the impression of portal inflammation in this case.

Treatment for AIH with steroids is contra-indicated in NASH.

Only suggest additional AIH if very conspicuous plasma cells and interface hepatitis.

Clinical follow up – no evidence that this patient had AIH as well as NASH.

**LW 2**

# LW 2

- Female 56 years

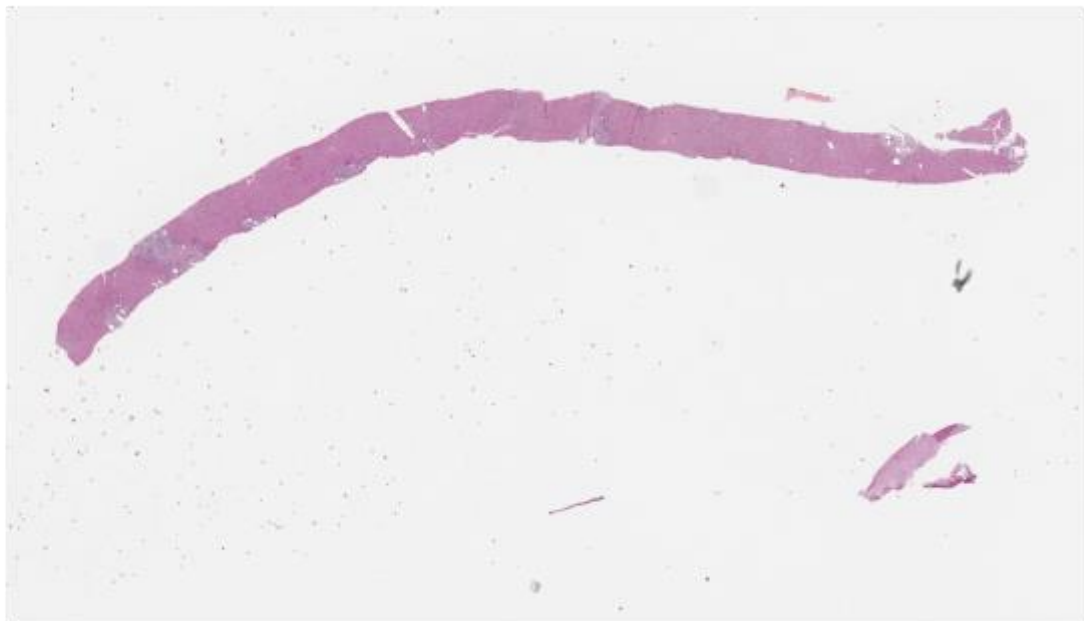
Post cholecystectomy. Cholestatic LFT's. 3x previous episodes of sepsis - klebsiella 2x E coli. Liver abscess March 2017. Repeat MRCP - possible progressive extrahepatic duct dilatation and mild central intrahepatic duct dilatation. Bili 7, ALP 135, ALT 95, GGT 195, AST 73. ?Cause of deranged LFT's. Positive soluble live antigen. ?Degree fibrosis.

Specimen: Medical liver biopsy.

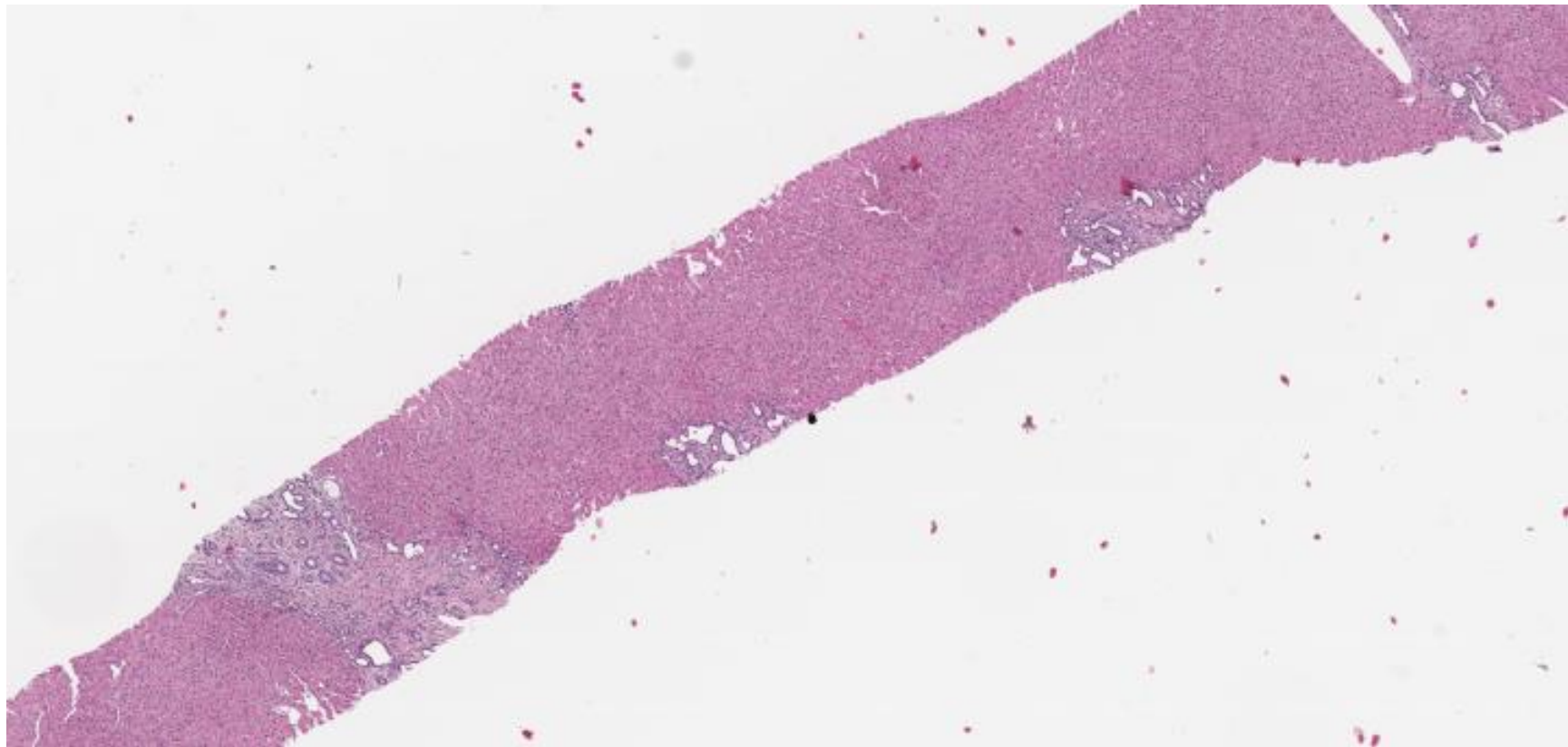
Macroscopic description: A core of tan tissue 19mm in length. Processed intact.

Immunohistochemistry: None.

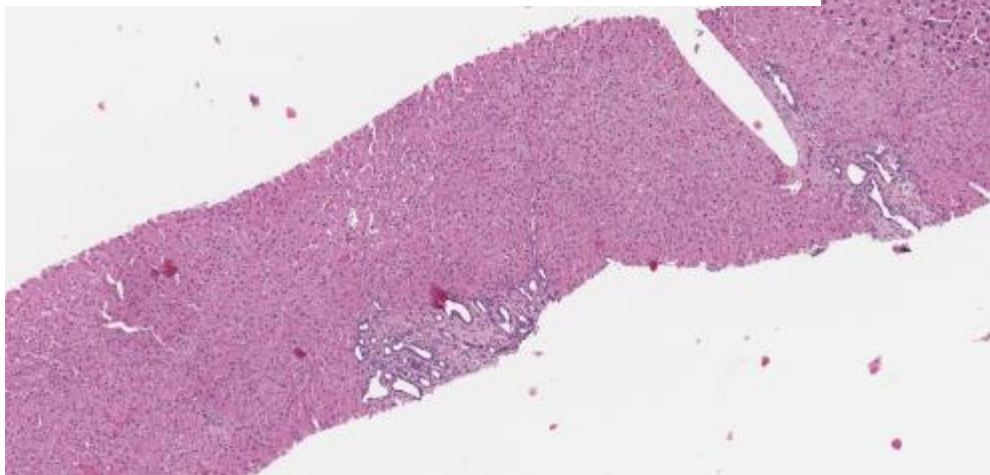
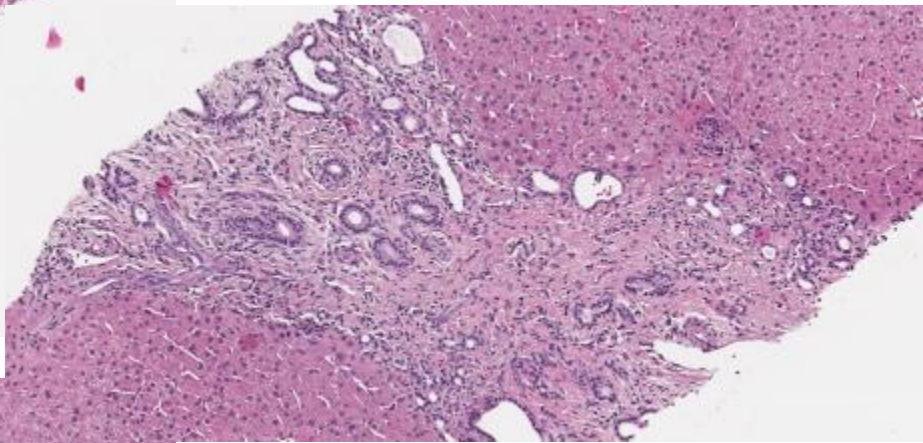
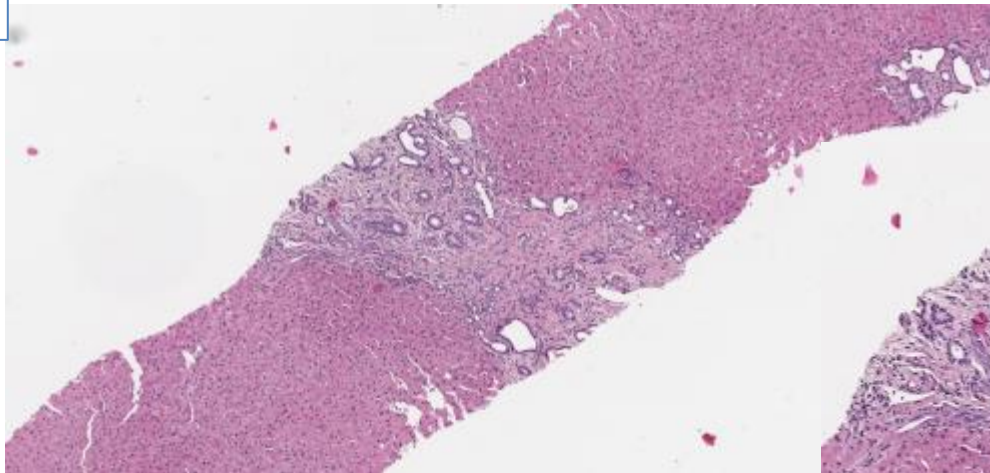
LW2



LW2



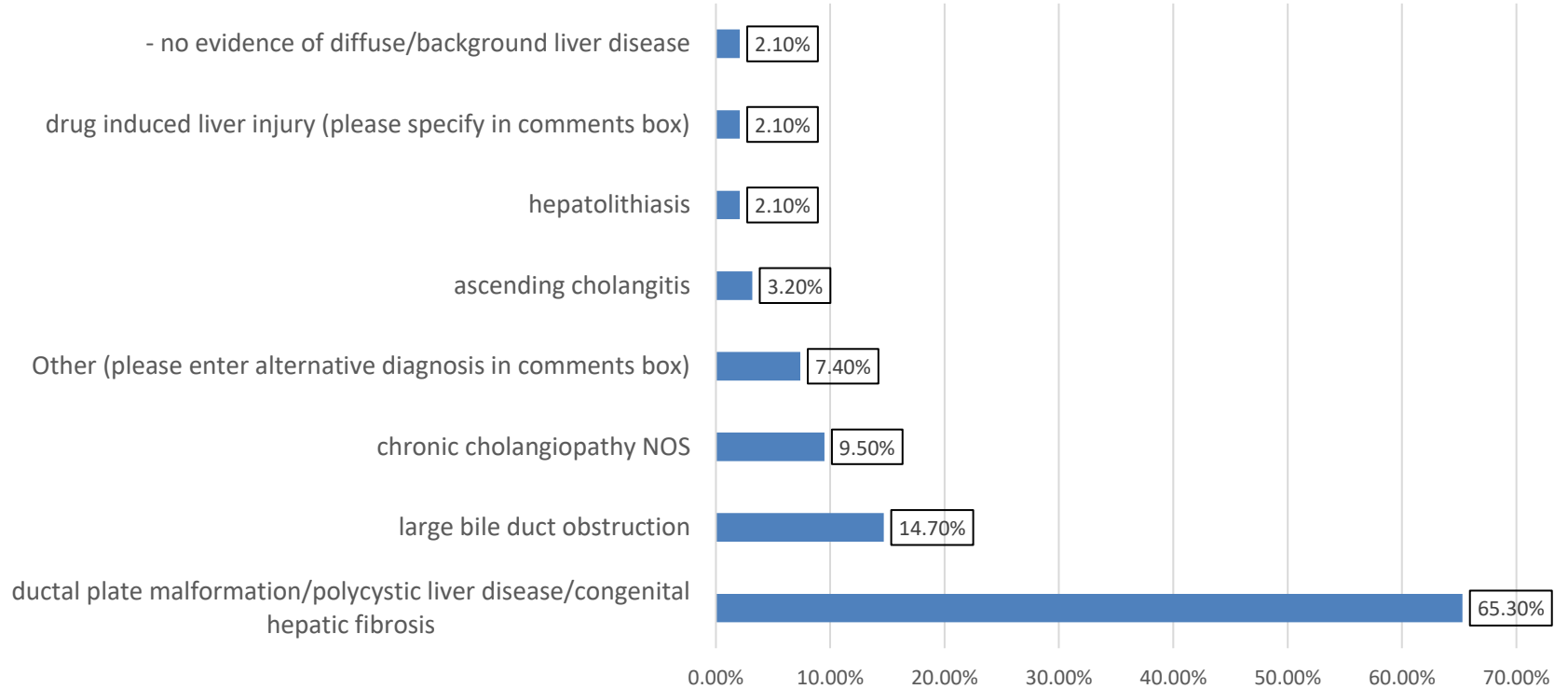
LW2



LW2

Pattern:	Popularity:
Other (please specify in Comments)	47.4%
chronic biliary disease	34.7%
within normal limits	10.5%
not applicable	5.3%
abnormal, no pattern discernible	4.2%
cholestasis, bilirubinostasis	2.1%
chronic hepatitis	1.1%
vascular disease	1.1%

Pattern 1:	Pattern 2:	Count :
Other (please specify in Comments)		37
chronic biliary disease		27
within normal limits		9
abnormal, no pattern discernible		4
Other (please specify in Comments)	not applicable	4
		3
chronic biliary disease	cholestasis, bilirubinostasis	2
Other (please specify in Comments)	Other (please specify in Comments)	2
chronic biliary disease	vascular disease	1
within normal limits	within normal limits	1
chronic biliary disease	chronic biliary disease	1
Other (please specify in Comments)	chronic biliary disease	1
chronic hepatitis	chronic hepatitis	1
not applicable	not applicable	1
chronic biliary disease	Other (please specify in Comments)	1

**Diagnostic category:**

Diagnosis Combination:	Count:
ductal plate malformation/polycystic liver disease/congenital hepatic fibrosis	58
large bile duct obstruction	10
chronic cholangiopathy NOS	7
Other (please enter alternative diagnosis in comments box)	5
[No selections made]	2
- no evidence of diffuse/background liver disease	2
ductal plate malformation/polycystic liver disease/congenital hepatic fibrosis, large bile duct obstruction	2
ductal plate malformation/polycystic liver disease/congenital hepatic fibrosis, Other (please enter alternative diagnosis in comments box)	2
ascending cholangitis	1
ascending cholangitis, hepatolithiasis	1
ascending cholangitis, large bile duct obstruction	1
chronic cholangiopathy NOS, drug induced liver injury (please specify in comments box)	1
chronic cholangiopathy NOS, large bile duct obstruction	1
drug induced liver injury (please specify in comments box)	1
hepatolithiasis	1

# Diagnostic combinations

- Conclusion – INSUFFICIENT FOR CONSENSUS
- Non-scoring (educational case)
- 62 with DPM; 5 mentioned DPM in comments
- 28 participants = no DPM
- Biliary disease (cholangitis, LDO, chronic cholangiopathy) ~ 22
- Outliers
  - No mention of anything biliary (3 participants) incl no background disease, and DILI

**Original Diagnosis:** Congenital hepatic fibrosis (ductal plate malformation)

# Discussion points

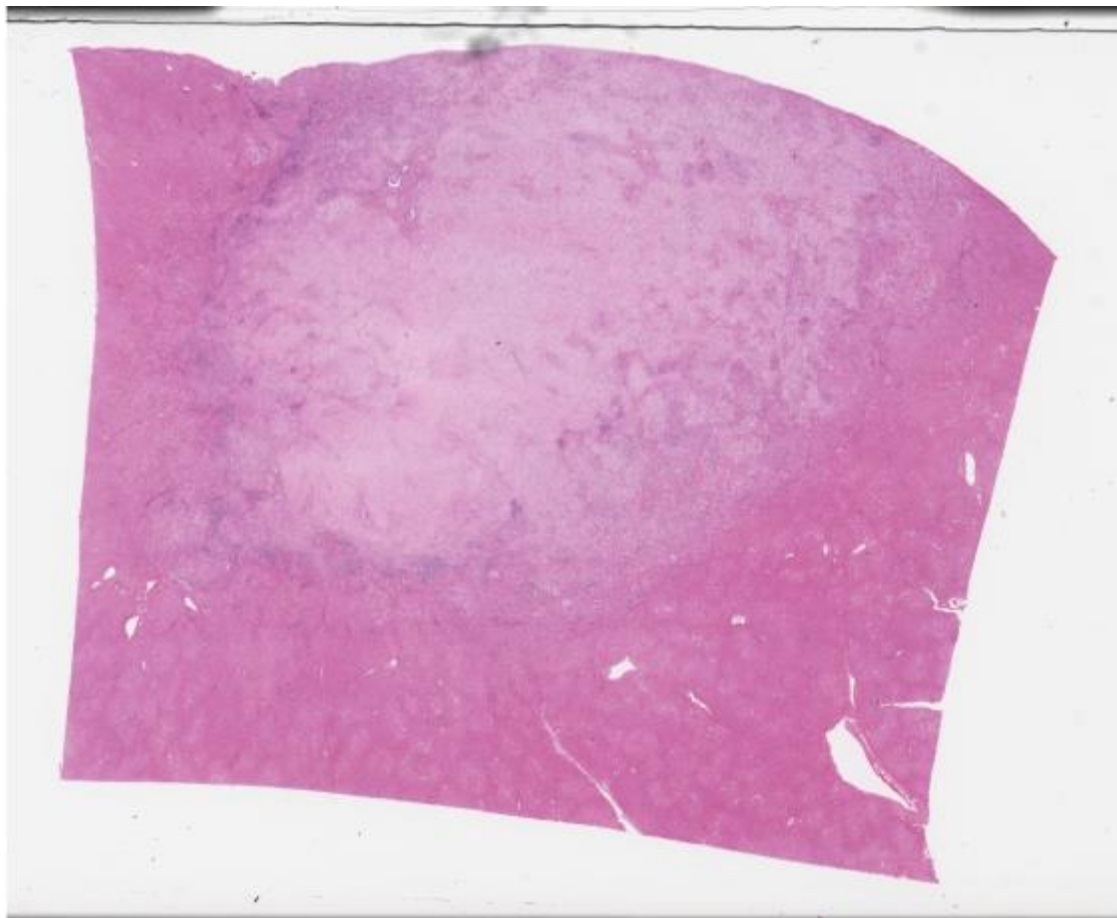
- Original diagnosis = Congenital hepatic fibrosis (ductal plate malformation)
- LDO as diagnosis – confusion of ductal plate malformation and ductular reaction (no lobular cholestasis)
  - “odd bile duct dilatation with focal ductular reaction”
- Awareness of spectrum of congenital hepatic fibrosis, and suspect this if multiple VMC-like structures.
- Late stage of chronic biliary disease can resemble congenital hepatic fibrosis without VMC – Copper associated protein would be abundant in late stage chronic biliary disease (Shikata not provided with this case)

**LW 3**

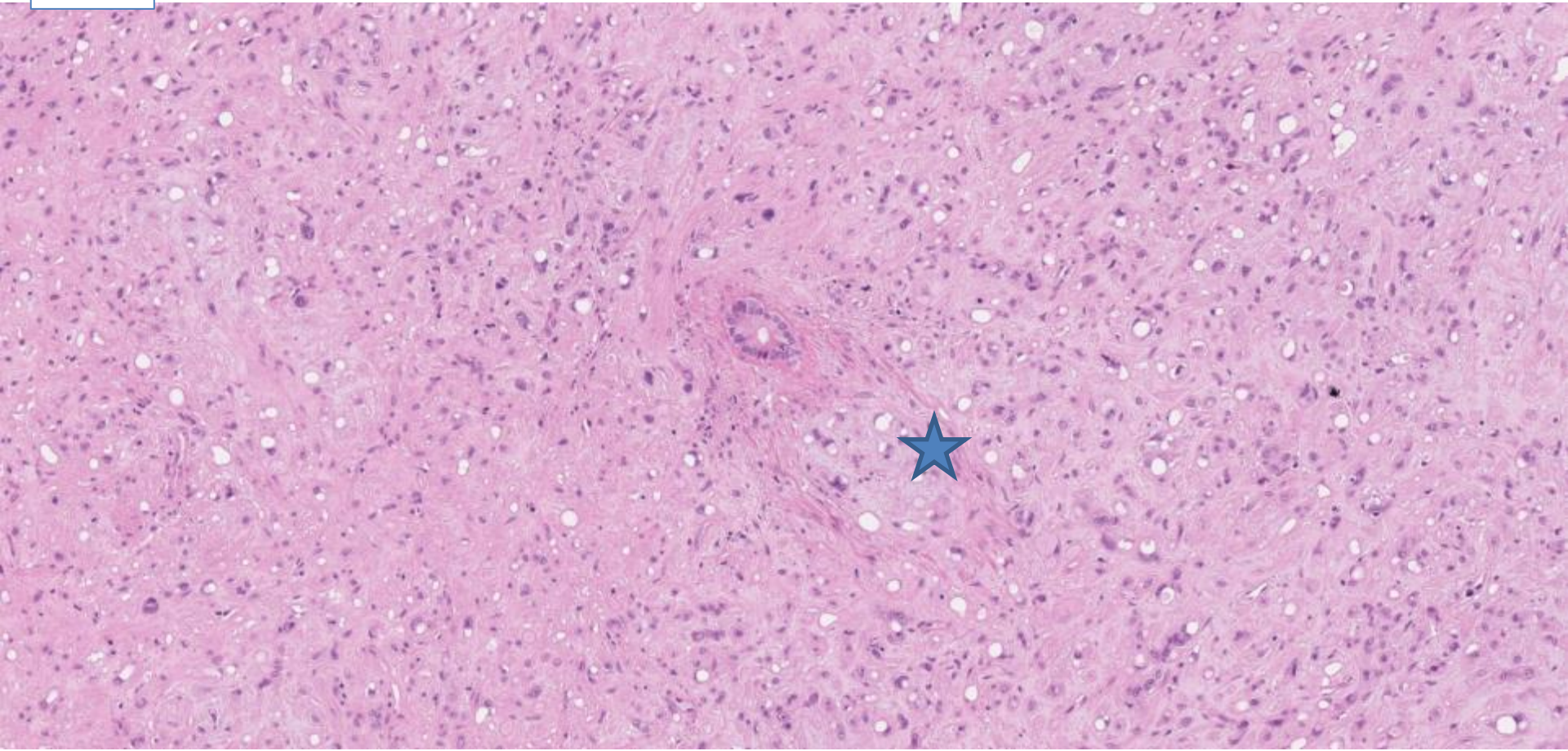
# LW3

- Male 72.
- Two lesions picked up incidentally on radiology. This section is from one of these (both lesions were similar ).
- Specimen: Liver segmentectomy
- Macroscopic: Ill defined white lesion, 33/17x15mm, below capsule
- Immunohistochemistry: CD34

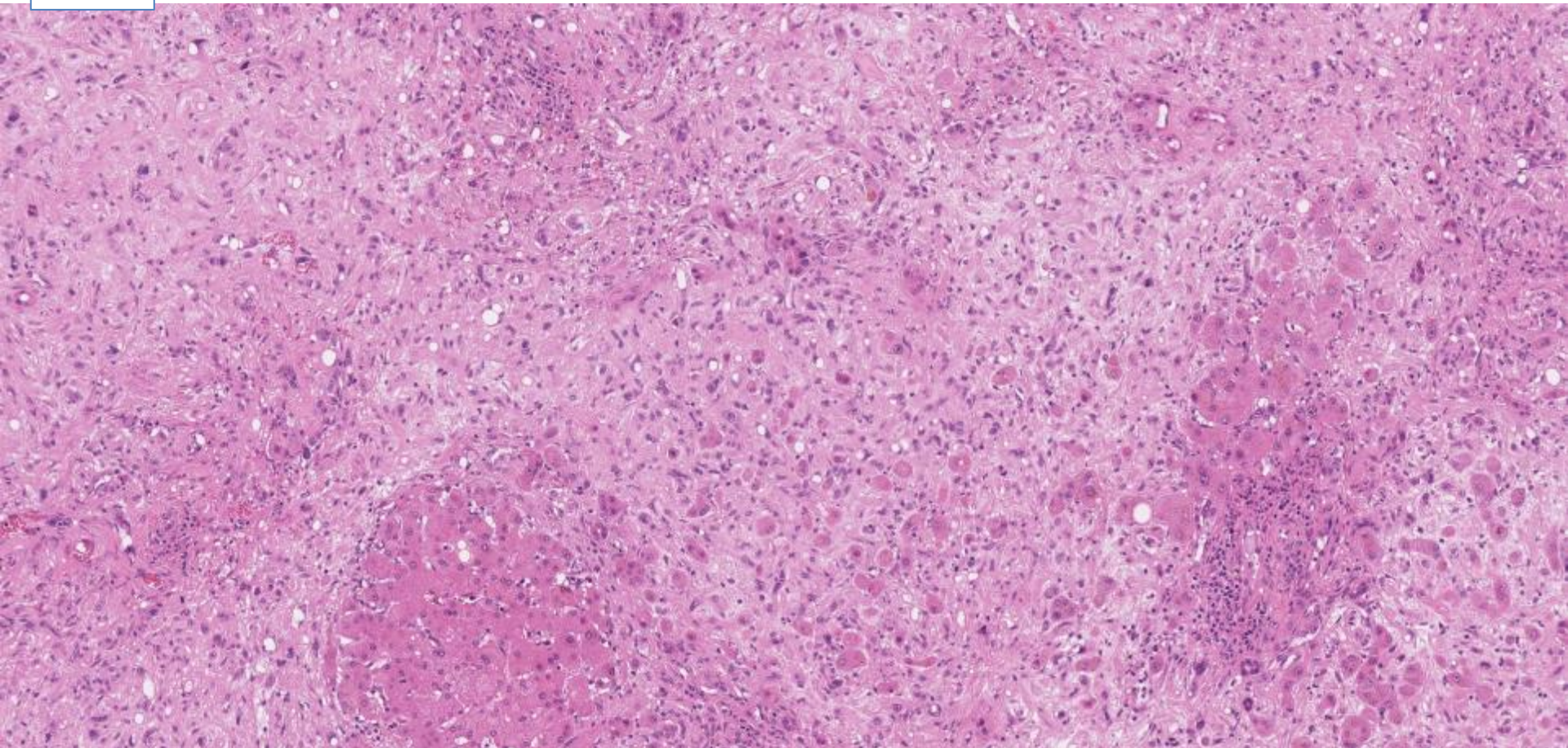
LW3



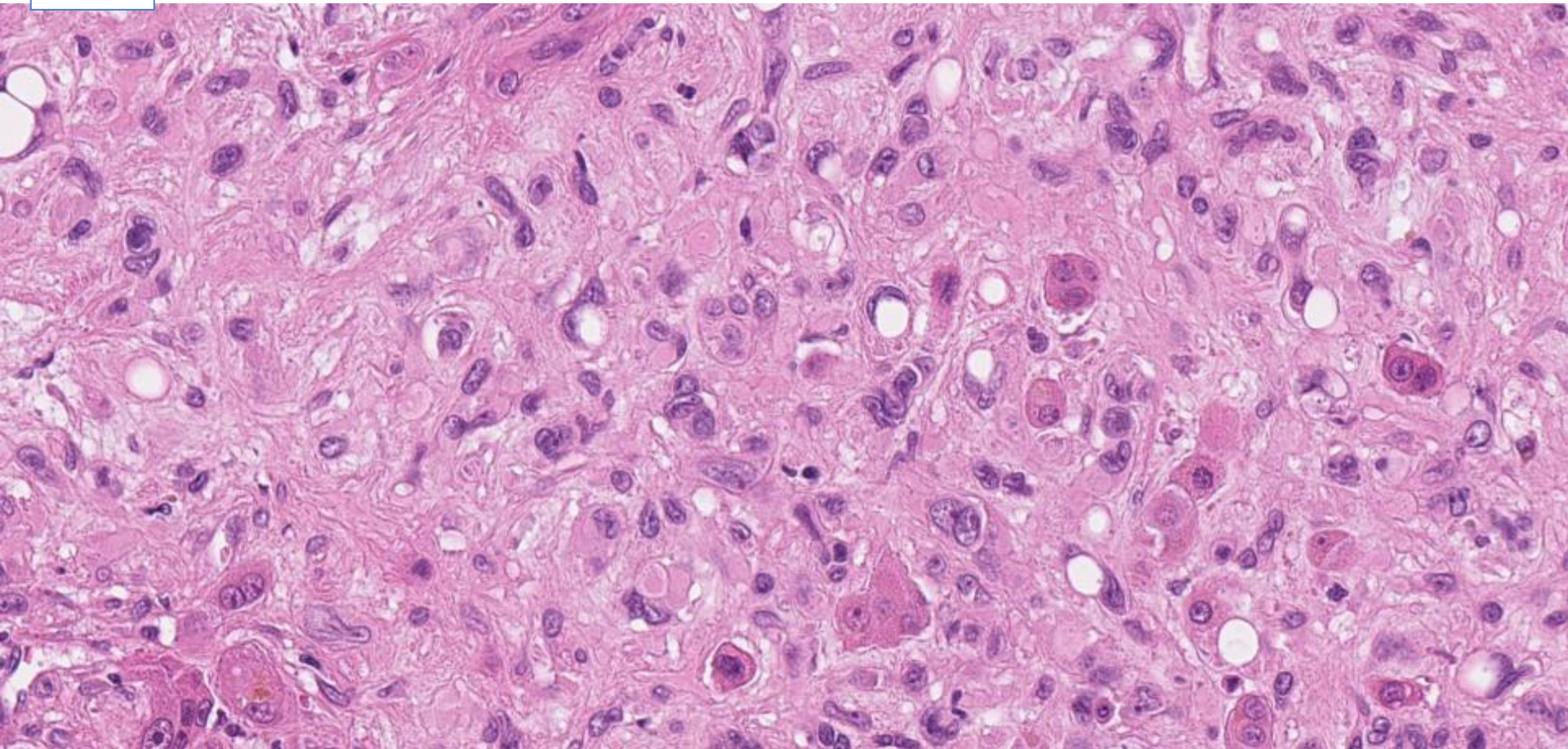
LW3



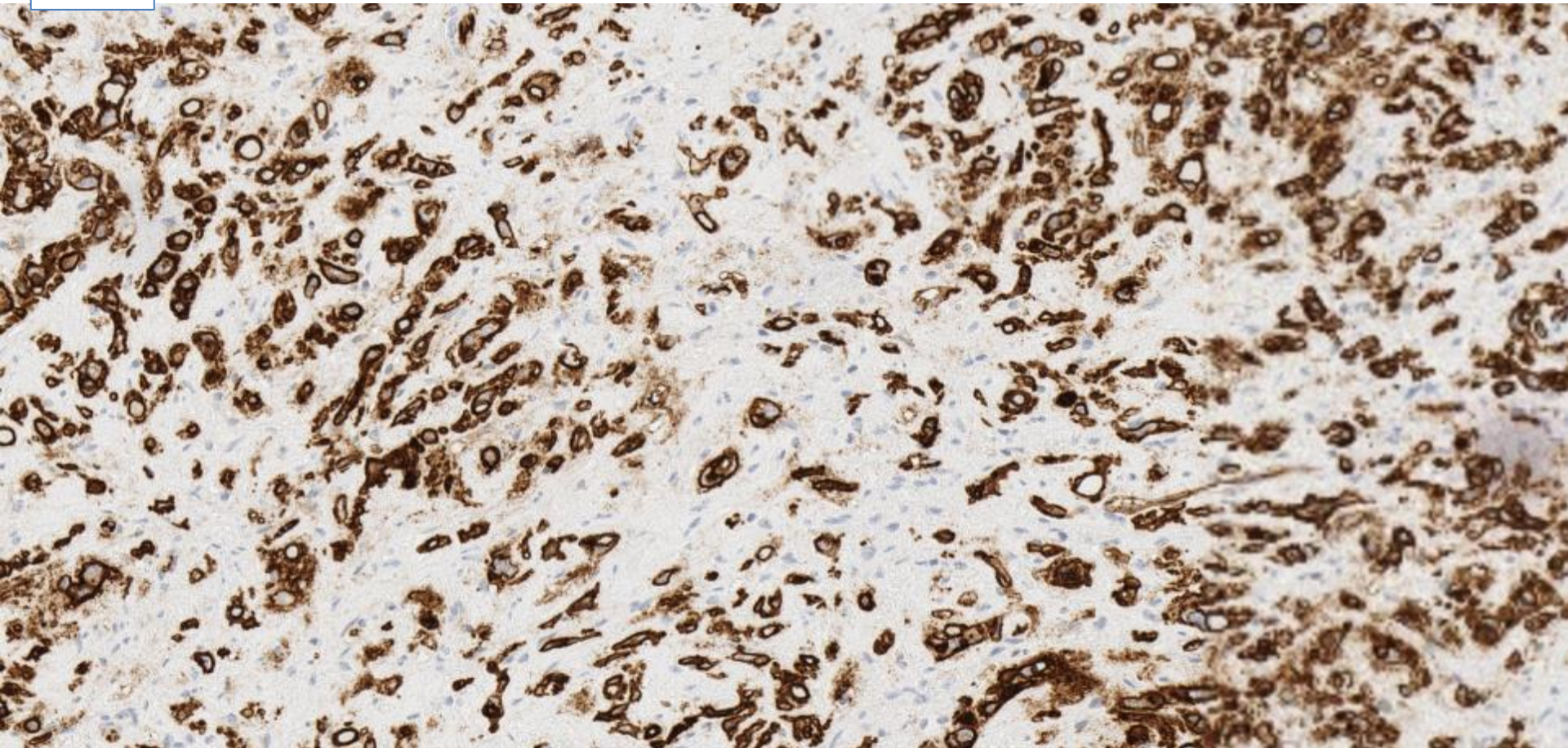
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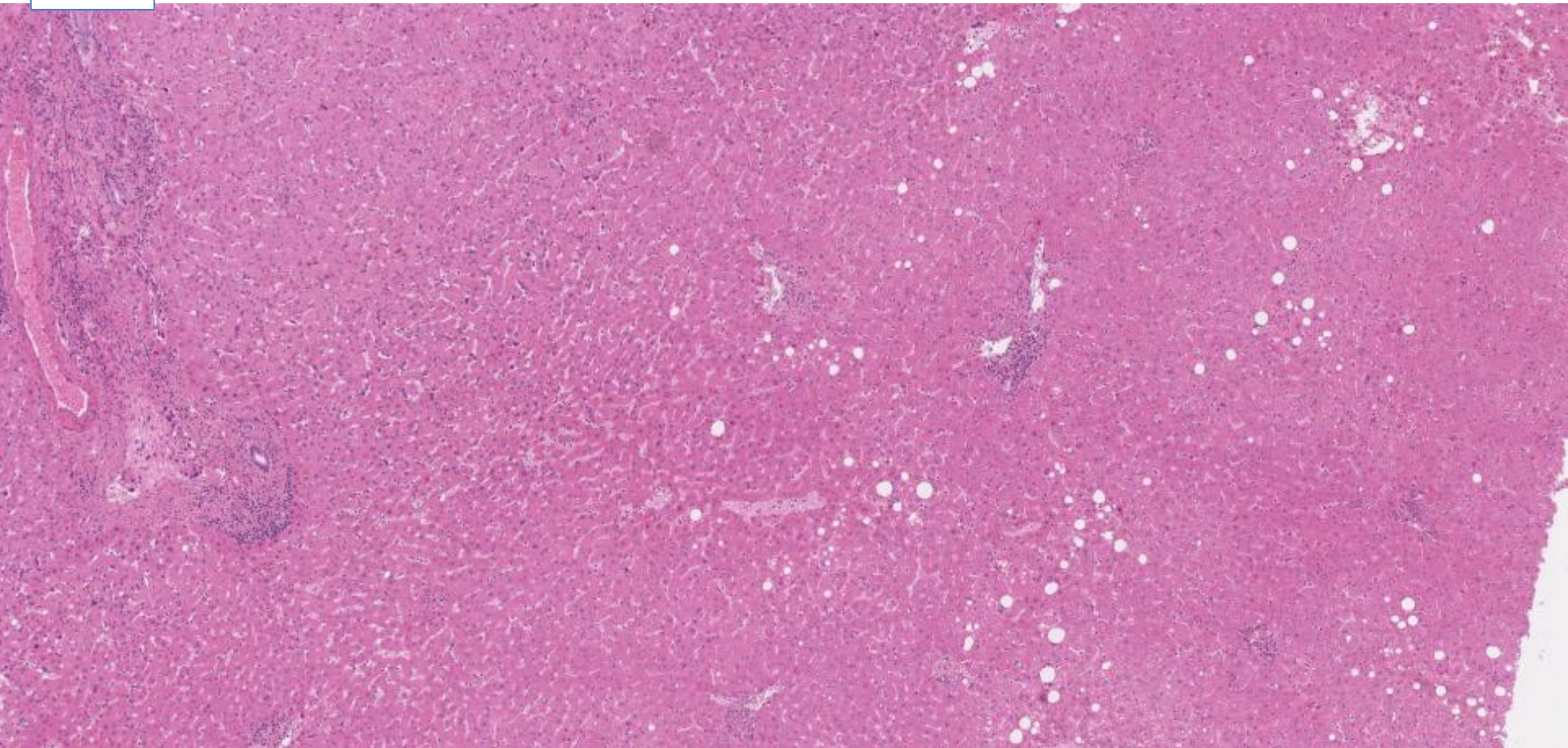
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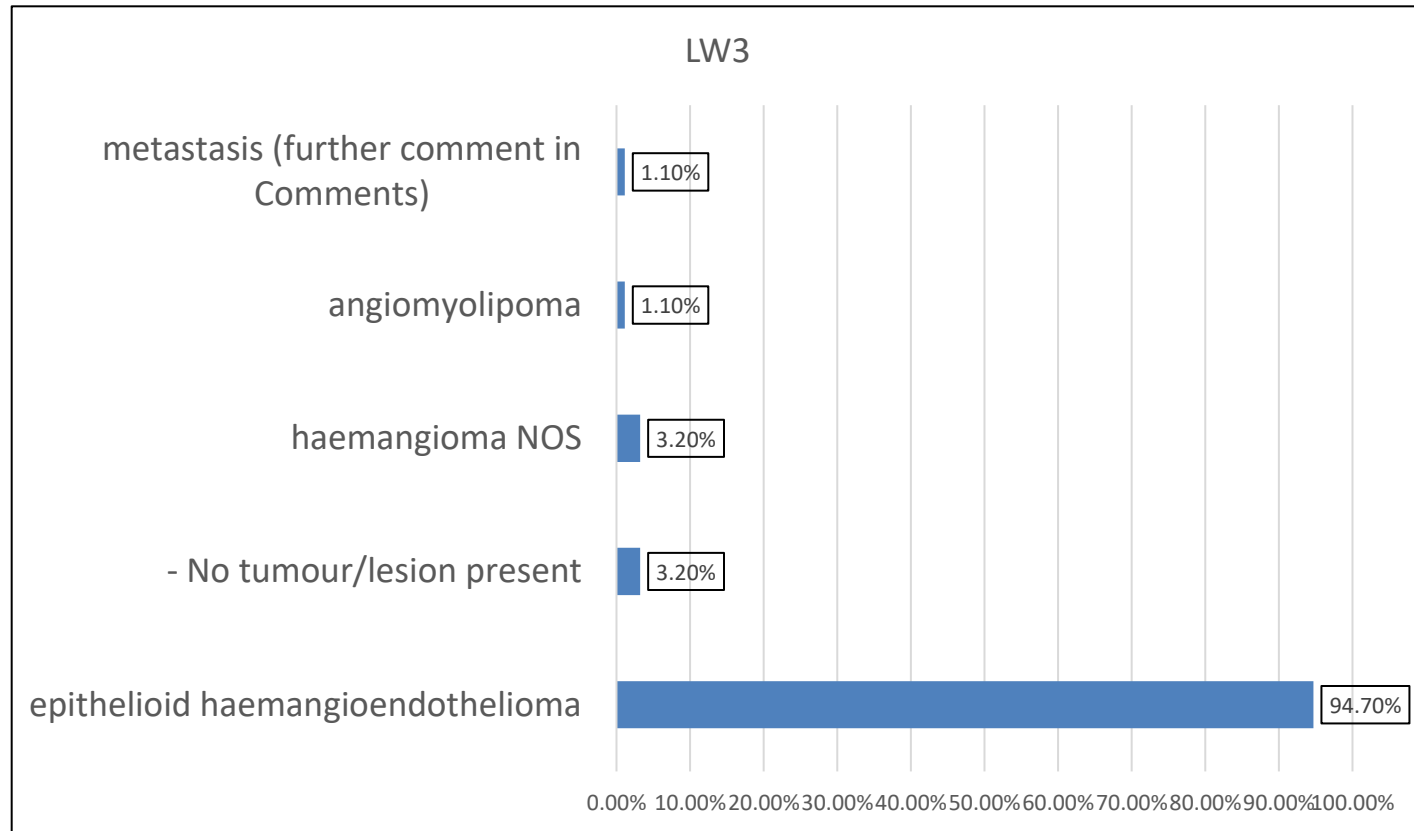


LW3



LW3





(EHE = 90/95 participants);  
haemangioma n = 3; metastasis n = 1;

# Background liver = no consensus

<b>Pattern:</b>	<b>Popularity:</b>
<b>steatosis</b>	52.6%
<b>within normal limits</b>	23.2%
<b>not applicable</b>	15.8%
<b>Other (please specify in Comments)</b>	5.3%
<b>cholestasis, bilirubinostasis</b>	1.1%

# Consensus complete response

- Epithelioid haemangioendothelioma.
  - Insufficient consensus on background to include in scoring (50 participants referred to steatosis).
- **Lose 5 marks – not applicable**
- **Lose 10 marks – if alternate diagnosis (haemangioma, AML, met GIST)**
- **Original diagnosis - EHE**

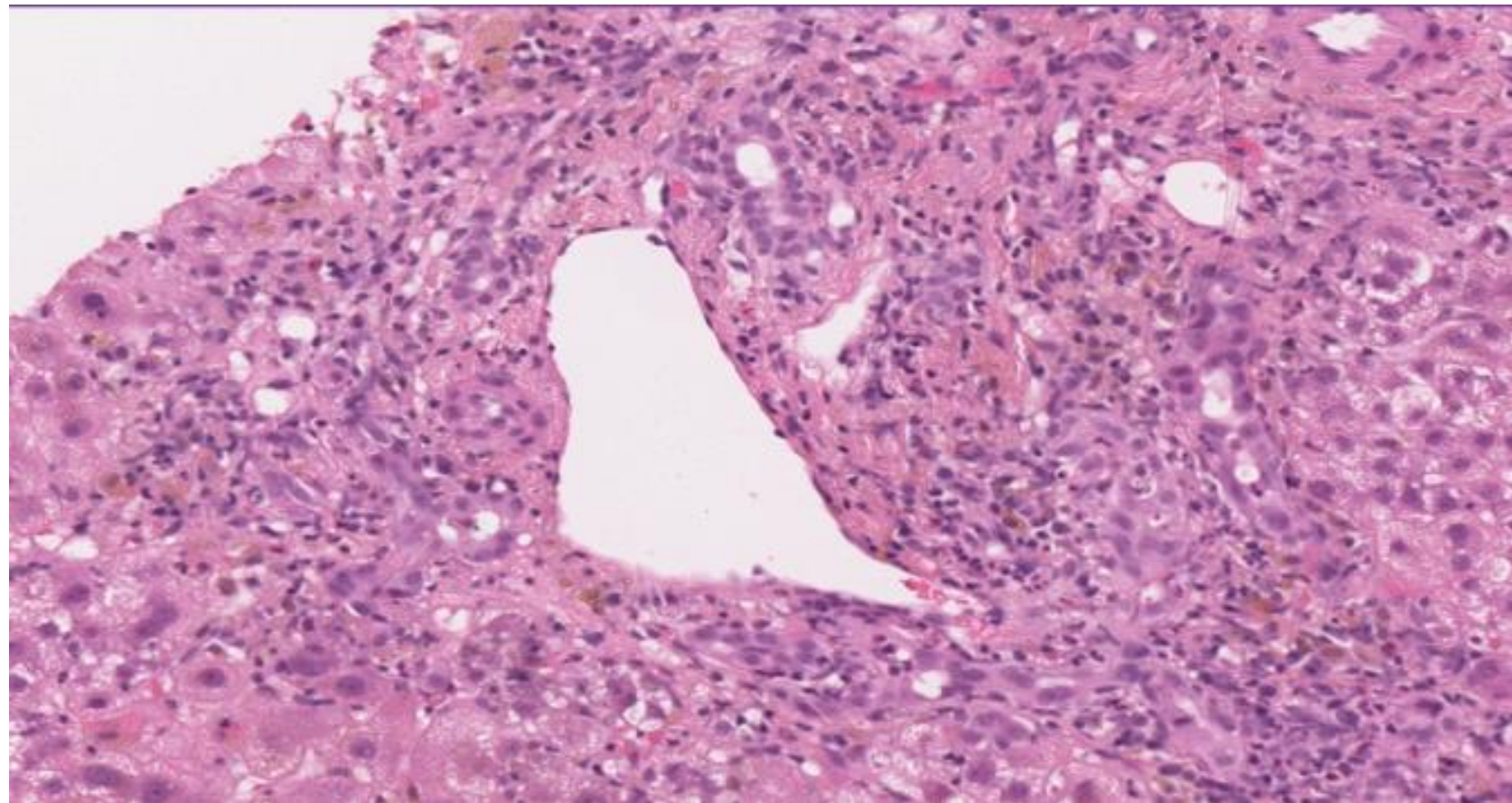
# Case Number: LW4

- **Clinical:** Male 58. AML. BM transplant 7 months previously. Initial GVH then settled. Abnormal LFTs following URTI 2 months previously, treated with erythromycin. Current ALT 557, br 193, ALP 789.
- **Specimen:** liver biopsy
- **Macroscopic:** Two needle cores, each 15mm
- **Immunohistochemistry:** N/A

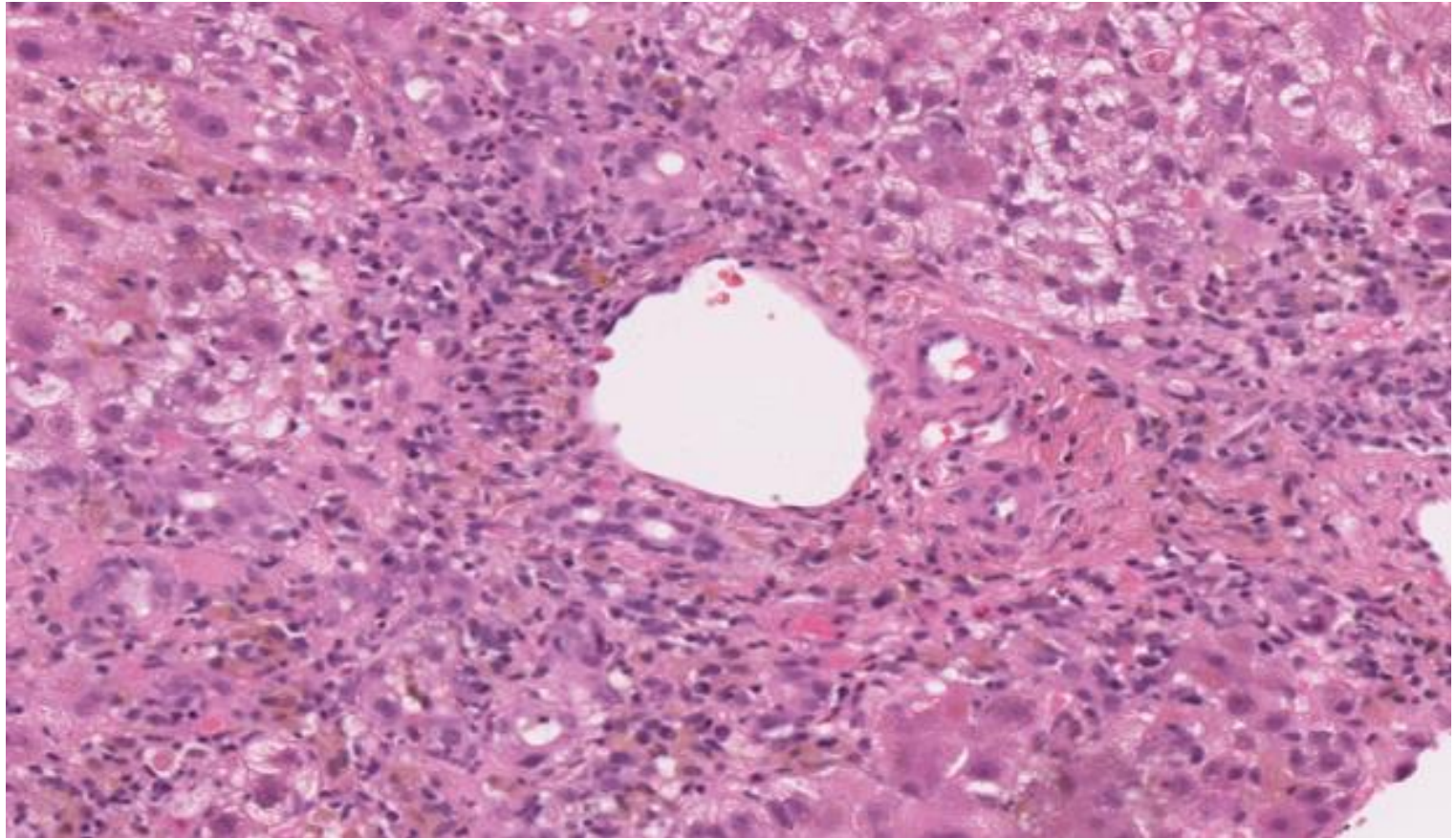
LW4



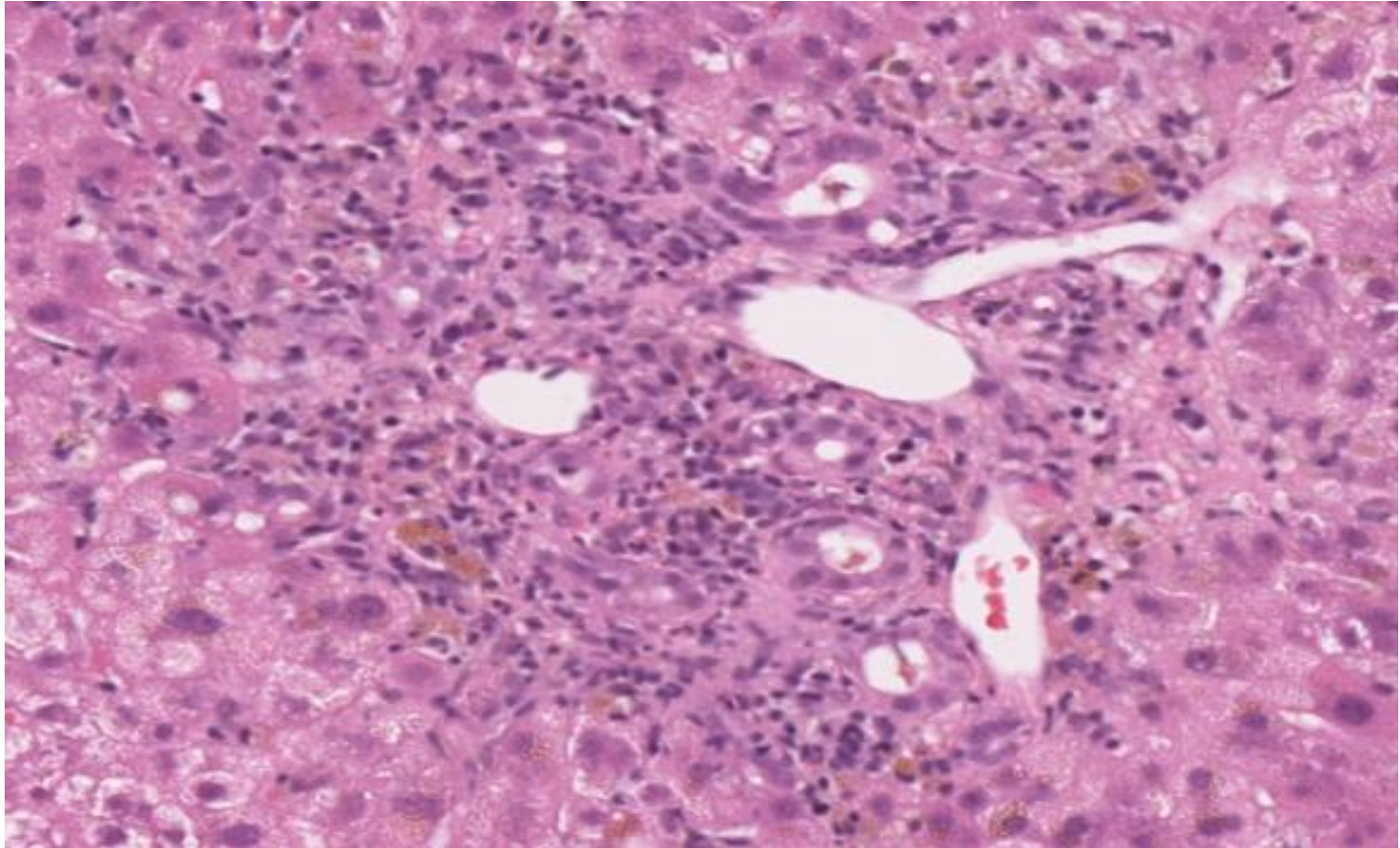
LW4



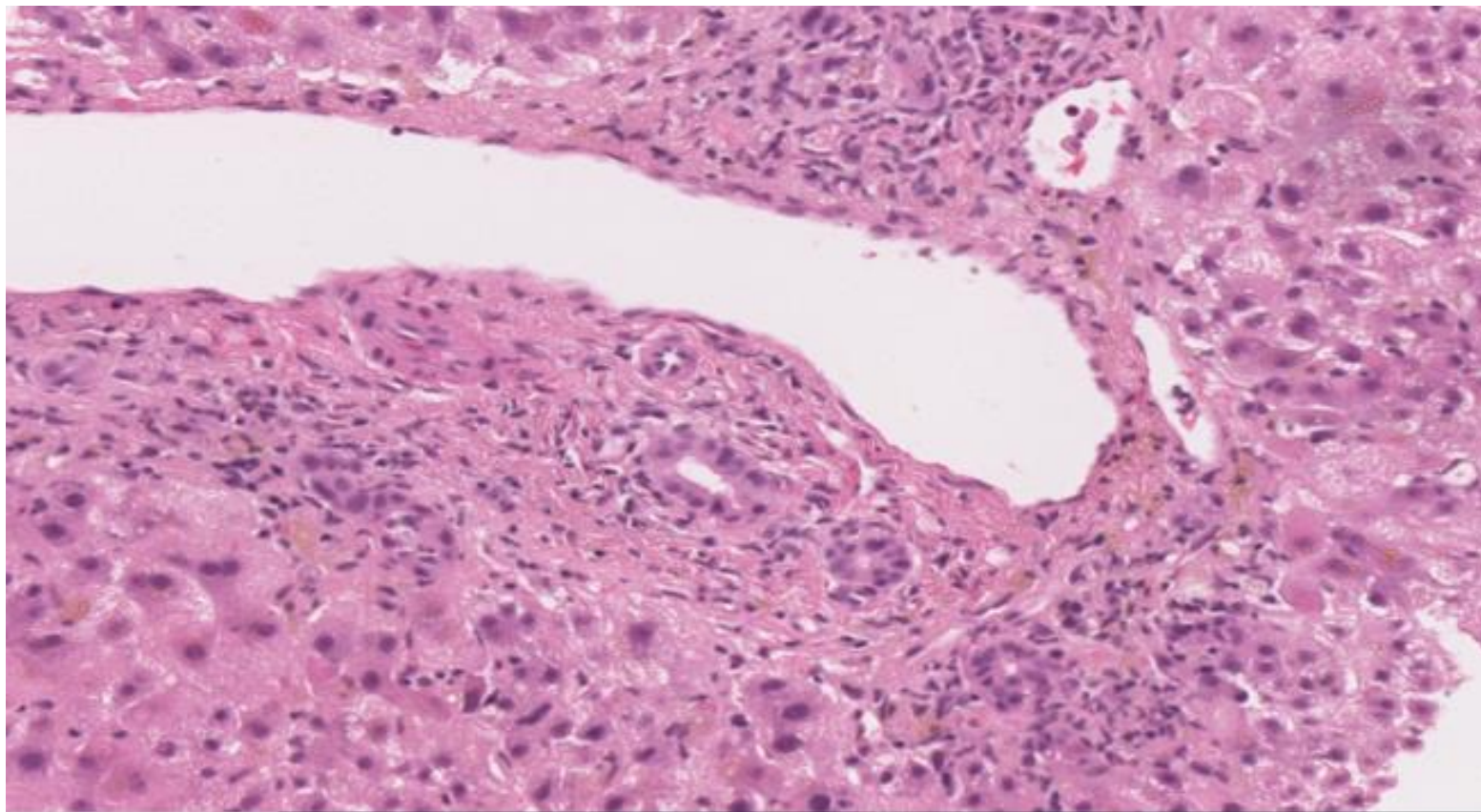
LW4



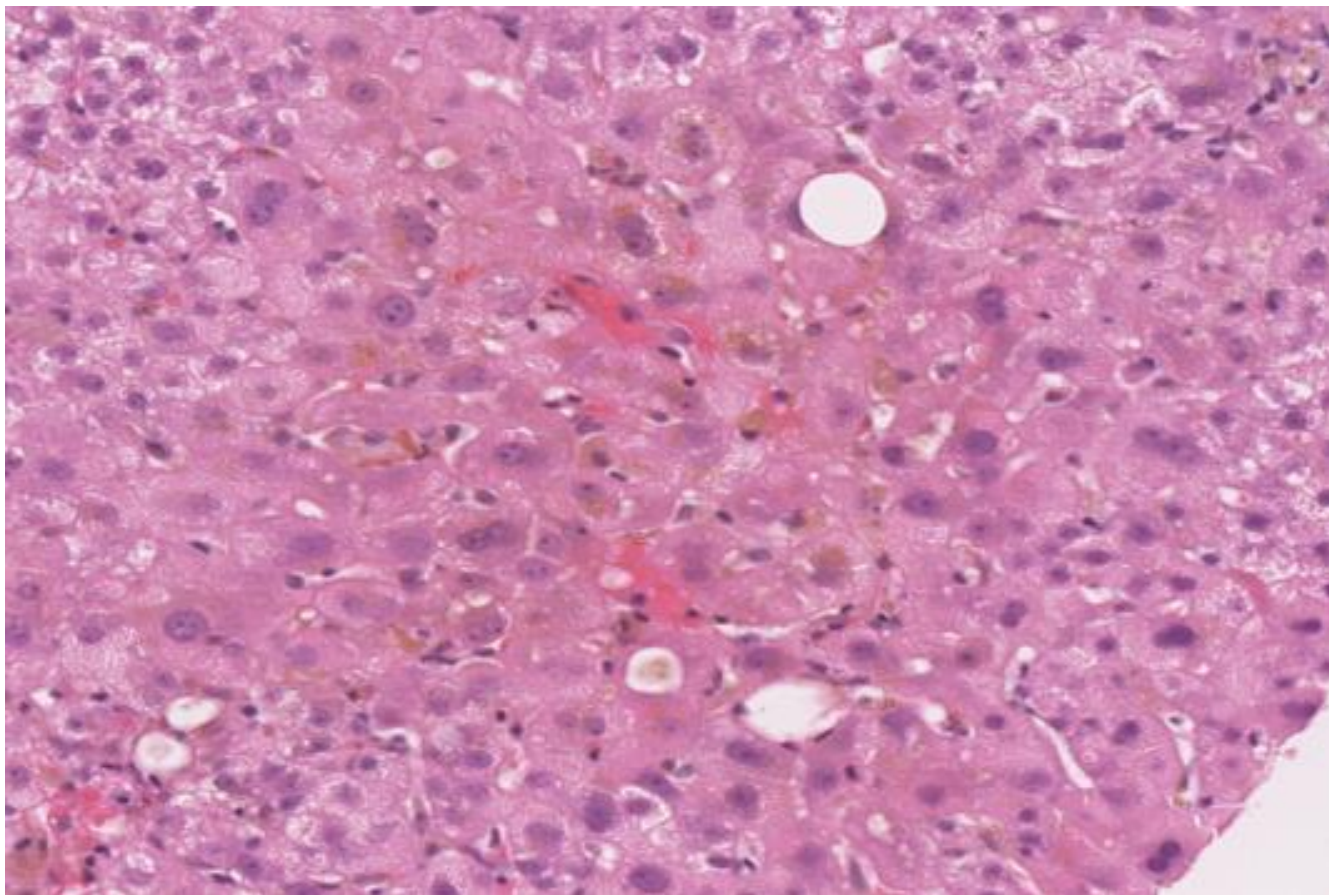
LW4



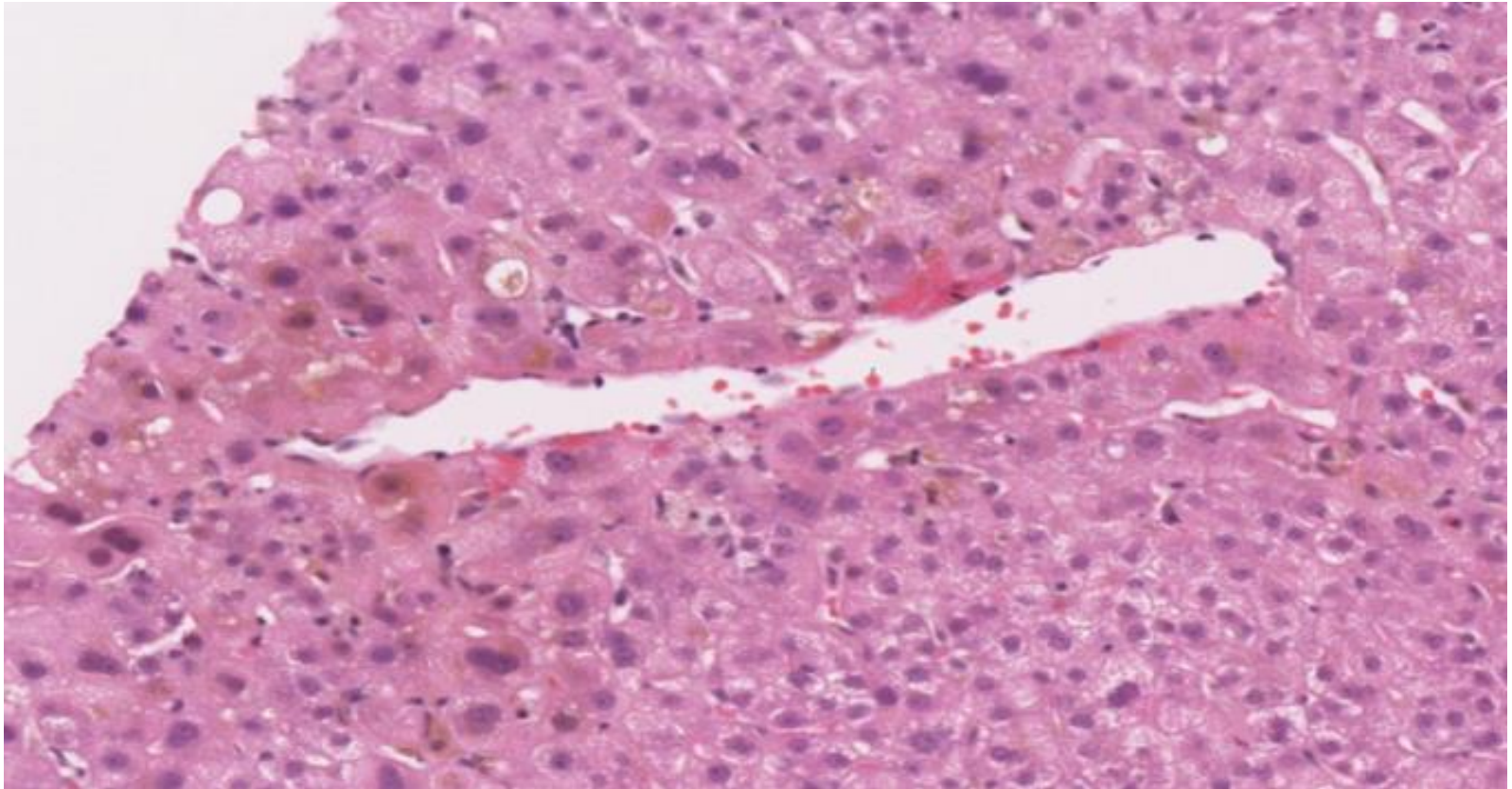
LW4



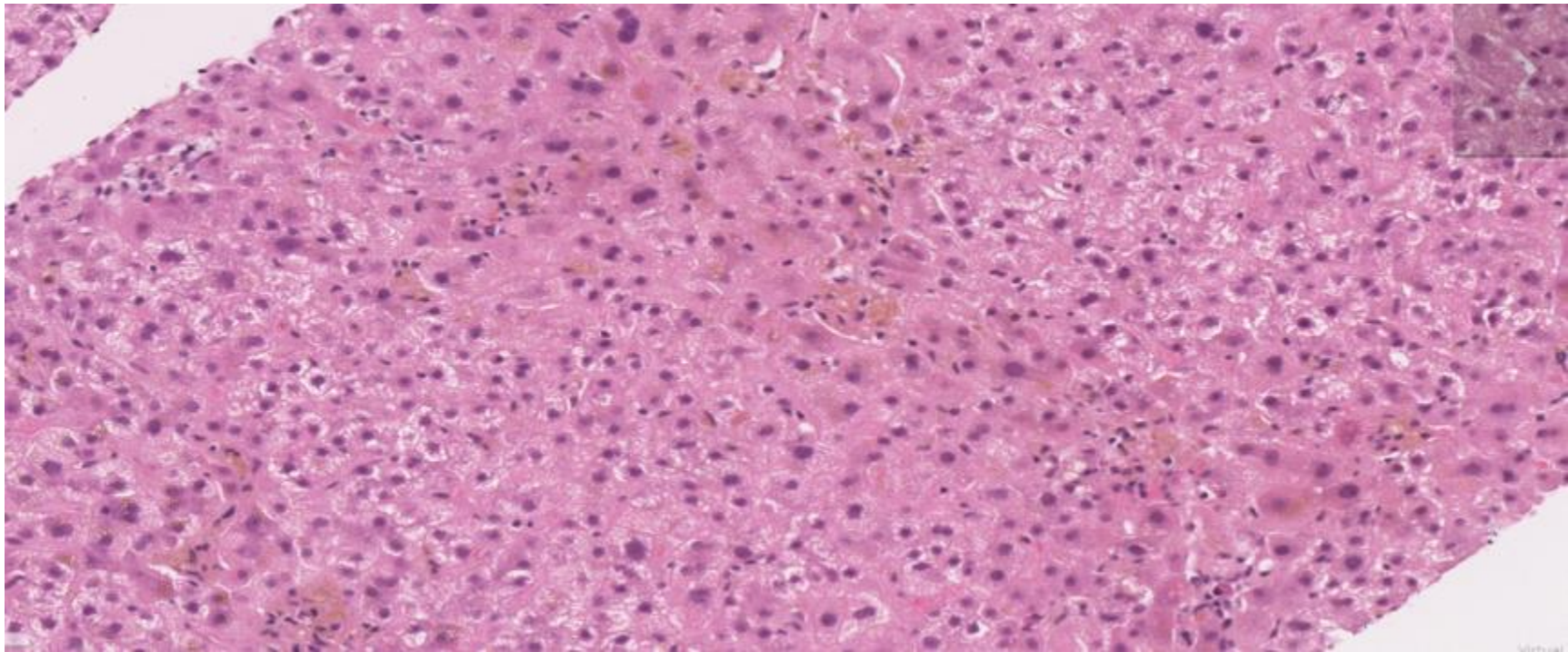
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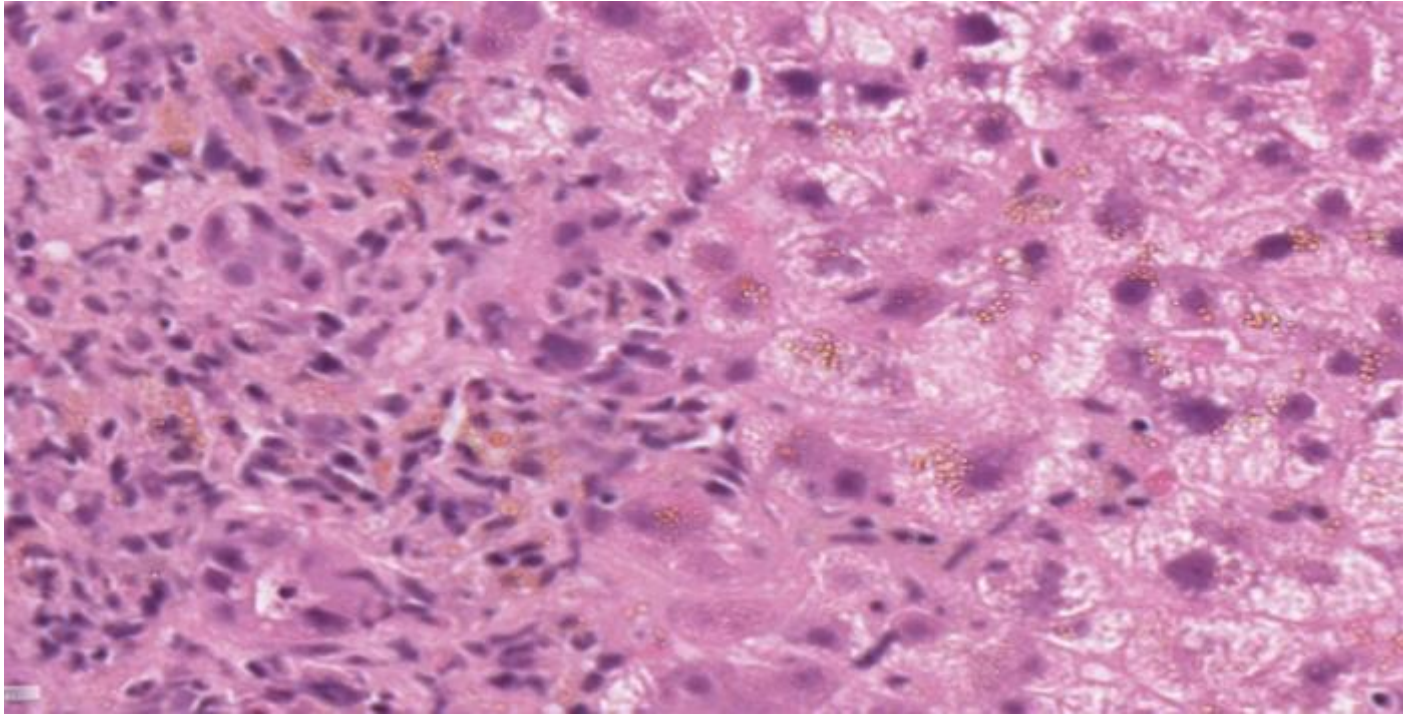
LW4



LW4



LW4



# Not applicable

Tumour:	Popularity:
- No tumour/lesion present	98.9%
Other (please specify in Comments)	1.1%

Tumour 1:	Tumour 2:	Count:
- No tumour/lesion present		77
- No tumour/lesion present	- No tumour/lesion present	17
Other (please specify in Comments)		1

## LW4

Pattern:	Popularity:
cholestasis, bilirubinostasis	87.4%
lobular hepatitis	26.3%
Other (please specify in Comments)	18.9%
chronic hepatitis	11.6%
iron overload	7.4%
chronic biliary disease	6.3%
abnormal, no pattern discernible	1.1%
not applicable	1.1%

Pattern 1:	Pattern 2:	
cholestasis, bilirubinostasis		28
cholestasis, bilirubinostasis	lobular hepatitis	16
cholestasis, bilirubinostasis	Other (please specify in Comments)	12
lobular hepatitis	cholestasis, bilirubinostasis	8
cholestasis, bilirubinostasis	chronic hepatitis	5
cholestasis, bilirubinostasis	iron overload	5
Other (please specify in Comments)		4
chronic hepatitis	cholestasis, bilirubinostasis	3
cholestasis, bilirubinostasis	chronic biliary disease	3
chronic biliary disease		2
chronic hepatitis		1
		1
abnormal, no pattern discernible		1
chronic biliary disease	cholestasis, bilirubinostasis	1
Other (please specify in Comments)	cholestasis, bilirubinostasis	1
chronic hepatitis	lobular hepatitis	1
cholestasis, bilirubinostasis	not applicable	1
chronic hepatitis	iron overload	1
Other (please specify in Comments)	iron overload	1

# Not applicable

Stages:	Popularity:
not applicable / no special stains to assess architecture	74.7%
no fibrosis/equivocal fibrosis	10.5%
mild/early fibrosis without bridging	7.4%
fibrosis with bridging between vascular structures	2.1%
hepatocyte loss or bridging - favour collapse not fibrosis	1.1%

Diagnostic categories:	Popularity:
drug induced liver injury (please specify in comments box)	80.0%
transplant complication NOS (please specify in comments box)	12.6%
iron overload - acquired, secondary	11.6%
Other (please enter alternative diagnosis in comments box)	6.3%
acute / subacute hepatitis - autoimmune / drug / viral	4.2%
- histologically indeterminate for cause	1.1%
large bile duct obstruction	1.1%

Diagnosis Combination:	Count:
drug induced liver injury (please specify in comments box)	62
drug induced liver injury (please specify in comments box), iron overload - acquired, secondary	8
transplant complication NOS (please specify in comments box)	7
Other (please enter alternative diagnosis in comments box)	5
drug induced liver injury (please specify in comments box), transplant complication NOS (please specify in comments box)	3
acute / subacute hepatitis - autoimmune / drug / viral, drug induced liver injury (please specify in comments box)	2
iron overload - acquired, secondary, transplant complication NOS (please specify in comments box)	2
[No selections made]	1
- histologically indeterminate for cause	1
acute / subacute hepatitis - autoimmune / drug / viral	1
acute / subacute hepatitis - autoimmune / drug / viral, iron overload - acquired, secondary	1
drug induced liver injury (please specify in comments box), Other (please enter alternative diagnosis in comments box)	1
large bile duct obstruction	1

**Points of consensus:**

Pattern – cholestasis in 83/95 - either in disease pattern or included in comments.

Diagnosis – DILI 76 (80%), acute/subacute hepatitis - autoimmune/drug/viral = 2, plus another 5 in comments – 83/95 (87%) consensus

**Suggested scoring: for 10 points** - Diagnostic category that includes DILI or 'acute/subacute hepatitis -

**Lose 5 marks** no mention of DILI in differential - most were GVHD (9/95) *committee agreed*

**Lose 5 marks** no mention of cholestasis *committee agreed*

*i.e. expecting both pattern and diagnosis in this case for full marks*

*Members suggesting both DILI and transplant complication (GVHD) are still scoring 10 marks n=3 , those favouring DILI alone (+/- Fe) just under consensus (75).*

*These two points for discussion with the membership – agreed 10 points for DILI + GVHD to achieve consensus and score*

**Lose 10 marks (score 0) if** acute cellular rejection – confused with liver transplant? *Large bile duct obstruction*

**Observations/potential learning points, suitable for masterclass?**

Differential diagnosis of GVHD v DILI.

**Original Diagnosis:** cholestatic hepatitis c/w DILI (erythromycin). No features GVH. Subsequently resolved

# Liver tox erythromycin

- Clinically apparent liver injury from **erythromycin** is rare, but because of the frequency of its use, **erythromycin** has been one of the most common causes of drug induced liver injury at least in previous years. Initially, liver injury was thought to be more common with, or perhaps limited to, **erythromycin** estolate. However, instances of jaundice and liver damage have been reported with virtually all formulations of **erythromycin**, and cross sensitivity to injury is common, although not universal. The hepatotoxicity of **erythromycin** resembles that described in other macrolide antibiotics and is typically a mild and self-limiting cholestatic hepatitis. The latency period between starting **erythromycin** and onset of liver injury is short, typically 1 to 3 weeks and is shorter (<1 week) with reexposure. Symptoms may include right upper quadrant pain and jaundice, clinical features that might suggest cholecystitis. [Eosinophilia](#) and fever are common, but not universal; rash is reported less commonly. The pattern of enzyme elevations is often mixed or variable, but the disease is usually cholestatic and symptoms of pruritus may be prominent. The liver injury is usually mild and self-limited with recovery in 4 to 8 weeks. However, instances of prolonged jaundice and cholestasis with paucity of bile ducts due to erythromycin have been reported. Furthermore, cases of abrupt onset of liver injury after a short latency (<1 week) and a hepatocellular pattern of liver enzyme elevations have been reported, particularly with repeat exposure, and some of these cases have led to acute liver failure and death or need for liver transplantation. Rapid recurrence occurs with rechallenge even within 24 hours of a single dose.

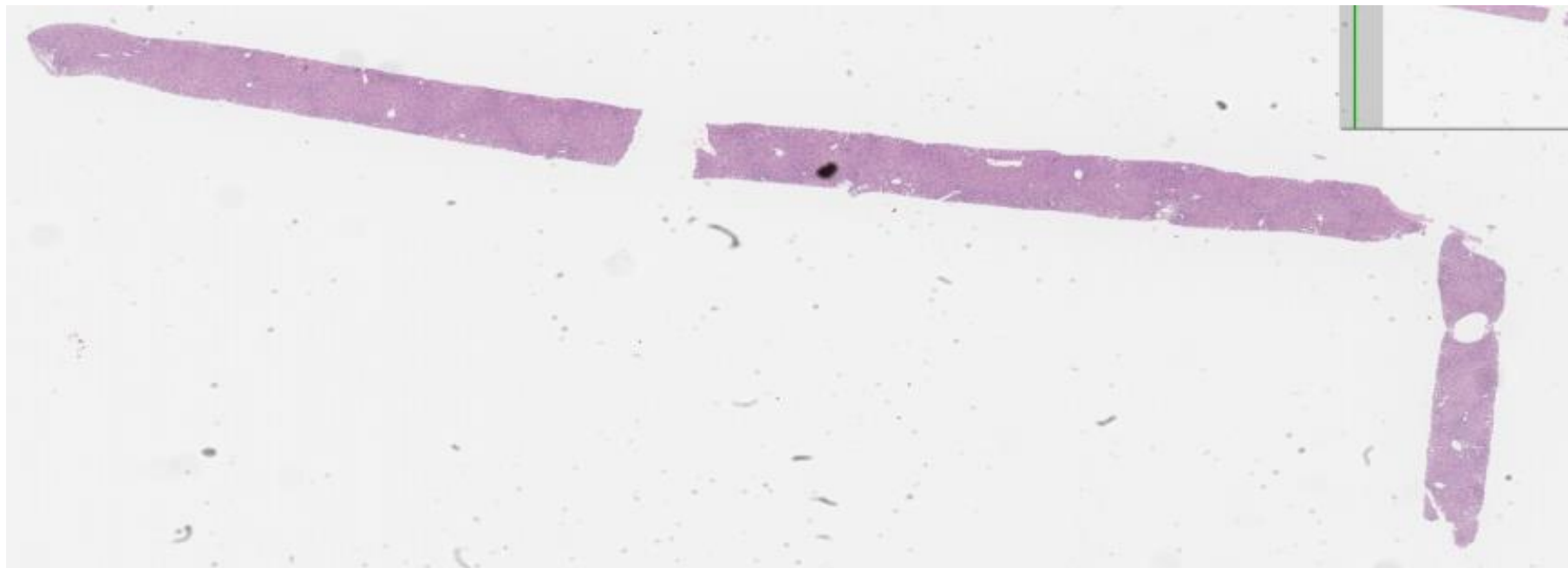
# MacSween

- GVHD usually multisystemic
- Raised ALP and bilirubin transaminase elevation mild (this case ALT 557) but can see hepatitic GVHD
- Bile duct damage expected in GVHD even in hepatitic variant

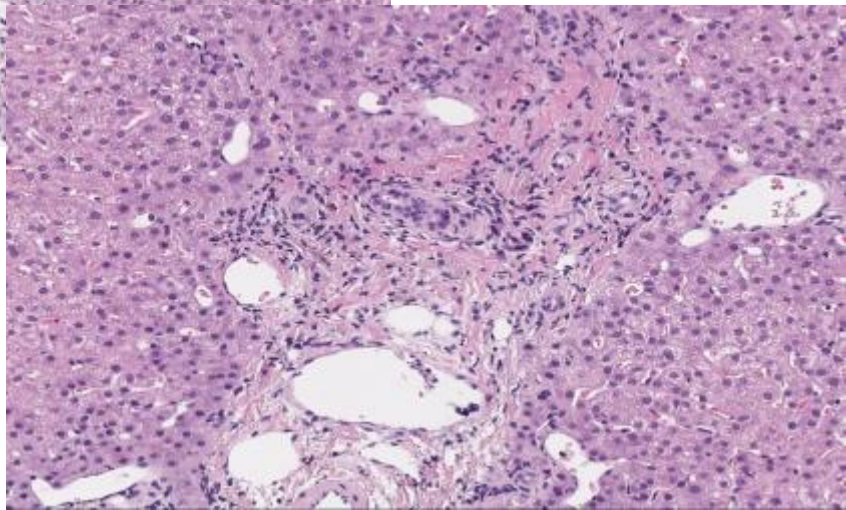
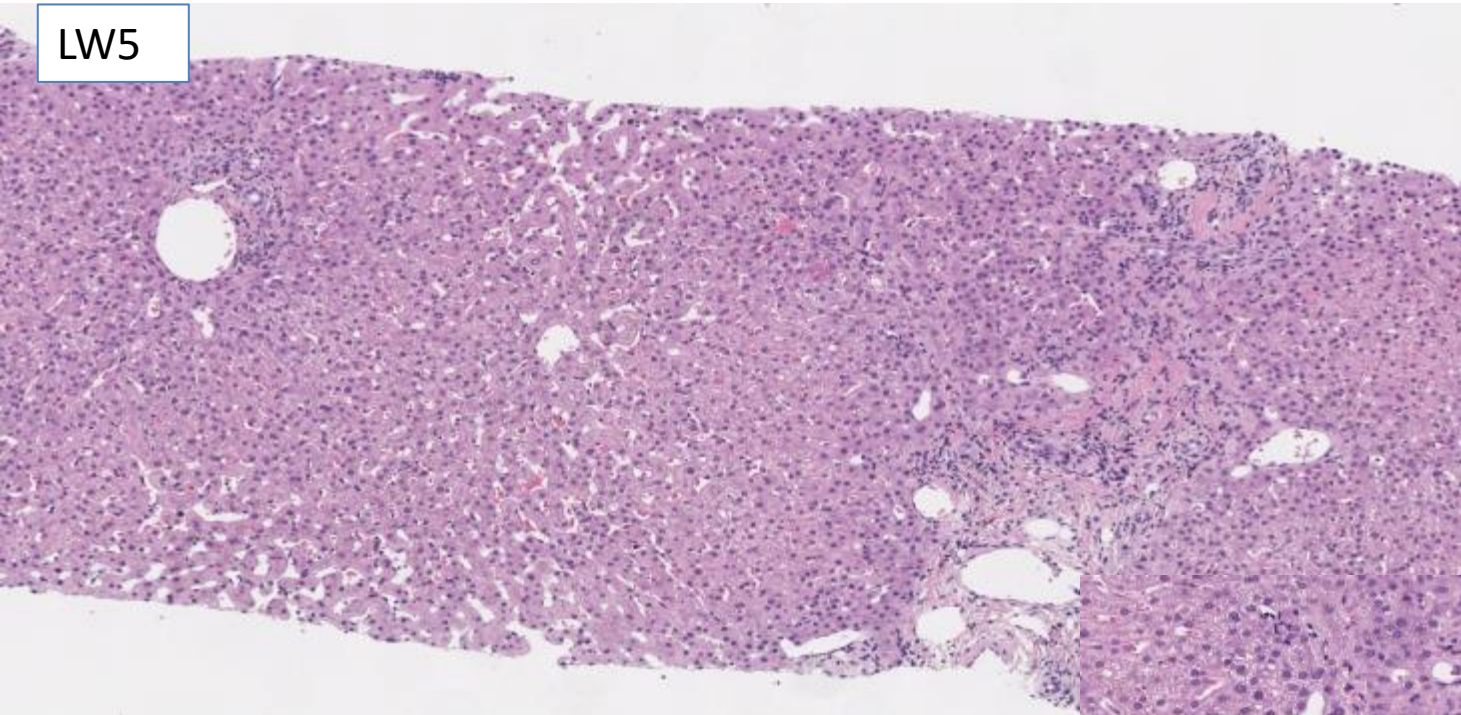
# Case Number: LW5

- **Clinical:** Male 17. Recent diagnosis of UC and admitted with acute severe flare. Treated with hydrocortisone and then infliximab. Marked transaminitis for last 9 months. NILS negative. MRCP does not show large duct PSC. ? small duct PSC/? seronegative AIH. From EPR: recent ALT 161; alk phos 537, max 765 at presentation 9 months ago. Autoantibodies -ve apart from pANCA. Immunoglobulins normal.
- **Specimen:** liver biopsy    **Macroscopic:** liver biopsy core 28mm long
- **Immunohistochemistry:** van Gieson, reticulin, Shikata, CK7

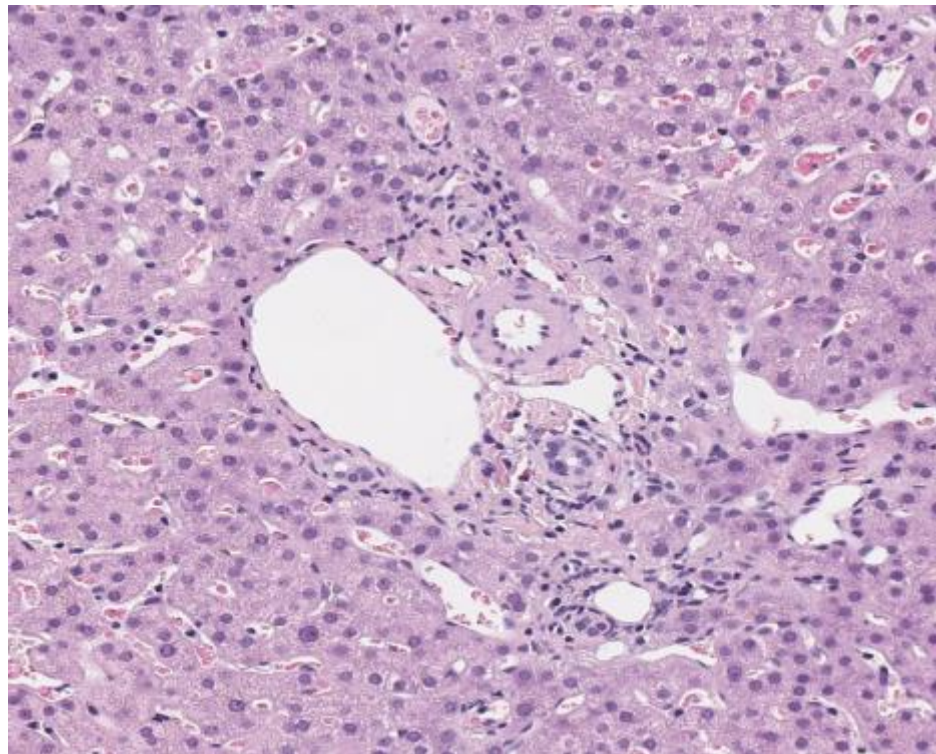
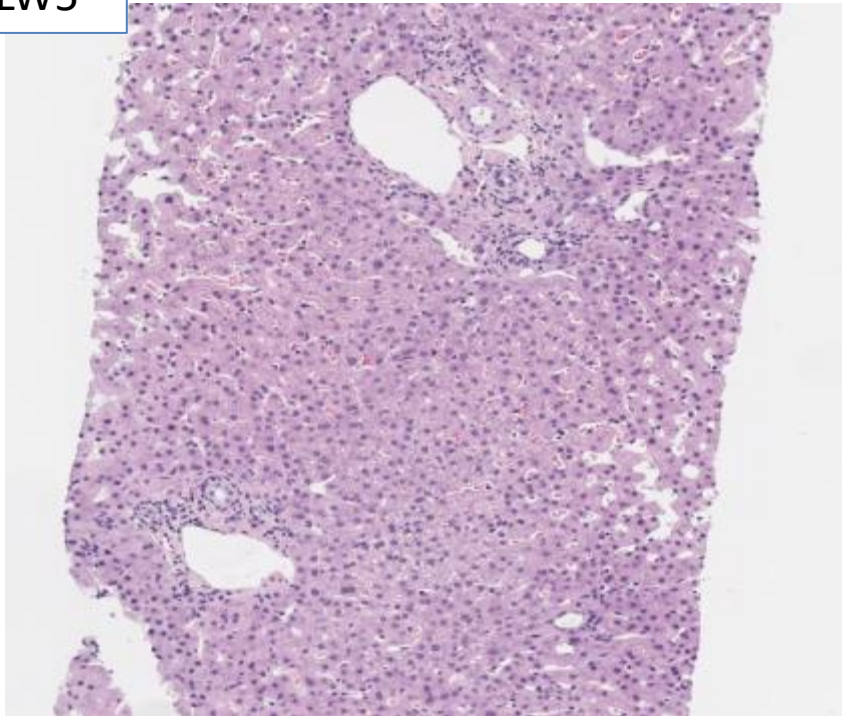
LW5

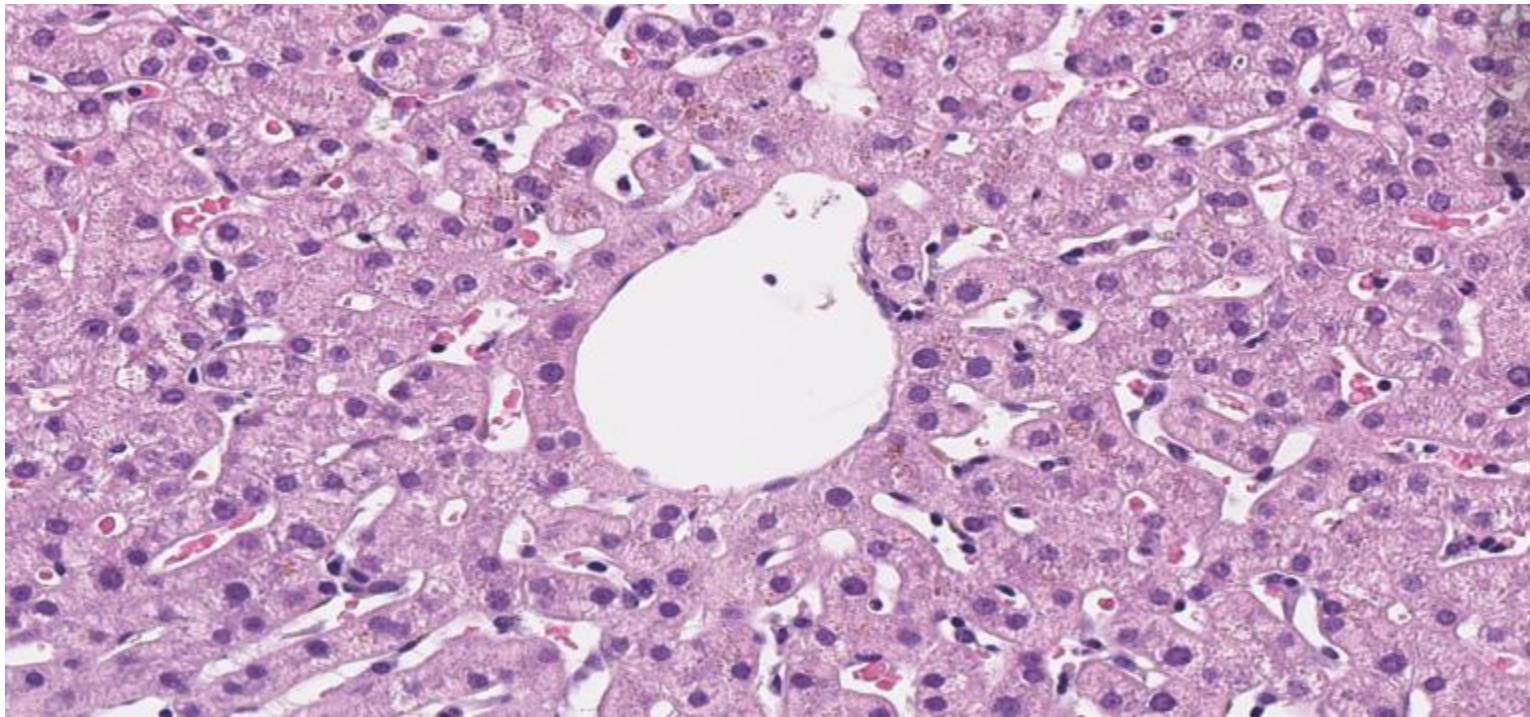


LW5

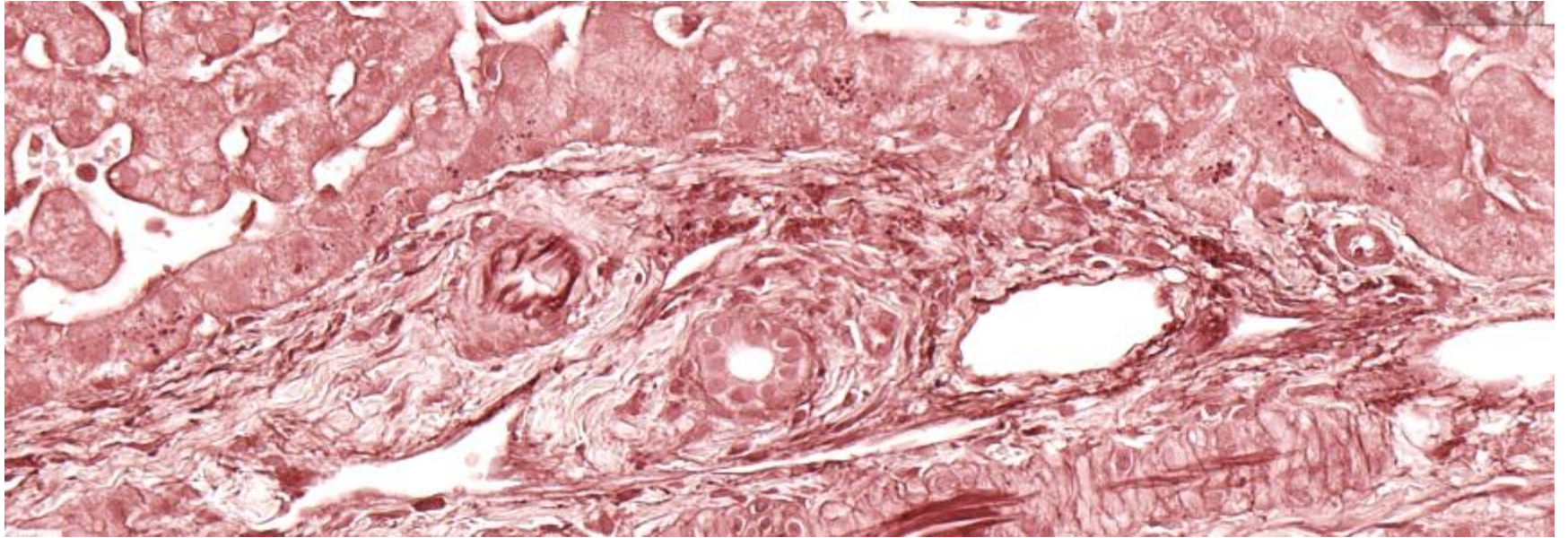


LW5



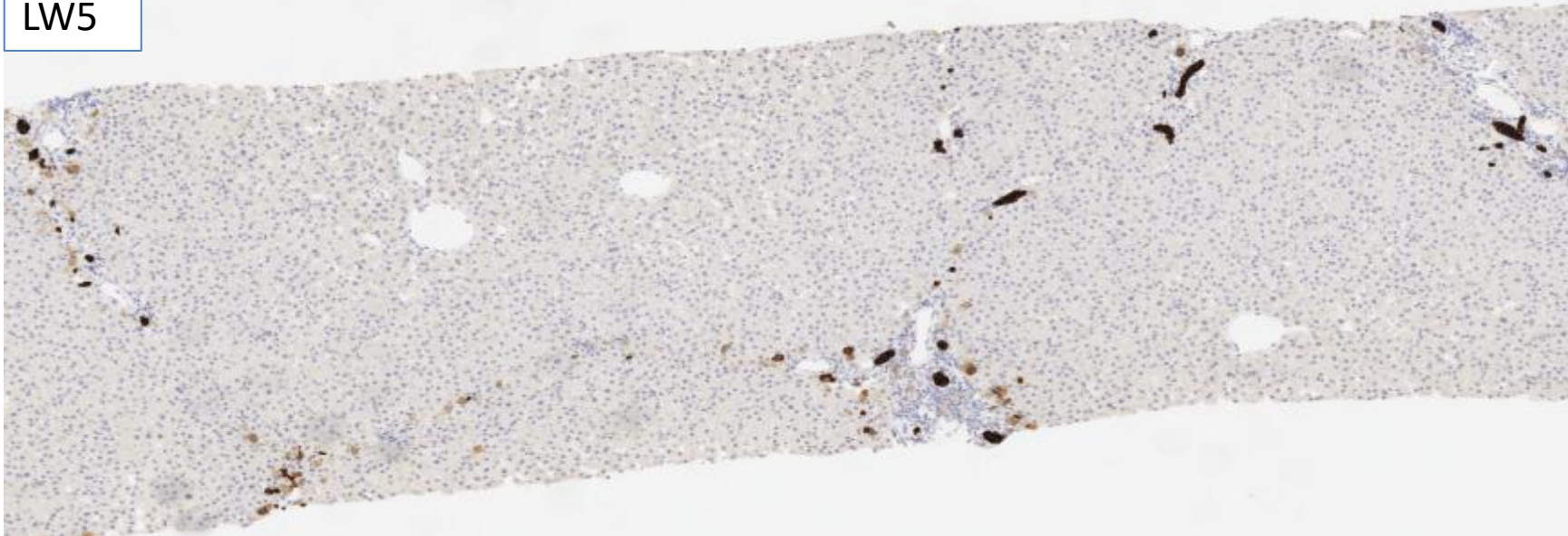


LW5



Shikata

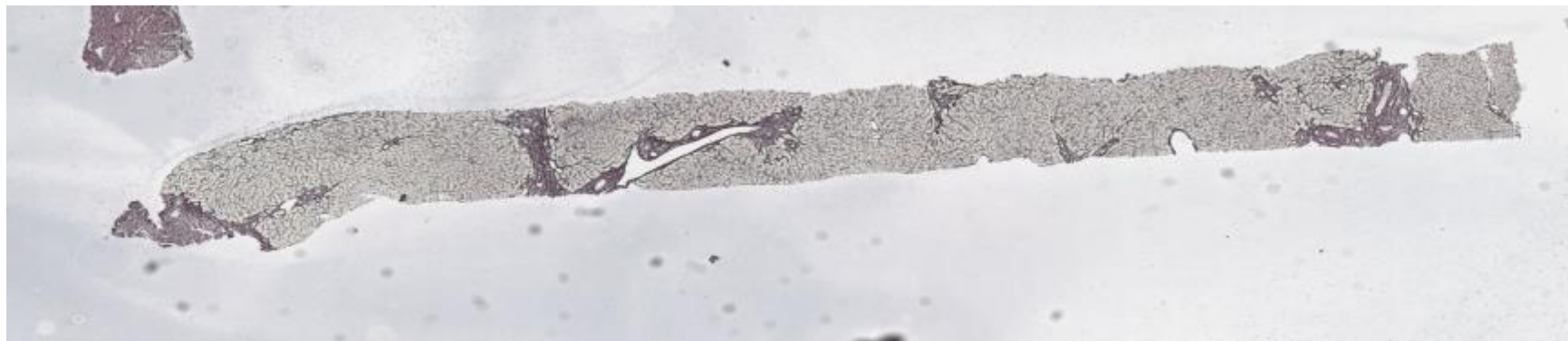
LW5



CK7

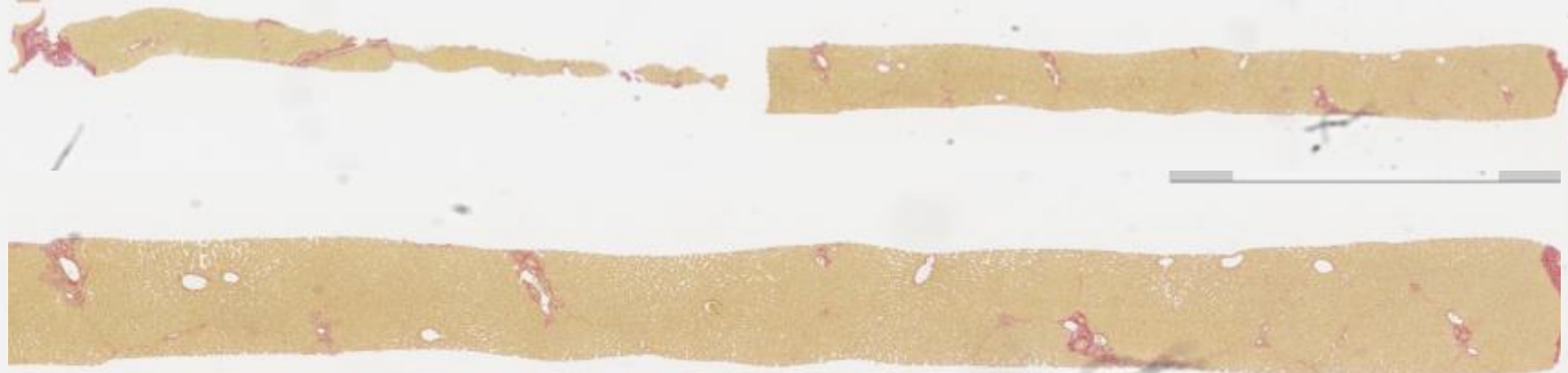


LW5



reticulin

LW5



Van Gieson

# Not applicable

Tumour:	Popularity:
- No tumour/lesion present	98.9%
Other (please specify in Comments)	1.1%

Tumour 1:	Tumour 2:	Count:
- No tumour/lesion present		78
- No tumour/lesion present	- No tumour/lesion present	16
Other (please specify in Comments)		1

LW5

Pattern:	Popularity:
chronic biliary disease	87.4%
Other (please specify in Comments)	6.3%
cholestasis, bilirubinostasis	6.3%
not applicable	3.2%
within normal limits	3.2%
abnormal, no pattern discernible	2.1%
vascular disease	2.1%
lobular hepatitis	1.1%
chronic hepatitis	1.1%

Pattern 1:	Pattern 2:	Count:
chronic biliary disease		68
Other (please specify in Comments)		3
cholestasis, bilirubinostasis	chronic biliary disease	3
within normal limits		3
chronic biliary disease	not applicable	3
chronic biliary disease	Other (please specify in Comments)	3
chronic biliary disease	cholestasis, bilirubinostasis	2
chronic biliary disease	chronic biliary disease	2
		2
abnormal, no pattern discernible		1
cholestasis, bilirubinostasis		1
vascular disease		1
chronic hepatitis	chronic biliary disease	1
chronic biliary disease	lobular hepatitis	1
abnormal, no pattern discernible	vascular disease	1

Stages:	Popularity:
mild/early fibrosis without bridging	68.4%
no fibrosis/equivocal fibrosis	20.0%
fibrosis with bridging between vascular structures	6.3%
advanced fibrosis with bridging and nodularity/cirrhosis	2.1%
Other (please specify in Comments)	2.1%
subtle architectural abnormalities, vascular disease	1.1%

Diagnostic categories:	Popularity:
primary sclerosing cholangitis	77.9%
chronic cholangiopathy NOS	12.6%
- histologically indeterminate for cause	4.2%
drug induced liver injury (please specify in comments box)	4.2%
Other (please enter alternative diagnosis in comments box)	4.2%
- no evidence of diffuse/background liver disease	2.1%

Diagnosis Combination:	Count:
primary sclerosing cholangitis	70
chronic cholangiopathy NOS	8
- histologically indeterminate for cause	3
chronic cholangiopathy NOS, primary sclerosing cholangitis	3
drug induced liver injury (please specify in comments box)	3
- no evidence of diffuse/background liver disease	2
Other (please enter alternative diagnosis in comments box)	2
[No selections made]	1
- histologically indeterminate for cause, Other (please enter alternative diagnosis in comments box)	1
chronic cholangiopathy NOS, Other (please enter alternative diagnosis in comments box)	1
drug induced liver injury (please specify in comments box), primary sclerosing cholangitis	1

## LW5

**Points of consensus:** chronic biliary disease (83/95), PSC as diagnosis (74) or mentioned in text (10) = 84/95, 88.4%. No or early fibrosis.

**Suggested scoring: for 10 points** chronic biliary disease pattern, suggest PSC, and no or early fibrosis without bridging.

**Lose 5 marks** if doesn't consider PSC specifically - but include cholangiopathy? - ask the audience? *Committee felt if biliary selected or described in comments but PSC not specifically mentioned lose 5*

**Lose 5 marks** if advanced fibrosis/cirrhosis

**Lose 5 marks** if no mention of PSC, DILI as only entry in diagnosis – *(did have biliary features in comments)*

**Lose 10 marks (score 0) if** something else e.g. - within normal limits - Nothing to suggest chronic biliary disease. - within normal limits - Mostly normal appearance  
- vascular disease, Features of a chronic venopathy - outflow tract obstruction. No evidence of AIH.

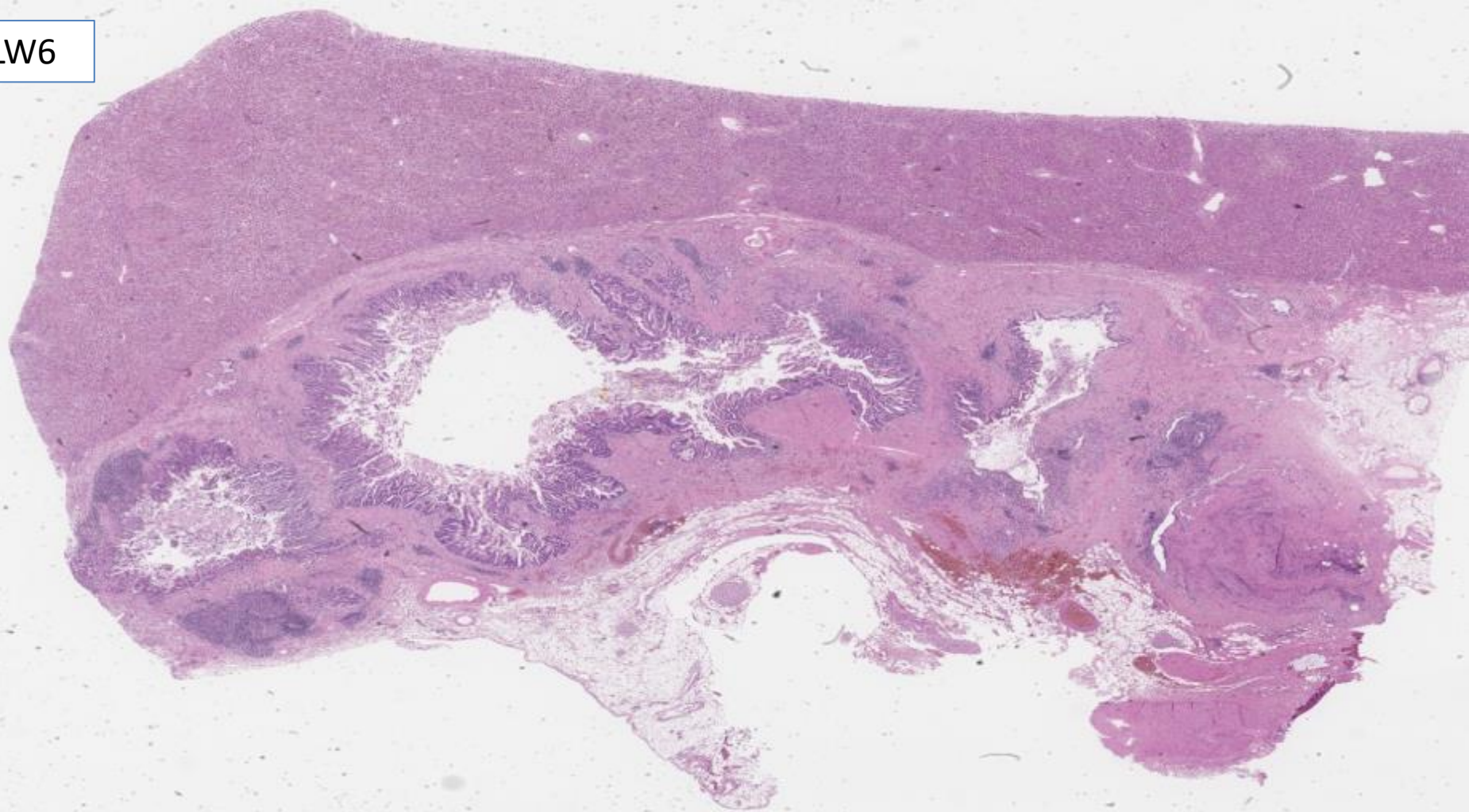
**Original Diagnosis:** Diagnosis of small duct PSC based on this biopsy. Some hydrocortisone around the time of the biopsy.

- Utility of good orcein (or supplemented with rhodanine) and CK7 immunohistochemistry in subtle biliary disease.
- Also had useful history in this case, can answer question – not seronegative AIH
- Infliximab?

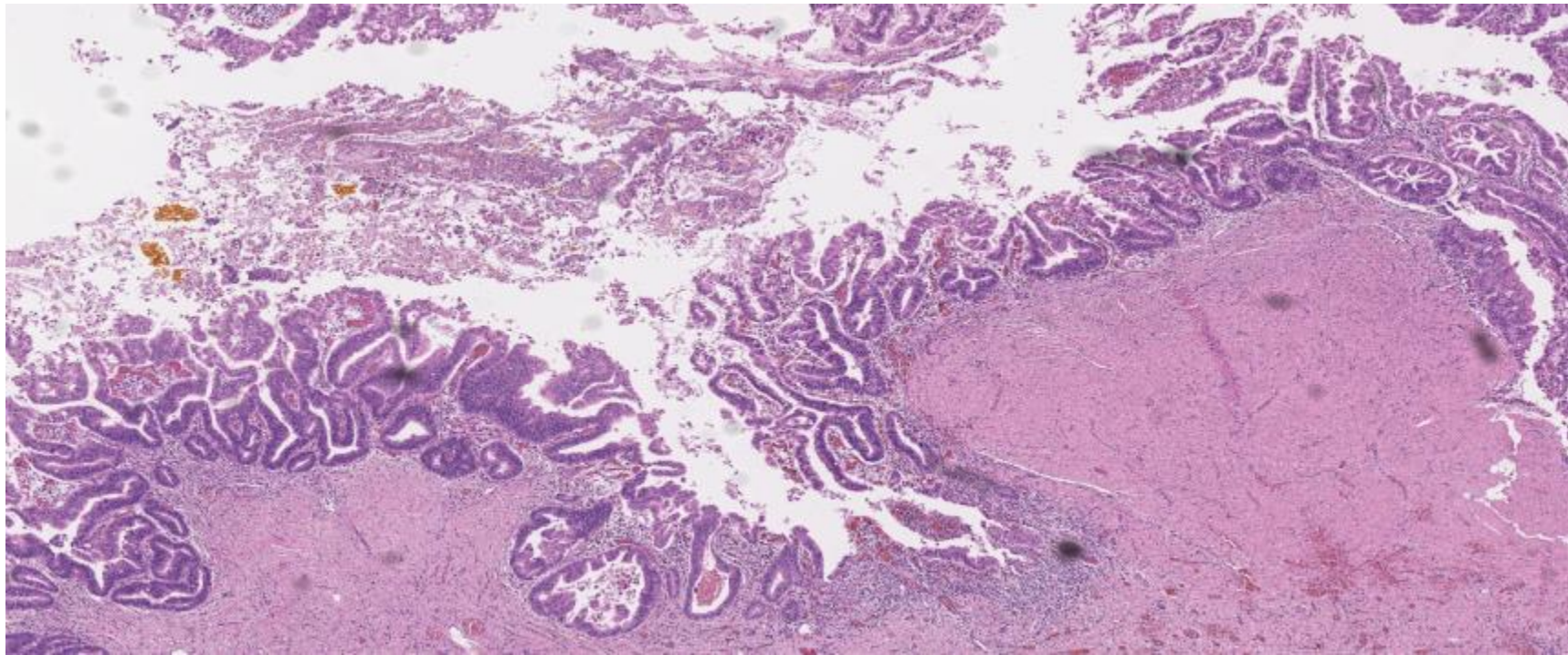
# Case Number: LW6

- **Clinical:** Male 53. None given, from electronic record indication for transplantation PSC.
- **Specimen:** liver removed at transplantation (explant)
- **Macroscopic:** Green liver, mildly dilated bile ducts towards the hilum, no grossly visible mass lesions. Both of the sections (C6 and C8) are from the hilum - random sections, no lesion visible.
- **Immunohistochemistry:** None (2x H&E slides)

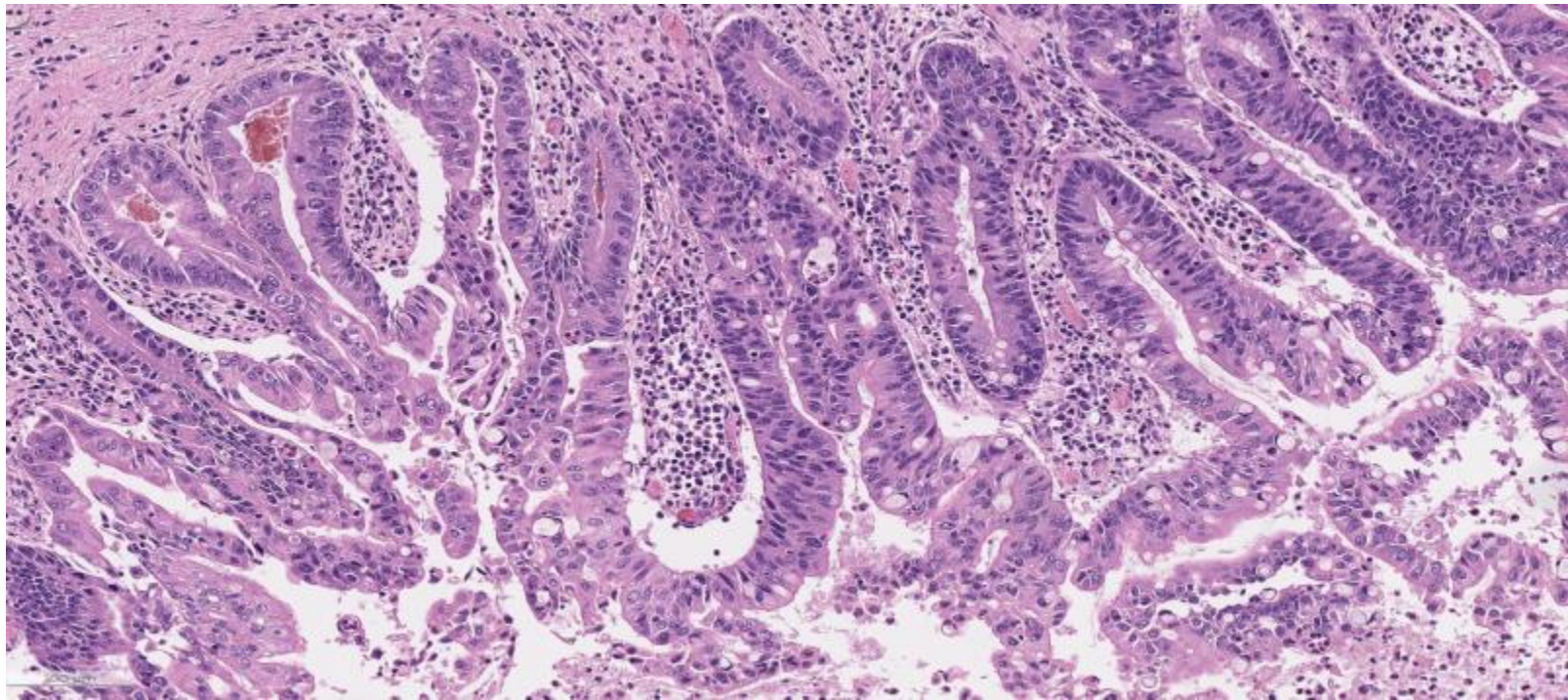
LW6



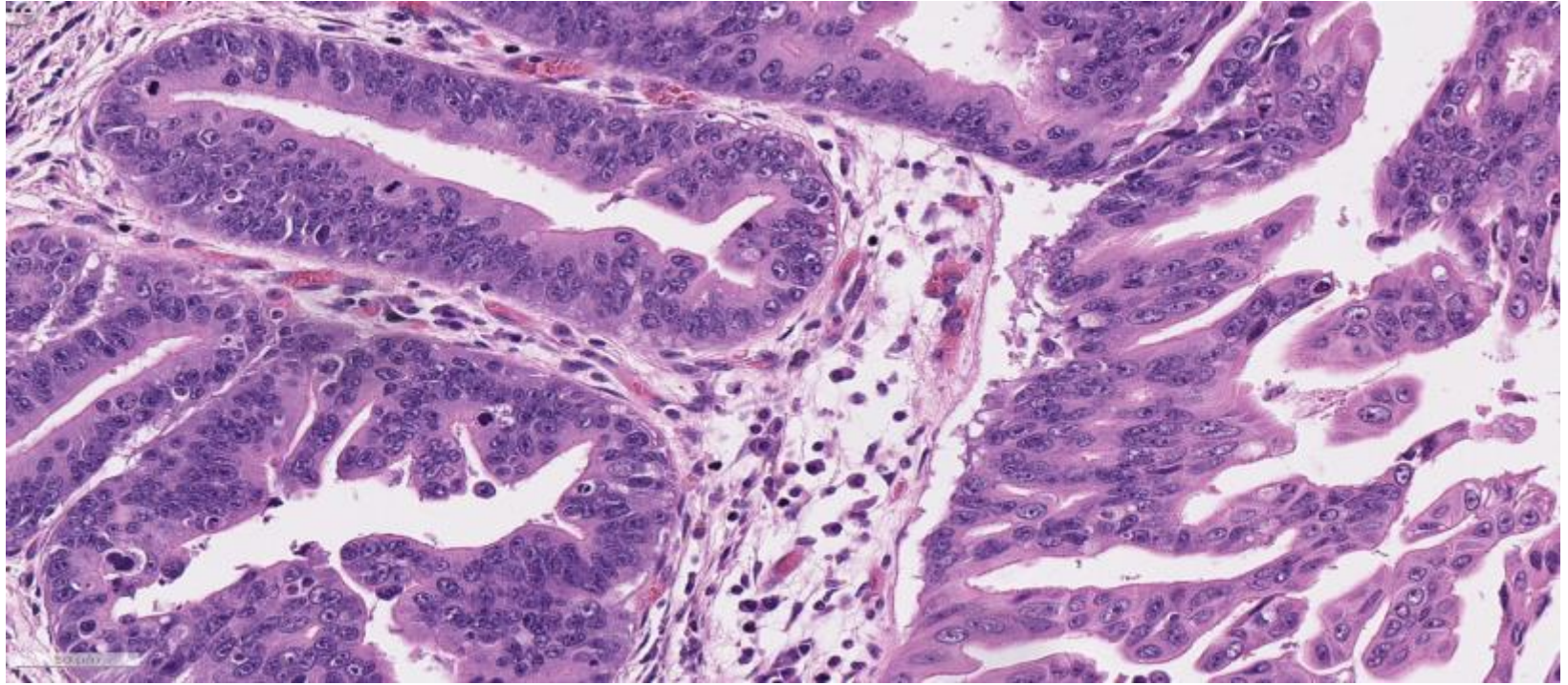
LW6



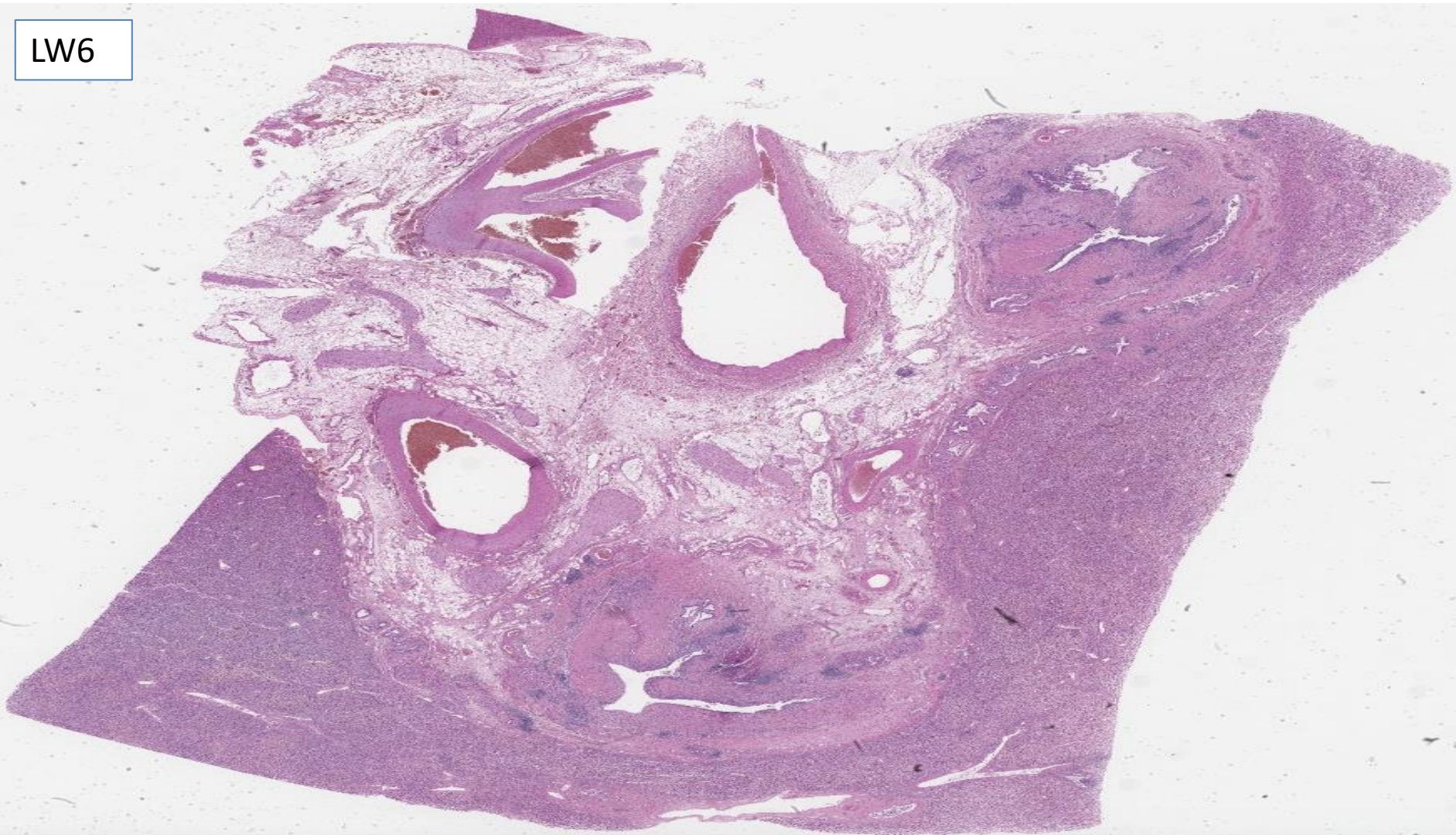
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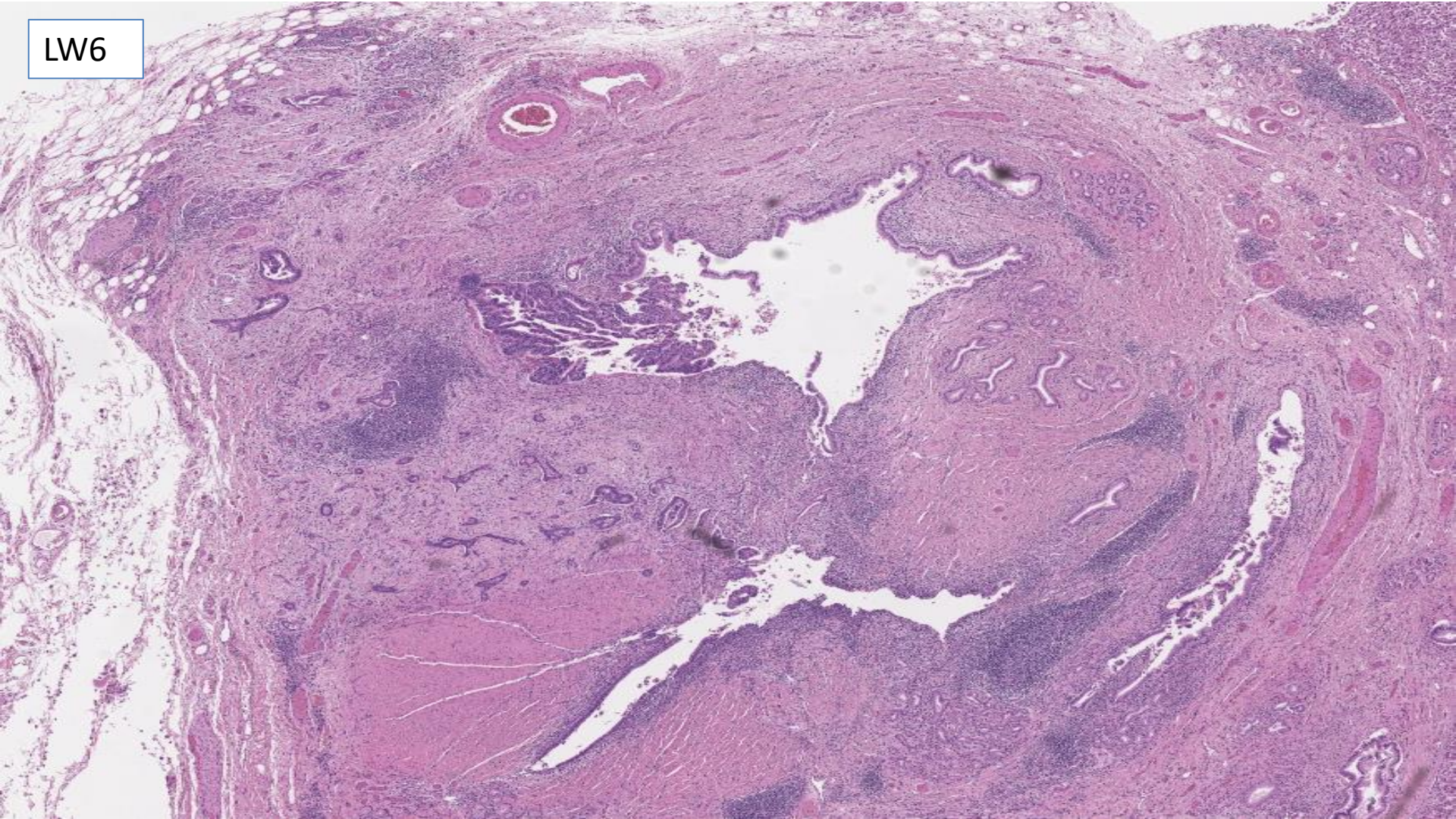
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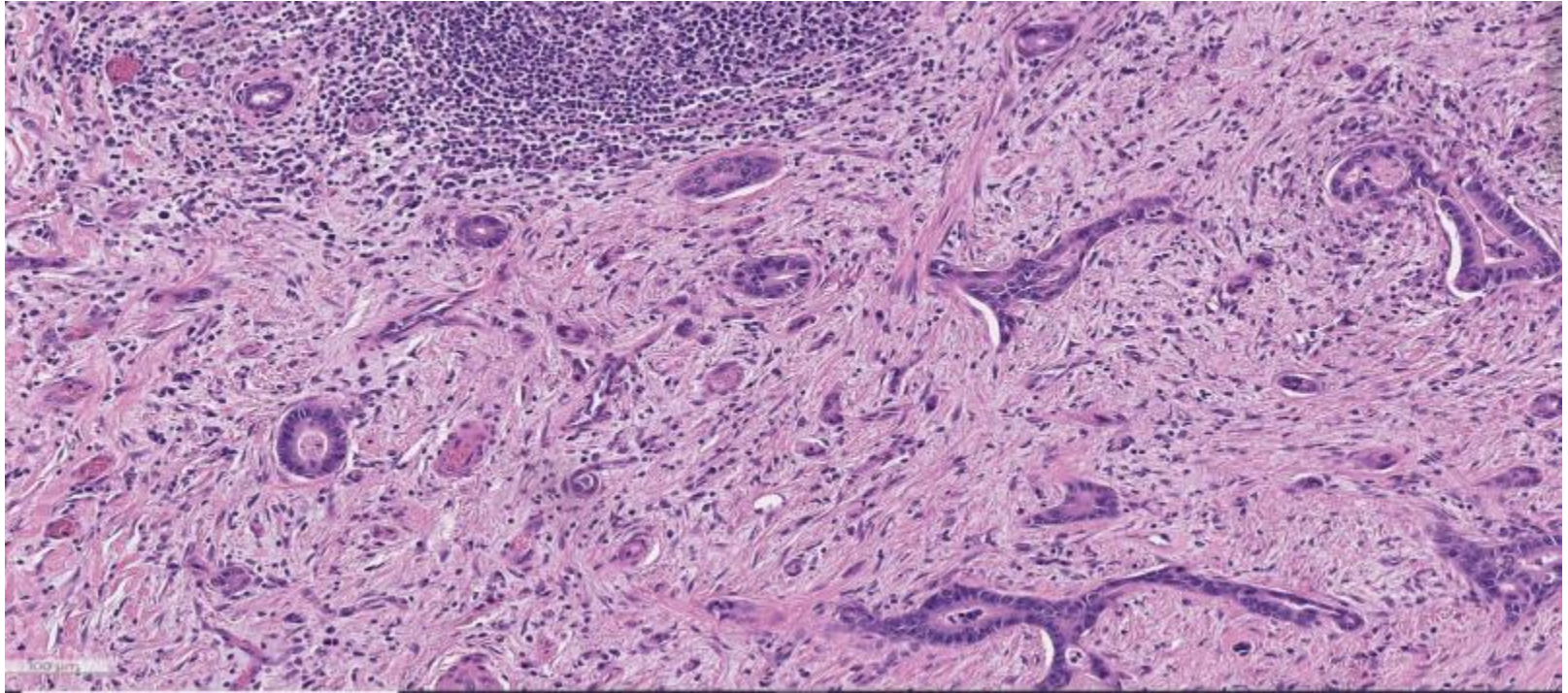
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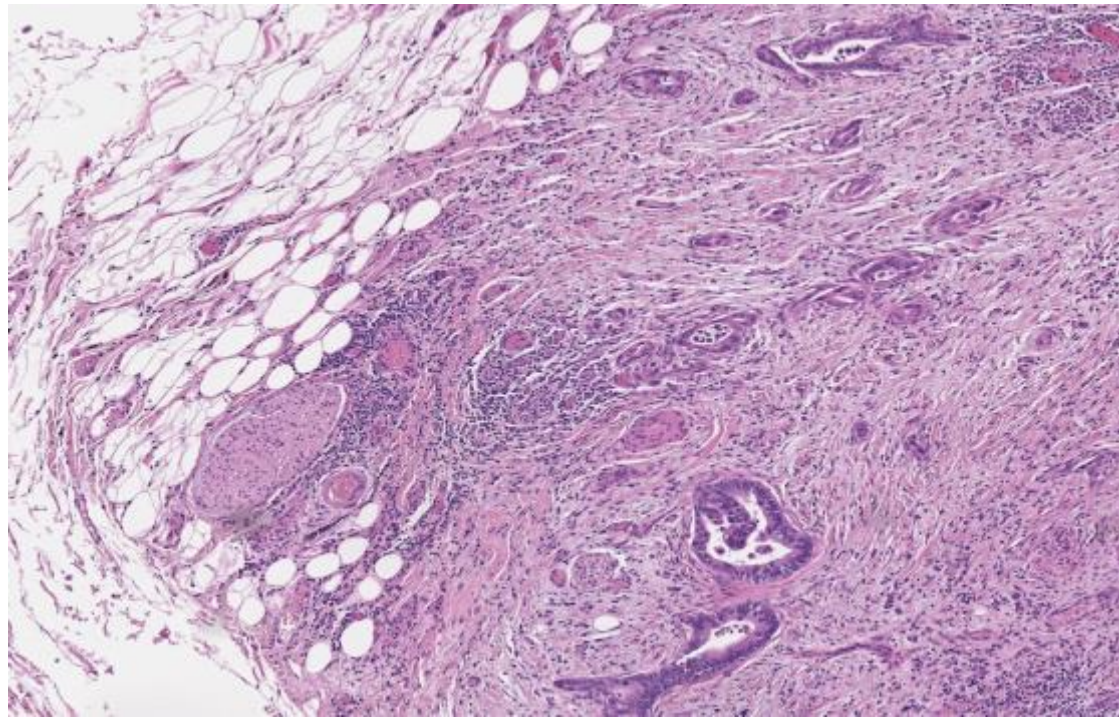
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LW6



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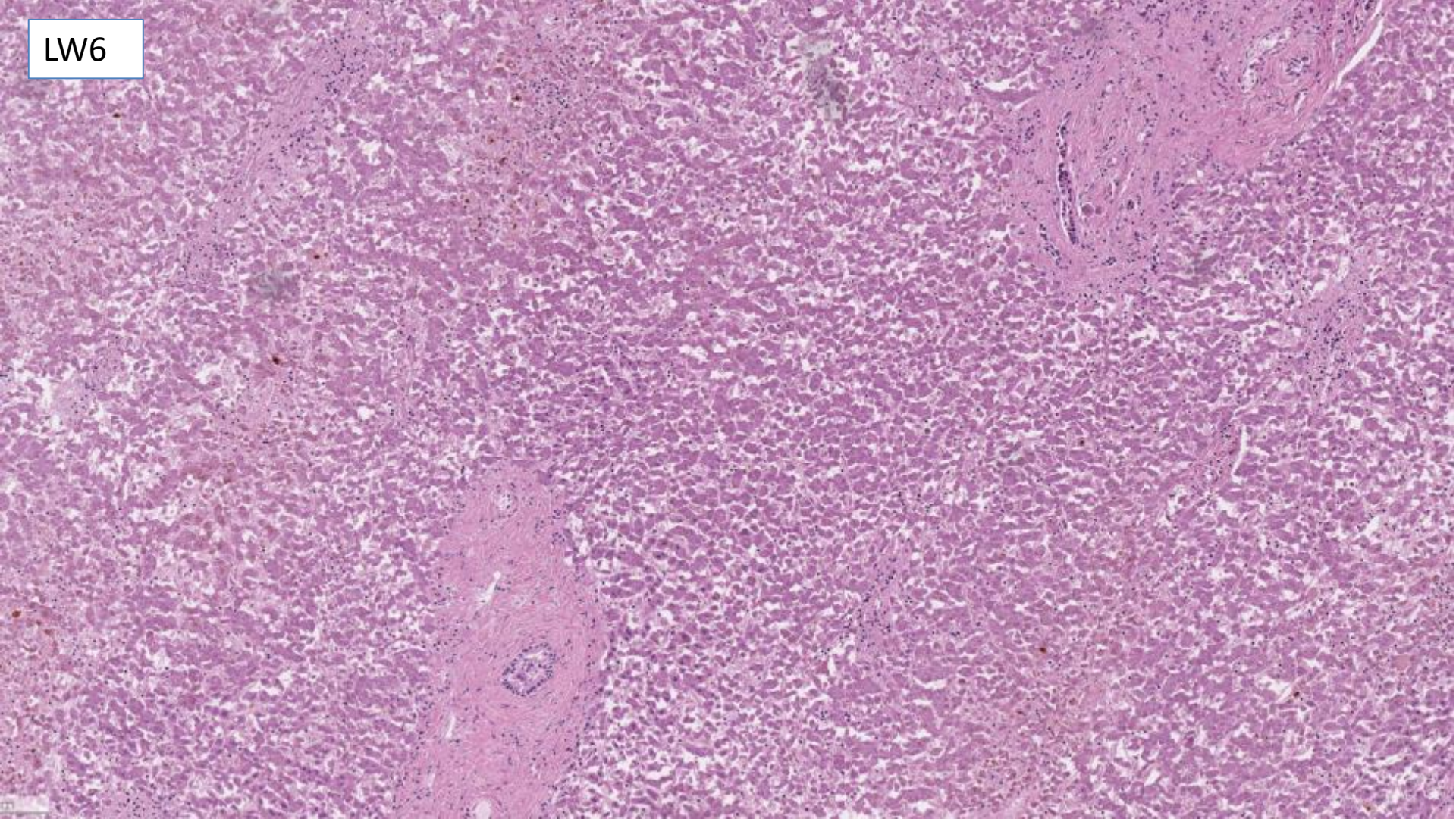


## LW6

Tumour:	Popularity:
cholangiocarcinoma	90.5%
biliary intra-epithelial neoplasia (BillIN)	57.9%
biliary intraductal papillary neoplasia	29.5%
- No tumour/lesion present	1.1%

Tumour 1:	Tumour 2:	Count:
cholangiocarcinoma	biliary intra-epithelial neoplasia (BillIN)	35
biliary intra-epithelial neoplasia (BillIN)	cholangiocarcinoma	15
cholangiocarcinoma	biliary intraductal papillary neoplasia	14
cholangiocarcinoma		12
biliary intraductal papillary neoplasia	cholangiocarcinoma	10
biliary intraductal papillary neoplasia		4
biliary intra-epithelial neoplasia (BillIN)		4
biliary intra-epithelial neoplasia (BillIN)	- No tumour/lesion present	1

LW6



# Re background (greyed out)

Pattern:	Popularity:
chronic biliary disease	56.8%
cholestasis, bilirubinostasis	40.0%
Other (please specify in Comments)	11.6%
not applicable	8.4%
within normal limits	1.1%

Pattern 1:	Pattern 2:	
chronic biliary disease		35
cholestasis, bilirubinostasis		16
chronic biliary disease	cholestasis, bilirubinostasis	9
cholestasis, bilirubinostasis	chronic biliary disease	8
Other (please specify in Comments)		7
		6
not applicable		5
cholestasis, bilirubinostasis	Other (please specify in Comments)	3
chronic biliary disease	Other (please specify in Comments)	1
within normal limits		1
cholestasis, bilirubinostasis	cholestasis, bilirubinostasis	1
cholestasis, bilirubinostasis	not applicable	1
chronic biliary disease	not applicable	1
not applicable	not applicable	1

# Re background (greyed out)

Stages:	Popularity:
not applicable / no special stains to assess architecture	57.9%
fibrosis with bridging between vascular structures	11.6%
advanced fibrosis with bridging and nodularity/cirrhosis	10.5%
Diagnostic categories:	Popularity:
primary sclerosing cholangitis	60.0%
large bile duct obstruction	5.3%
Other (please enter alternative diagnosis in comments box)	5.3%
- not applicable (insufficient non-lesional tissue)	2.1%
- histologically indeterminate for cause	1.1%
- no evidence of diffuse/background liver disease	1.1%
chronic cholangiopathy NOS	1.1%
Diagnosis Combination:	Count:
primary sclerosing cholangitis	53
[No selections made]	27
Other (please enter alternative diagnosis in comments box)	5
large bile duct obstruction, primary sclerosing cholangitis	3
- not applicable (insufficient non-lesional tissue)	2
large bile duct obstruction	2
- histologically indeterminate for cause	1
- no evidence of diffuse/background liver disease	1
chronic cholangiopathy NOS, primary sclerosing cholangitis	1

## LW6

**Points of consensus:** Cholangiocarcinoma and background of biliary dysplasia - accept either BilIN or biliary intraductal papillary neoplasia.

Background insufficient for consensus.

**Suggested scoring: for 10 points** cholangiocarcinoma **and** BilIN or IPNB

86/95 (90%) had cholangiocarcinoma

83/95 (87.4%) included BilIN or IPNB.

**Lose 5 marks** 12 had cholangiocarcinoma but no BilIN or IPNB – ask the audience – added after the meeting 60% felt just cholangiocarcinoma would still score 10 marks

i.e. no marks deducted for omitting dysplastic lesion if Cholangiocarcinoma diagnosed.

**Lose 10 marks (score 0) if** no cholangiocarcinoma

**Observations/potential learning points, suitable for masterclass?** terminology for biliary dysplasias

**Original report and further information (if any):** High grade dysplasia / biliary intraepithelial neoplasia with focal invasive cholangiocarcinoma. Background features of PSC not well demonstrated in this material but seen elsewhere

May 2021 Patient remains well, no recurrence cholangiocarcinoma, has UC awaiting surveillance colonoscopy

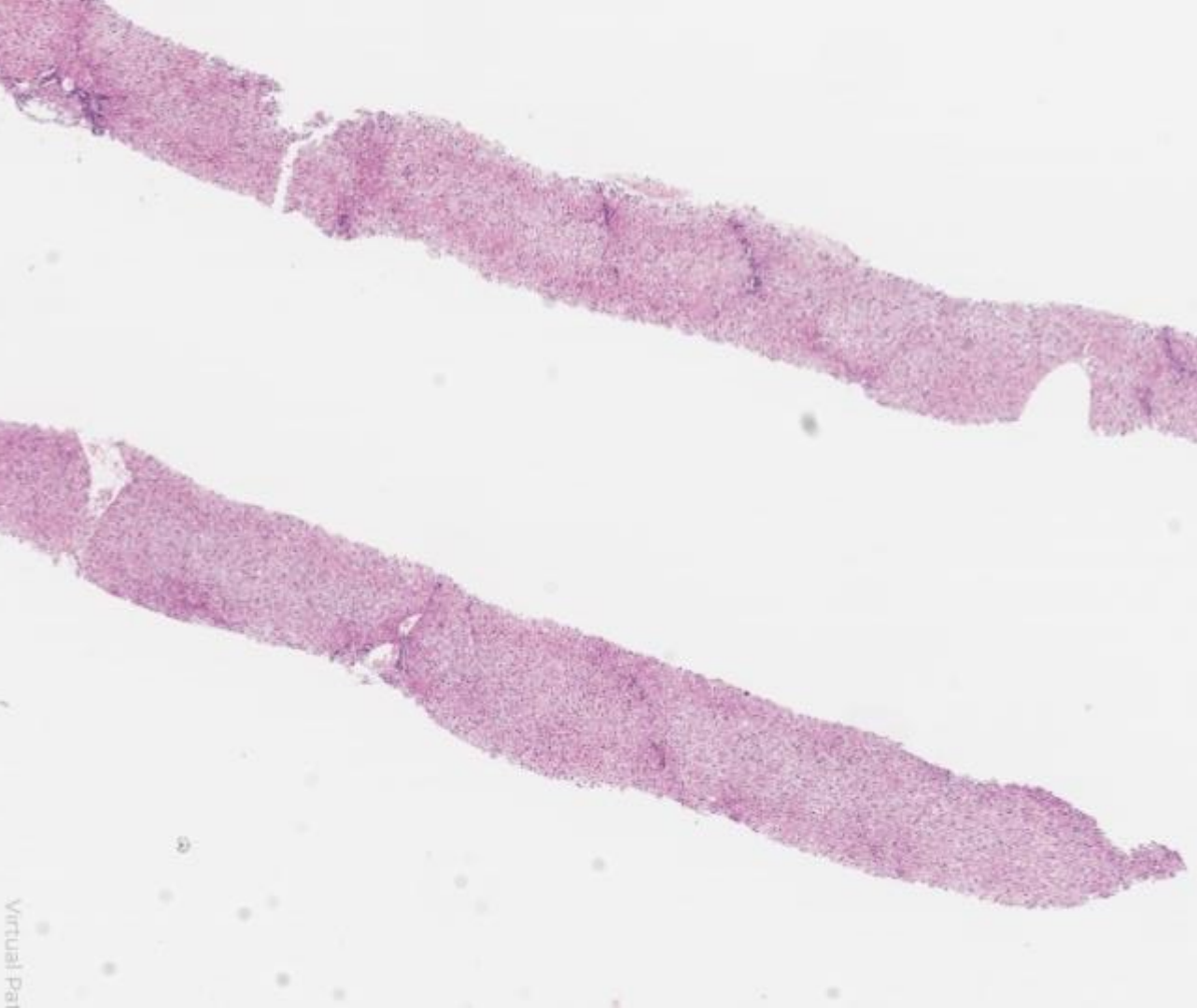
## WHO classification 5<sup>th</sup> ed

- BiLIN biliary intraepithelial neoplasia, **microscopic**, flat or (micro) papillary.
- IPNB Intraductal papillary neoplasm of the bile ducts. (our EQA nomenclature 'biliary intraductal papillary neoplasia' needs tweaking!) **grossly visible** premalignant neoplasm.

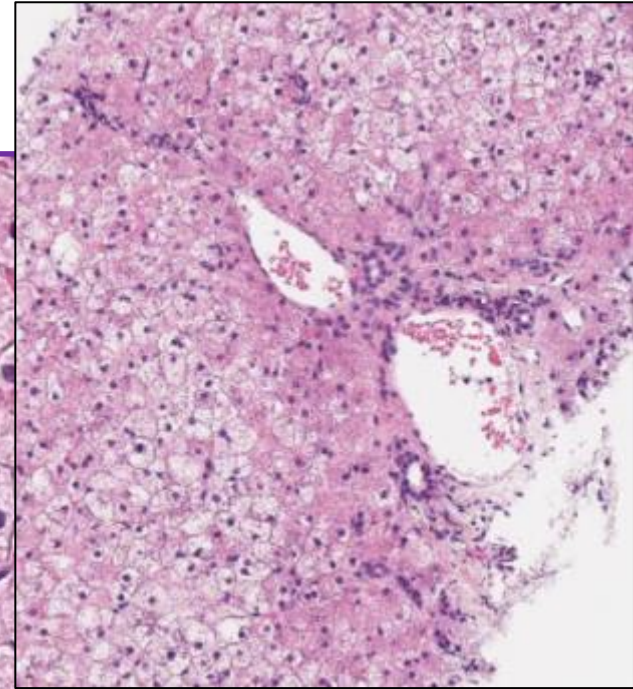
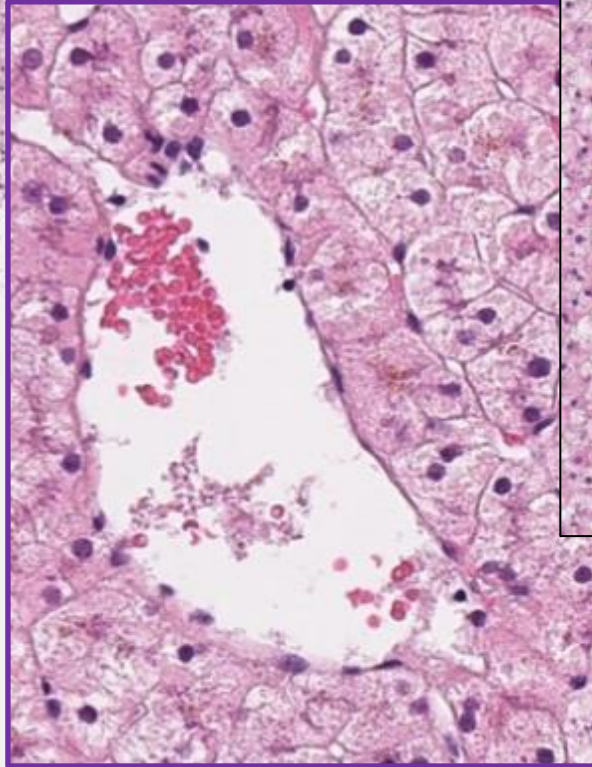
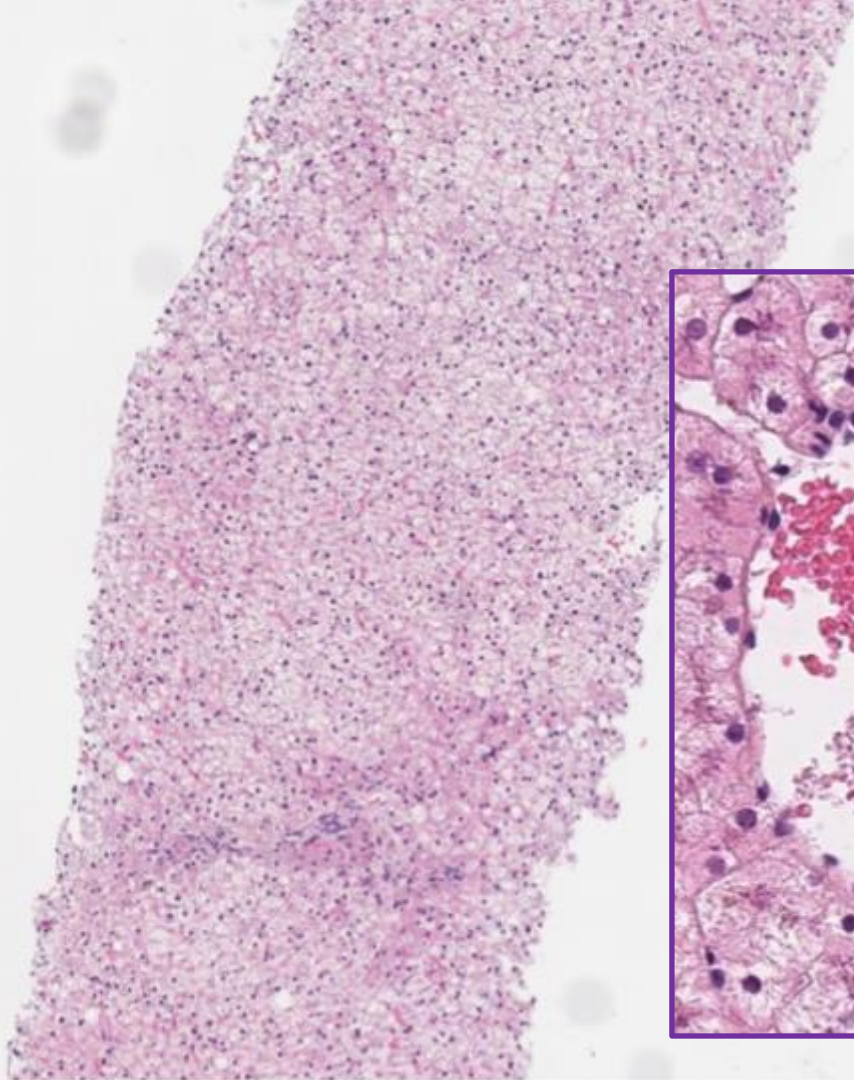
# LW – Case 7

<b>Case number:</b>	7
<b>Clinical Information:</b>	18, T1DM, Sturge Weber syndrome & epilepsy. Admitted with DKA, Back on normal insulin. Persistently raised LFTs for 4 months (ALT 302, ALP 178, Bili 5). INR normal. NILS negative apart from positive pANCA. USS previously normal ?cause of deranged LFTS ?drug induced. Patient on Carbamazepine for epilepsy
<b>Specimen:</b>	Liver biopsy
<b>Age:</b>	18
<b>Sex:</b>	Female
<b>Macroscopic description:</b>	One core of tissue measuring up to 27mm in length, plus three smaller fragments
<b>Additional Stains:</b>	Liver specials show no significant changes.
<b>View Slides:</b>	H&E, van Gieson, retic, PAS, DPAS

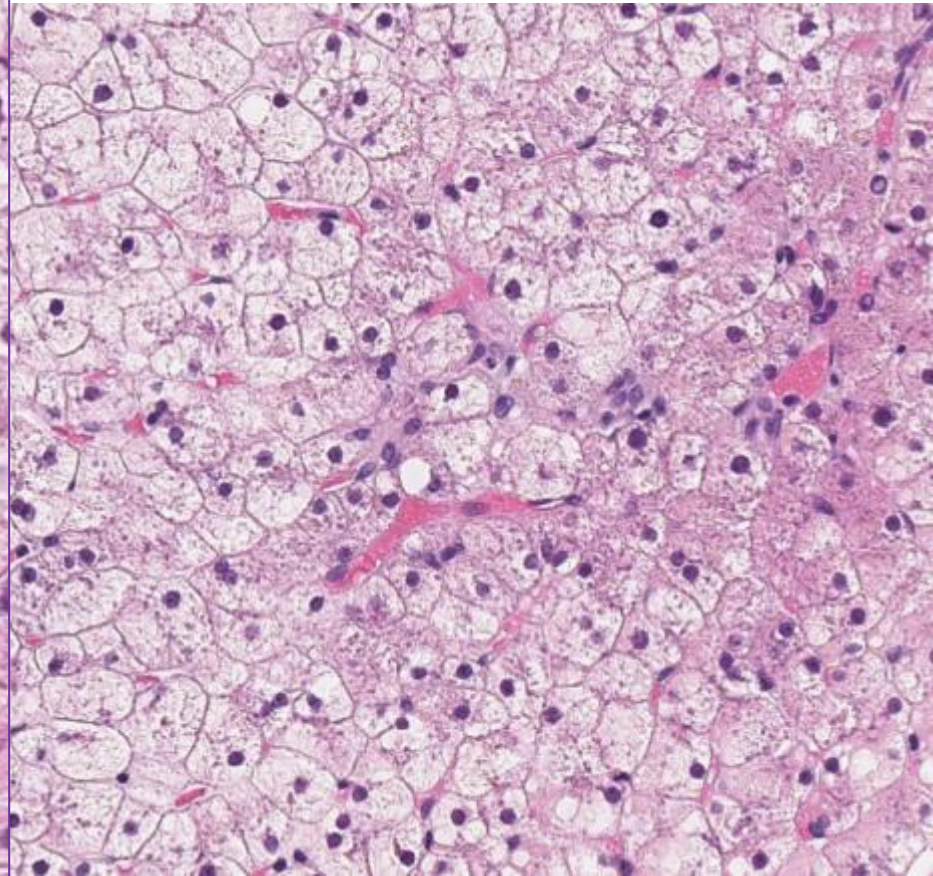
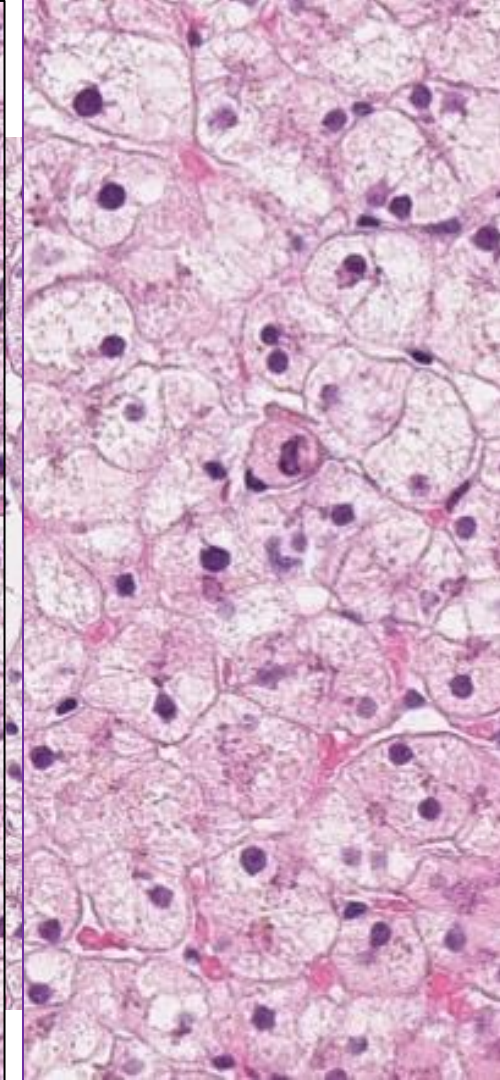
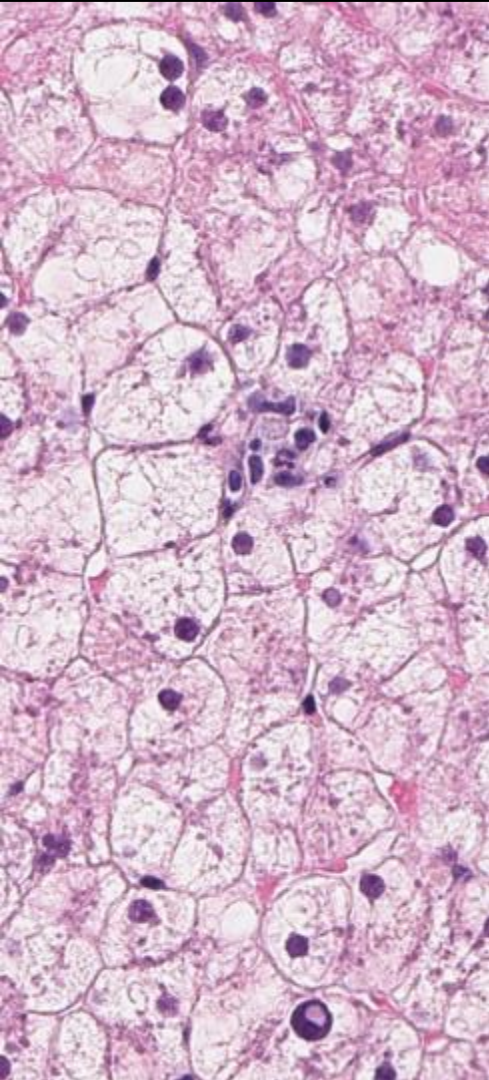
# LW – Case 7



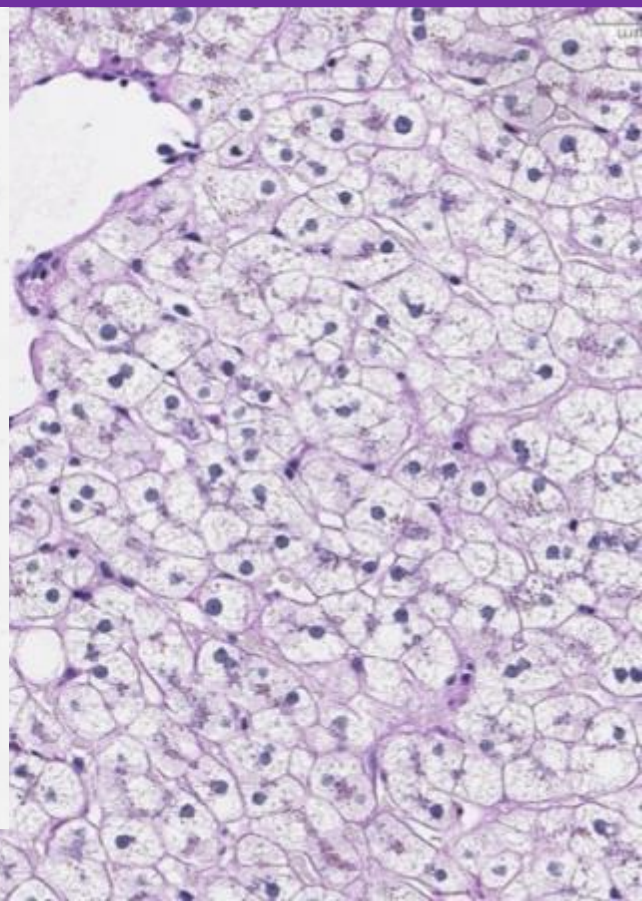
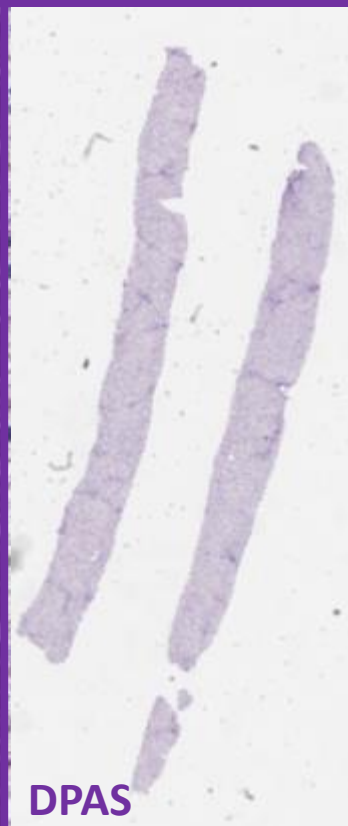
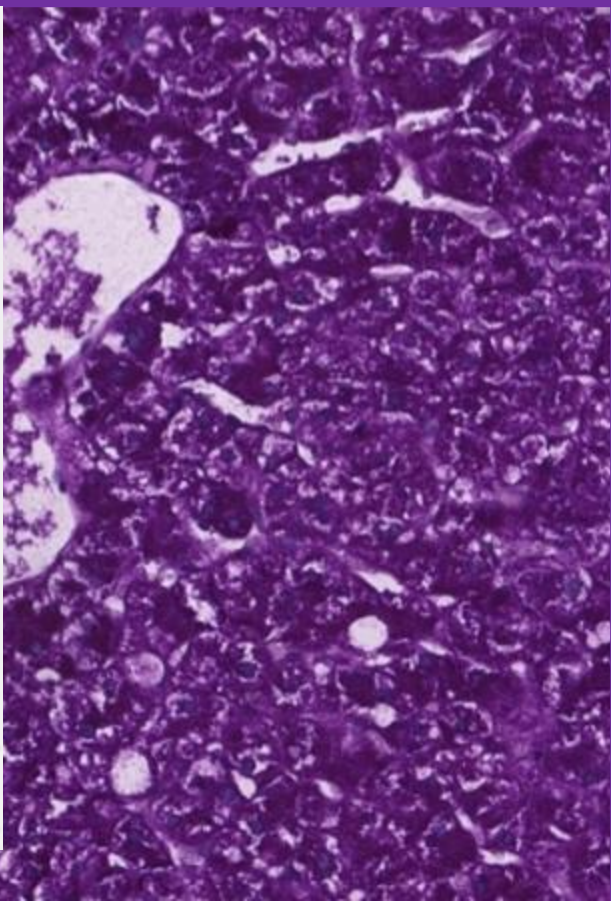
# LW – Case 7



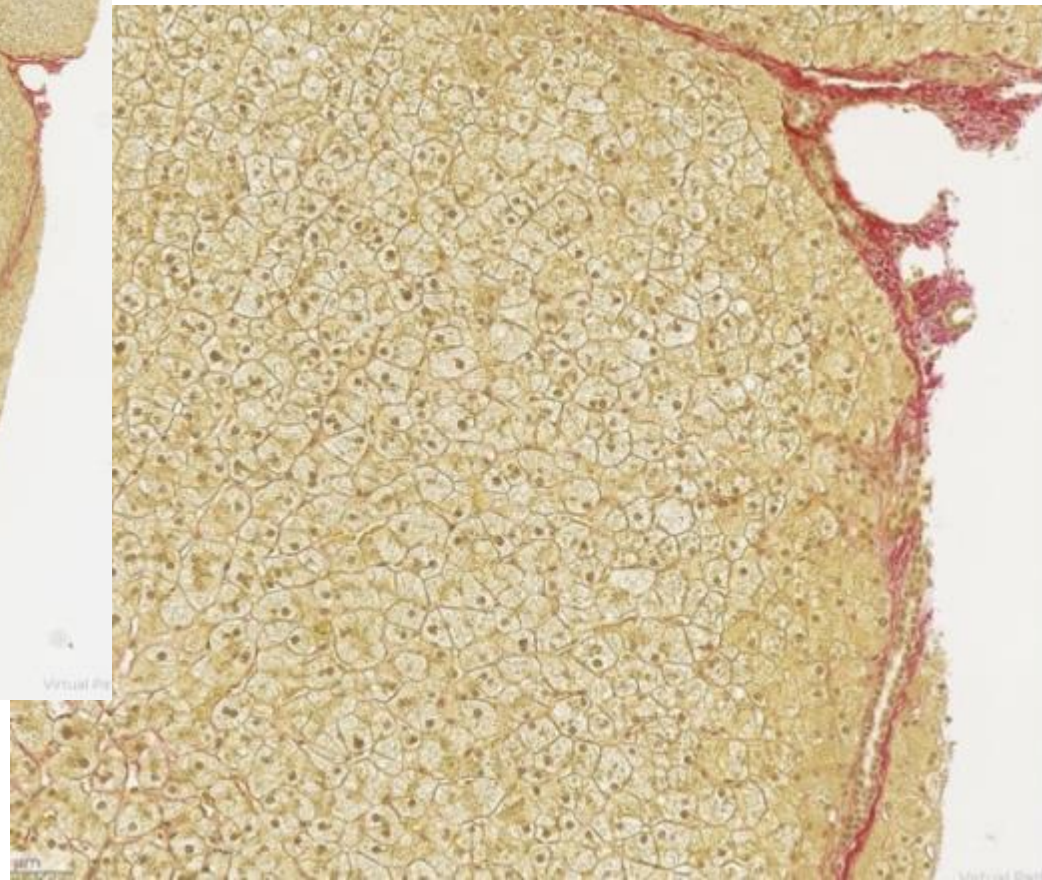
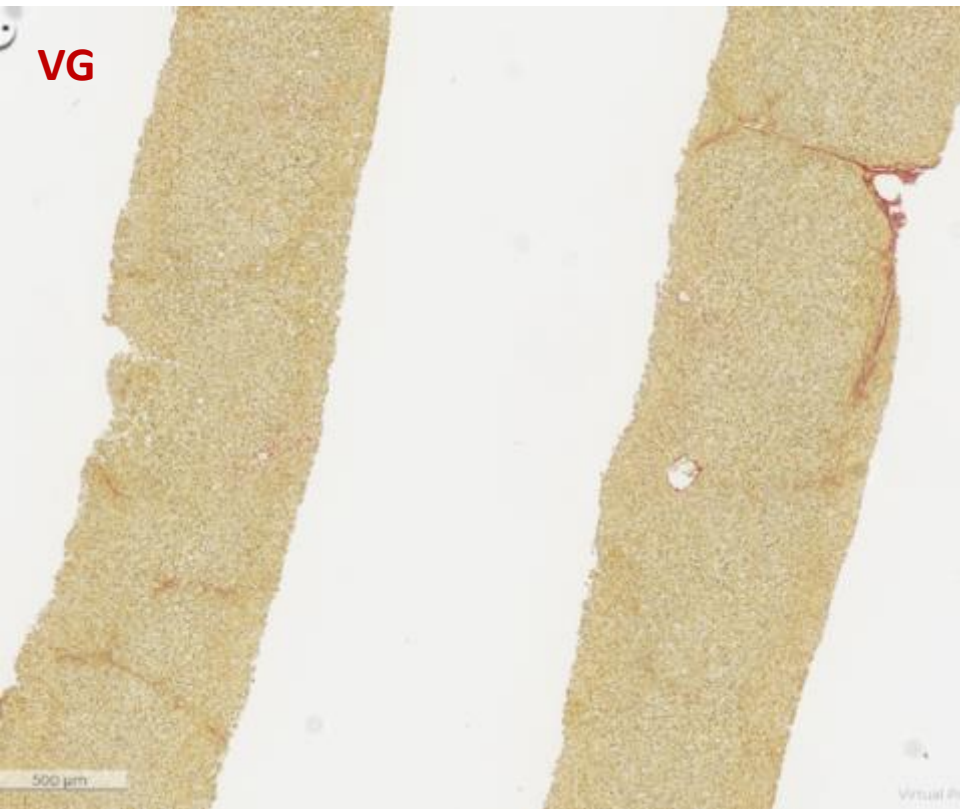
# LW – Case 7



# LW – Case 7



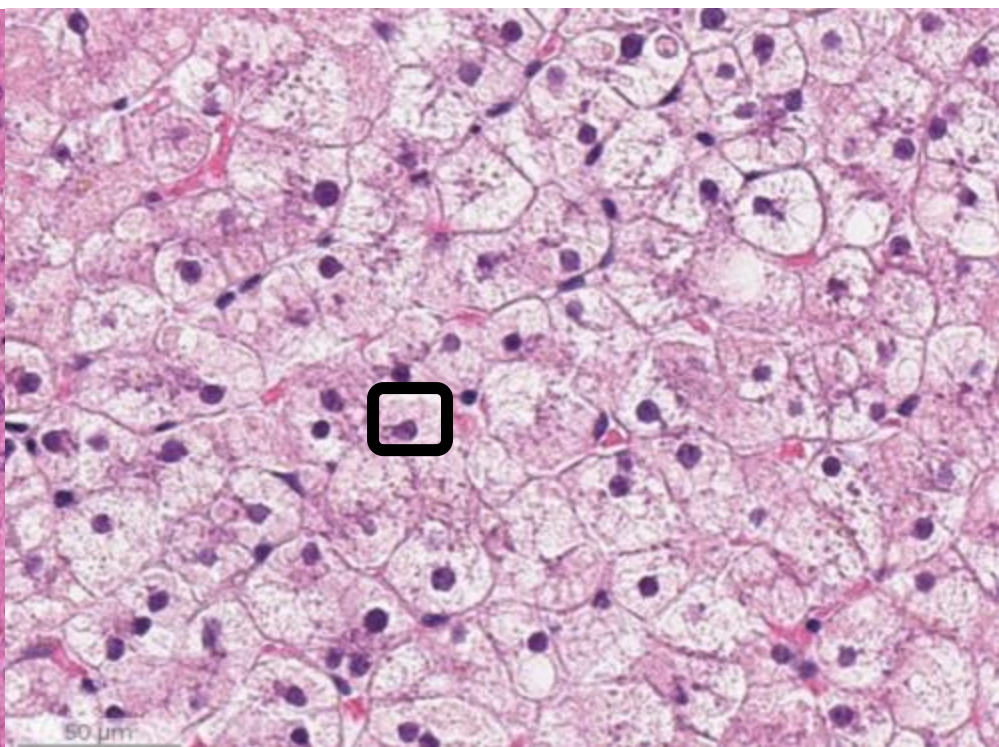
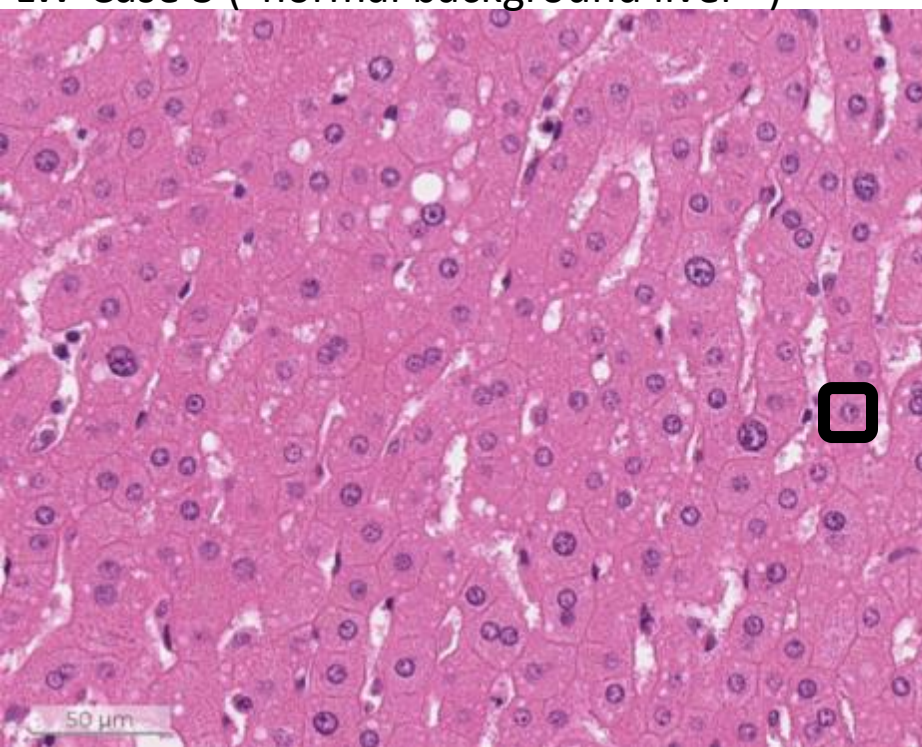
# LW – Case 7



# LW – Case 7



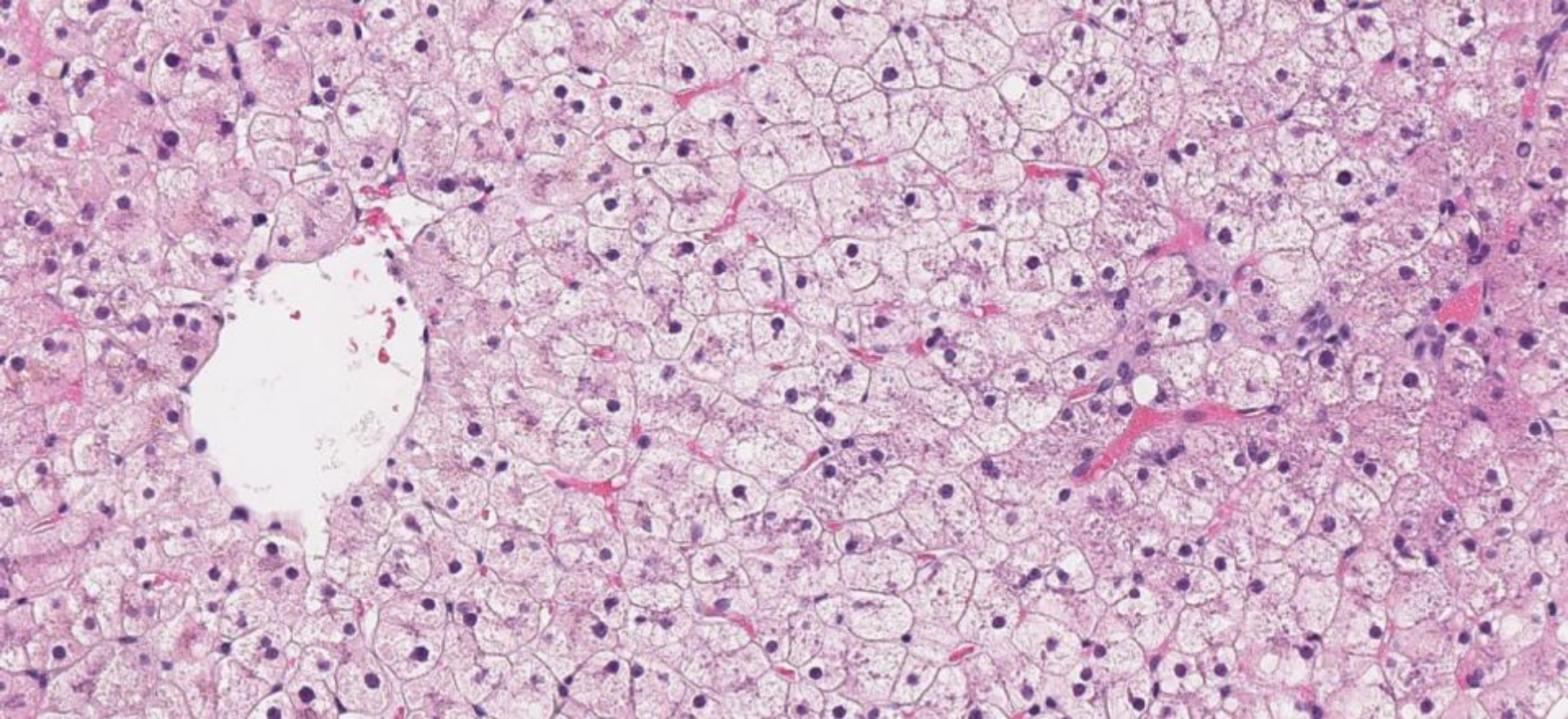
LW-Case 3 (“normal background liver “)



Original reporting pathologist diagnosis:

LW – Case 7

**Glycogenic hepatopathy**



# LW – Case 7

Case not suitable for scoring, no consensus on pattern of injury or diagnosis

<b>Pattern:</b>	<b>Popularity:</b>
Other (please specify in Comments)	82.1%
Abnormal, no pattern discernible	6.3%
<u>Steatosis</u>	6.3%
<u>Steatohepatitis</u>	3.2%
<u>Within normal limits</u>	3.2%
<u>Lobular hepatitis</u>	2.1%
<u>Cholestasis, bilirubinostasis</u>	2.1%
Not applicable	2.1%

<b>Diagnostic categories:</b>	<b>Popularity:</b>
Manifestation of systemic or extrahepatic disease	30.5%
Other	30.5%
Storage disorder	23.2%
Drug induced liver injury	13.7%
Histologically indeterminate for cause	4.2%
fatty liver disease - non-alcohol related fatty liver disease	4.2%
fatty liver disease - either alcohol or non-alcohol	1.1%

**LW7: Diagnosis Combination:**

	<b>Count:</b>
<b>Manifestation of systemic or extrahepatic disease</b> (please specify in comments box)	<b>25</b>
<b>Other</b> (please enter alternative diagnosis in comments box)	<b>25</b>
<b>Storage disorder</b> (please specify in comments box)	<b>17</b>
<b>drug induced liver injury</b> (please specify in comments box)	<b>8</b>
<b>[No selections made]</b>	<b>3</b>
<b>Histologically indeterminate for cause</b>	<b>3</b>
<b>Fatty liver disease - non-alcohol related fatty liver disease</b>	<b>3</b>
Drug induced liver injury storage disorder	2
Manifestation of systemic or extrahepatic disease storage disorder	2
<b>Histologically indeterminate for cause, Other</b>	1
Drug induced liver injury, fatty liver disease - non-alcohol related fatty liver disease	1
Drug induced liver injury, manifestation of systemic or extrahepatic disease	1
Drug induced liver injury, Other	1
Fatty liver disease - either alcohol or non-alcohol	1
Manifestation of systemic or extrahepatic disease, Other	1
Other (please enter alternative diagnosis in comments box), storage disorder	1

# LW – Case 7

Case not suitable for scoring,  
no consensus on pattern of injury or diagnosis

## In Comments:

<b>Glycogenic hepatopathy</b>	<b>31</b>
<b>Glycogen hepatopathy</b>	<b>2</b>
<b>Hepatic glycogenosis, glycogen</b>	<b>25</b>
Glycogenosis related to diabetes	20
Mauriac Syndrome	4
<b>GSD – Glycogen Storage Disease</b>	<b>12</b>
<b>DILI – Carbamazepin/anti-epileptics</b>	<b>12</b>

<b>Pattern:</b>	<b>Popularity:</b>
Other (please specify in Comments)	82.1%
Abnormal, no pattern discernible	6.3%
<u>Steatosis</u>	6.3%
<u>Steatohepatitis</u>	3.2%
<u>Within normal limits</u>	3.2%
<u>Lobular hepatitis</u>	2.1%
<u>Cholestasis, bilirubinostasis</u>	2.1%
Not applicable	2.1%

# LW – Case 7

Case not suitable for scoring,  
no consensus on pattern of injury or diagnosis

## GSD in diagnosis box 22

### Comments:

GSD, genetic disorder	12
GSD related to diabetes, if GSD excluded	1
GSD = glycogenosis related to diabetes	8
GSD = glycogen accumulation	1

### Diagnostic categories:

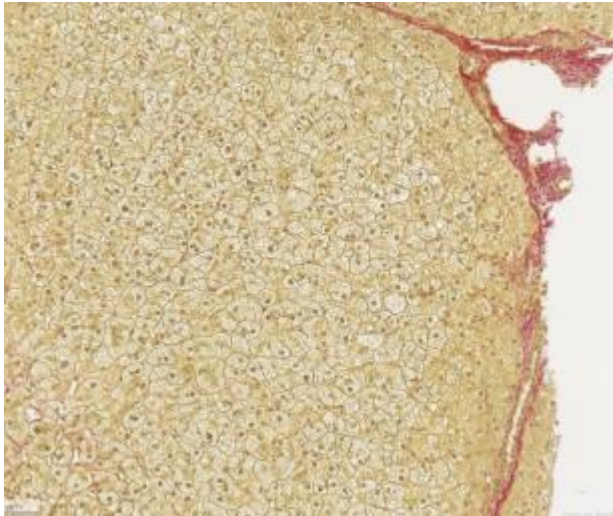
#### Popularity:

Manifestation of systemic or extrahepatic disease	30.5%
Other	30.5%
Storage disorder	23.2%
Drug induced liver injury	13.7%
Histologically indeterminate for cause	4.2%
fatty liver disease/non-alcohol related fatty liver disease	4.2%
fatty liver disease - either alcohol or non-alcohol	1.1%

Glycogenosis is a broad term to define morphological features of the cells accumulating glycogen, resulting in clear cytoplasmic appearance, which may be secondary to genetic or acquired causes.

GSD- glycogen storage disease, is a terminology that is used in general to refer to genetic disorders, particularly in Paediatrics.

Stages:	Popularity:
no fibrosis/equivocal fibrosis	61.1%
mild/early fibrosis without bridging	25.3%
fibrosis with bridging between vascular structures	4.2%
Other (please specify in Comments)	1.1%
not applicable / no special stains to assess architecture	1.1%



**Educational point: Total of 6 participants staged as or commented on the presence of bridging fibrosis. Portal ramification (bile ducts or vasculature cut longitudinally, accompanied by structural fibrosis) may be mistaken for bridging septa. This features should not account for bridging fibrosis.**

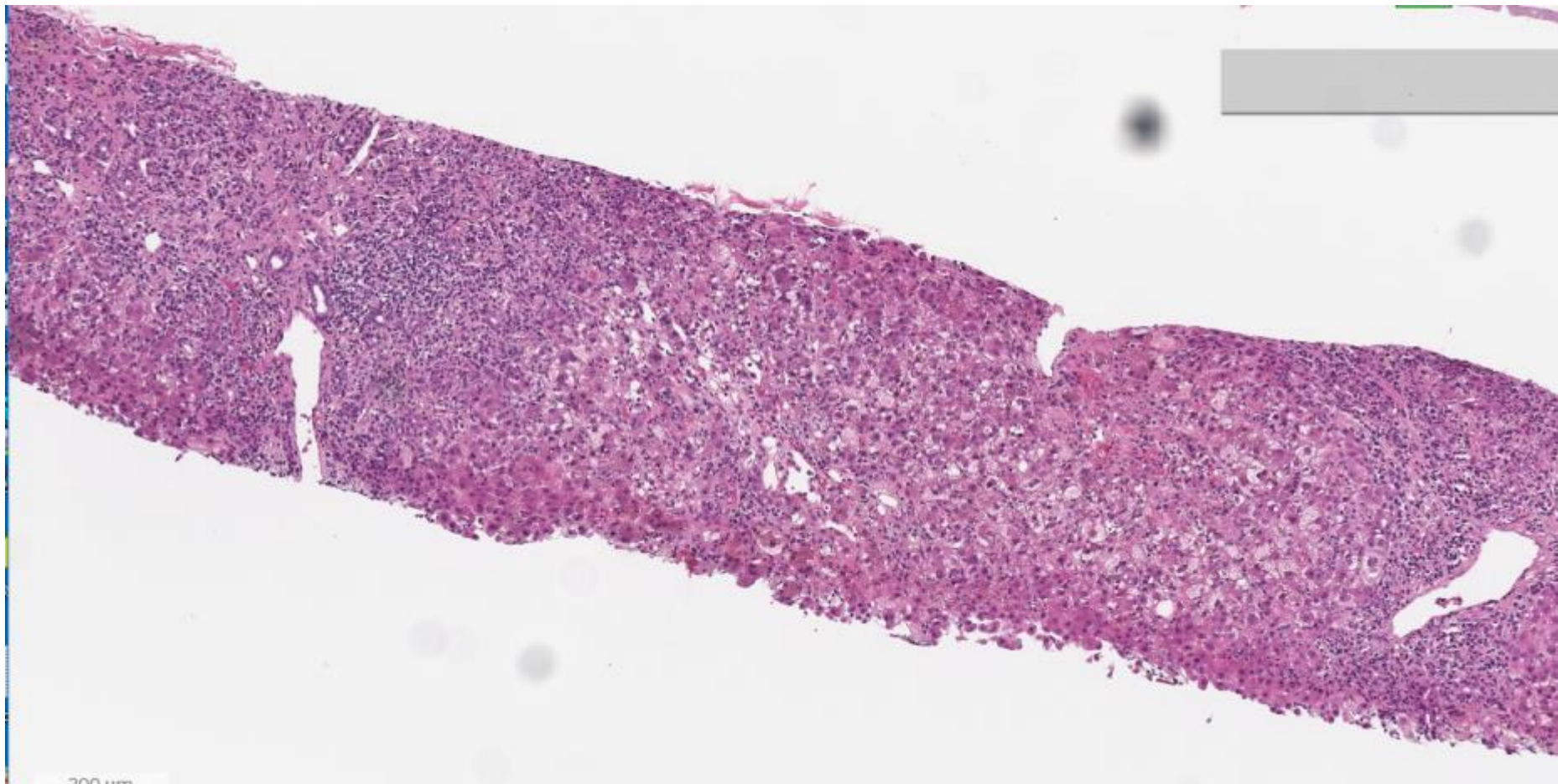
# LW – Case 8

<b>Clinical Information:</b>	Bil 267, ALT 2803, ALP 132, IgG 26.5, ANA 1:640. ?Auto immune hepatitis triggered by Infliximab (x2 doses). Azathioprine previously. Previous medical history: IBD, likely Crohn's. 6/7 steroids before biopsy.
<b>Specimen:</b>	Medical liver biopsy
<b>Age:</b>	40
<b>Sex:</b>	Male
<b>Macroscopic description:</b>	A tan core measuring 22mm, embedded intact.
<b>Additional Stains:</b>	None
<b>View Slides:</b>	<a href="#">H&amp;E</a>

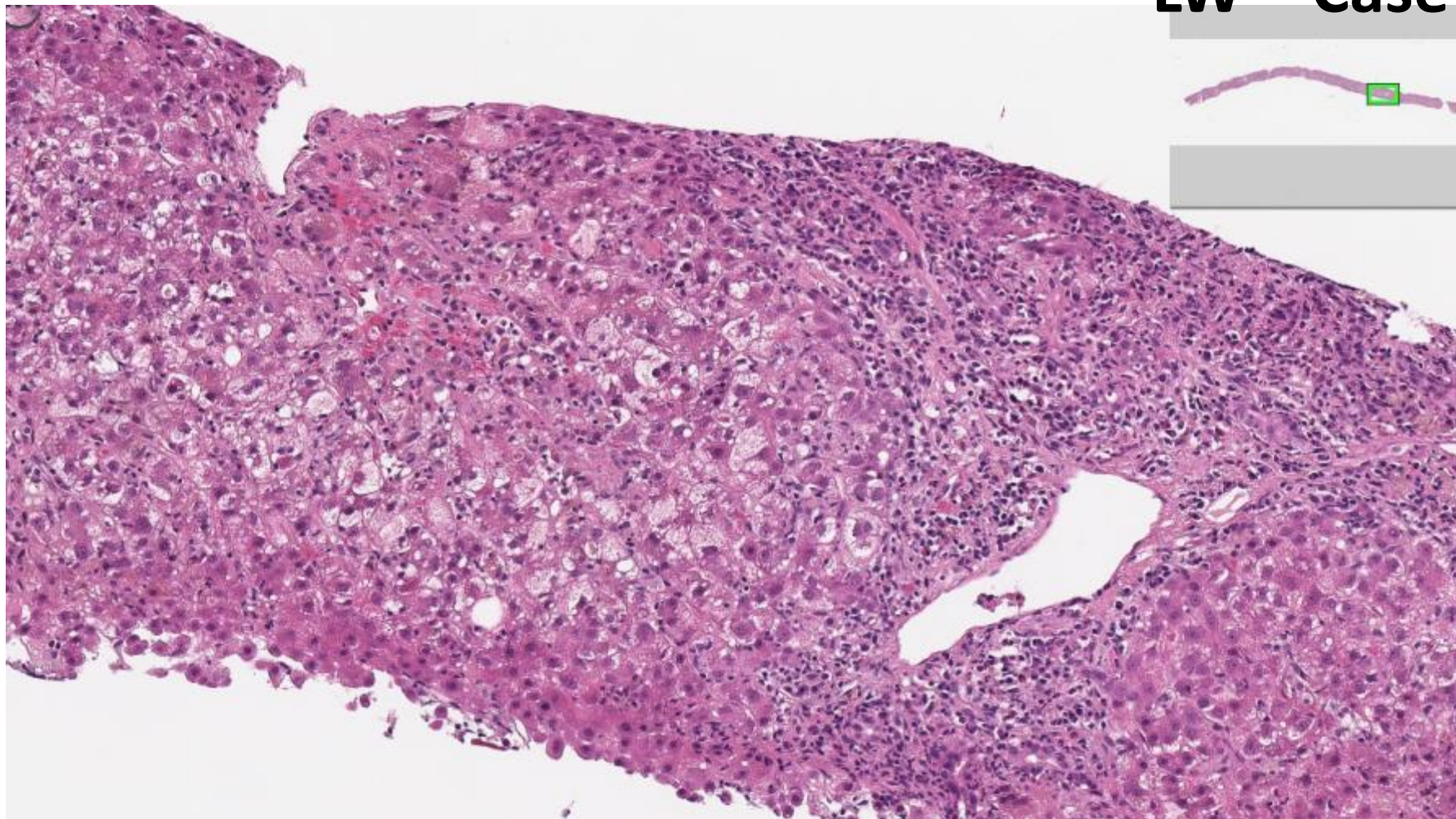
# LW – Case 8



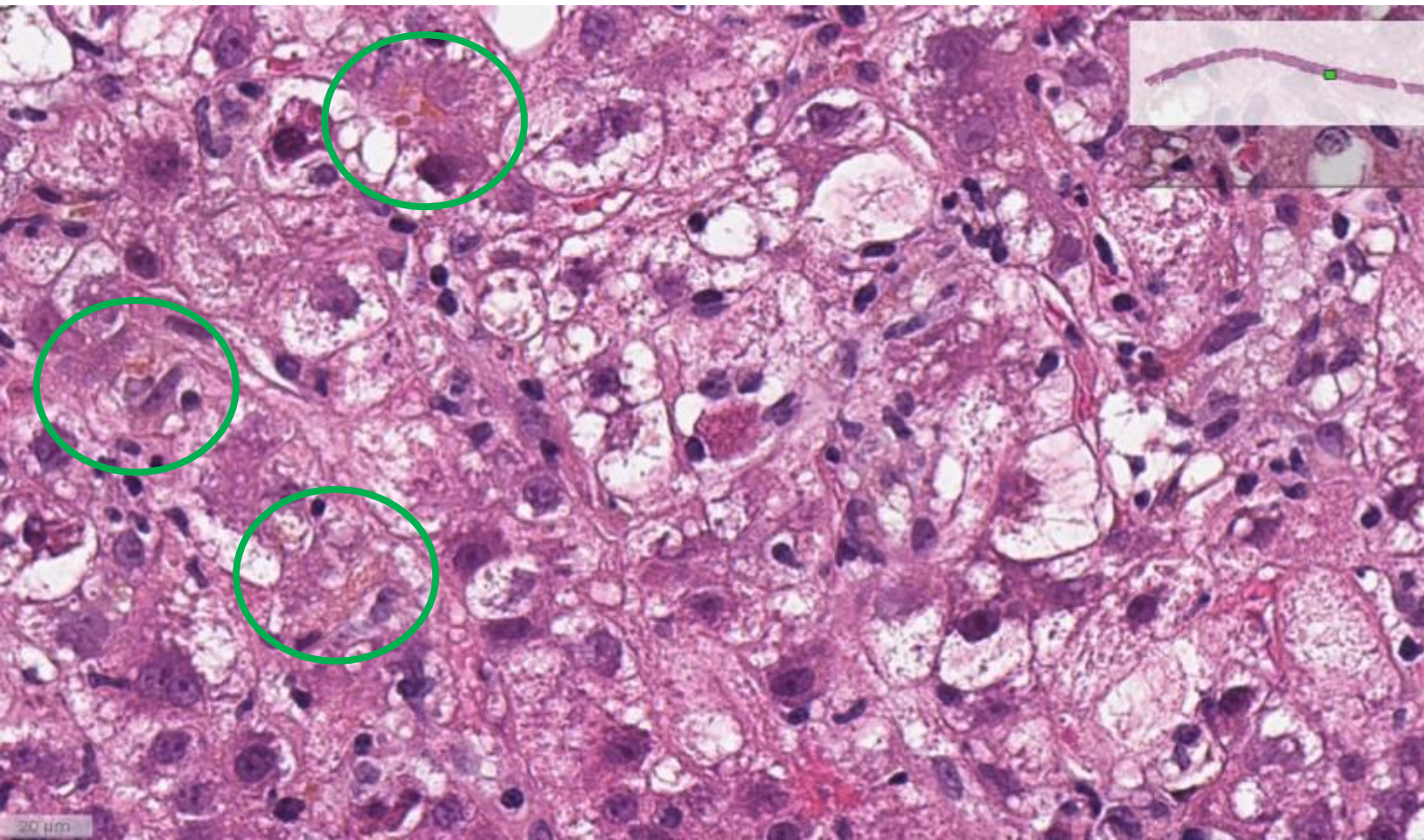
# LW – Case 8



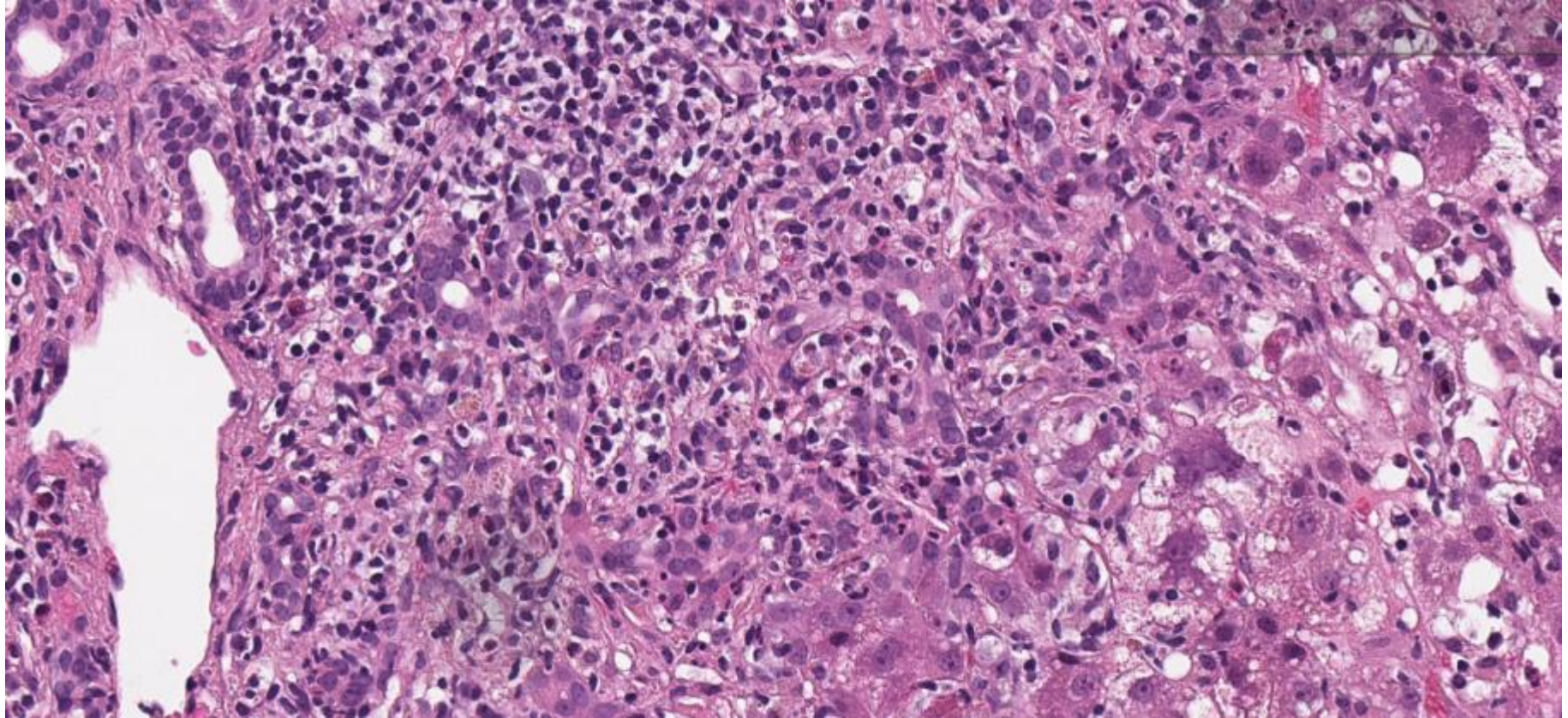
# LW – Case 8



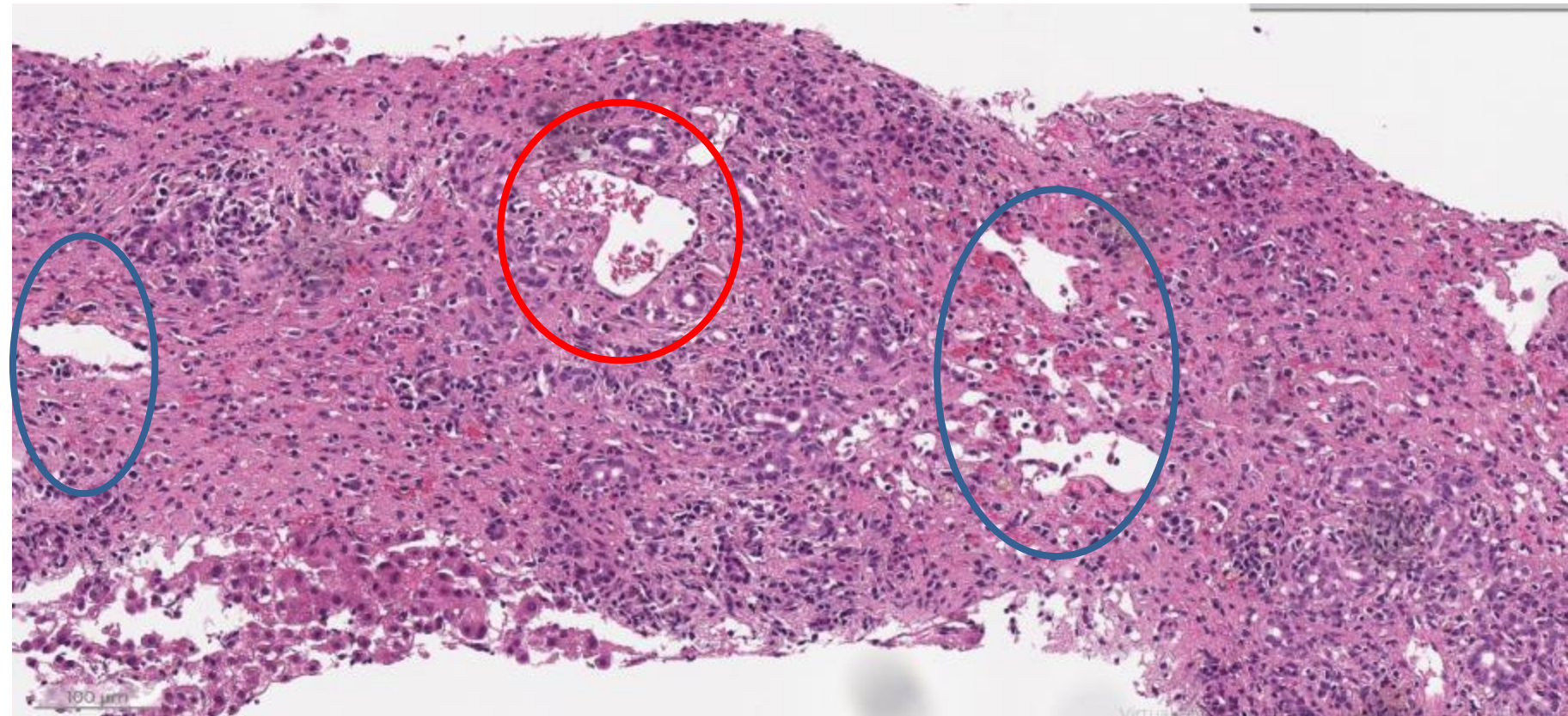
Bilirubinostasis



# LW – Case 8

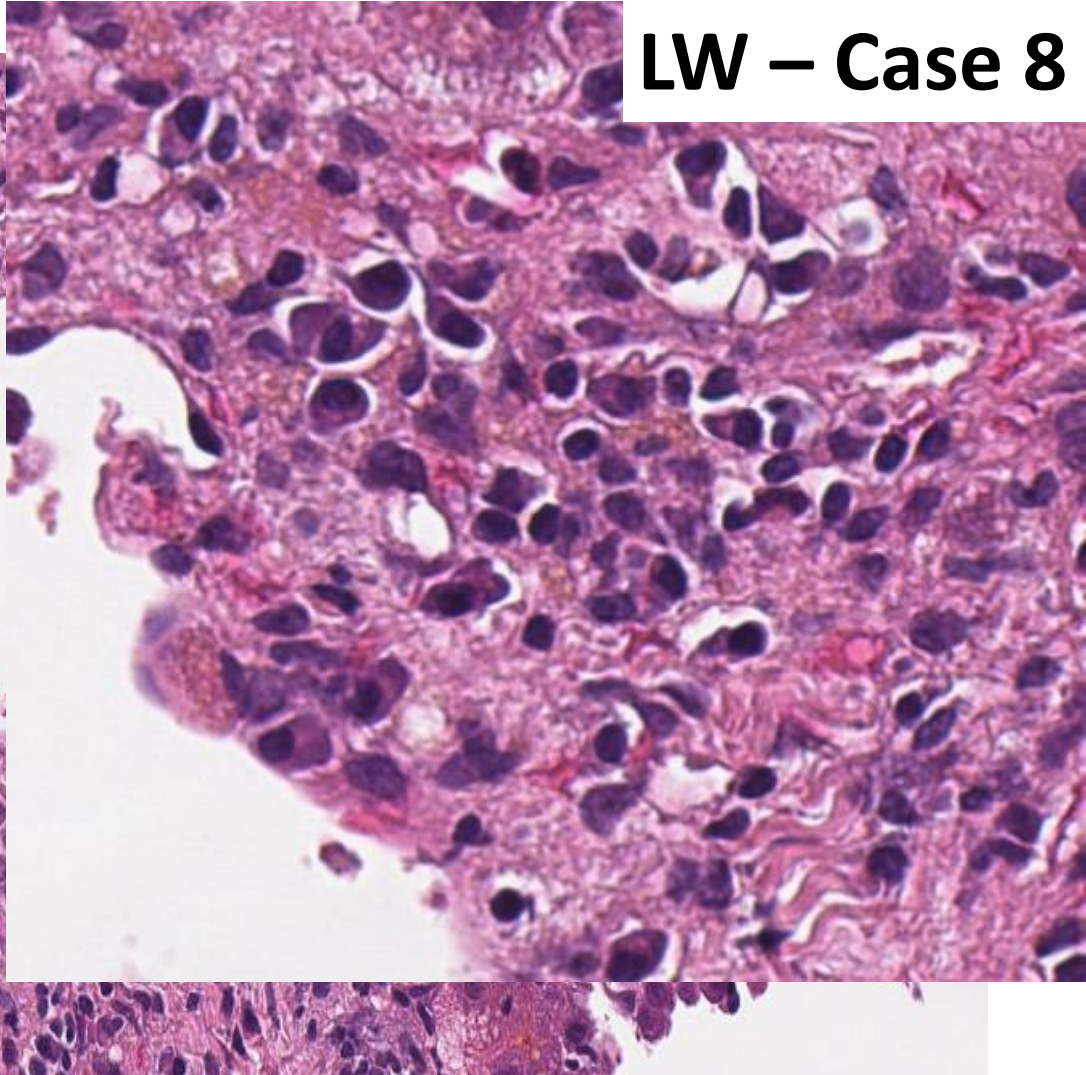
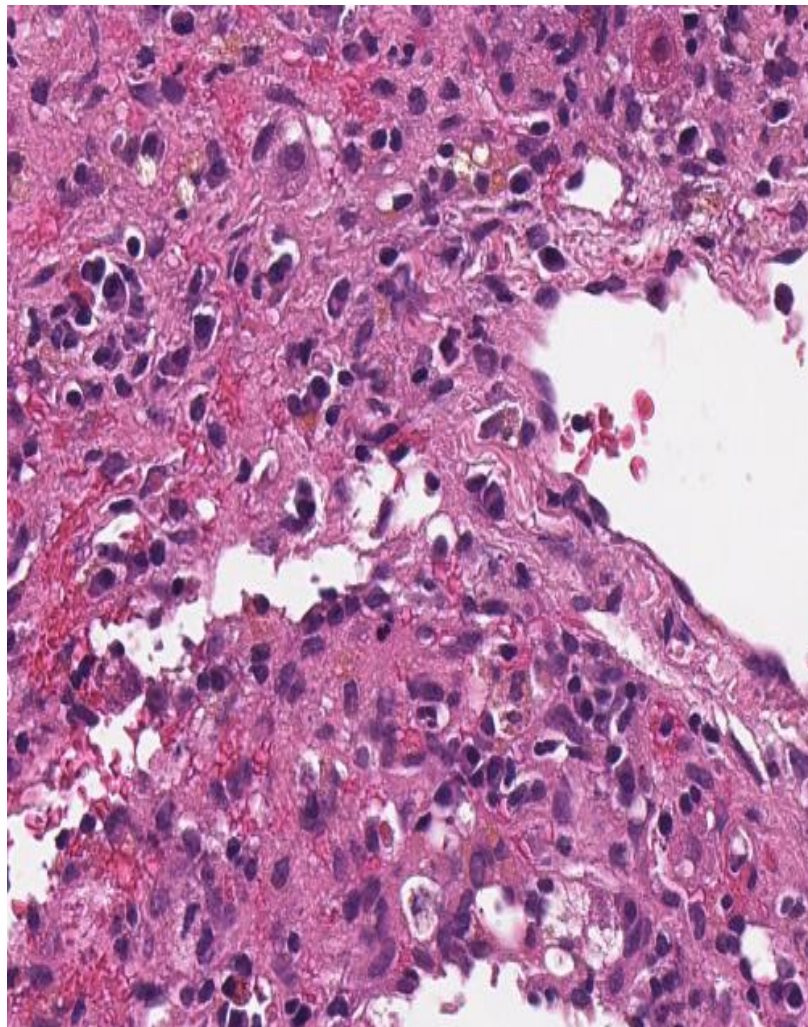


# LW – Case 8

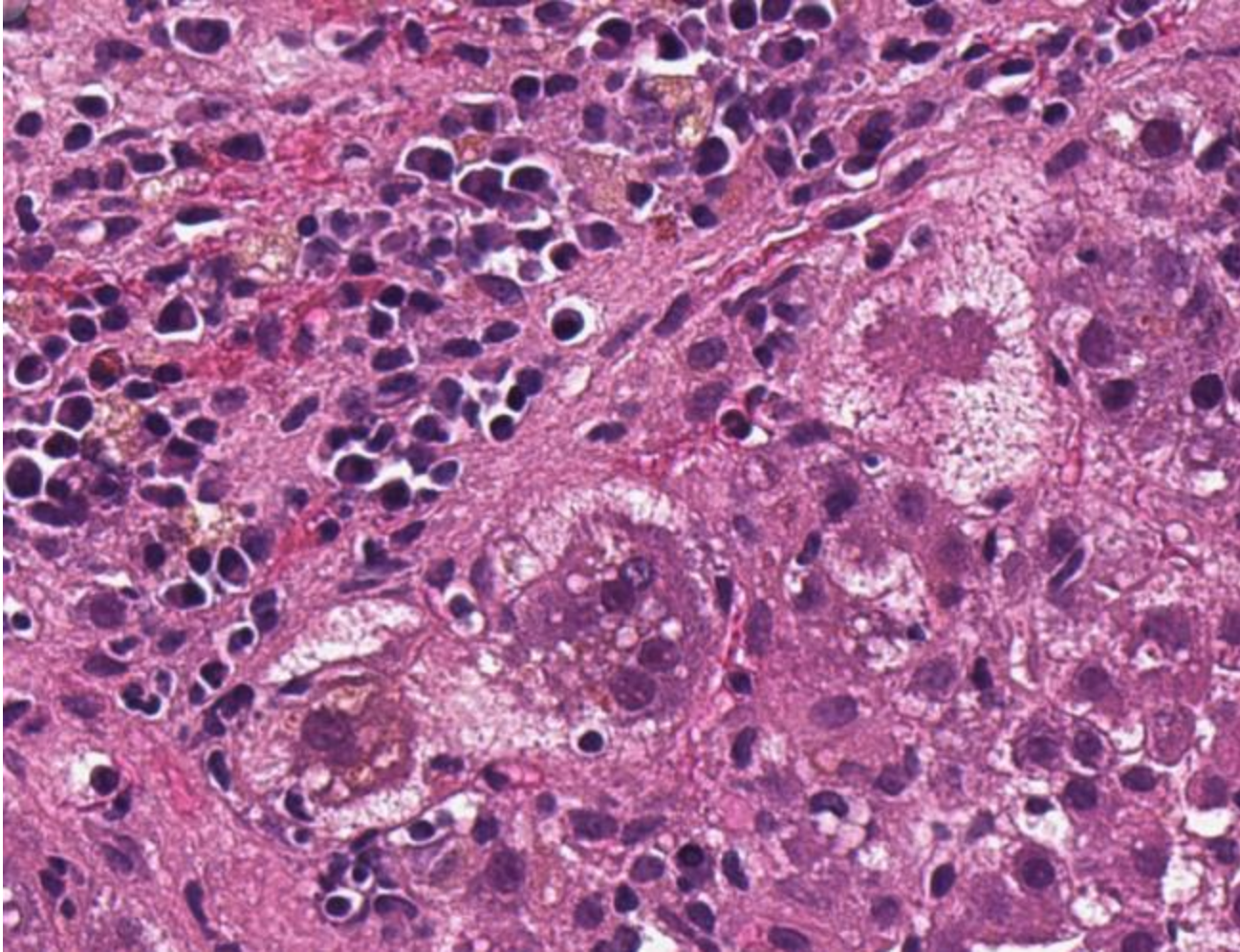


Preserved vascular relationships, with massive hepatocyte loss and collapse

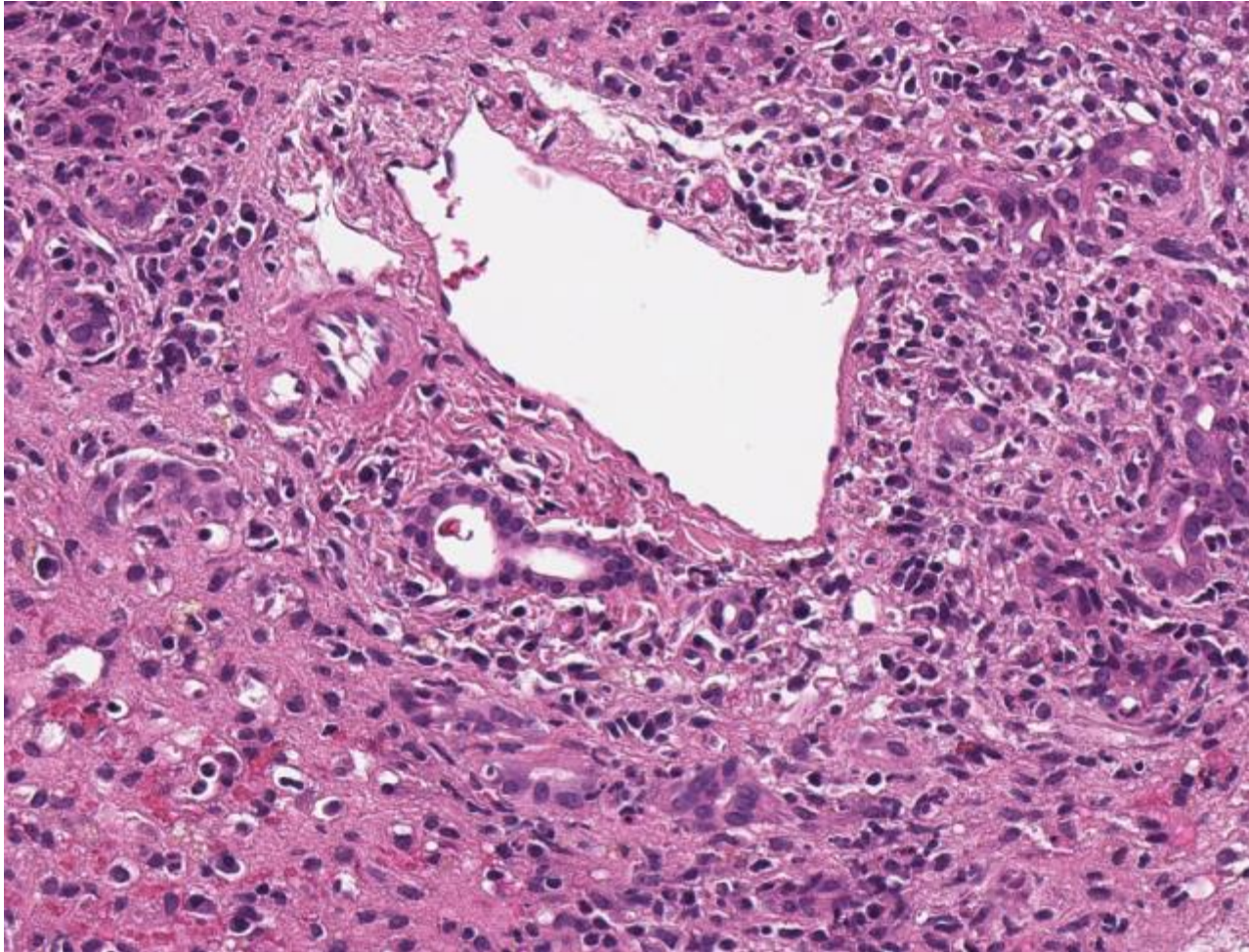
**LW – Case 8**



# LW – Case 8

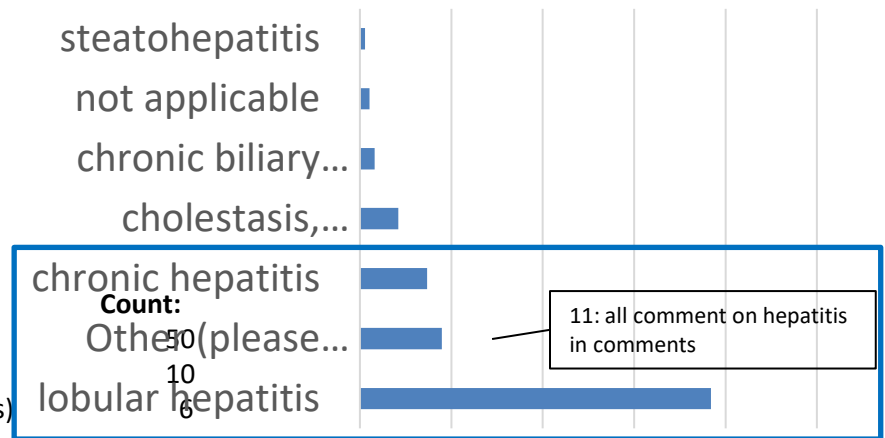


# LW – Case 8



Pattern:	Popularity:
lobular hepatitis	76.8%
Other (please specify in Comments)	17.9%
chronic hepatitis	14.7%
cholestasis, bilirubinostasis	8.4%
chronic biliary disease	3.2%
not applicable	2.1%
Steatohepatitis	1.1

LW8 pattern



Pattern 1:	Pattern 2:	Count:
lobular hepatitis		5
Other (please specify in Comments)	Other (please specify in Comments)	5
lobular hepatitis	cholestasis, bilirubinostasis	5
lobular hepatitis	chronic hepatitis	4
chronic hepatitis	lobular hepatitis	4
lobular hepatitis	not applicable	3
chronic biliary disease		2
Blank		2
cholestasis, bilirubinostasis	chronic biliary disease	1
chronic hepatitis	chronic hepatitis	1
chronic hepatitis	cholestasis, bilirubinostasis	1
Other (please specify in Comments)	Other (please specify in Comments)	1
	steatohepatitis	1
lobular hepatitis	lobular hepatitis	1
lobular hepatitis		1
cholestasis, bilirubinostasis	lobular hepatitis	1

## LW8 Staging: No special stains available, not for scoring

**Stages:**

**Popularity:**

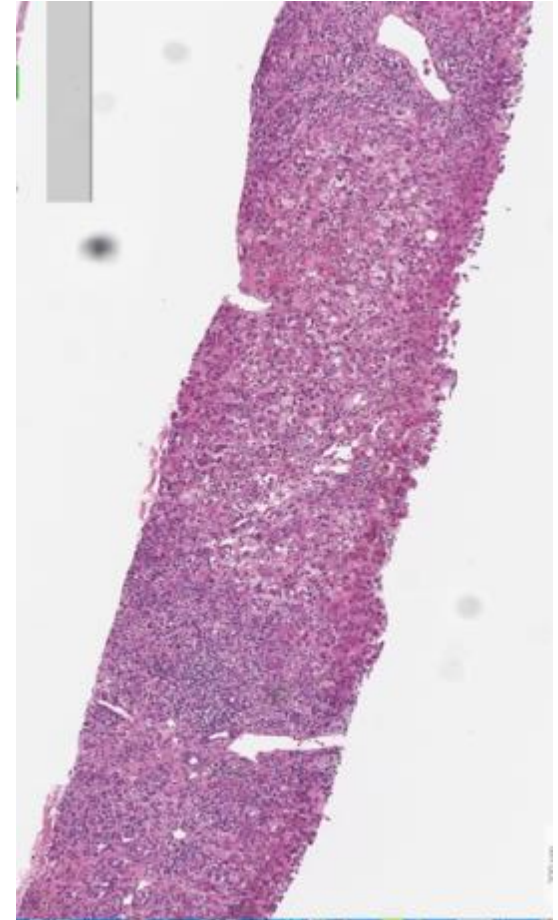
<b>not applicable / no special stains to assess architecture</b>	<b>46.3%</b>
hepatocyte loss or bridging - favour collapse not fibrosis	36.8%
advanced fibrosis with bridging and nodularity/cirrhosis	5.3%
no fibrosis/equivocal fibrosis	4.2%
Other (please specify in Comments)	3.2%
fibrosis with bridging between vascular structures	2.1%
mild/early fibrosis without bridging	1.1%



## LW8 Original report and further information (if any):

### Recent severe hepatitis.

- severe hepatitic pattern with bridging and multi-/panacinar necrosis and autoimmune features including hepatocyte rosetting, prominent plasma cells and emperipolesis.
- also significant numbers of eosinophils observed.
- changes appear relatively recent and collagen stains do not highlight evidence of mature pre-existing fibrosis.
- main differential diagnosis lies between genuine autoimmune hepatitis, potentially triggered by infliximab, or true infliximab induced liver injury of immunoallergic type, provided infection has been reliably excluded clinically. Temporal correlation with exposure to infliximab, previous liver function test abnormalities and clinical course is essential.
- Close clinicopathological correlation with medication history, clinical, imaging and serological features is recommended.



**LW8 Points of consensus:** Consider a **pattern of hepatitis** (lobular or chronic, including description in comments, **autoimmune hepatitis** (93) (in diagnosis or differential in comments). Many refer to drugs in diagnosis (62) or in comments (11) but not reach consensus (73/95).

**Suggested scoring for 10 points:** **Hepatitis, in pattern, diagnosis or comments, and mention on autoimmune hepatitis.**

**Lose 5 marks if:** **Steatohepatitis**  
**Chronic biliary disease**  
(important second diagnosis, outliers) **agreed by vote at meeting**

**Lose 10 marks if:** **Only chronic biliary disease (primary biliary cholangitis), with no comment on hepatitis pattern or autoimmune hepatitis**

**Observations/potential learning points, suitable for masterclass?**

Infliximab is a well known cause of autoimmune-induced hepatitis. Implication of this drug in case 8 is highly possible, but scoring for DILI did not reach consensus.

Liver biopsies in patients treated with biologics are becoming more and more frequent in clinical practice and pathologists should be aware of the patterns of liver injury associated with these drugs.

In practice it is VERY IMPORTANT to include that infliximab is a cause of AIH in the report.

# LW – Case 9

**Case number:** 9

**Clinical Information:**

Previous lung cancer 4.5cm lesion in left lobe of liver. MRI: ?HCC (adenoma less likely). (Metastases also less likely). To characterise. Bili 10, ALP 66, ALT 8, AFP 3. 4 years ago Left upper lobectomy and regional lymph nodes (L5, L6, L9, L11, and station 7). Moderately to poorly differentiated, (15mm) papillary predominant, invasive adenocarcinoma of left upper lobe with background multiple foci of atypical adenomatous hyperplasia and incidental (4mm at least) focus of adenocarcinoma in situ: (TNM 7) pT2a, N0, Mx - PL1. 2012 Ampullectomy: Tubulovillous adenoma with low grade and very focal high grade dysplasia. Previous targeted liver biopsies at at different trust negative.

**Specimen:** **Lesional liver biopsy**

**Age:** 79

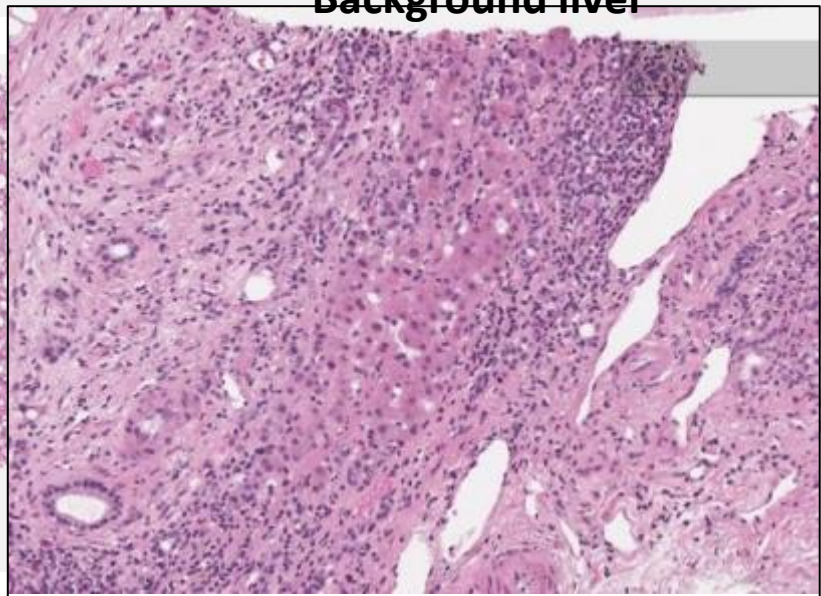
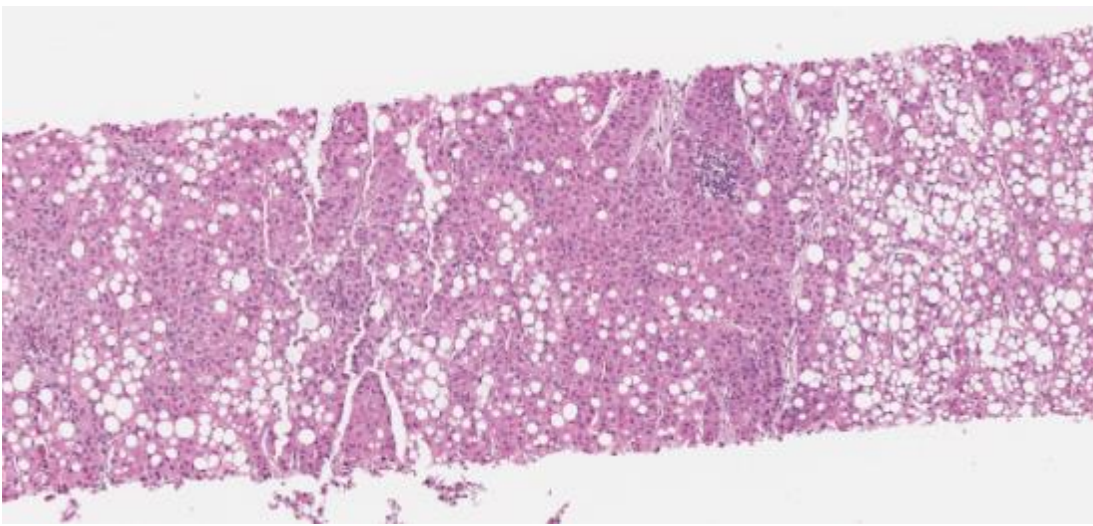
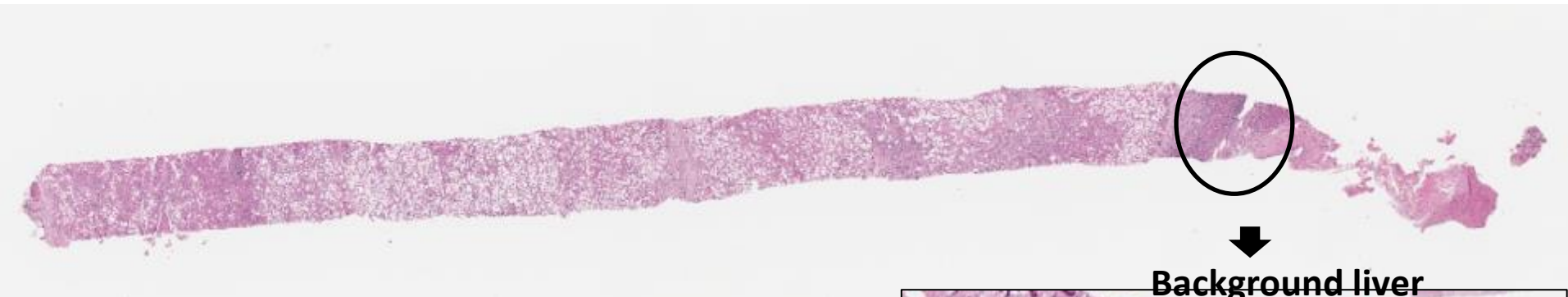
**Sex:** Female

**Macroscopic description:** A cream core 16mm embedded intact.

**Additional Stains:** None

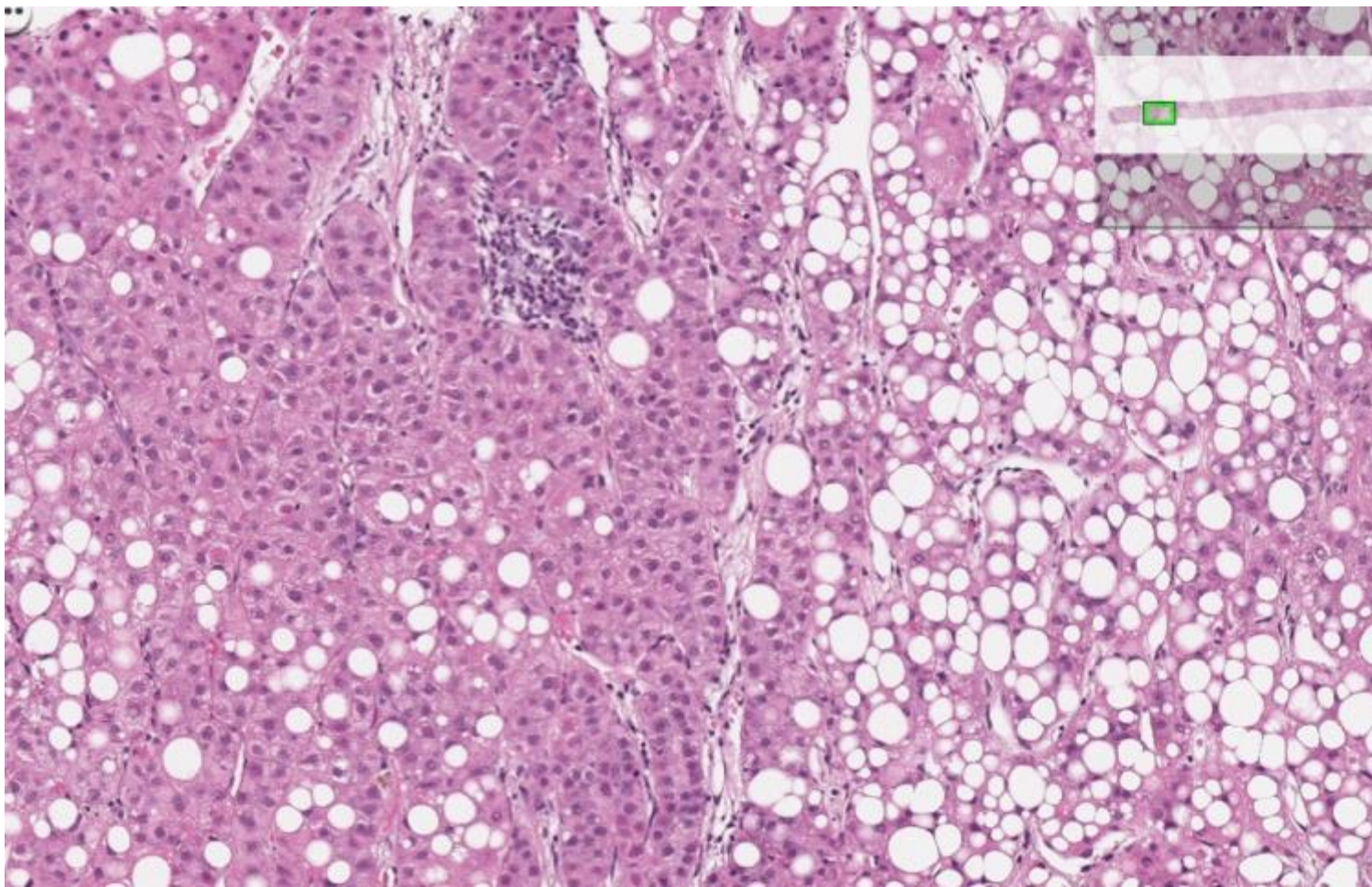
**View Slides:** [H&E](#)

# LW – Case 9

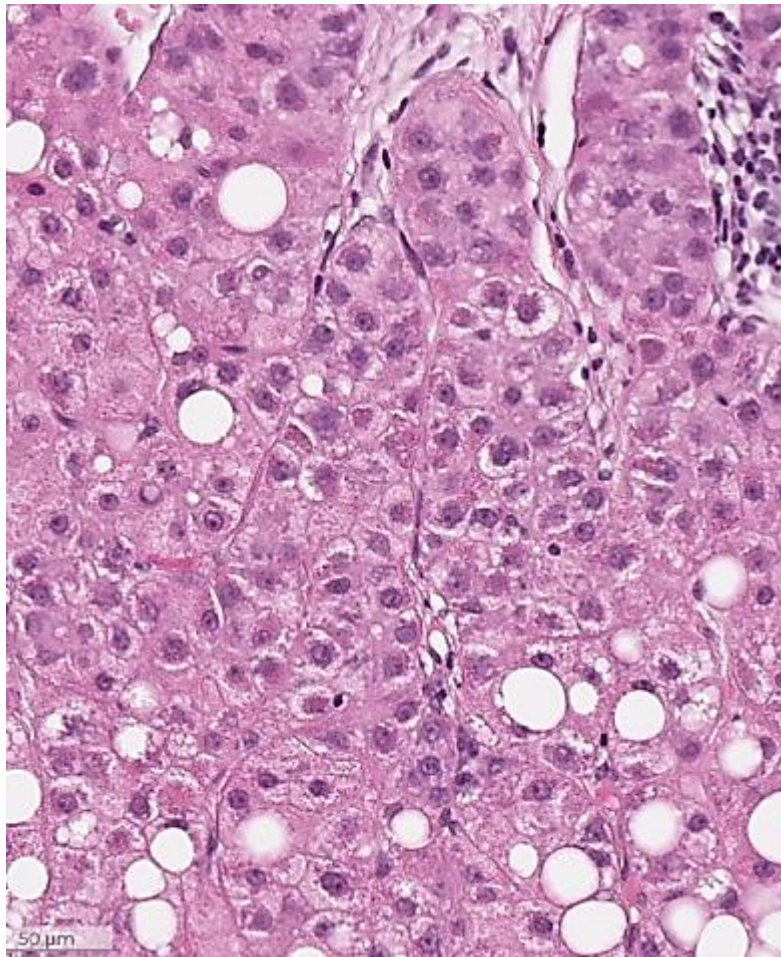


Background liver

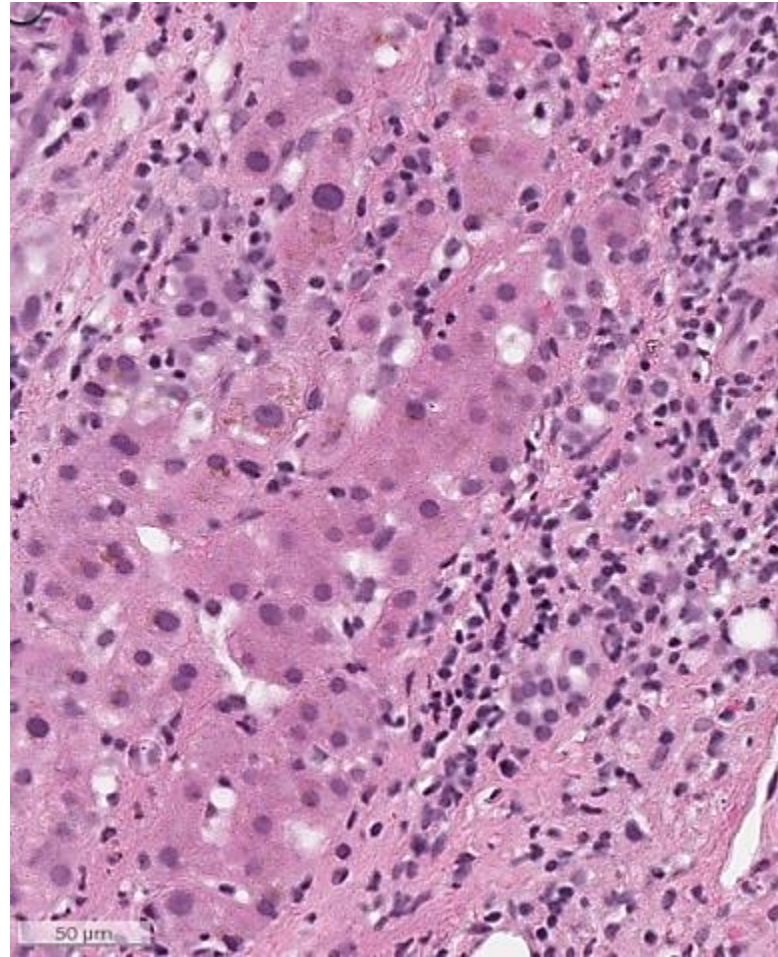
# LW – Case 9



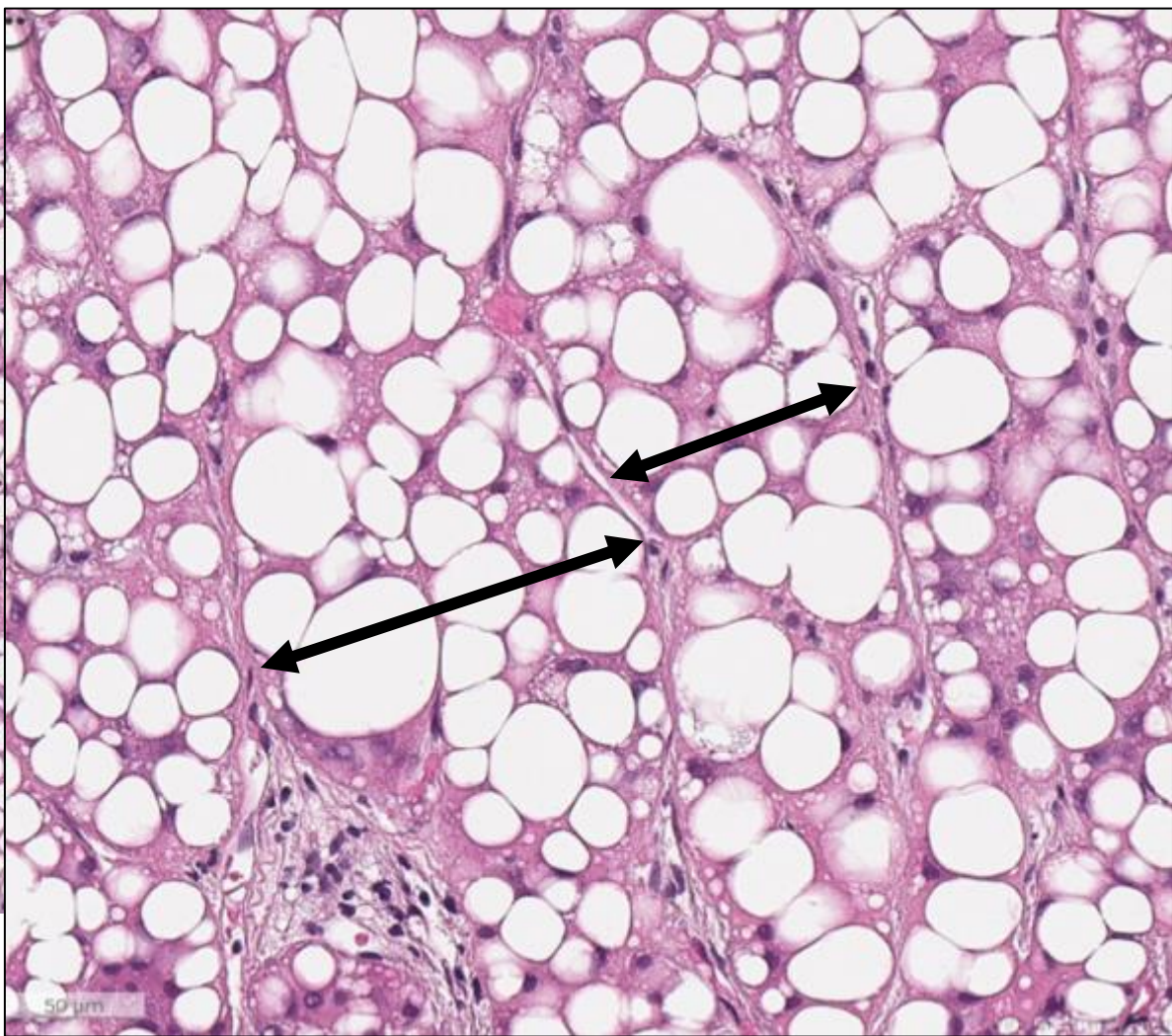
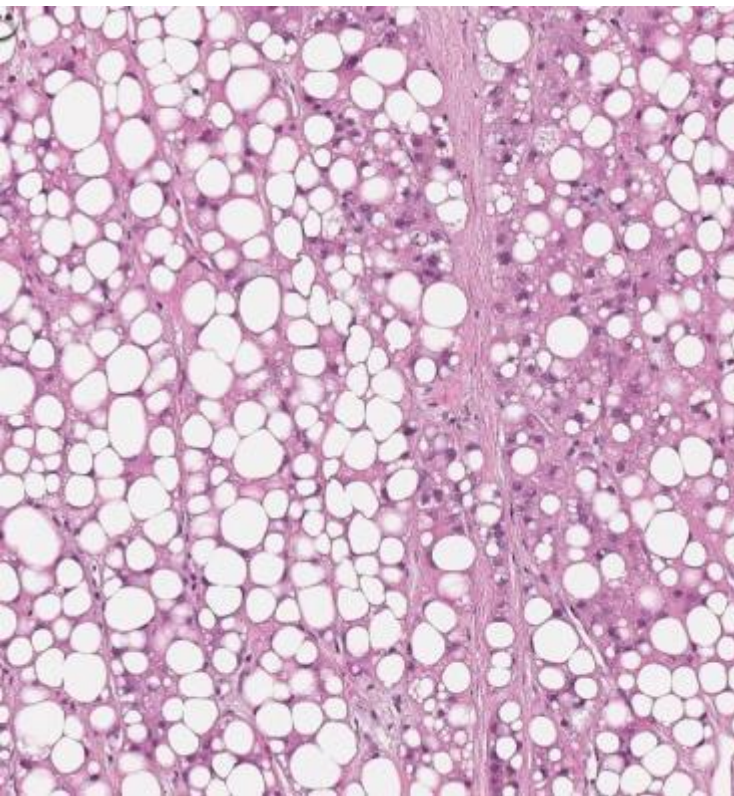
**Lesional tissue**



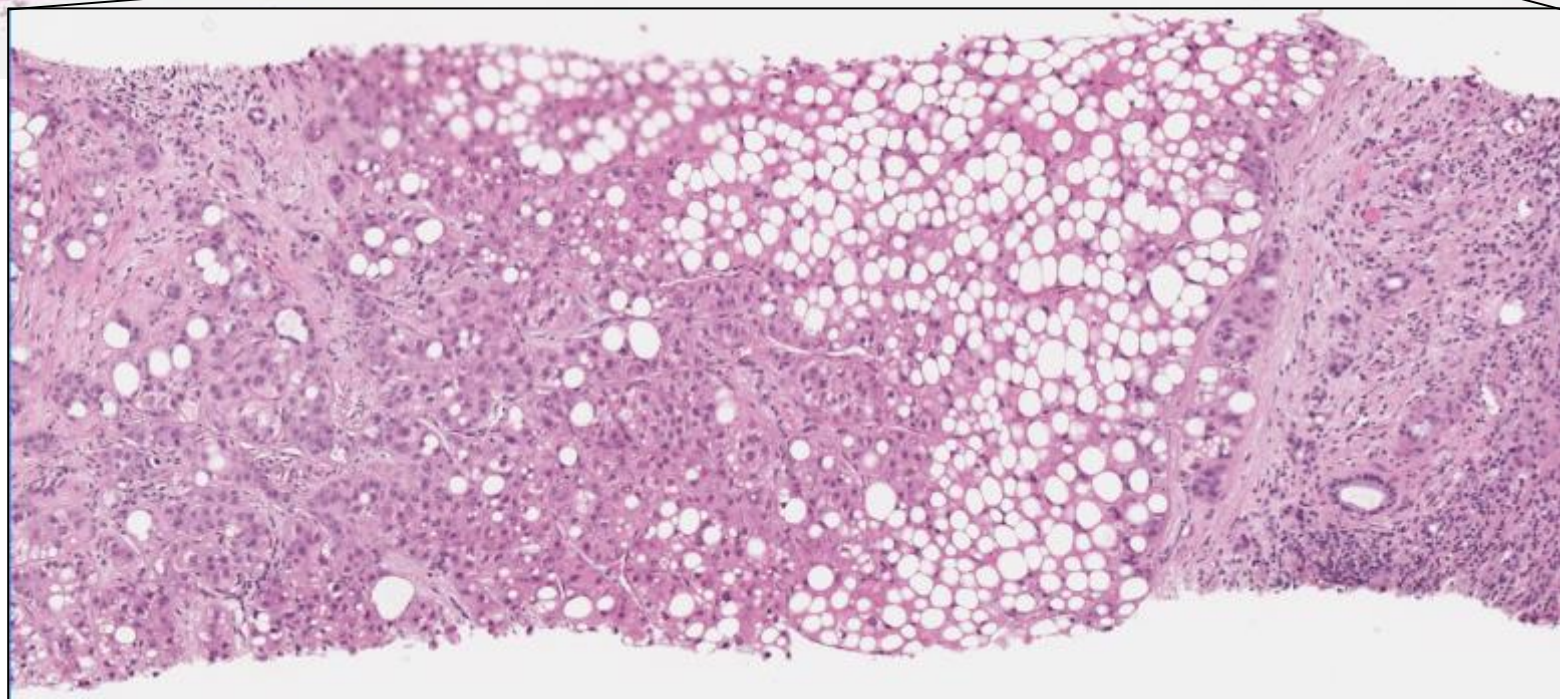
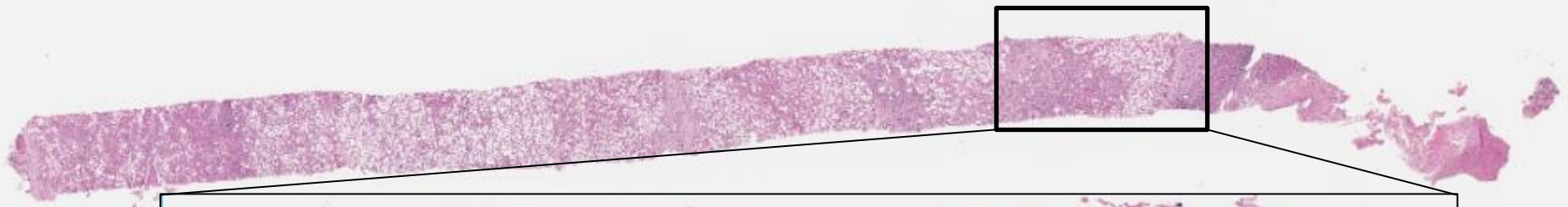
**Background liver**



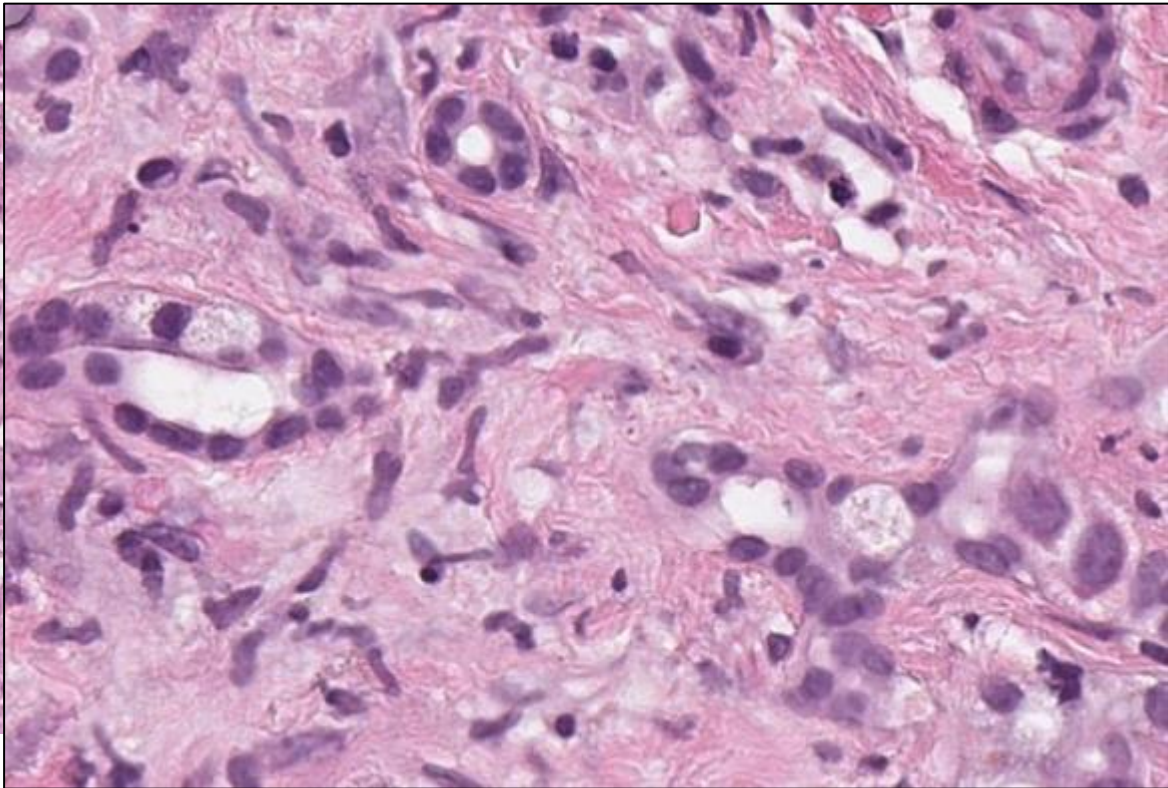
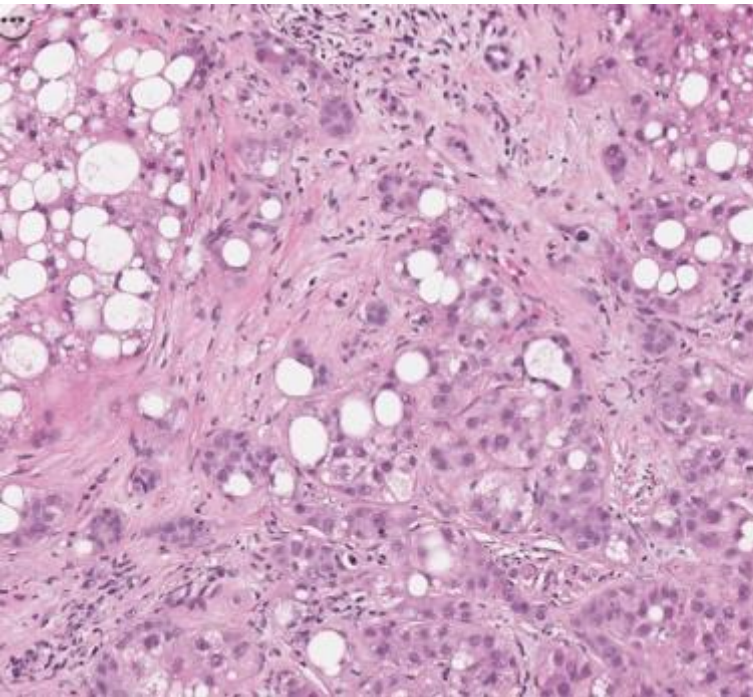
# LW – Case 9



# LW – Case 9



# LW – Case 9

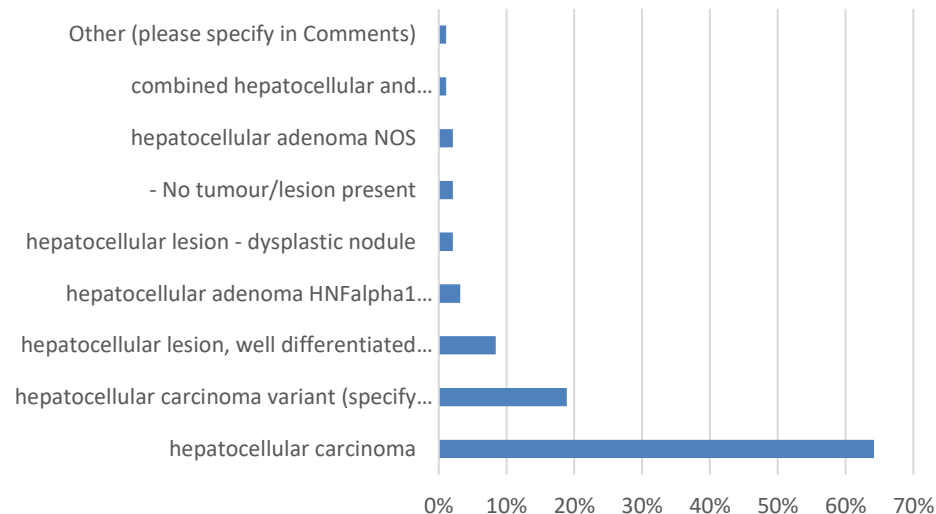


# LW – Case 9

Tumour:	Popularity:
hepatocellular carcinoma	64.2%
hepatocellular carcinoma variant (specify in Comments)	18.9%
hepatocellular lesion, well differentiated NOS (please add comment)	8.4%
hepatocellular adenoma HNFalpha1 inactivated	3.2%
hepatocellular lesion - dysplastic nodule	2.1%
- No tumour/lesion present	2.1%
hepatocellular adenoma NOS	2.1%
combined hepatocellular and cholangiocarcinoma	1.1%
Other (please specify in Comments)	1.1%

83.1%  
(78)

LW9 tumour



Original reporting pathologist diagnosis: **Hepatocellular Carcinoma**

## LW9 No consensus on background liver

<b>Pattern:</b>	<b>Popularity</b>	<b>Stages:</b>	<b>Popularity:</b>
not applicable	54.7%	not applicable / no special stains to assess architecture	57.9%
steatohepatitis	13.7%	advanced fibrosis with bridging and nodularity/cirrhosis	15.8%
steatosis	12.6%	mild/early fibrosis without bridging	3.2%
Other (please specify in Comments)	7.4%	fibrosis with bridging between vascular structures	2.1%
chronic hepatitis	1.1%	Other (please specify in Comments)	1.1%

<b>Diagnostic categories:</b>	<b>Popularity:</b>
- not applicable (insufficient non-lesional tissue)	30.5%
fatty liver disease - either alcohol or non-alcohol	12.6%
- no evidence of diffuse/background liver disease	1.1%
- histologically indeterminate for cause	1.1%
fatty liver disease - non-alcohol related fatty liver disease	1.1%

## LW – Case 9

**Points of consensus:** Hepatocellular carcinoma, included in diagnosis, or comment on HCC favoured with stains that would confirm it.

**Suggested scoring for 10 points:** Hepatocellular carcinoma, definite (78) in diagnosis, or HCC suspected / favoured with confirmatory stains in comments (5).

**Lose 5 marks if:** Hepatocellular lesion (adenoma/dysplastic nodule) with HCC in differential but not the most likely diagnosis.  
Combined HCC/CCA. – this was confirmed by vote at meeting.

**Lose 10 marks if:** No mention of HCC,  
No lesion,  
Blank answer.

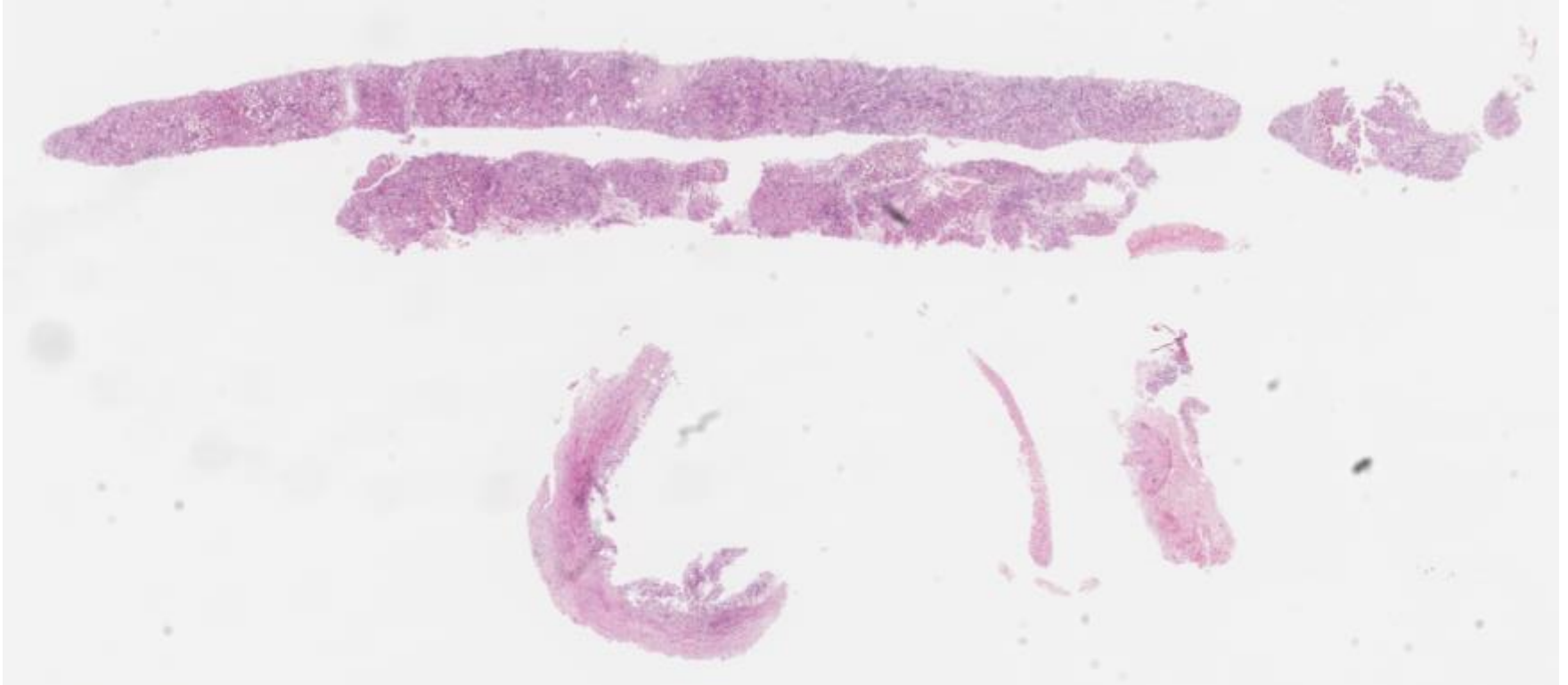
**Observations/potential learning points, suitable for masterclass?**

**Case Number: LW10**

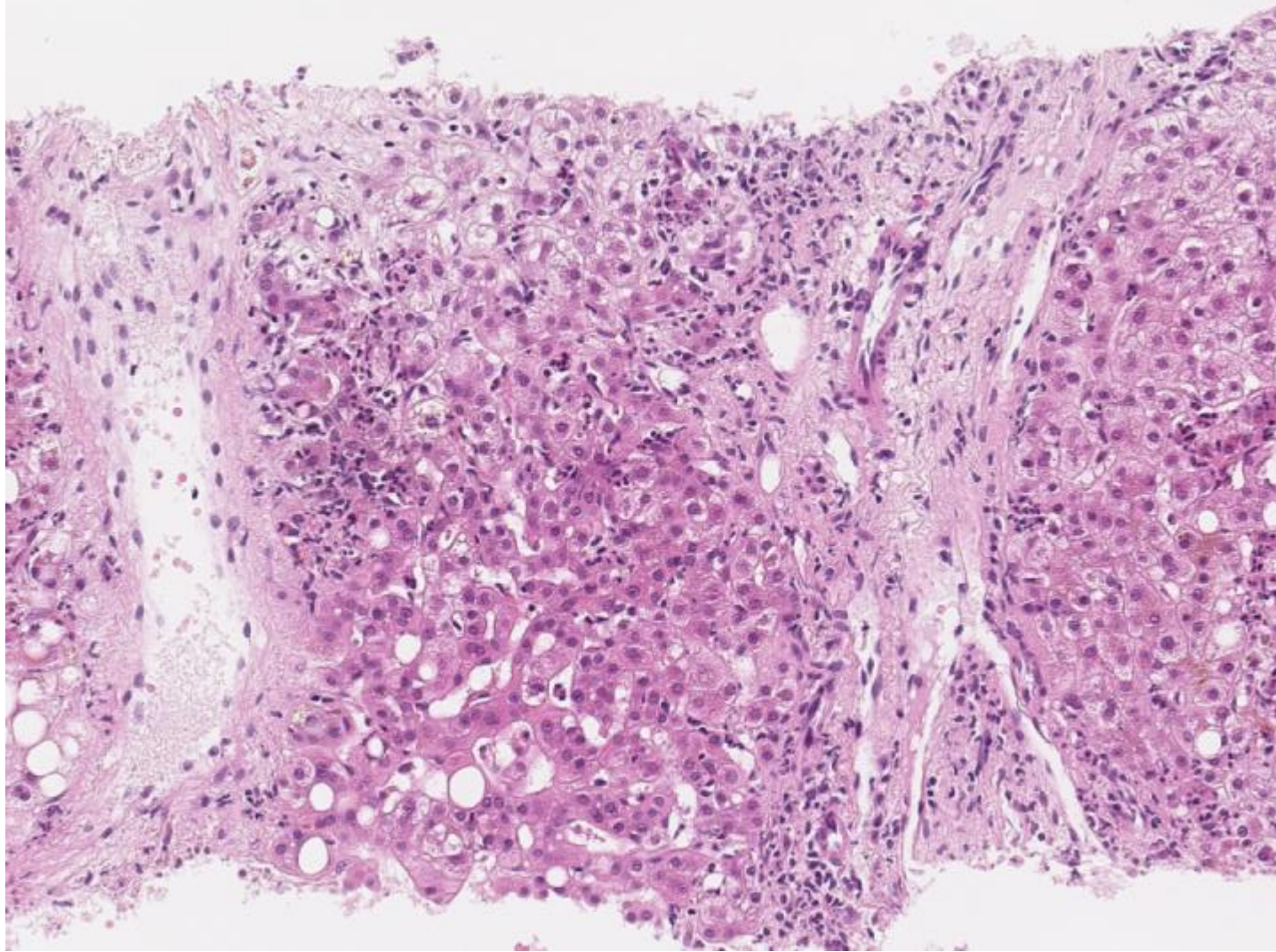
**Clinical:** Male 38. Alcoholic hepatitis on a background of probable cirrhosis.  
We are considering starting steroids.

**Specimen:** Liver biopsy     **Macroscopic:** 2 cores of tissue, 1.5cm + frags.

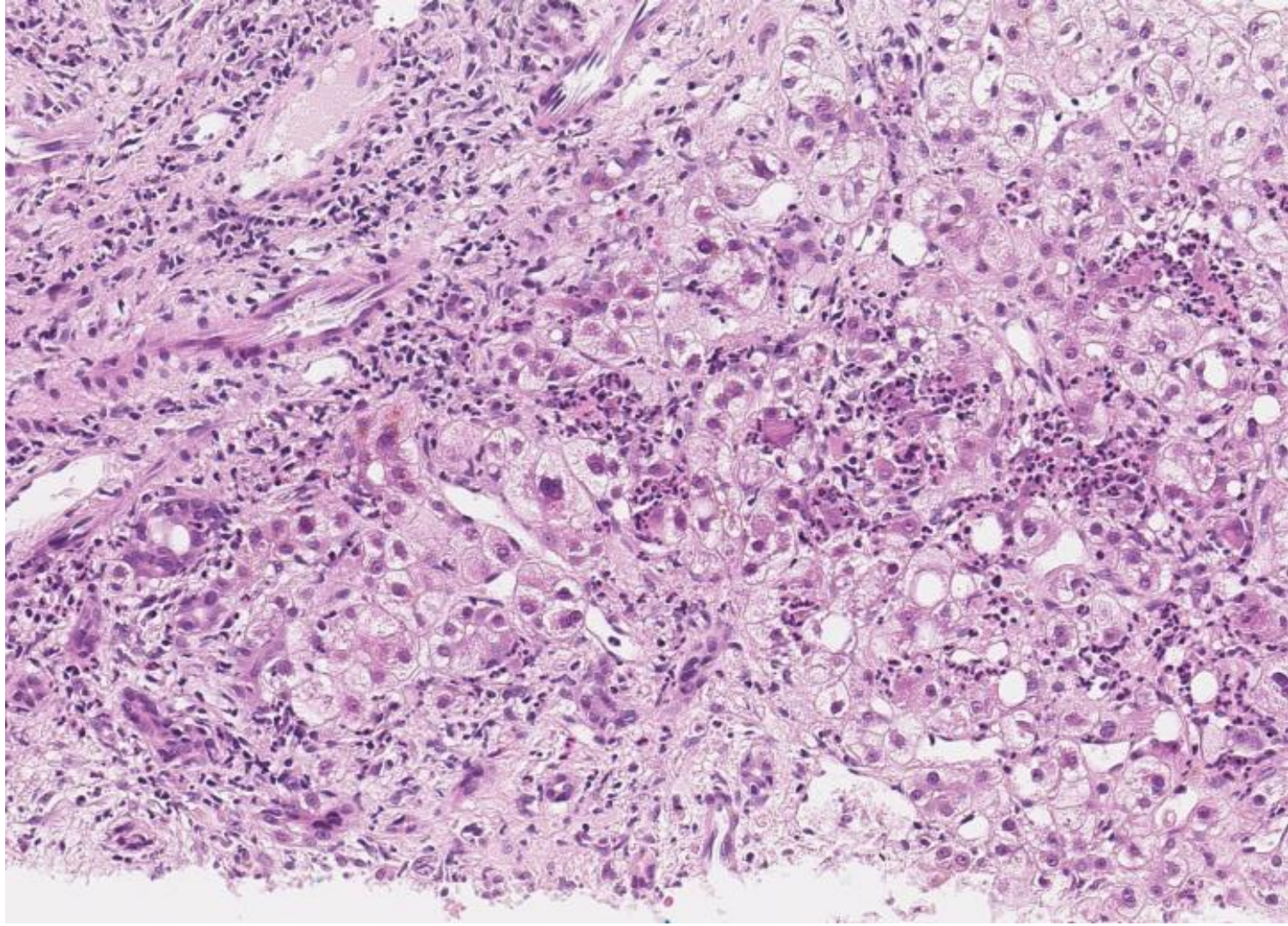
**Immunohistochemistry:** EPSR, retic, PASD, Perls, Orcein



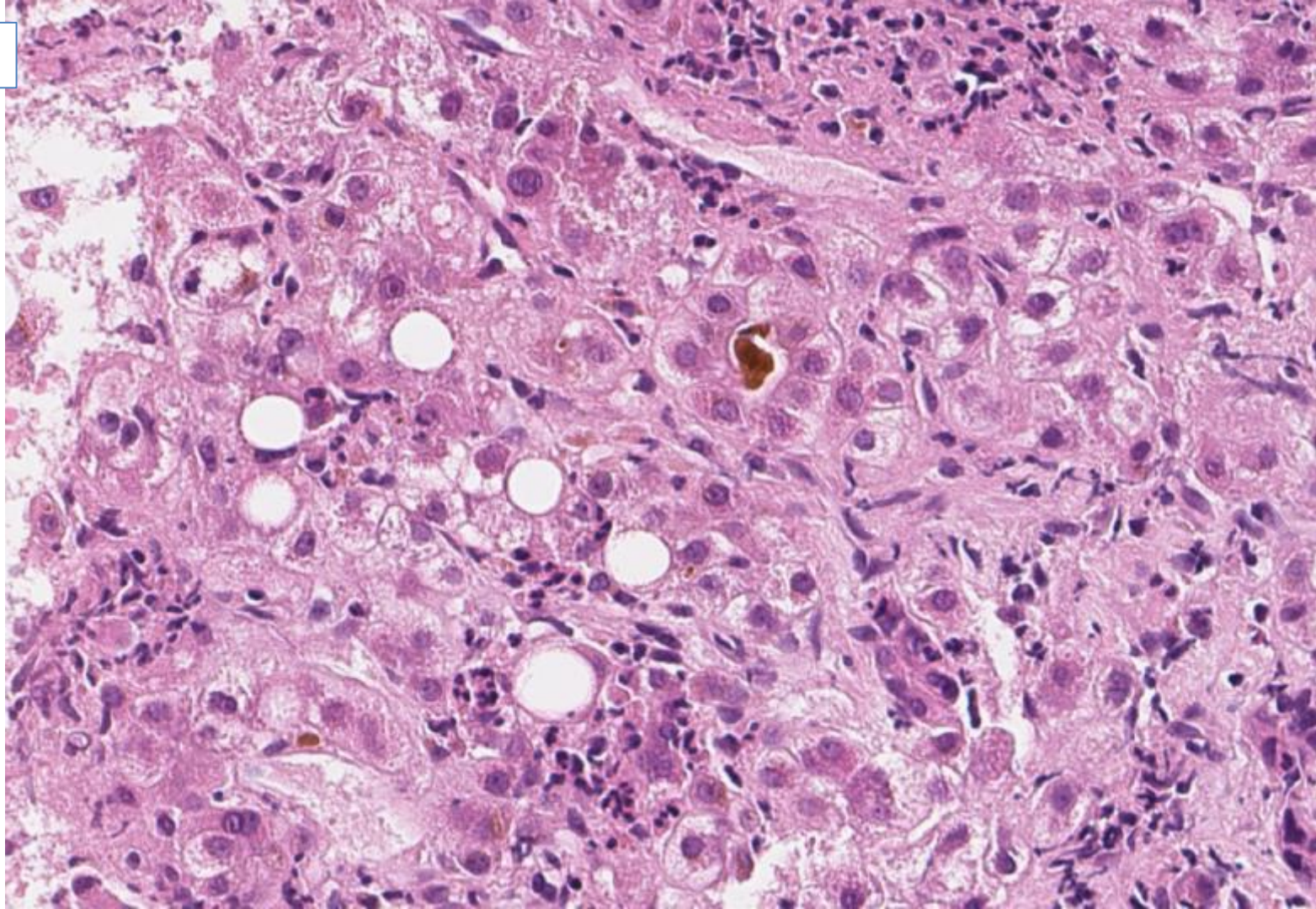
LW10



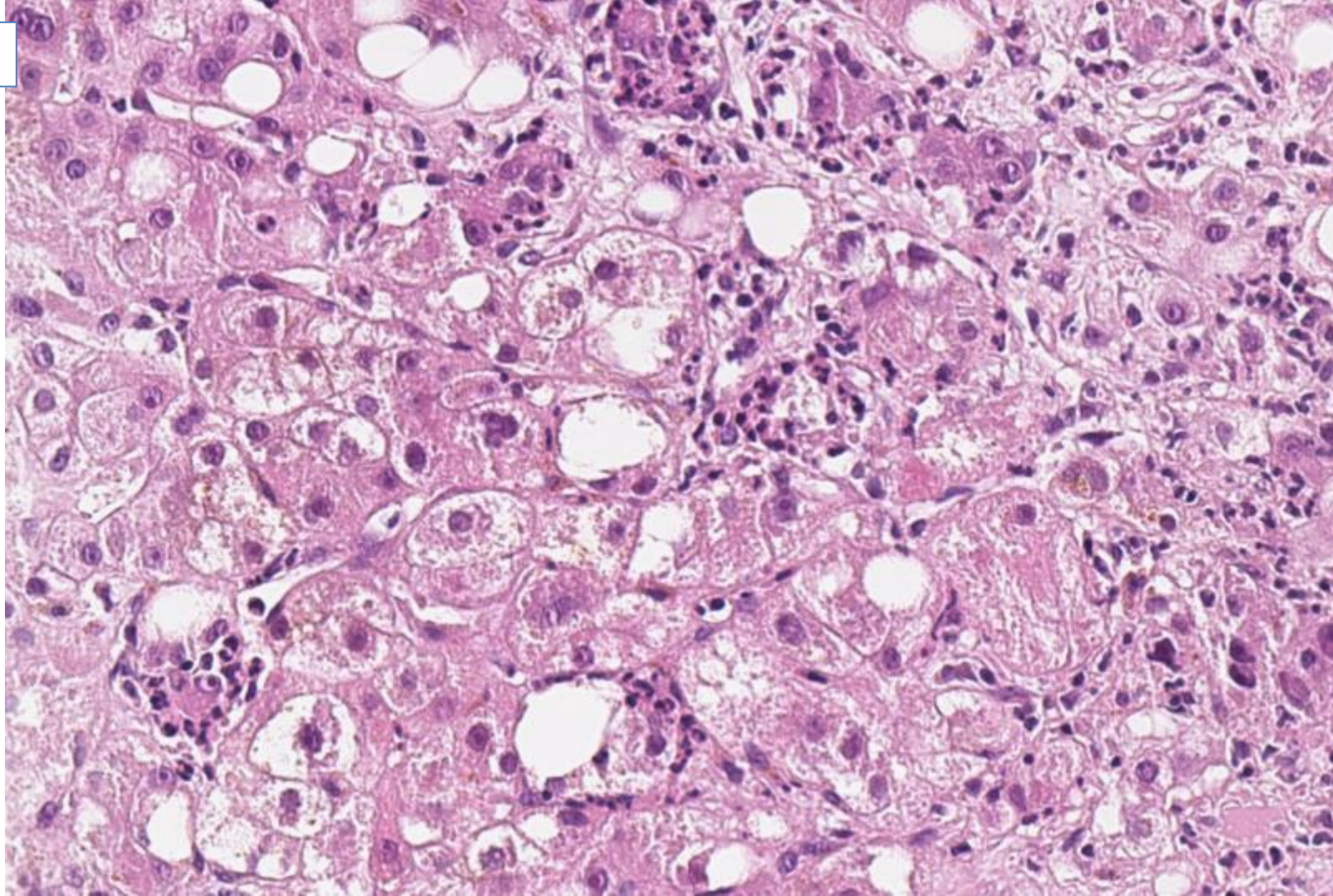
LW10



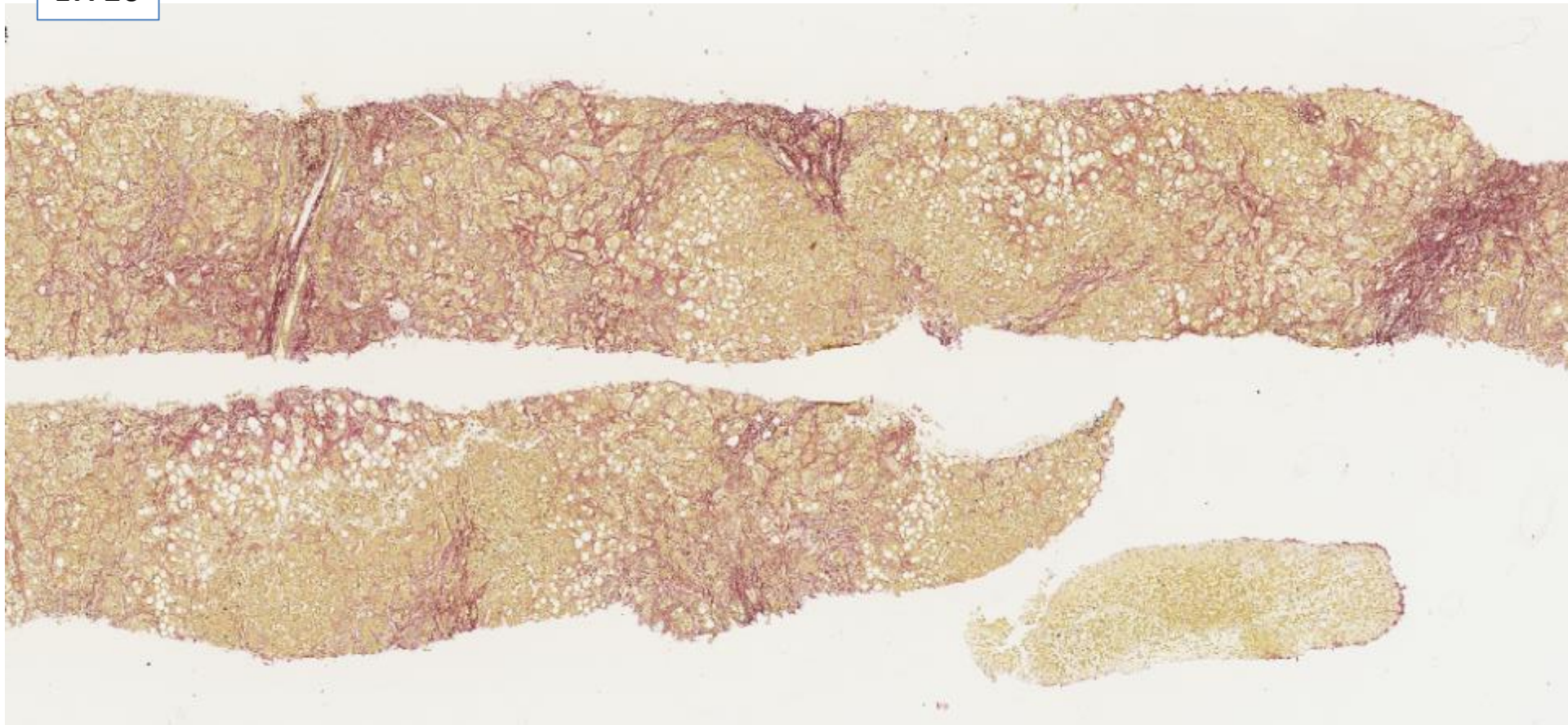
LW10



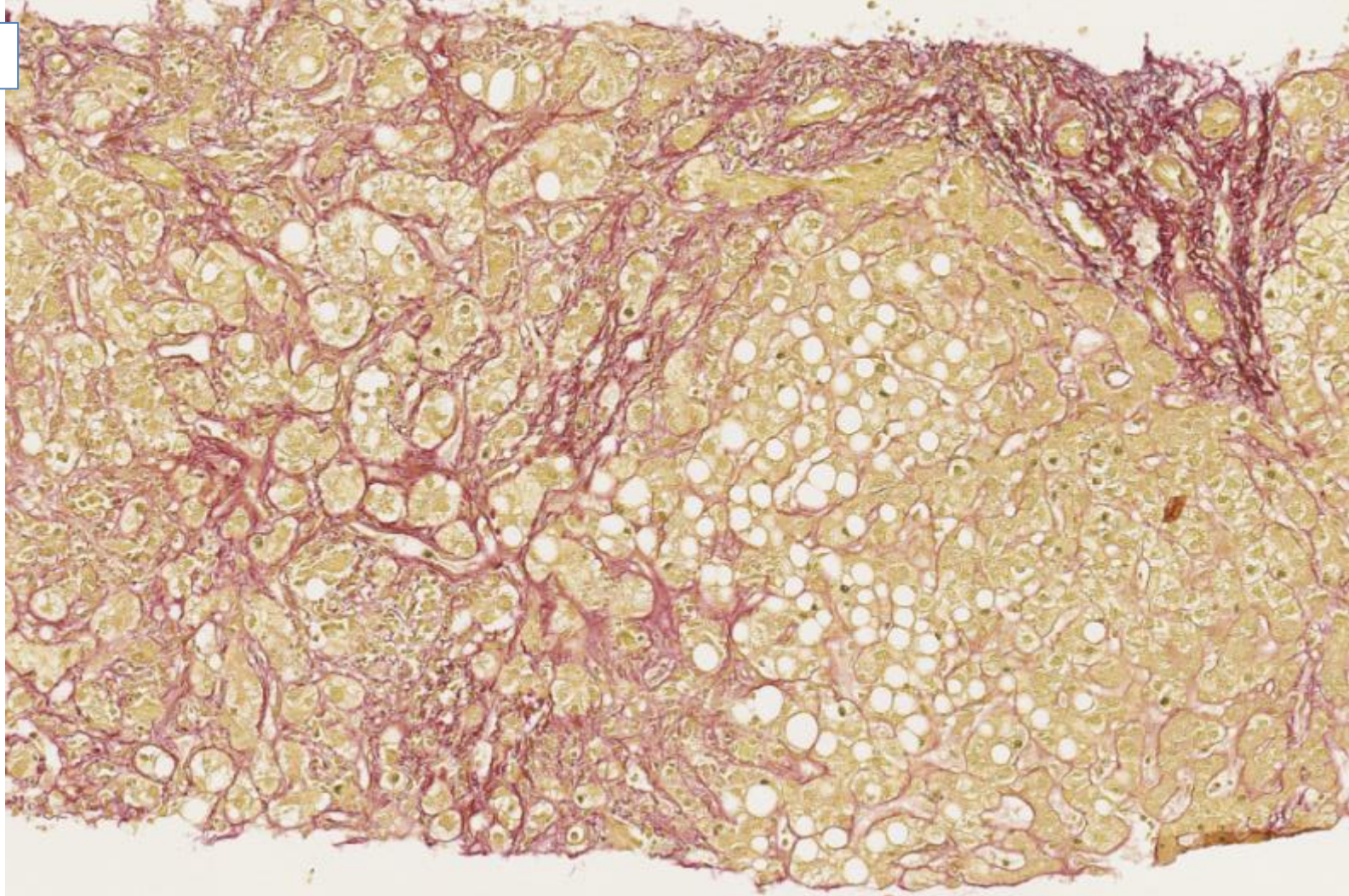
LW10



LW10

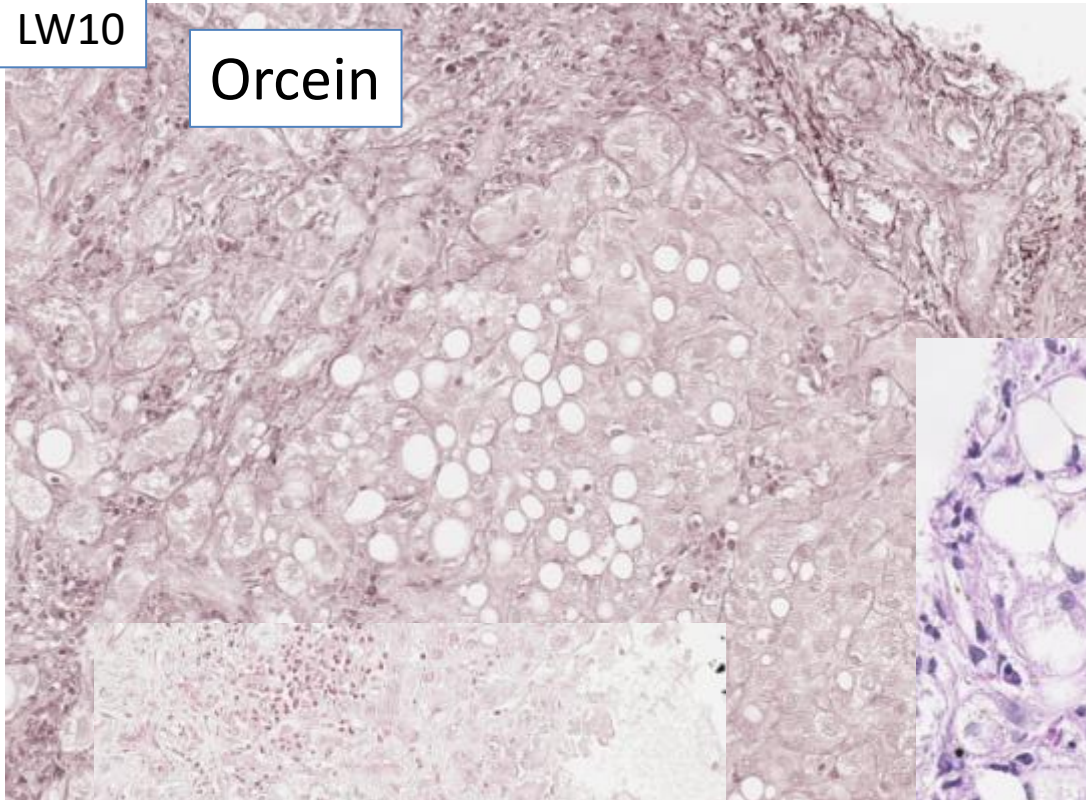


LW10



LW10

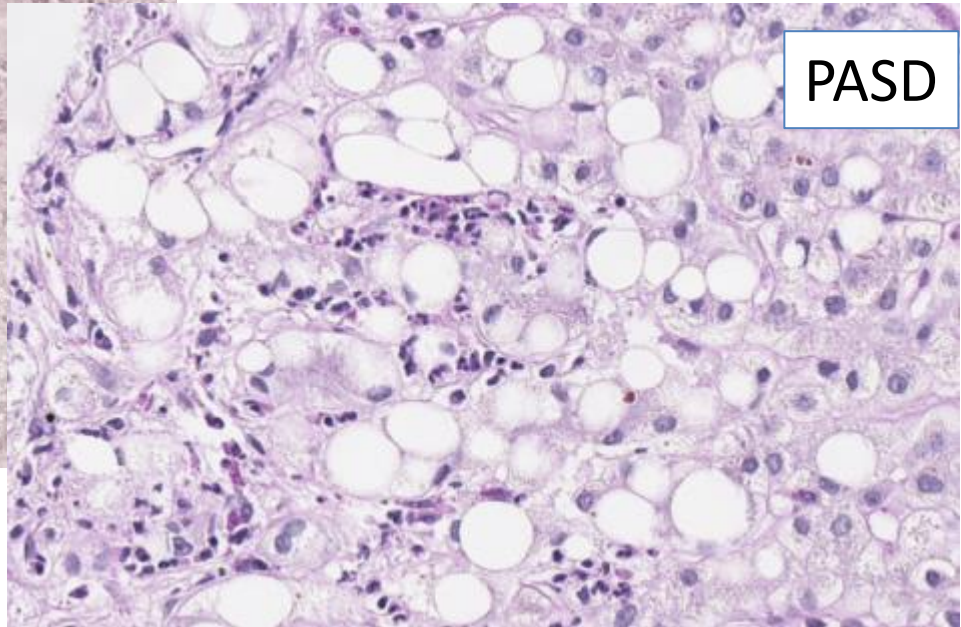
Orcein



Perls



PASD



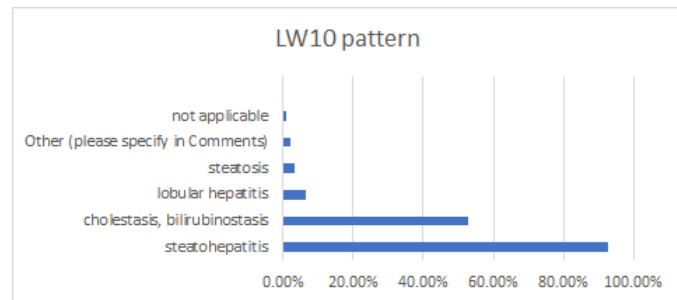
## LW10

<b>Tumour:</b>	<b>Popularity:</b>
- No tumour/lesion present	97.9%
Other (please specify in Comments)	2.1%

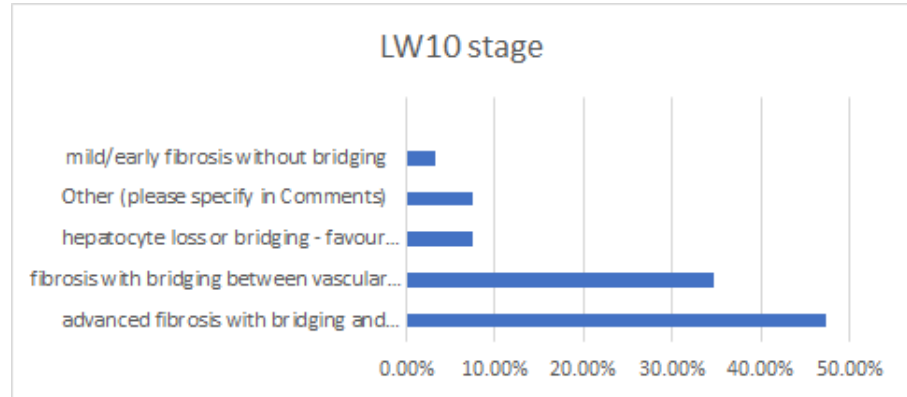
<b>Tumour 1:</b>	<b>Tumour 2:</b>	<b>Count:</b>
- No tumour/lesion present		77
- No tumour/lesion present	- No tumour/lesion present	15
- No tumour/lesion present	Other (please specify in Comments)	1
Other (please specify in Comments)		1
		1

# LW10

Pattern:	Popularity:
steatohepatitis	92.6%
cholestasis, bilirubinostasis	52.6%
lobular hepatitis	6.3%
steatosis	3.2%
Other (please specify in Comments)	2.1%
not applicable	1.1%



Pattern 1:	Pattern 2:	Count:
steatohepatitis	cholestasis, bilirubinostasis	46
steatohepatitis		34
Other (please specify in Comments)		2
lobular hepatitis	steatohepatitis	2
steatohepatitis	steatohepatitis	2
steatosis	steatohepatitis	1
lobular hepatitis	steatosis	1
		1
lobular hepatitis	cholestasis, bilirubinostasis	1
steatosis	cholestasis, bilirubinostasis	1
cholestasis, bilirubinostasis	lobular hepatitis	1
steatohepatitis	lobular hepatitis	1
steatohepatitis	not applicable	1
cholestasis, bilirubinostasis	steatohepatitis	1



Stages:	Popularity:
advanced fibrosis with bridging and nodularity/cirrhosis	47.4%
fibrosis with bridging between vascular structures	34.7%
hepatocyte loss or bridging - favour collapse not fibrosis	7.4%
Other (please specify in Comments)	7.4%
mild/early fibrosis without bridging	3.2%

Advanced fibrosis with bridging + fibrosis with bridging = 82.1%

LW10

Diagnostic categories:

Popularity

fatty liver disease - alcohol related liver disease

88.4%

Other (please enter alternative diagnosis in comments box)

6.3%

drug induced liver injury (please specify in comments box)

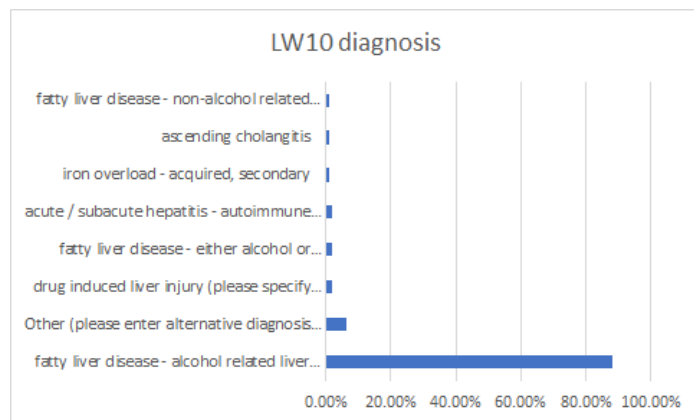
2.1%

fatty liver disease - either alcohol or non-alcohol

2.1%

acute / subacute hepatitis - autoimmune / drug / viral

2.1%



Diagnosis Combination:

Count:

iron fatty liver disease - alcohol related liver disease

76

asce [No selections made]

4

fatty fatty liver disease - alcohol related liver disease, Other (please enter alternative diagnosis in comments box)

4

fatty liver disease - either alcohol or non-alcohol

2

Other (please enter alternative diagnosis in comments box)

2

acute / subacute hepatitis - autoimmune / drug / viral

1

acute / subacute hepatitis - autoimmune / drug / viral, fatty liver disease - alcohol related liver disease

1

ascending cholangitis, fatty liver disease - alcohol related liver disease

1

drug induced liver injury (please specify in comments box)

1

drug induced liver injury (please specify in comments box), fatty liver disease - alcohol related liver disease

1

**Points of consensus;** steatohepatitis and alcohol related FLD and fibrosis with bridging or advanced fibrosis or 'other' for stage with description of pericellular fibrosis.

**Suggested scoring: for 10 points** - steatohepatitis, alcohol related and more than mild fibrosis.

**Lose 5 marks** for mild/early fibrosis, or bridging/collapse

**Lose 5 marks** for steatohepatitis with no mention of alcohol

**Lose 5 marks** – some other responses may score 5 ?

ascending cholangitis as well as ARLD steatohepatitis - **lose 5 no consensus for a second pattern/diagnosis**

cholestasis, acute hepatitis, consistent with alcohol - **lose 5 for no steatohepatitis**

lobular hepatitis and steatosis - **lose 5 for no steatohepatitis**

**Lose 10 marks (score 0)** for lobular hepatitis, cholestasis, DILI, alcohol not mentioned = neither alcohol nor steatohepatitis mentioned

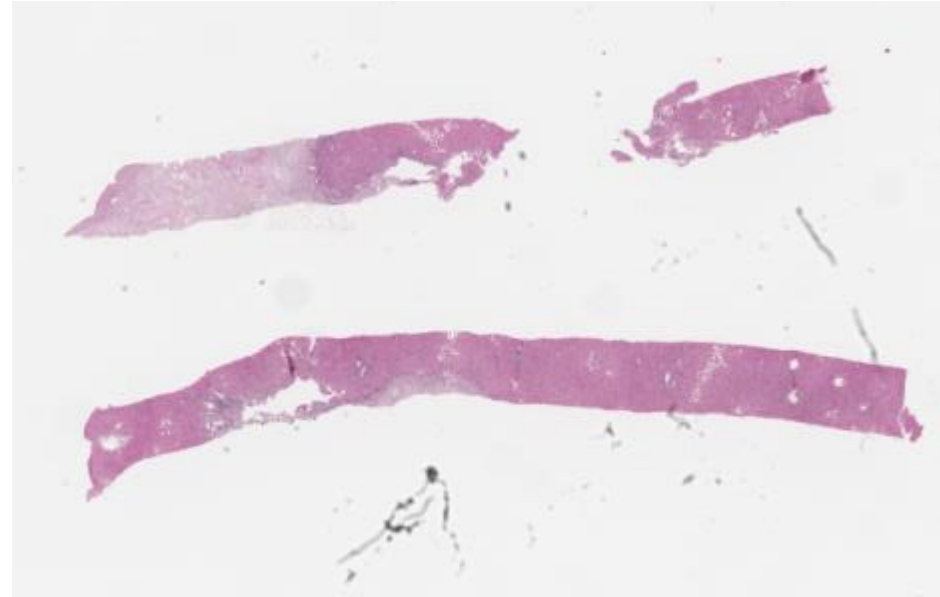
**Original report and further information (if any):** The features are those of a floridly active alcoholic steatohepatitis with cholestasis, raising the suggestion of secondary sepsis. There is clearly abundant fibrosis, but mainly in a pattern associated with acute steatohepatitis. There is a suggestion of nodule formation towards one edge, although without features of well-established cirrhosis within limits of the sample.

**Case Number: LW11**

**Clinical:** Female 69.

**Liver lesion. ?Aetiology. Hyper vascular, indeterminate on CT/MR.** Difficult biopsy (basically invisible on B mode, navigated by capsular indentation). 1cm core I think lesional. MRI **13mm with capsular retraction**, mildly high signal on T2 and low on T1-weighted imaging. Bili 9, ALP 58, ALT 22. Non-insulin dependent diabetes, osteoarthritis, palindromic rheumatism and migraines. Current medications include Loratidine, Sumatriptan, Lansoprazole, Lisinopril, and Co-codamol. She has allergies to Metformin, Hydroxychloroquine, Amitriptyline, Tramadol, Codeine and Imipramine.

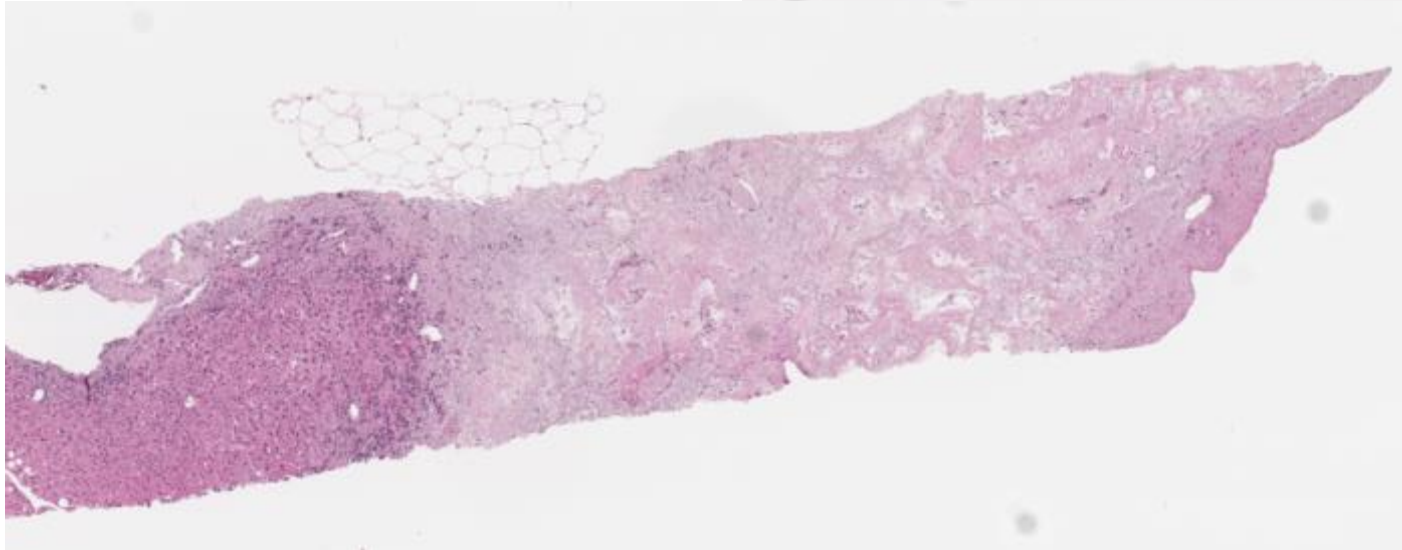
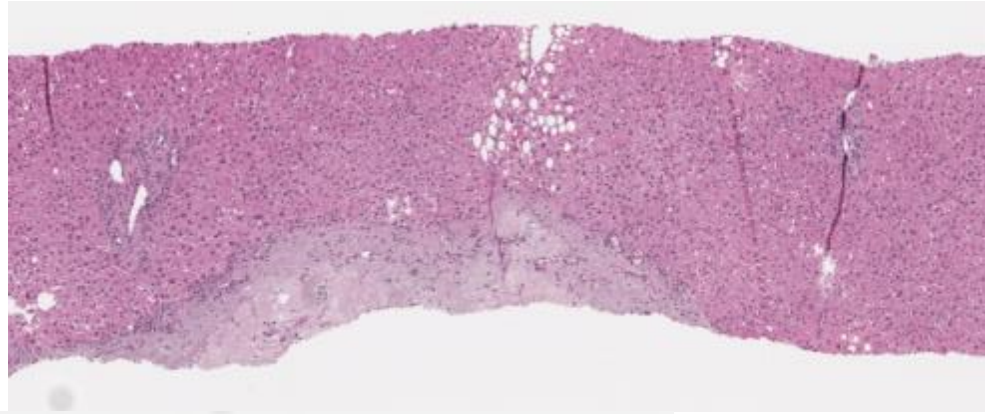
**Specimen:** **Lesional liver biopsy**



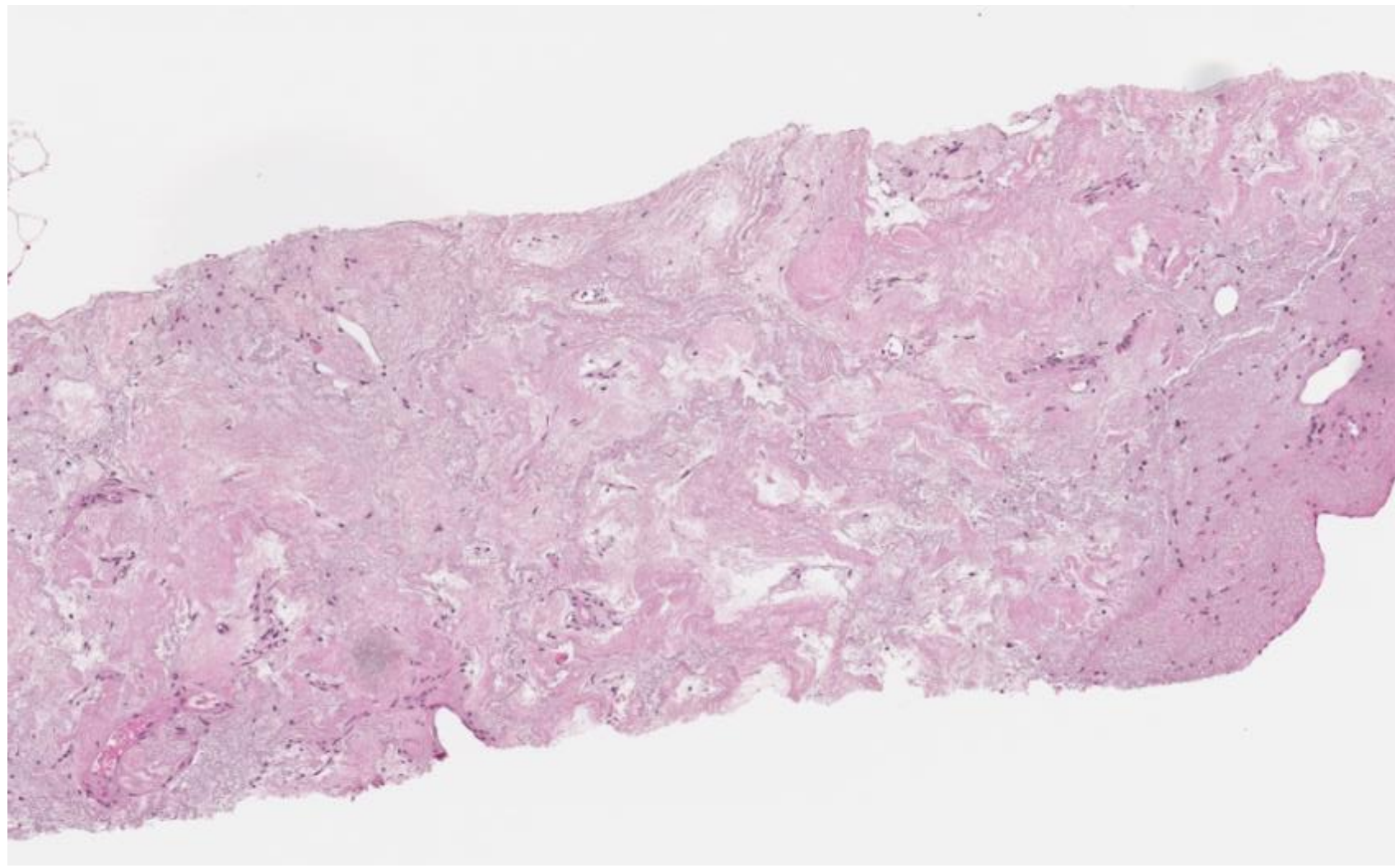
**Case Number: LW11**

**Clinical:** Female 69.

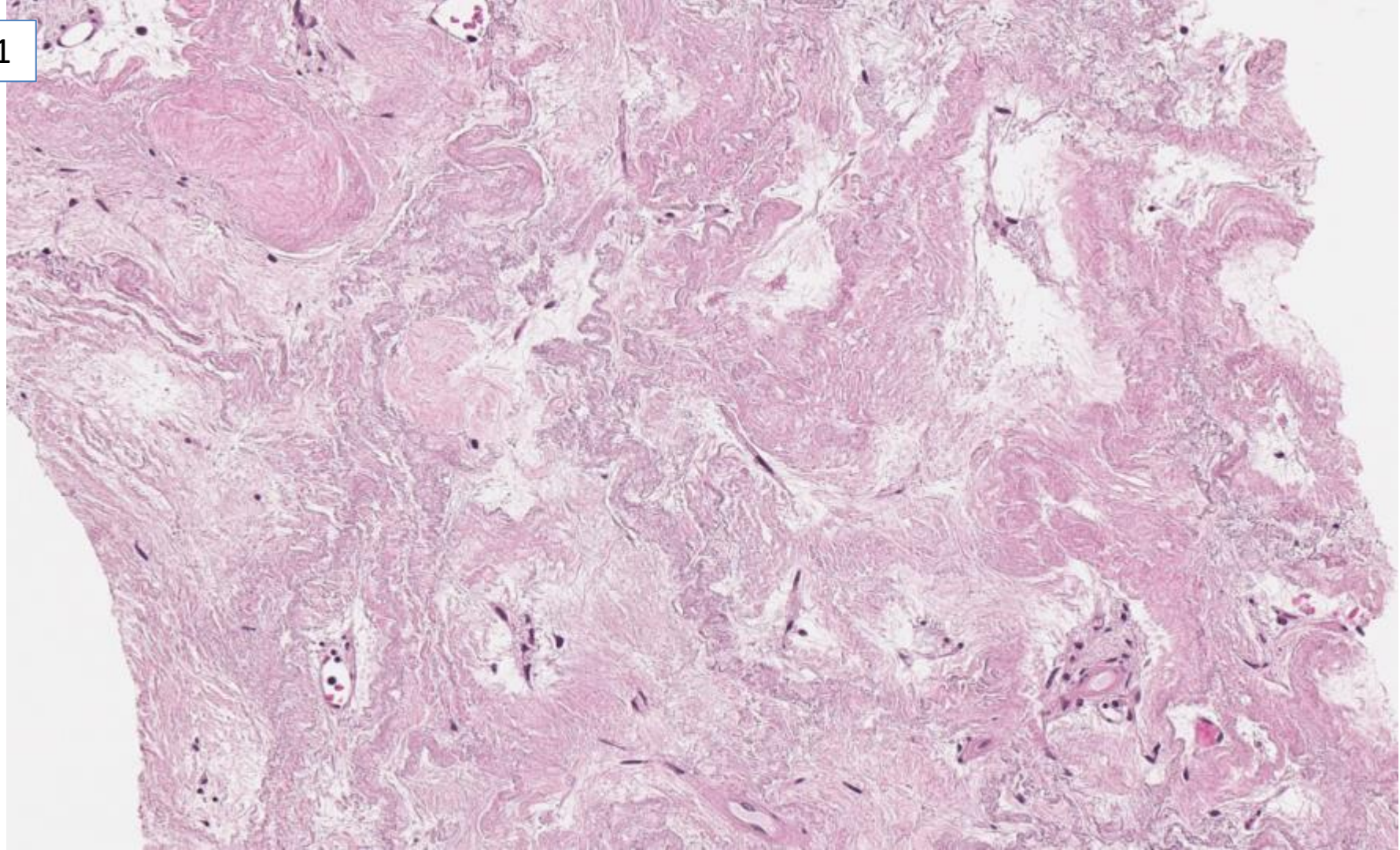
Liver lesion. ?Aetiology. Hyper vascular,  
indeterminate on CT/MR.



LW11



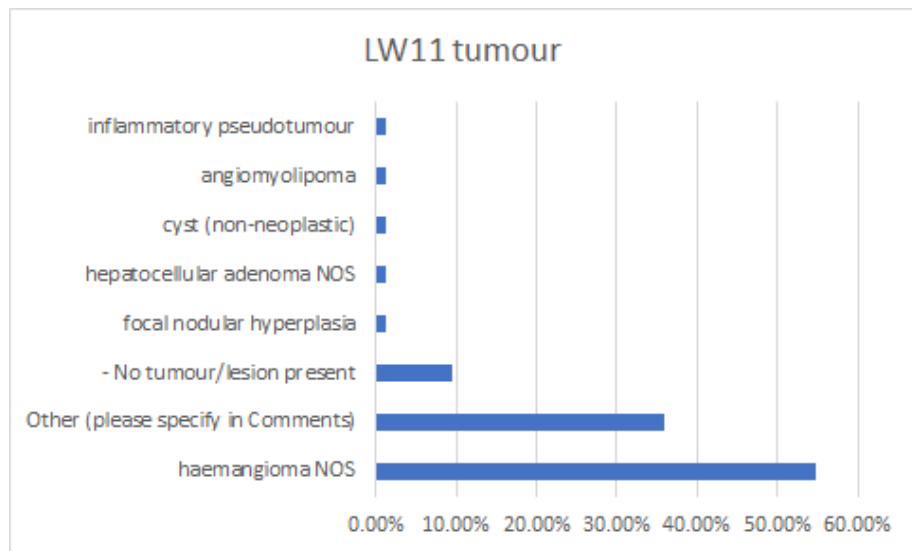
LW11



**Case Number: LW11**

**Clinical: Female 69.**

**Liver lesion. ?Aetiology. Hyper vascular,  
indeterminate on CT/MR.**



Tumour:	Popularity:
haemangioma NOS	54.7%
Other (please specify in Comments)	35.8%
- No tumour/lesion present	9.5%
focal nodular hyperplasia	1.1%
hepatocellular adenoma NOS	1.1%
cyst (non-neoplastic)	1.1%
angiomyolipoma	1.1%
inflammatory pseudotumour	1.1%

## Case Number: LW11

### Points of consensus:

haemangioma (52) or include haemangioma in comments (15) = 67/95, 70.5% not consensus.

Can score if also accept any benign fibrotic lesion – amyloid, elastosis, - then 88/95. **Is this reasonable? – excluding amyloid, accepted for elastosis, segmental atrophy,**

**Suggested scoring: for 10 points** haemangioma or alternative benign sclerotic lesion.

**Lose 5 marks** for diagnosis of amyloid, unless in differential and dependant on Congo red to confirm.

**Lose 5 marks** for other - "Myxoid spindle cell lesion with prominent vasculature. Mild nuclear atypia, difficult to distinguish if low grade malignant neoplasm or benign. Would do immuno and show soft tissue colleagues."

**Lose 10 marks** for ‘no lesion present’

**Lose 10 marks** for specific cellular focal lesion, i.e. FNH, HCA, angiomyolipoma,

**Original report and further information (if any):** Sclerosed haemangioma

## Case Number: LW11

Discussion, learning points:

Differential diagnosis between sclerosed (cavernous) haemangioma and segmental atrophy of the liver in the nodular elastosis stage may not be possible.



› [Am J Surg Pathol.](#) 2011 Mar;35(3):364-71. doi: 10.1097/PAS.0b013e31820b0603.

### **Segmental atrophy of the liver: a distinctive pseudotumor of the liver with variable histologic appearances**

Aatur D Singhi<sup>1</sup>, Hala R Maklouf, Anupamjit K Mehrotra, Zachary D Goodman, Uta Drebber, Hans P Dienes, Michael Torbenson

*Histopathology* 2019, 75, 876–881. DOI: 10.1111/his.13961

### **Hepatic sclerosing cavernous haemangioma can mimic the nodular elastosis stage of segmental atrophy**

Jennifer J Findeis-Hosey,  Zhongren Zhou\* & Raul S Gonzalez<sup>†</sup> 

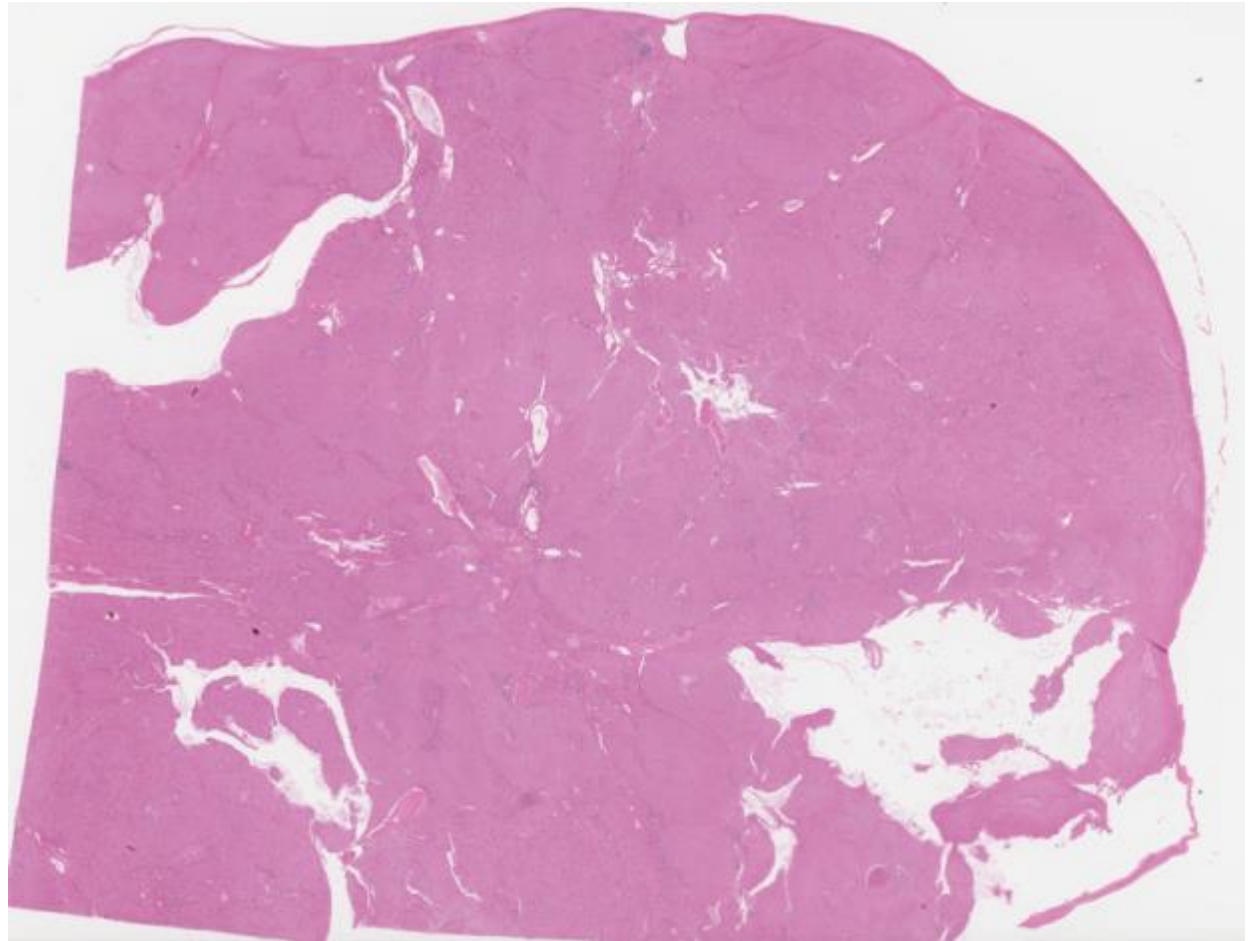
*Department of Pathology and Laboratory Medicine, University of Rochester Medical Center, Rochester, NY, USA*

**Case Number:**

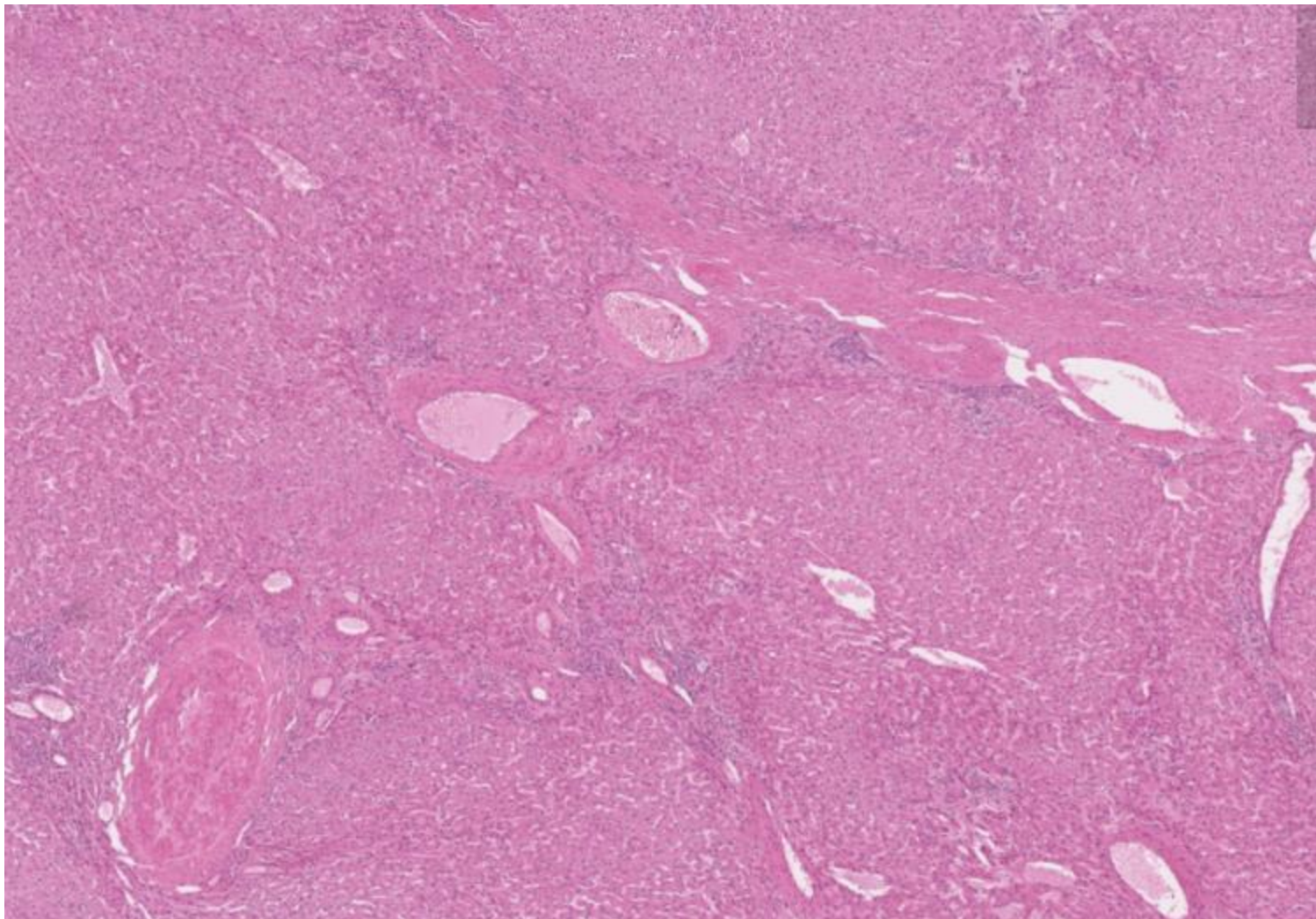
**LW12**

**Clinical:** Female 32.

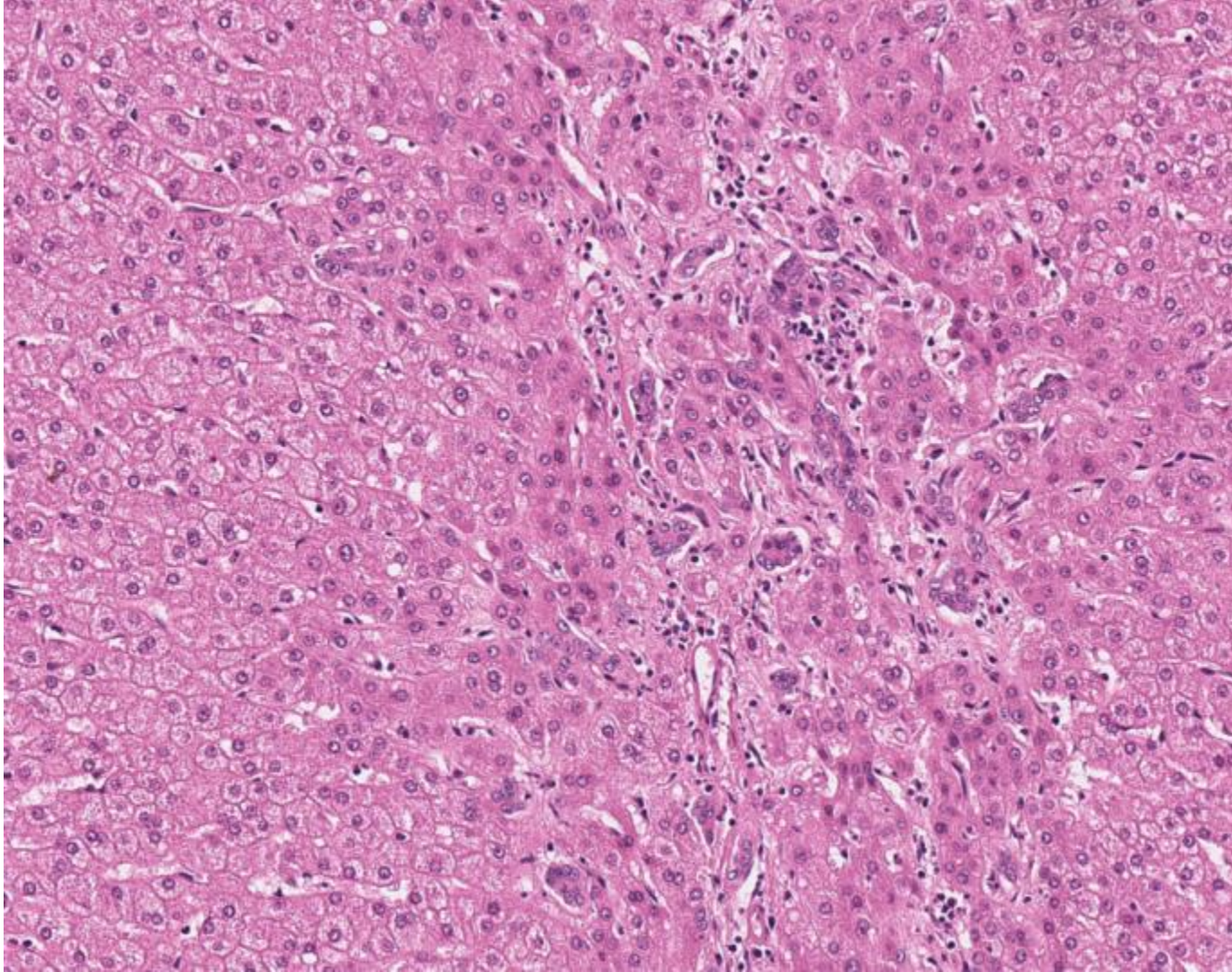
Non-anatomical  
liver resection  
segment VI



LW12



LW12



# Case Number: LW12

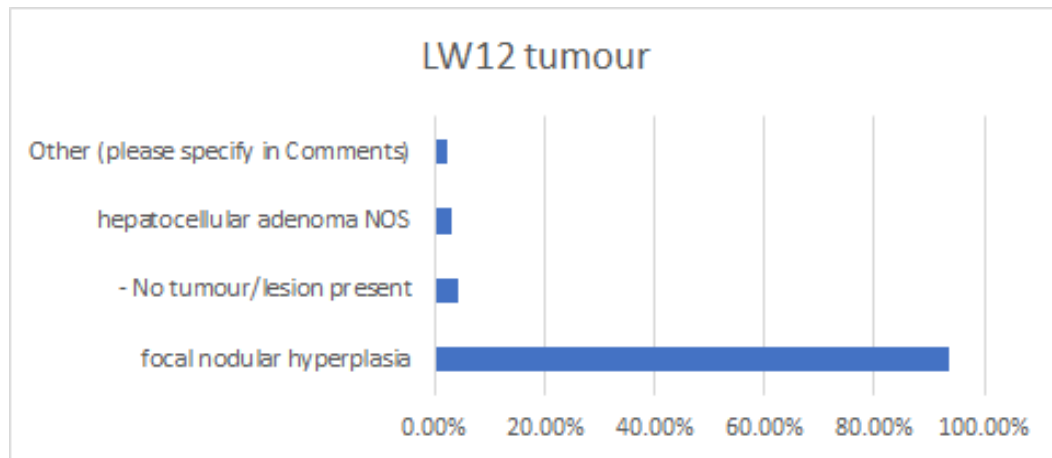
## Clinical: Female 32. Non-anatomical liver

Tumour:	Popularity:
focal nodular hyperplasia	93.7%
- No tumour/lesion present	4.2%
hepatocellular adenoma NOS	3.2%
Other (please specify in Comments)	2.1%

Pattern:	Popularity:
not applicable	64.2%
within normal limits	18.9%
vascular disease	2.1%

Stages:	Popularity:
not applicable / no special stains to assess architecture	69.5%
no fibrosis/equivocal fibrosis	2.1%
mild/early fibrosis without bridging	2.1%
Other (please specify in Comments)	2.1%

Diagnosis Combination:	Count:
[No selections made]	58
- not applicable (insufficient non-lesional tissue)	28
- no evidence of diffuse/background liver disease	5
Other (please enter alternative diagnosis in comments box)	3
- histologically indeterminate for cause	1



Tumour 1:	Tumour 2:	Count:
focal nodular hyperplasia		82
focal nodular hyperplasia	focal nodular hyperplasia	4
- No tumour/lesion present		2
hepatocellular adenoma NOS		2
Other (please specify in Comments)		2
focal nodular hyperplasia	- No tumour/lesion present	1
- No tumour/lesion present	focal nodular hyperplasia	1
focal nodular hyperplasia	hepatocellular adenoma NOS	1

Case number	Pathology ref	Tumour 1	Tumour 2	Text Diagnosis	proposed score
12	154	-No tumour/lesion present		venoocclusive disease	1
12	228	Other (please specify in Comments)		Paraneoplastic atrophy	1
12	18	focal nodular hyperplasia	hepatocellular adenoma NOS	Liver has features of both FNH and adenoma. Stain for Glutamine synthetase and for Beta catenin, SAA and LFBOP.	5
12	53	hepatocellular adenoma NOS		I think adenoma rather than FNH.	5
12	66	hepatocellular adenoma NOS		'Telangiectatic FNH'	5
12	3	focal nodular hyperplasia		Focal nodular hyperplasia with multiple large abnormal vessels - some septa, but not diffusely nodular throughout, would be Glutamine synthetase for confirmation, as difficult background liver tissue	
12	7	focal nodular hyperplasia			
12	8	focal nodular hyperplasia			
12	11	focal nodular hyperplasia			
12	12	focal nodular hyperplasia		This looks like FNH; would do some connective tissue stain	
12	15	focal nodular hyperplasia			
12	16	focal nodular hyperplasia			
12	24	focal nodular hyperplasia			
12	22	focal nodular hyperplasia			
12	24	focal nodular hyperplasia		would like IHC against adenoma panel	
12	25	focal nodular hyperplasia		Beta and Glutamine synthetase to confirm (will have normal periportal vessels in background)	
12	28	focal nodular hyperplasia			
12	31	focal nodular hyperplasia			
12	33	focal nodular hyperplasia			
12	34	focal nodular hyperplasia	focal nodular hyperplasia		
12	35	focal nodular hyperplasia	focal nodular hyperplasia		
12	37	focal nodular hyperplasia			
12	38	focal nodular hyperplasia			
12	48	focal nodular hyperplasia			
12	44	focal nodular hyperplasia			
12	56	focal nodular hyperplasia		Diagnosed Focal Nodular Hyperplasia (FNH)	
12	57	focal nodular hyperplasia		Other (please specify in Comments)	
12	58	focal nodular hyperplasia			
12	64	focal nodular hyperplasia		Differential of FNH would like some special stains and IHC.	
12	65	focal nodular hyperplasia			
12	67	focal nodular hyperplasia			
12	74	focal nodular hyperplasia			
12	72	focal nodular hyperplasia			
12	75	focal nodular hyperplasia			
12	76	focal nodular hyperplasia			
12	77	focal nodular hyperplasia			
12	84	focal nodular hyperplasia			
12	82	focal nodular hyperplasia		FNH	
12	83	focal nodular hyperplasia		Largely like FNH. Looks prominent scar and bile ductular prol	3
12	85	focal nodular hyperplasia	focal nodular hyperplasia	FNH with vascular scar	7
12	88	focal nodular hyperplasia		Macrolicly and nodular scar and dividing fibrous septa with des	8
12	38	focal nodular hyperplasia		Central with focal nodular hyperplasia	11
12	35	focal nodular hyperplasia			
12	33	-No tumour/lesion present	focal nodular hyperplasia		
12	188	focal nodular hyperplasia			
12	181	focal nodular hyperplasia			
12	183	focal nodular hyperplasia		Young female single node containing irregular vascular area	16
12	143	focal nodular hyperplasia			
12	128	focal nodular hyperplasia			
12	126	focal nodular hyperplasia		No background liver present for assessment.	22
12	123	focal nodular hyperplasia			
12	158	focal nodular hyperplasia	-No tumour/lesion present		
12	151	focal nodular hyperplasia			
12	157	focal nodular hyperplasia			
12	153	focal nodular hyperplasia			

Participant	Tumour 1	Tumour 2	Text Diagnosis	proposed score
14	Other (please specify in Comments)		Peliosis Variably sized spaces in liver, with no vascular or epithelial lining.	0
114	- No tumour/lesion present		venoocclusive disease	0
228	Other (please specify in Comments)		? segmental atrophy	0
10	focal nodular hyperplasia	hepatocellular adenoma NOS	Lesion has features of both FNH and adenoma. Stain for Glutamine synthetase and for Beta catenin, SAA and	5
59	hepatocellular adenoma		I think adenoma rather than FNH.	5
66	hepatocellular adenoma		'Telangiectatic FNH'	5
3	focal nodular hyperplasia		Focal nodular hyperplasia with multiple large abnormal vessels + some septa, but not diffusely nodular	
7	focal nodular hyperplasia			
8	focal nodular hyperplasia			
11	focal nodular hyperplasia			
12	focal nodular hyperplasia		This looks like FNH; would do some connective tissue	
15	focal nodular hyperplasia			
16	focal nodular hyperplasia			
21	focal nodular hyperplasia			
22	focal nodular hyperplasia			
24	focal nodular hyperplasia		would like IHC against adenoma panel	

## **Case Number: LW12**

**Clinical:** Female 32. Non-anatomical liver resection segment VI

**Points of consensus;** focal nodular hyperplasia

**Suggested scoring: for 10 points** Focal nodular hyperplasia

**Lose 5 marks ?**

hepatocellular adenoma NOS - I think adenoma rather than FNH - as not further qualified score 5

hepatocellular adenoma NOS - 'telangiectatic FNH' - as not further qualified score 5

**Lose 10 marks (score 0) if**

Other - Peliosis Variably sized spaces in liver, with no vascular or epithelial lining.

Other - ? segmental atrophy

no tumour present - venoocclusive disease

**Original report and further information (if any):** FNH

The end