

# National Liver Histopathology EQA Scheme

Circulation D1

Spring/Summer 2011

## **Liver EQA scheme - business meeting**

Responses received for D1 = 69; 66 electronically, 3 entered by Laura from paper copies. For E1 = 44 by the closing date, another 16 in following week = 60 (2 by paper).

Current number of members = 97 – rather low response rate, ?  
Why – questionnaire after D1 closing date, half wanted more time, 20% circulation problem, 15% not submitting due to insufficient time.

Were my suggested scoring schemes OK?

D1 – comments from committee and 3 sets from other members

E1 – comments from committee and 1 other member

Review at the end of the afternoon discussion.

## Case number 362

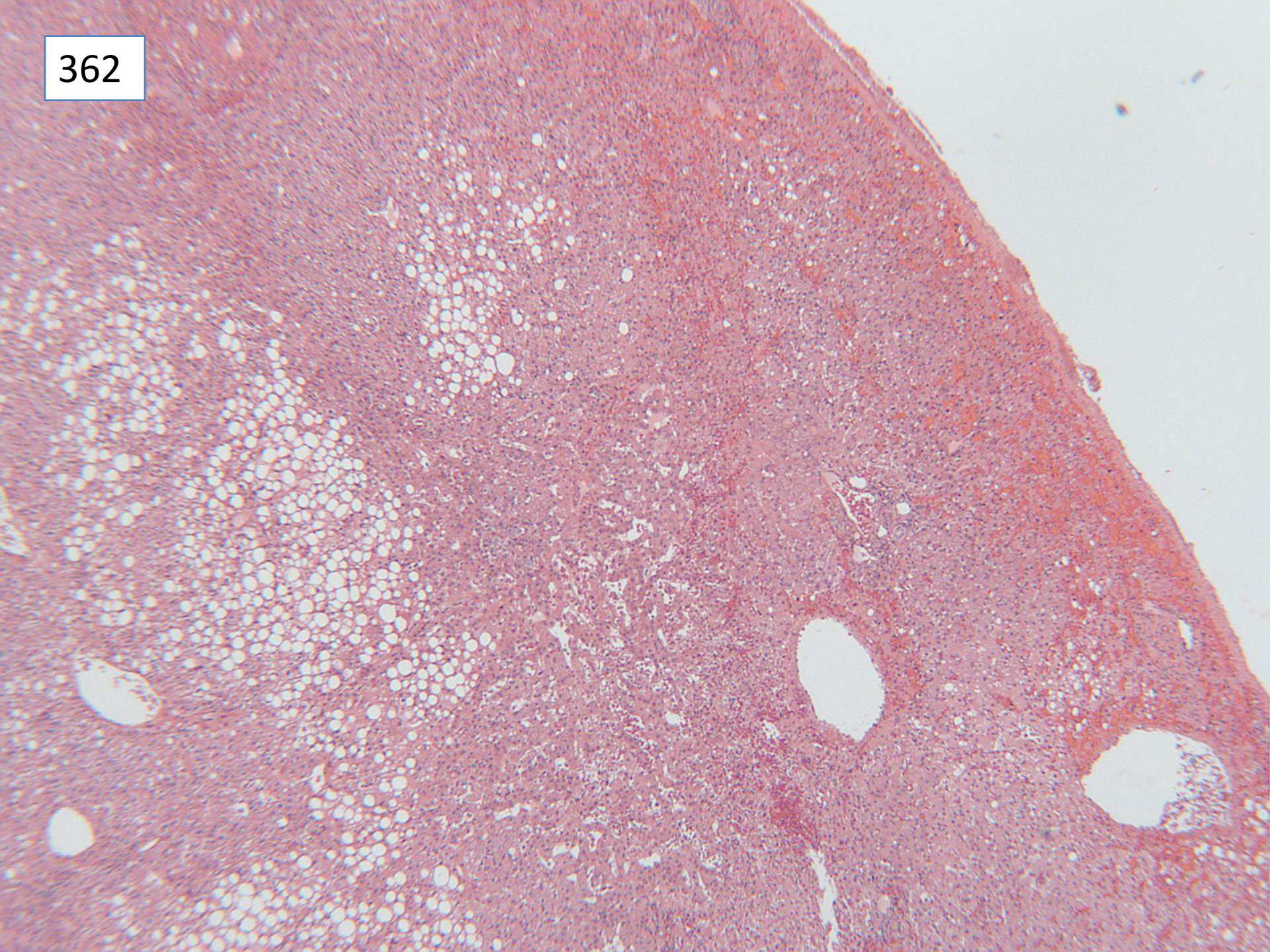
Female 48 years

Gallstones, cholecystitis, lesion gall bladder bed.

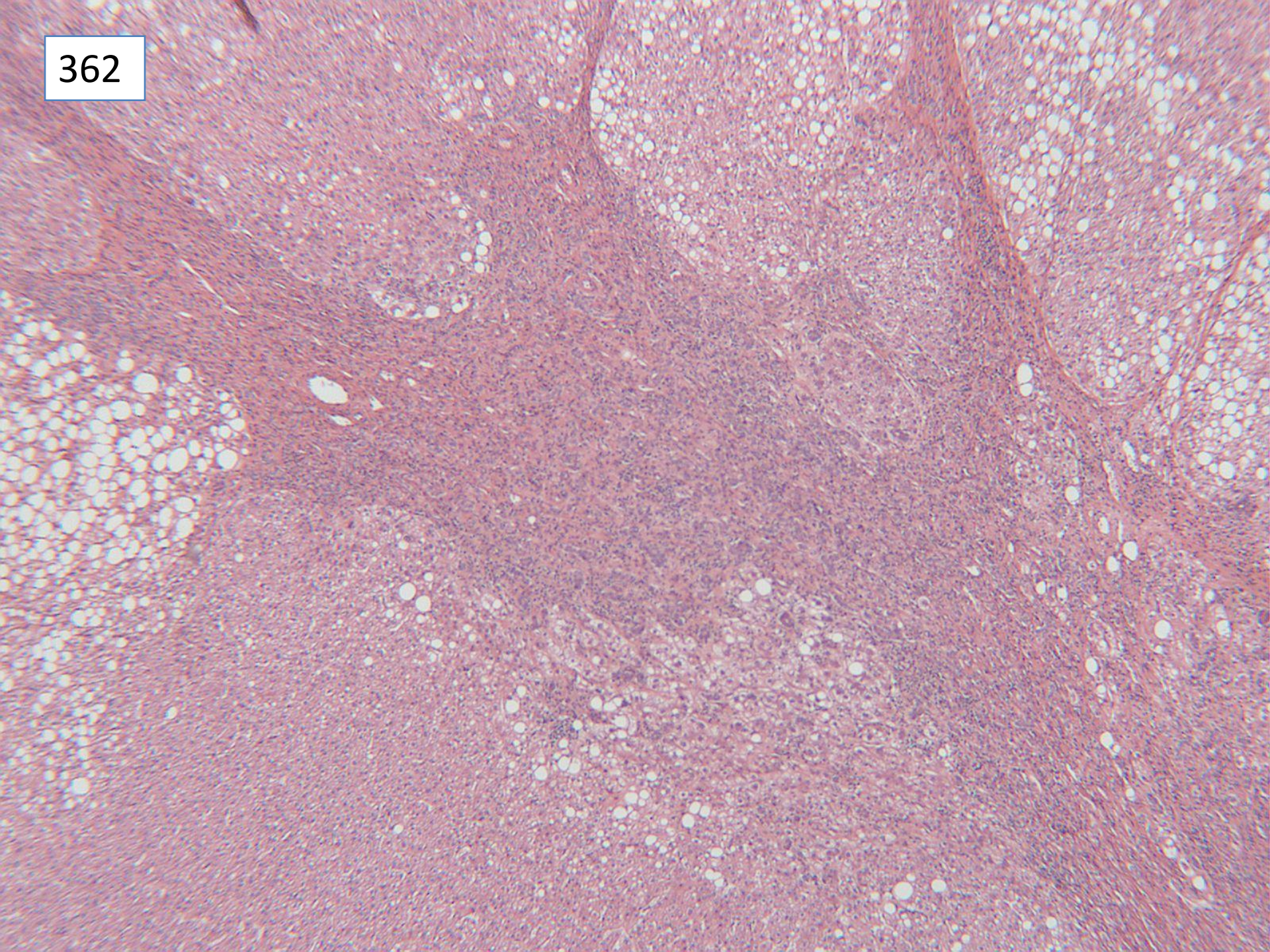
MRI benign.

Liver resection: lobulated liver nodule 3.5x2.5x2.5cm.

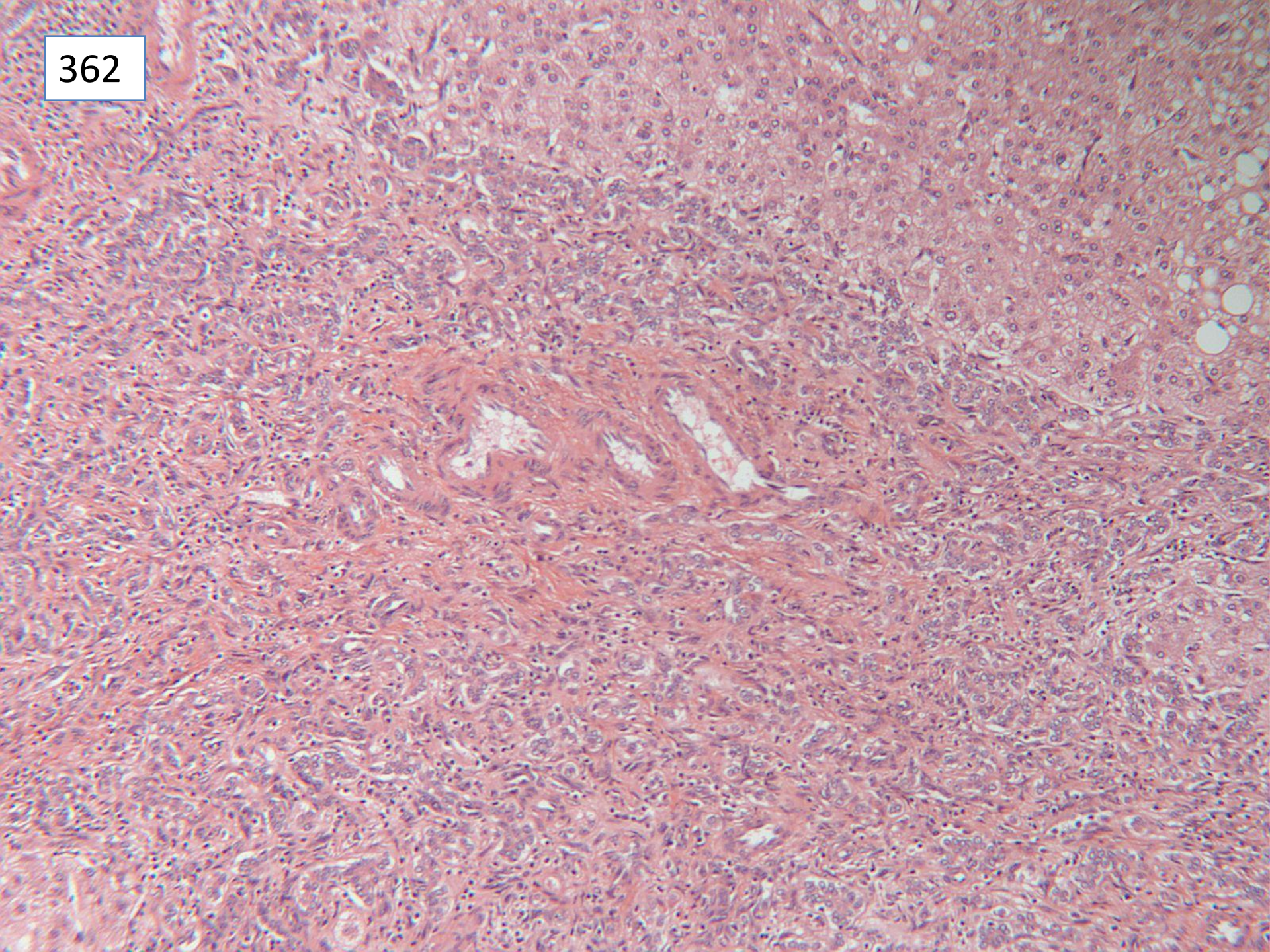
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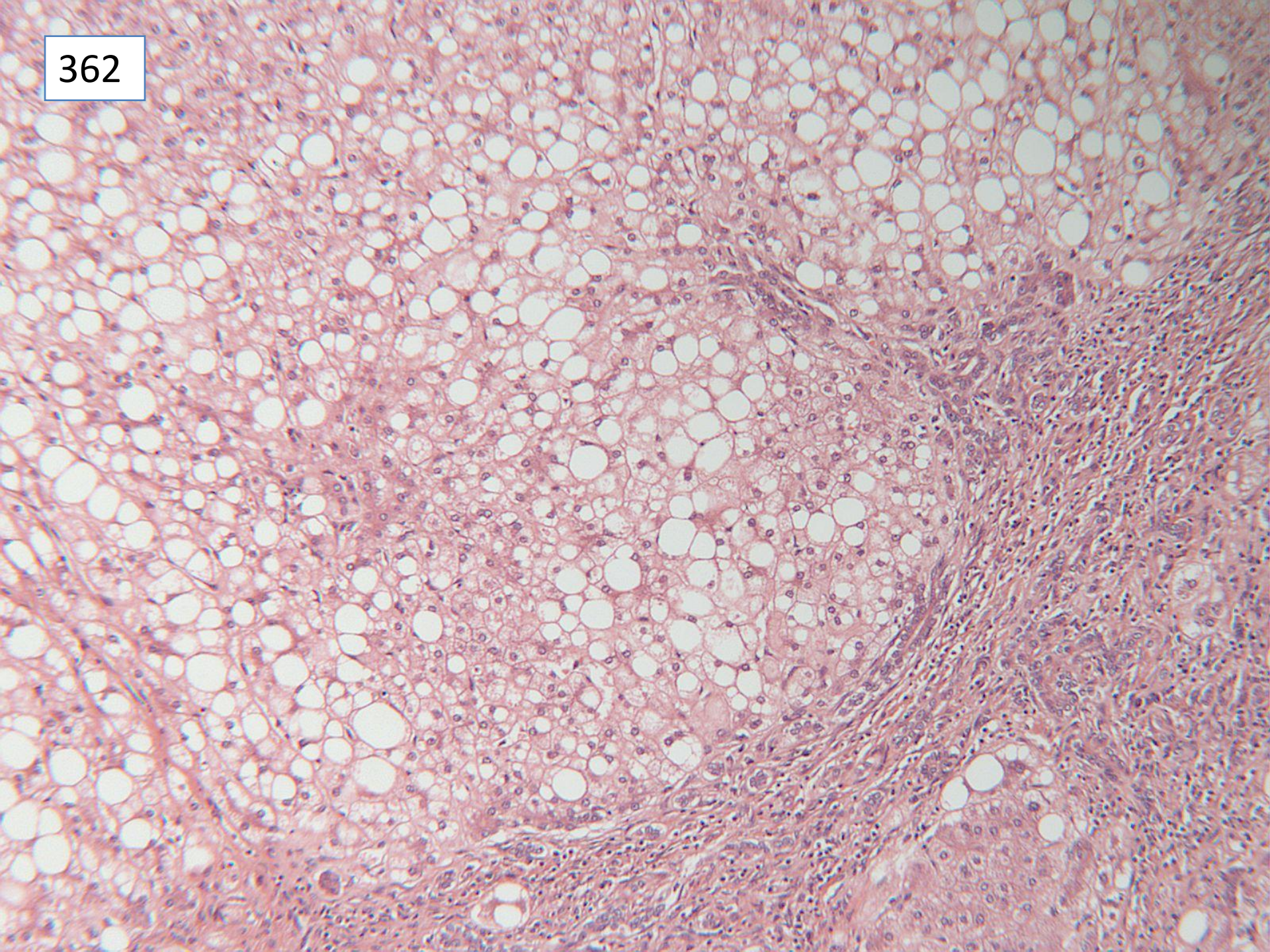
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## Case number 362

### Results:

67 Focal Nodular Hyperplasia (+/- comment on steatosis or steatohepatitis)

1 fibrosis/cirrhosis; biliary process and ASH/NASH

1 macro-regenerative nodule, background active cirrhosis

Scoring: clear consensus, 10 points for diagnosis of FNH

Submitting pathologist's diagnosis: Focal nodular hyperplasia

## **Case number 363**

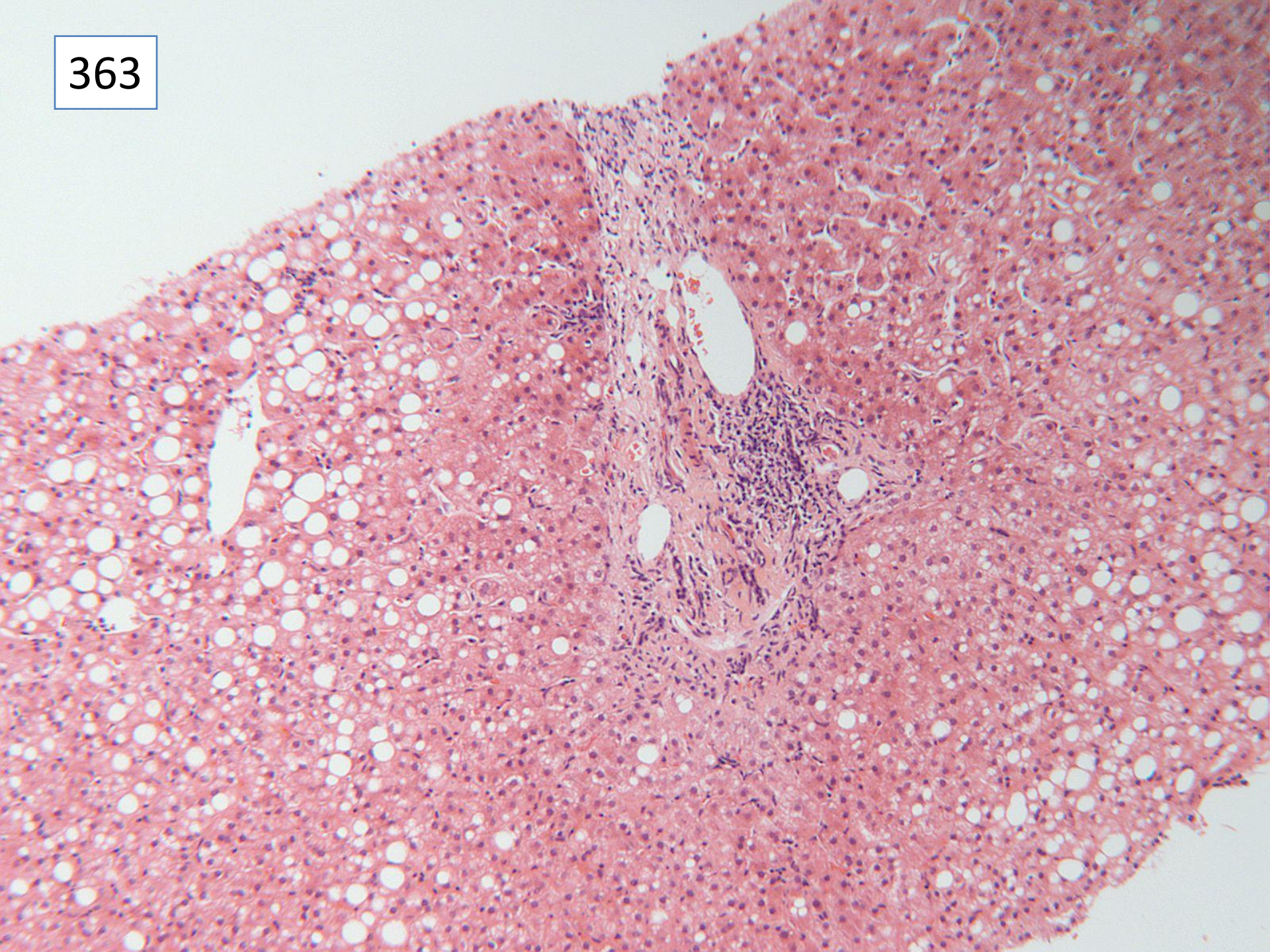
Male 25 years

No clinical information provided with specimen.

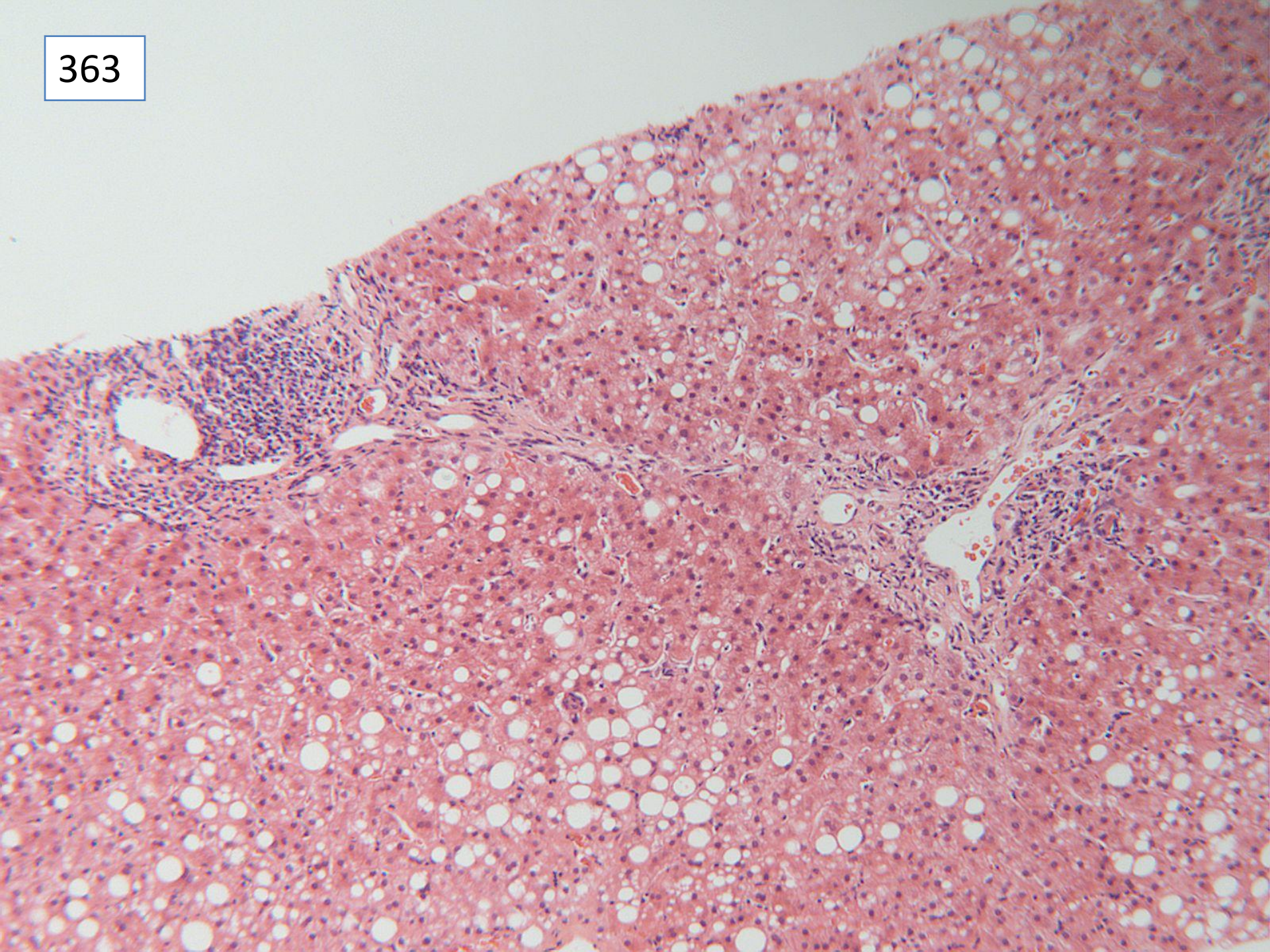
Electronic patient record suggests hepatitis C.

Liver needle core biopsy, 11mm long.

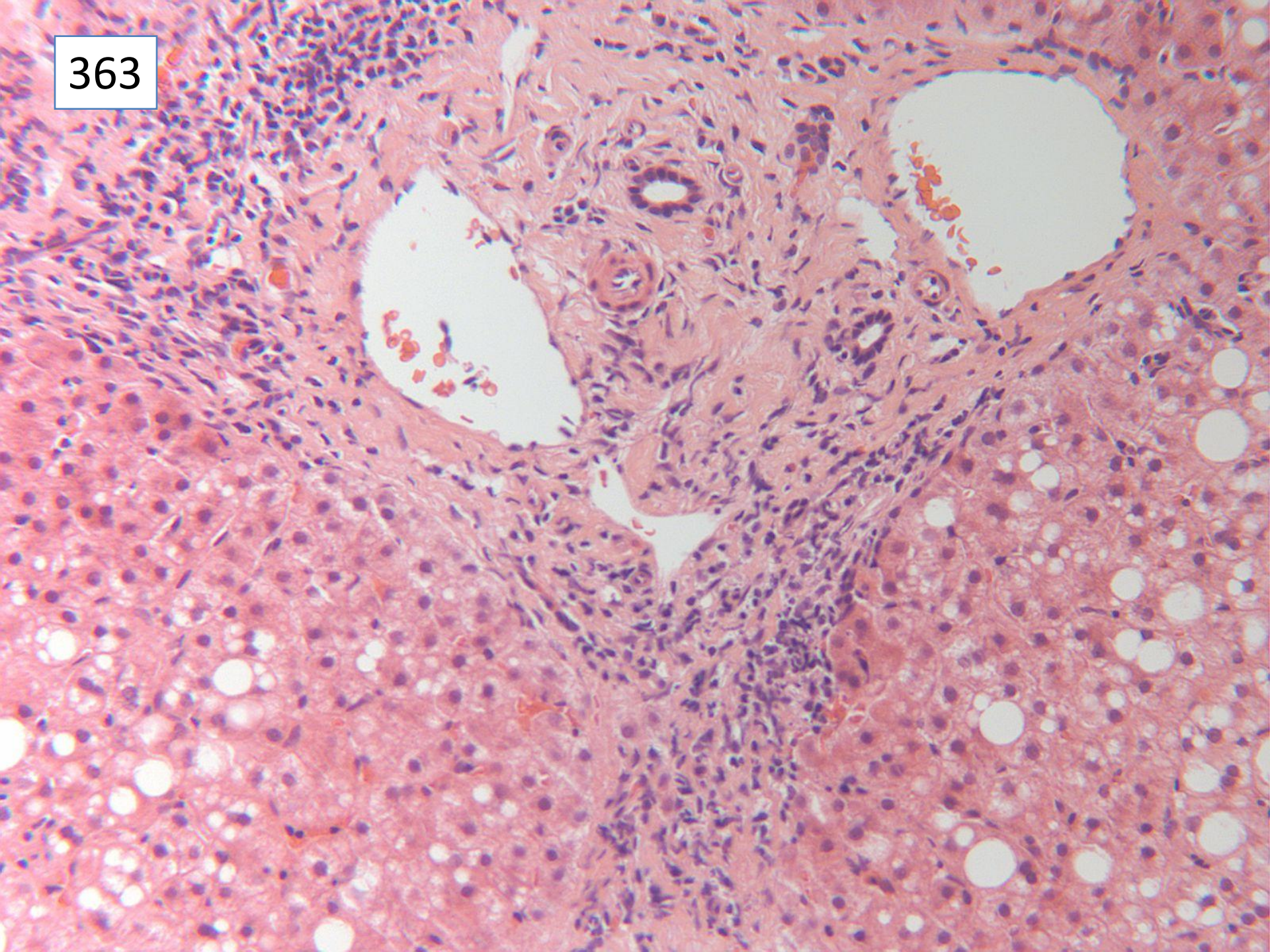
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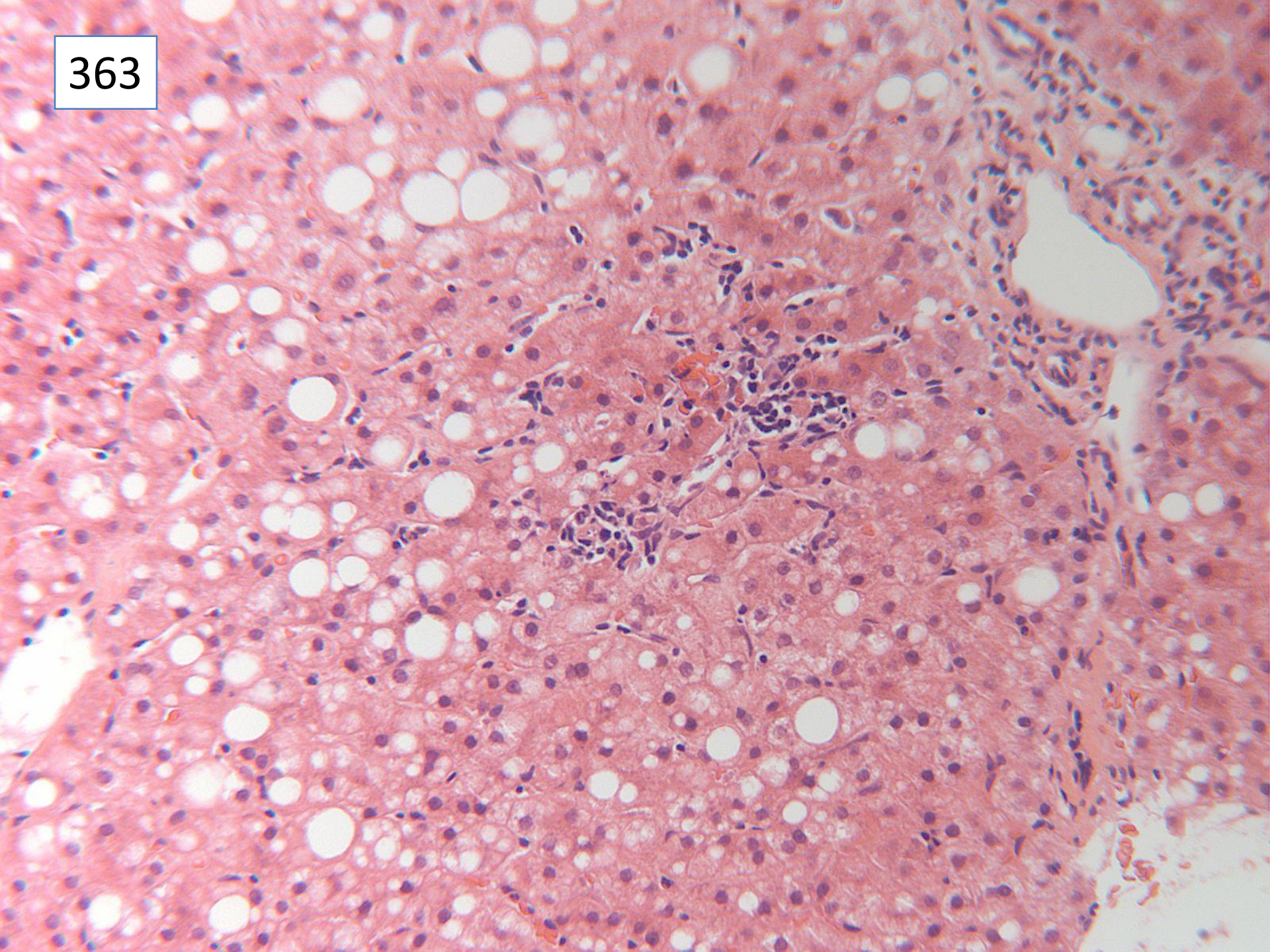
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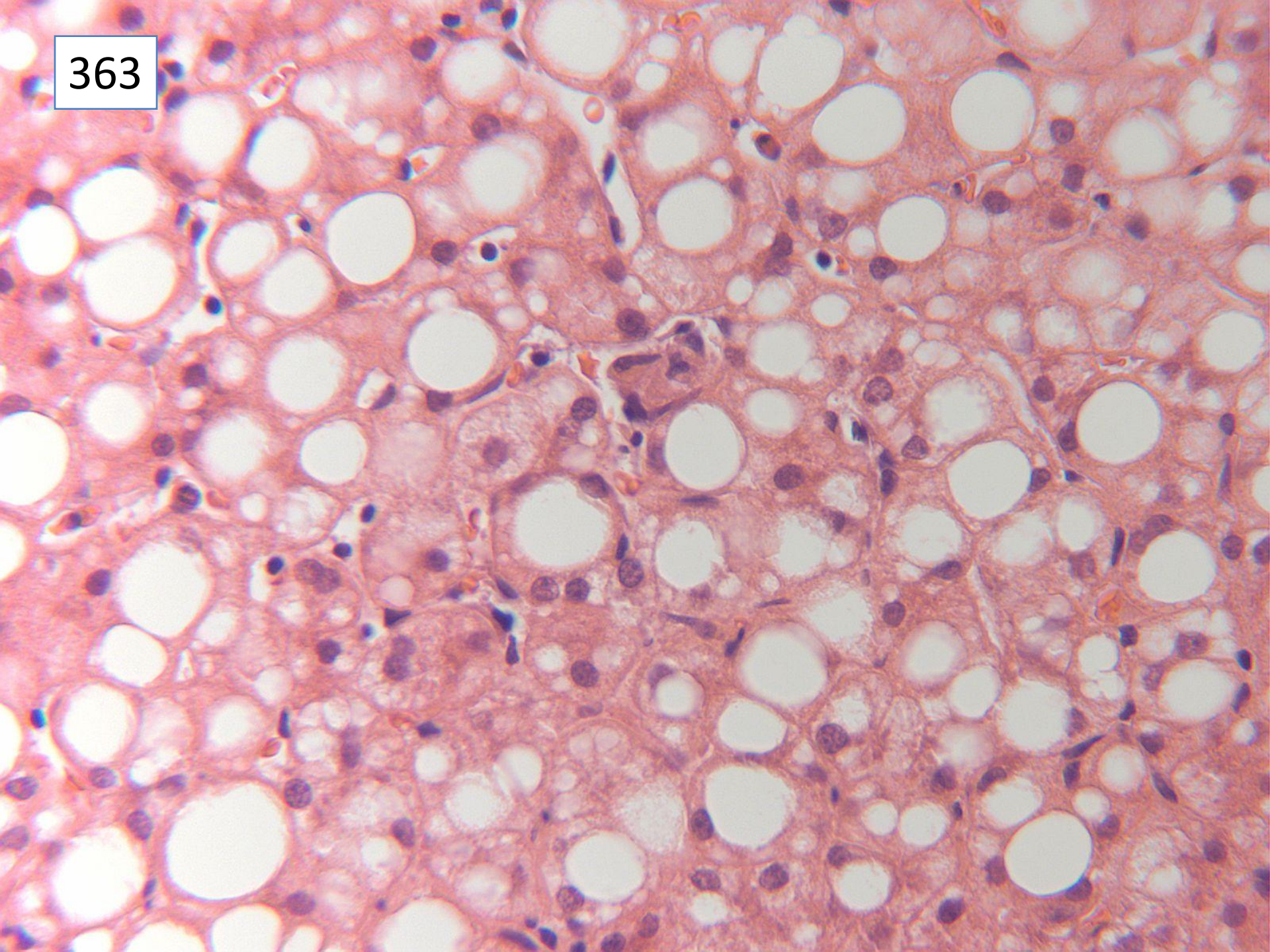
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# Case number 363

## Results:

1 hepatitis C not mentioned in report

68 description of chronic hepatitis, consistent with hepatitis C

Of these:

61 also commented on steatosis

3 no comment on steatosis

46 some comment on fibrosis stage

18 need connective tissue stain for staging

5 no comment on stage

57 some comment on grade/activity

7 no comment on grade/activity

## Suggested scoring:

The reason for biopsy is to assess severity of chronic hepatitis C. From previous EQA discussions – for 10 points, need features consistent with hepatitis C, and a comment on stage and activity/grade.

Also, steatosis influences progression and response to treatment, so is important in report. Lose 5 points if any of these are missing.

Discussion during the meeting: agreed not to penalise for no comment on stage, but in future required connective tissue stain for biopsies like this.

## Case number 363

### Other comments:

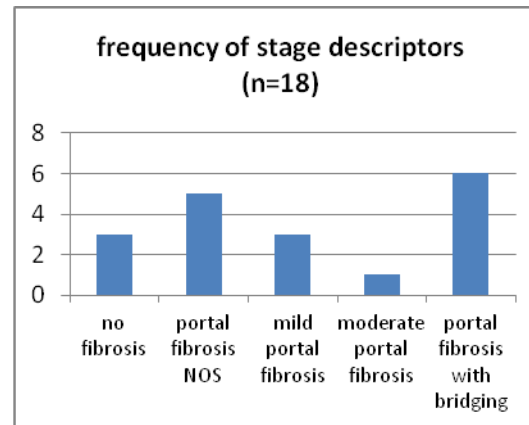
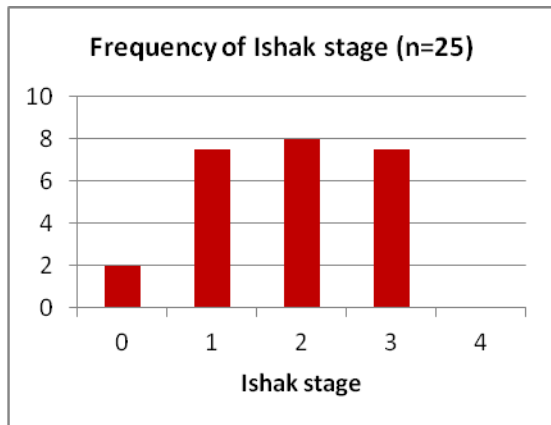
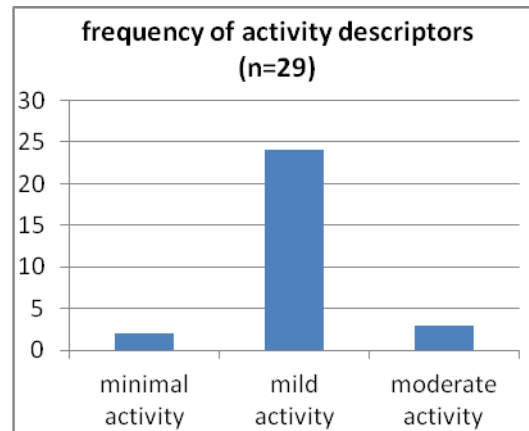
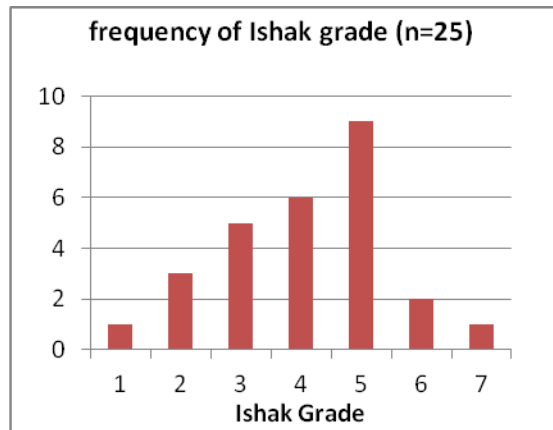
Of responses including steatosis or steatohepatitis, 28/61 included comment on the possible cause (hep C type 3, alcohol, NAFLD)

Reason for biopsy also to rule out other causes of liver disease.  
7 commented on prominent plasma cells and/or possibility of autoimmune hepatitis.

Extra information: Opportunity for participants to compare their assessment of grade/stage with the whole group:

For severity, 25 Ishak stage, 2 Metavir stage, 18 descriptive text  
27 Ishak grade, 1 Metavir grade, 29 descriptive text

# Case number 363



Original pathologist's diagnosis:  
chronic hepatitis consistent with chronic hepatitis C, stage 3

## Example of responses on spreadsheet:

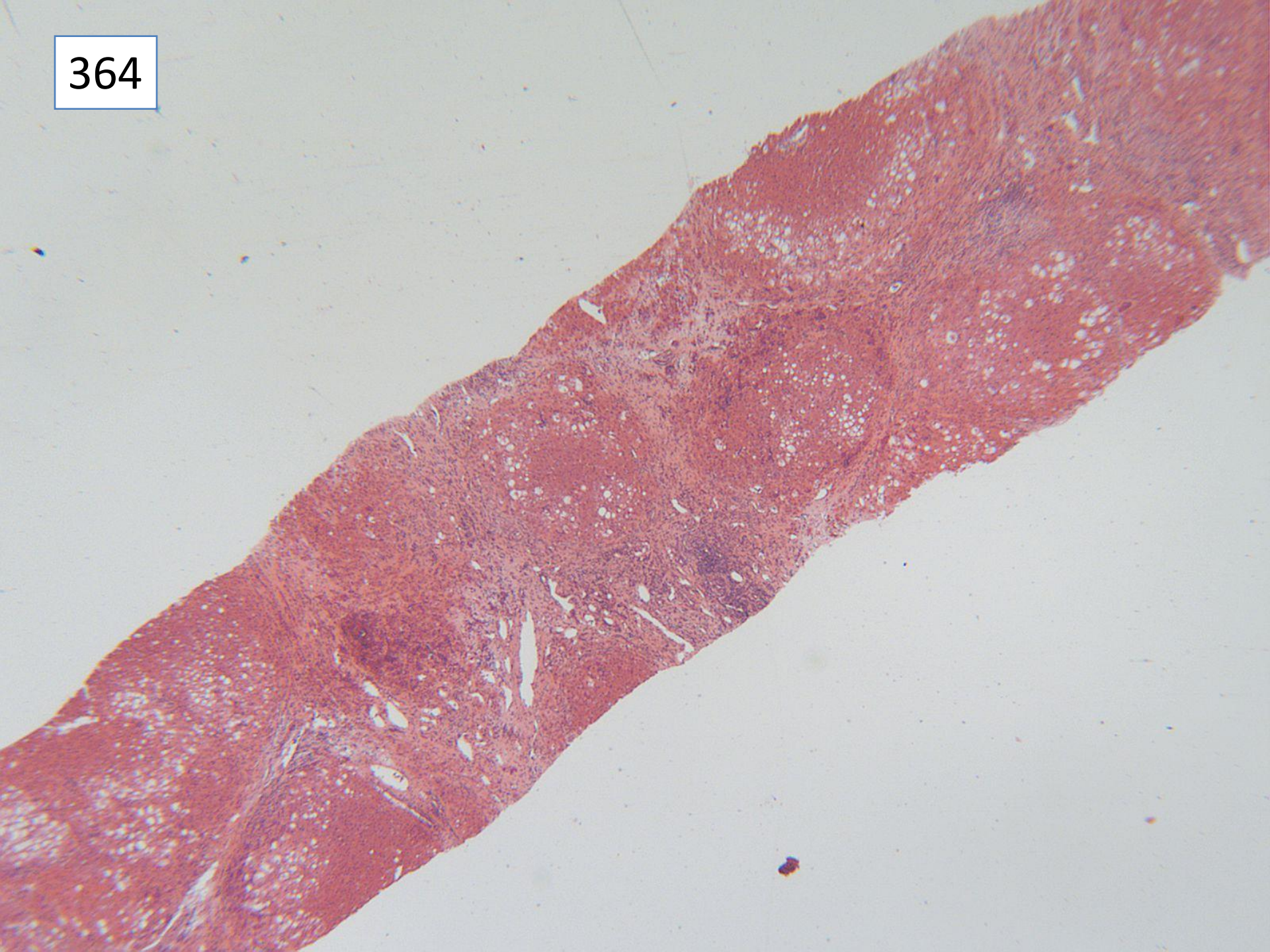
<p>Chronic hepatitis, interface hepatitis, fatty change, incomplete fibrous septa formation</p>	<p>Chronic hepatitis with mild inflammatory activity in keeping with hepatitis C virus infection. ISHAK Grade <b>6/18</b>; Stage possibly <b>2-3/6</b> (to be confirmed by special stains)</p>
<p>Moderate fibrous expansion of portal tracts. Moderate steatosis. Chronic inflammation in portal tracts. Focal mild interface hepatitis. Moderate to marked lobular inflammation. No steatohepatitis.</p>	<p>Chronic HCV Necro-inflammatory score = <b>5/18</b> Fibrosis <b>stage = 2/6</b></p>
<p>Mild fibrous expansion of portal tracts. Mild chronic hepatitis (portal tract and lobular). Plasma cells within infiltrate. Minimal interface hepatitis. Mild to moderate macrovesicular steatosis but no steatohepatitis.</p>	<p>Consistent with HCV infection - <b>low grade chronic hepatitis</b>. Steatosis may be direct result of HCV although consider co-morbid condition.</p>
<p>Mild chronic hepatitis, mild fibrosis and moderate steatosis (60% hepatocytes) <b>Stage 1, Grade 4 (A1,B0,C2,D1)</b></p>	<p>MILD CHRONIC HEPATITIS AND MODERATE STEATOSIS In keeping with HCV but need to confirm serologically. Needs correlation with genotype to see if HCV is responsible for all the steatosis</p>
<p>Mild chronic hepatitis with steatosis</p>	<p>Cons with mild chronic hepatitis C, <b>Ishak grade 1 stage 0</b></p>

## Case number 364

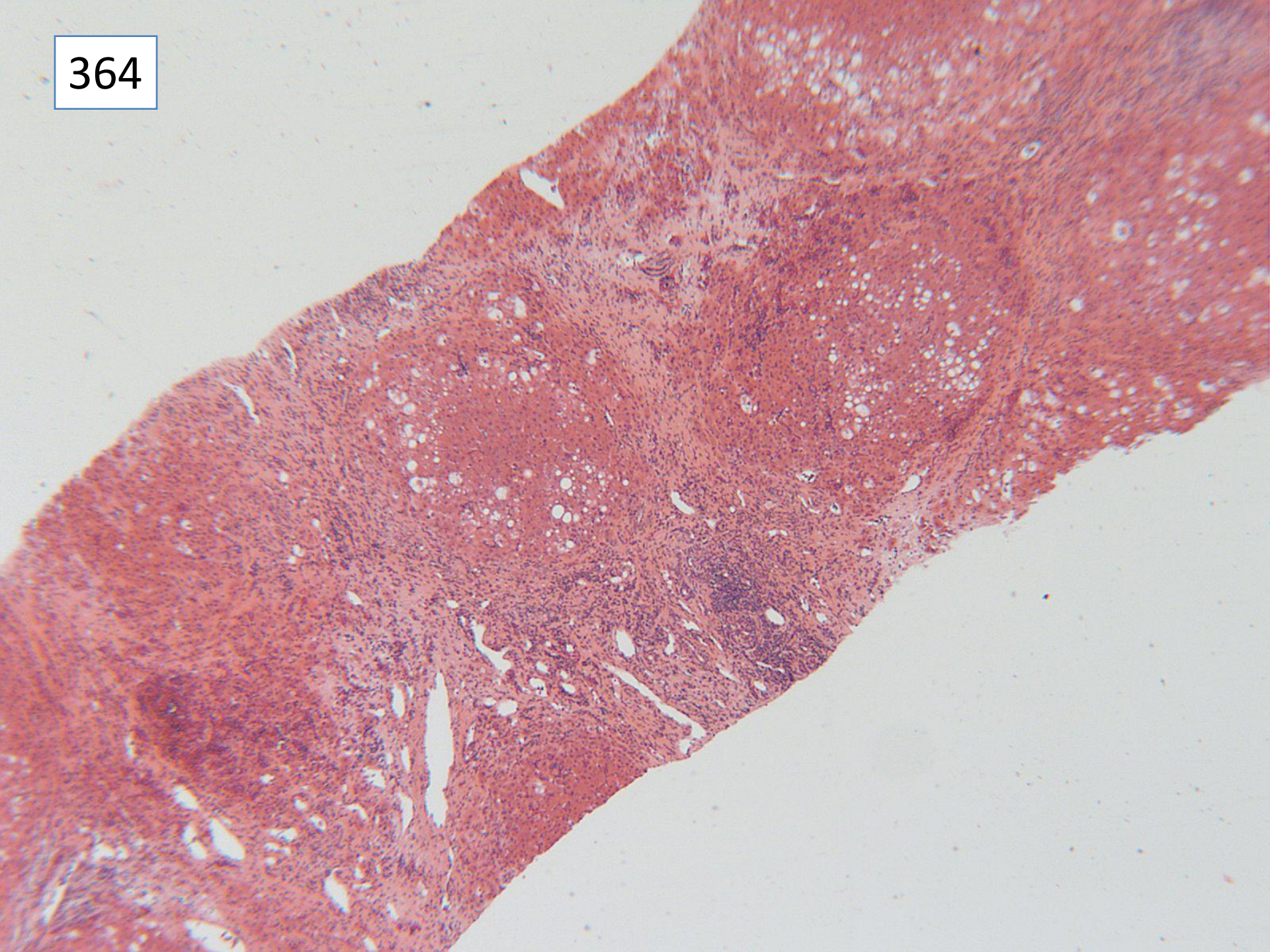
Female 48 years

?NASH cirrhosis, FH of cirrhosis. Percutaneous core biopsy, 15mm core.

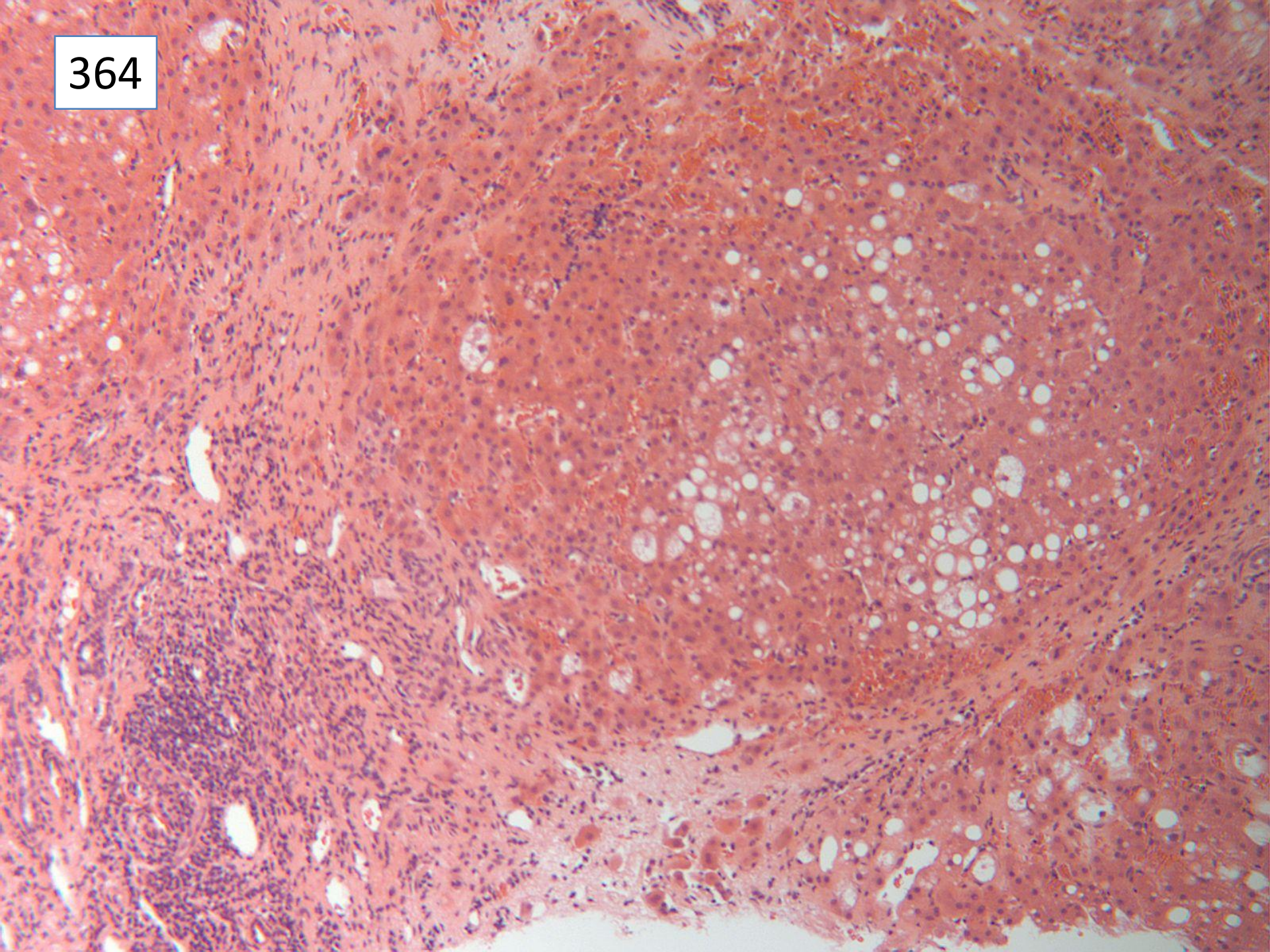
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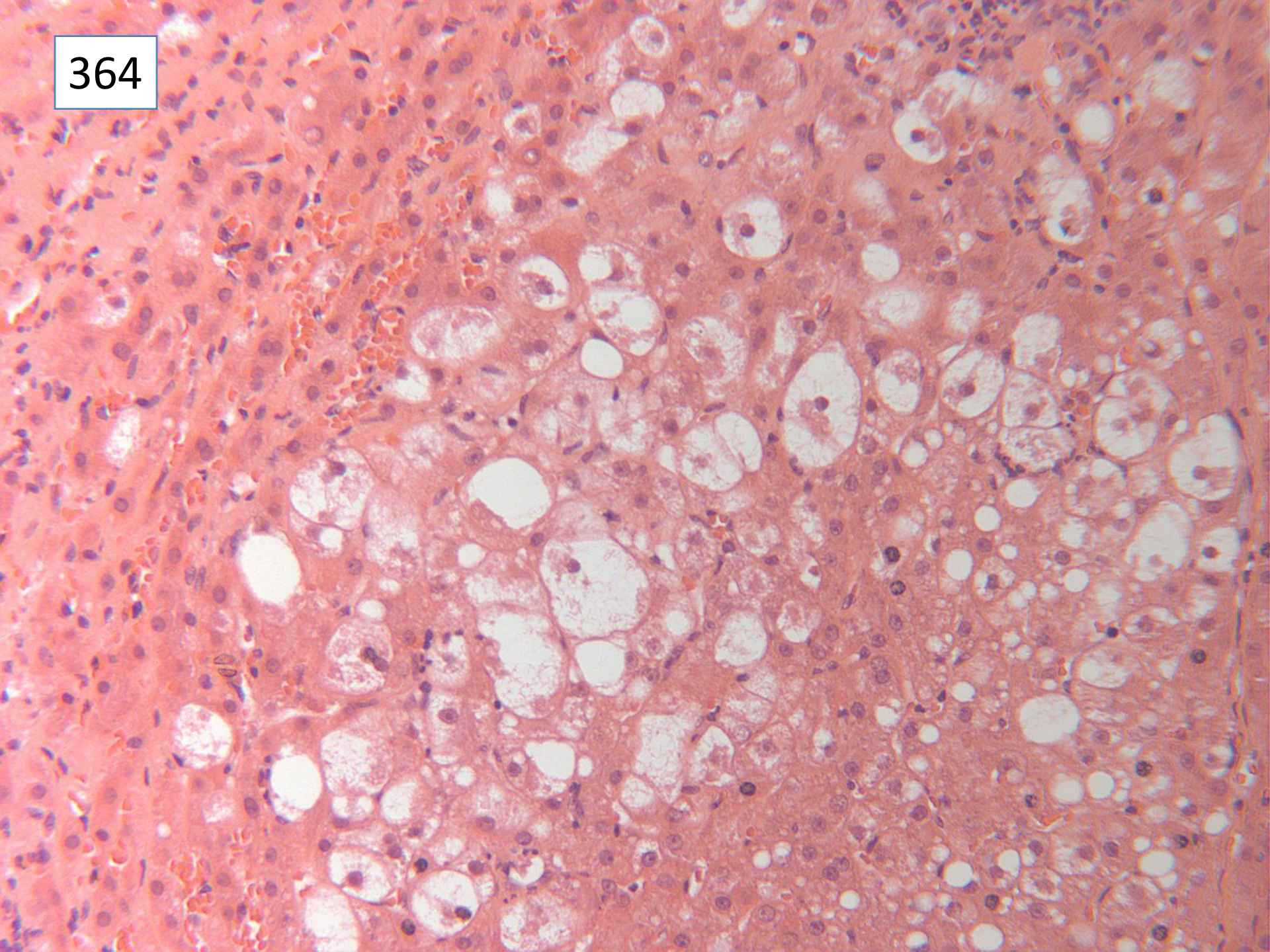
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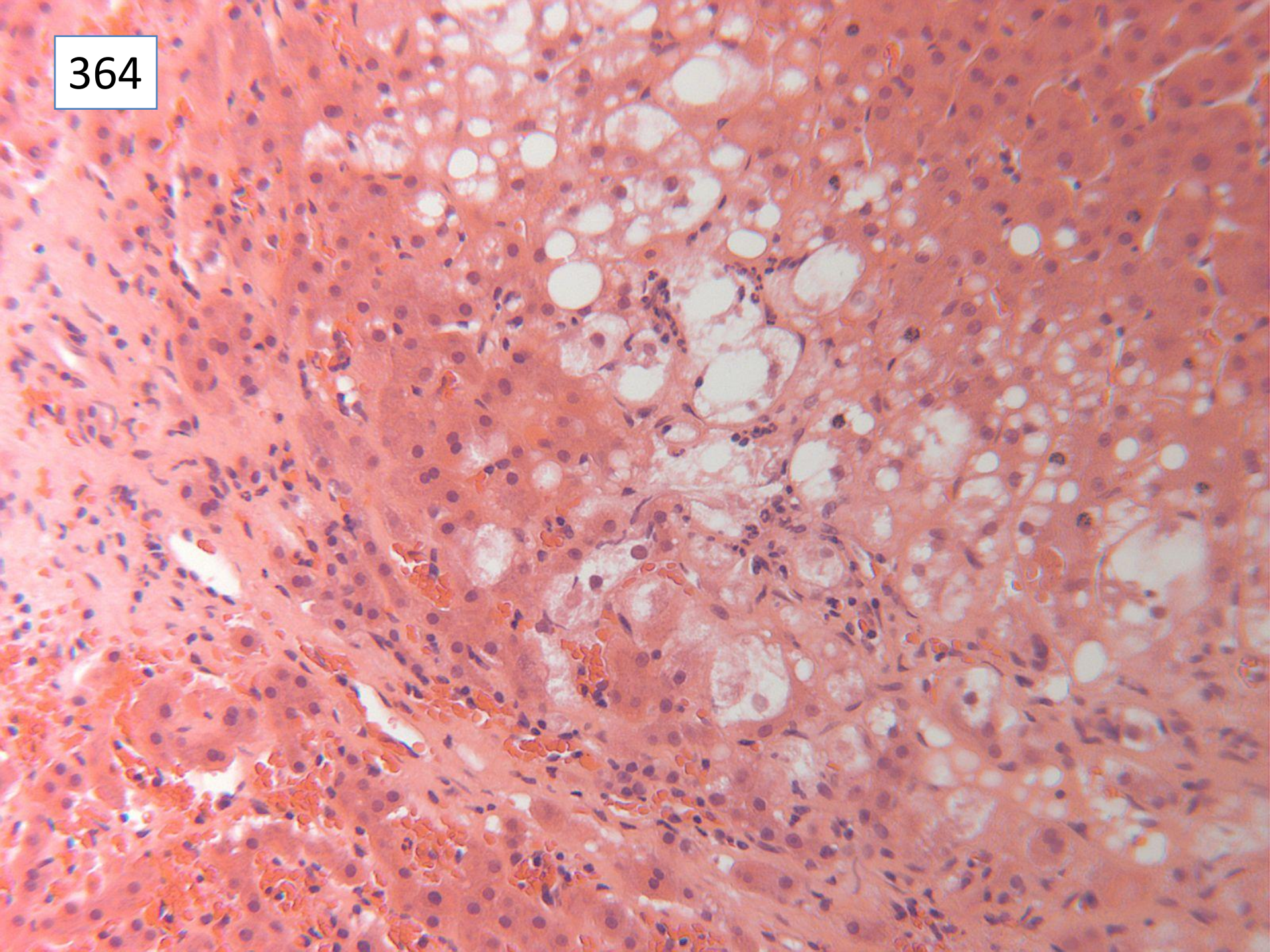
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# Case number 364

## Results

67 Cirrhosis

1 'chronic hepatitis, fibrosis/incipient cirrhosis,

1 'acute liver injury on background of steatohepatitis'; stage not mentioned

63 steatohepatitis in description and/or

51 consistent with NASH

25 alcohol should be excluded

1 alcoholic cirrhosis, no differential

6 favours alcohol, NASH not mentioned as a differential

5 ? aetiology, neither NASH nor alcohol mentioned

## Suggested scoring:

For 10 points, responses should include a diagnosis of cirrhosis and steatohepatitis/consistent with NASH. Lose 5 points if steatohepatitis but no mention of NASH, and score 0 for diagnoses in red.

## Other comments:

3 gave Brunt or Kleiner grade/stage

10 special stains to exclude Iron, A1ATD etc. – often with comment on family history

3 PCs prominent, ? also AIH

1 prominent Mallory-Denk, favours alcohol

## Case number 364

### Discussion on terminology for steatosis –

macrovesicular can have small or large droplets; size of droplets relevant to prognosis in ALD- small droplets tend to do worse. True microvesicular steatosis just looks like pale hepatocytes, needs frozen section fat stain for diagnosis, and is associated with mitochondrial defects; these may be acquired in patches of hepatocytes in chronic liver disease.

### Submitting pathologist's diagnosis:

Cirrhosis and background nodules with steatohepatitis

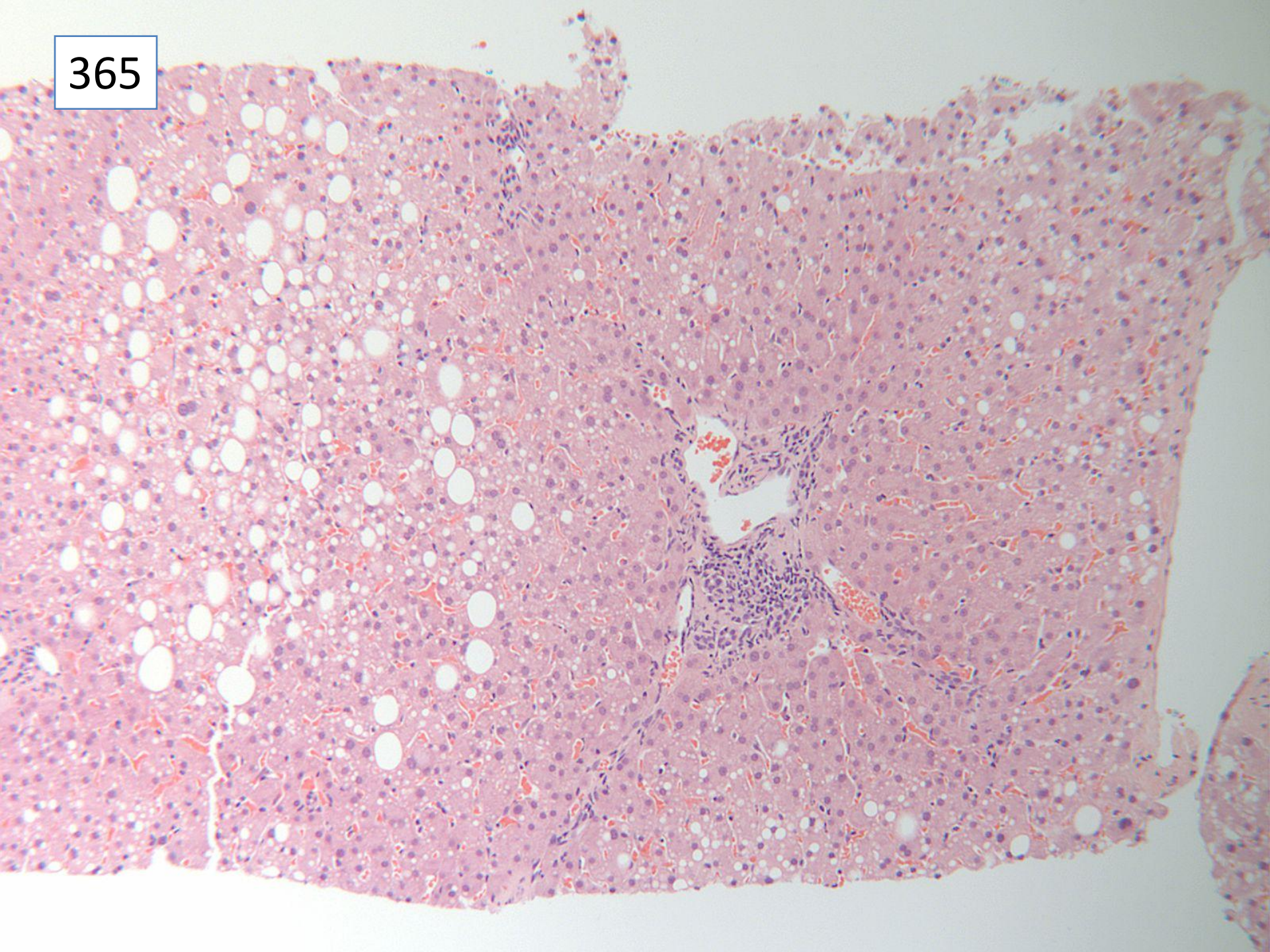
Further clinical information: Clinicians were happy there was no significant alcohol intake and patient would 'fit with' NASH.

## Case number 365

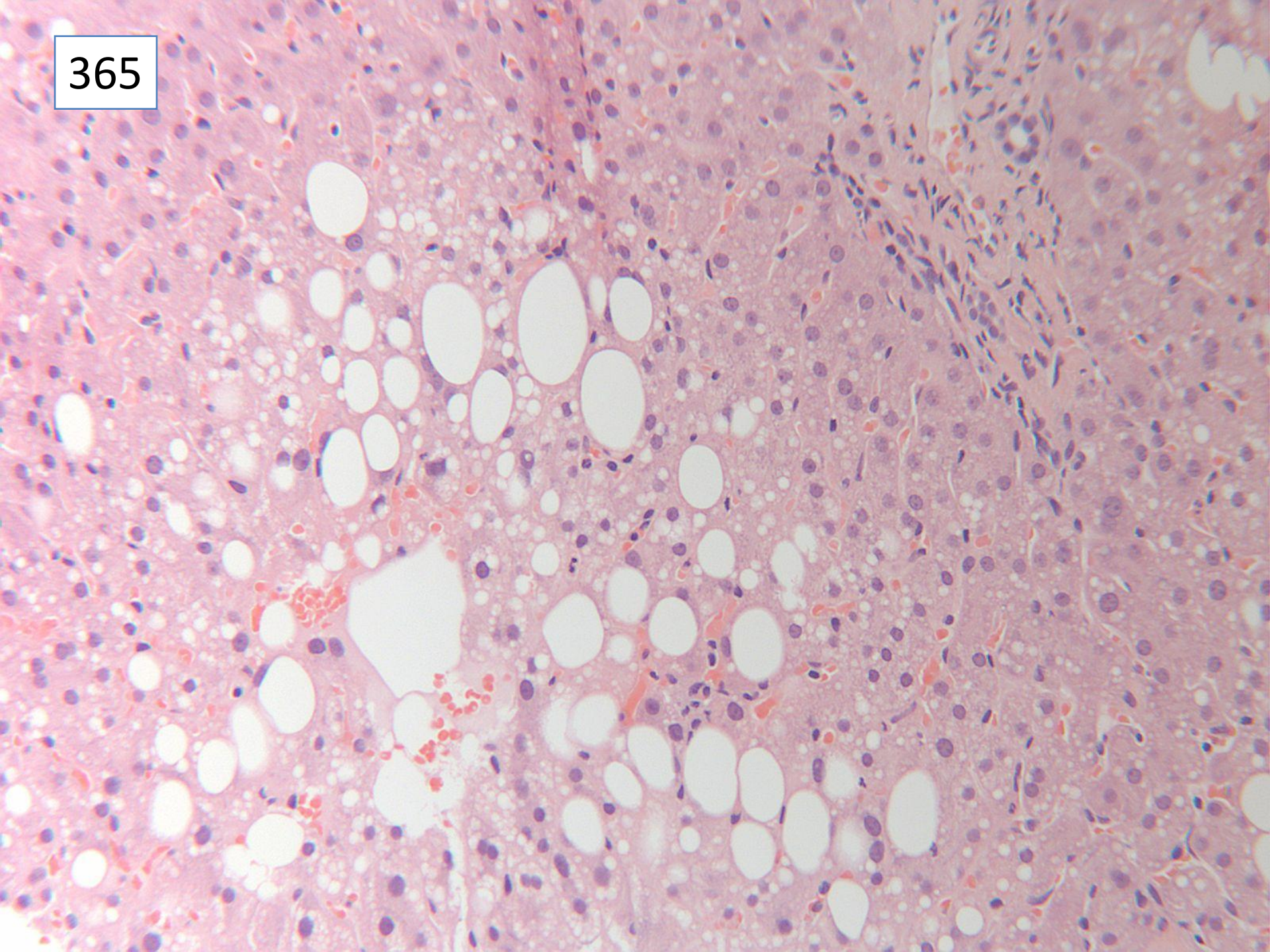
Male 23 years

Ulcerative colitis, deranged LFTs, mildly elevated ALT and GGT, normal bilirubin and alk phos. HBV,HCV neg; AIP normal. Alcohol history and BMI not given. 18G liver biopsy.

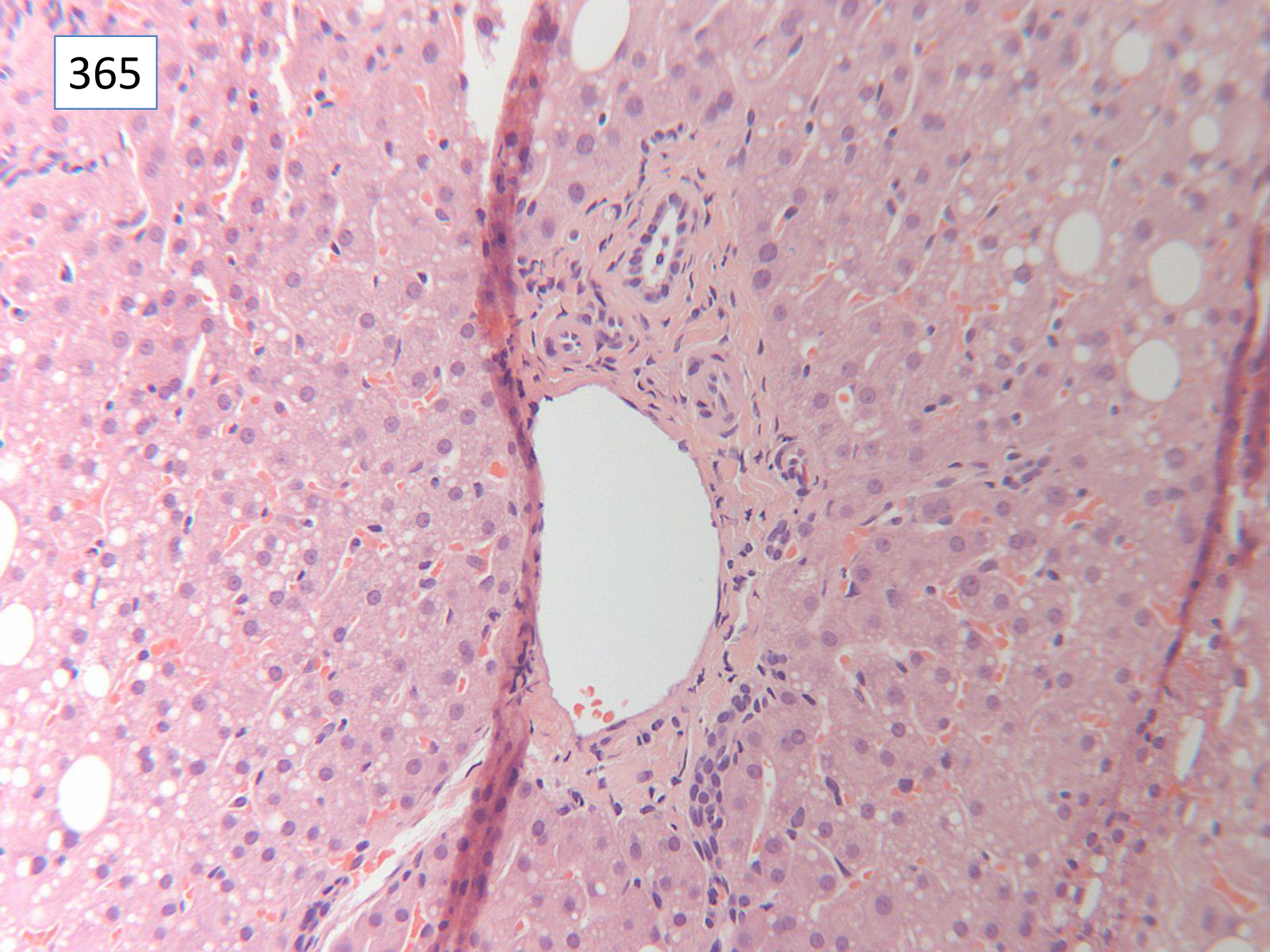
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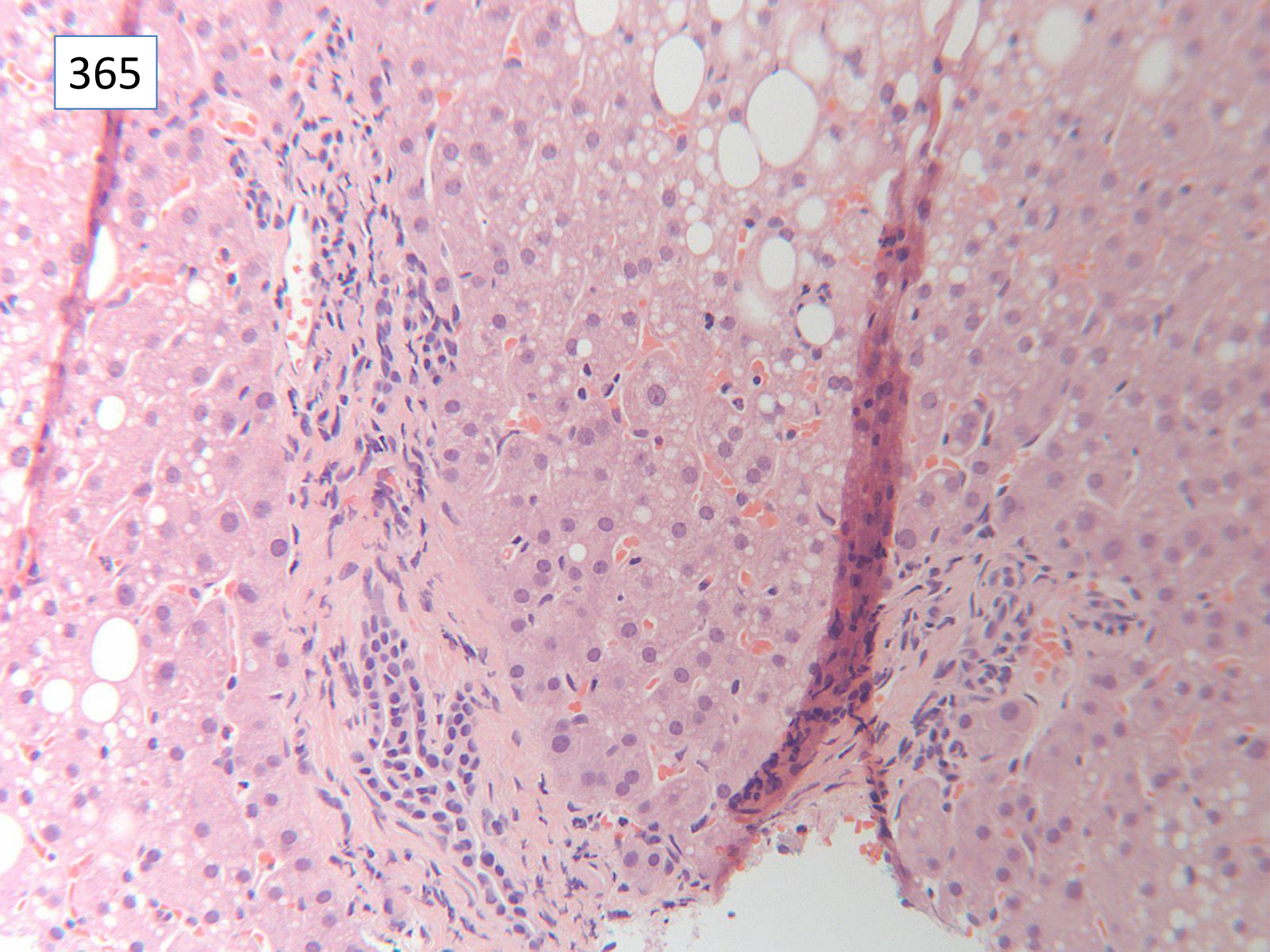
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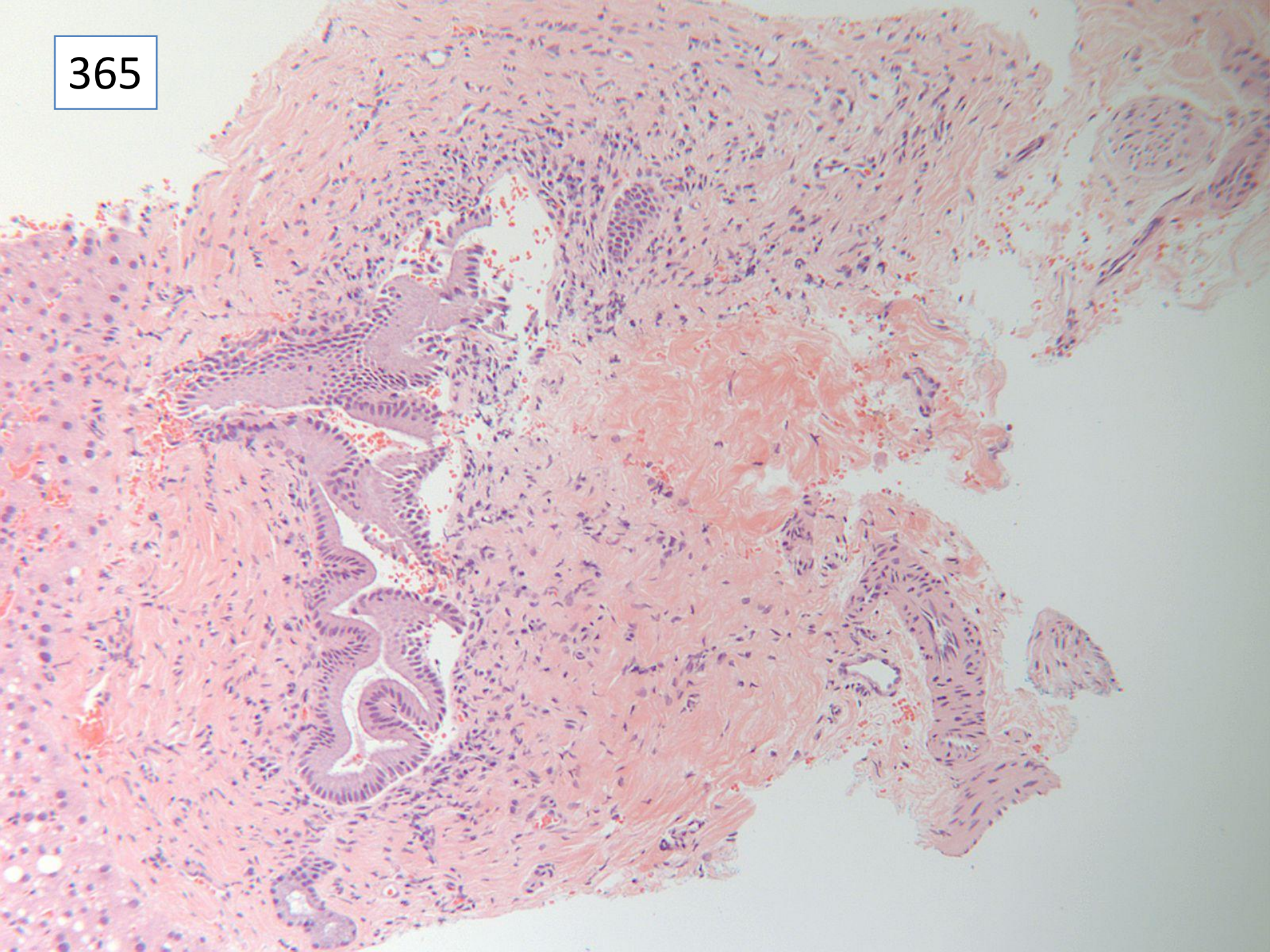
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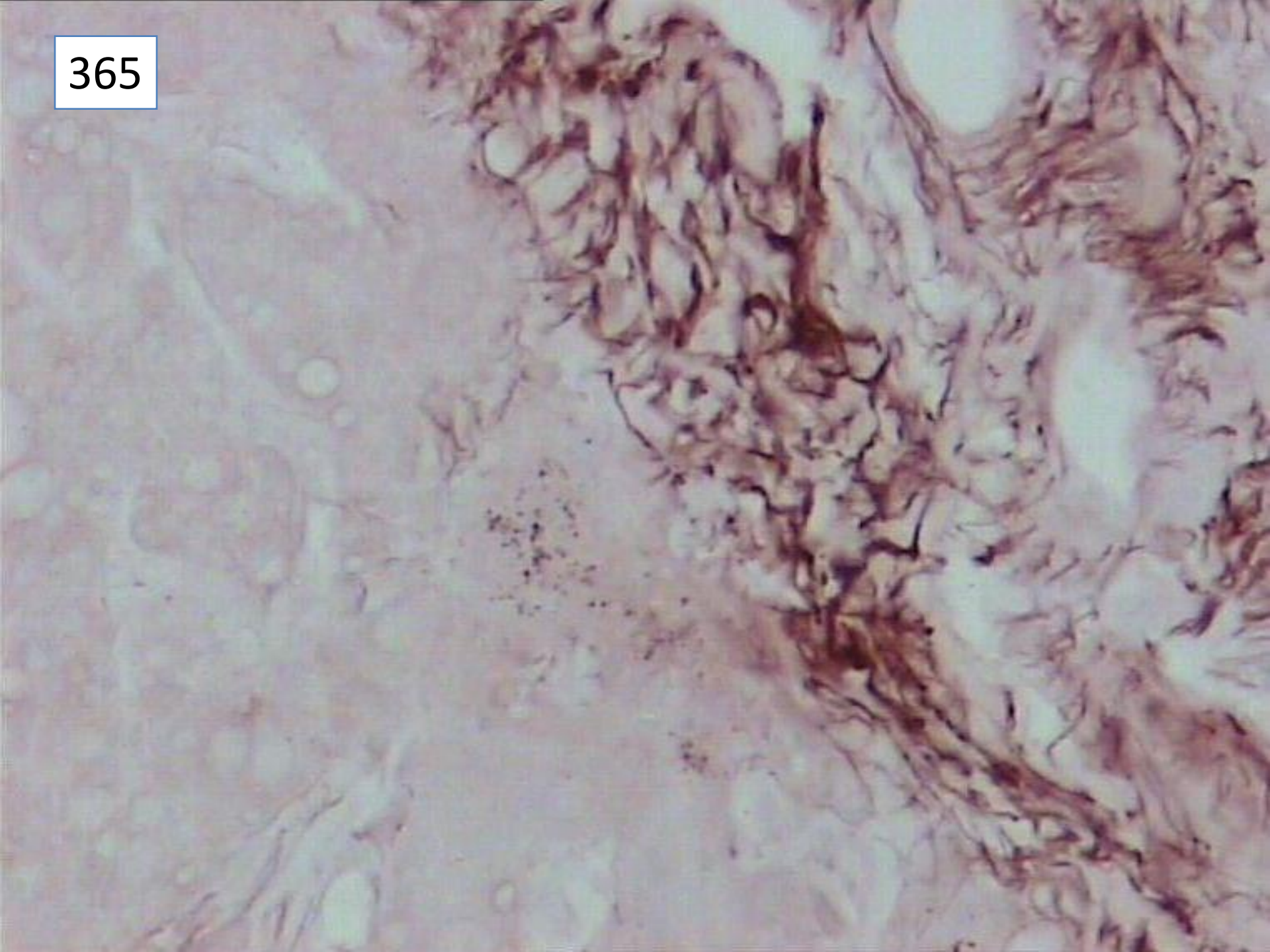
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# Case number 365

## Results:

- 58 steatosis
- 9 steatohepatitis
- 2 steatosis not mentioned
  
- 21 alcohol
- 7 steatosis associated with UC or its treatment
- 4 NASH
- 12 NAFLD
- 4 ? drug related
- 25 no cause for steatosis suggested
  
- 56 biliary features and/or
- 53 investigate for PSC
- 1 'sclerosing cholangitis' (as only clinicopath diagnosis)
- 3 no mention of any biliary features
- 4 no evidence of PSC
- 2 no mention of PSC

## Suggested Scoring:

For 10 points should include steatosis as well as biliary features and/or comment on possibility of PSC.

## Other comments:

- 8 ? Wilson's

## Case number 365

Discussion: the biliary features were very subtle in this case, but the copper associated protein demonstrated by Shikata in early stage disease is a strong indicator of biliary disease. The clinical context is important: young man with UC, so high index of suspicion for PSC.

Original pathologist's diagnosis: Mild steatohepatitis c/w NASH and accumulation of CAP is suspicious of PSC.

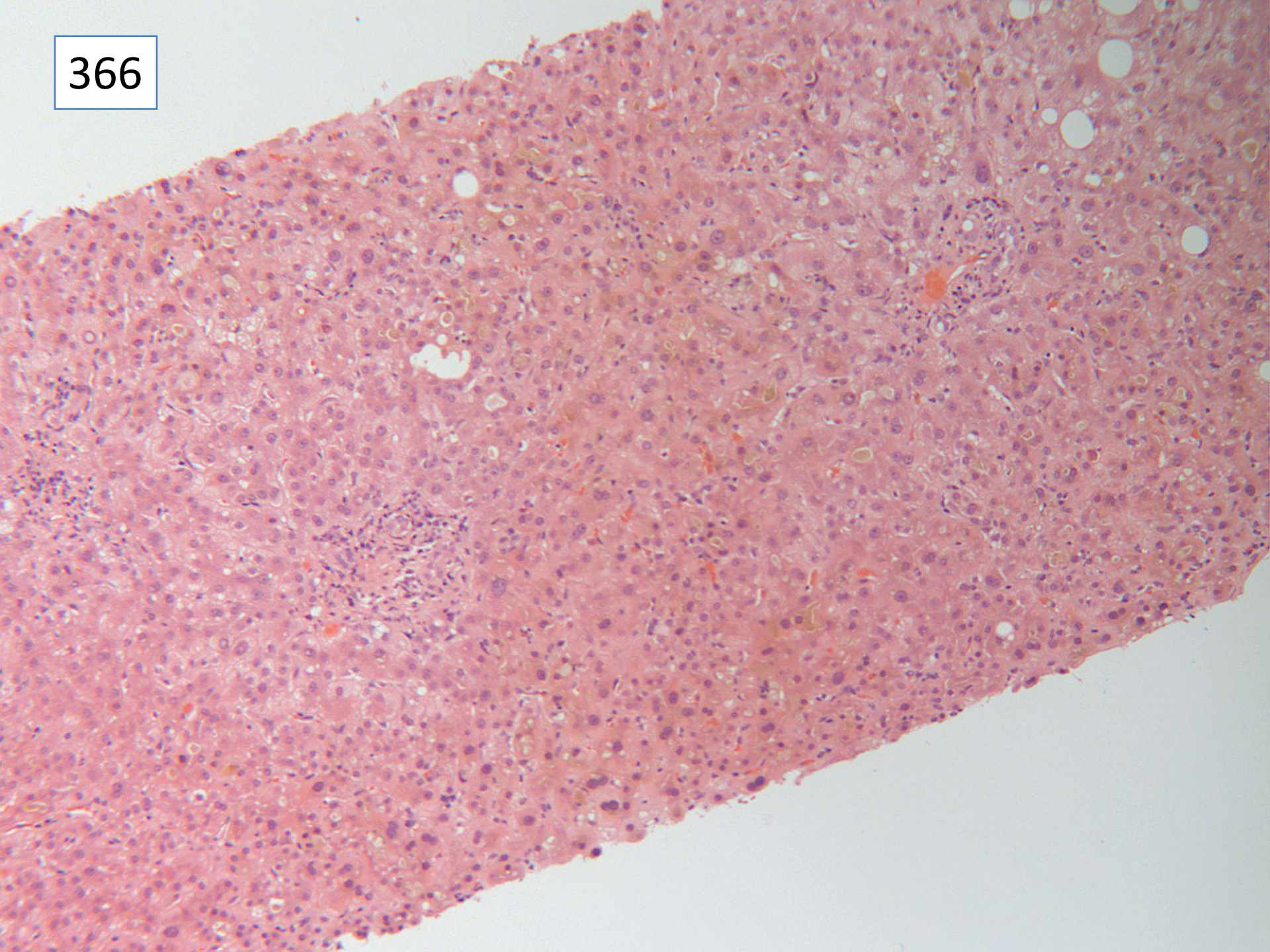
## Case number 366

Male 73 years

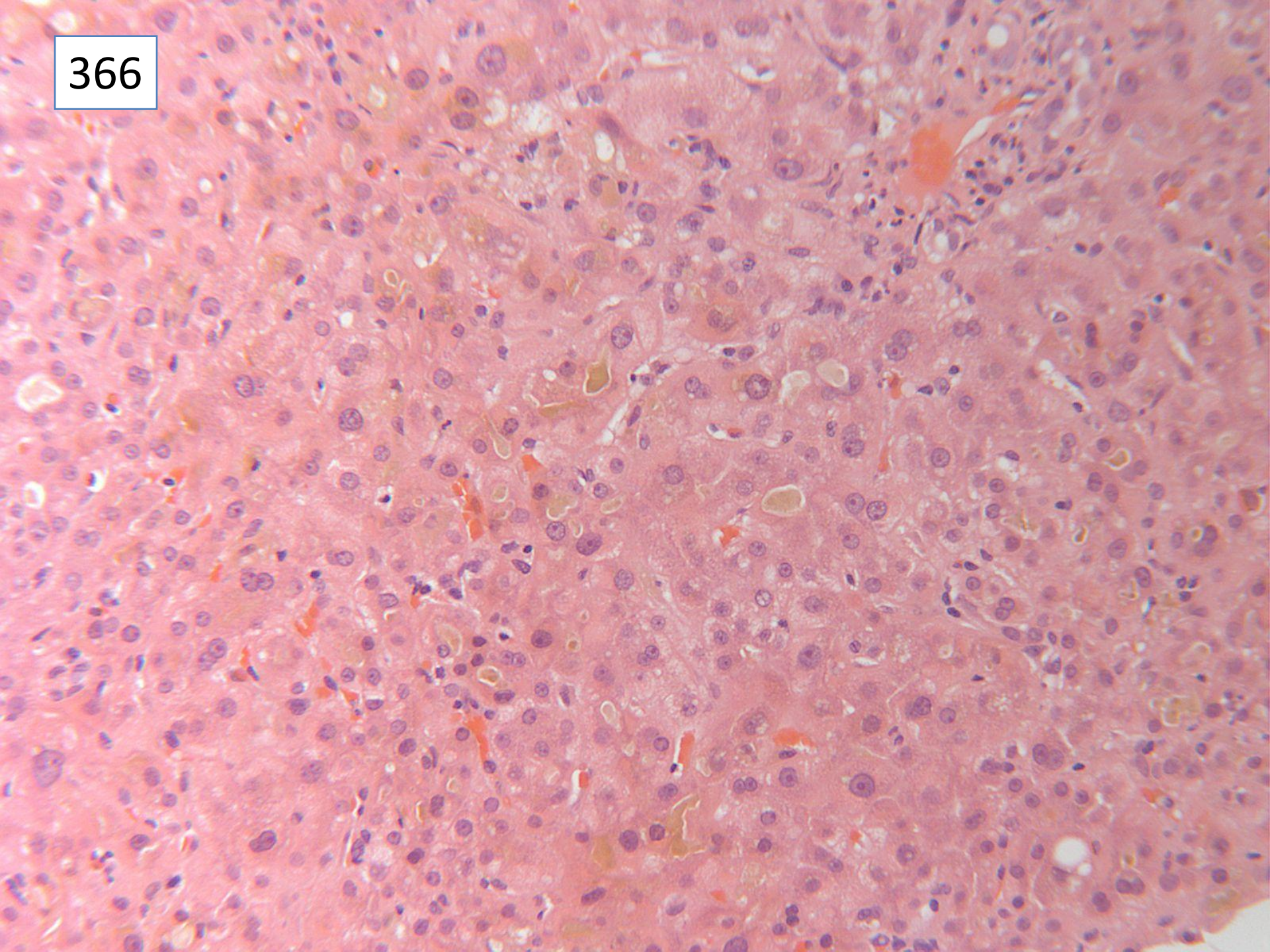
Jaundice, no obstruction on CT. Ferritin >1000.

Liver biopsy, single core 17mm long.

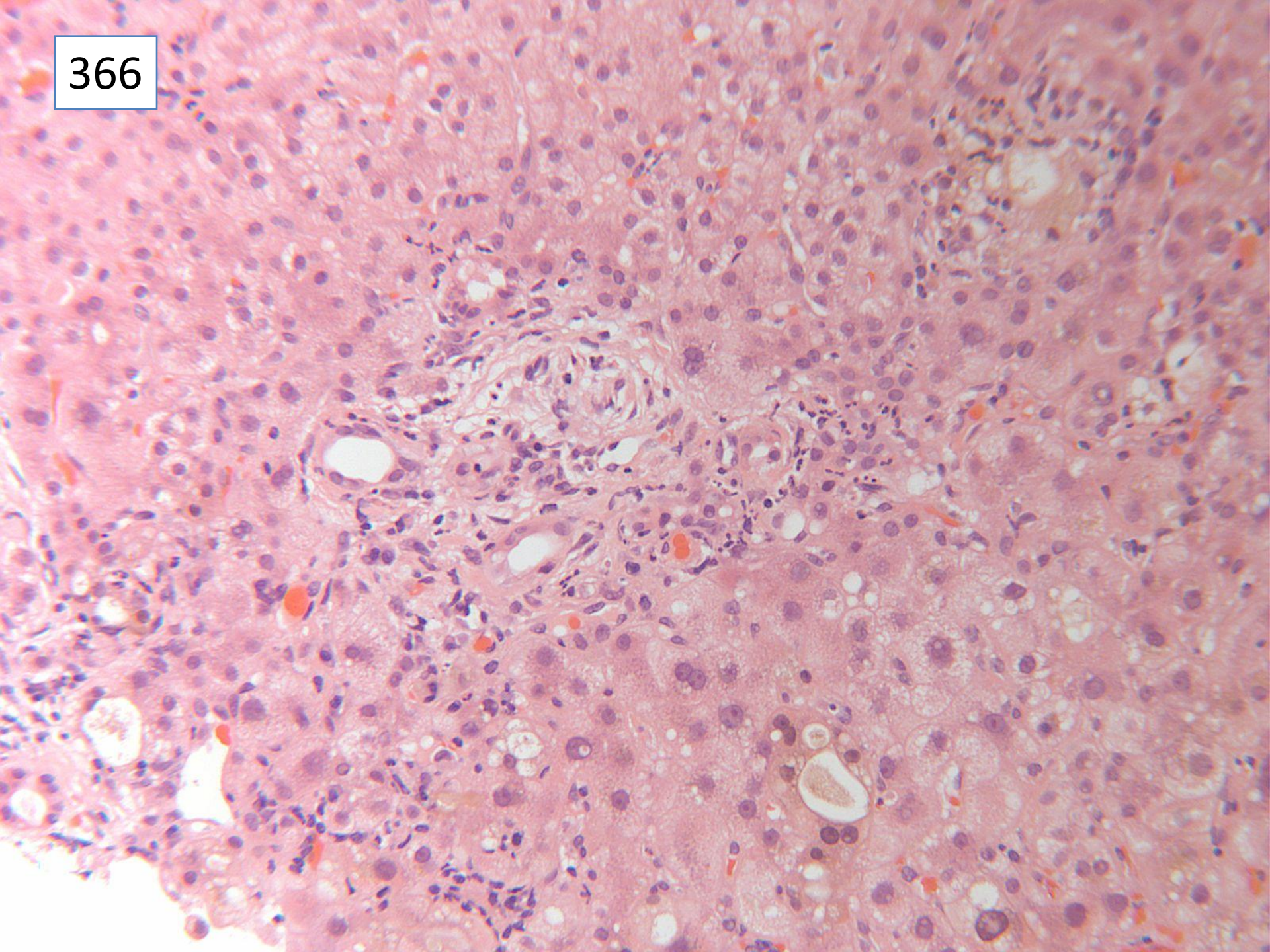
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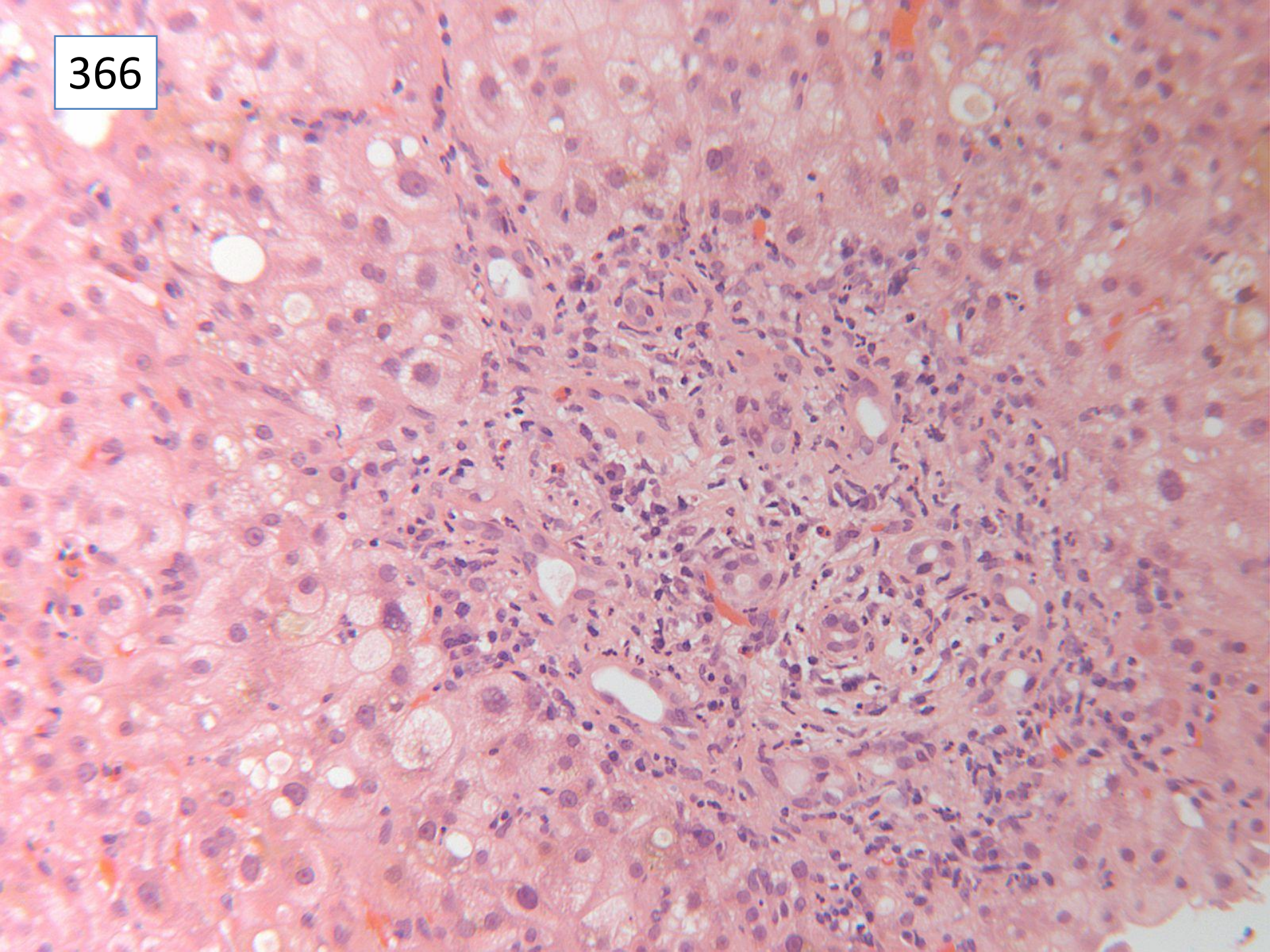
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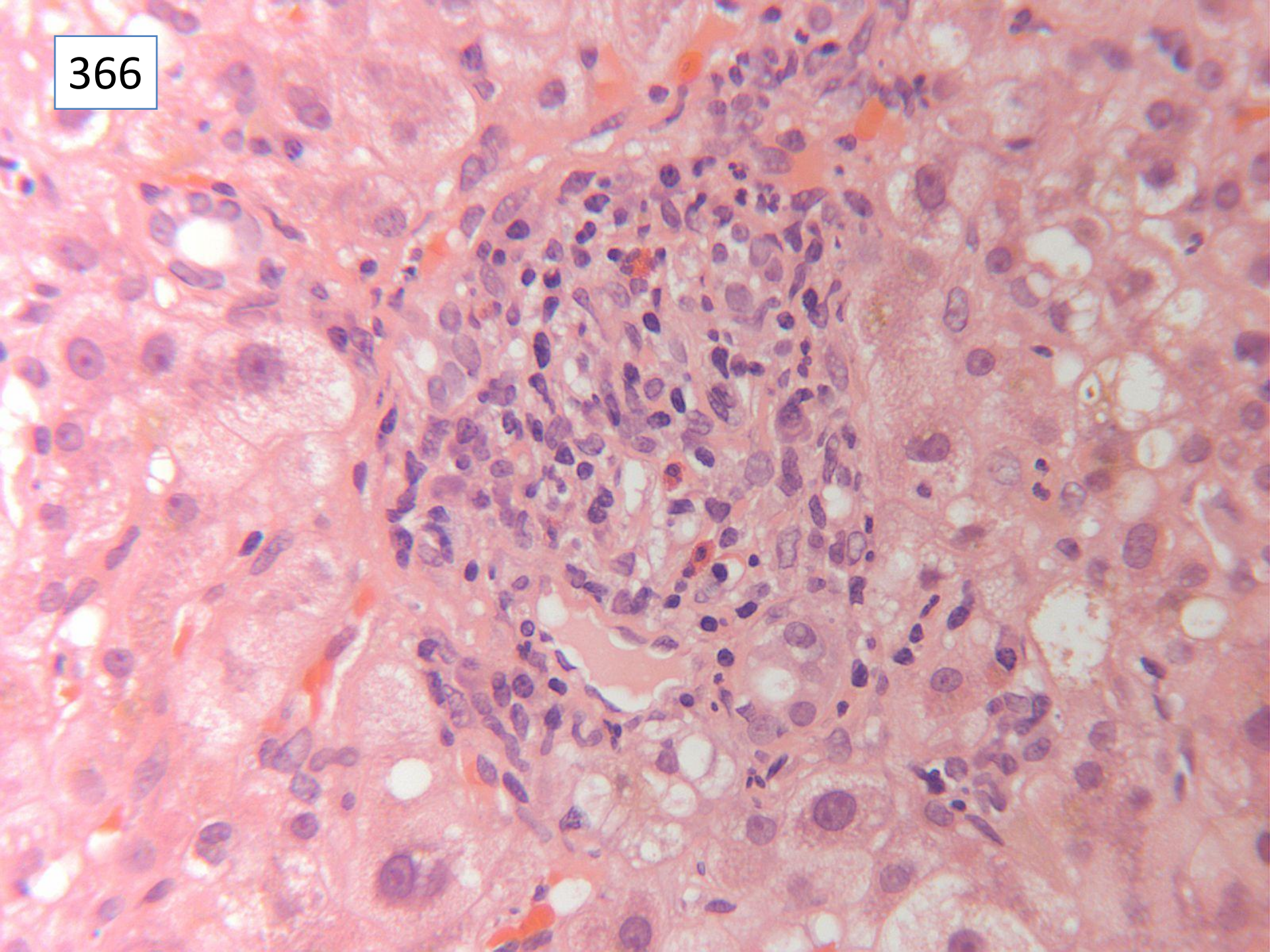
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# Case number 366

## Results:

- 34 cholestasis
- 18 cholestatic hepatitis
- 7 cholangiopathy
- 4 cholangitis
- 1 cholestasis not mentioned

## Aetiology:

- 16 differential diagnosis without obvious favourite
- 46 Probably drug related:
  - 6 drugs as only cause mentioned
  - 24 drugs as most likely cause
- 6 no mention of drugs
  
- 21 probably obstructive
  - 8 large bile duct obstruction as only cause mentioned
  - 13 LBDO as most likely

## Examples of individual responses:

- 'chronic hepatitis and siderosis – genetics for haemochromatosis'
- 'cholestasis with portal tract plasma cells, diagnosis AIH'
- 'acute hepatitis, cholestasis, eosinophils, most likely drug related'
- 'cholestatic granulomatous hepatitis with cholangitis, ?PBC or drug'
- 'cholestasis, cholangitis', NOS

## Suggested scoring:

For 10 points should include cholestasis in some form. Deduct 5 points for responses that do not include any possibility of drug related cholestasis - this was modified during discussion at the meeting – see next slide.

## Other comments:

- 20 comment on need for Perl's stain in view of history of high ferritin

## Case number 366

Discussion during meeting: difficult case with no clear diagnosis.

The appropriate diagnosis would be cholestasis with drugs or obstruction as most likely causes. Agreed to include for scoring with penalty of 5 points for responses that clearly implied the cause of cholestasis was drugs or obstruction without a differential – wording of responses reviewed by organiser to assign scores.

Original pathologist's diagnosis: severe cholestasis with features favouring LBDO mild siderosis. Conspicuous eosinophils ?parasitic infestation. Further clinical information – no clear drug history; history of pancreatic disease.

## Case number 367

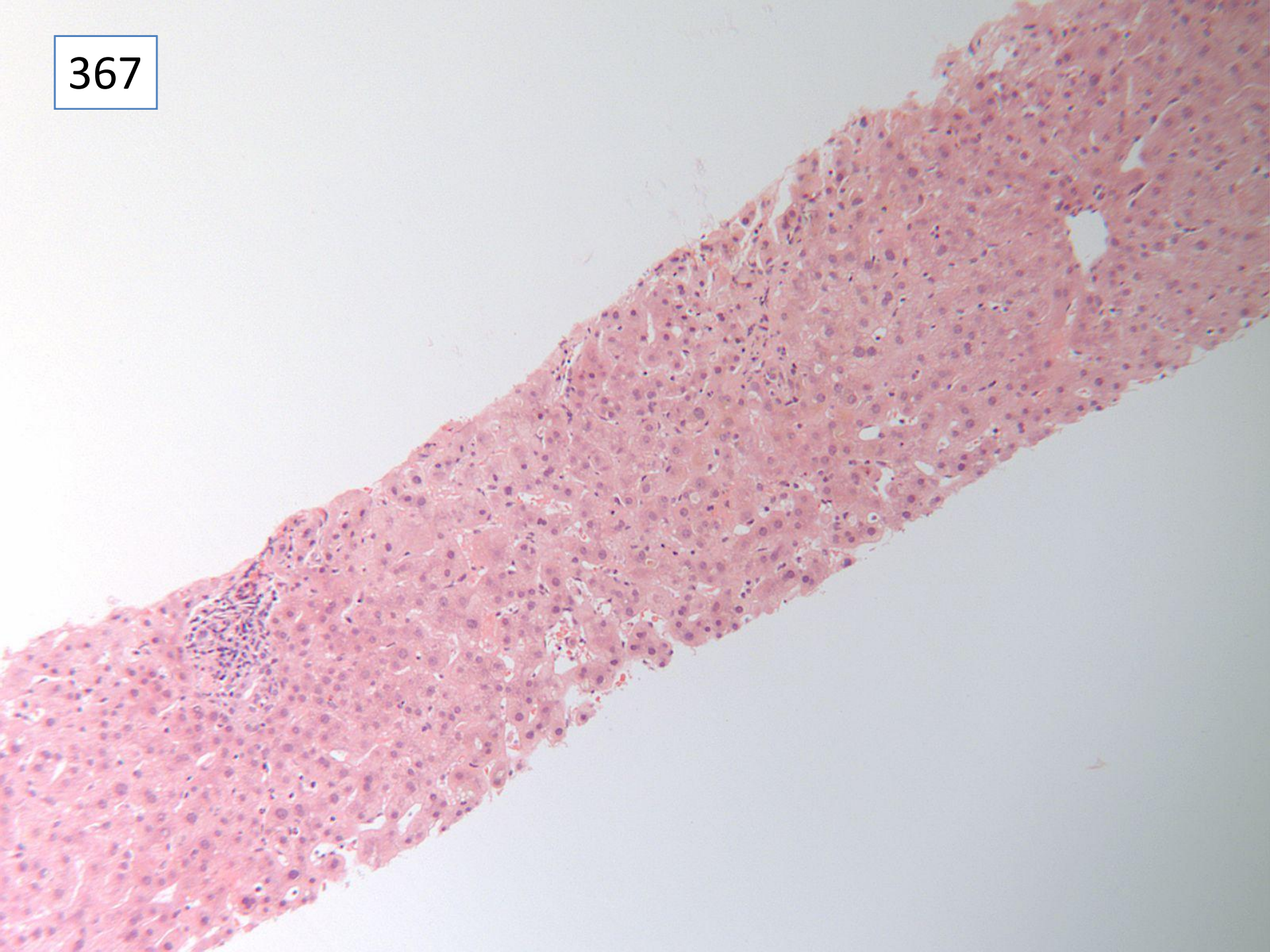
Female 78 years

Painless jaundice, deranged LFTs, normal liver screen.

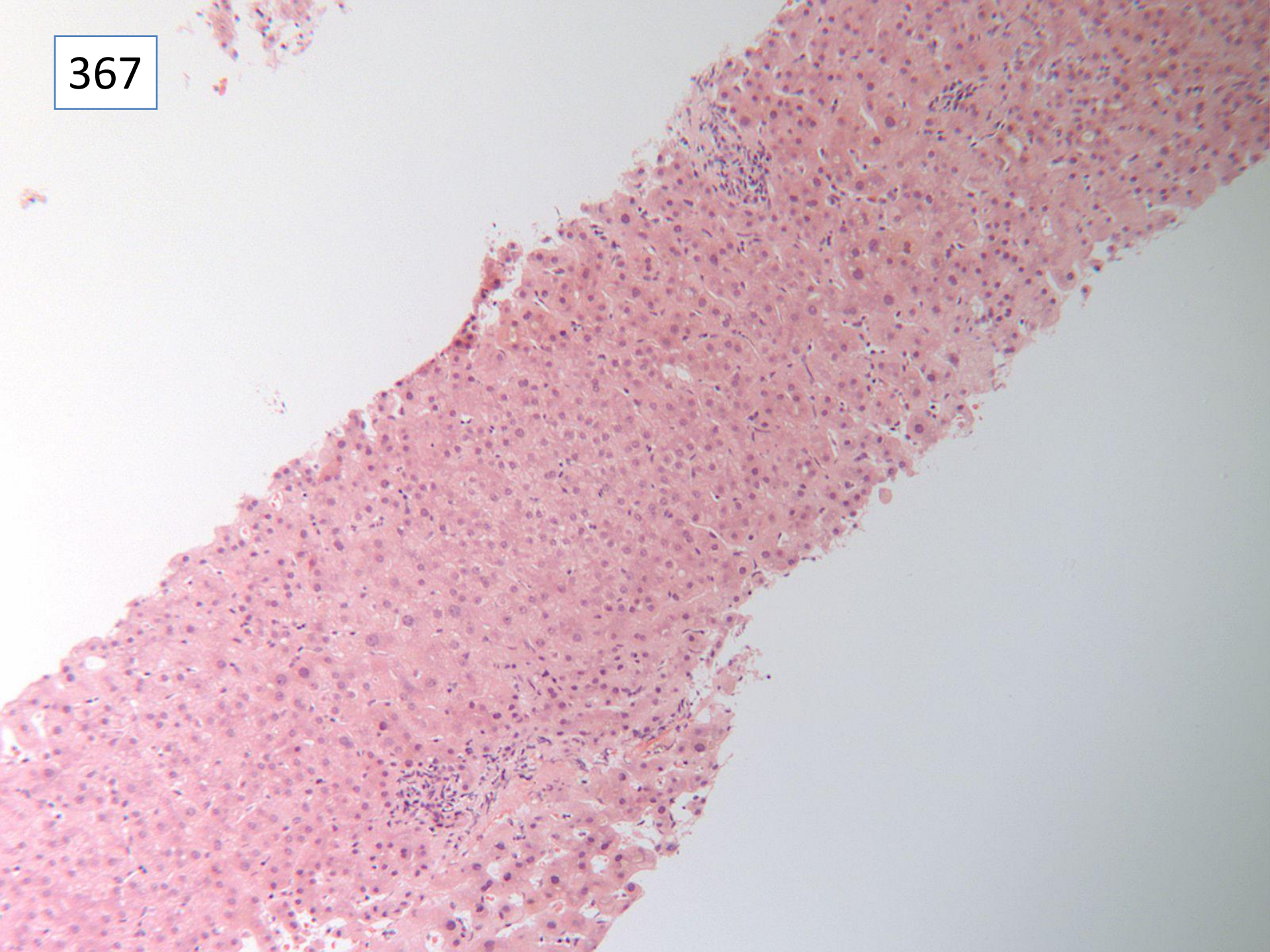
?duct dilatation on CT, not confirmed on ERCP.

Recent ear infection. ALT 503, BR 88, ALP 260. 19G liver biopsy (trans-jugular), 4 cores up to 9mm long.

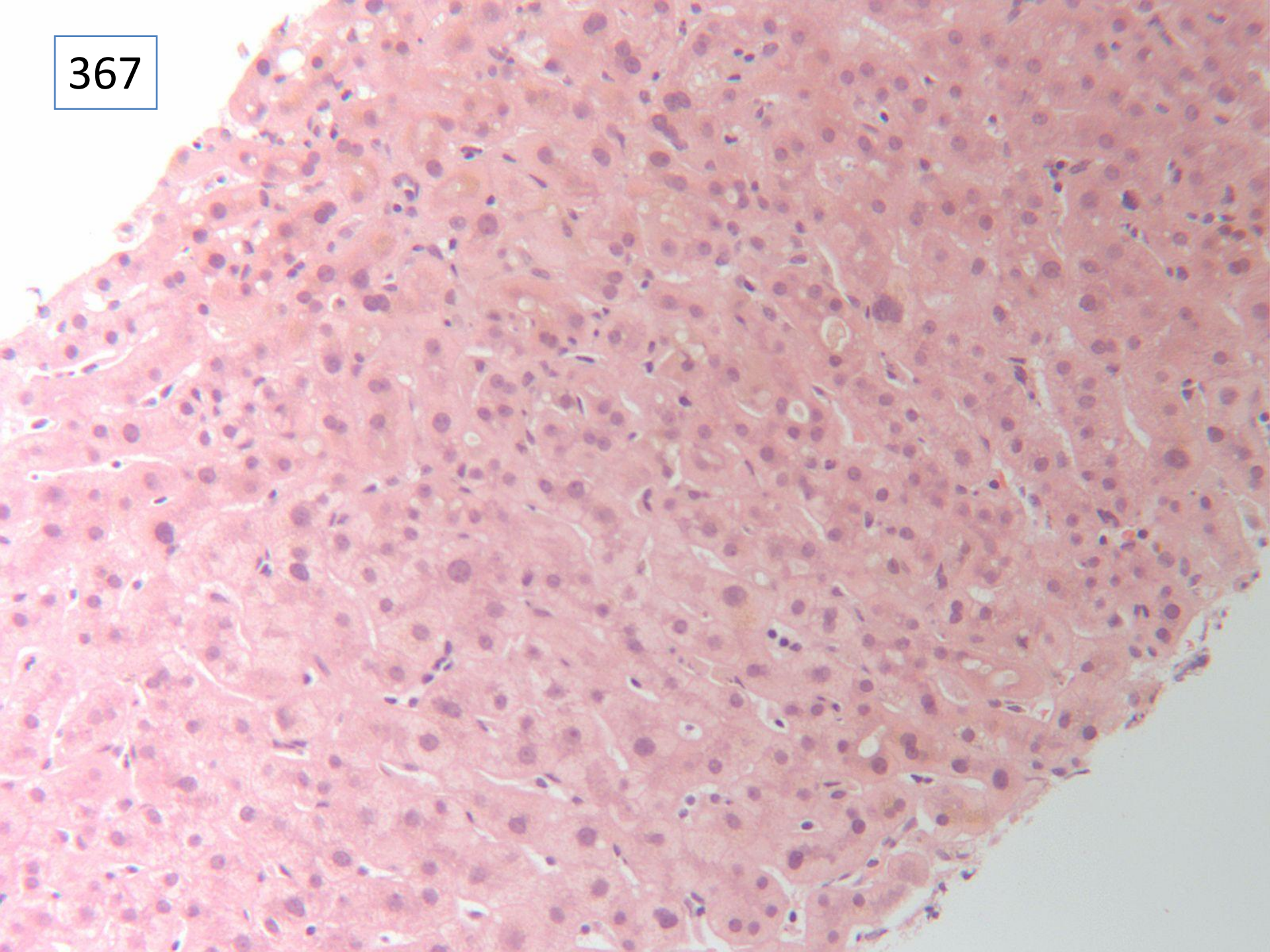
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# Case number 367

## Results:

- 41 Cholestasis
- 19 Cholestatic hepatitis
- 2 cholangiopathy
- 1 pigment- looks like bile
- 2 cholestasis not mentioned
  
- 44 Drugs as only cause mentioned
- 11 drugs as favoured cause
- 8 differential includes drugs
- 4 drugs not mentioned
  
- 2 obstruction as only cause mentioned
- 13 obstruction included in differential diagnosis
- 1 Chronic hepatitis, cholestasis and bile duct damage: PSC/PBC (unqualified)

## Suggested Scoring:

For 10 points should include cholestasis in some form. Deduct 5 points for responses that do not include any possibility of drug related cholestasis

## Other comments:

- 8 Shikata/comment on need to exclude chronic cholestasis
- 6 exclude other hepatitis – AIH, viral, etc.

## Case number 367

Discussion at meeting: Similar issues to the last case, and to be scored in the same way.

This time a clear history of recent infection'

Submitting pathologist's diagnosis: cholestatic hepatitis secondary to drug (recent augmentin for ear infection)

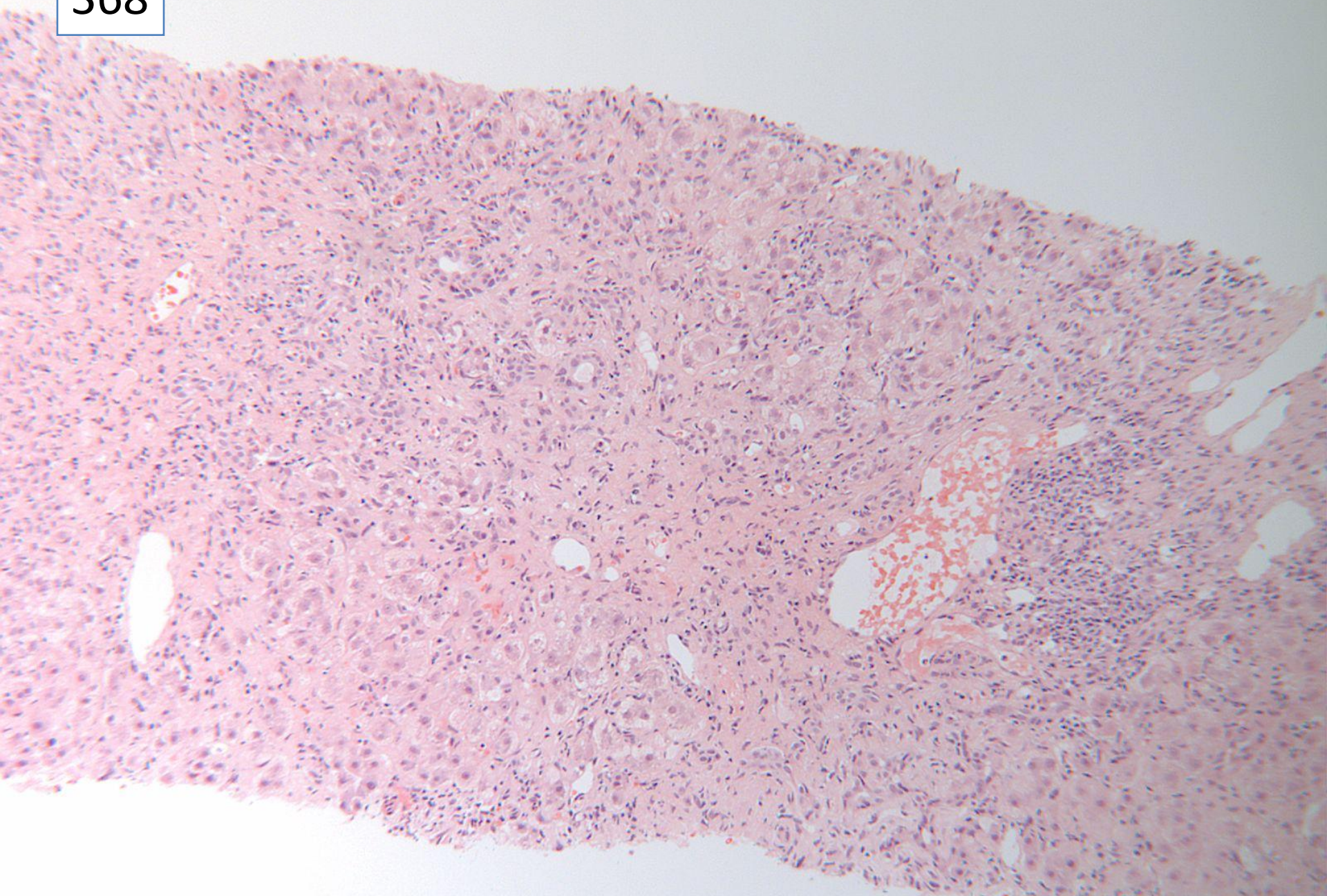
## Case number 368

Male 23 years

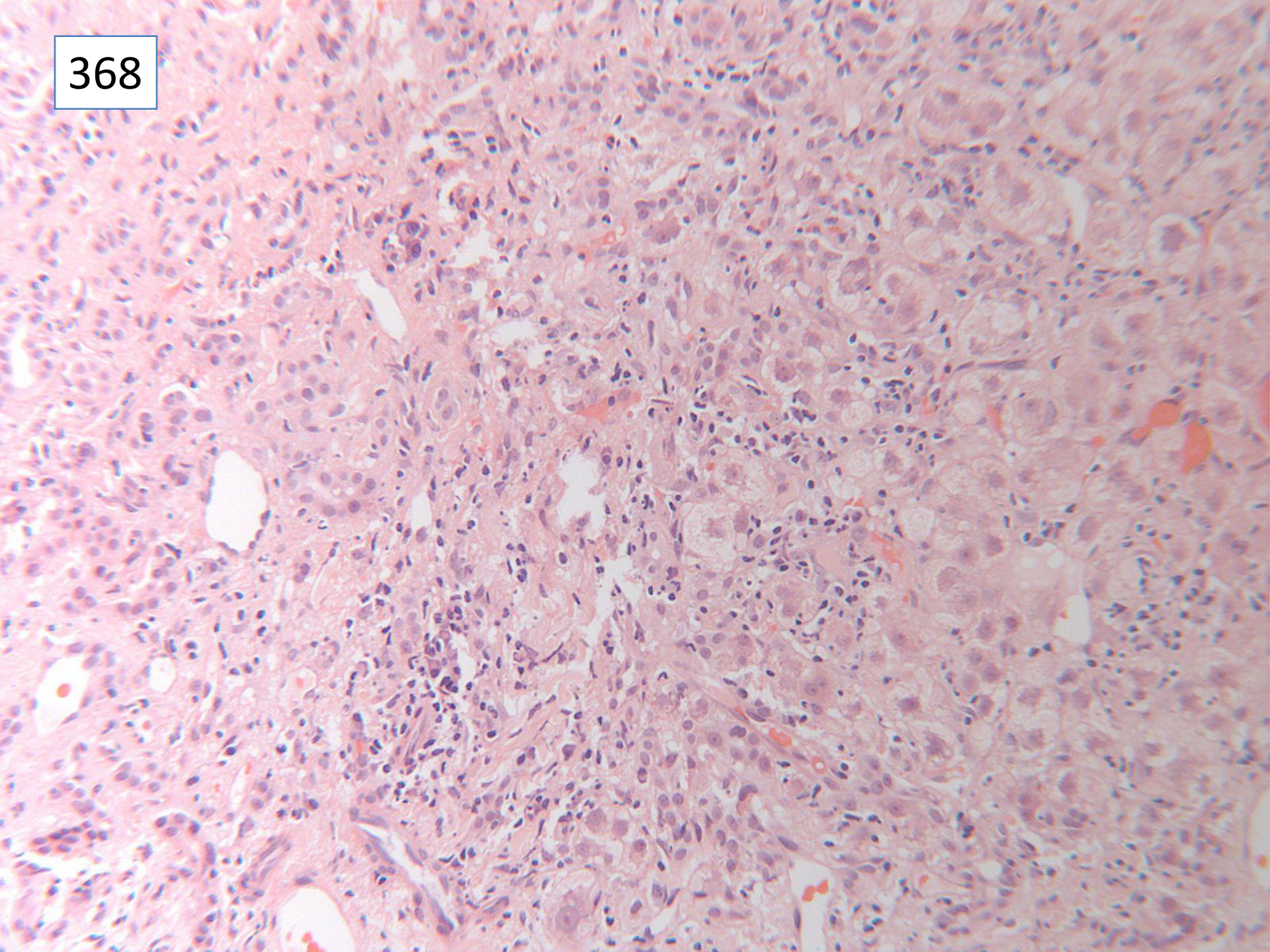
ALT 500. ?Drug. ?EtOH

Liver biopsy

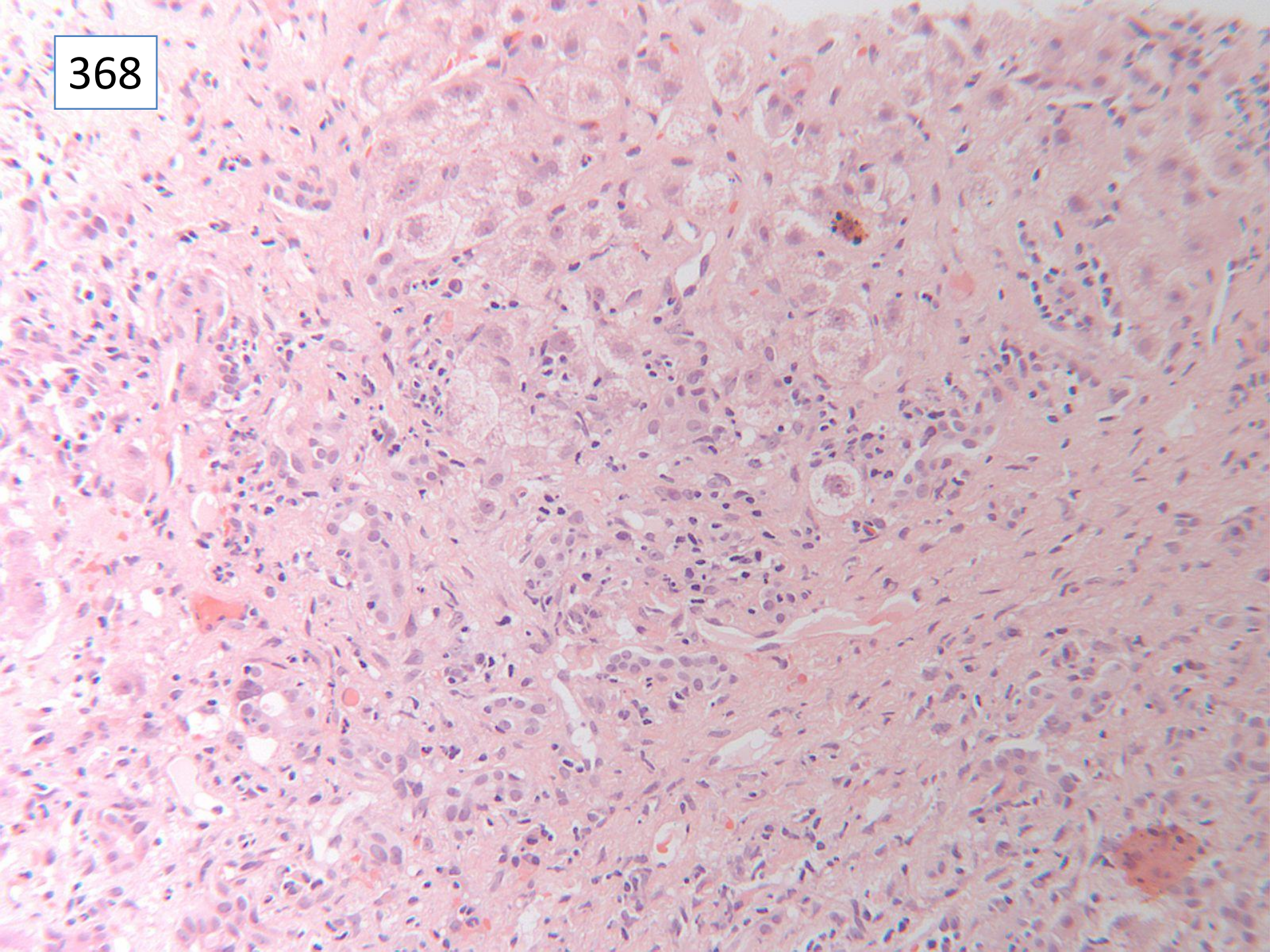
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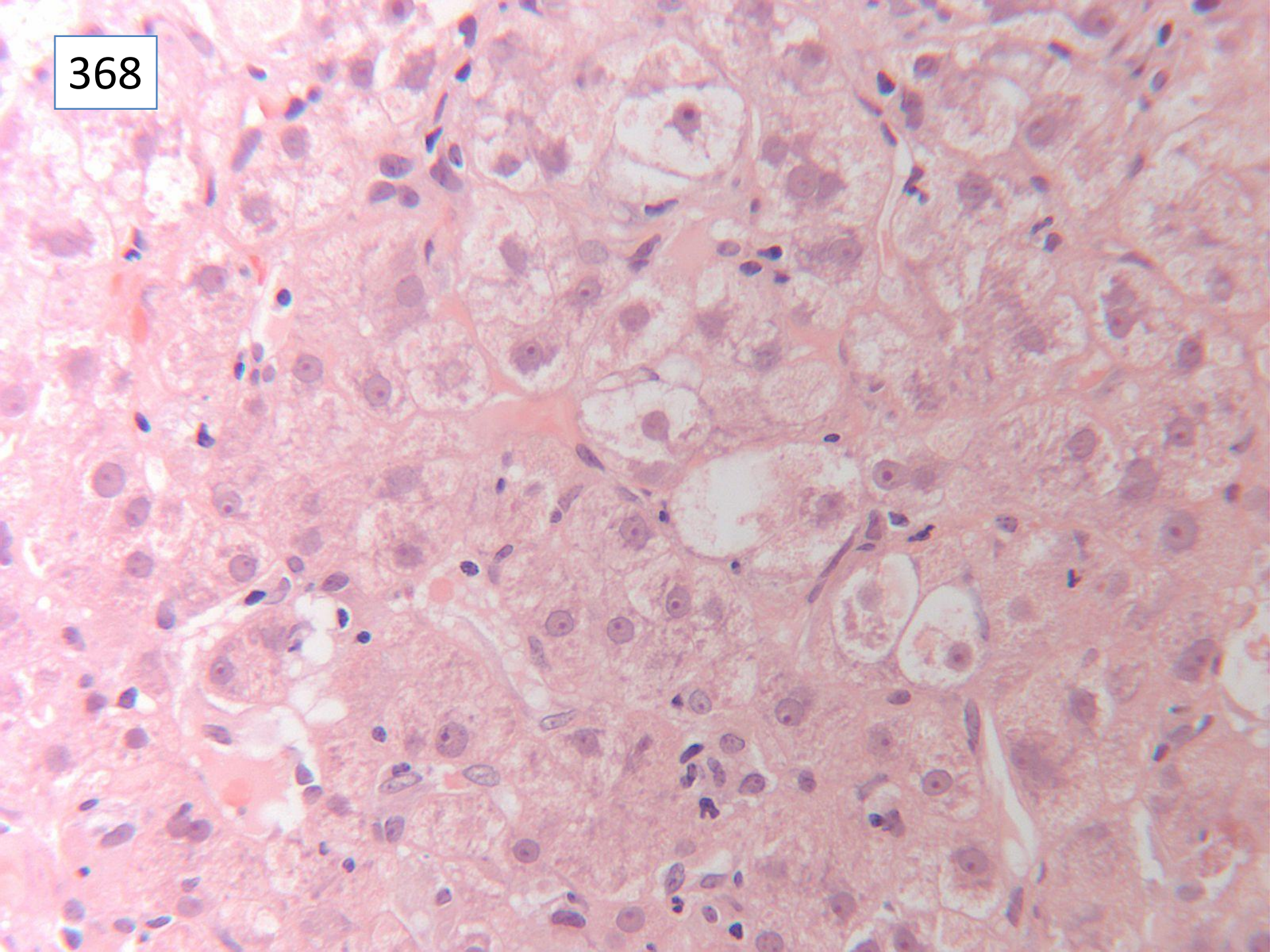
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# Case number 368

## Results:

- 33 Probable/definite cirrhosis
  - Of which 9 also steatohepatitis
- 5 acute on chronic hepatitis/active cirrhosis
- 1 cirrhosis plus superimposed acute collapse
- 5 cirrhosis OR acute hepatitis with collapse – can't tell without special stains
- 20 acute hepatitis with bridging/confluent necrosis
- 1 acute hepatitis, bridging necrosis not mentioned
- 1 massive necrosis, alcoholic liver disease
- 1 cholestatic hepatitis with wide differential
- 1 active chronic inflammation, plasma cells, suspicious for AIH
  
- 1 acute alcoholic hepatitis
- 23 alcoholic liver disease
- 11 alcohol included in differential
- 8 not alcoholic liver disease
- 18 acute hepatitis – differential includes drugs/virus/AIH
- 3 acute, due to drugs
- 8 chronic, due to drugs/viral
- 2 AIH with differential
- 1 AIH or PBC
- 5 exclude Wilson's

## Suggested scoring:

Unsuitable for scoring – no consensus.

Interesting split between alcoholic liver disease/cirrhosis and acute hepatitis/confluent necrosis.

## Follow up info?

## Case number 368

Discussion during meeting: unsuitable for scoring, but of great educational value. Responses split between alcoholic liver disease and drug-related hepatitis with necrosis. Depends on pattern recognition of process, when there are many histological features, which are most important? Among inflammation, fibrosis and hepatocyte loss, the ballooned hepatocytes with Mallory bodies point to alcoholic hepatitis.

### Follow up information:

His clinical diagnosis is cirrhosis with varices secondary to alcohol.

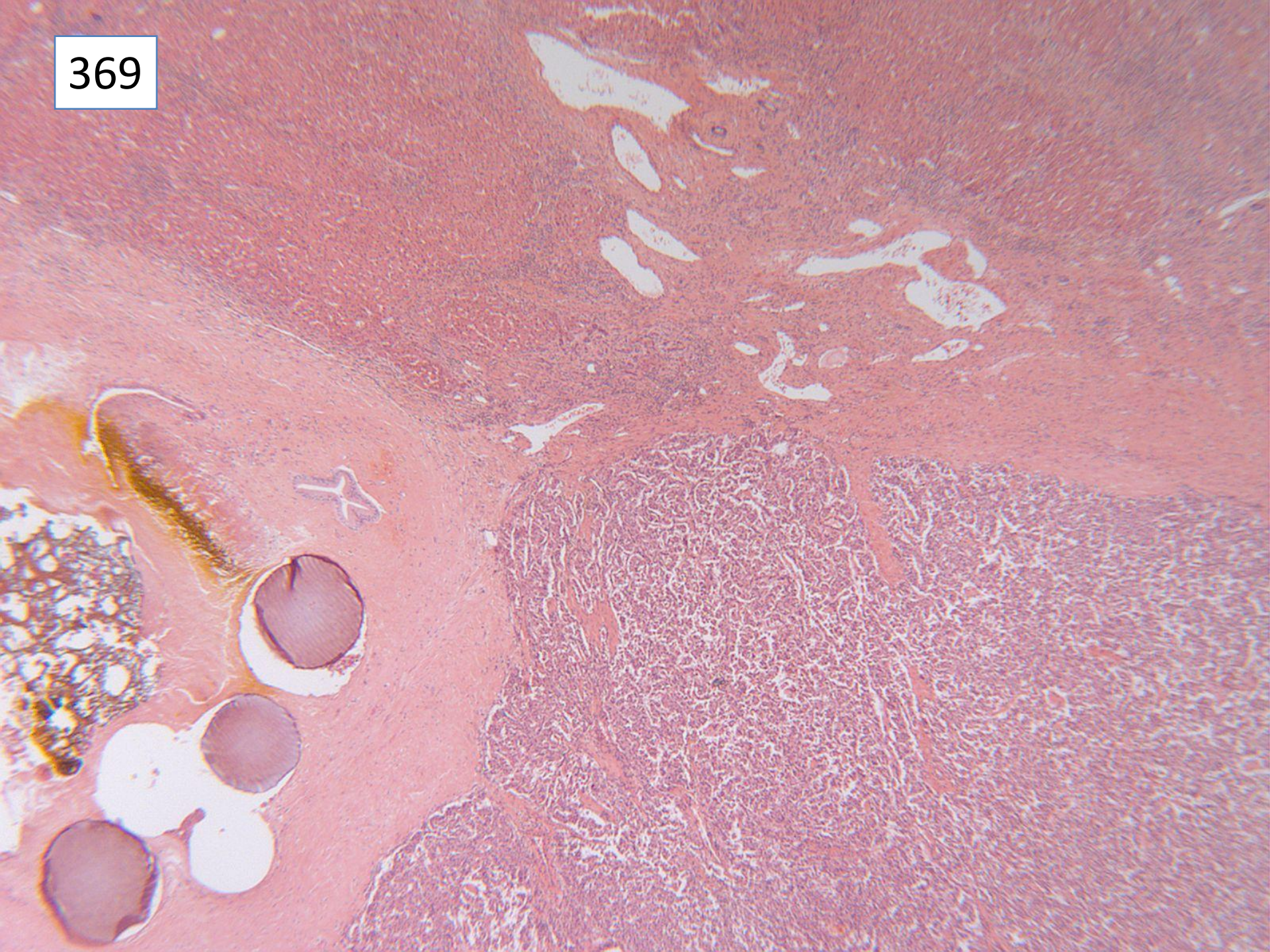
Seen once in 2010 for a transplant opinion but it was decided he was too well, and he is asymptomatic and well according to his last clinic letter here.

## Case number 369

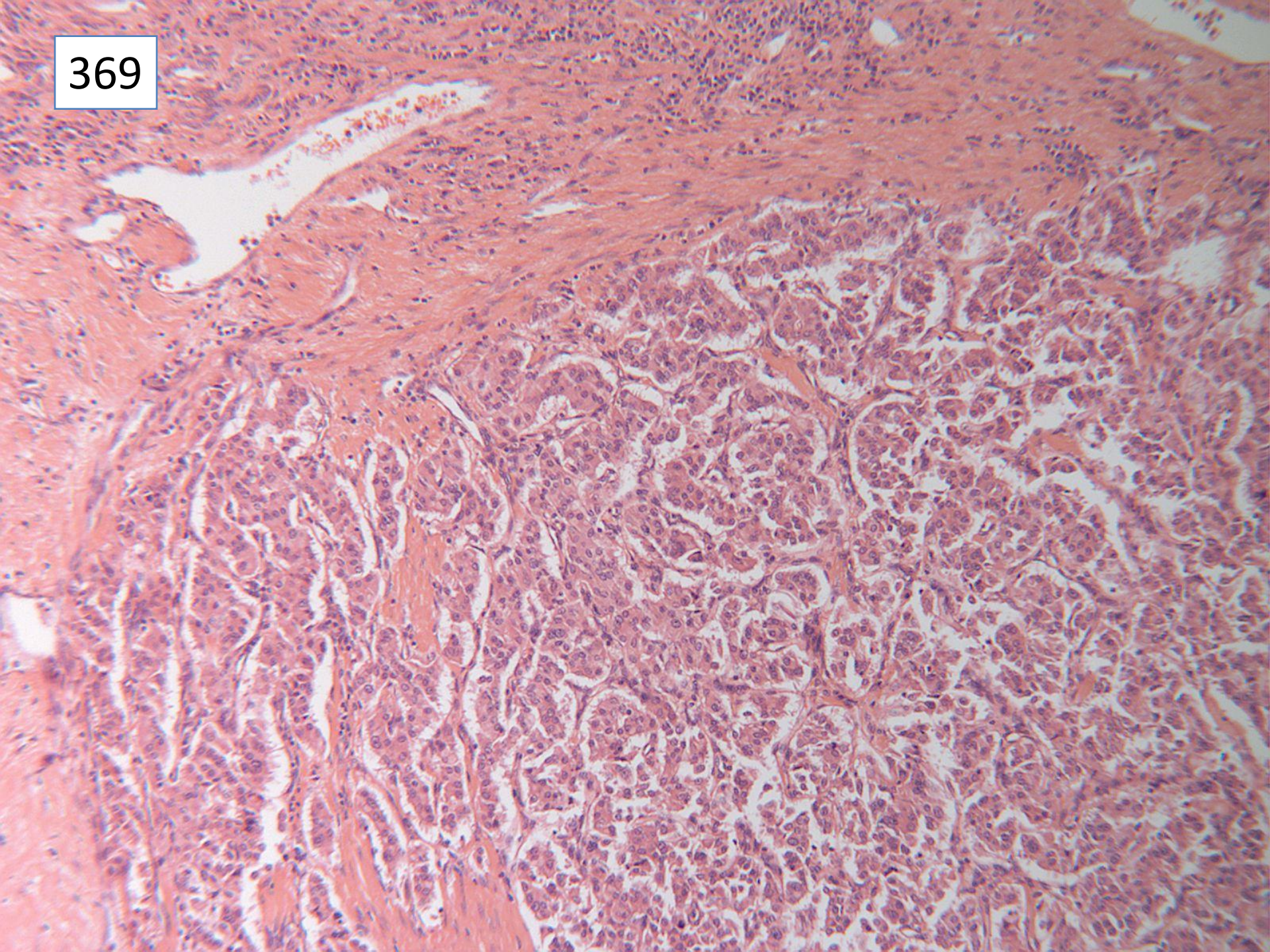
Male 59 years

Left trisectionectomy post TACE x 5. Presumed HCC.  
Left trisectionectomy - 1967g, measures 21.5cm transversely, 18cm high and 12cm antero-posterior.  
Large subcapsular tumour in segment IV. 13cm maximum dimension with extensive haemorrhagic and coagulative necrosis.

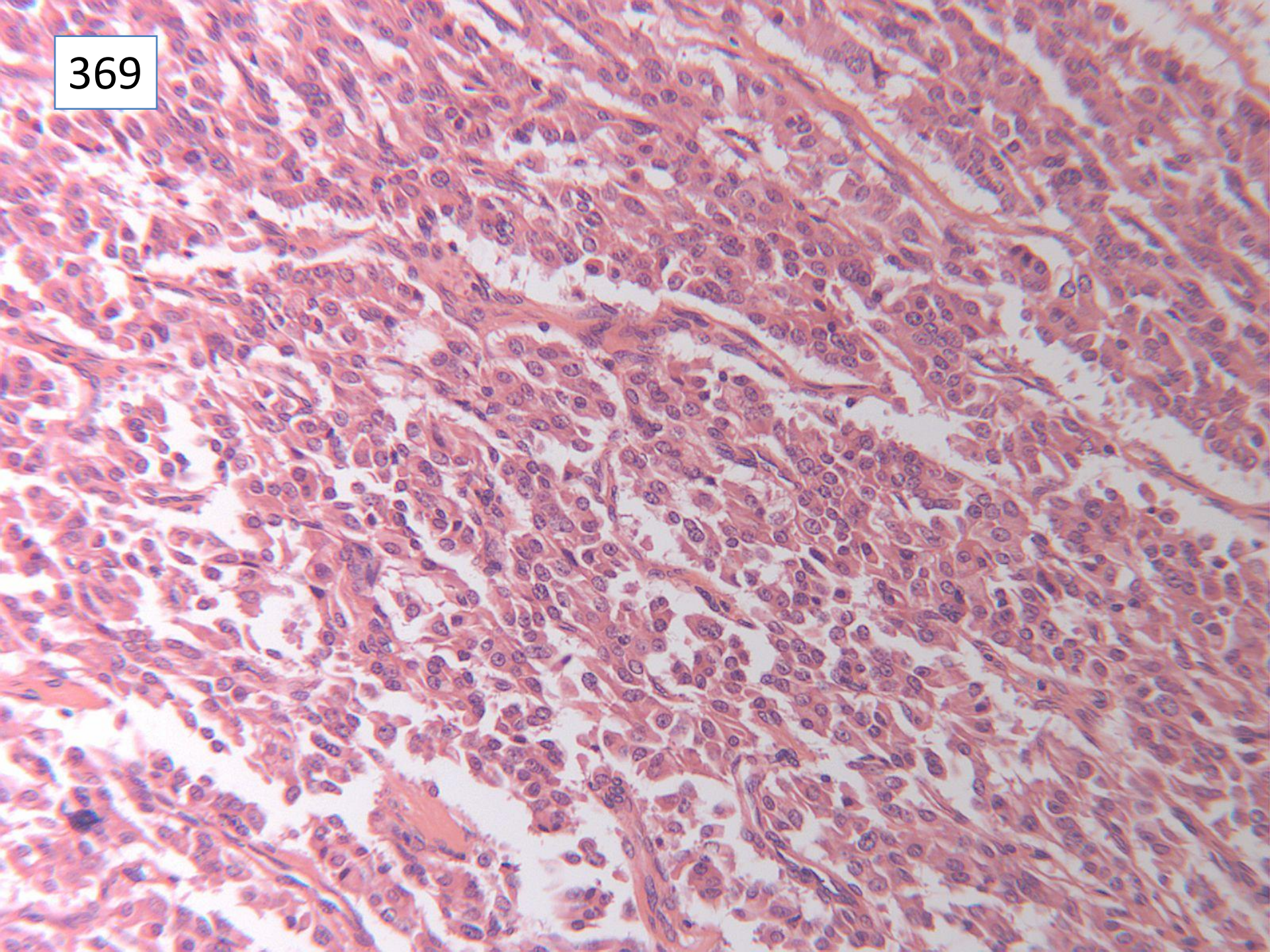
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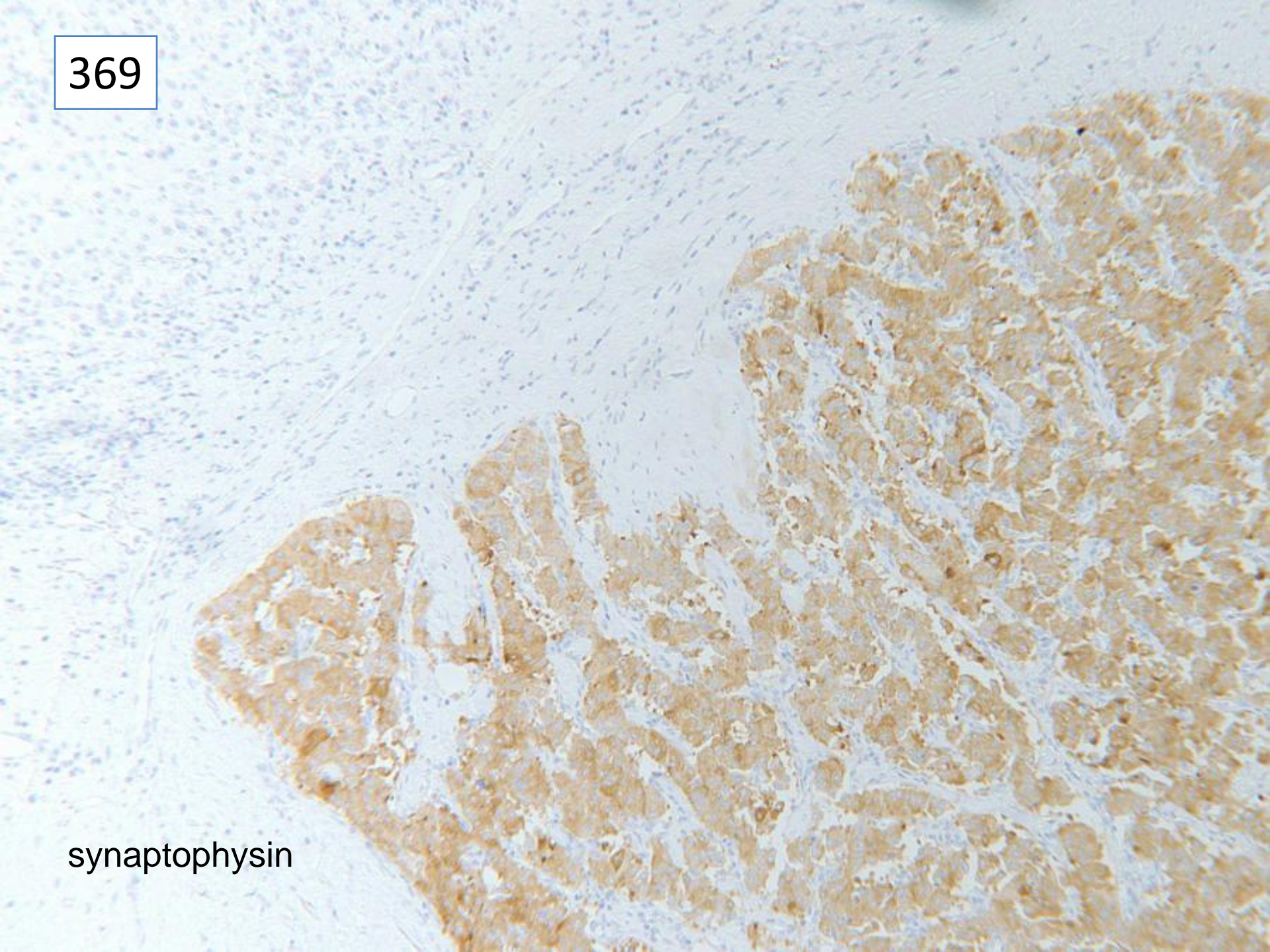
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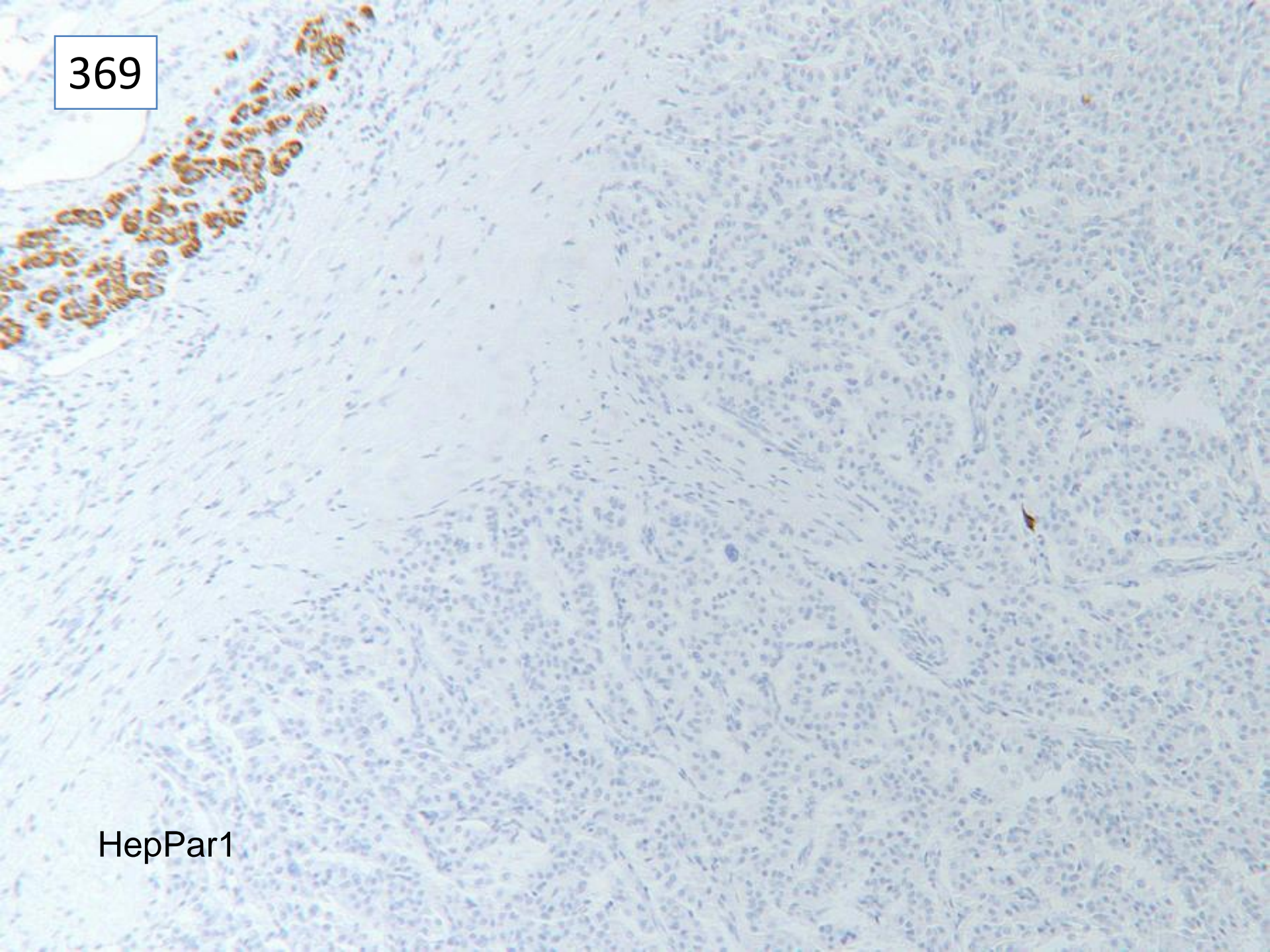


369



synaptophysin

369



HepPar1

# Case number 369

## Results:

62 neuroendocrine carcinoma/neoplasm

Of which: 28 metastatic NEC

19 could be primary or metastatic

13 no comment on primary or metastatic

1 ? NEC, needs more immunos

5 HCC or NEC, needs more immunos

1 HCC (no other comment)

29 comment on embolic material

5 comment on need for Ki67/mitotic count

## Suggested scoring:

For 10 points, clear diagnosis of neuroendocrine carcinoma. 5 points for tentative diagnosis requiring more immunos. No points for HCC.

## Case number 369

Discussion during meeting: agreed that the IHC supplied is sufficient to make the diagnosis, except in very rare circumstances.

### Follow up information:

Few days of liver failure post op,  
now good recovery 1 year post-surgery

Ki 67 intermediate, 10%

Octreotide scan –ve; no evidence of primary lesion outside liver,  
so may be liver primary.

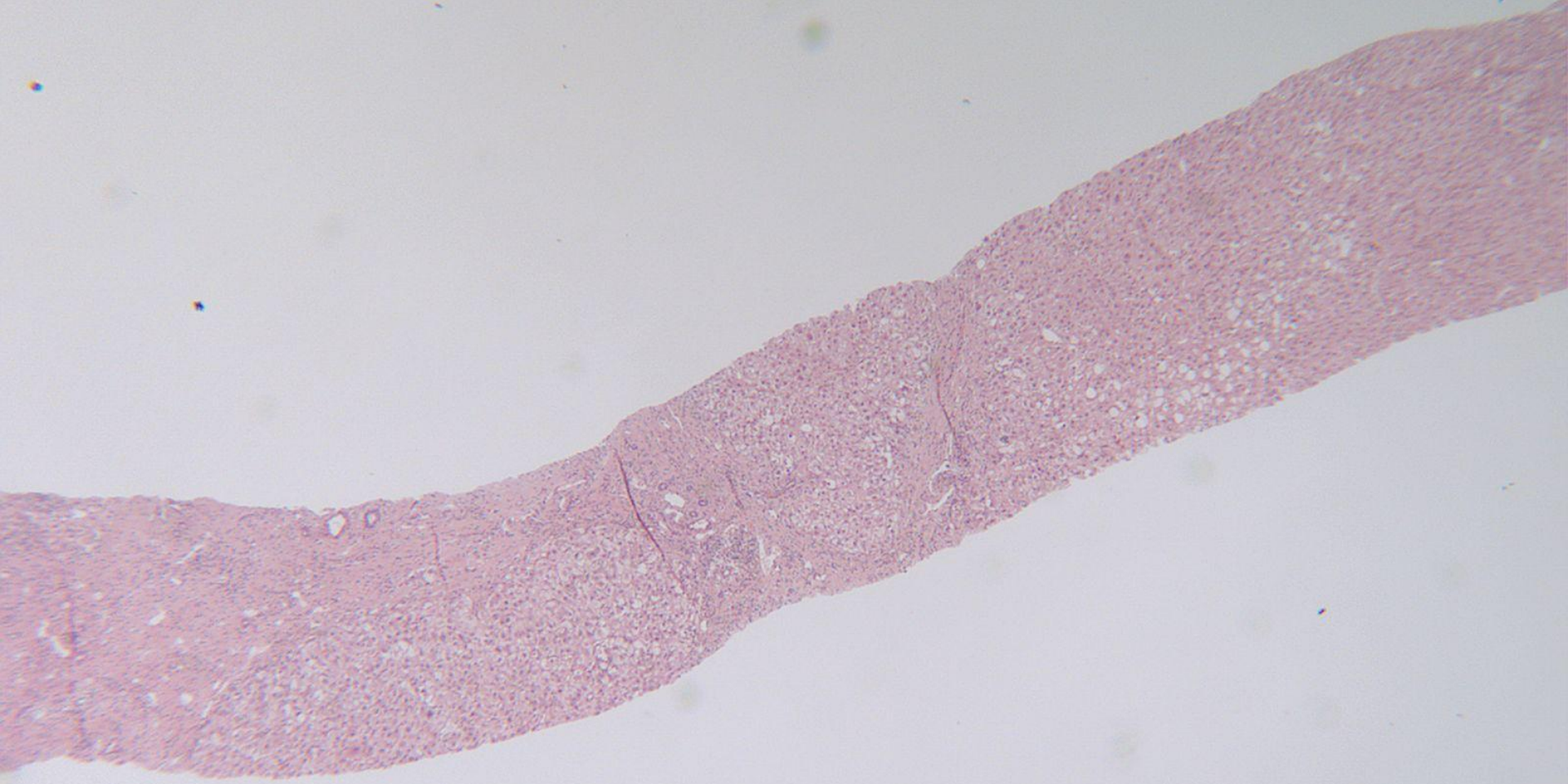
## Case number 370

Female 59 years

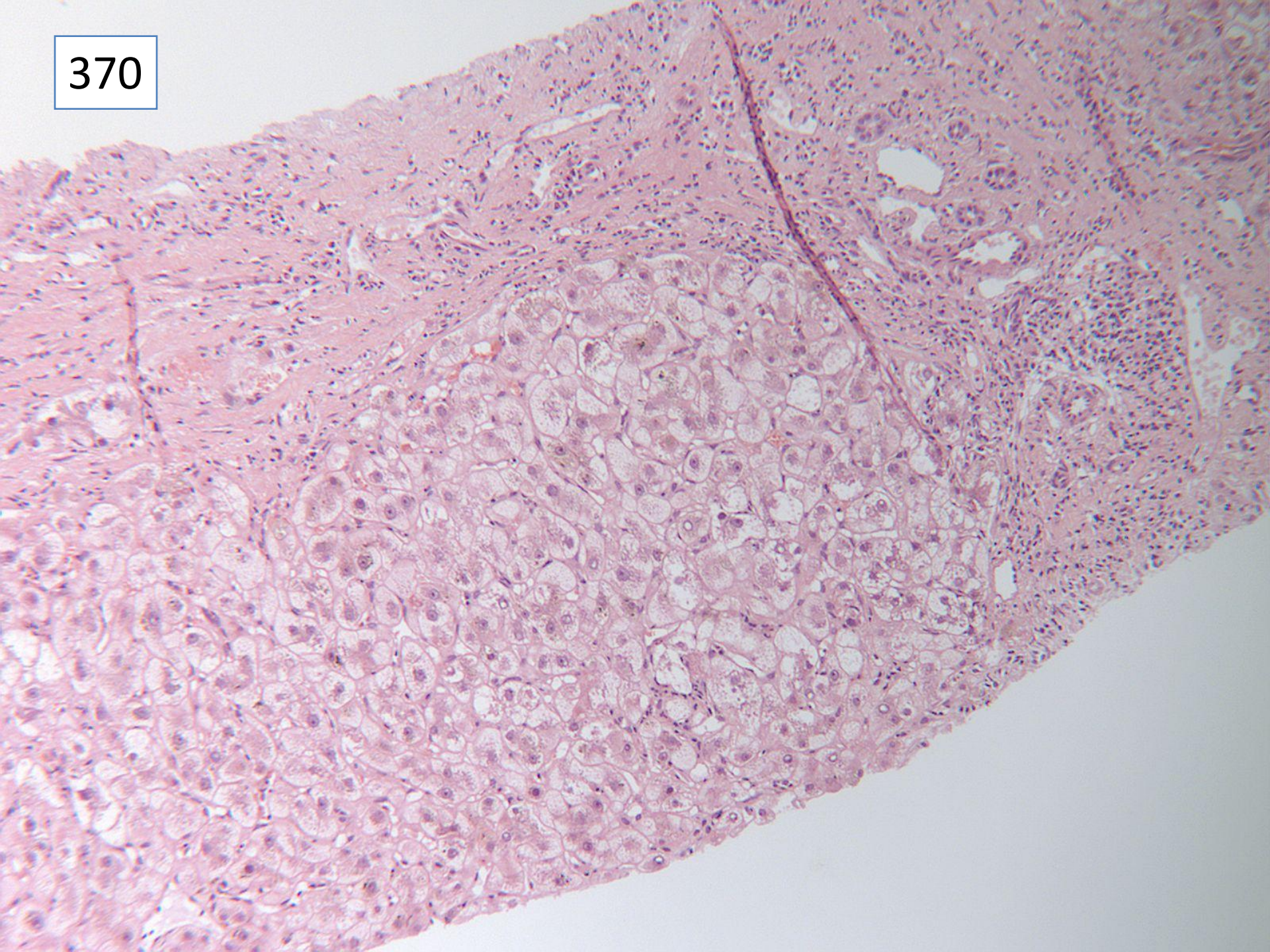
Obesity and diabetes, on methotrexate. ?cause of liver failure. Low platelets.

Liver biopsy, one core 16mm.

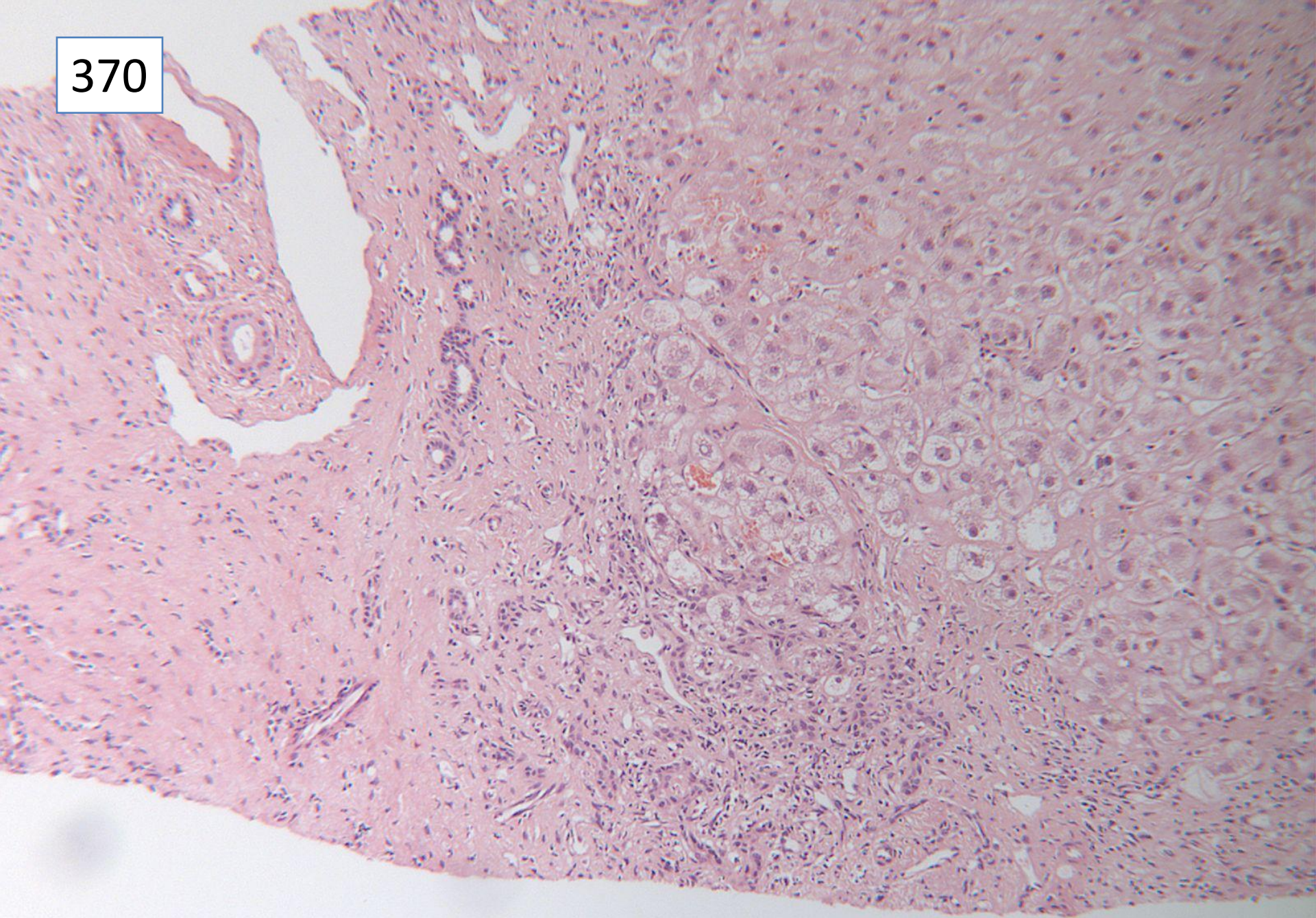
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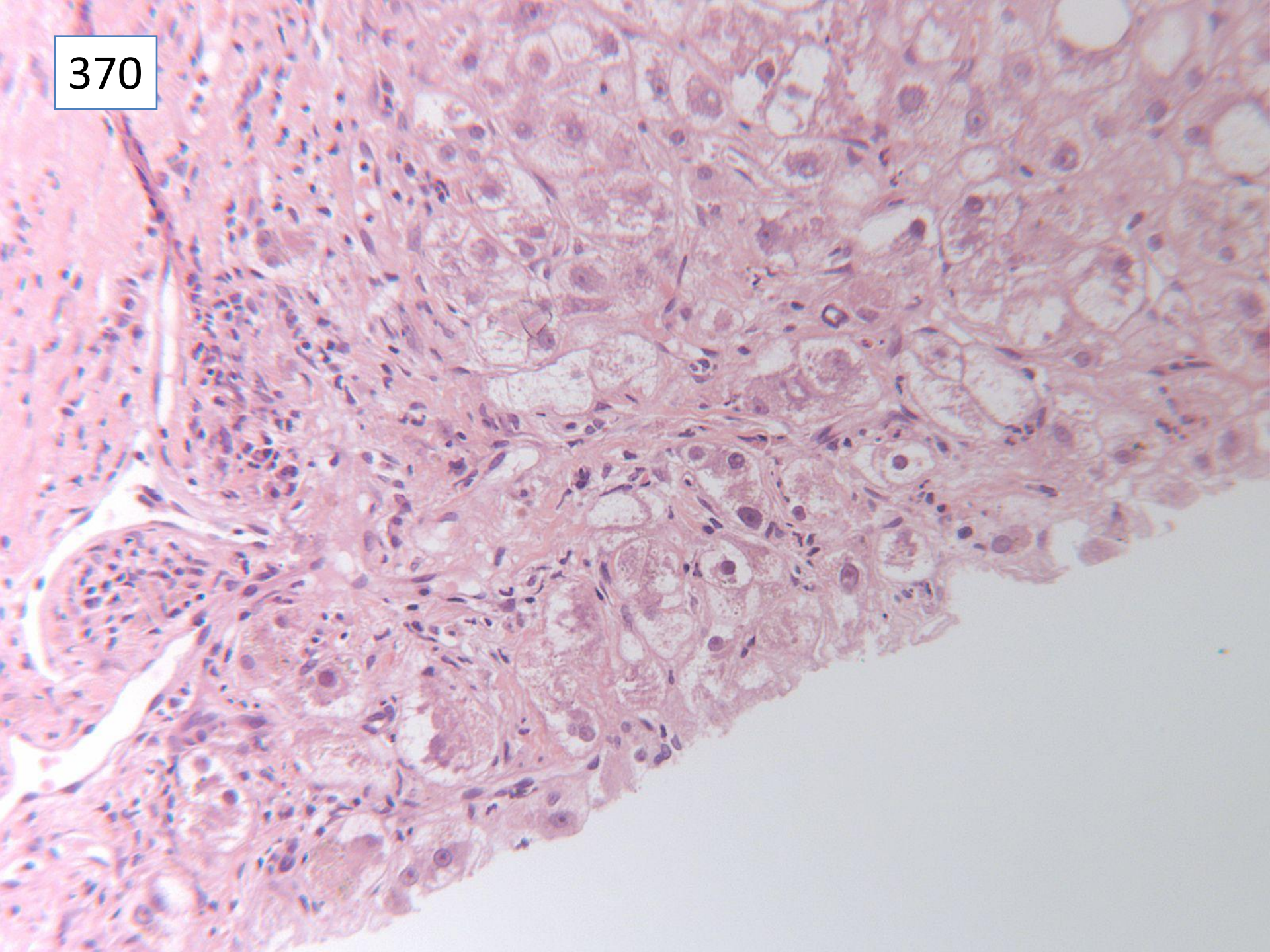
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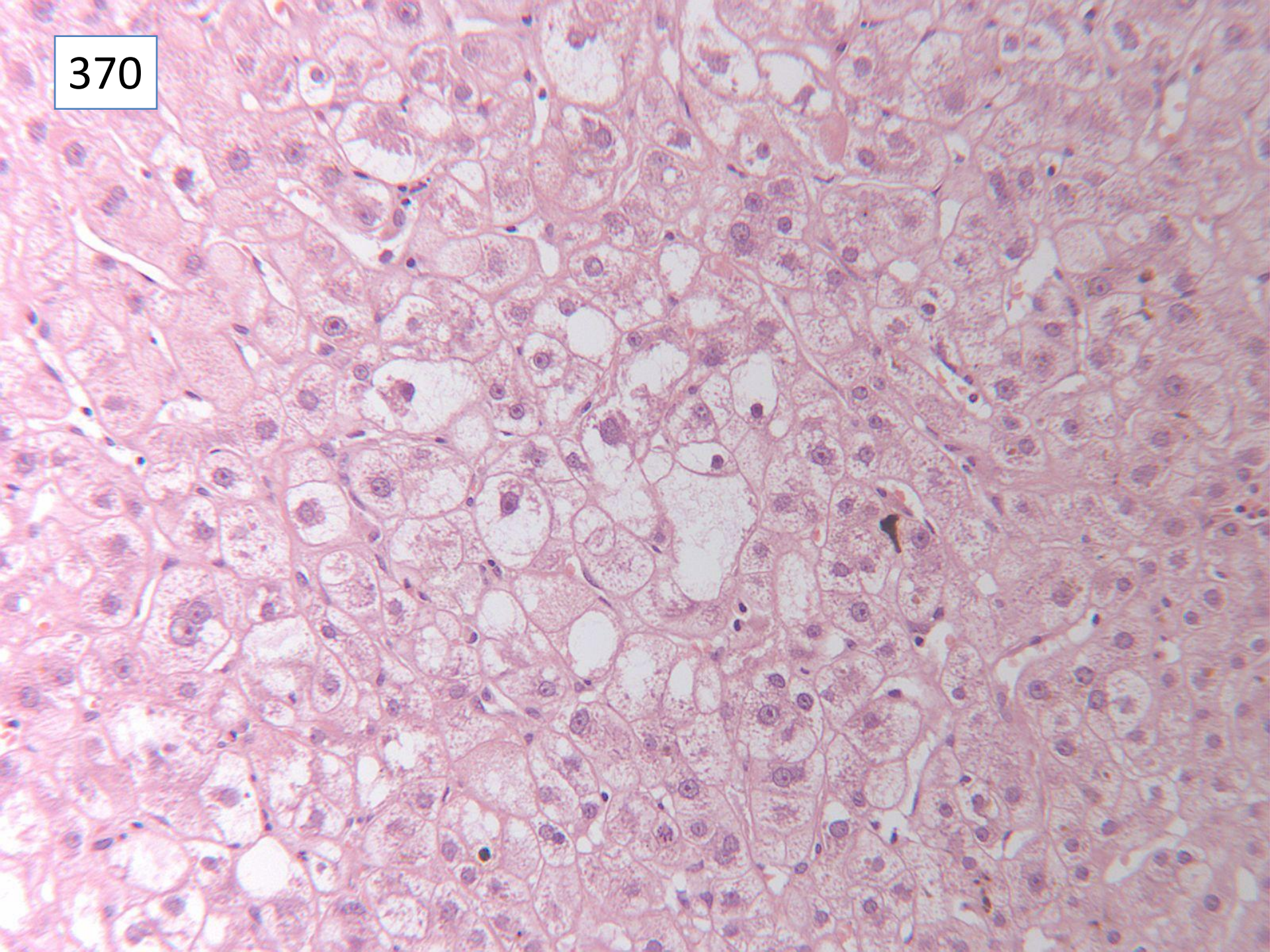
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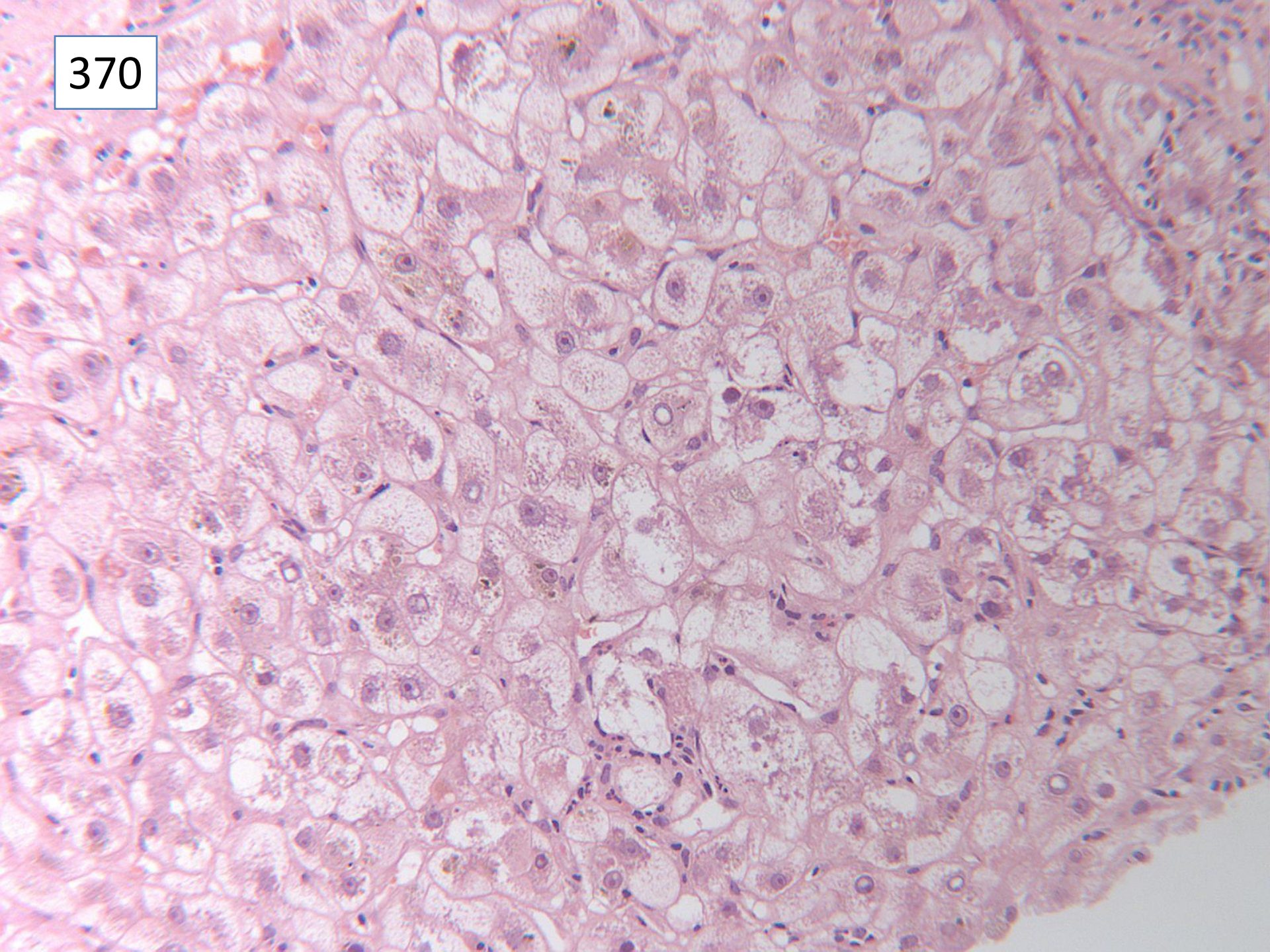
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370



370



# Case number 370

## Results:

- 64 Cirrhosis
- 2 incipient cirrhosis
- 1 portal fibrosis
- 1 'cholestasis with necrosis, fibrosis, nodule formation, no steatosis, ?methotrexate effect'
- 1 'rheumatoid associated portal fibrosis with methotrexate hepatitis'
  
- 39 steatohepatitis
- 47 cholestasis
  
- 48 Mention of methotrexate as potential cause/contributory cause
- 43 NAFLD or NASH
- 14 alcohol
- 21 no mention of NAFLD/NASH
- 11 'methotrexate induced cirrhosis and cholestasis' or similar, no mention of fatty liver disease
- 4 no aetiology given or 'cause not clear'
- 2 ?chronic biliary problem, ?PBC
- 1 chronic hepatitis
- 1 haemochromatotic cirrhosis

## Suggested scoring: - difficult!

For 10 points, cirrhosis/incipient cirrhosis; lose 5 marks for no mention of cirrhosis

In reality, methotrexate NAFLD/NASH are both potential contributory factors, so should both be mentioned for full marks? – in which case this does not achieve a sufficient consensus for scoring. Or lose 5 points if no reference to either methotrexate or NAFLD as a potential contributory factor.

## Comment:

Assumed that cholestasis is due to end stage cirrhosis or sepsis – few included any comment on significance of cholestasis.

## Case number 370

### Discussion during the meeting:

Agreed with proposed scoring – should relate to clinical details given. It is not possible to distinguish effects of methotrexate – the drug aggravates fatty liver disease of either metabolic or alcoholic cause. Worse in psoriasis than rheumatoid because the dose of methotrexate is much higher.

Submitting pathologist's diagnosis: cirrhosis, steatohepatitis.

Further clinical information: Psoriatic arthritis

Considered for liver transplant for NAFLD – not suitable

Clinically suspicion of alcohol

## Case number 371

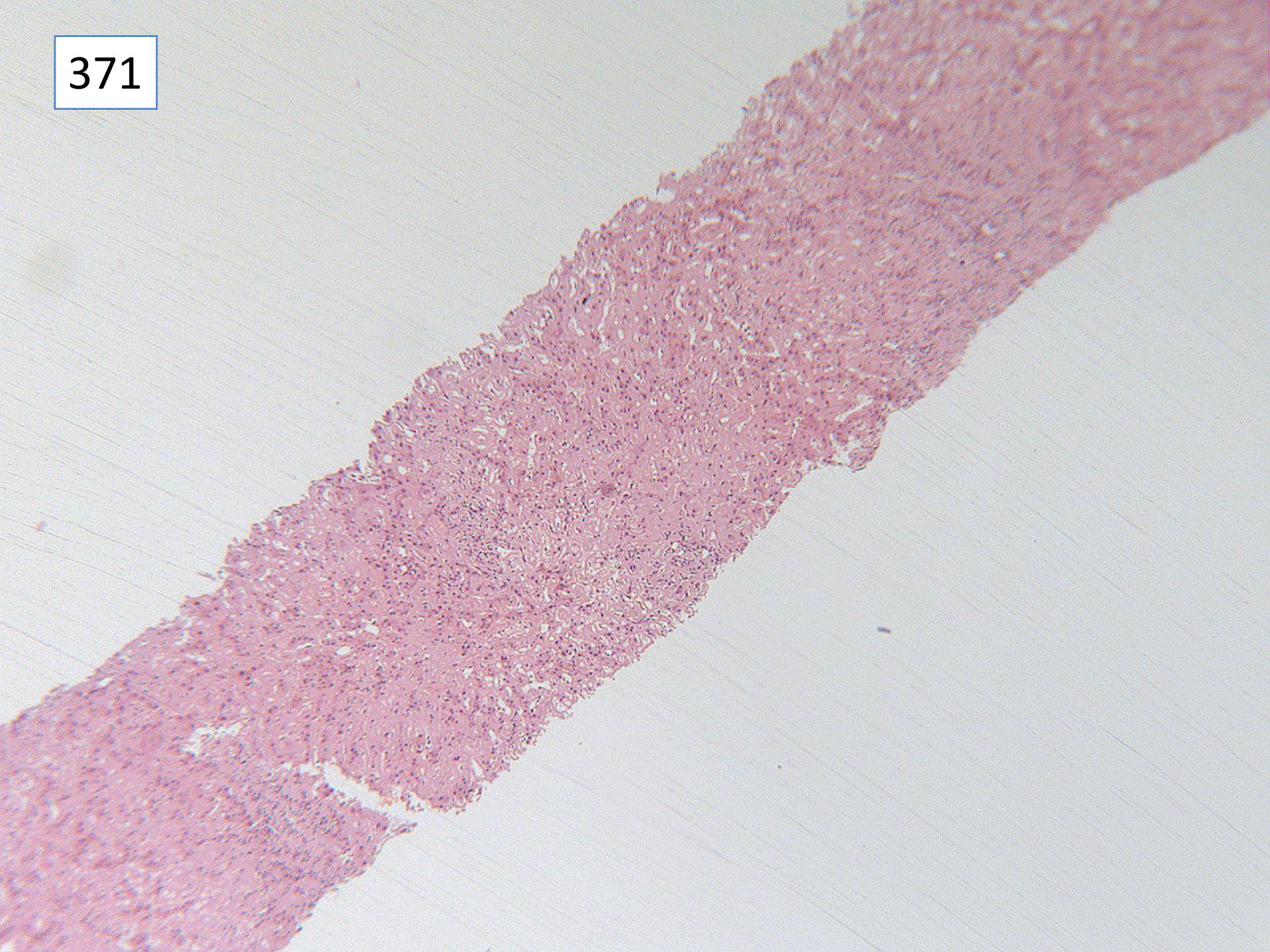
Female 75 years

Raised alkaline phosphatase for 1 year.

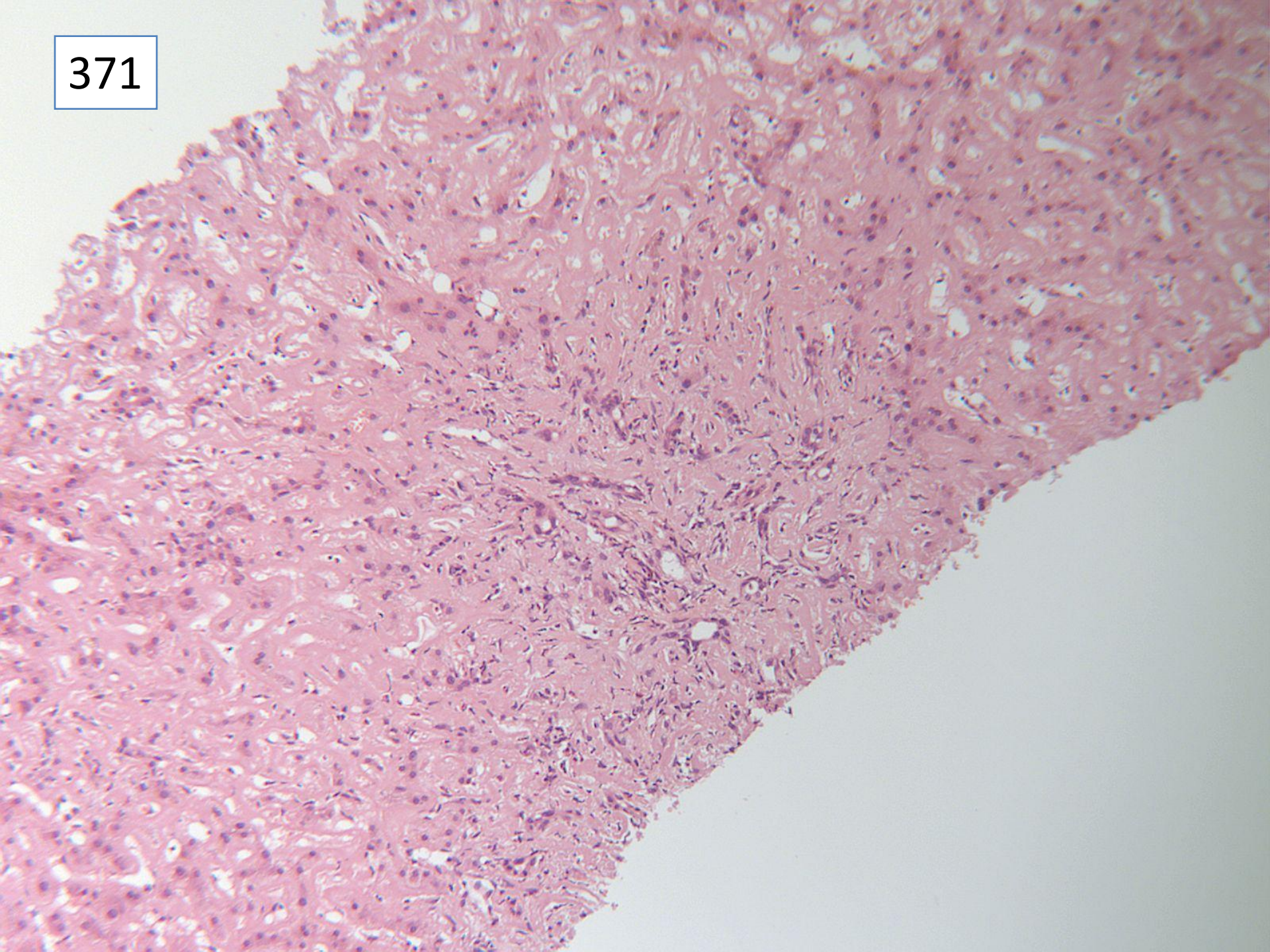
Hepatomegaly on CT. MRCP-unable to demonstrate aetiology. No lymphoma on CT. Peripheral oedema.  
?Cause.

Liver biopsy, one core 12mm long.

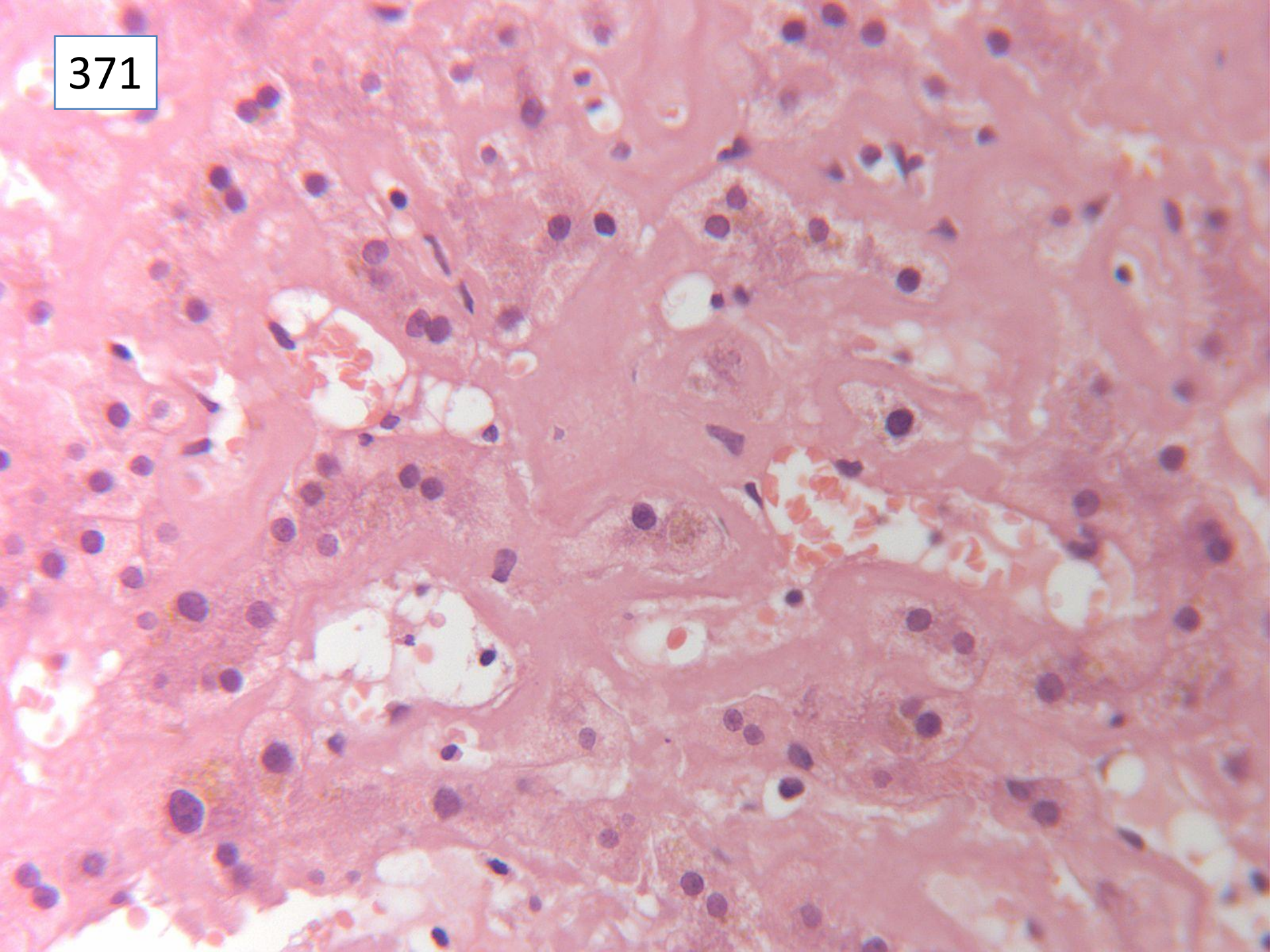
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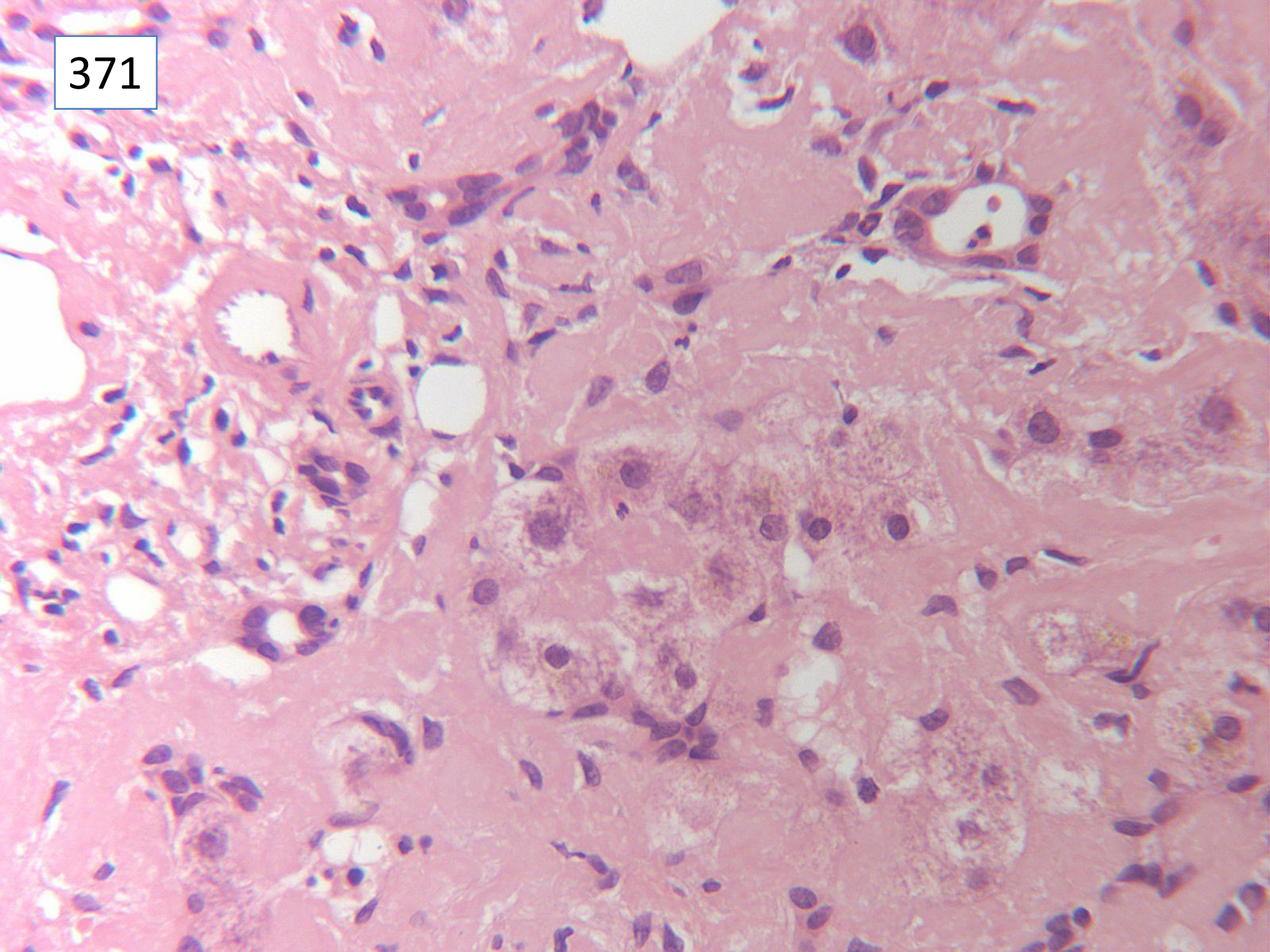
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# Case number 371

## Results:

64 amyloidosis

Of which: 39 needs Congo red/other stain

27 suggest additional investigations to determine the cause

1 biliary process, exclude amyloid by special stains

1 bile duct proliferation, necrosis, inflammation; Large bile duct obstruction

1 extensive sclerosis, bile ductular reaction, favours cardiac cirrhosis over amyloid, do stains

1 odd staining portal fibrosis, dilated sinusoids, ? venous outflow obstruction

1 zone 2/3 ischaemia and sinusoidal dilatation, ? venous outflow obstruction

## Suggested scoring:

For 10 points clear diagnosis of amyloid. 5 points if amyloid within differential and stains for amyloid included. No points if no mention of amyloid.

- Comment (CB) amyloid most likely but needs supporting stain, and need to establish the type.

## Case number 371

Discussion during meeting: related to usefulness of typing amyloid histologically - felt to be not contributory. Many cases referred to National Amyloidosis Centre at RFH.

### Follow up:

Significant bleed after biopsy, needed hepatic artery embolisation.

IgM kappa paraprotein,

Bone marrow – marginal zone lymphoma.

Palliative care, died 10 weeks later.

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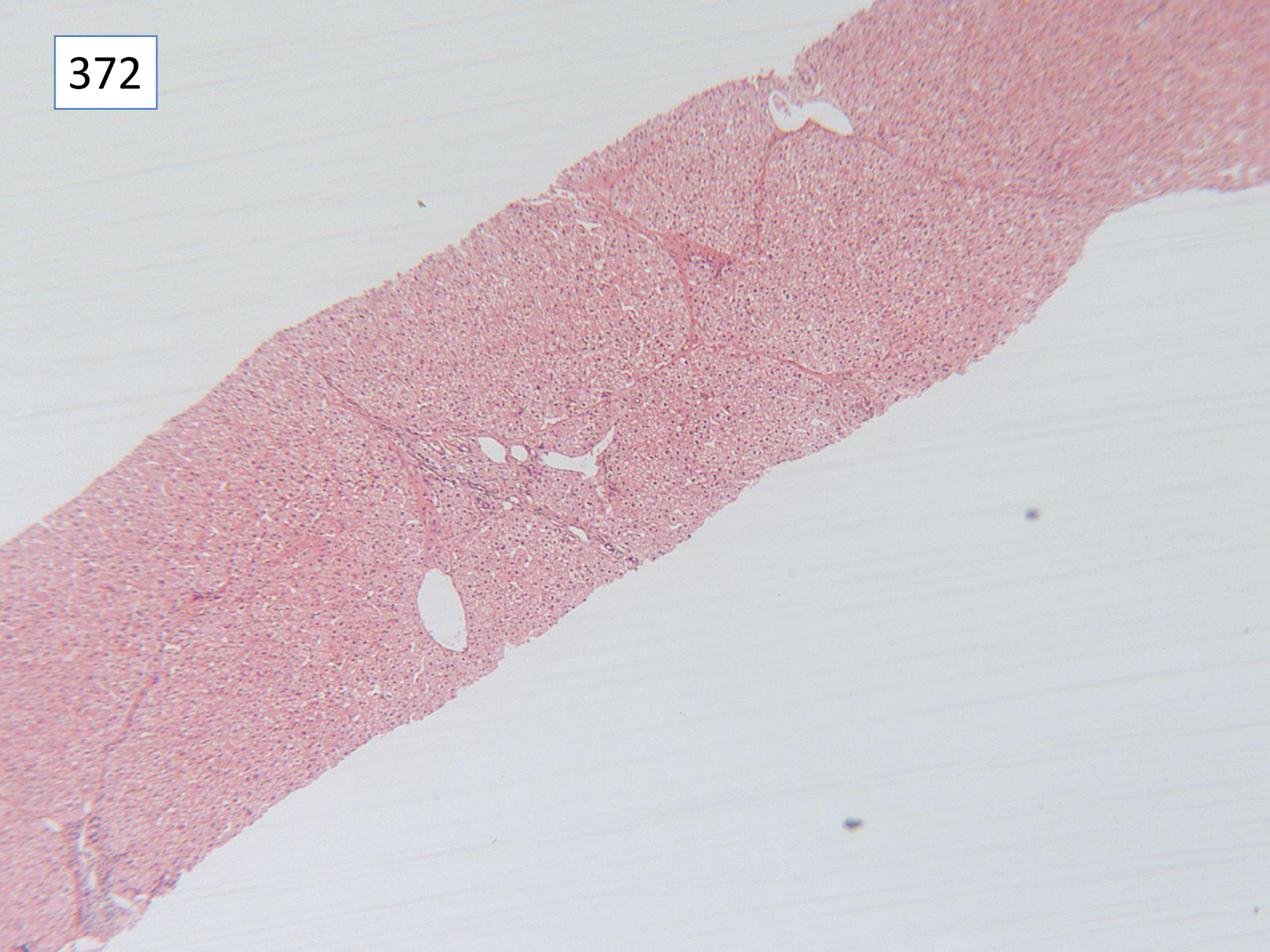
Female 52 years

Deranged LFT's.

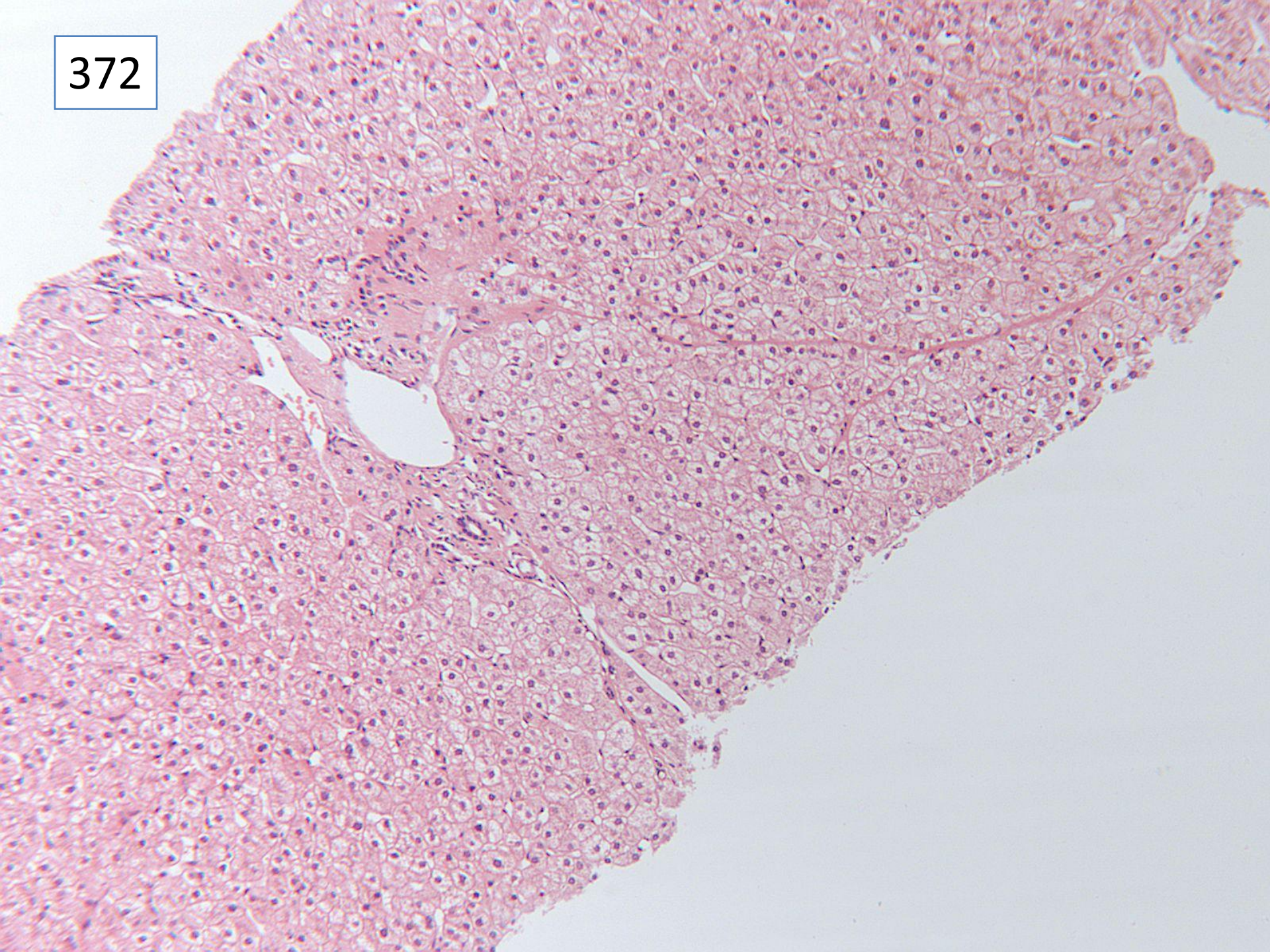
Additional information from electronic patient record:  
previous high alcohol intake, jaundice and ascites 7  
years ago. LFTs now normal. ? now abstinent,  
? cirrhosis.

One core of liver tissue measuring 18mm in size.

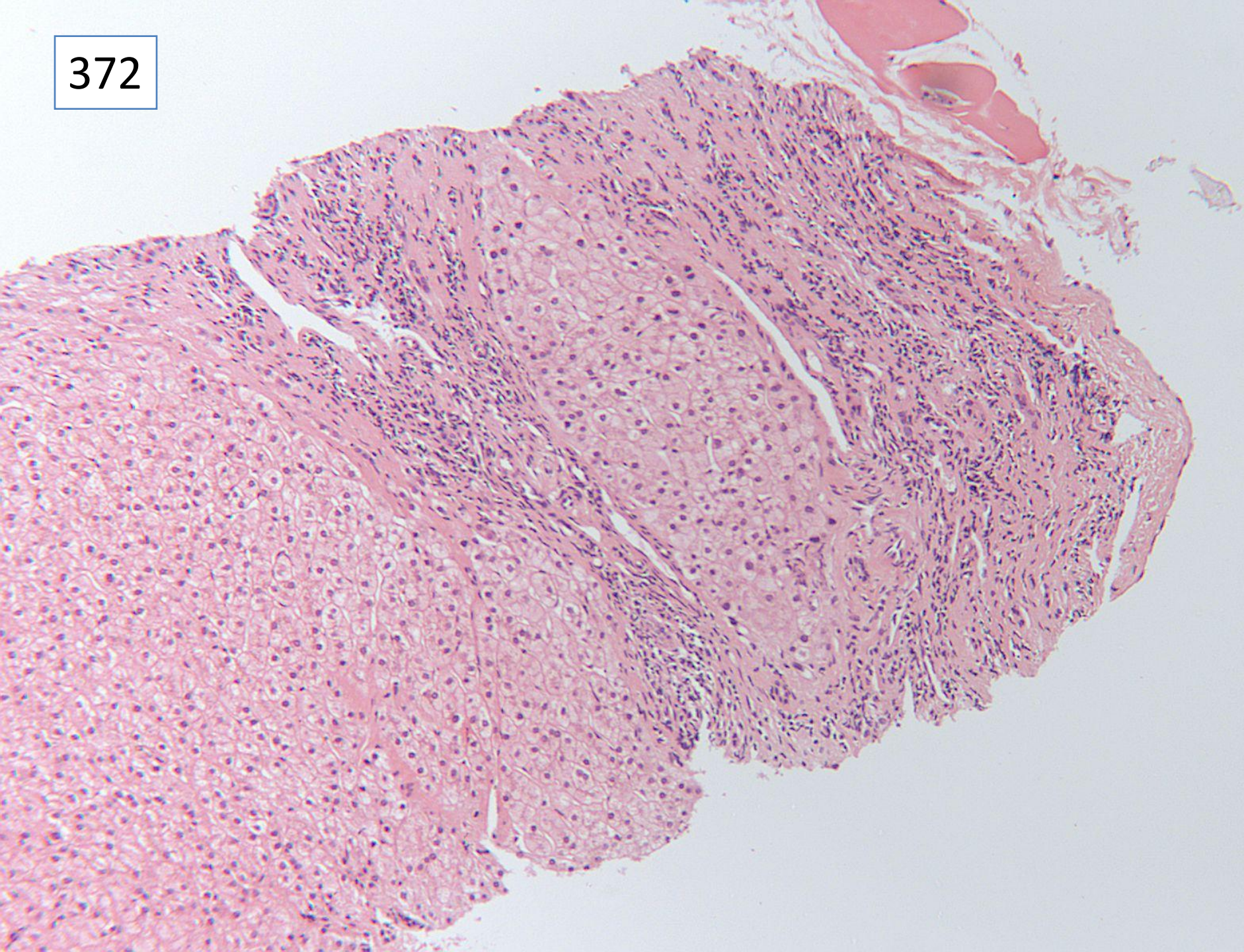
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# Case number 372

## Results:

- 19 incomplete septal cirrhosis
- 16 bridging fibrosis
- 7 incipient cirrhosis/pre-cirrhosis
- 15 cirrhosis
- 7 post-cirrhotic hepatic regeneration/regression of cirrhosis
- 4 nodular regenerative hyperplasia
  
- 35 consistent with previous alcoholic liver disease
- 5 consistent with alcoholic injury (not indicating previous/current abstinence)
- 3 no features of alcohol
- 23 no comment on aetiology
- 1 post hepatitis rather than alcoholic
- 1 chronic hepatitis likely PSC or PBC
- 1 ? storage disorder
- 1 no answer submitted

Suggested scoring: no consensus, unsuitable for scoring

## Case number 372

Submitting pathologist's diagnosis: incomplete septal cirrhosis, consistent with previous alcoholic liver disease now abstinent.

### Further comment:

Submitted as good example of 'incomplete septal cirrhosis' due to regression of previous alcoholic cirrhosis. Clear history of admission for liver failure from alcoholic cirrhosis 7 years earlier. Successfully abstinent since then.

Biopsy done to determine if cirrhotic to guide clinical management.

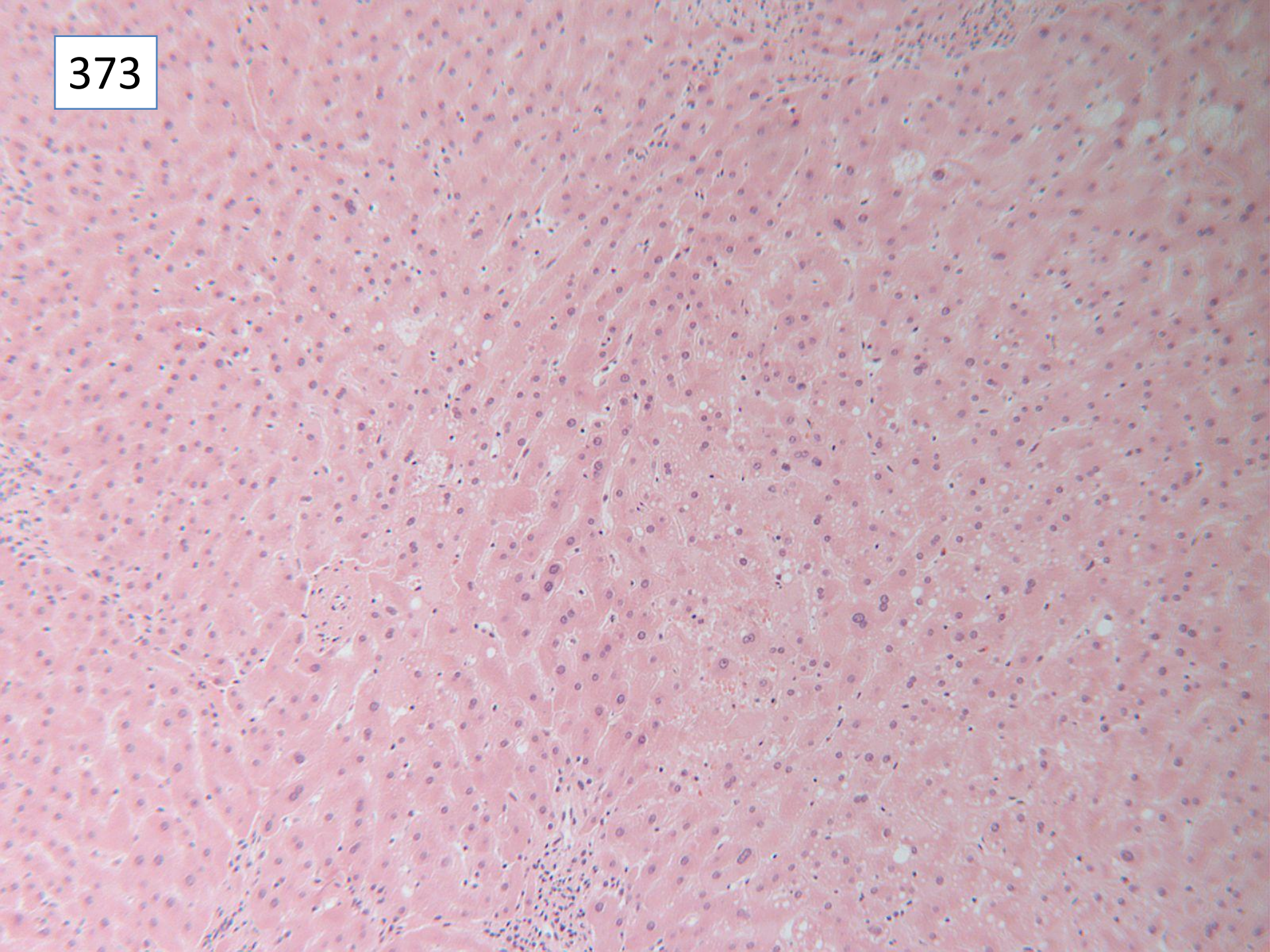
? Needs surveillance for HCC

## Case number 373

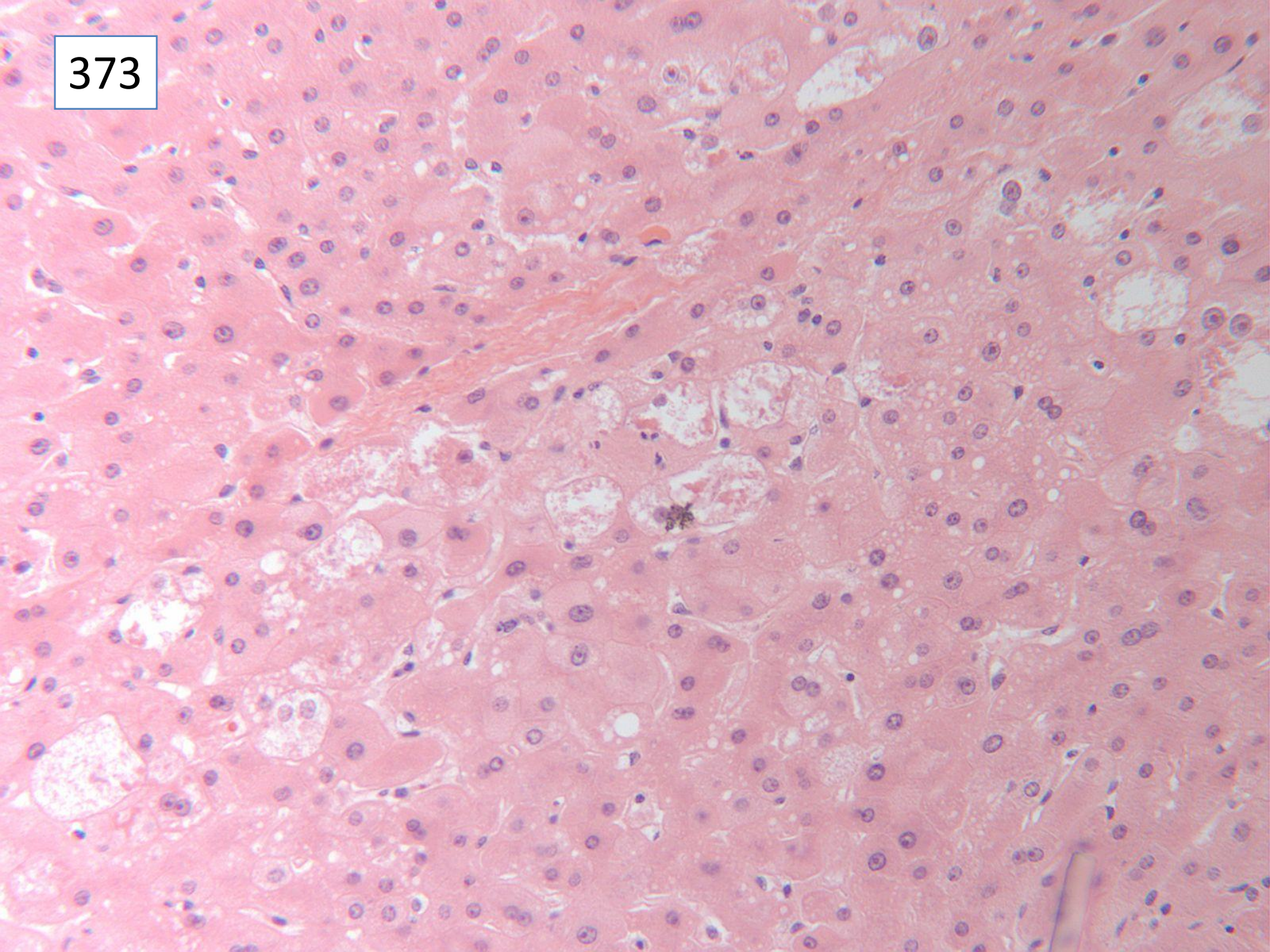
Female 66 years

Biliary colic. History of Wegener's granulomatosis, hence request for biopsy. Currently controlled on prednisolone 10mg and azathioprine. Also has type II diabetes. Mildly raised bilirubin and ALT. Antibody screen negative. Hepatitis B&C screen negative. Wedge biopsy taken at cholecystectomy for gallstones.

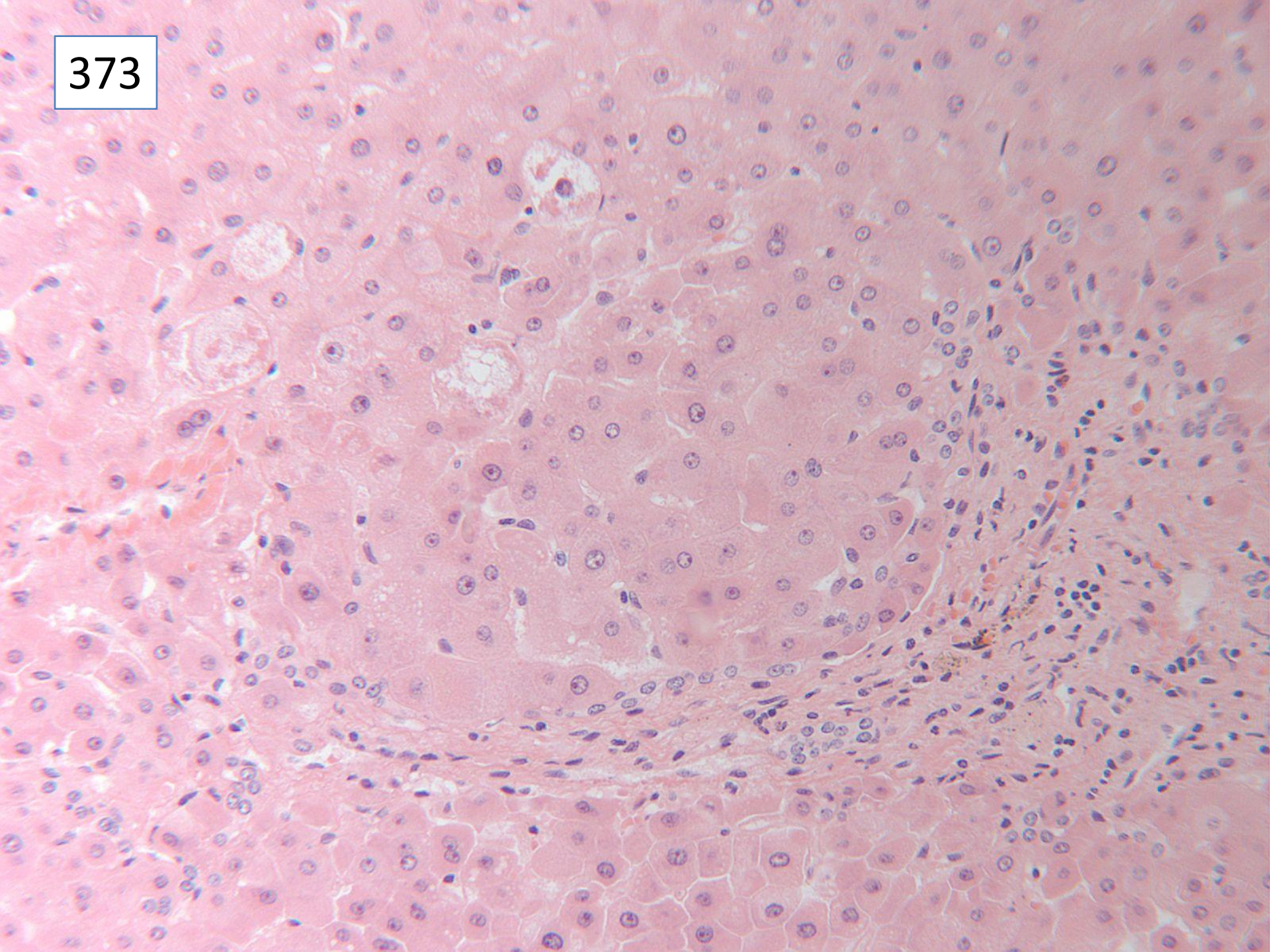
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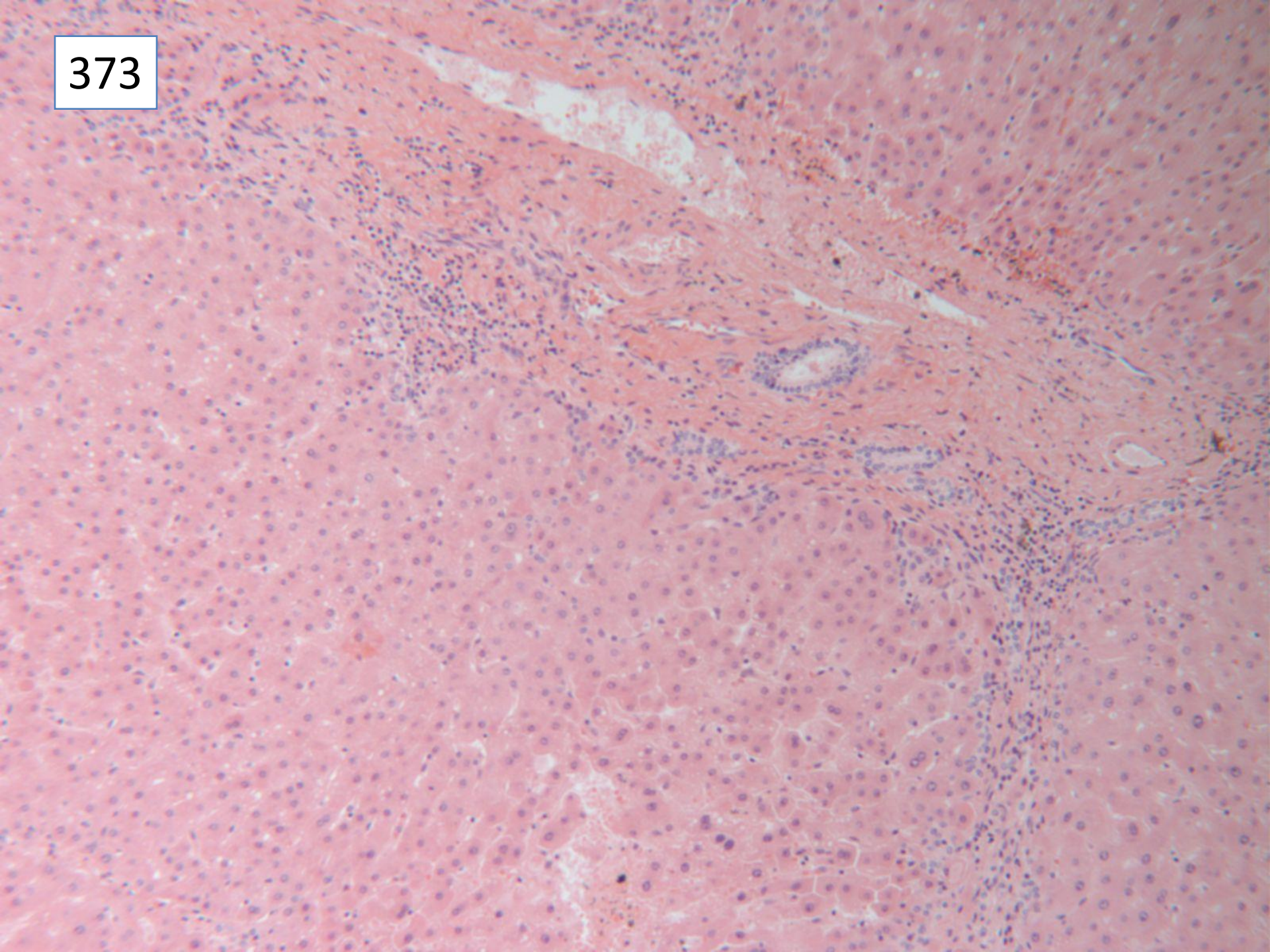
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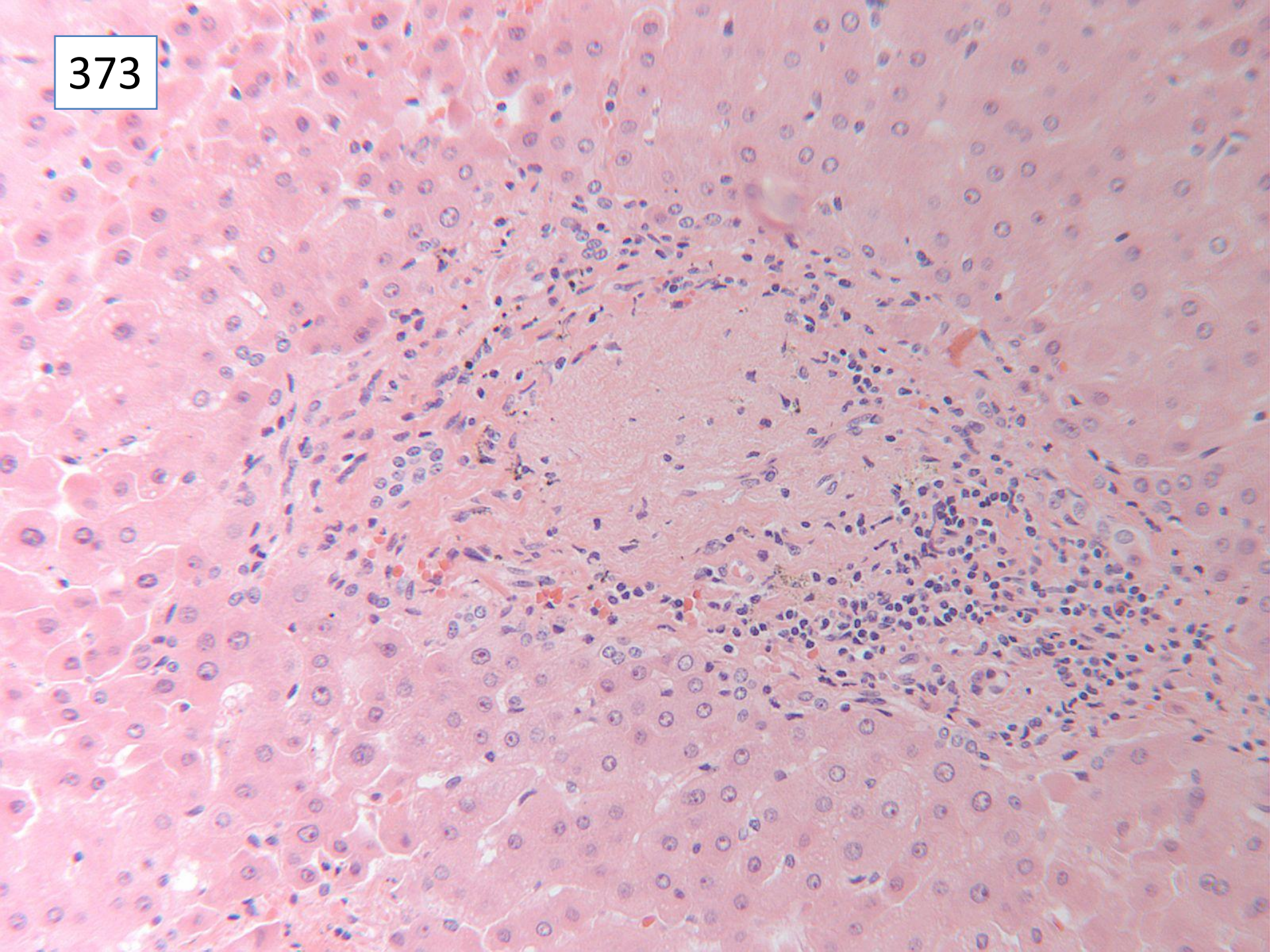
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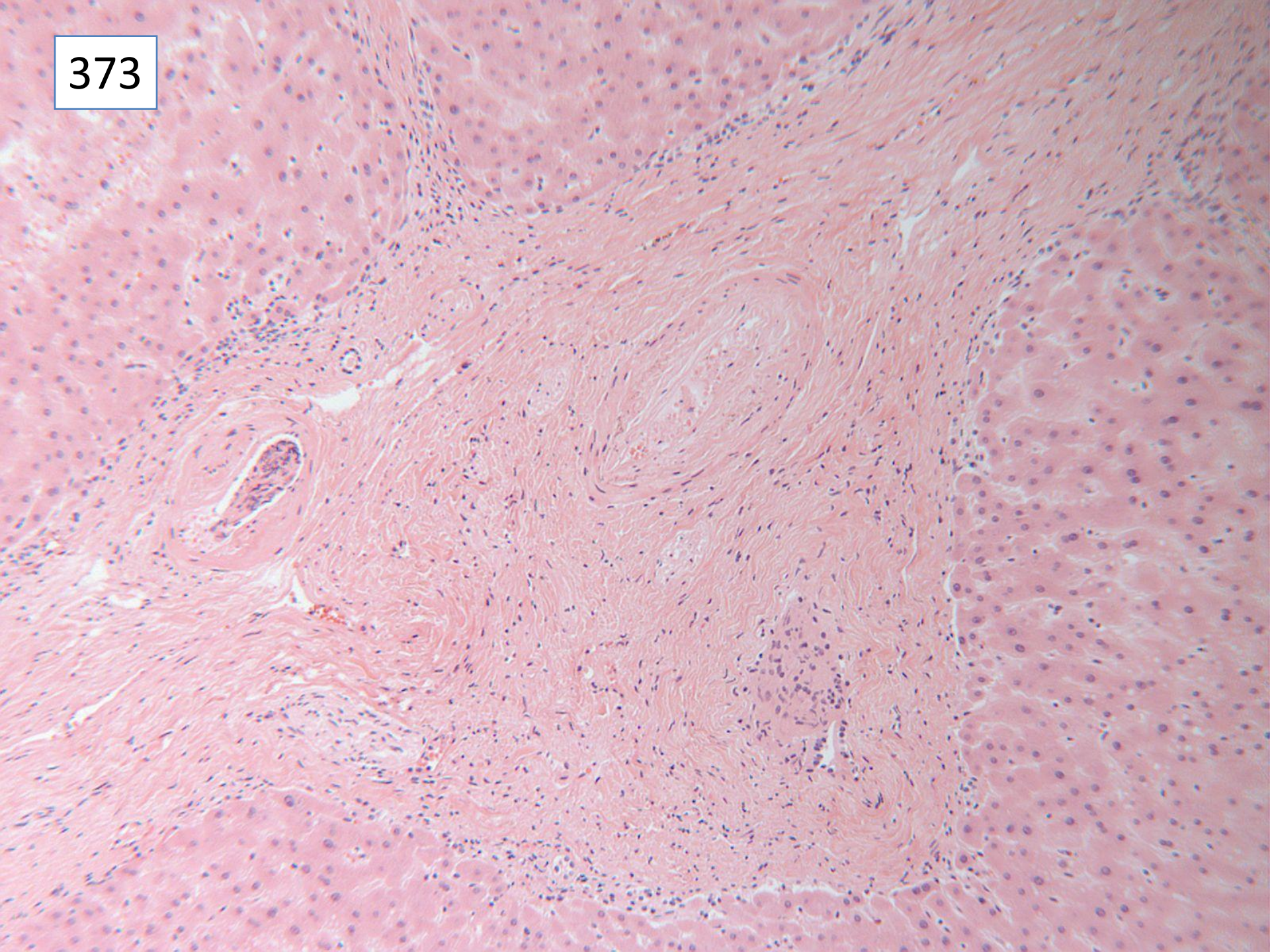
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# Case number 373

## Results:

- 20 nodular regenerative hyperplasia,  
Of which 9 may be effect of azathioprine
- 22 NASH/NAFLD/ASH
- 6 non-specific chronic hepatitis
- 4 non-specific ? due to gall stone disease
- 5 non-specific, consistent with treated giant cell vasculitis
- 3 vasculitis with intimal fibrosis, ?Wegener's related
- 5 various other comments about abnormal vessels
- 1 perivenular congestion and necrosis, ?BCS/SOS associated with azathioprine
- 1 ?CMV, ?VOD, ?SOS
- 1 secondary sclerosing cholangitis

Suggested scoring: no consensus, not suitable for scoring

## Case number 373

Submitting pathologist's diagnosis: nodular regenerative hyperplasia and mild portal inflammation

Follow up information:

Still taking azathioprine, Wegener's well controlled.

Probably has Gilbert's syndrome.

That's all for circulation D1