

# National Liver Histopathology EQA Scheme

Circulation Z

July 2009

# Business meeting

## 1. Circulation Z – problems with circulation?

58 responses, several seem to have difficulties seeing the slides?

Three weeks each slot, is this about right?

## 2. Circulation A1 – starts 20<sup>th</sup> July,

finishes 20<sup>th</sup> November, discussion after

liver meeting on 10<sup>th</sup> December, London.

## **Case 314**

33F.

Large cyst on CT. Hydatid serology negative.

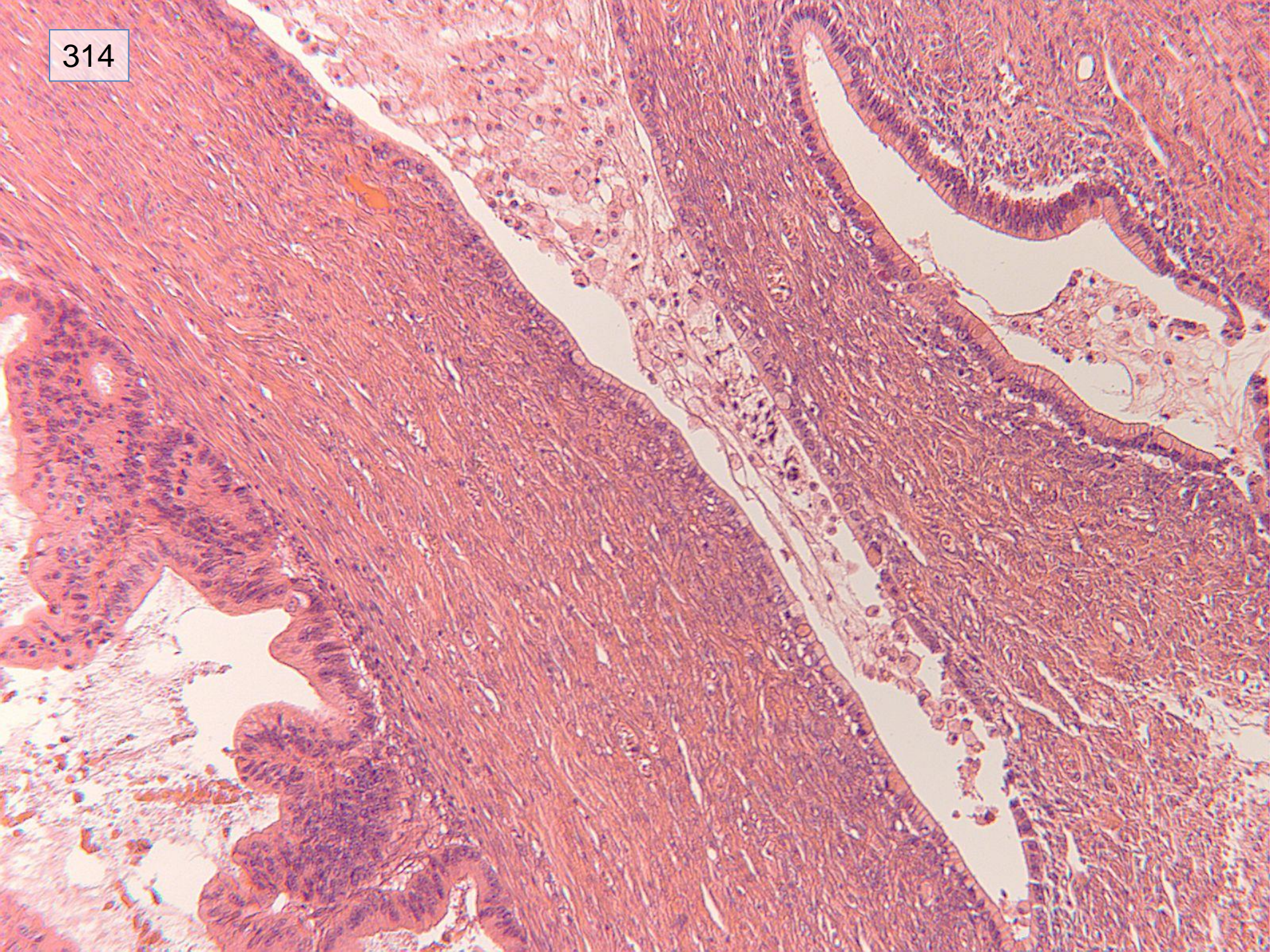
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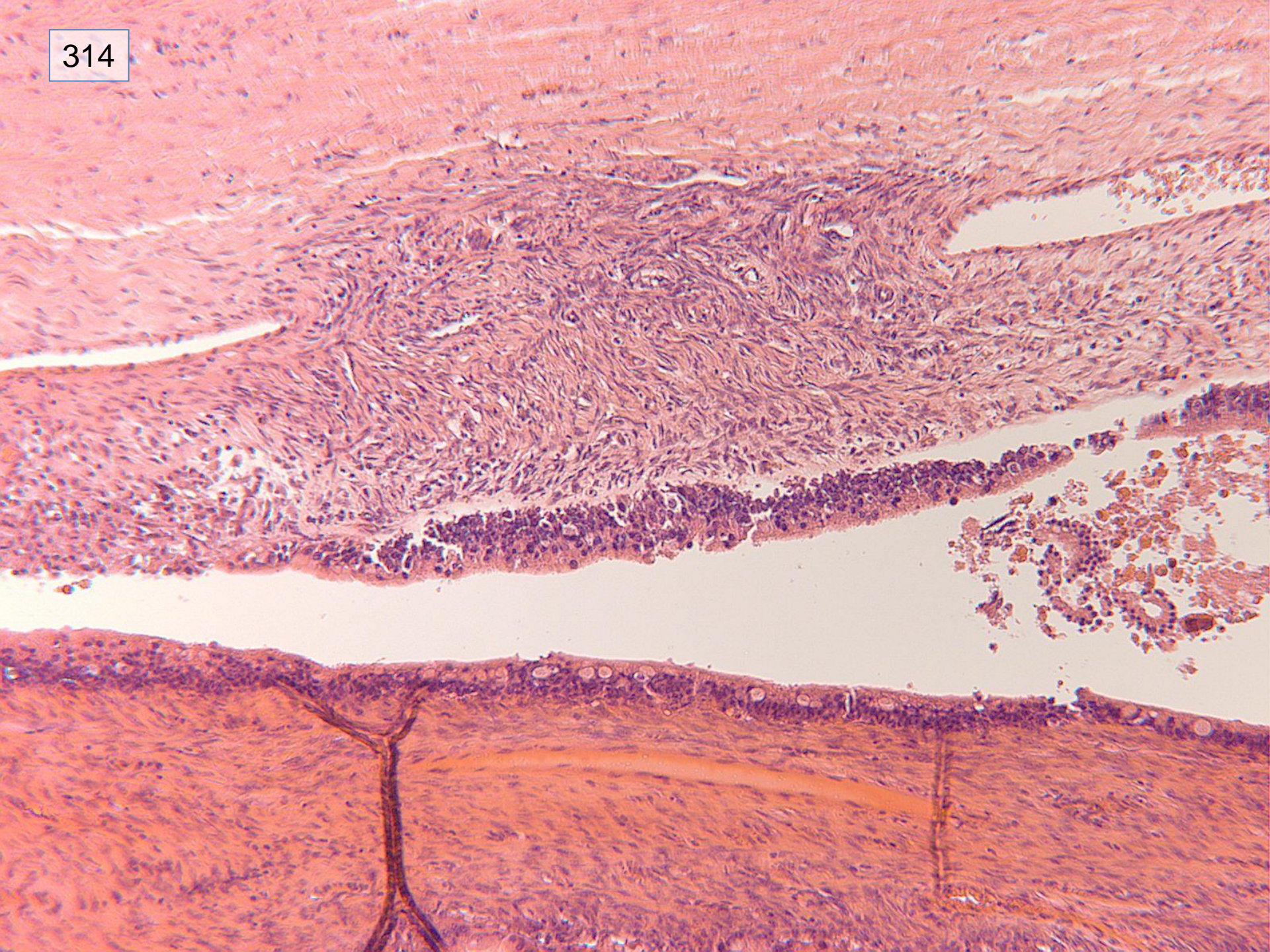
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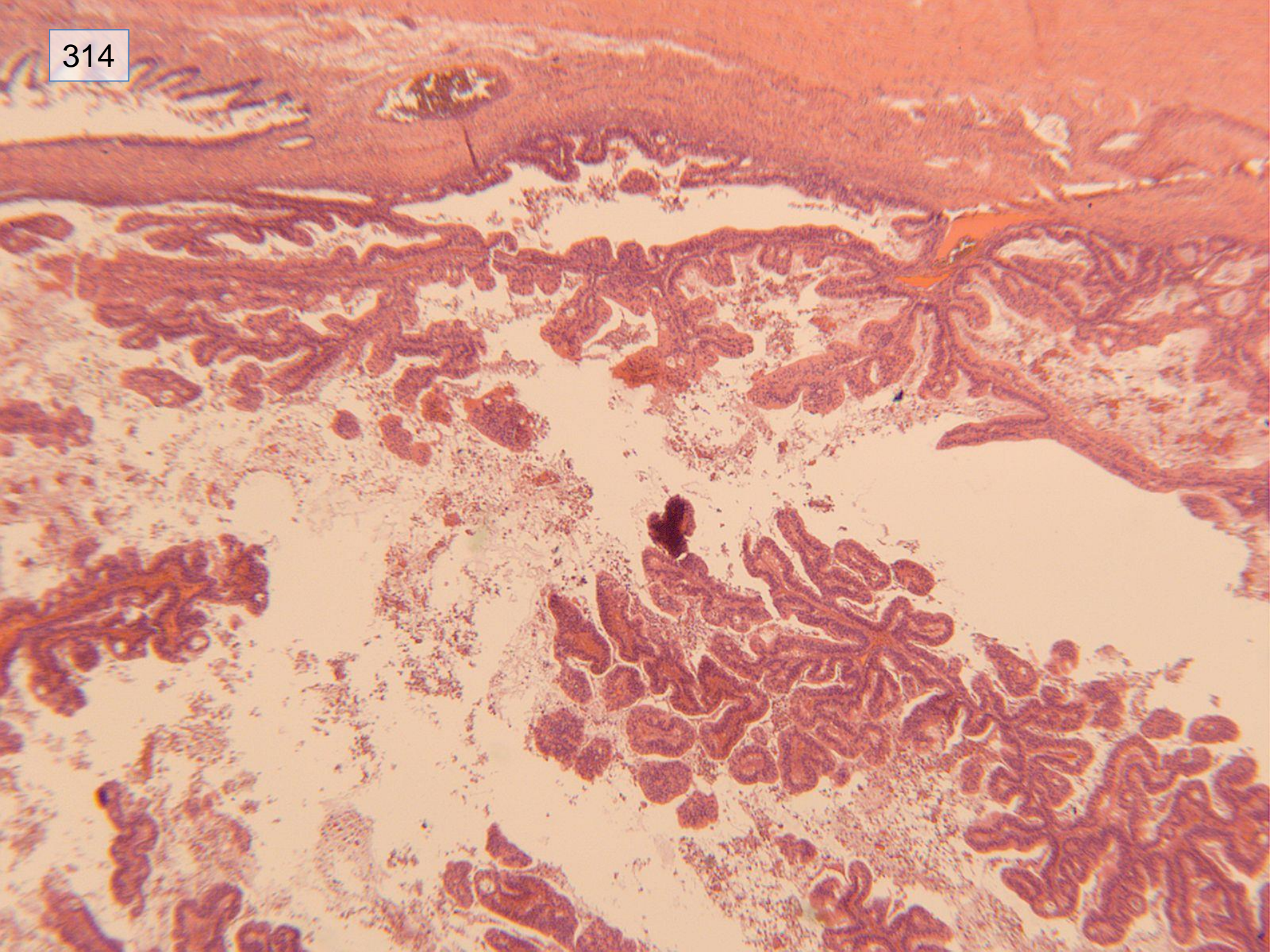
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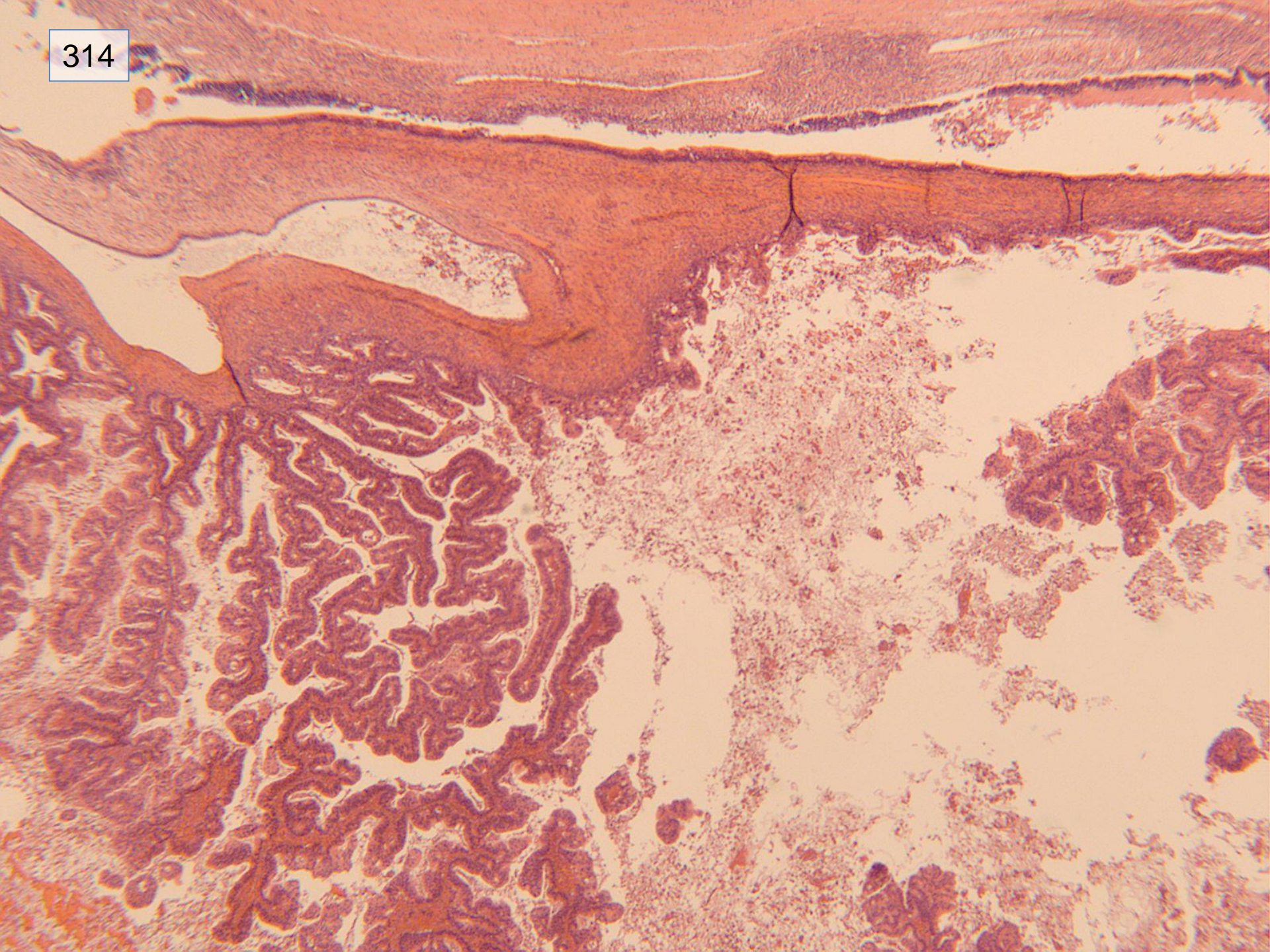
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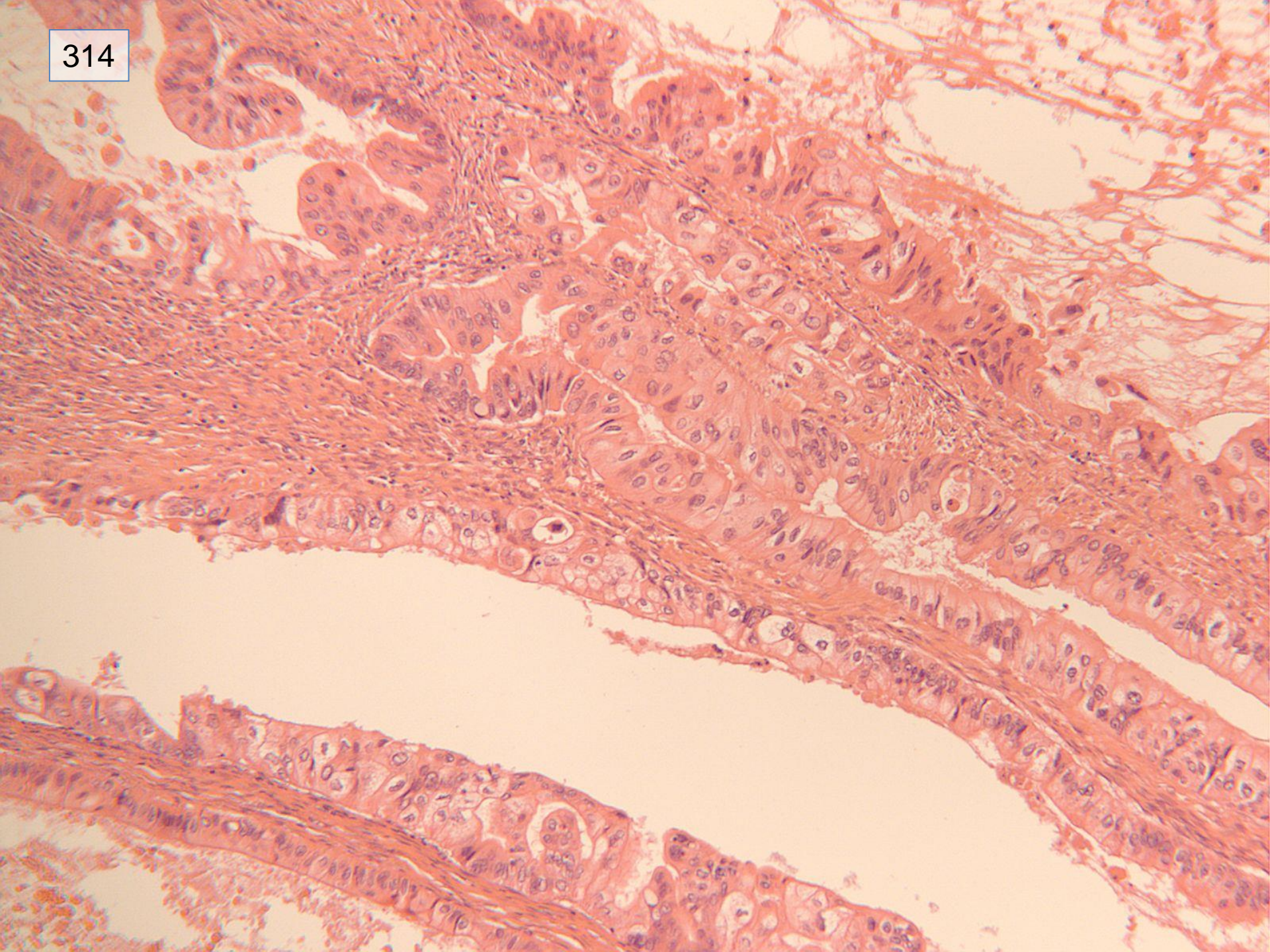
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314



314



# Case 314

## *Responses:*

35 cystadenocarcinoma

(of which 22 'hepatobiliary' and/or mention mesenchymal stroma)

10 cystadenoma, borderline malignancy

(of which 5 hepatobiliary/mesenchymal stroma)

6 cystadenoma with (high grade) dysplasia

(4 hepatobiliary/mesenchymal stroma)

1 cystadenoma or cystadenocarcinoma

1 biliary cystadenoma, no obvious invasion

3 adenocarcinoma, probably secondary

1 papillary adenocarcinoma NOS

*Original diagnosis: biliary cystadenocarcinoma*

## Case 314

### Scoring and discussion:

For 10 marks – cystadenocarcinoma or an indication that the lesion may behave aggressively. 5 marks for imprecise terminology (cystadenoma or cystadenocarcinoma, papillary adenocarcinoma).

Score 0 for adenocarcinoma, probably secondary - the presence of mesenchymal stroma and benign epithelial component are evidence that this is not a metastasis. Also score 0 for biliary cystadenoma.

Clinical follow up – cyst was excised intact; no recurrence.

## Case 315

70M.

Rectal carcinoma with liver metastases and known lung metastases. Post chemotherapy.

Segment 6 resection. Subcapsular area of scarring 8mm diameter, background liver diffusely nodular.

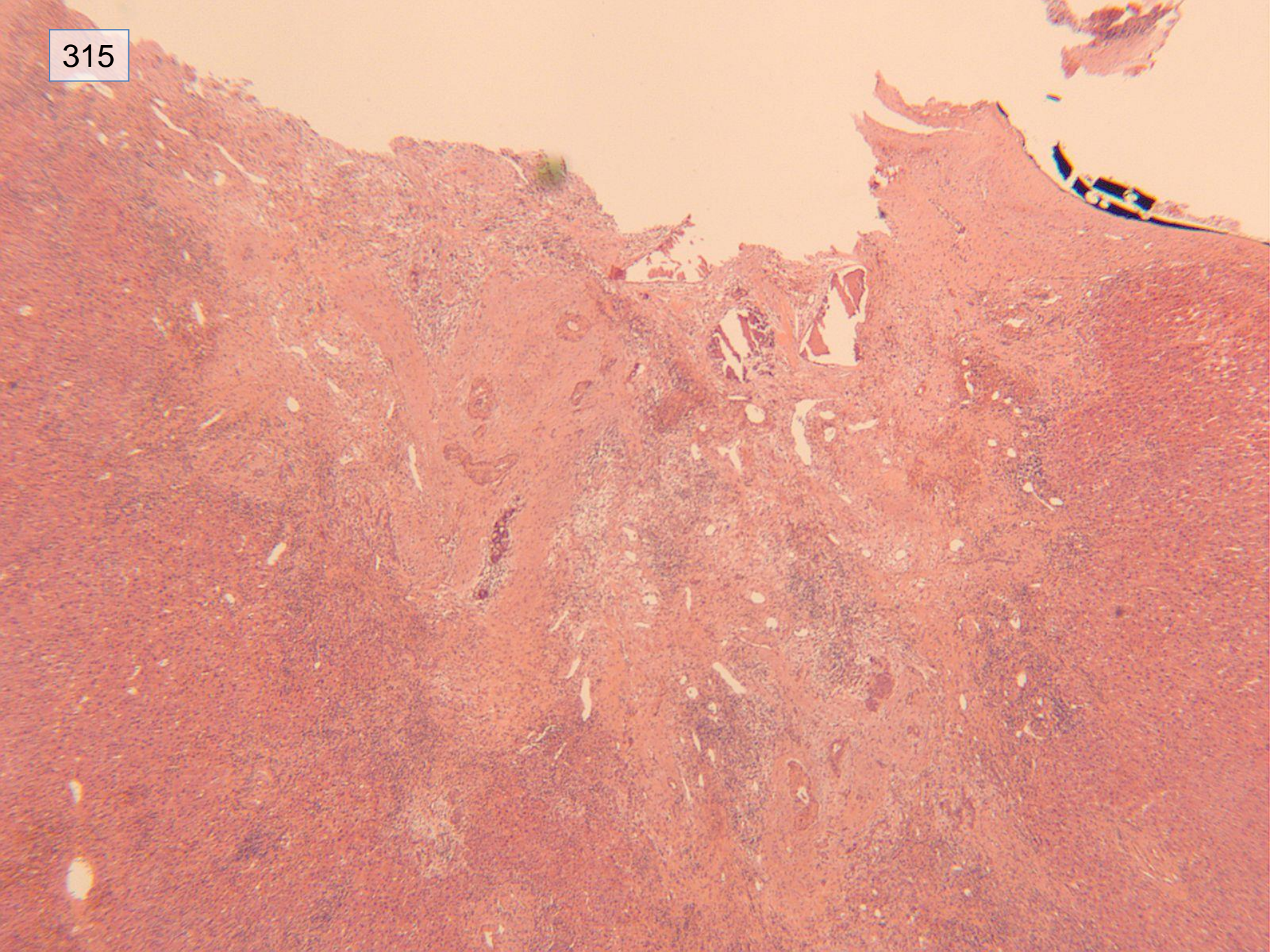
(Specimen photograph and 2x photomicrographs of reticulin stain included).

315

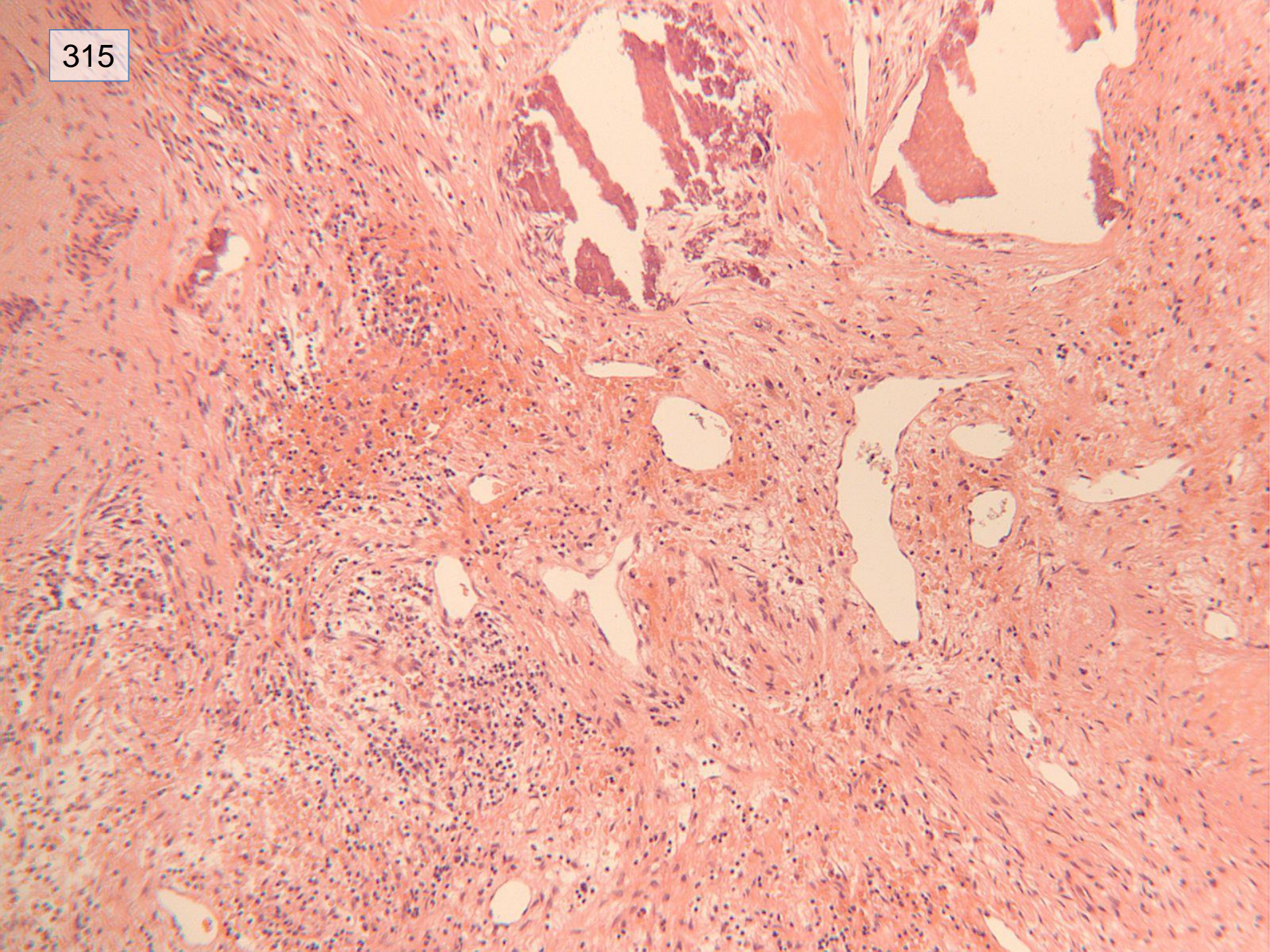




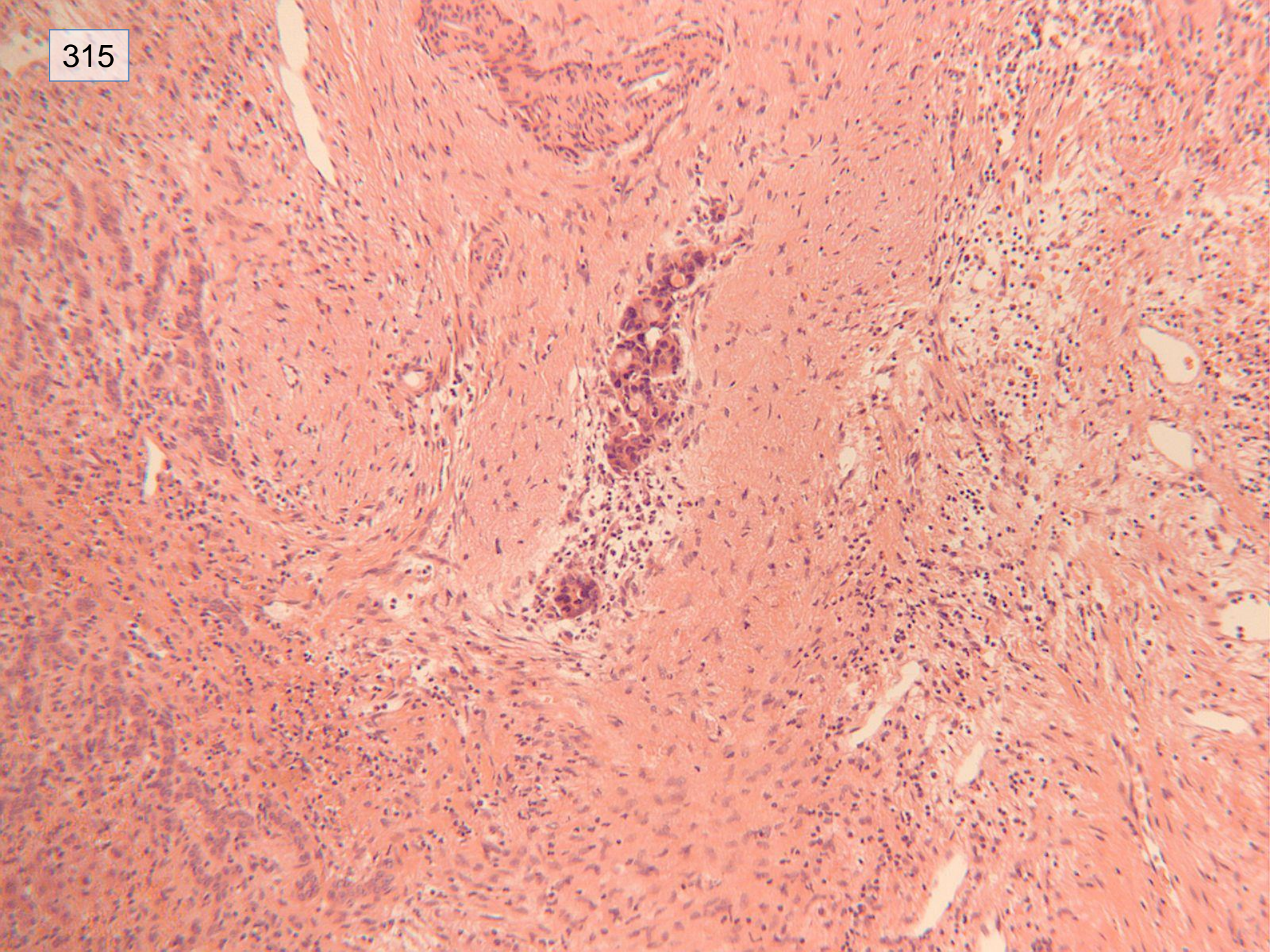
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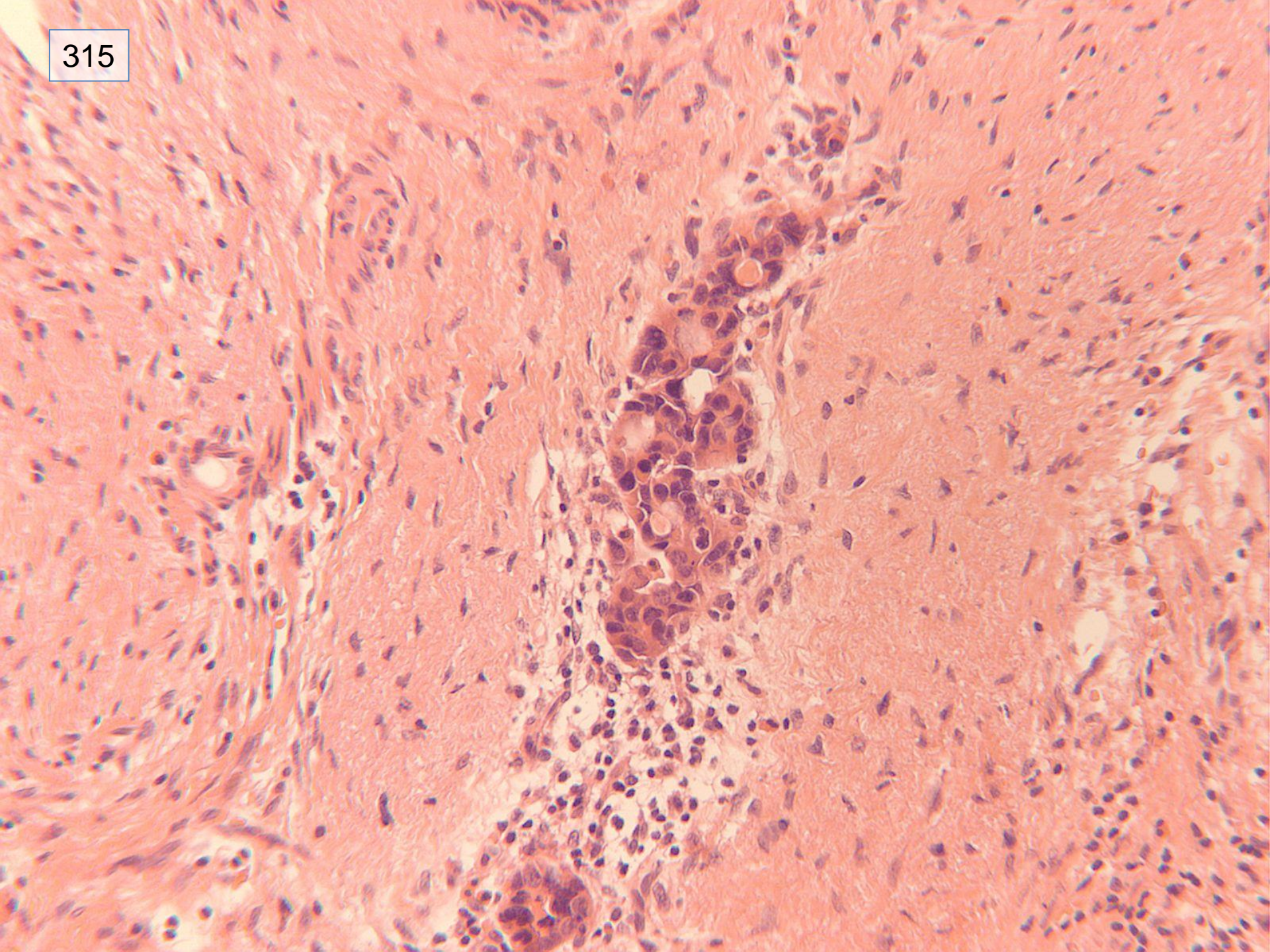
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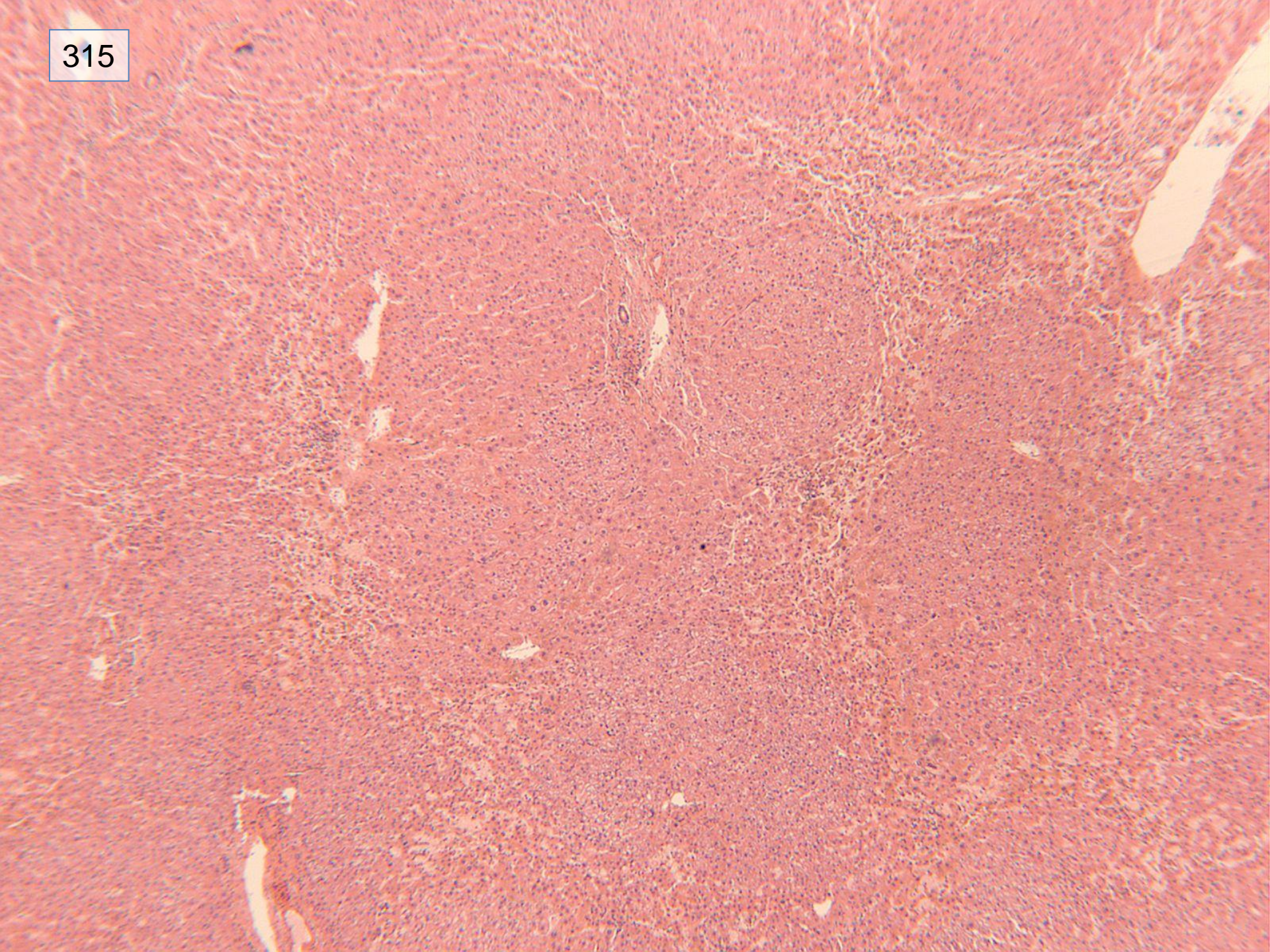
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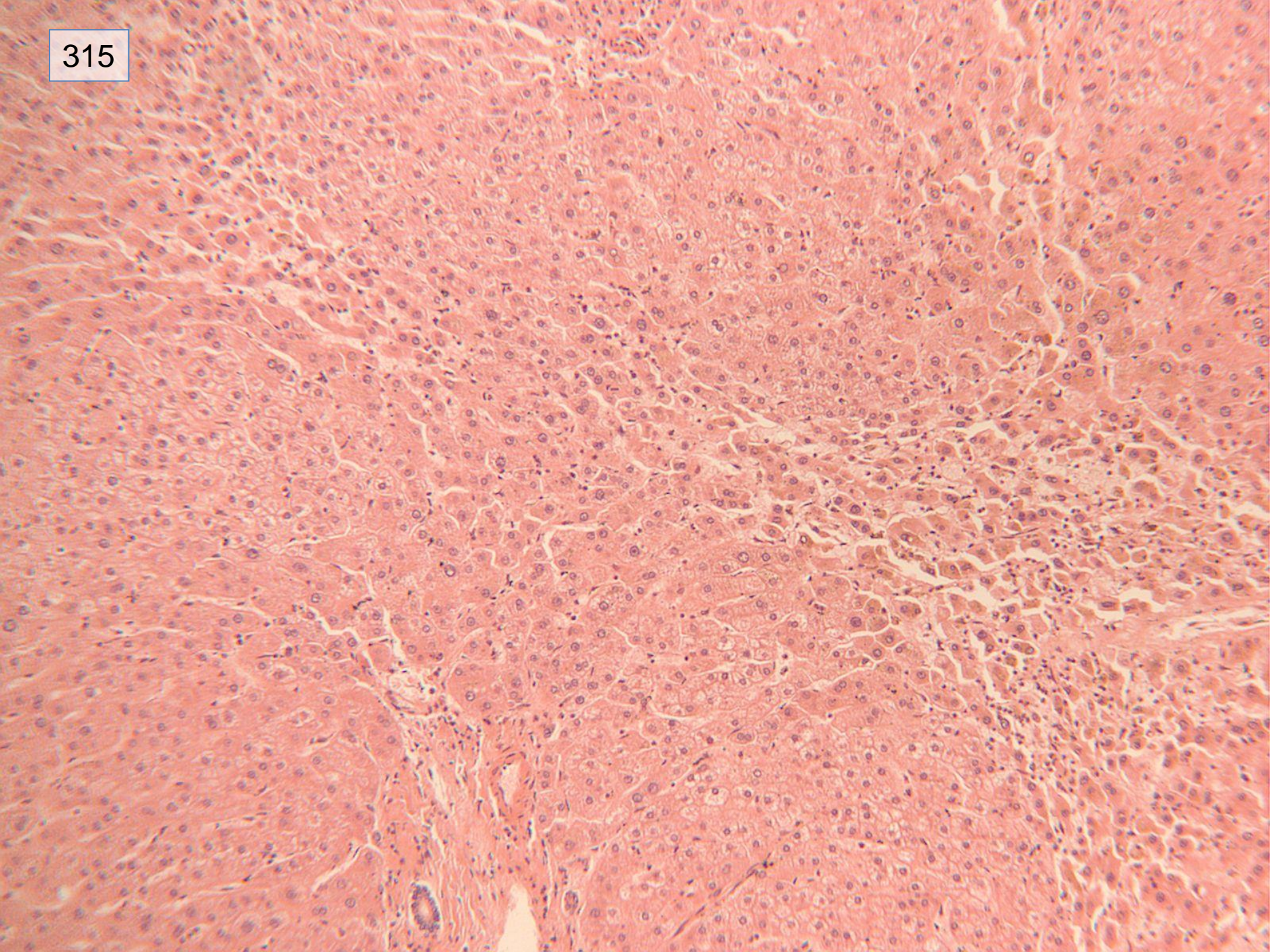
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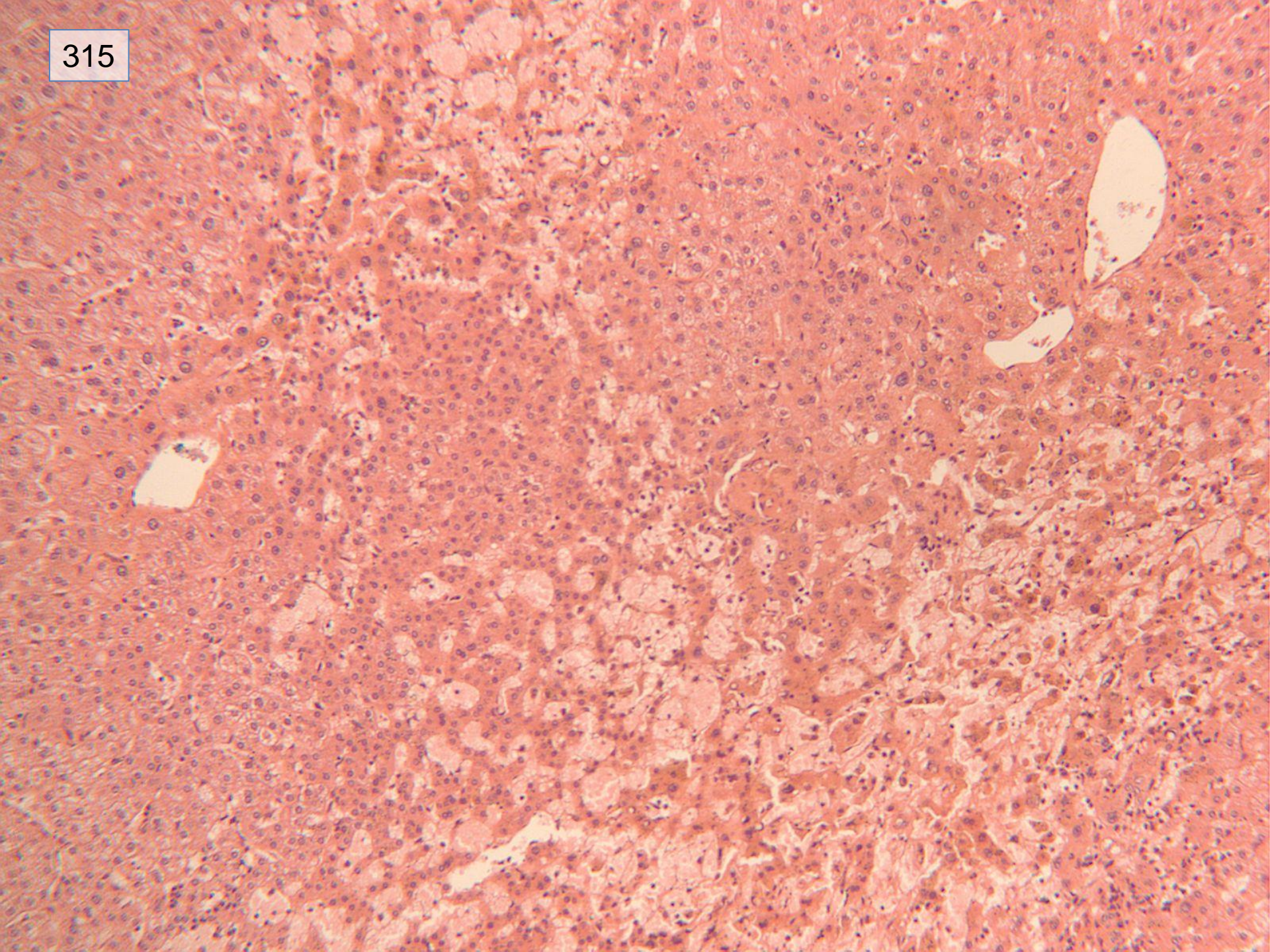


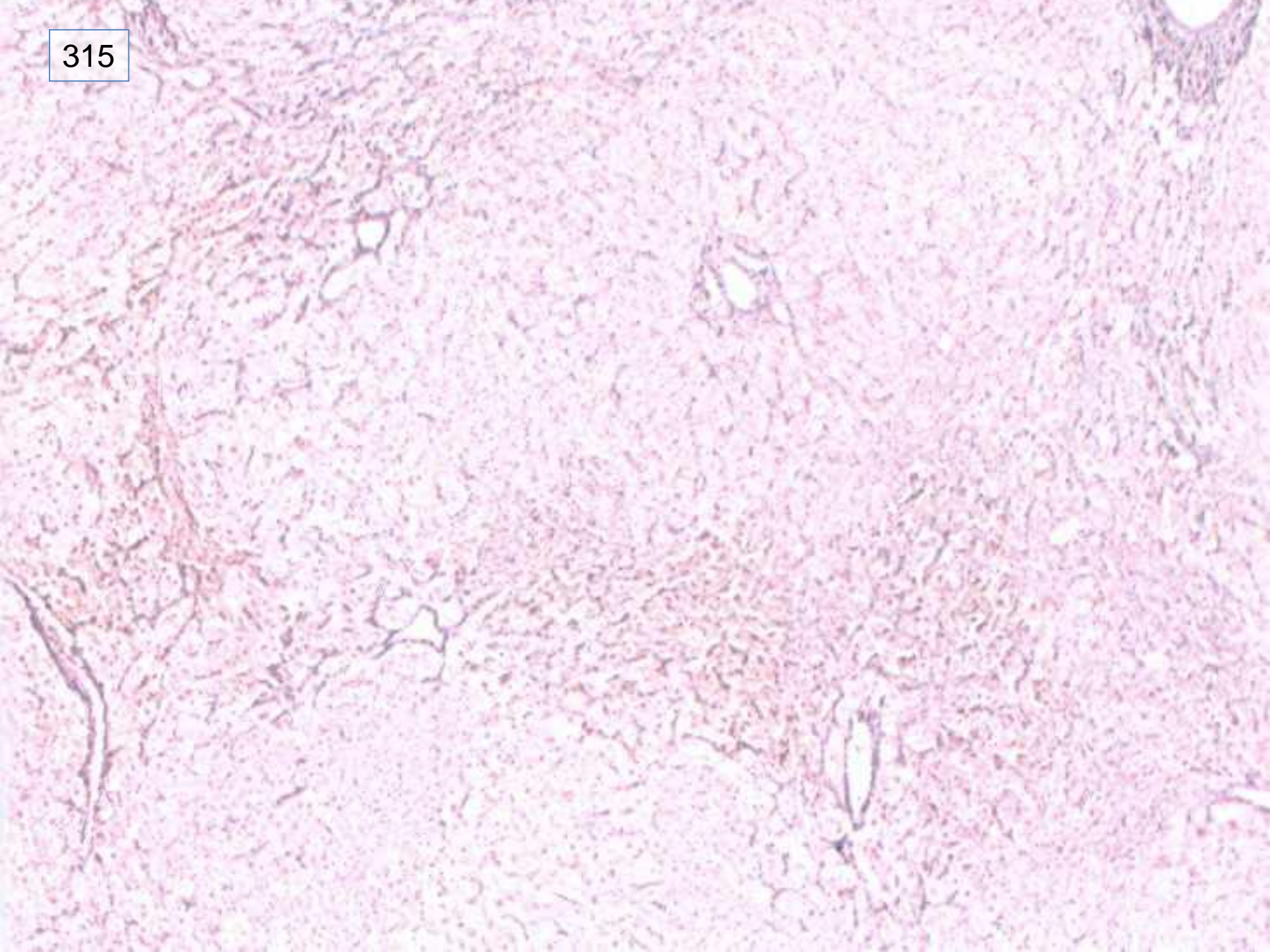
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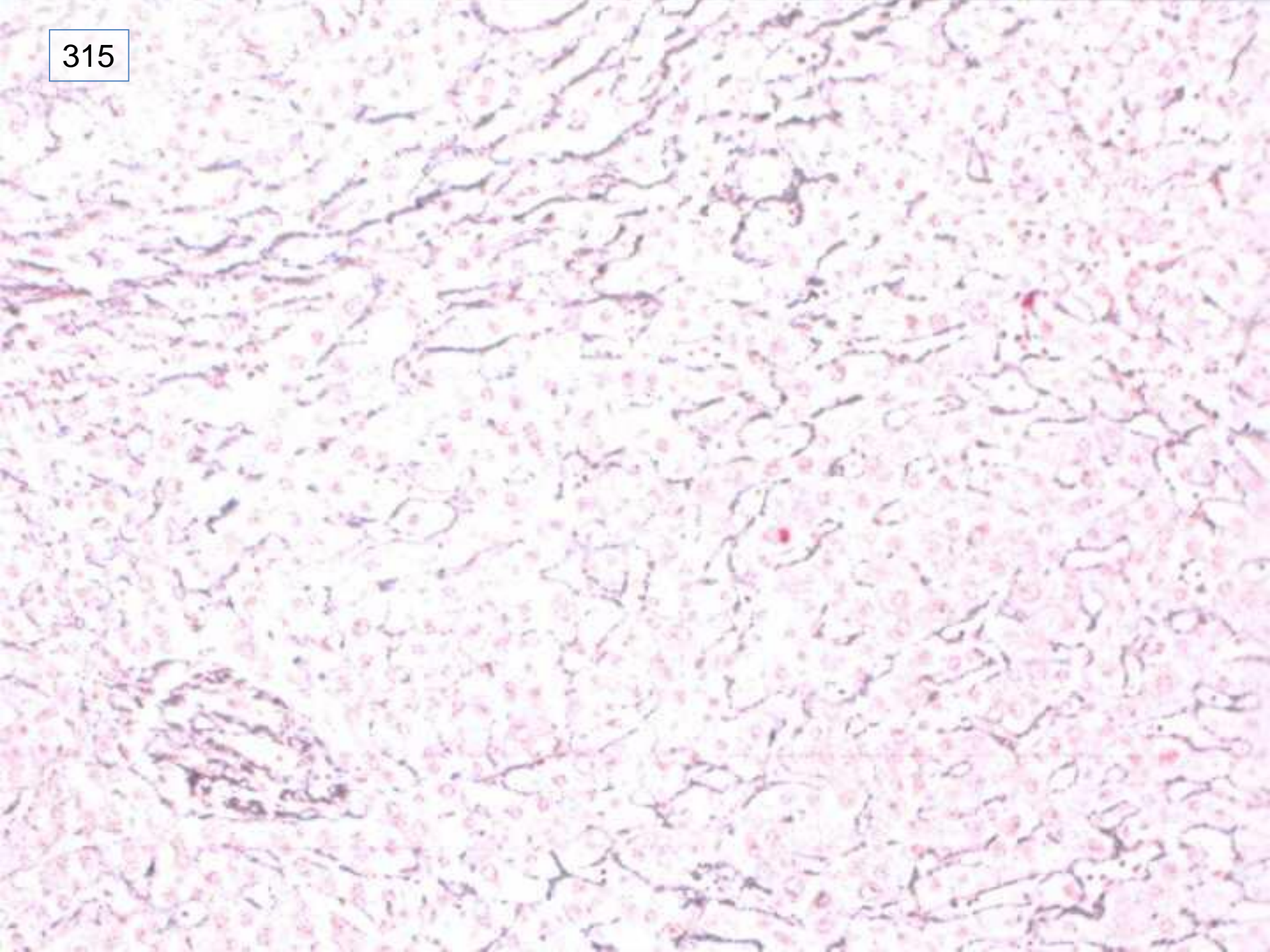


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## Case 315

*Responses:*

Comment on tumour:

45 metastatic adencarcinoma

3 suspect metastatic adenocarcinoma

7 scar, no cancer identified

3 no mention of a scar/tumour

Comment on background liver:

44 nodular regenerative hyperplasia

5 sinusoidal obstruction syndrome

6 morphological description e.g. chronic congestion, collapse and haemorrhage, zones of necrosis etc.

3 no mention of changes in background liver.

35 background liver abnormality due to chemotherapy

1 background liver abnormality due to adjacent space occupying lesion

19 no comment on cause of background abnormality

## Case 315 - scoring

Deduct 5 marks if no mention of scar/tumour or no mention or description of background changes of nodular hyperplasia/sinusoidal obstruction syndrome. The amount of residual adenocarcinoma may have varied among slides, and so as long as the scar of likely previous tumour site was included no marks were deducted.

This case was submitted as a good example of sinusoidal obstruction syndrome (SOS) changes that are a complication of chemotherapy with oxaliplatin<sup>1</sup>.

This patient had a protracted post-operative course.

1. Rubbia-Brandt L et al. Ann Oncol. 2004 Mar;15(3):460-6

## Case 315

Original diagnosis:

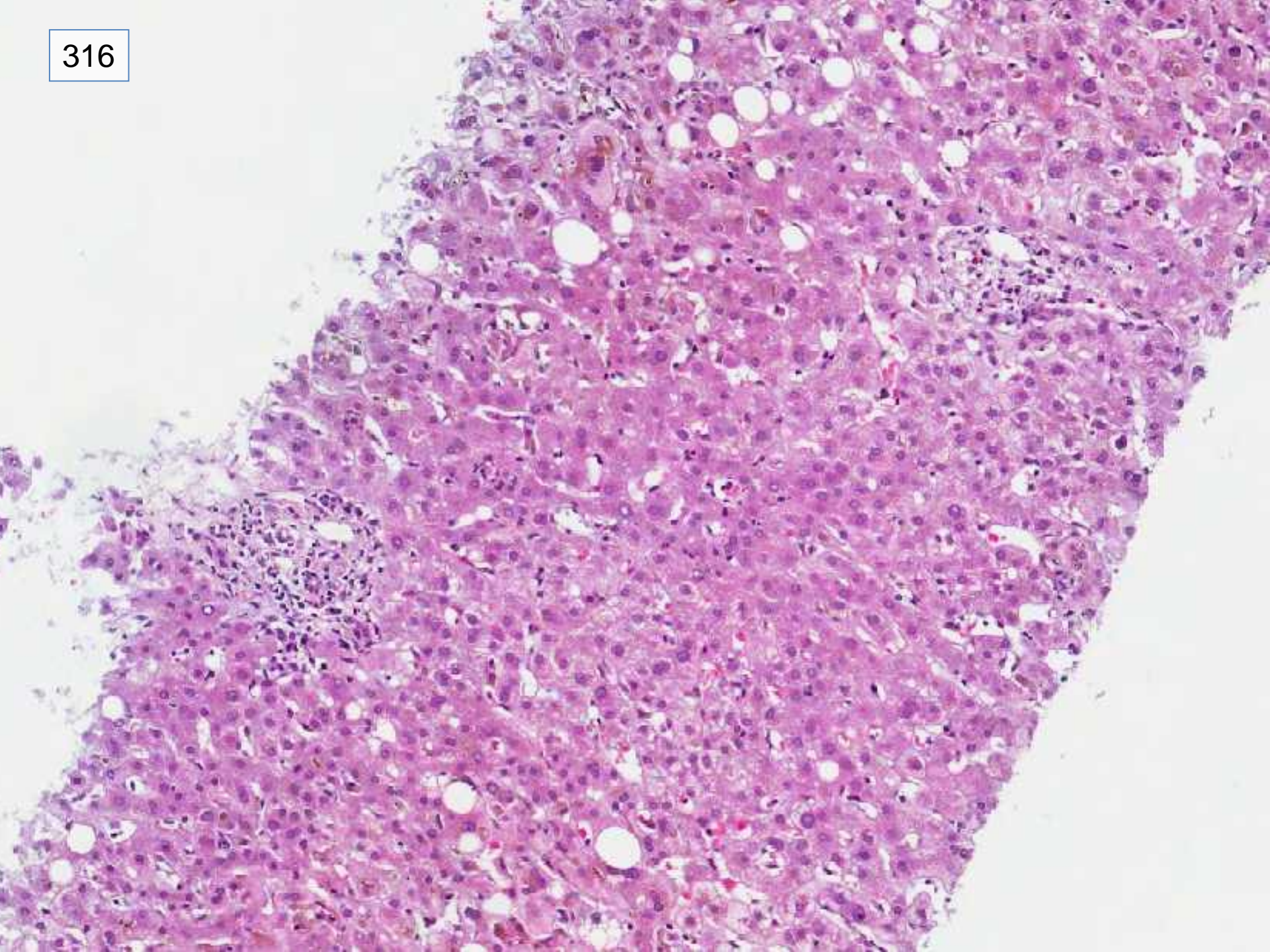
sinusoidal obstruction syndrome including  
nodular regenerative hyperplasia and  
subcapsular scar with focal residual  
adenocarcinoma

## **Case 316**

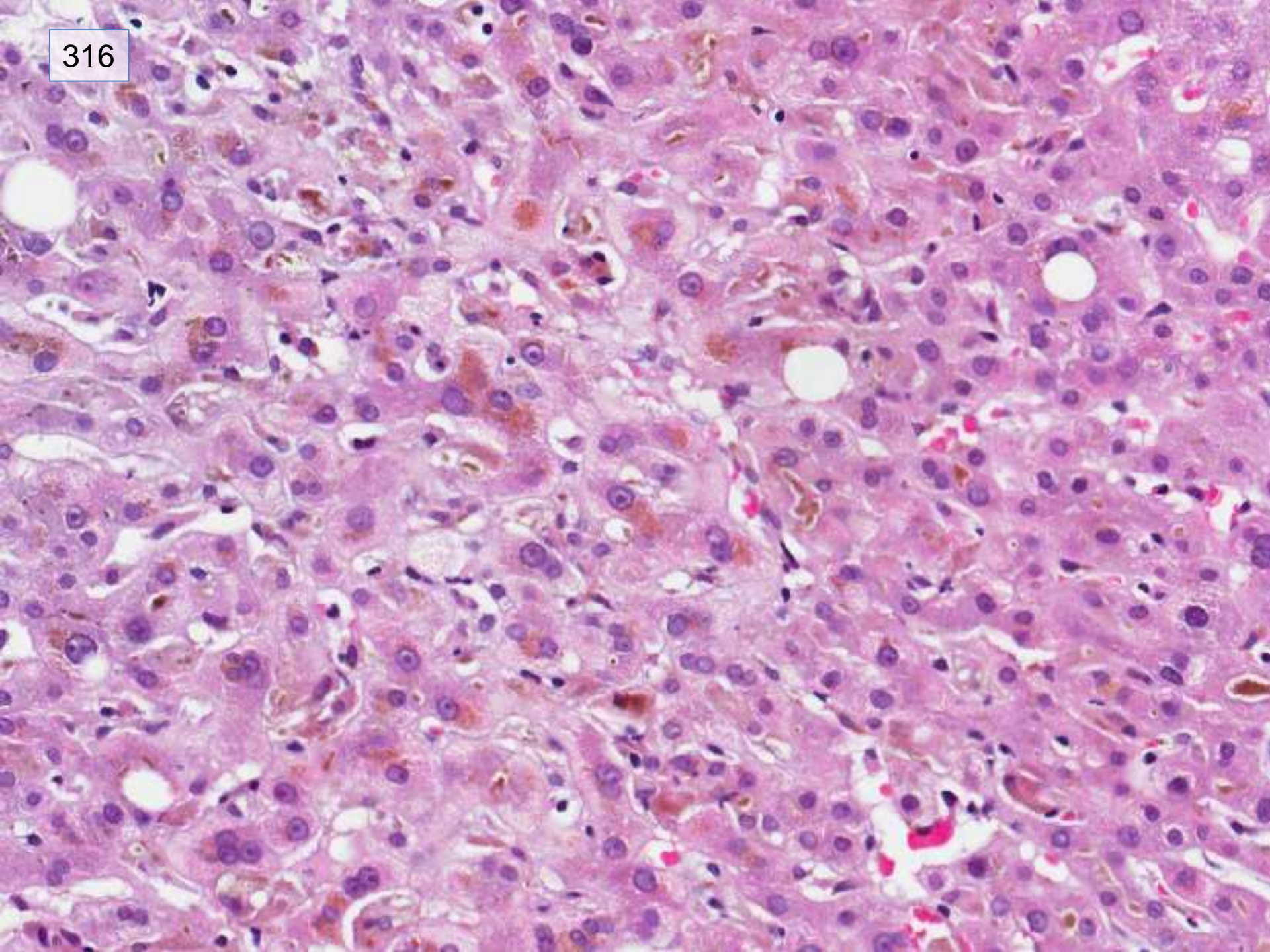
65M Common bile duct stone extracted by ERCP but progressive jaundice since.



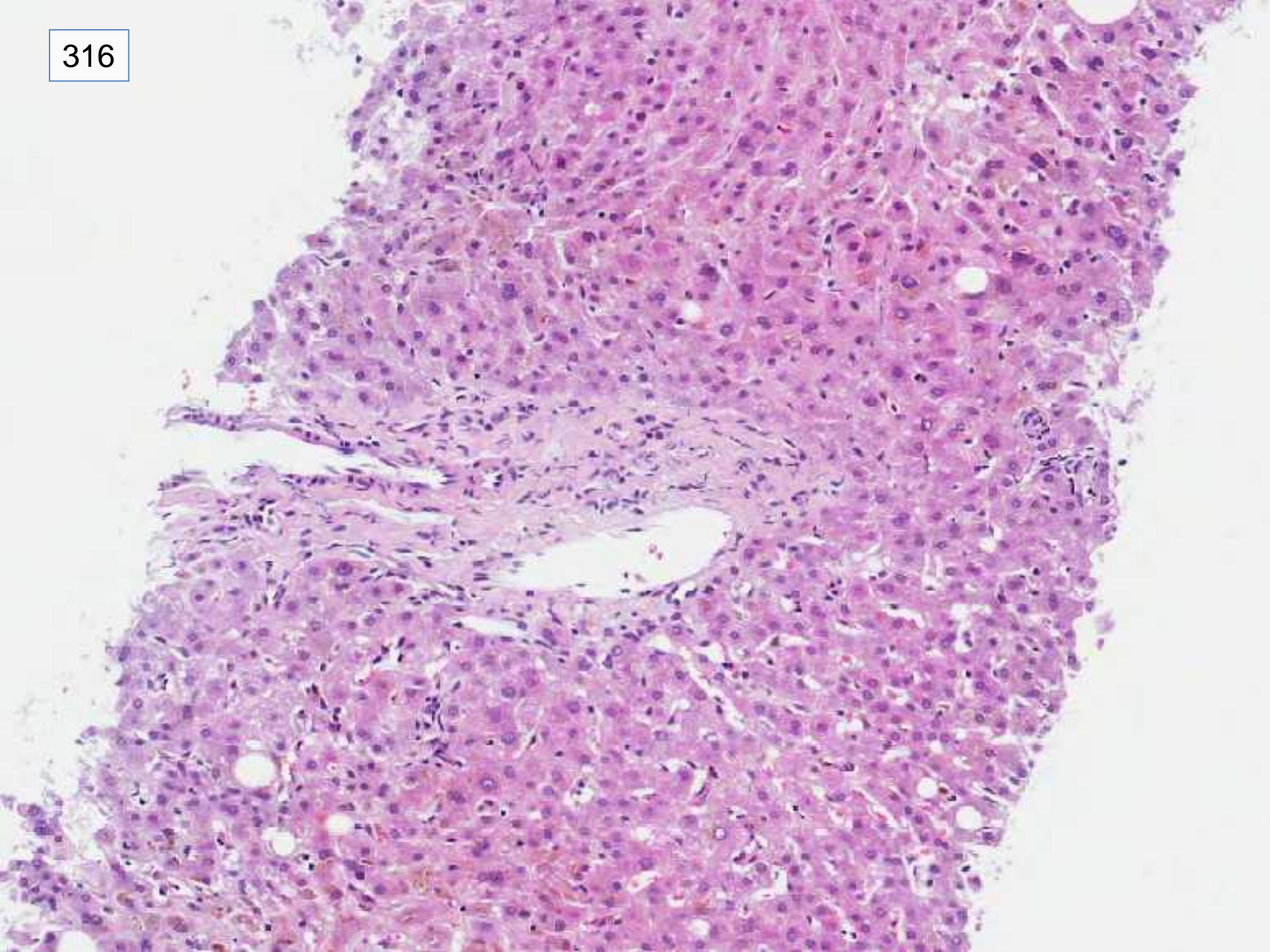
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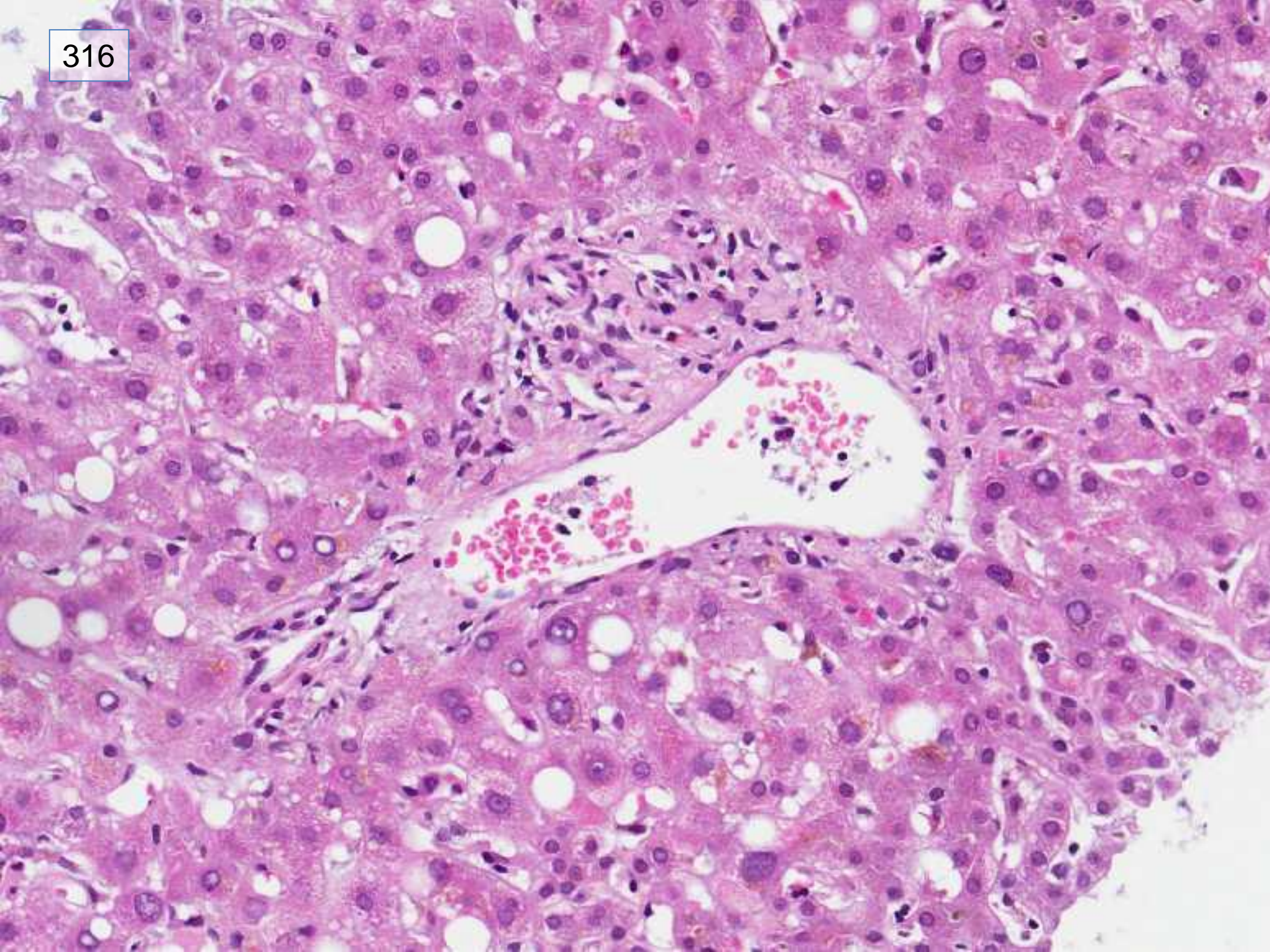
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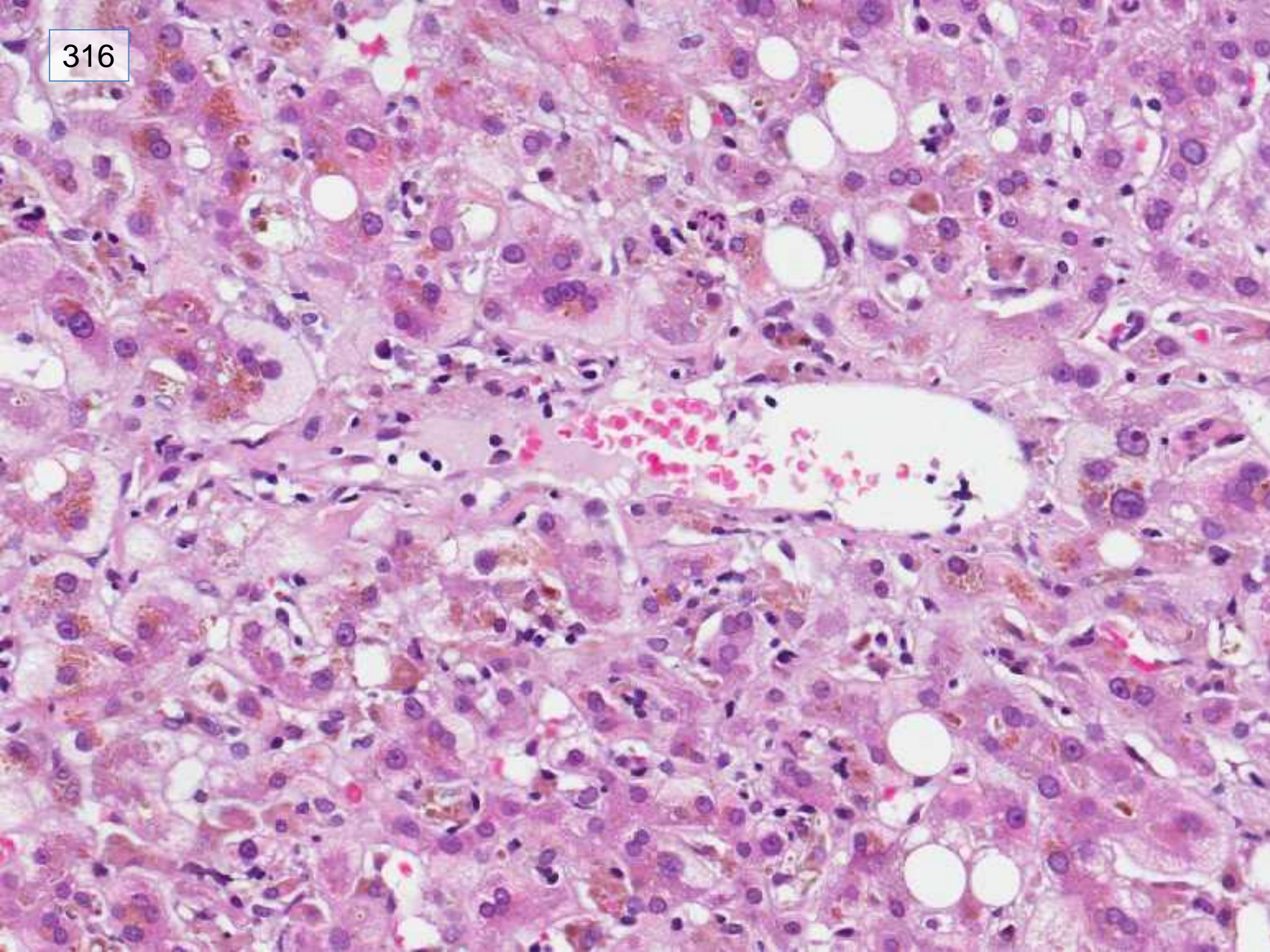
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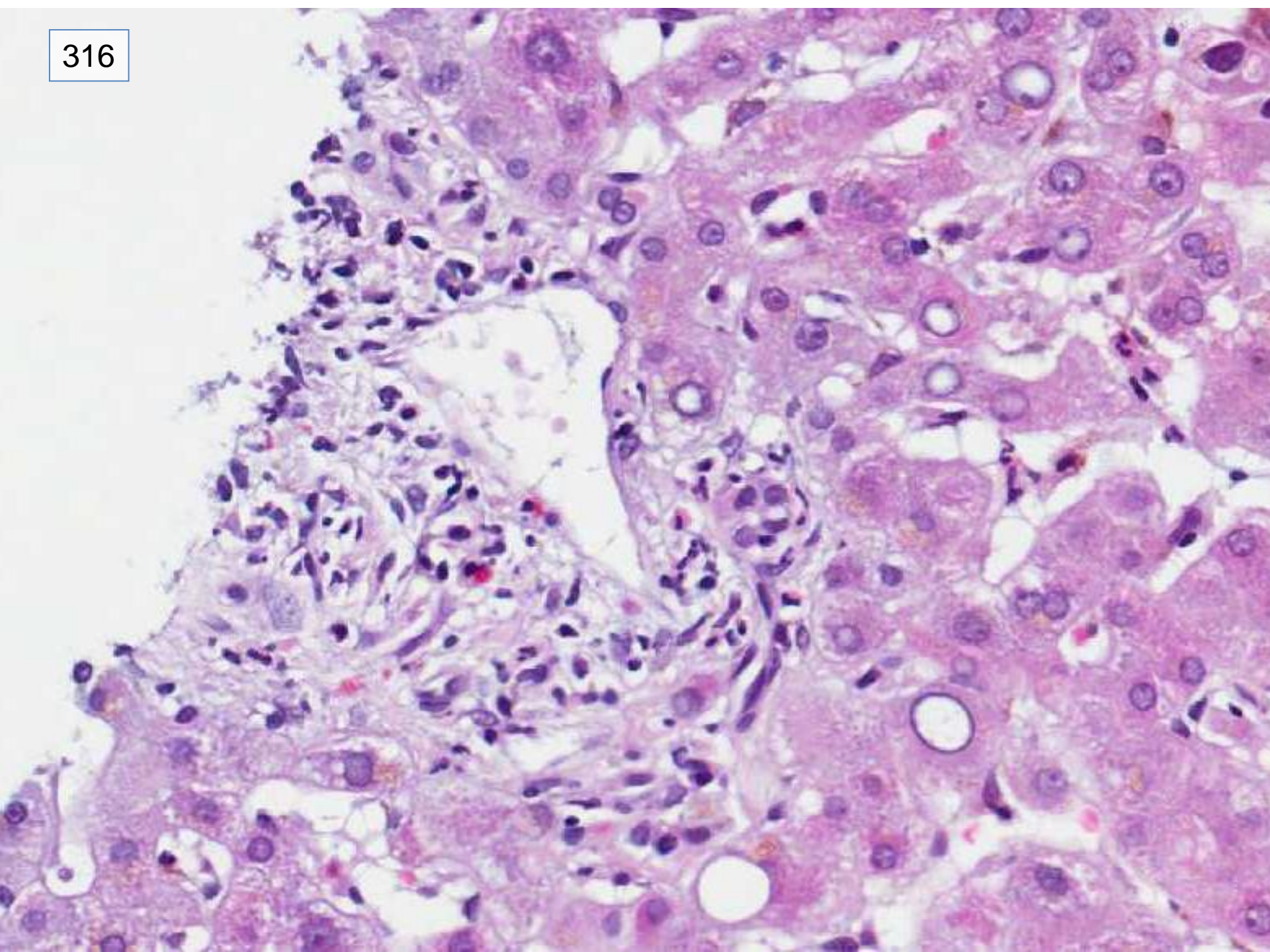


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316





## Case 316

### *Responses:*

All included mention of cholestasis.

41 cholestasis, +/- cholestatic hepatitis, drugs main/most likely cause  
(of which 13 included comment on ductopaenia)

.....  
14 differential diagnosis including drug reaction

14 no mention of drug induced liver injury

13 extra-hepatic biliary obstruction

4 possible ascending cholangitis

5 not suggestive of biliary obstruction

3 cholestatic hepatitis NOS

1 'sepsis following obstruction' as only diagnosis

1 'obstructive cholangiopathy' as only diagnosis

1 'severe canalicular cholestasis, paucity of bile ducts – do cytokeratin, orcein,  
autoantibodies and viral serology'

also mentioned:

18 steatosis

3 steatohepatitis

9 needs Orcein for copper associated protein

# Case 316 scoring and discussion

Score 10 as long as differential diagnosis includes drug reaction. Score 0 if no mention of drugs induced cholestasis anywhere in the response.

Discussion related to use of terminology 'cholestatic hepatitis' vs. cholestasis – the degree of inflammatory infiltrate and Kupffer cell hyperplasia in this case may be purely a reaction to bilirubinostasis, and insufficient for a diagnosis of cholestatic hepatitis.

Differential diagnosis with large duct obstruction – although drugs are the most likely cause of this cholestasis, the differential diagnosis of obstruction remains a possibility and the clinicians should consider further investigation of the biliary tree if jaundice does not settle.

Although more ductular reaction would be expected if this degree of cholestasis were due to large duct obstruction, experience shows that ductular reaction is not invariably present in obstructive jaundice (e.g. post transplant patient biopsied during surgical intervention for stricture).

## Case 316

Original diagnosis:

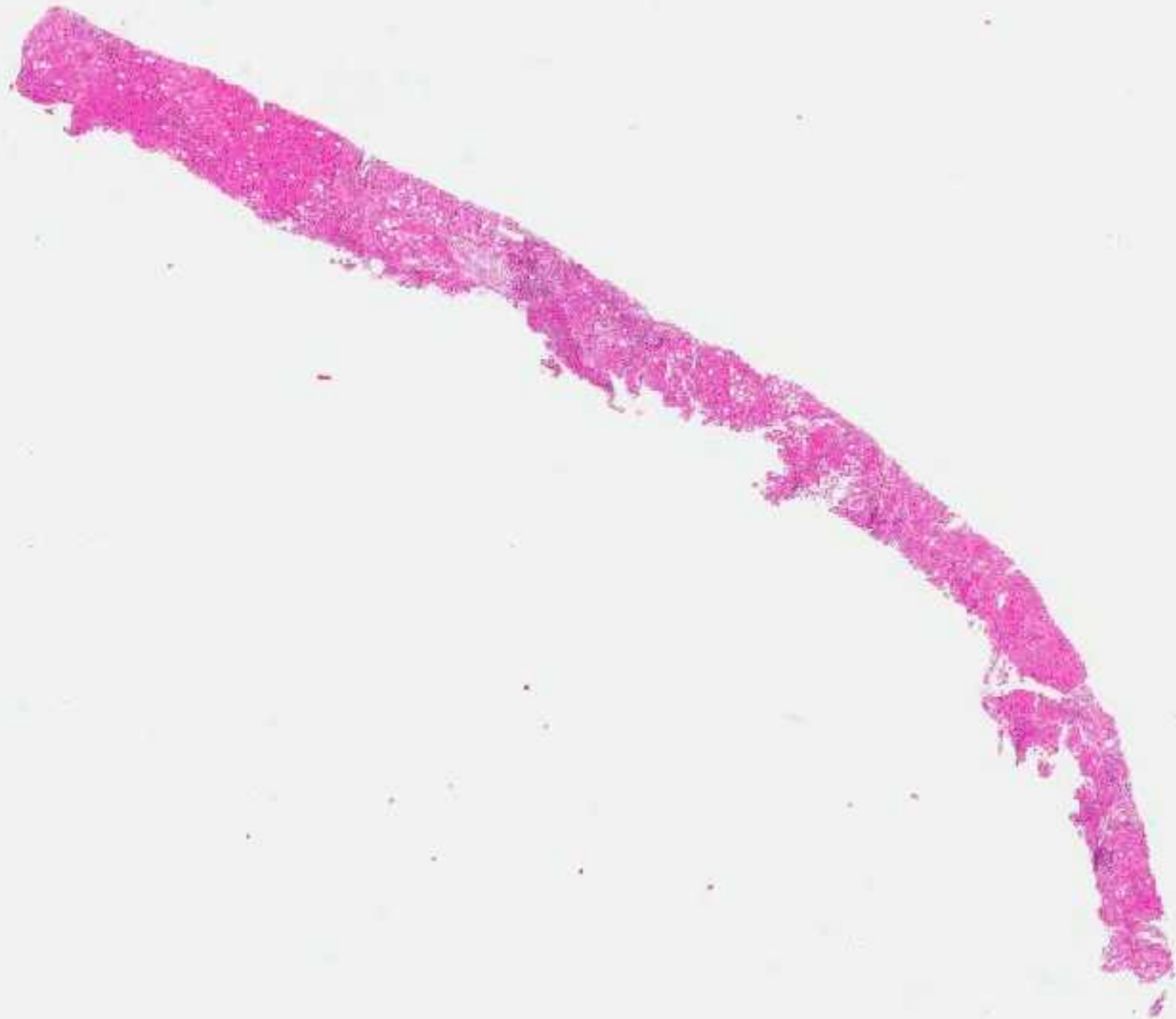
Cholestasis most likely due to drug-induced liver injury.

Further enquiry revealed history of antibiotic use prior to the onset of jaundice.

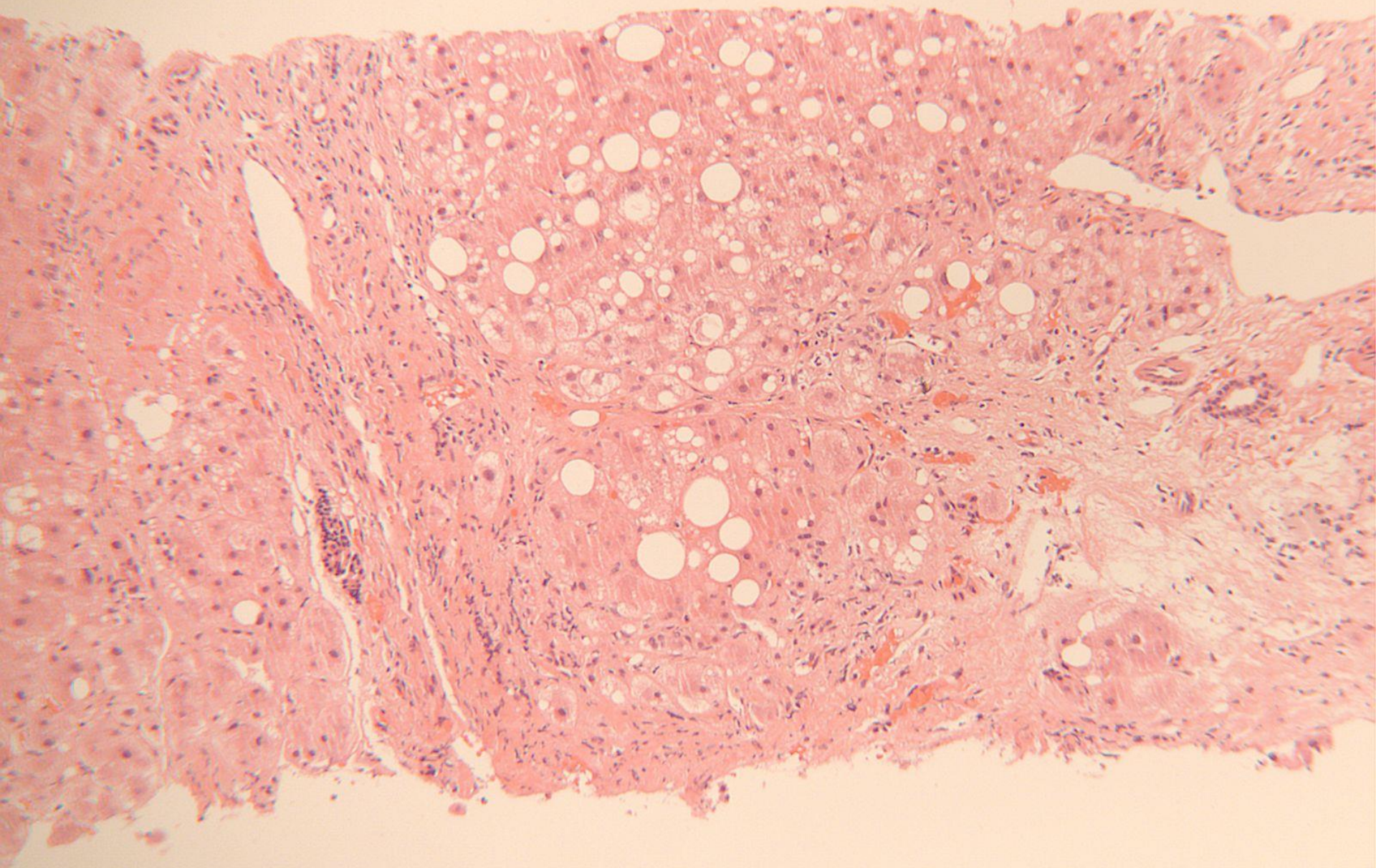
The orcein stain was negative for copper-associated protein.

## **Case 317**

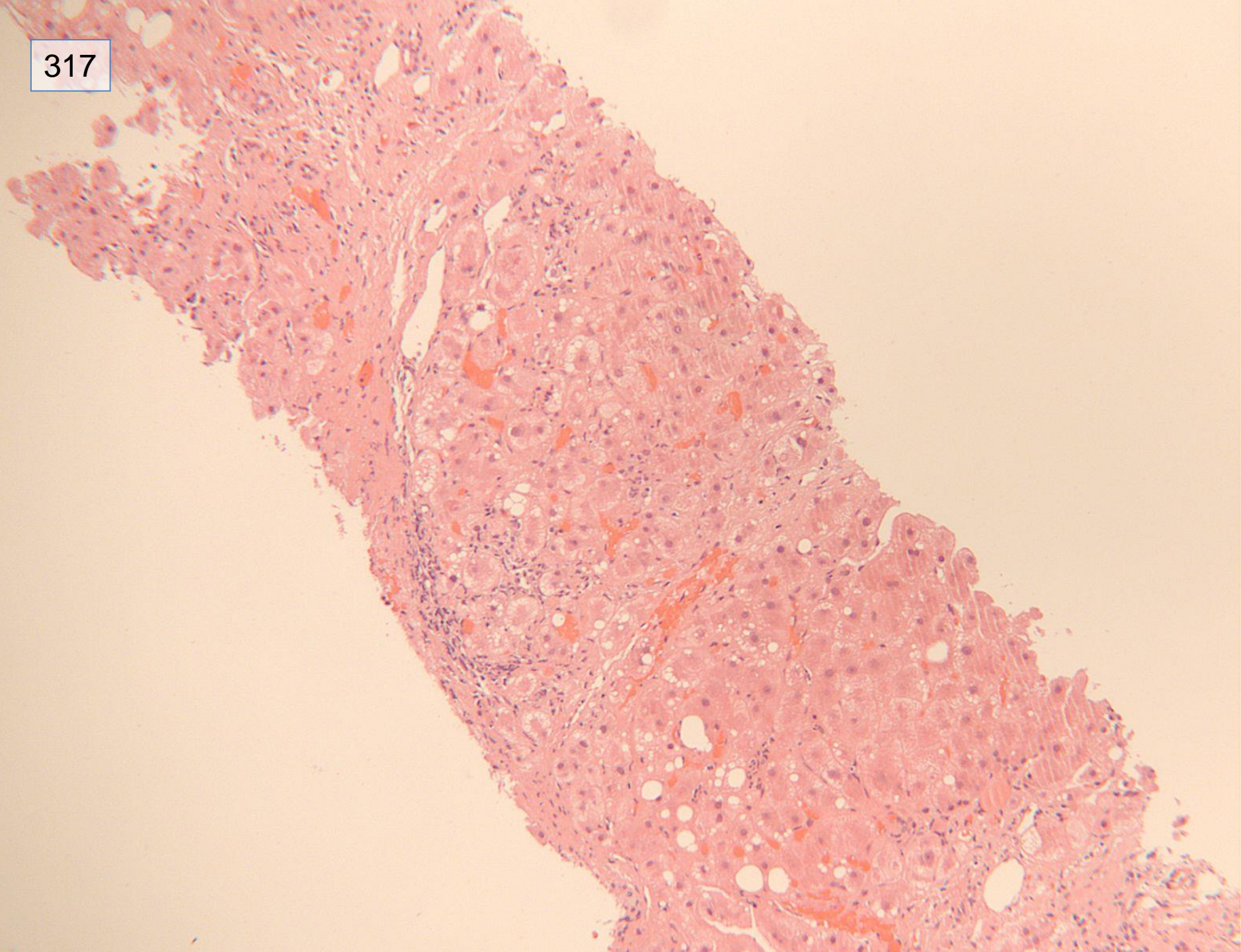
58M Abnormal LFTs. GGT 1064, previous alcohol excess.



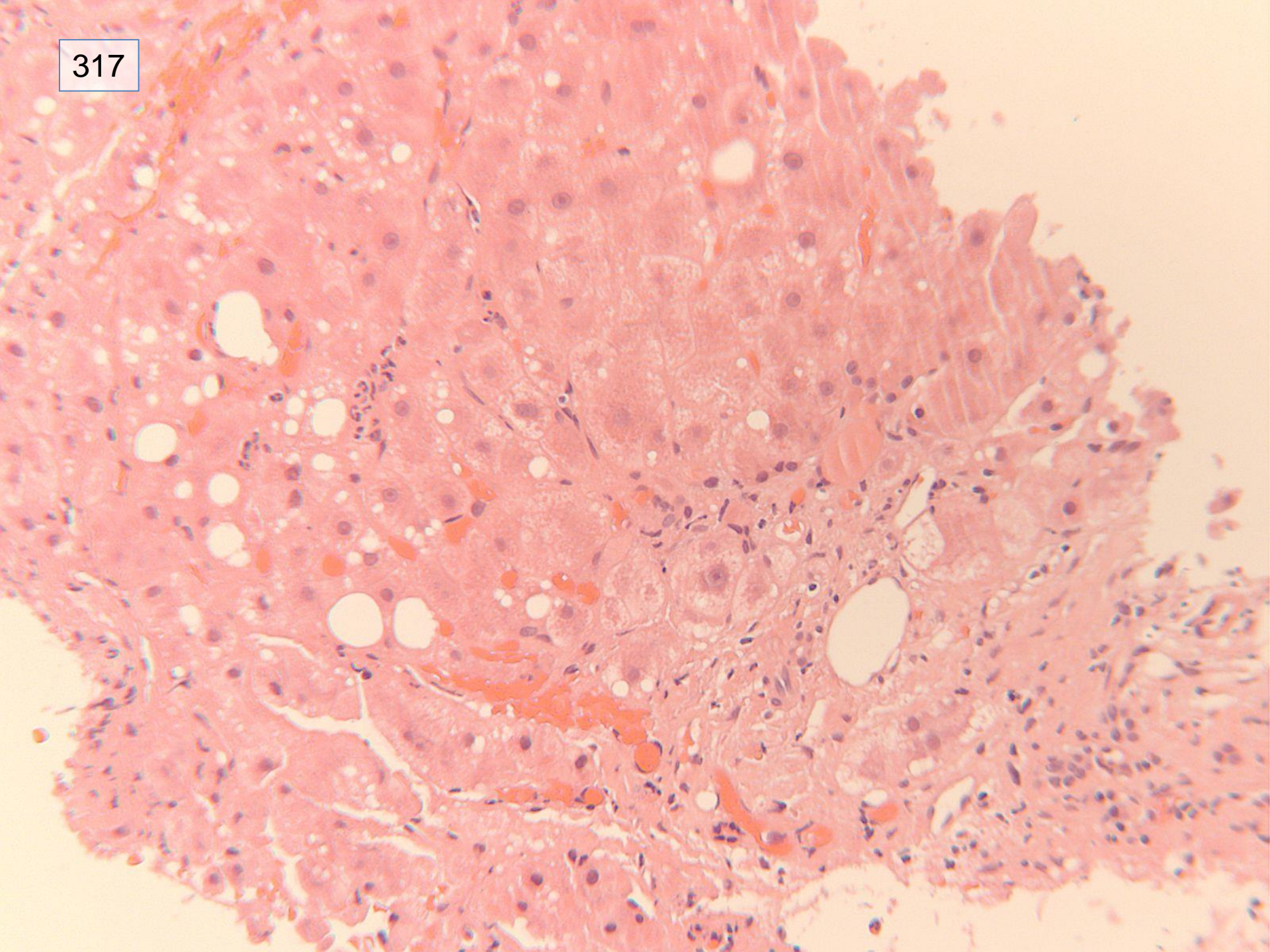
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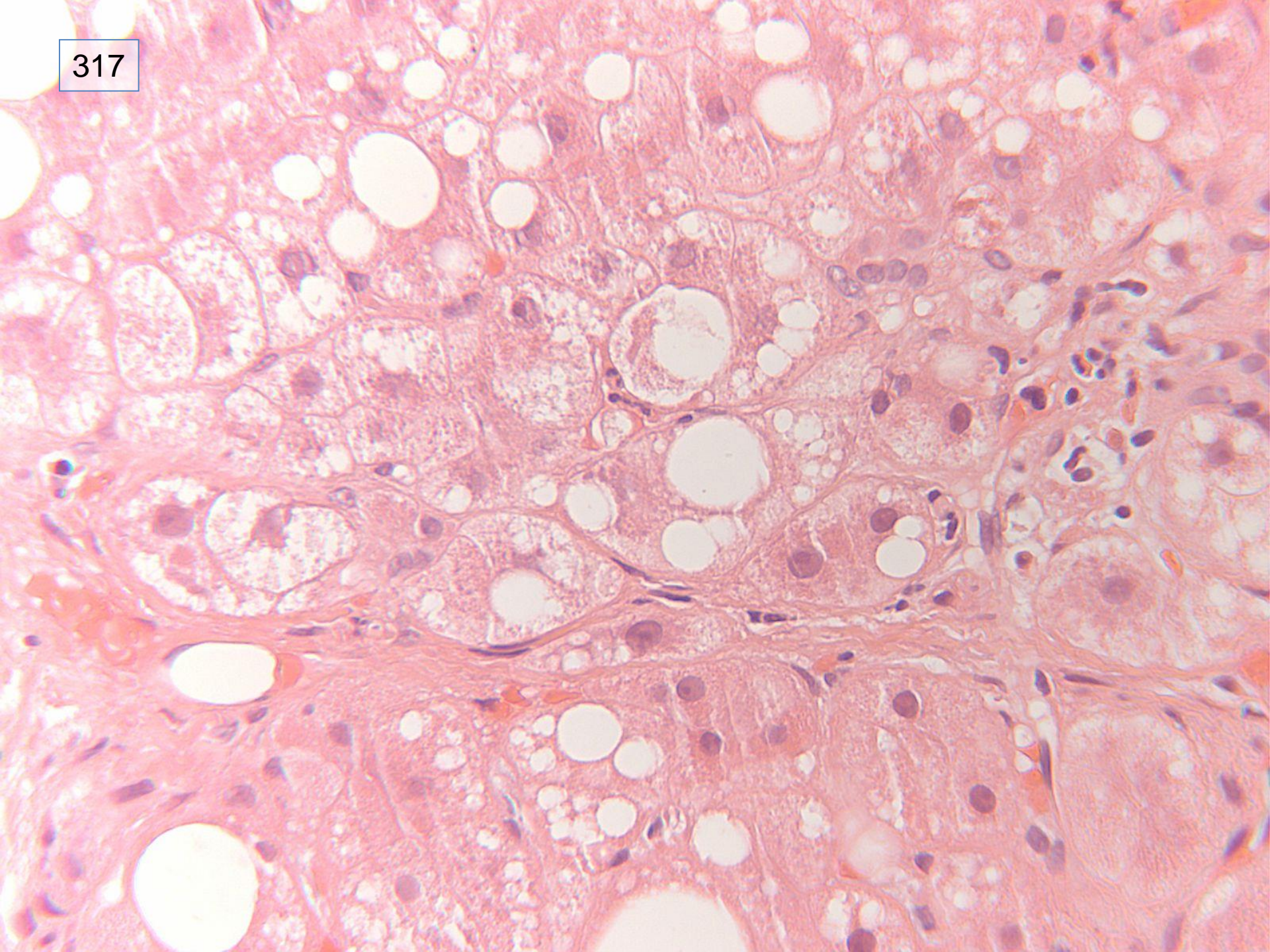
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317



## Case 317

### *Responses*

- 46 Cirrhosis, steatohepatitis, alcohol
- 8 fibrosis, steatohepatitis, alcohol
- 1 cirrhosis, steatosis, alcohol
- 1 micronodular cirrhosis with steatohepatitis,  
alcohol not mentioned
- 2 cirrhosis, consistent with alcoholic aetiology

*Original diagnosis: cirrhosis with steatohepatitis,  
features in keeping with alcoholic liver disease.*

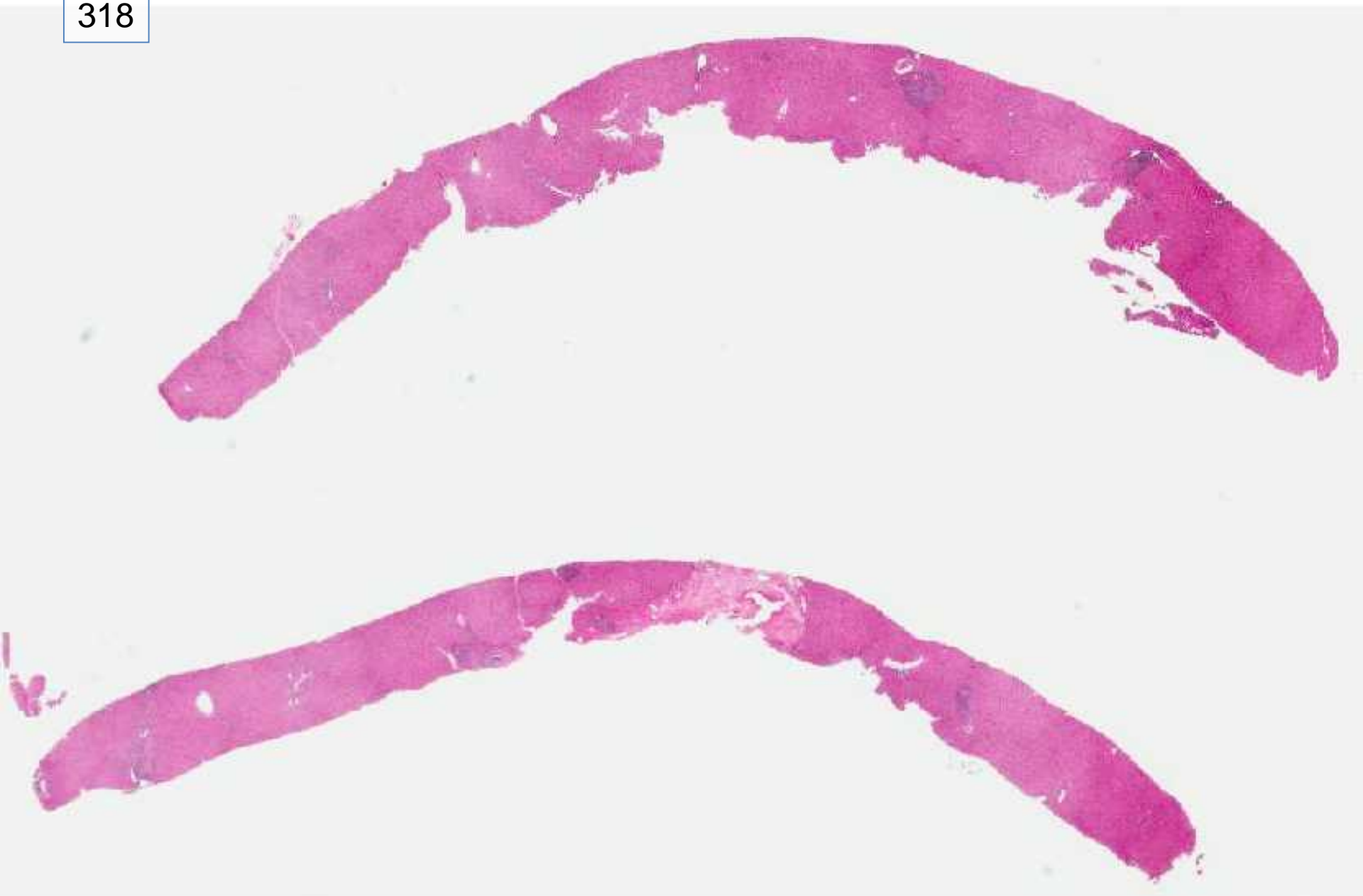
## Case 317, scoring and discussion

This case showed all the diagnostic features of steatohepatitis - hepatocyte ballooning, Mallory bodies, lobular neutrophil inflammation and fibrosis all present.

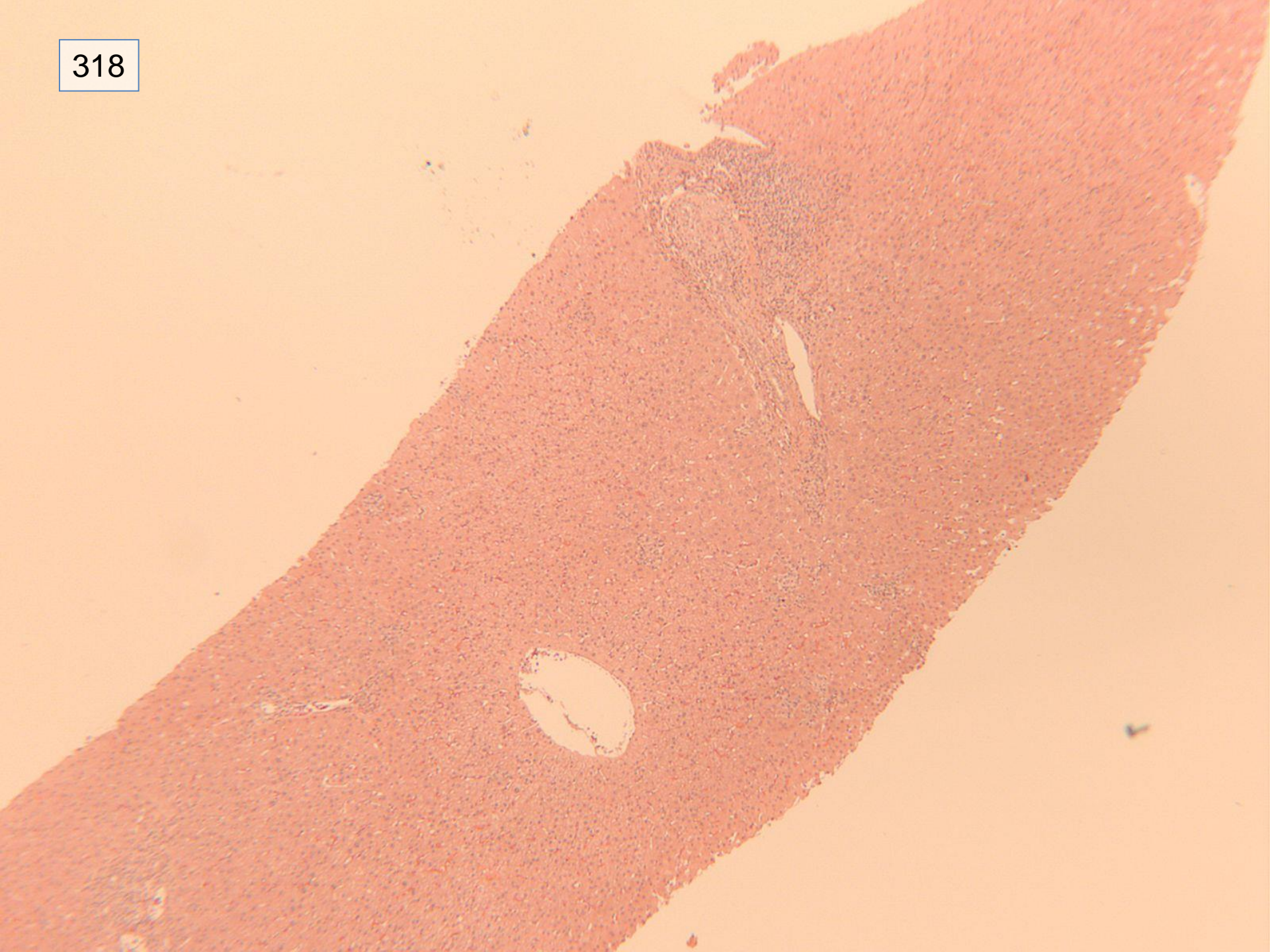
Score 5 points for responses that do not include steatohepatitis, or the clinical comment that this was attributable to alcohol.

## **Case 318**

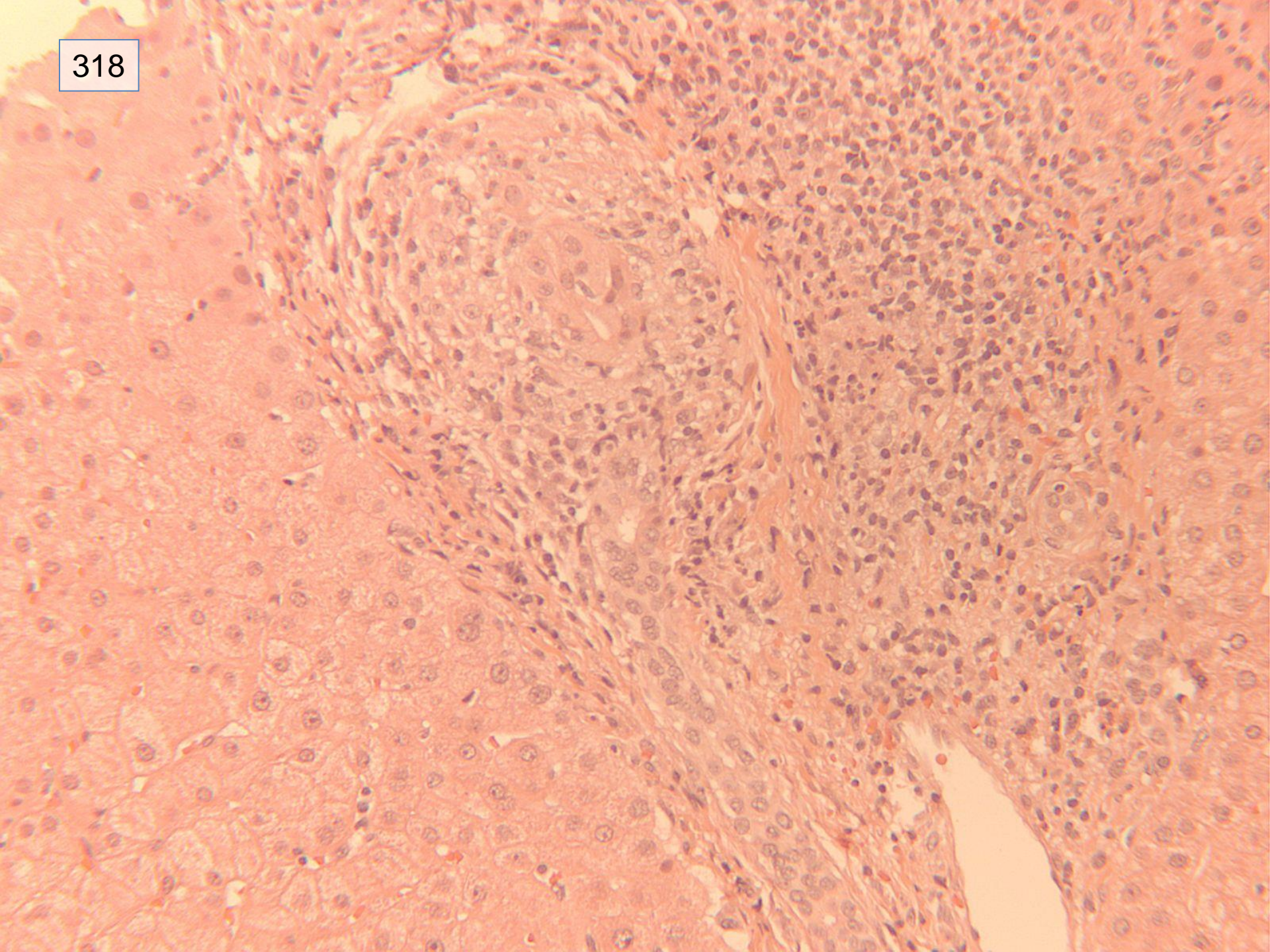
44F Deranged LFTs – raised alkaline phosphatase, raised gamma GT, normal bilirubin



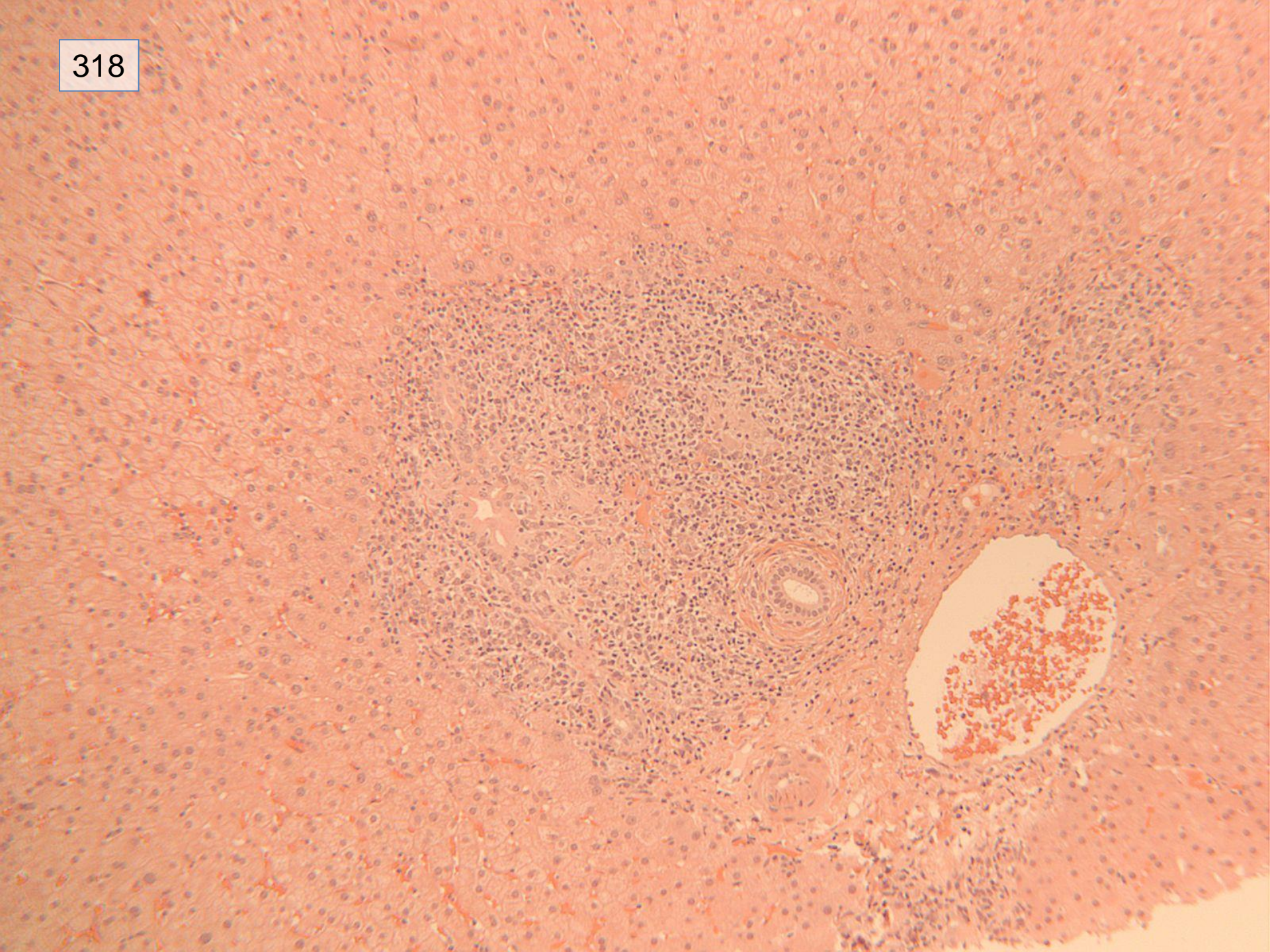
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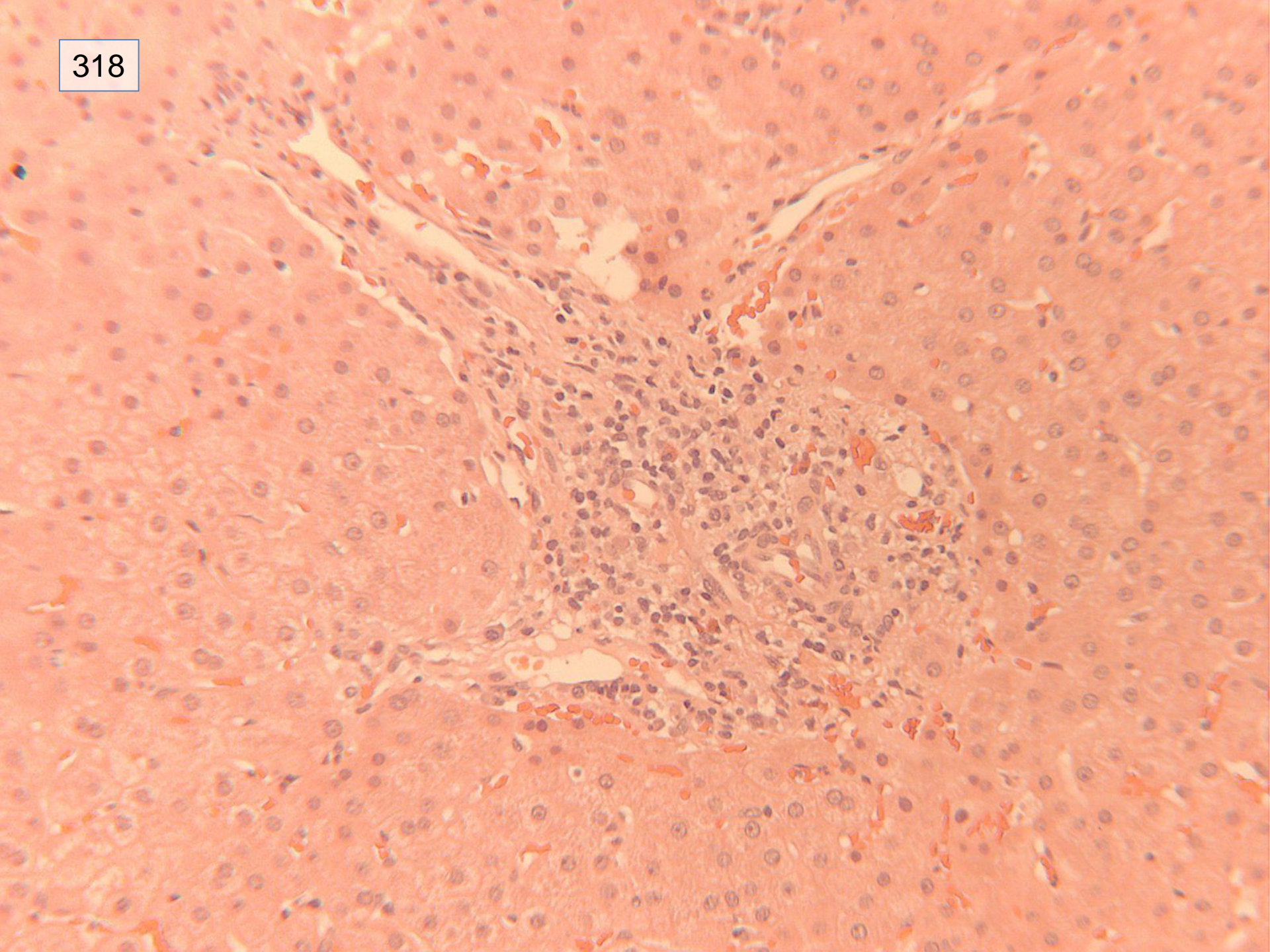
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318



# Case 318

## *Responses:*

50 Primary biliary cirrhosis as only diagnosis

5 PBC included in differential diagnosis:

2 AIH or PBC/AIH overlap, no mention of granulomas

1 granulomatous hepatitis, differential PBC, sarcoid, Hodgkin's

1 chronic active hepatitis, ?PBC, ?AIH, ?drug

1 early biliary (cholestatic) liver disease, Differential PBC/PSC/overlap

2 no mention of PBC:

1 AIH, needs autoantibodies, Hepatitis C

1 granulomatous hepatitis, ?parasitic cyst in one portal tract, differential sarcoid, TB etc. (no mention of PBC or autoantibodies)

## *Comments:*

43 needs AMA/'serology'

19 needs orcein

## Case 318 scoring and discussion

The bile duct granulomas were felt to be so characteristic of PBC that the diagnosis should be unqualified. Score 5 marks for responses that included PBC in a differential diagnosis, and no marks for those without PBC at all.

Autoantibodies would be requested, although if AMA were negative, this would still be best regarded as AMA negative PBC.

‘Granulomatous hepatitis’ is not an appropriate terminology for this case, as there is no hepatitic component. ‘Granulomatous liver disease’ is a preferred description where granulomas are not associated with a lobular necroinflammatory component.

## Case 318

Original diagnosis: primary biliary cirrhosis.

AMA >1:640, other autoantibodies negative

## Case 319

70M ? HCC in cirrhosis.

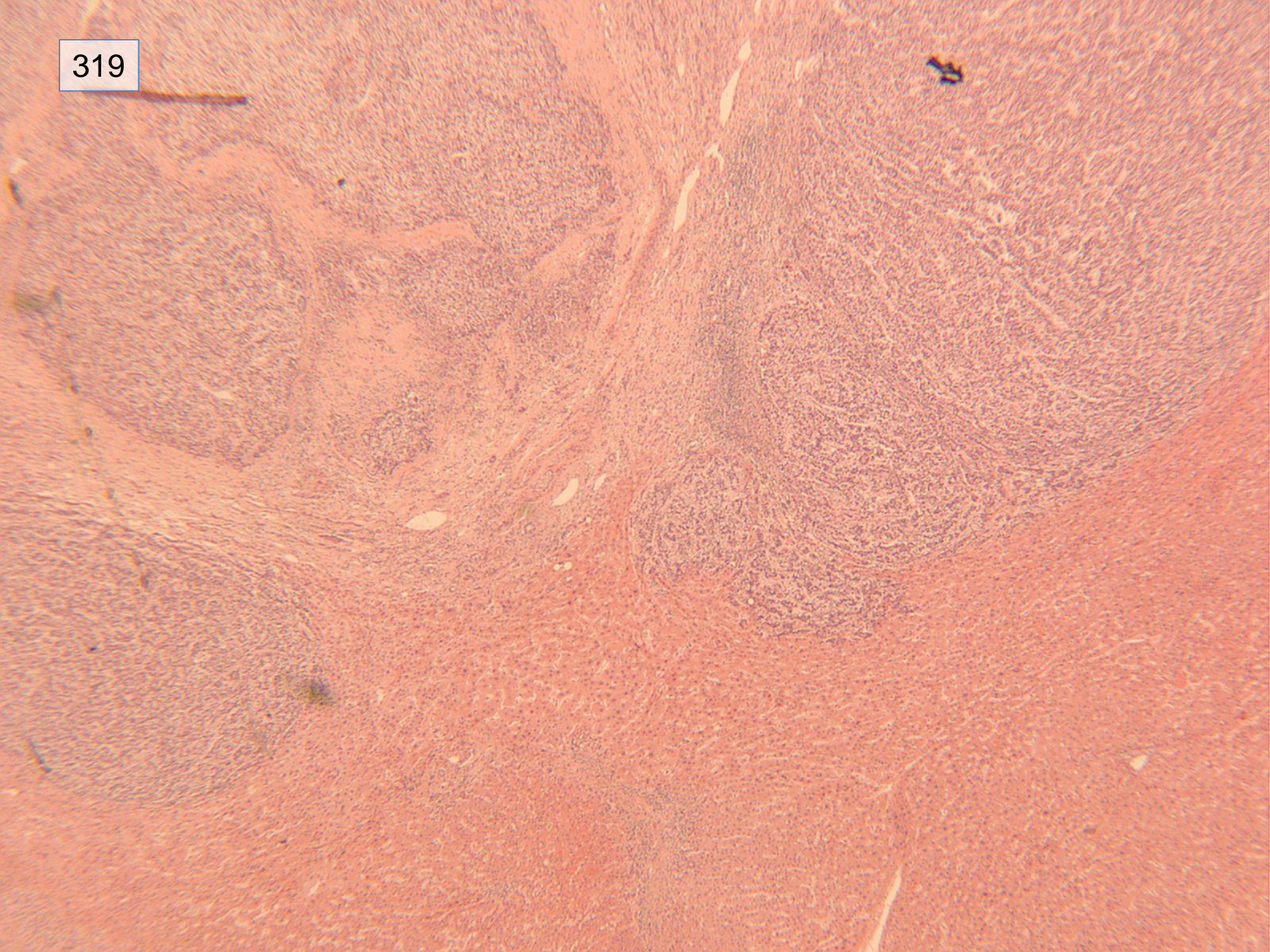
Liver resection for tumour – portion of liver measuring 135x120x70mm, micronodular cirrhosis and with several scattered pale nodules the largest 16mm.

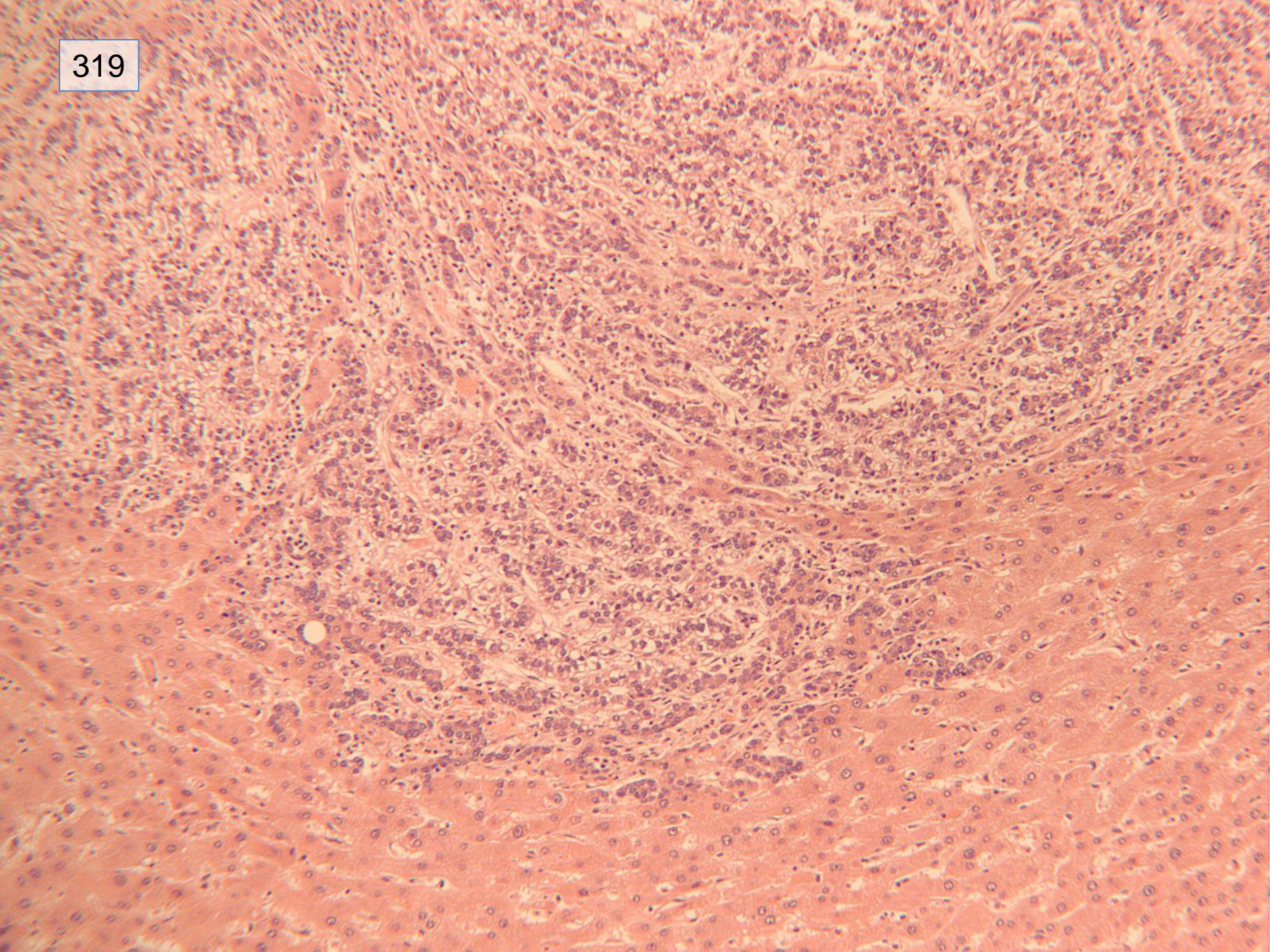
One nodule present in the centre of the submitted section.

319

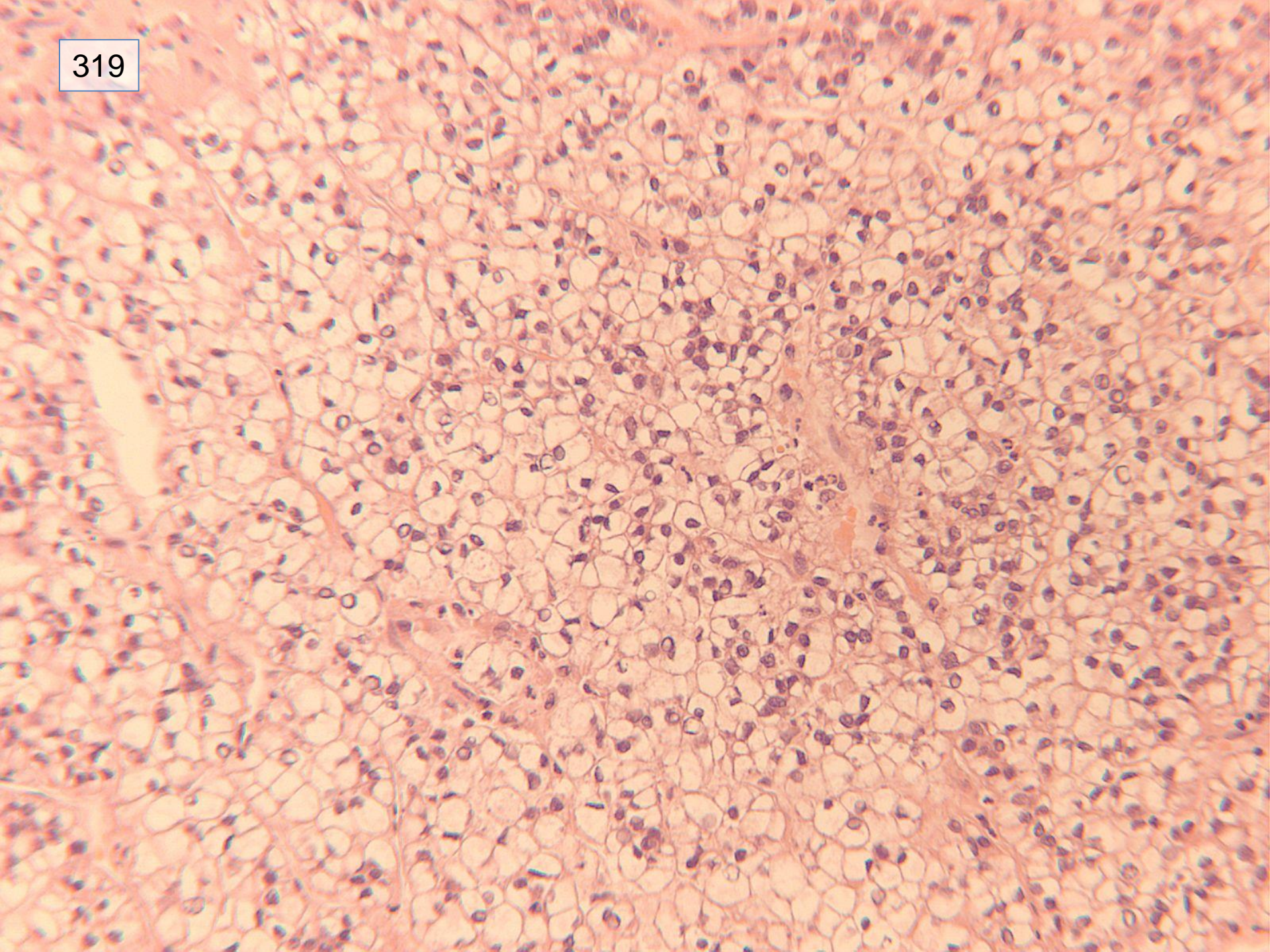


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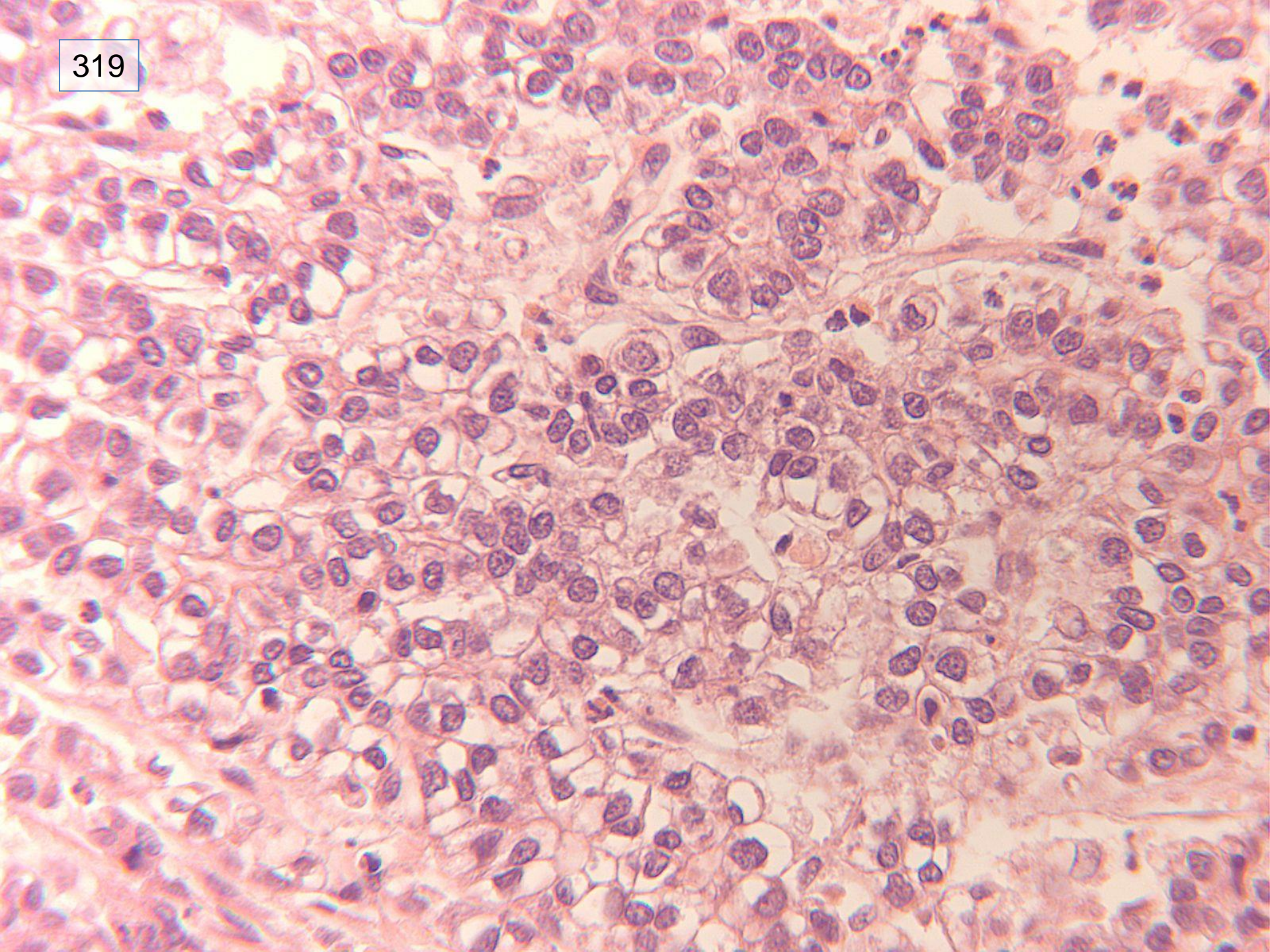




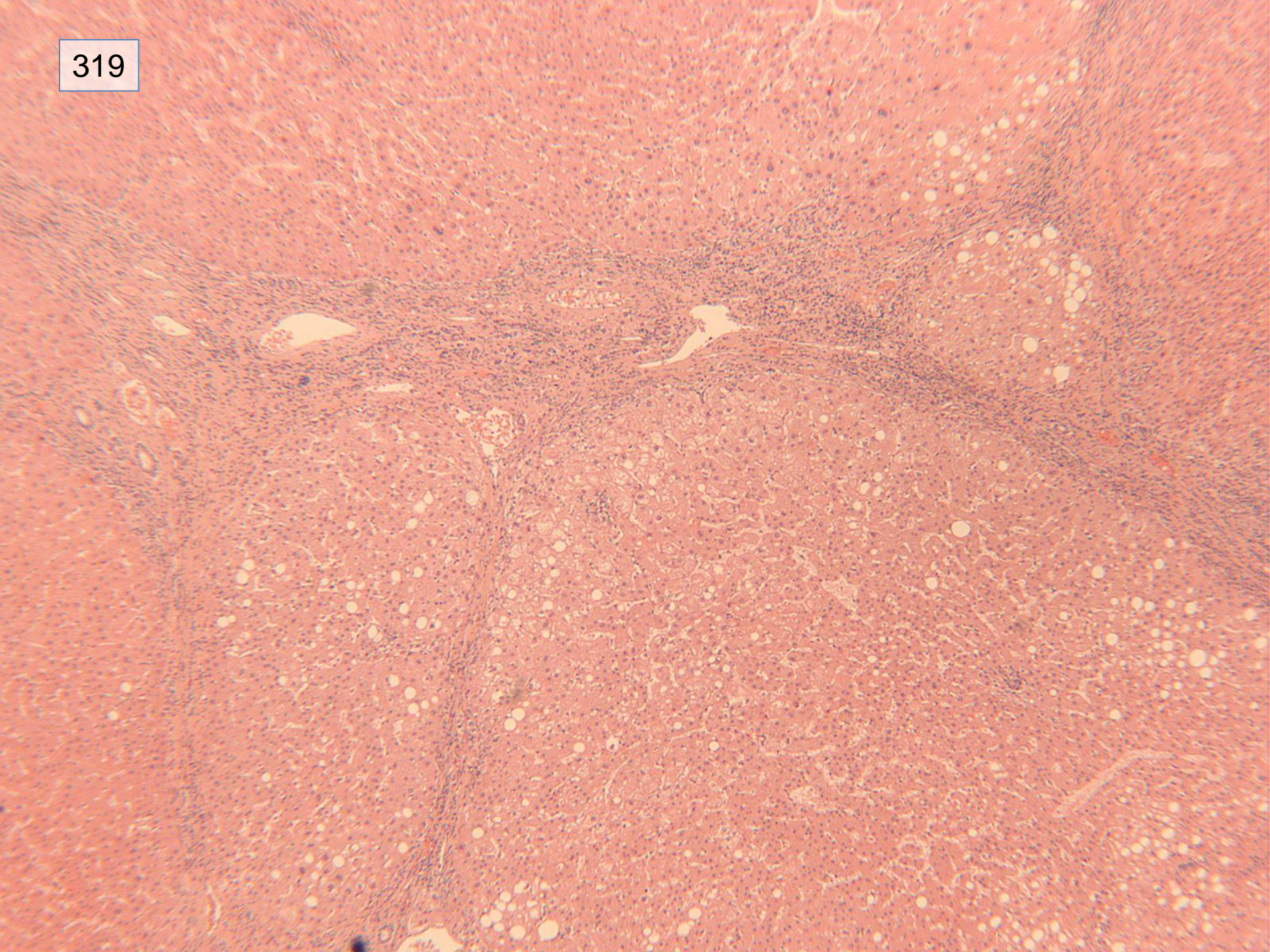
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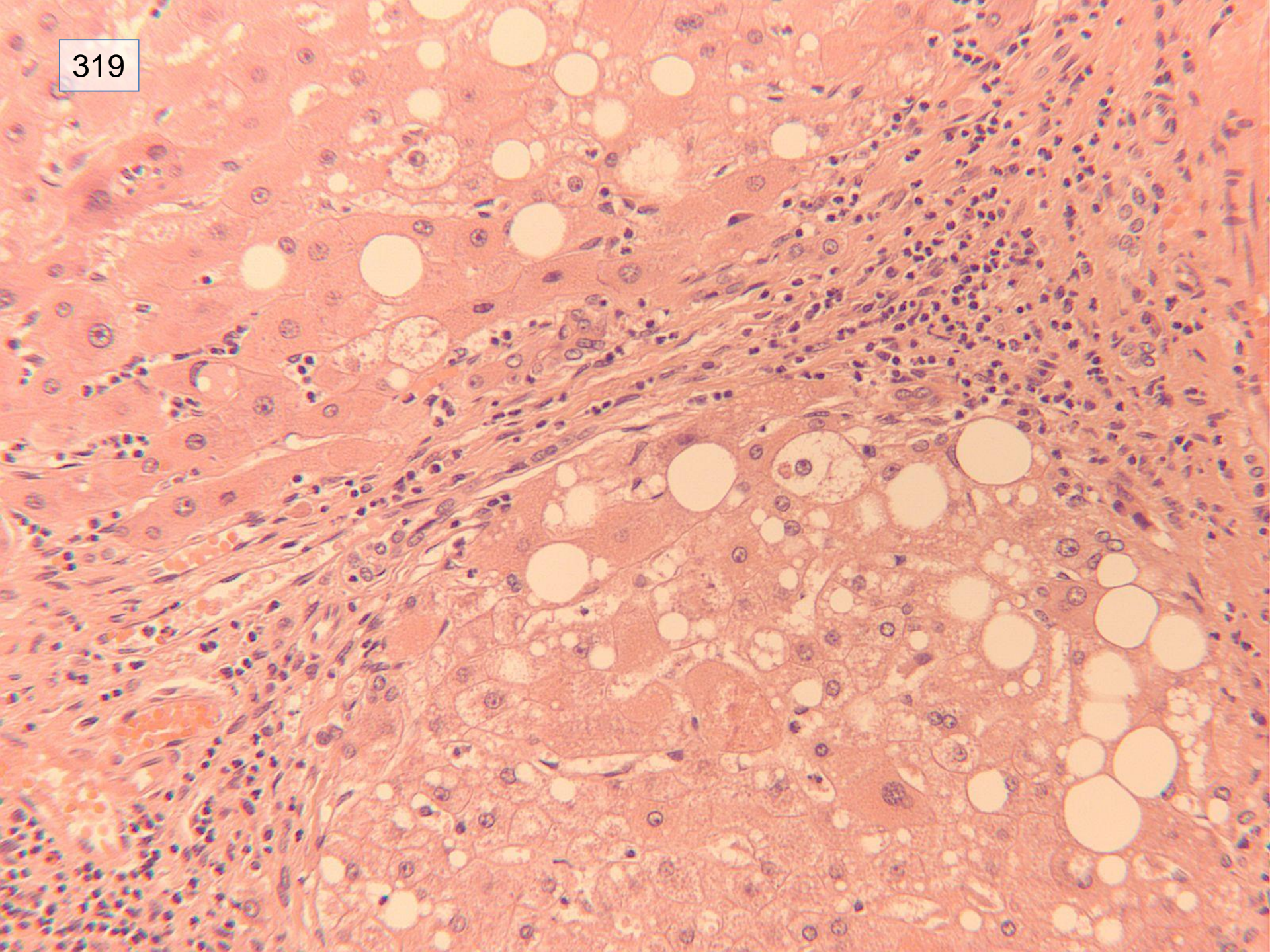
319



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319



# Case 319

## *Responses:*

### Background liver:

54 cirrhosis (of which 14 suspect due to fatty liver disease)

4 cirrhosis not mentioned

### Tumour:

13 probable/definite HCC, immunohistochemistry not mentioned.

33 probably HCC but would request confirmatory immunohistochemistry

1 HCC but imaging to rule out RCC (no immunos)

7 favour other cancer but differential diagnosis includes HCC – would request immunos for diagnosis

3 other cancer – HCC not included in differential diagnosis

1 ? renal cell carcinoma, immunos not mentioned

1 adenocarcinoma, c/w clear cell variant of cholangiocarcinoma, exclude metastasis

1 clear cell carcinoma, ?metastasis from urinary bladder

## Case 319 scoring and discussion

Score 10 marks for clear diagnosis of hepatocellular carcinoma, or where HCC was clearly the most likely diagnosis. The use of confirmatory immunohistochemistry varies among members – and would depend on clinical context. A requirement to exclude metastatic renal cell carcinoma was mentioned in several responses; it was commented that although metastatic malignancy is very rare in cirrhotic livers, it may occur on occasion.

Score 5 marks if HCC is included as a differential, but is not the most likely diagnosis, and no marks if the differential does not include HCC.

Cirrhosis should be mentioned in the response – deduct 5 marks for responses where cirrhosis is omitted.

Case 319

*Original diagnosis: HCC arising in cirrhosis*

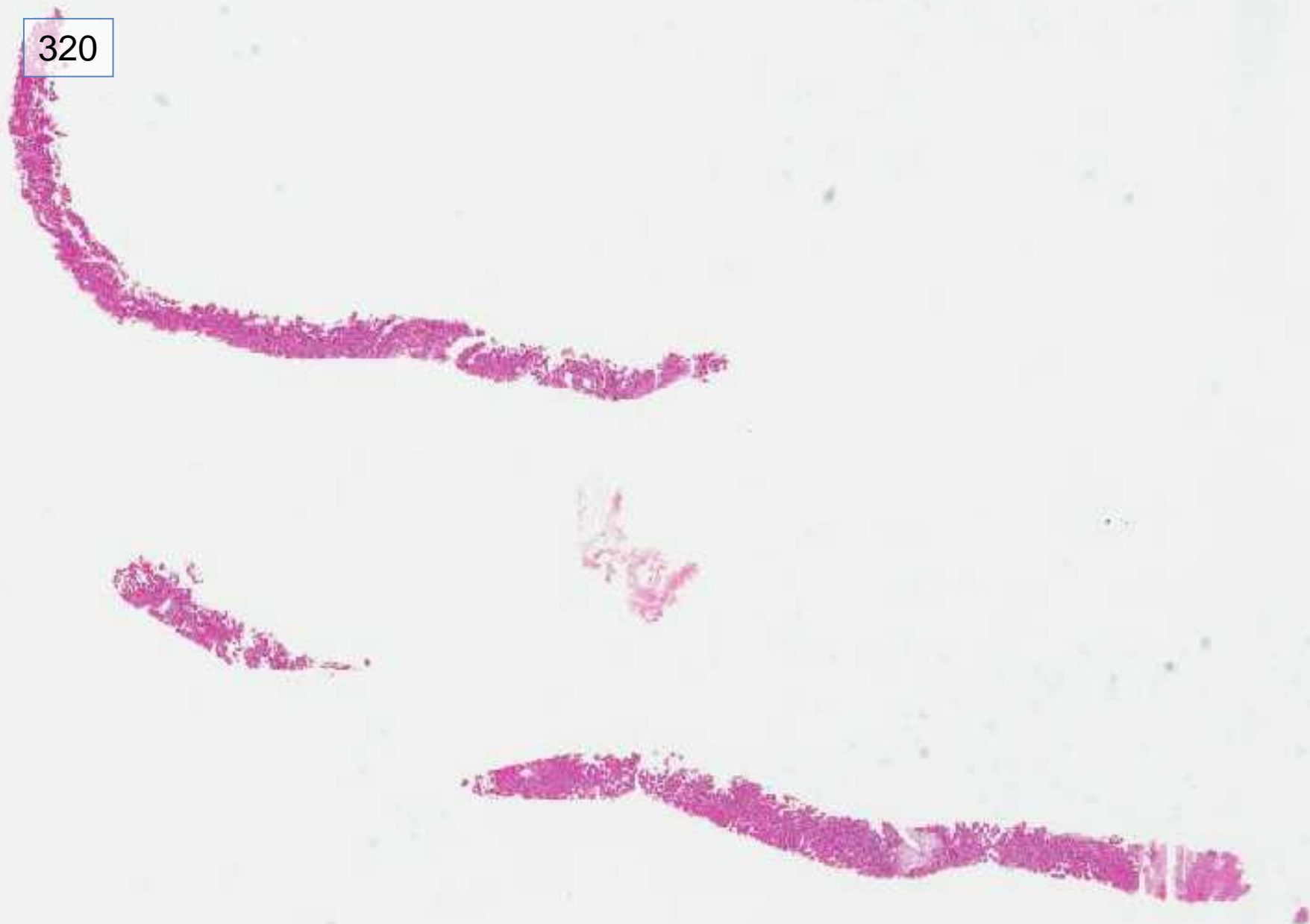
## Case 320

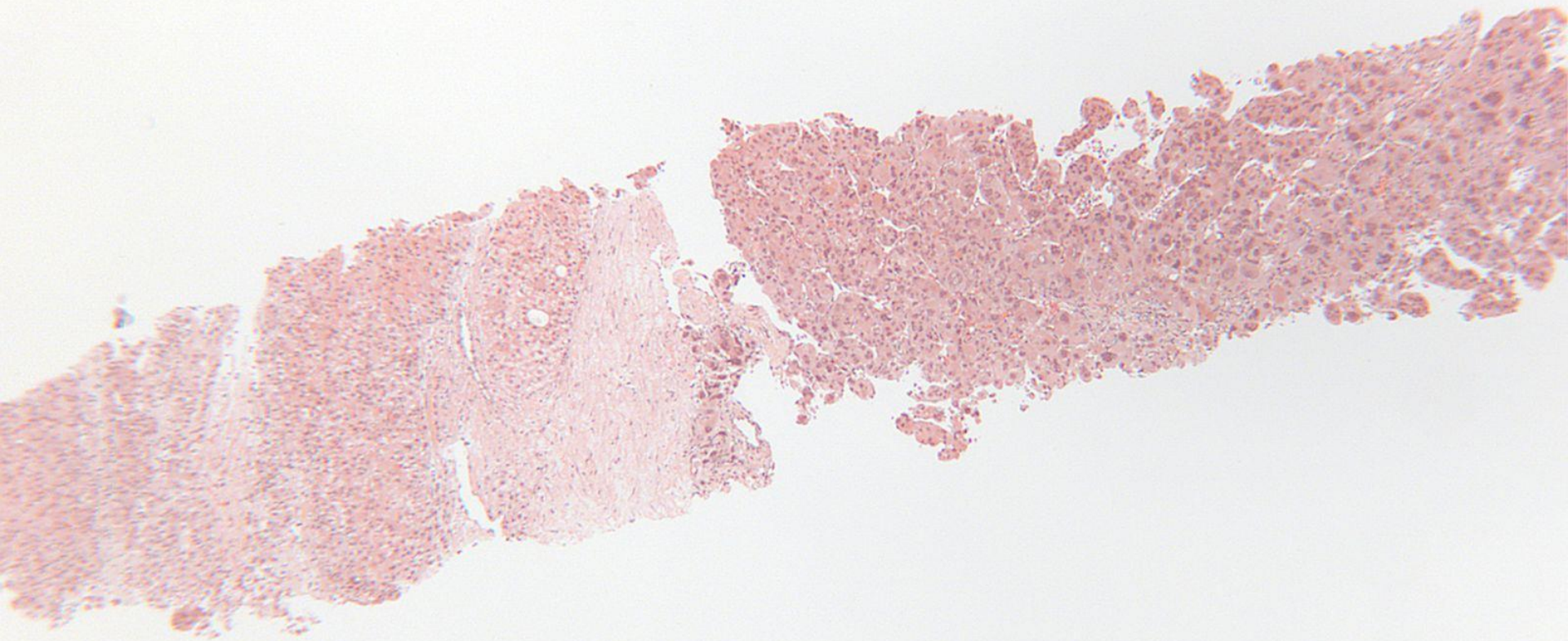
46M Weight loss, deranged LFTs, previous hepatitis B infection, hepatitis C positive.

CT showed mass in right lobe of liver.

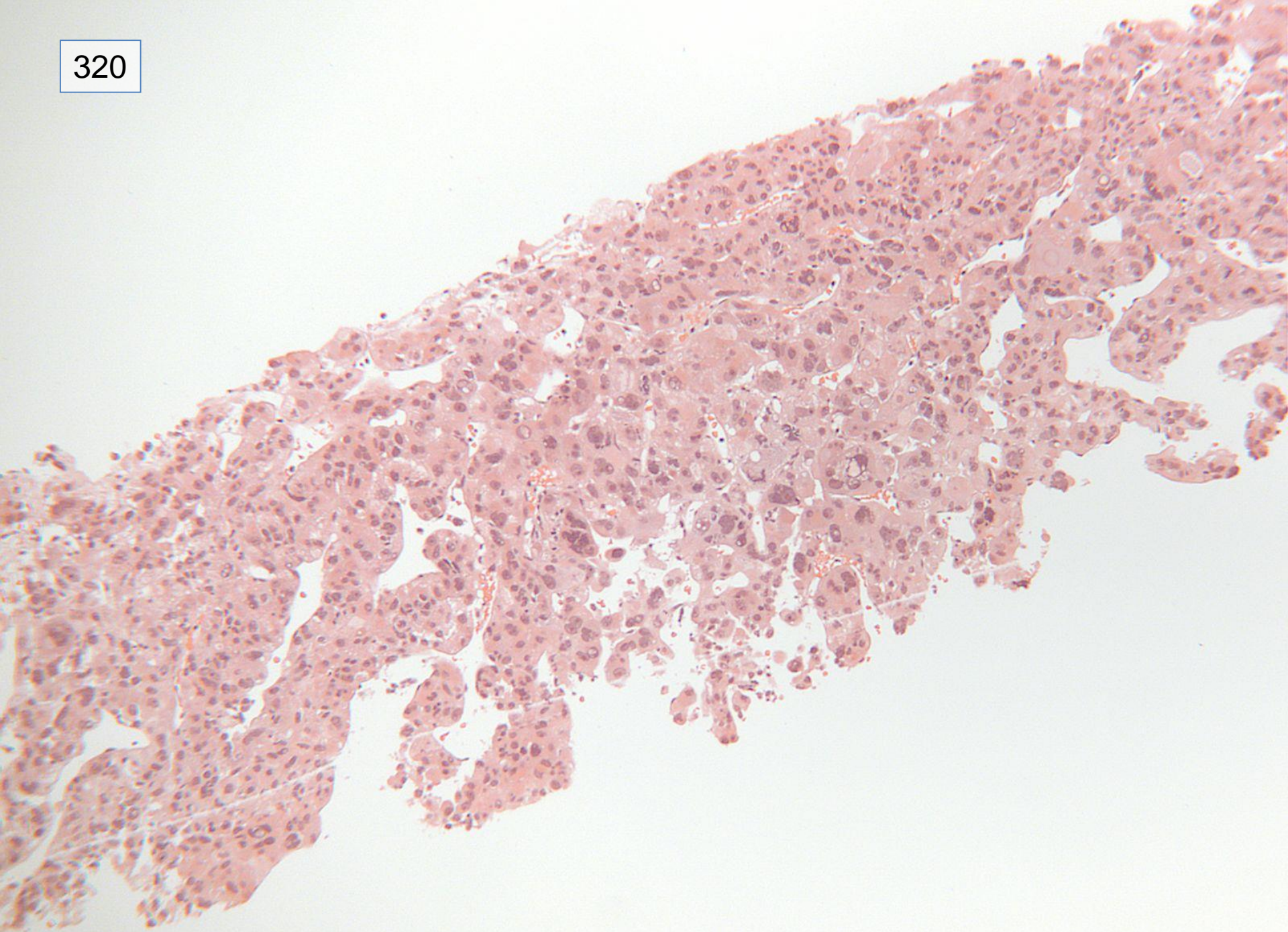
Liver biopsy – 2 cores 17 and 16mm.

320

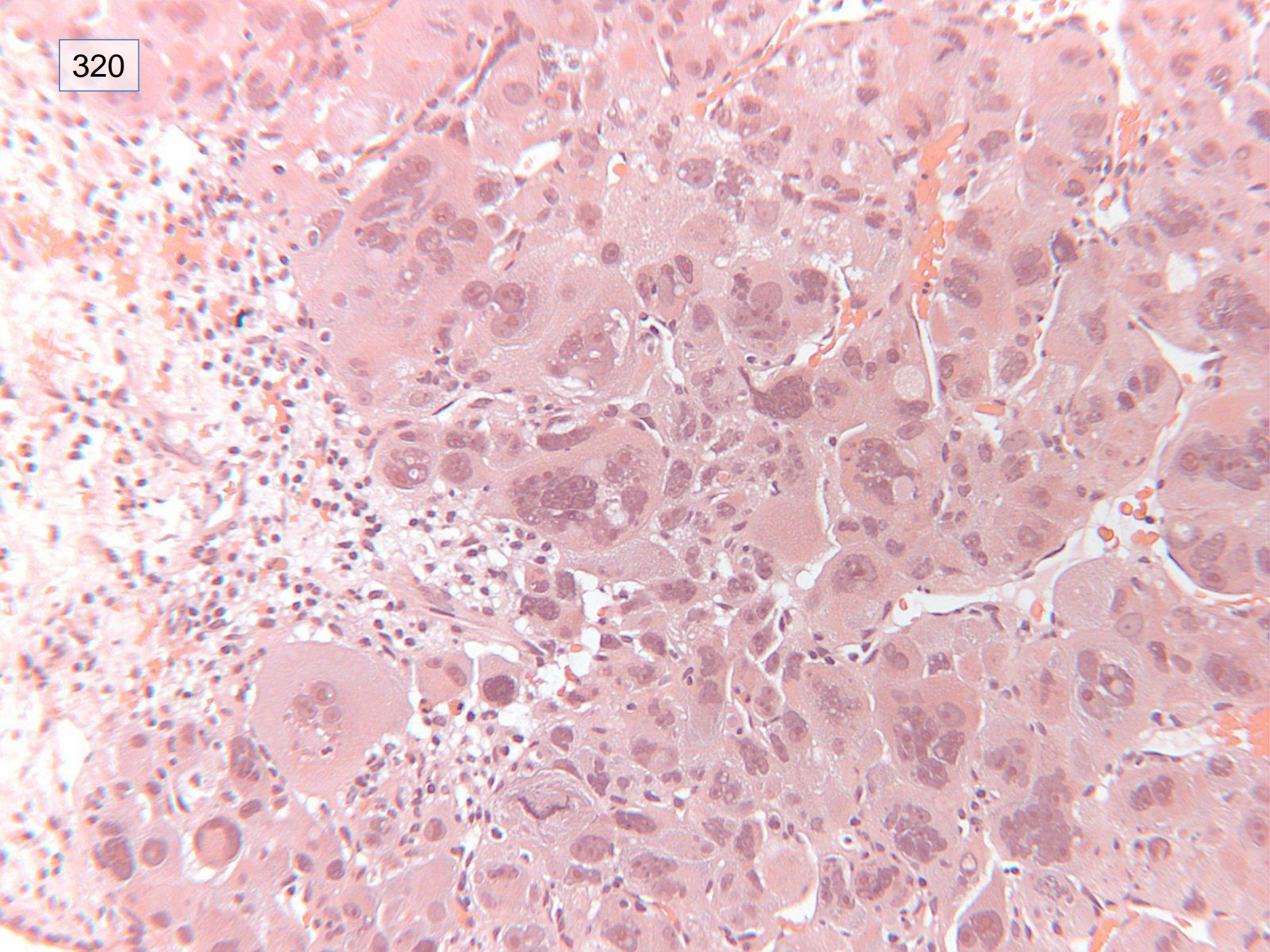




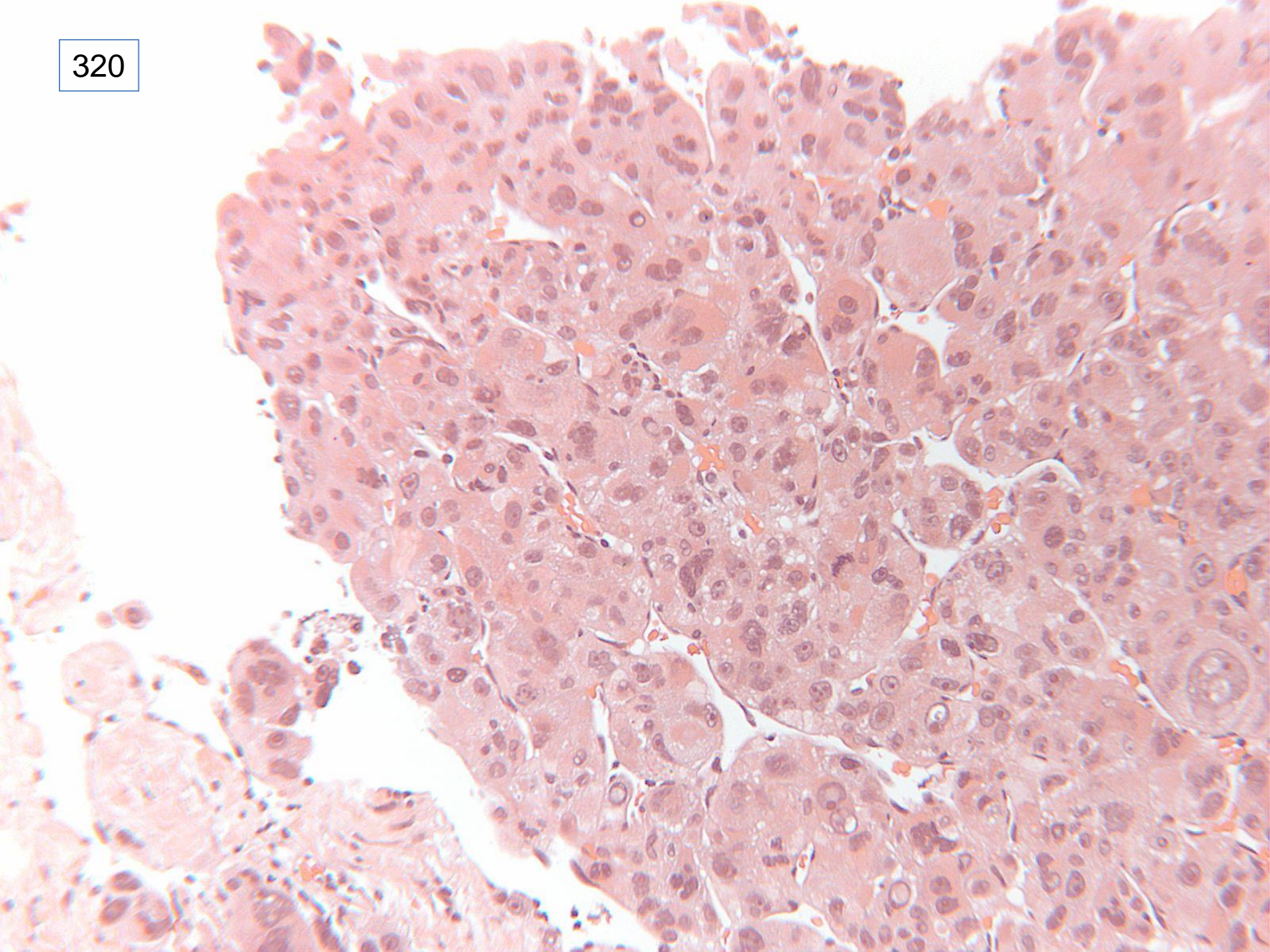
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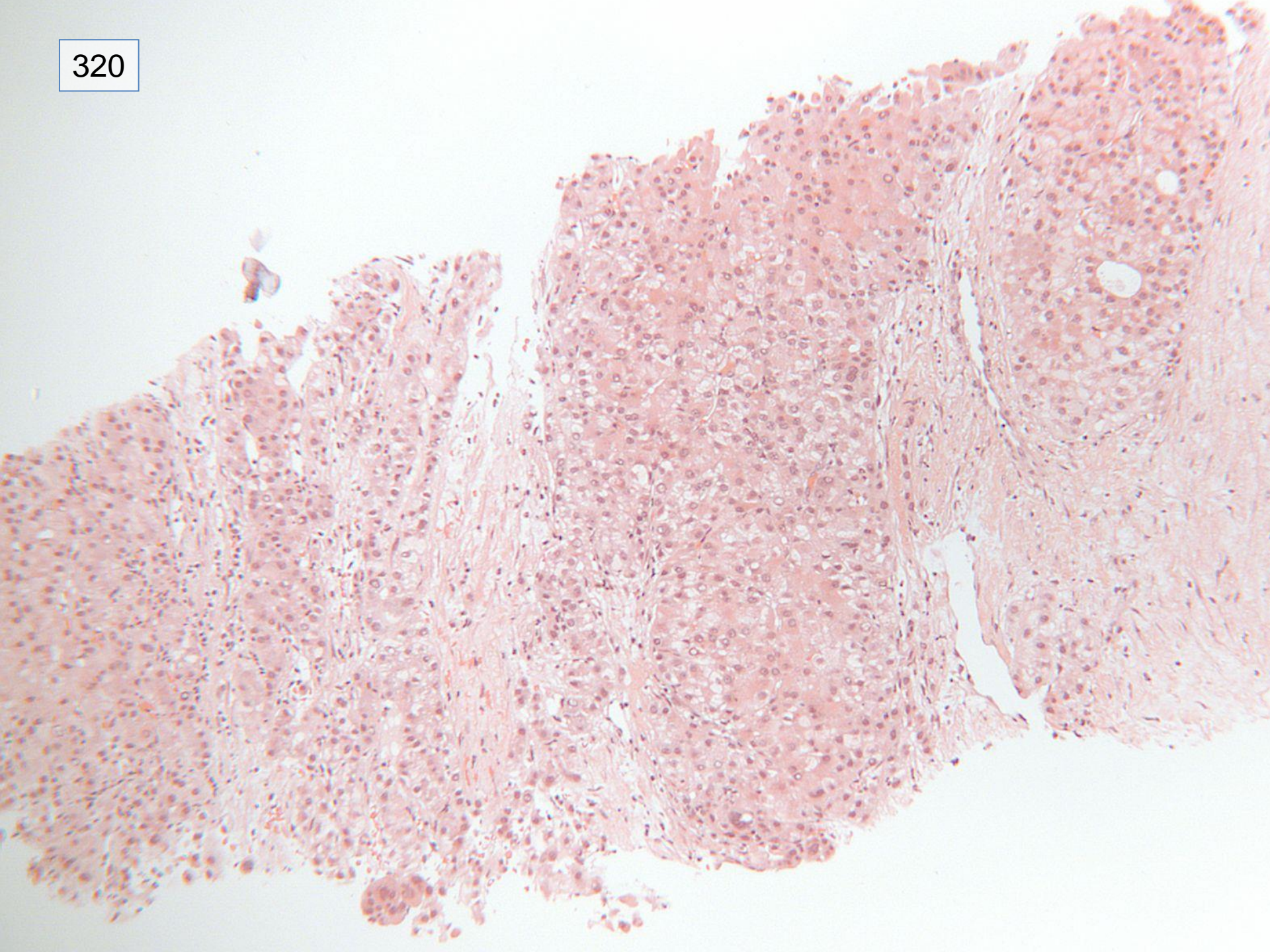
320



320



320



# Case 320

## *Responses:*

36 HCC as definite diagnosis, no immunohistochemistry requested.

20 HCC but would request confirmatory immunohistochemistry

Of the 55, 22 included comment about the grade

– no consensus.

1 Carcinoma with differential diagnosis that included HCC,  
needs immunos for diagnosis

1 'liver cell carcinoma' as only diagnosis

18 background liver showed probable/definite cirrhosis,

Includes 4 who commented on ground glass hepatocytes

5 commented that there was no background liver included,

Rest made no comment on background liver.

## Case 320 Scoring and discussion

All responses scored 10 marks.

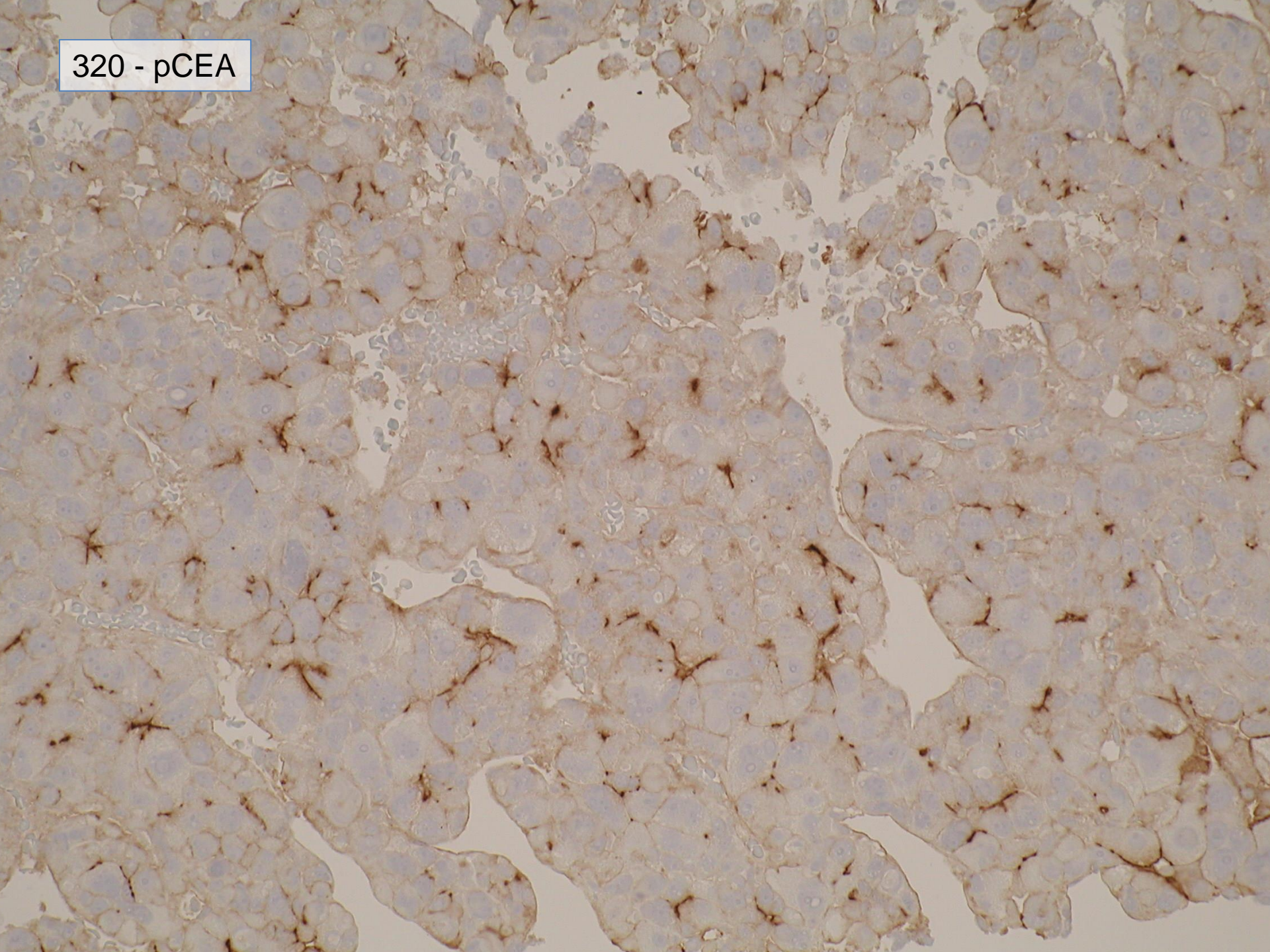
There was discussion about the use of the term 'liver cell carcinoma'; on discussion this was felt to be synonymous with hepatocellular carcinoma, and unambiguous, although not the usual terminology.

Case 320

Original diagnosis: Hepatocellular carcinoma.

Immunohistochemistry – CD10, CD13, pCEA  
positive.

320 - pCEA



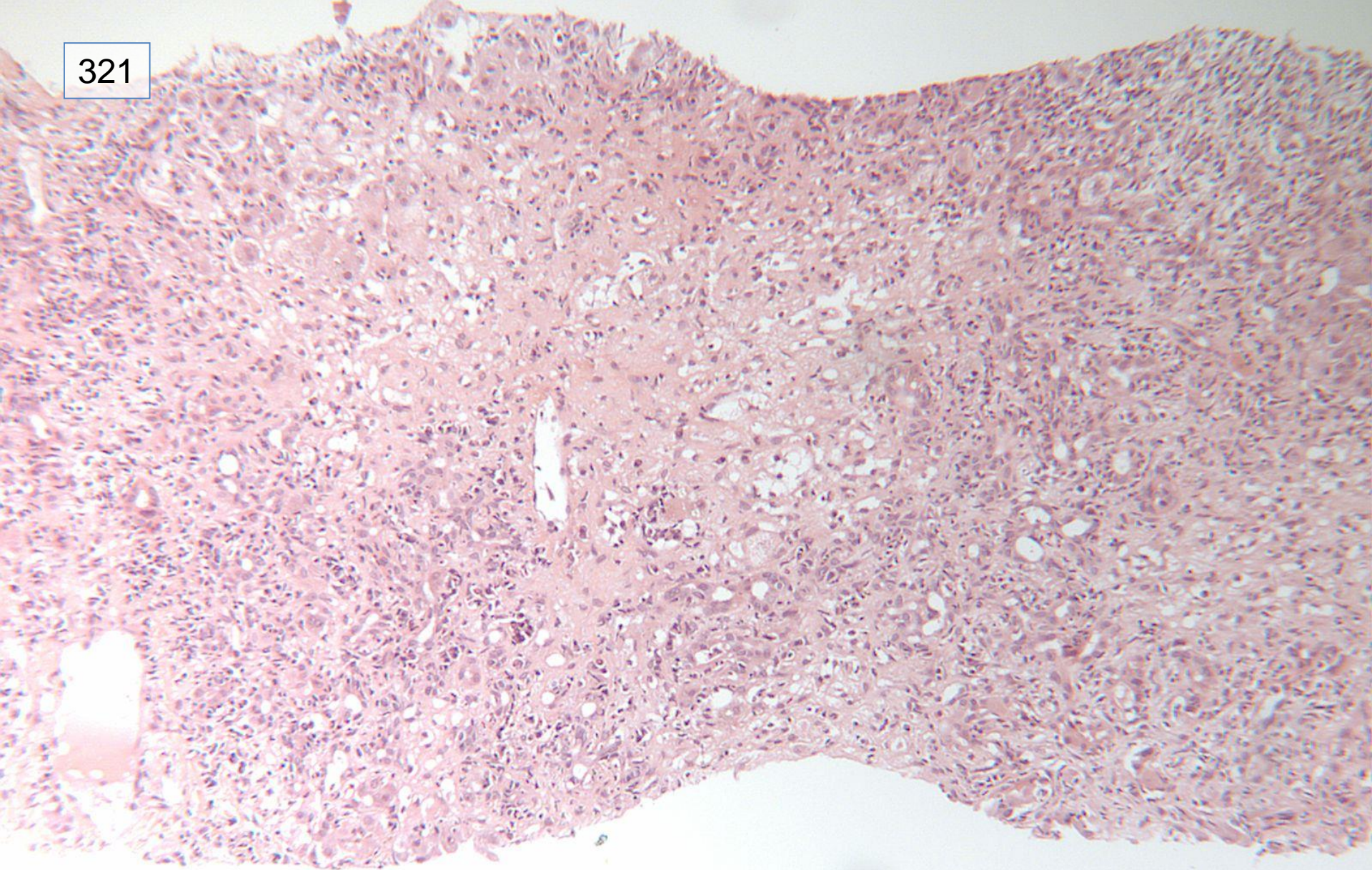
## Case 321

36M Diagnosed UC four months ago. Commenced mesalazine.

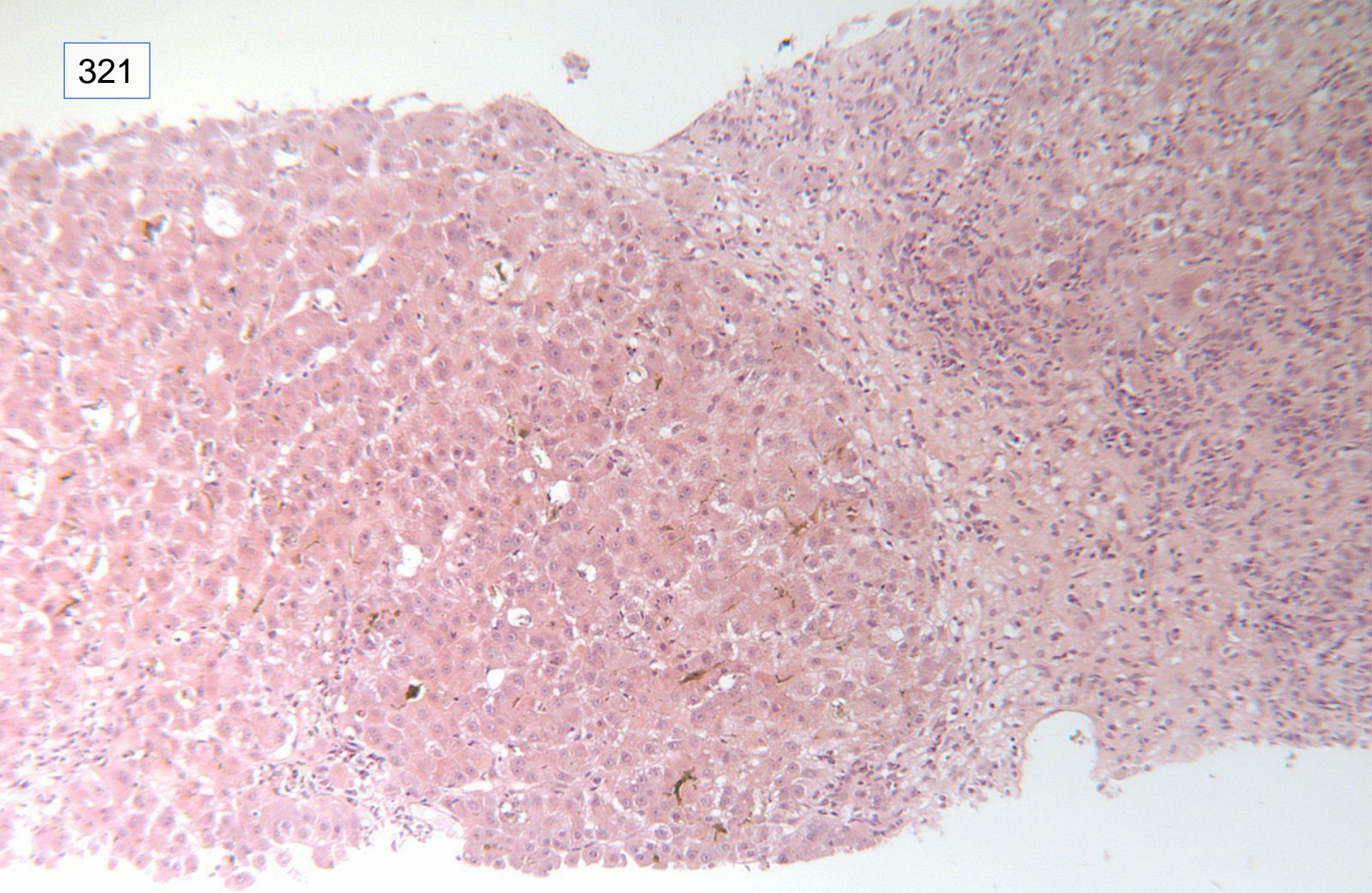
Three weeks of jaundice ? drug induced hepatitis.



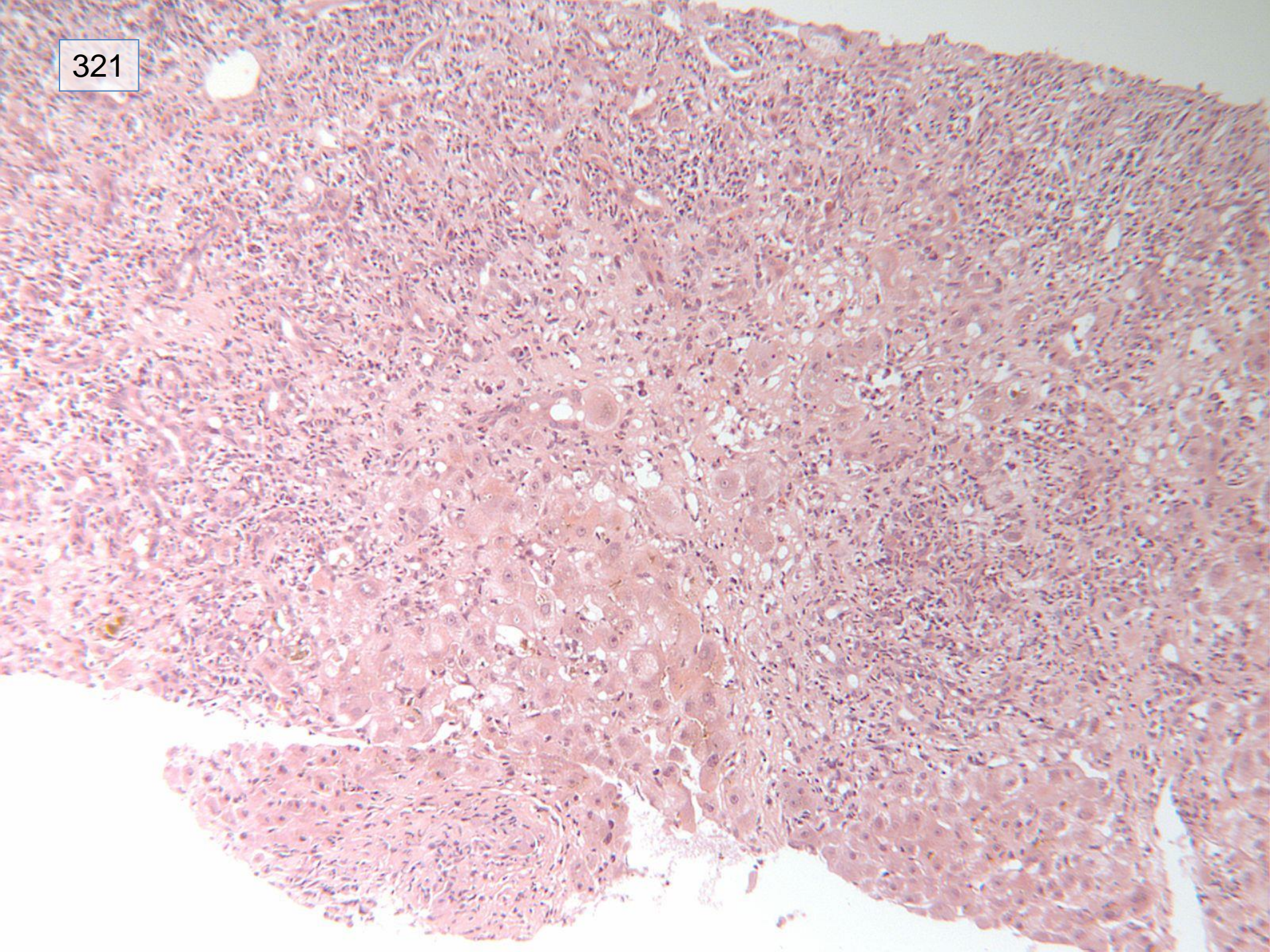
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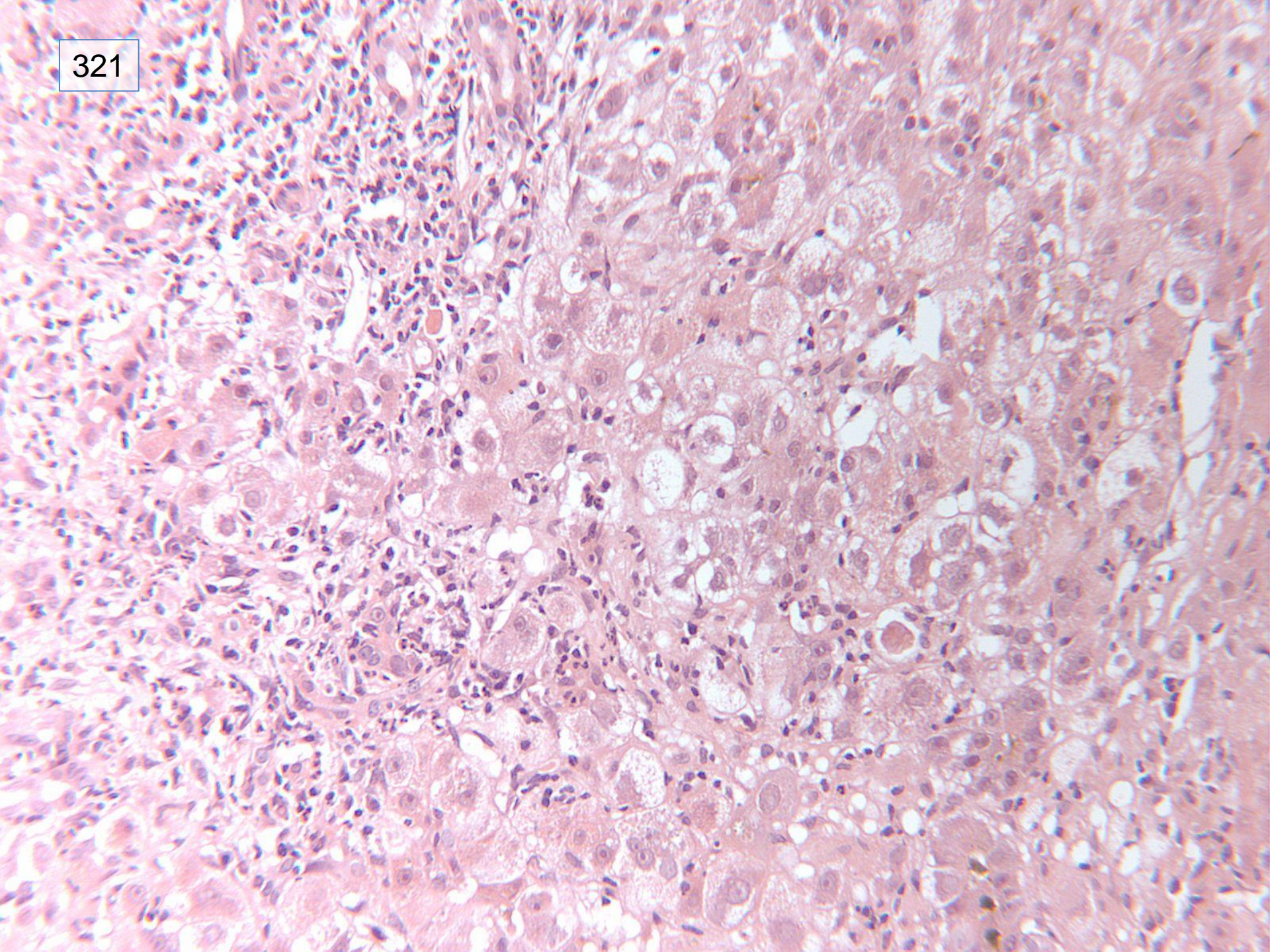
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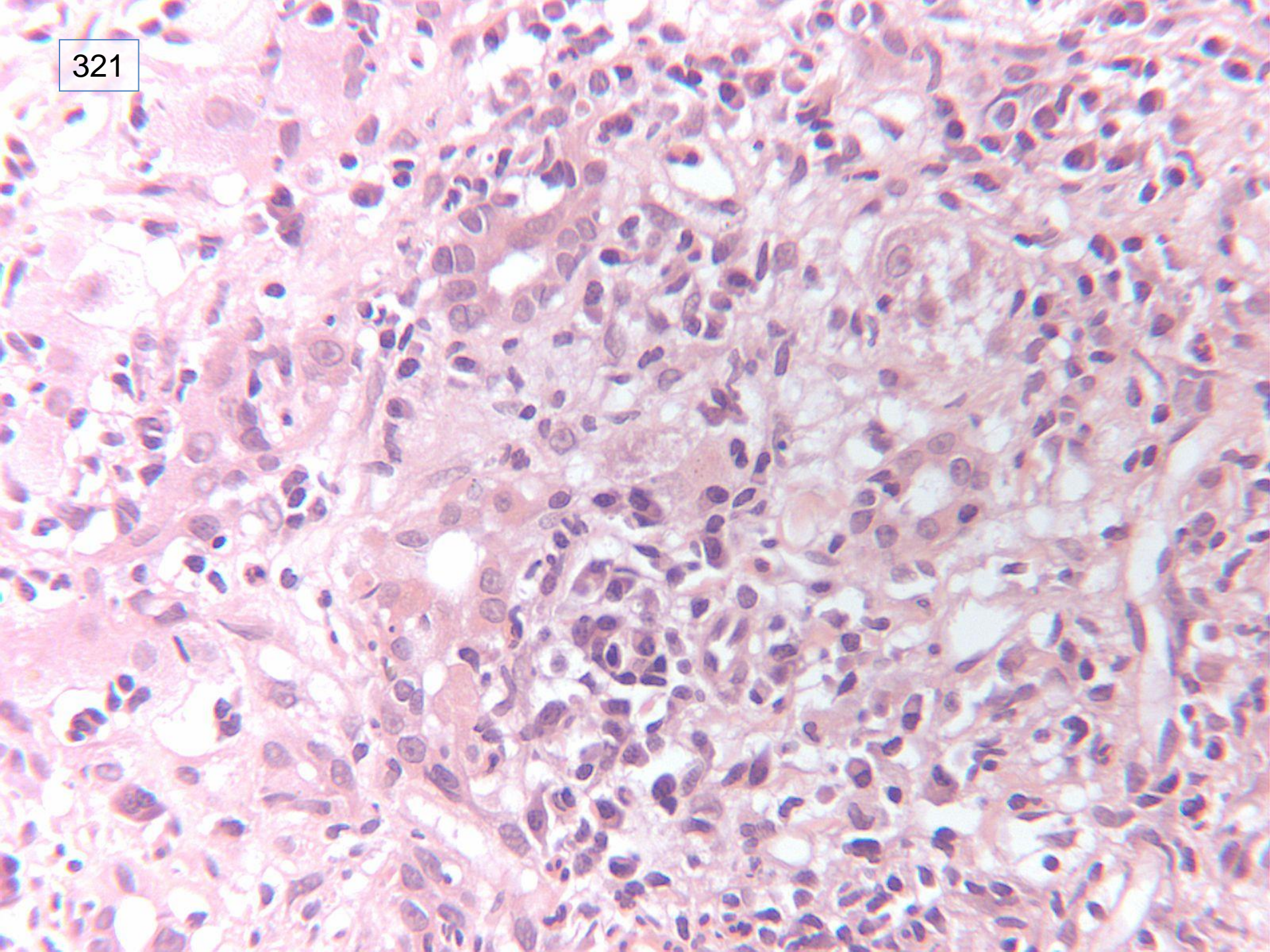
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# Case 321

## *Responses:*

48 drug related hepatitis

Of which: 18 specifically mentioned plasma cells/AIH like features

2 cirrhosis (early cirrhosis, or previously cirrhotic liver)

6 hepatitis, differential diagnosis includes drugs, but not as most likely

Of which: 5 probably autoimmune hepatitis,

1 biliary disease

6 drugs not mentioned

Of which: 3 PSC as main diagnosis

1 cholestasis with cholangiolitis, large duct obstruction/PSC

1 mixed cholangitis/hepatitis, probably PSC/AIH overlap

1 large duct obstruction with fibrosis

## Comments:

5 specifically mentioned the need to exclude PSC

## Case 321 scoring and discussion

This was cholestatic hepatitis, consistent with drug-induced liver injury.

Responses that included drug reaction as main diagnosis scored 10 marks, except those diagnosing cirrhosis, which scored 0 – mistaking the regenerative nodules of subacute hepatitis as cirrhosis is a recognised pitfall.

Prominent plasma cells are suggestive of autoimmune hepatitis – this pattern has been recognised in patients taking mesalazine.

This was clearly a hepatitis and therefore (unlike case 316) the features are not compatible with biliary obstruction. Responses with biliary disease as the main diagnosis scored 0 marks. It was commented that the ductular reaction that develops in areas of confluent panacinar necrosis could have contributed to the impression that this was a primarily a biliary disease.

## Case 321

Original diagnosis: subacute hepatitis with bridging and panacinar necrosis – histological features suggestive of autoimmune hepatitis.

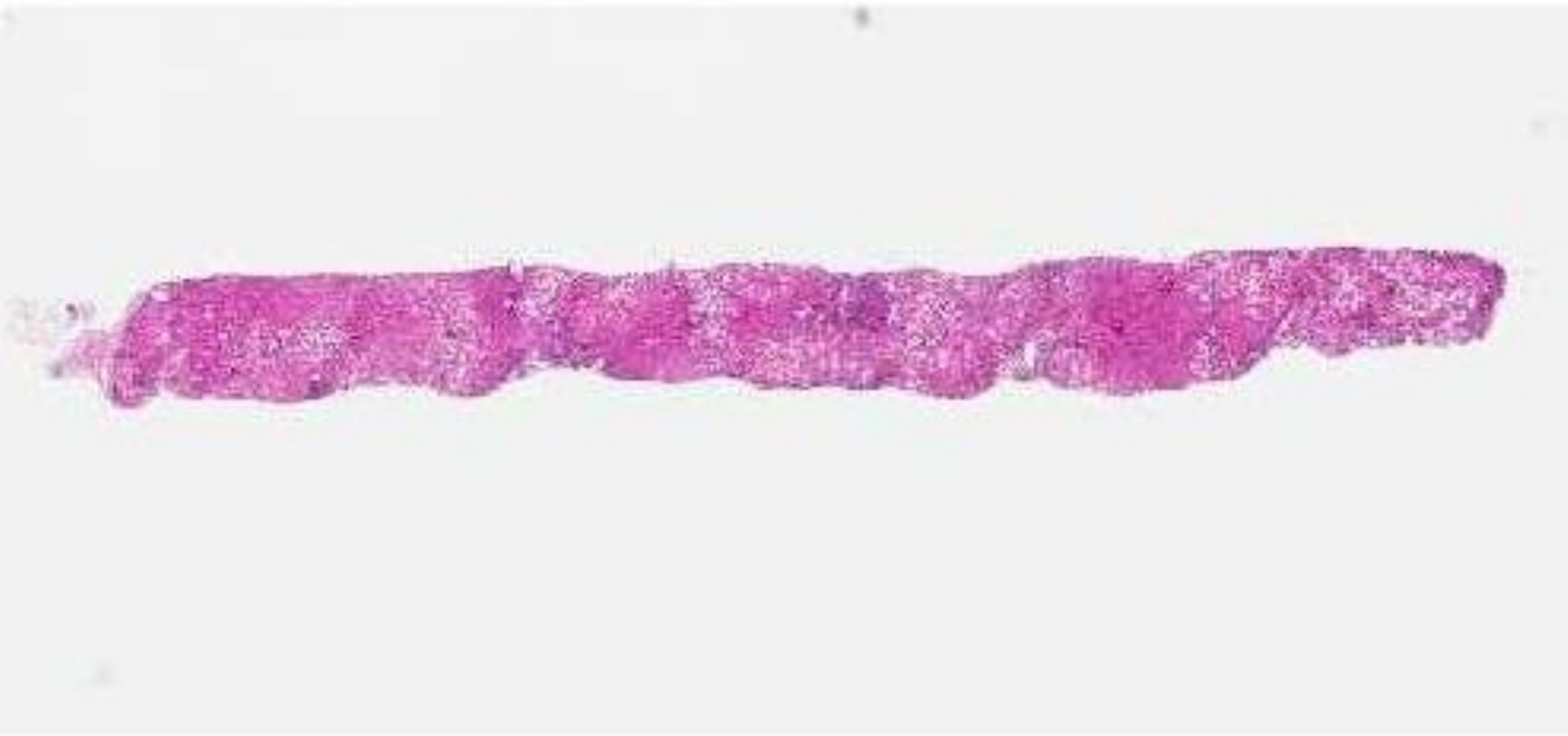
Mesalazine has been implicated in causing this pattern of liver injury. Orcein negative.

## **Case322**

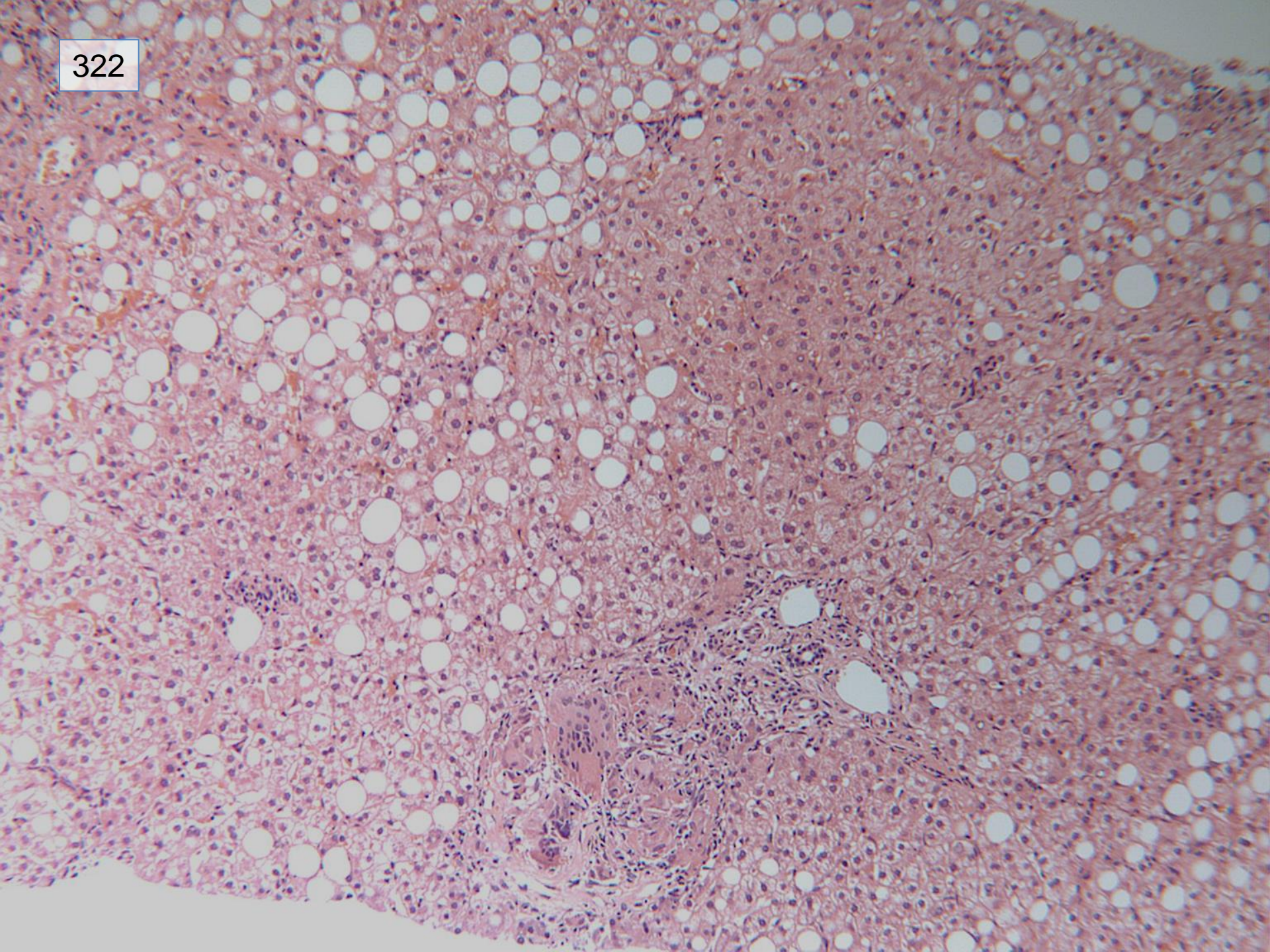
24M AIH on MMF.

Stopped prednisolone.

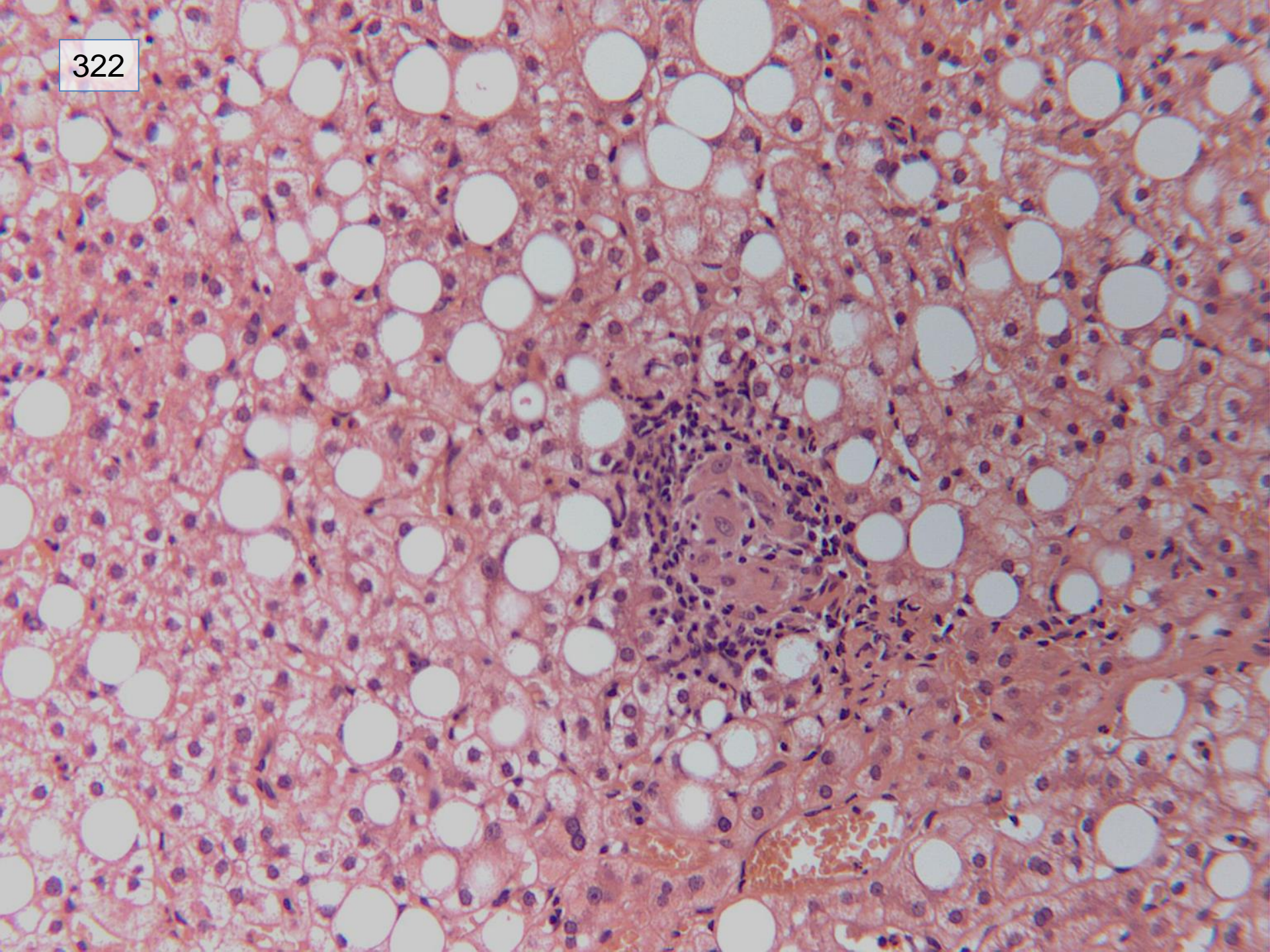
ALT still increased - ? on-going inflammatory activity



322

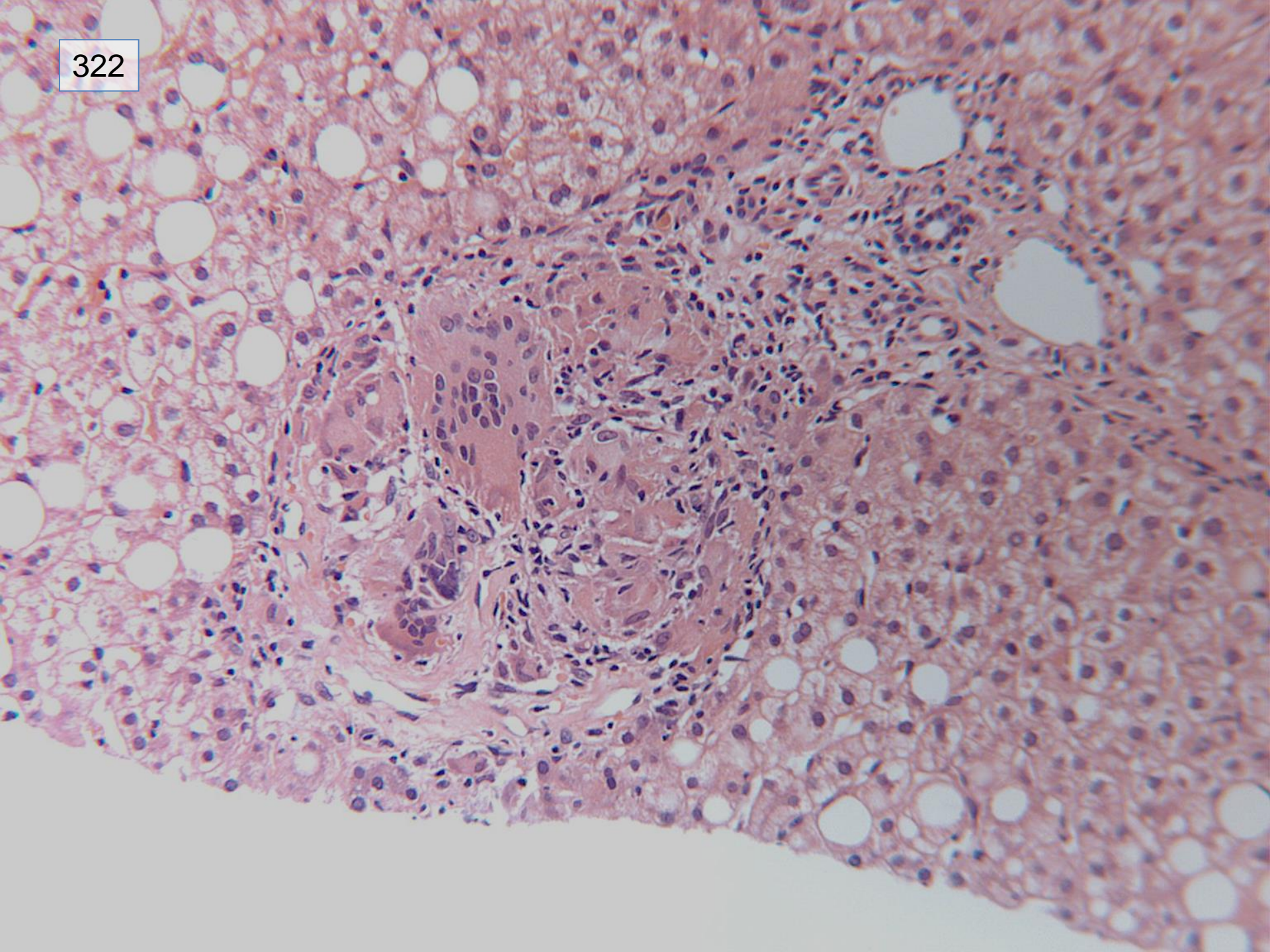


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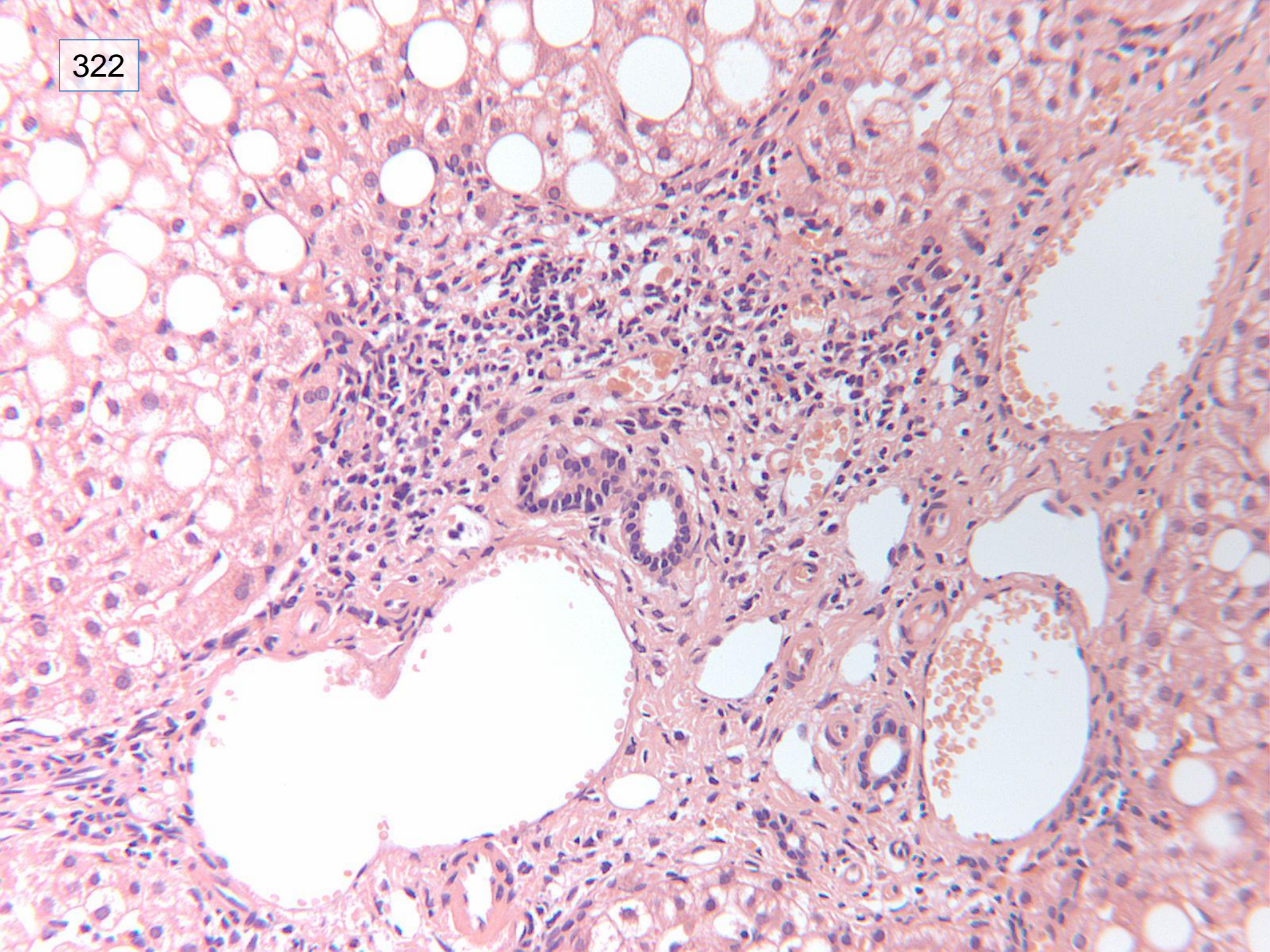




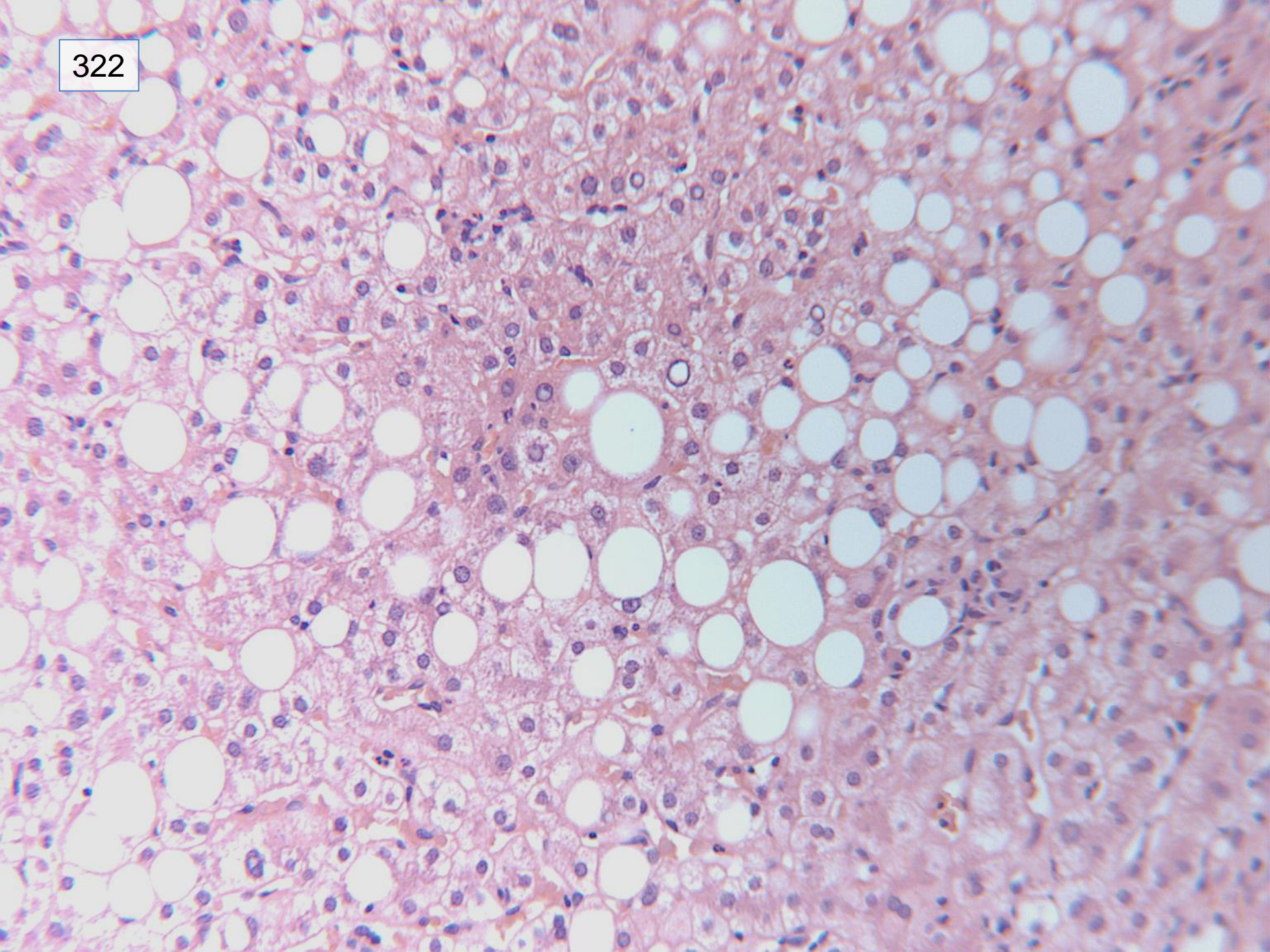
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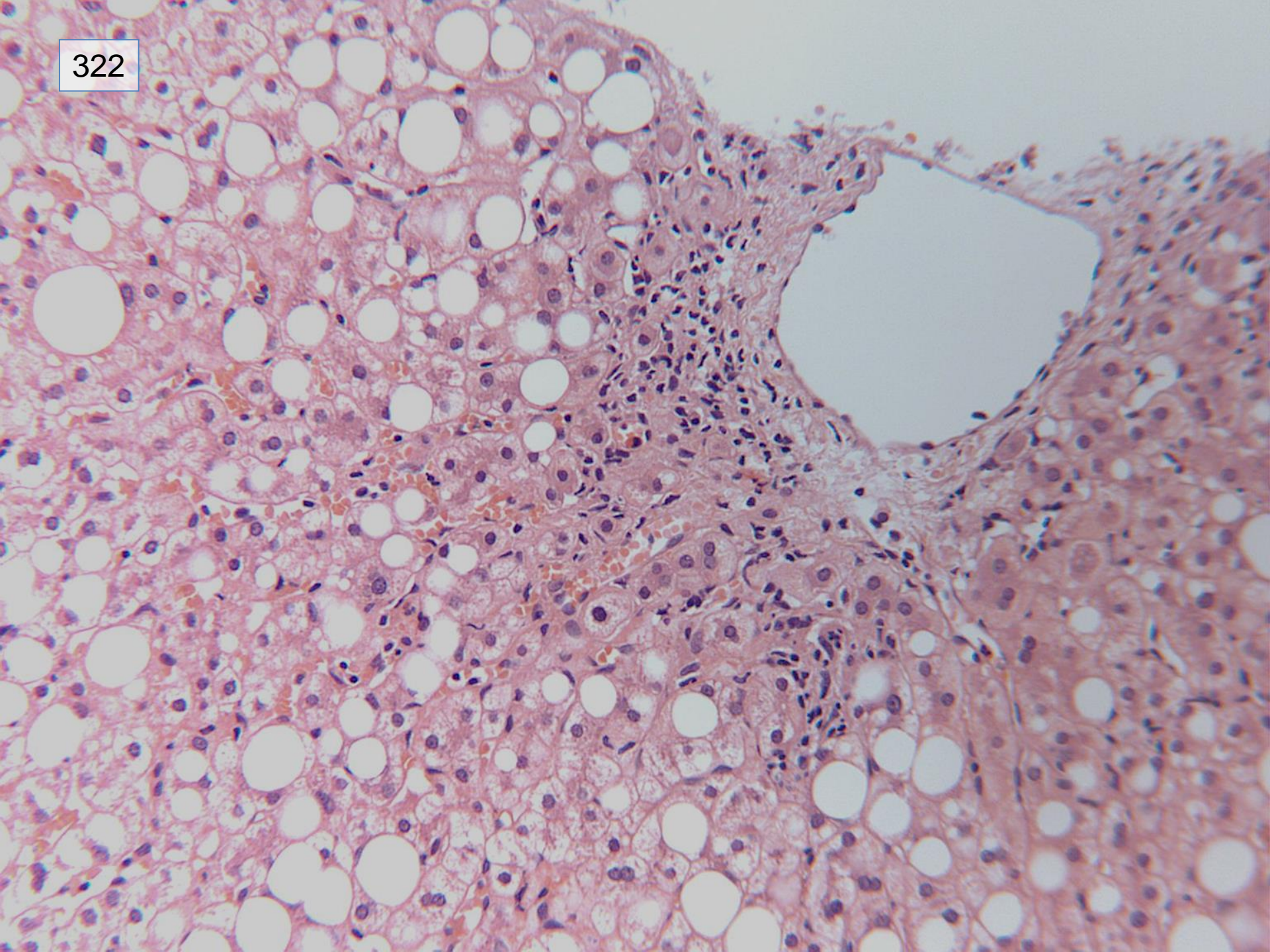
322



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322



# Case 322

*Responses:* Three components to the diagnosis:

## Granulomatous inflammation:

- 15 mentioned granulomas, but no comment about the cause
- 29 specifically commented on the need to exclude TB clinically  
(13 – no mention of possibility of infective cause)
- 17 consider PBC/overlap with AIH
- 16 included drugs in differential
- 10 included sarcoidosis in differential
- 1 no mention of granulomas

## Comment on AIH:

- 34 AIH as minor background feature, mild activity,  
or that changes are not typical of AIH
- 5 'active AIH' as main diagnosis
- 9 no mention of AIH anywhere in the response

## Comment on fatty change:

- 38 also steatosis
- 11 steatohepatitis
- 7 no mention of fatty change

## Case 322 scoring and discussion

This case was unsuitable for scoring – too complicated to evaluate three sets of diagnostic features.

The case was submitted because the presence of granulomas in a patient on immunosuppression should prompt clinical investigations for infectious disease, specifically TB. It was commented that the morphology of the granulomas in this case are not particularly suggestive of TB, and seem to be associated with some fibrosis.

## Case 322

Original diagnosis: evidence of chronic liver disease, stage 4 bridging fibrosis, currently little portal inflammation attributable to autoimmune hepatitis.

Granulomas – exclude TB in view of immunosuppression. Differential includes sarcoidosis; not typical for PBC and Orcein is negative for copper-associated protein.

Also steatosis, but not features of steatohepatitis.

.....

Further clinical information at CPC: patient with clinical features of lipodystrophy – would explain the steatosis.

ANA positive, diagnosed AIH on biopsy in May 2006, also steatosis at that time. Initial good response to immunosuppression with biopsy July 2007 showing improvement.

The circulated slide was the repeat biopsy November 2008 because ALT still raised. Subsequently seen in clinic in June 2009 – chest X-ray normal and no symptoms to suggest TB, no evidence of sarcoidosis, and alkaline phosphatase normal. Granulomas not further investigated.

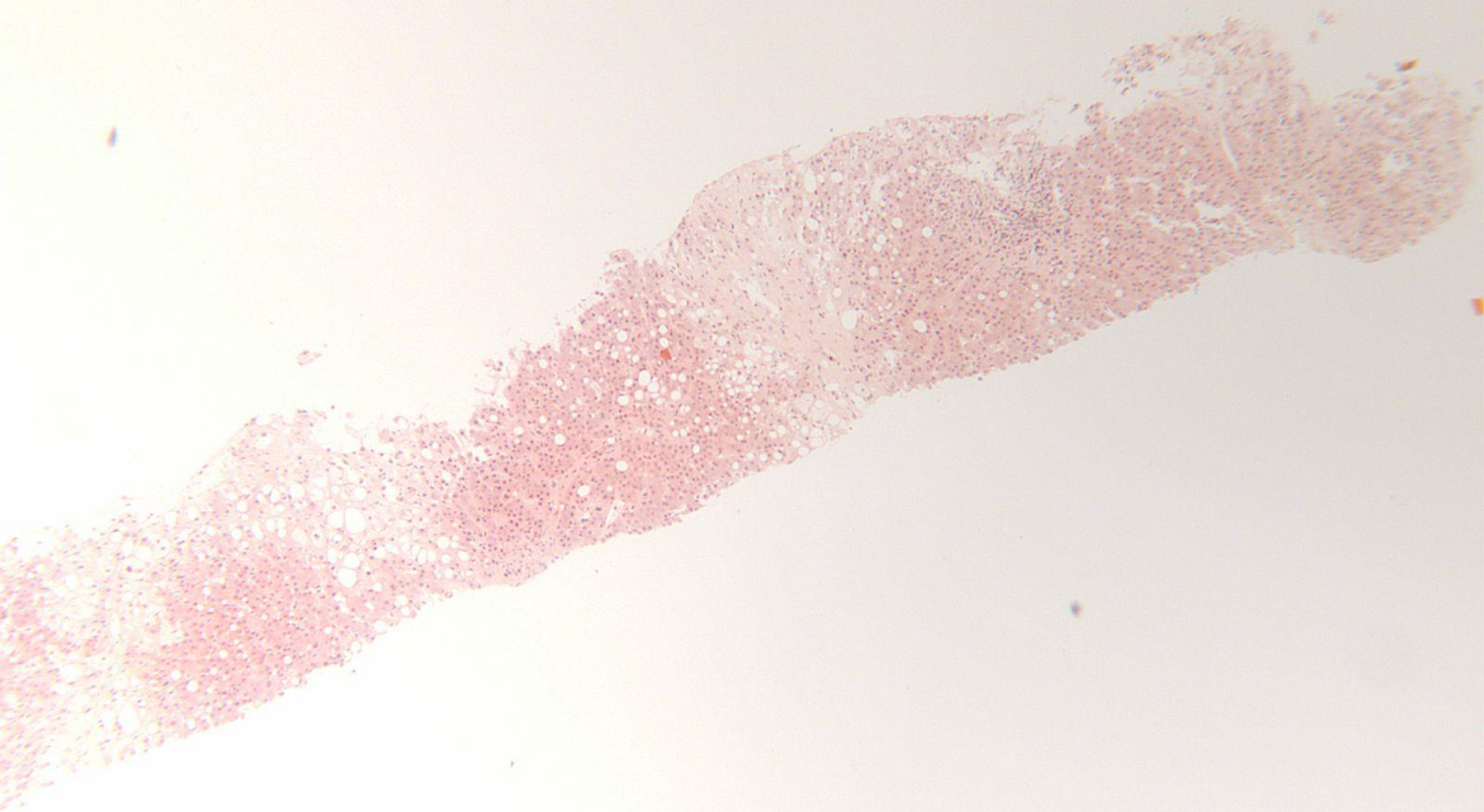
## **Case 323**

52M Cholestatic jaundice, previous high alcohol intake.  
Multiple organ failure.

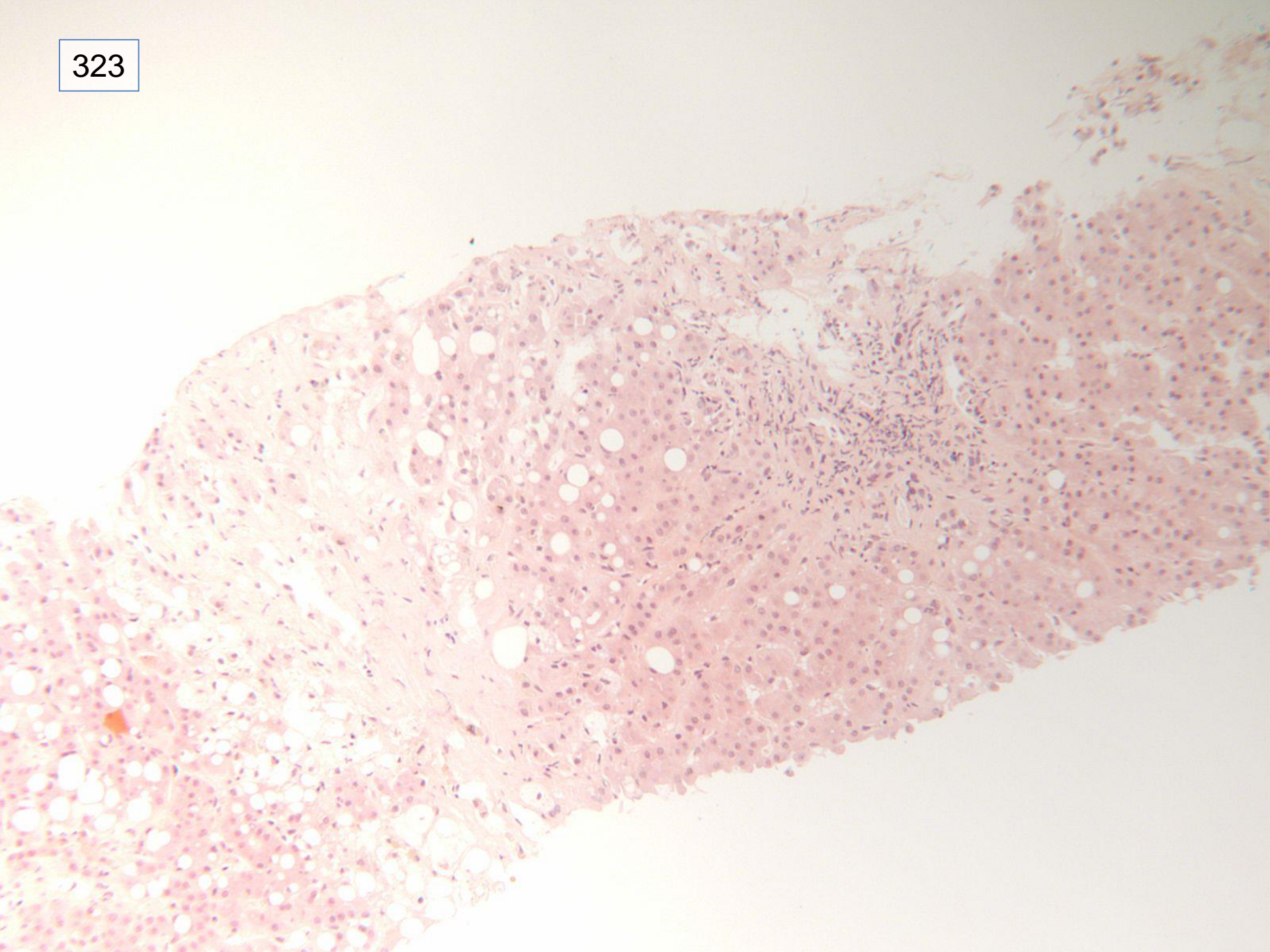
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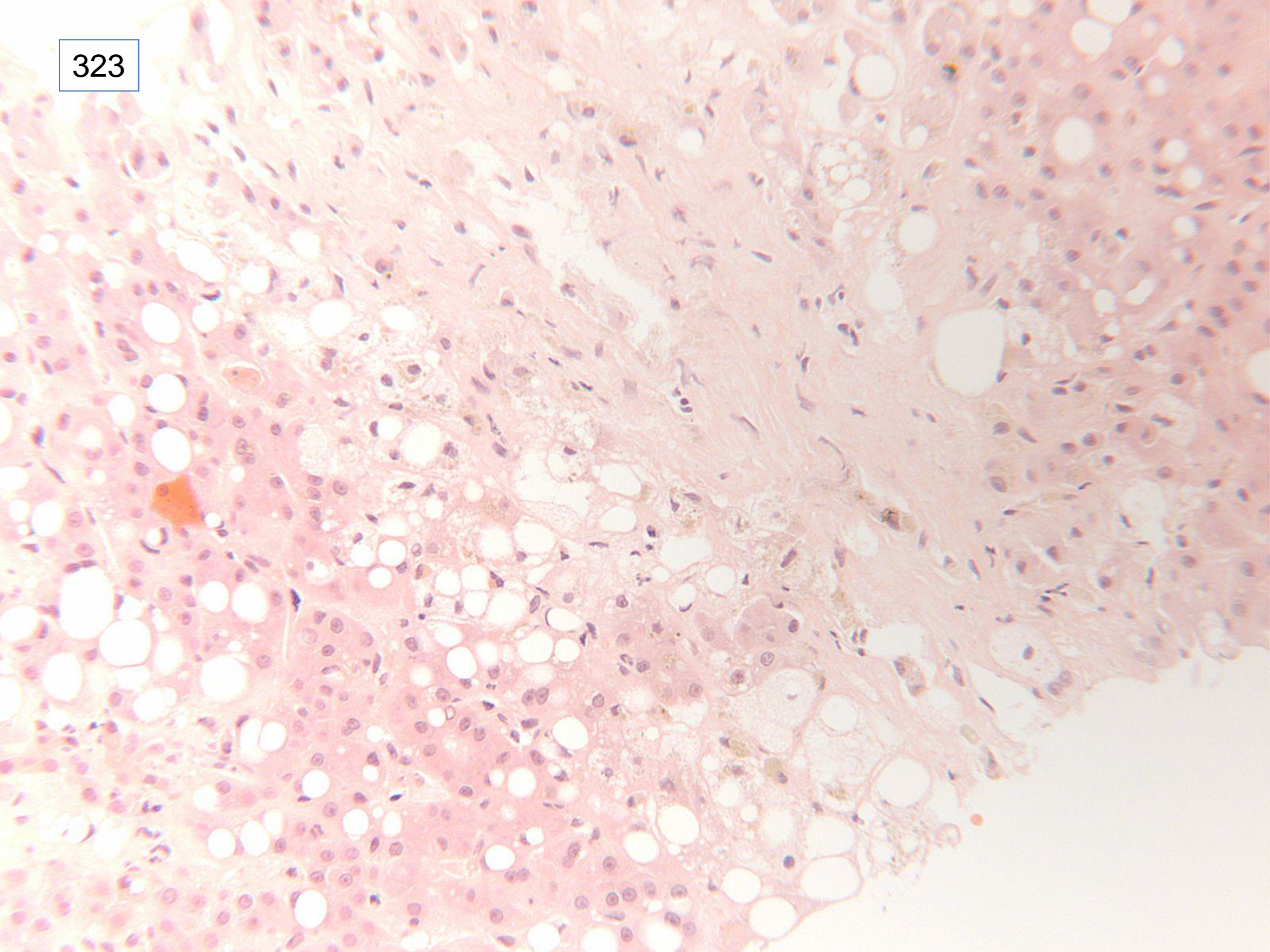
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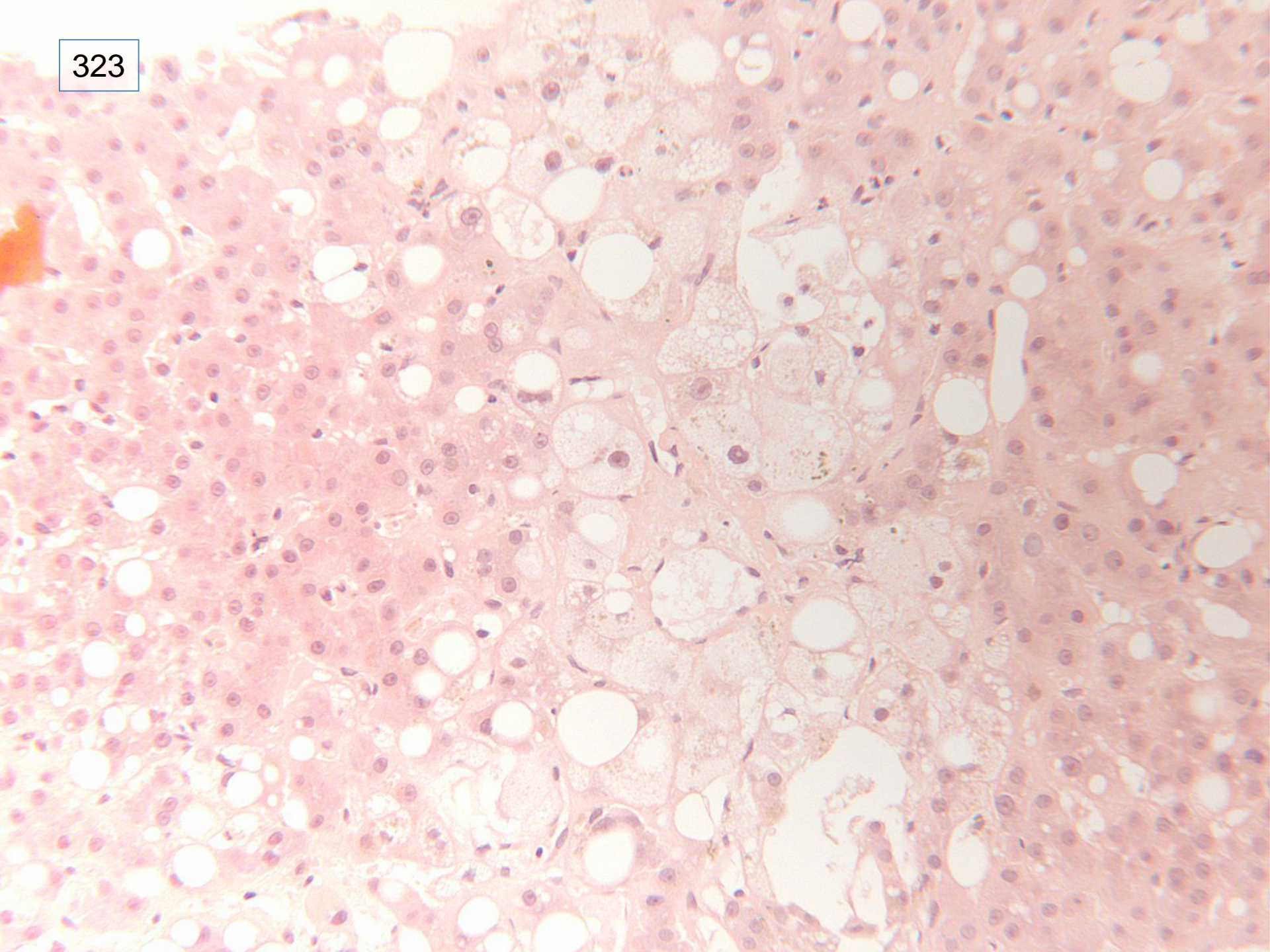
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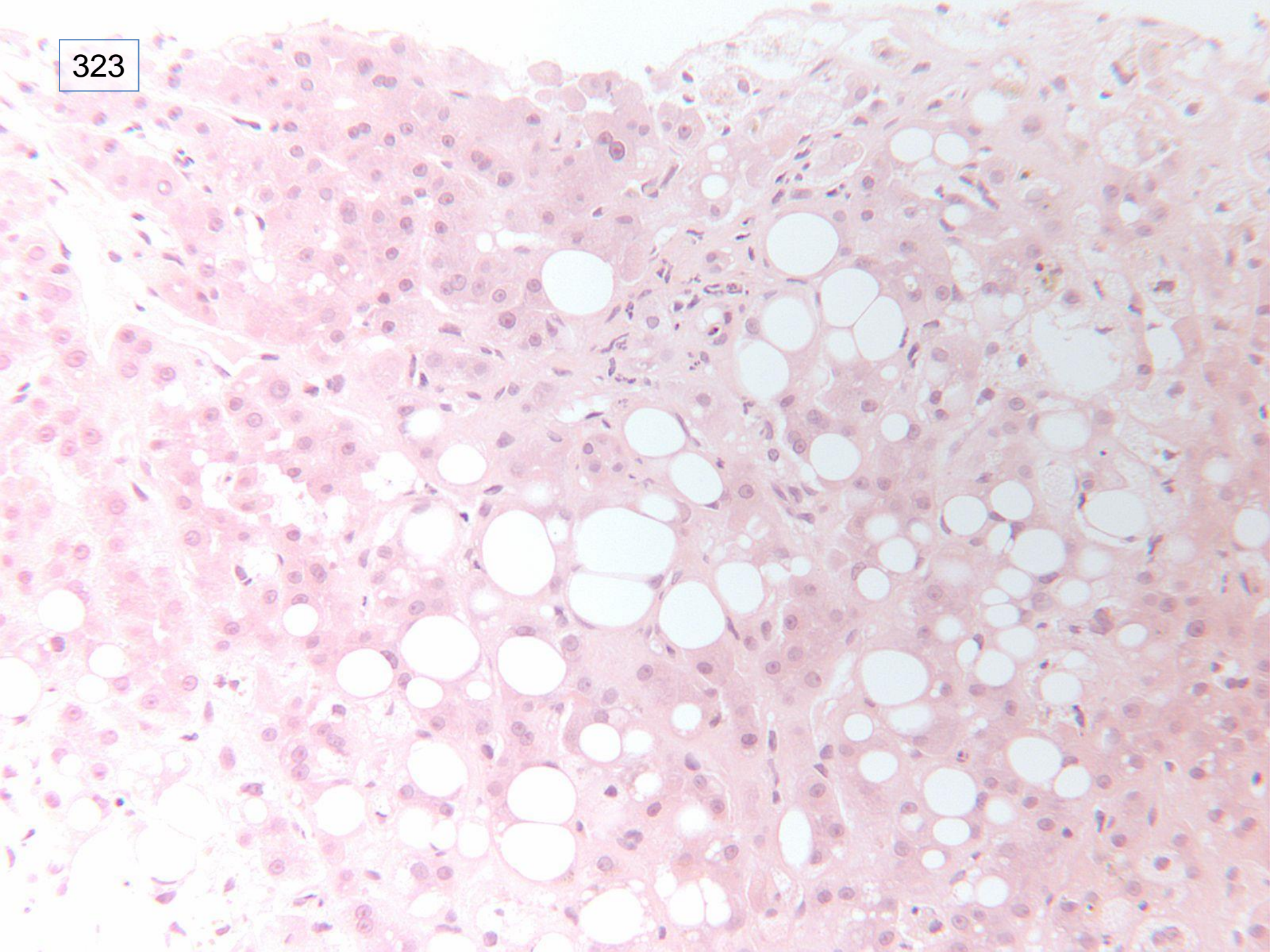
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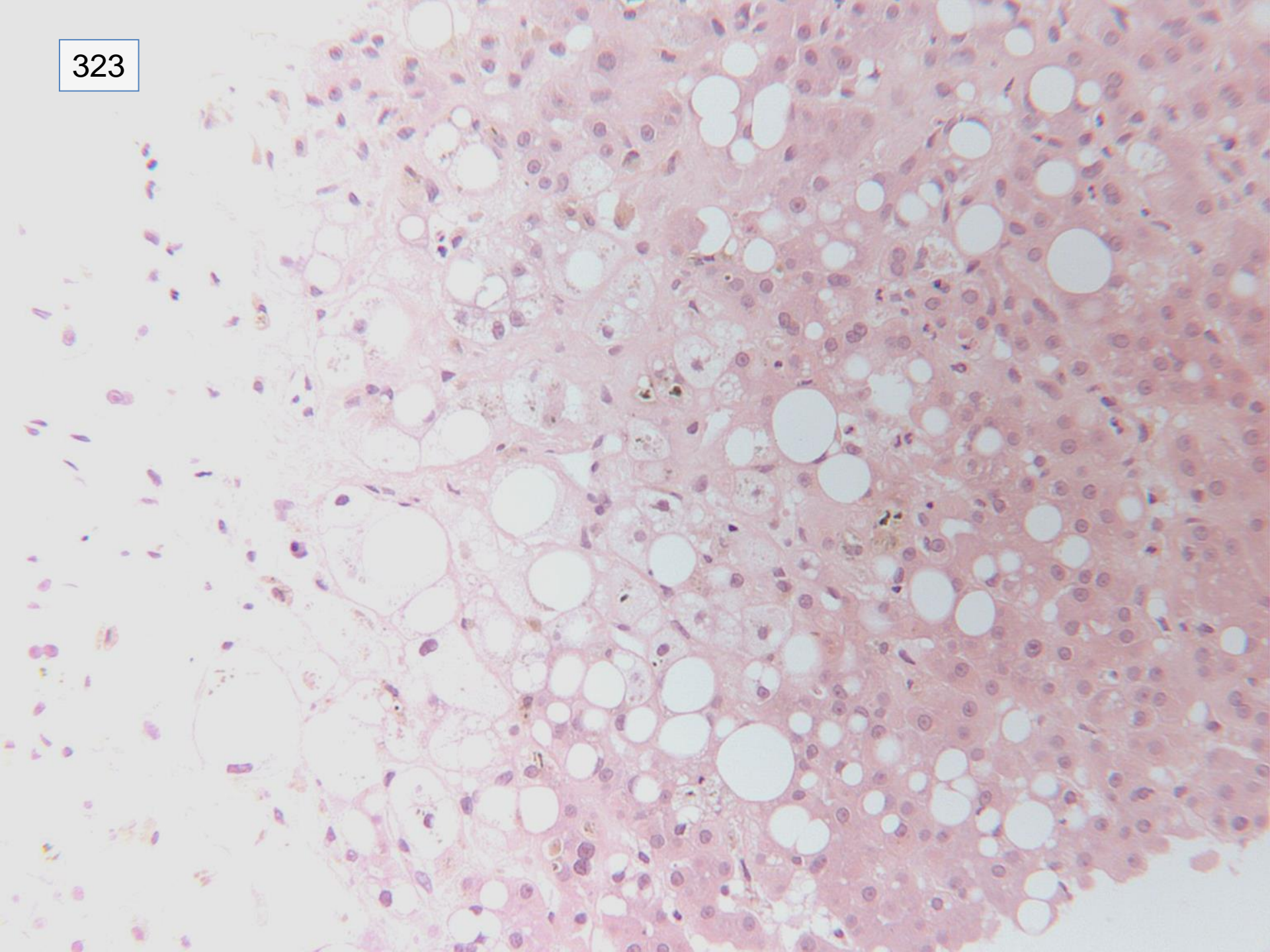
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# Case 323

## *Responses:*

44 had alcoholic liver disease as the dominant pathology:

33 alcoholic steatohepatitis as main/only diagnosis

of which 17 specified central hyaline necrosis pattern

5 alcoholic steatohepatitis plus centrilobular necrosis

6 alcoholic steatohepatitis plus a second cause for cholestasis

10 alcohol not mentioned anywhere in the response

Others included alcohol among background factors

7 centrilobular necrosis (ischaemic)

3 steatohepatitis and centrilobular necrosis (alcohol not mentioned)

1 steatosis and massive necrosis

1 drugs/paracetamol

1 descriptive – cholestasis, portal inflammation, ballooning, not typical of alcohol

1 acute cholestatic injury with steatosis, alcohol not mentioned

1 not typical of ALD – necrosis and cholestasis, ?drug/obstruction/sepsis

1 large duct obstruction and steatosis (alcohol)

1 cholestatic hepatitis with foamy degeneration – alcohol

1 cholestasis and steatosis and collapse – 'ITU liver'

## Case 323 scoring and discussion

A case of steatohepatitis with a marked degree of zone 3 fibrosis. It was felt that all the features in this case are attributable to alcoholic liver disease, an additional cause for cholestasis is not required. Although the staining was pale in perivenular zones, no zone 3 confluent necrosis was present.

The designation of central sclerosing hyaline necrosis is appropriate here, and is one pattern of alcoholic liver disease. There is zone 3 sclerosis, the 'hyaline' refers to Mallory's hyaline, (generally a prominent feature although not in this case) and 'necrosis' to the prior loss of perivenular hepatocytes. This can result in jaundice and liver failure without established cirrhosis.

Responses that did not include alcohol as the aetiology scored 0 marks.

## Case 323

Original diagnosis: steatohepatitis

Follow up information – recovered.

Many medical problems including obesity,  
‘past’ history of heavy alcohol consumption,  
type 2 diabetes, chronic renal failure,  
polycythaemia, hypoventilation syndrome.

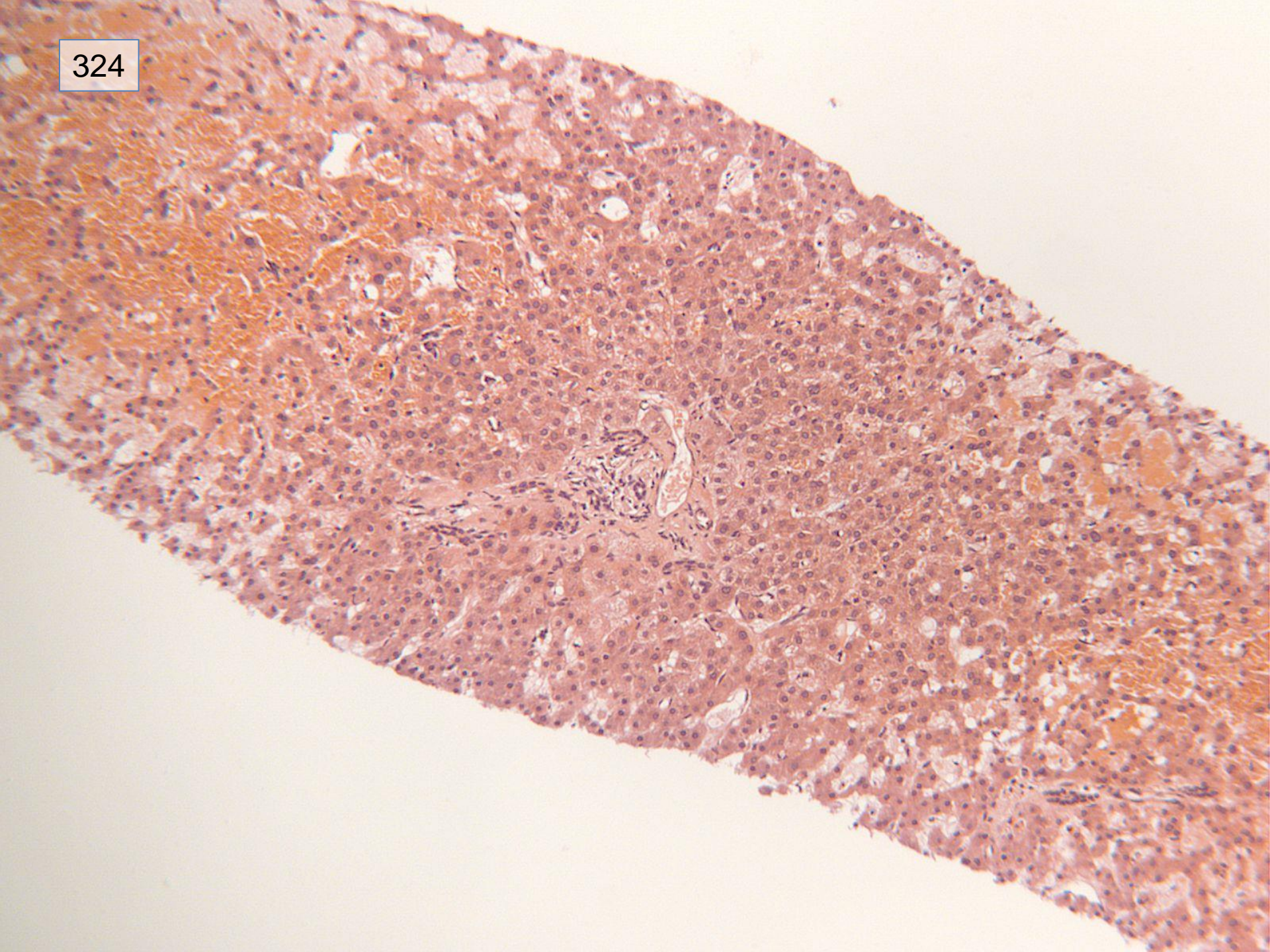
## **Case 324**

53M Oesophageal cancer. Liver failure.

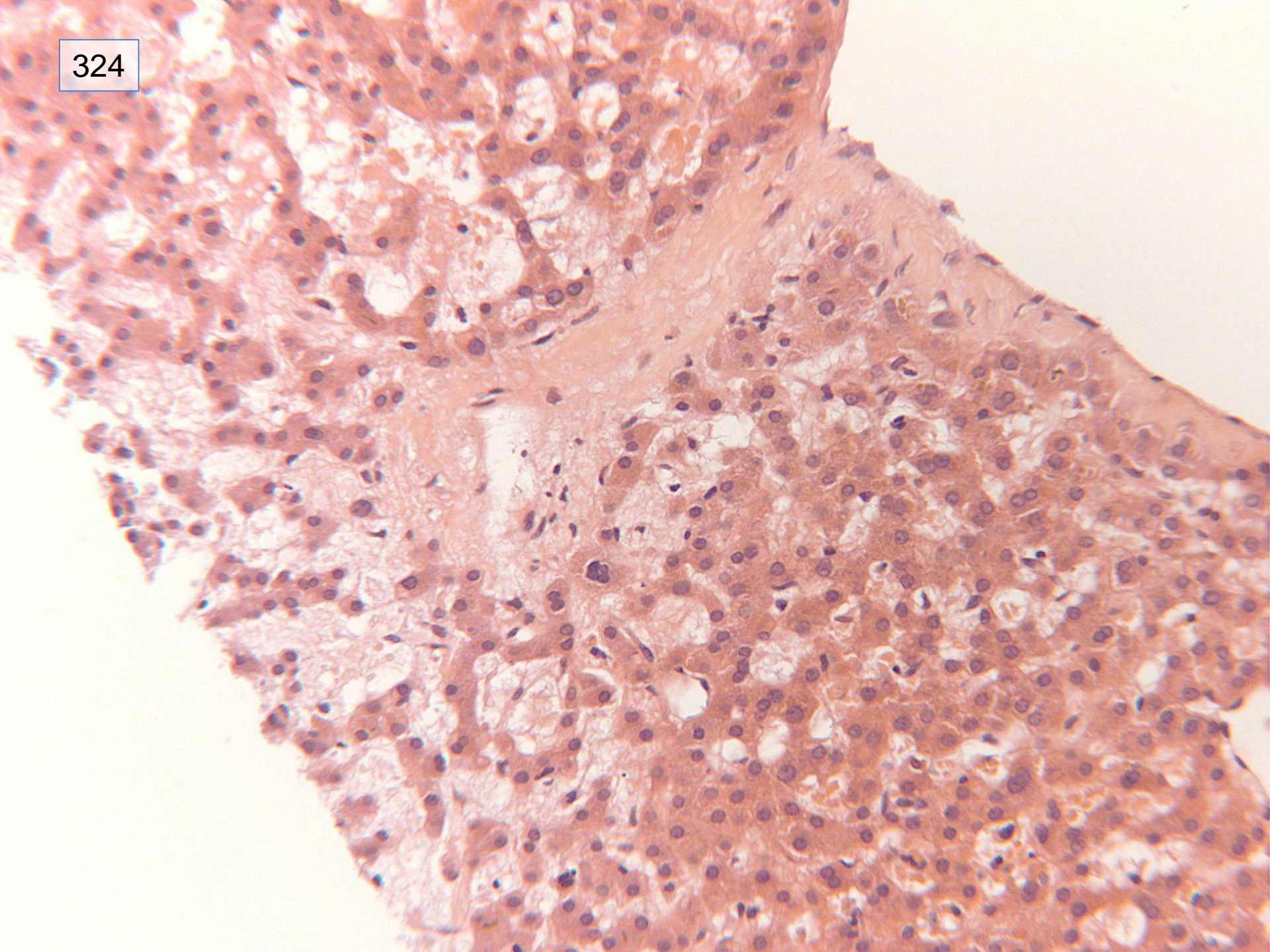
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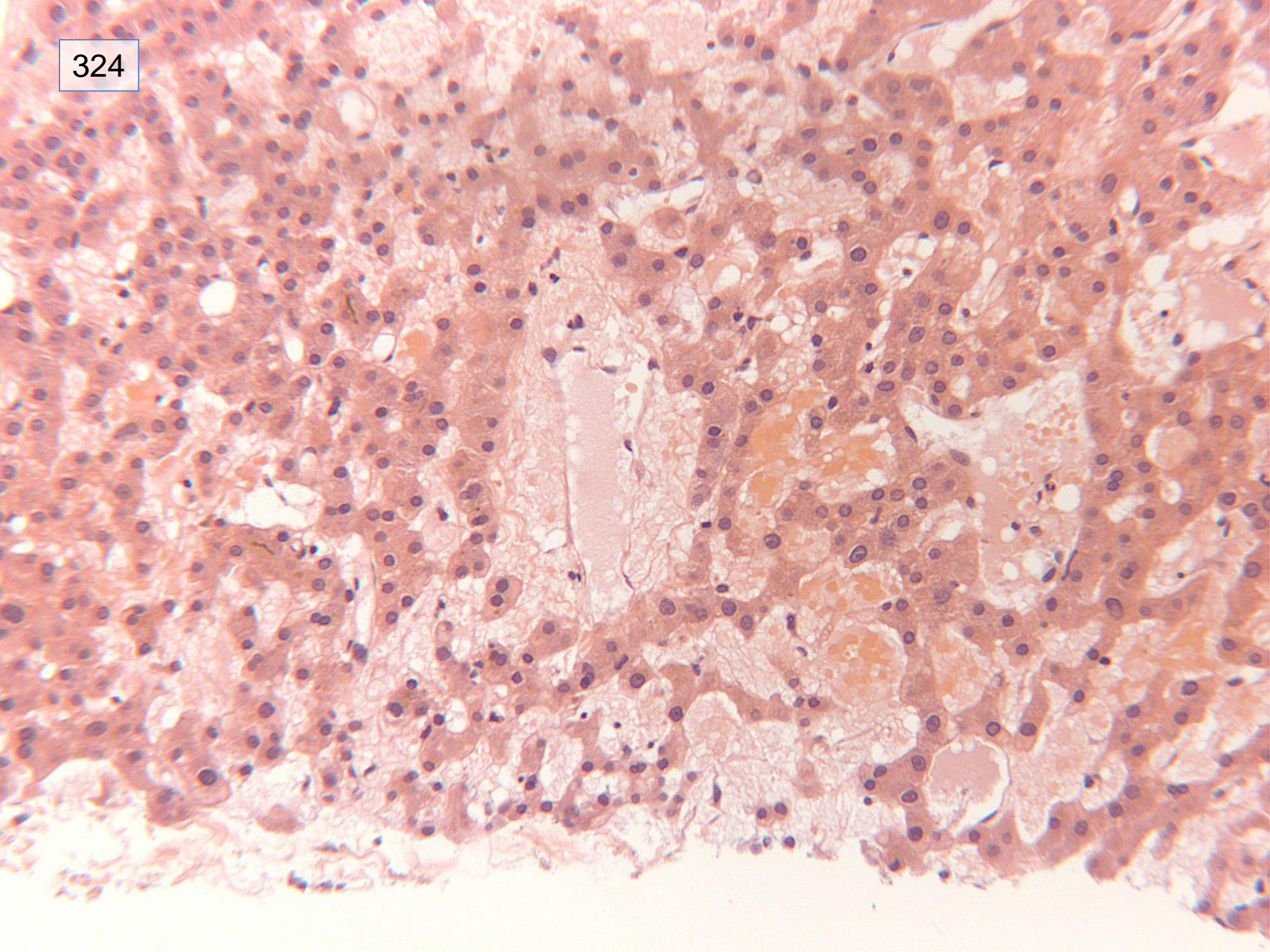
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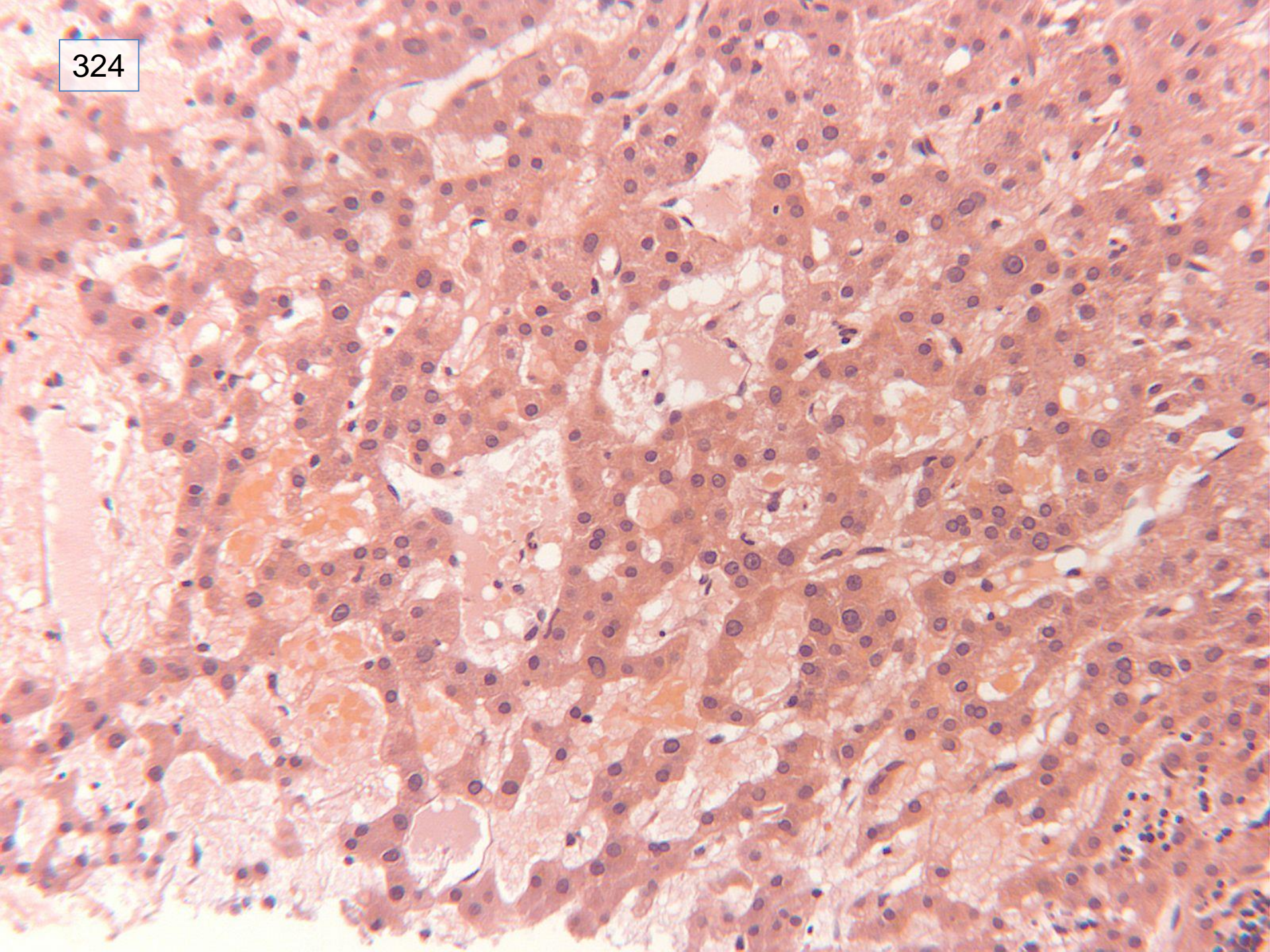
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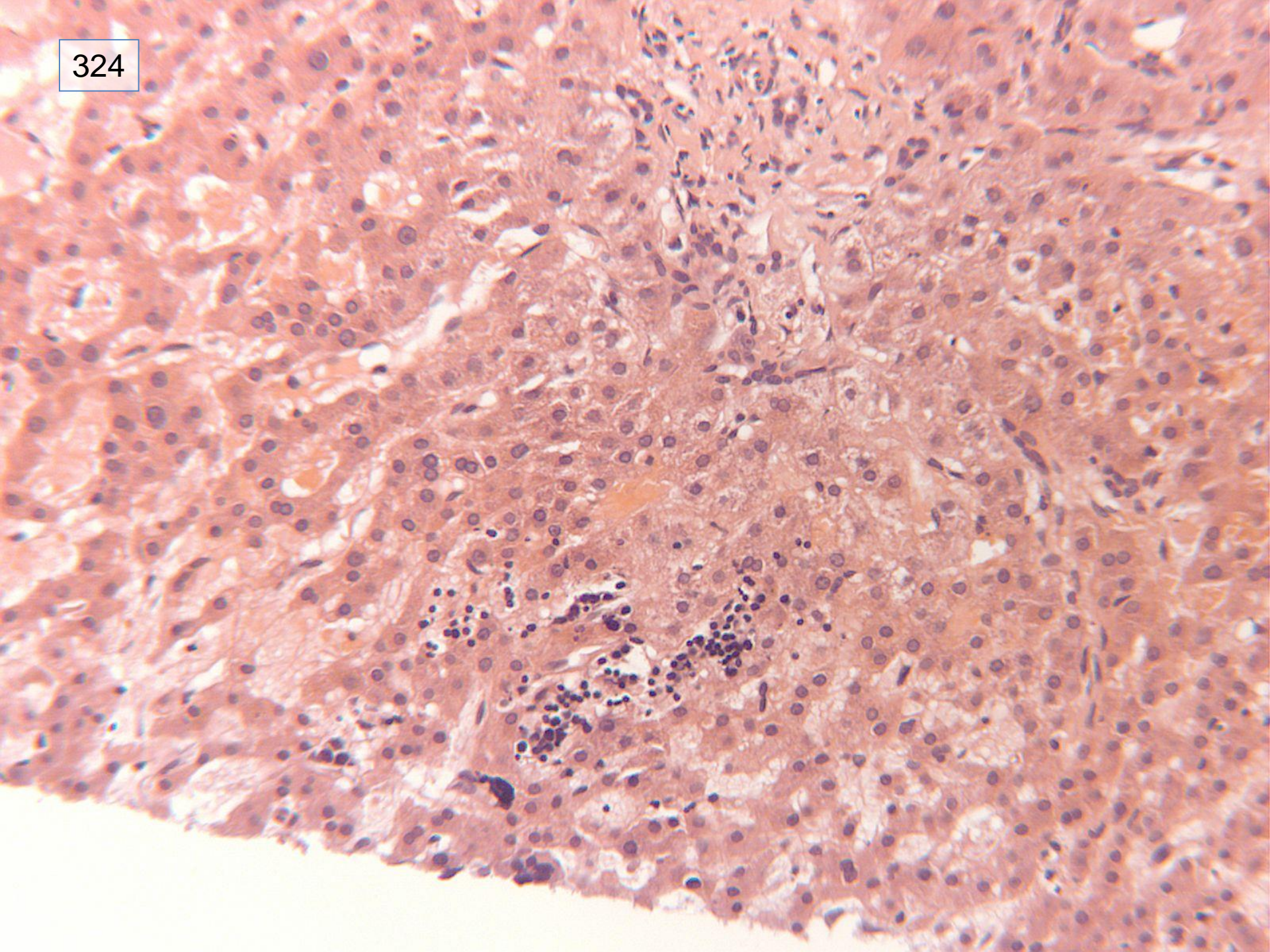
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# Case 324

## *Responses:*

- 48 venous outflow obstruction, of which
  - 17 hepatic vein obstruction/Budd Chiari Syndrome
  - 1 veno-occlusive disease
  - 3 sinusoidal obstruction syndromeOf this group, 12 suggested it may be due to chemotherapy
  
- 3 congestion and ischaemia suggestive of heart failure (one includes BCS among differentials)
- 2 sinusoidal dilatation and congestion NOS
- 1 chronic passive congestion (venous outflow obstruction)
- 2 peliosis hepatis NOS
- 1 nodular regenerative hyperplasia
- 1 sinusoidal dilatation and congestion secondary to space occupying lesion, likely met. cancer
  
- 22 also mentioned extra-medullary haematopoiesis, and possibility of marrow replacement by metastatic cancer, or associated myeloproliferative disease that could cause hyper-coagulability and BCS.

# Case 324 scoring and discussion

Score 10 marks for responses that included some form of venous outflow obstruction. There was discussion about whether these features could be due to acute cardiac failure and this was accepted as a possibility. The important clinical message is to investigate causes of venous outflow obstruction. Responses describing congestion/sinusoidal dilatation without mentioning venous outflow obstruction scored 5 marks.

Peliosis hepatis, nodular regenerative hyperplasia and changes adjacent to a space occupying lesion scored 0 marks.

It was commented that 'Budd Chiari Syndrome' strictly speaking refers to a clinical syndrome of hepatomegaly and ascites due to hepatic vein thrombosis, and a histological diagnosis of venous outflow obstruction is preferable.

## Case 324

Original diagnosis: venous outflow obstruction

VG stain shows loose fibrous tissue occluding some terminal hepatic venules – therefore acute veno-occlusive disease.

Differential diagnosis includes Budd Chiari syndrome.

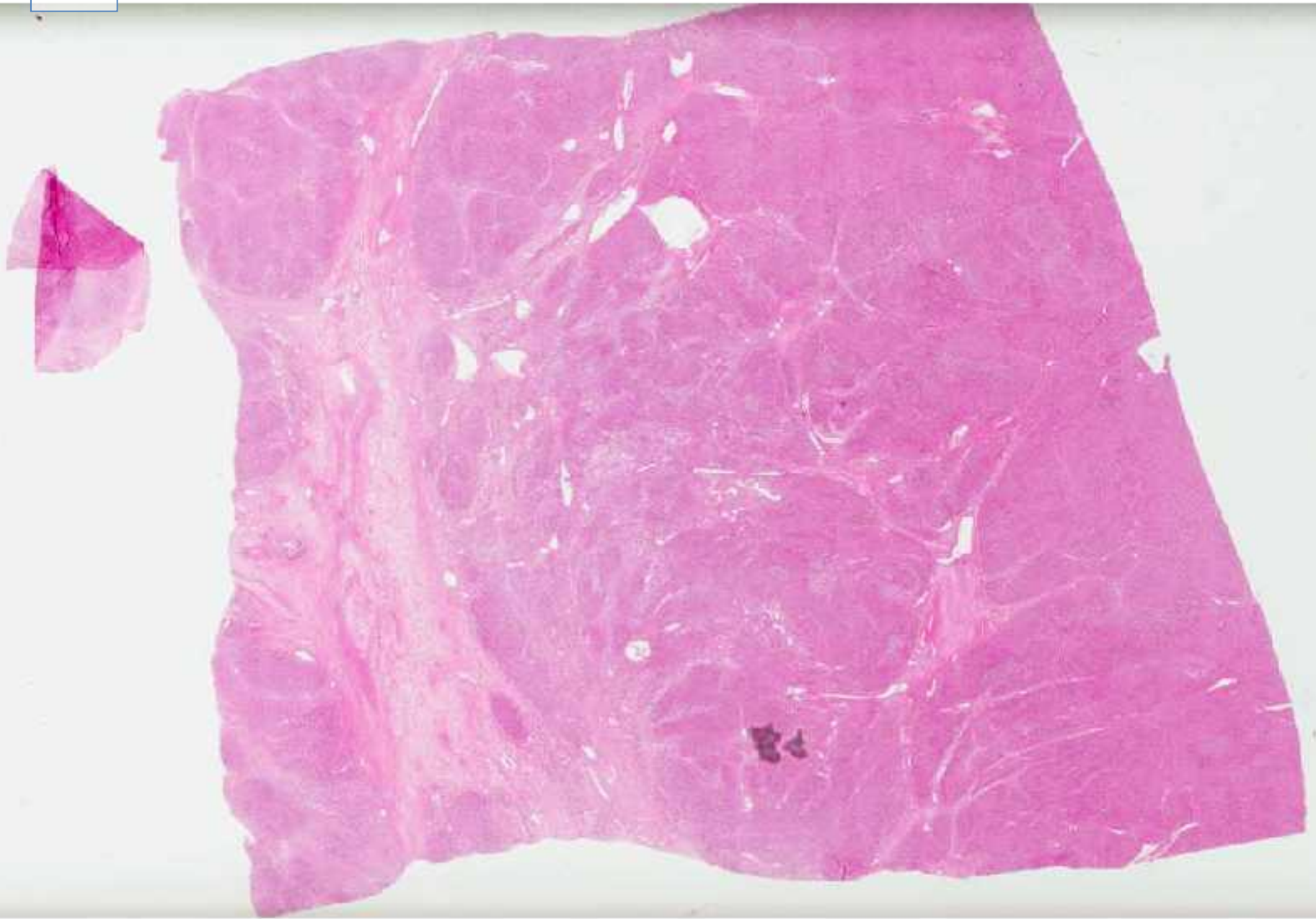
Further clinical information – patient has had treatment with a new taxane, discontinued after deterioration in LFTs about 4 weeks before this biopsy.

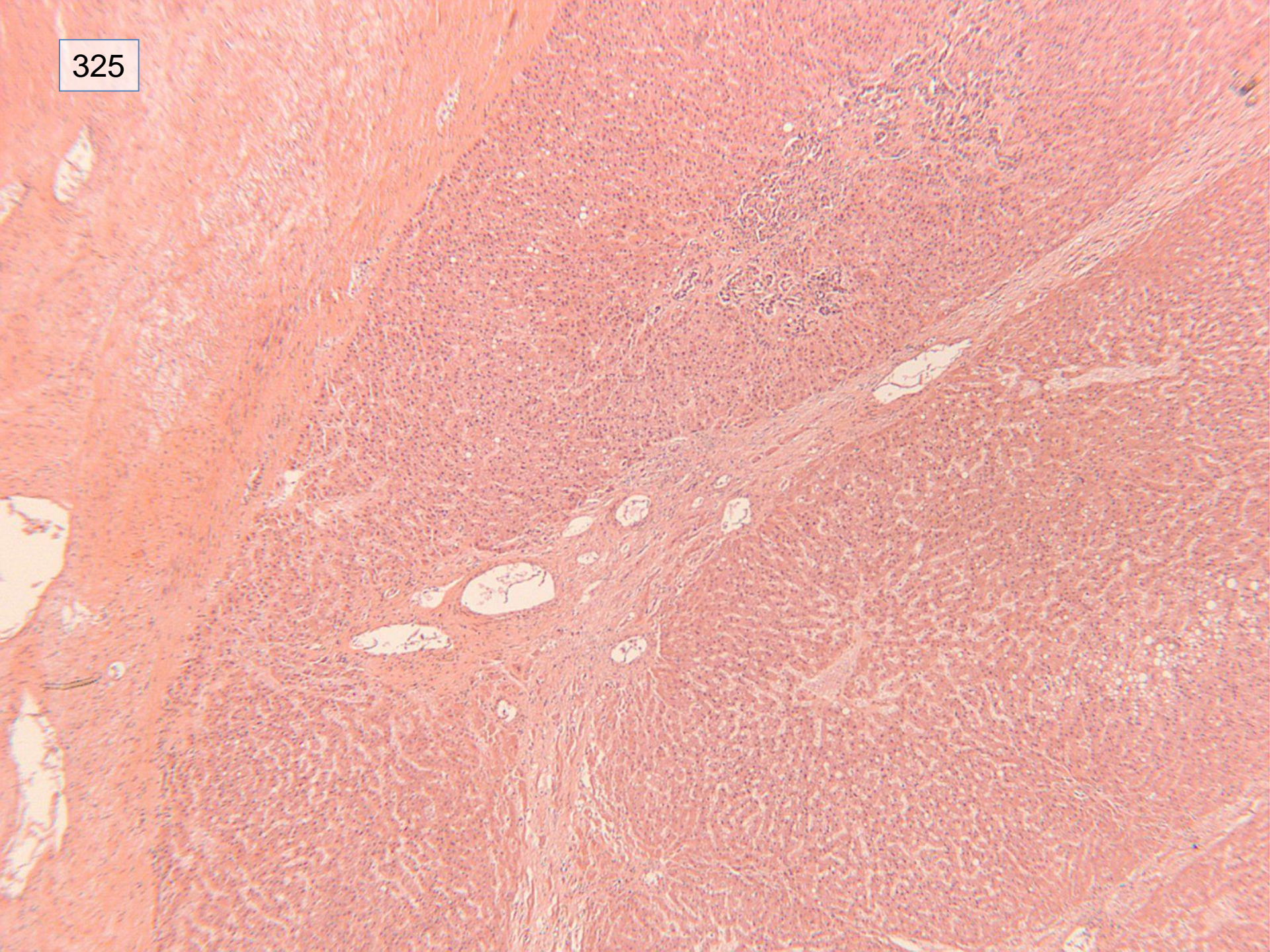
Alk phos and ALT improving but albumin is continuing to fall and bilirubin increasing.

## **Case 325**

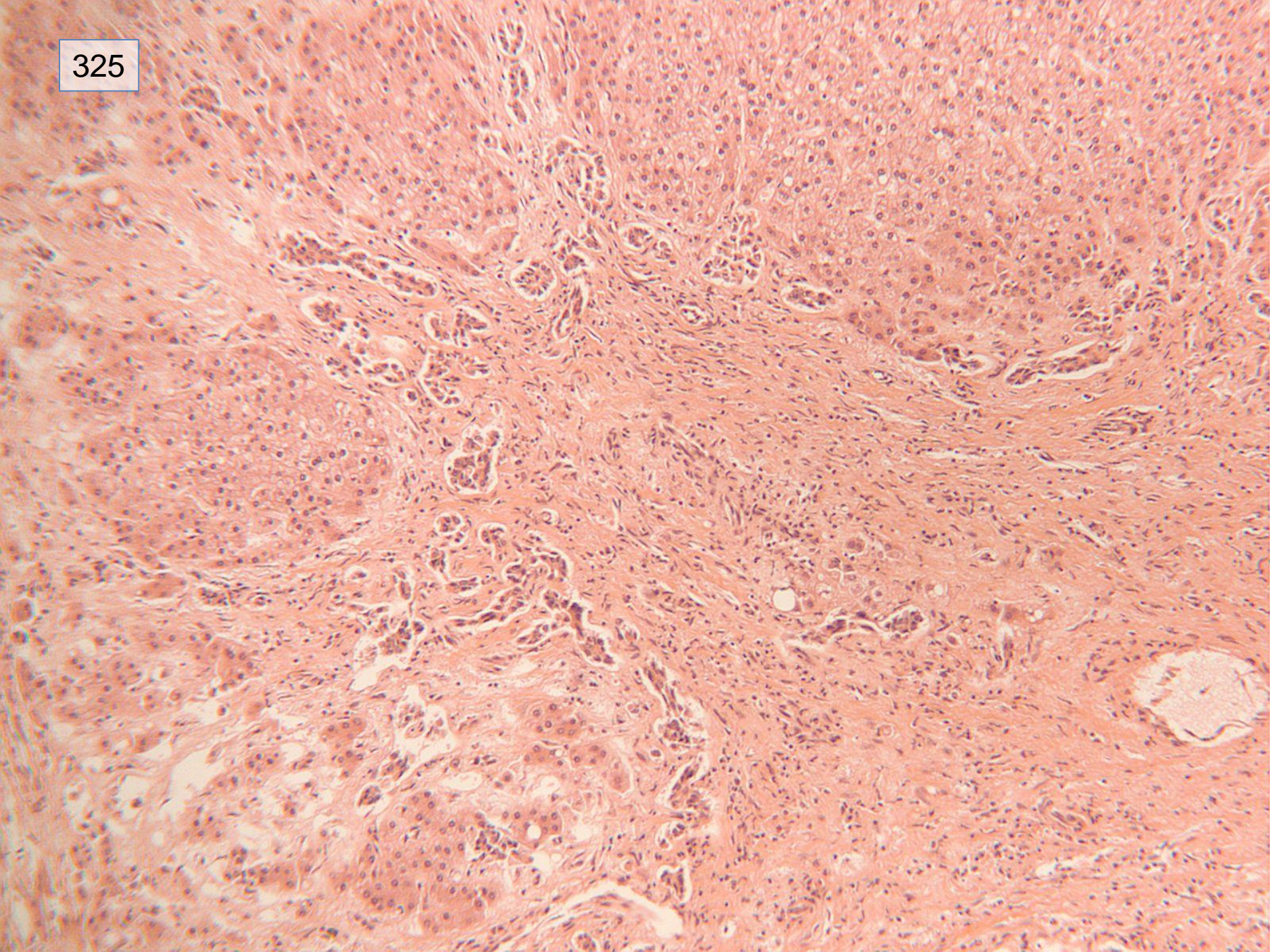
32F Lesion in liver. Left hepatectomy – lobulated, tan tumour 110x166x125mm with central stellate scar (specimen photograph included).



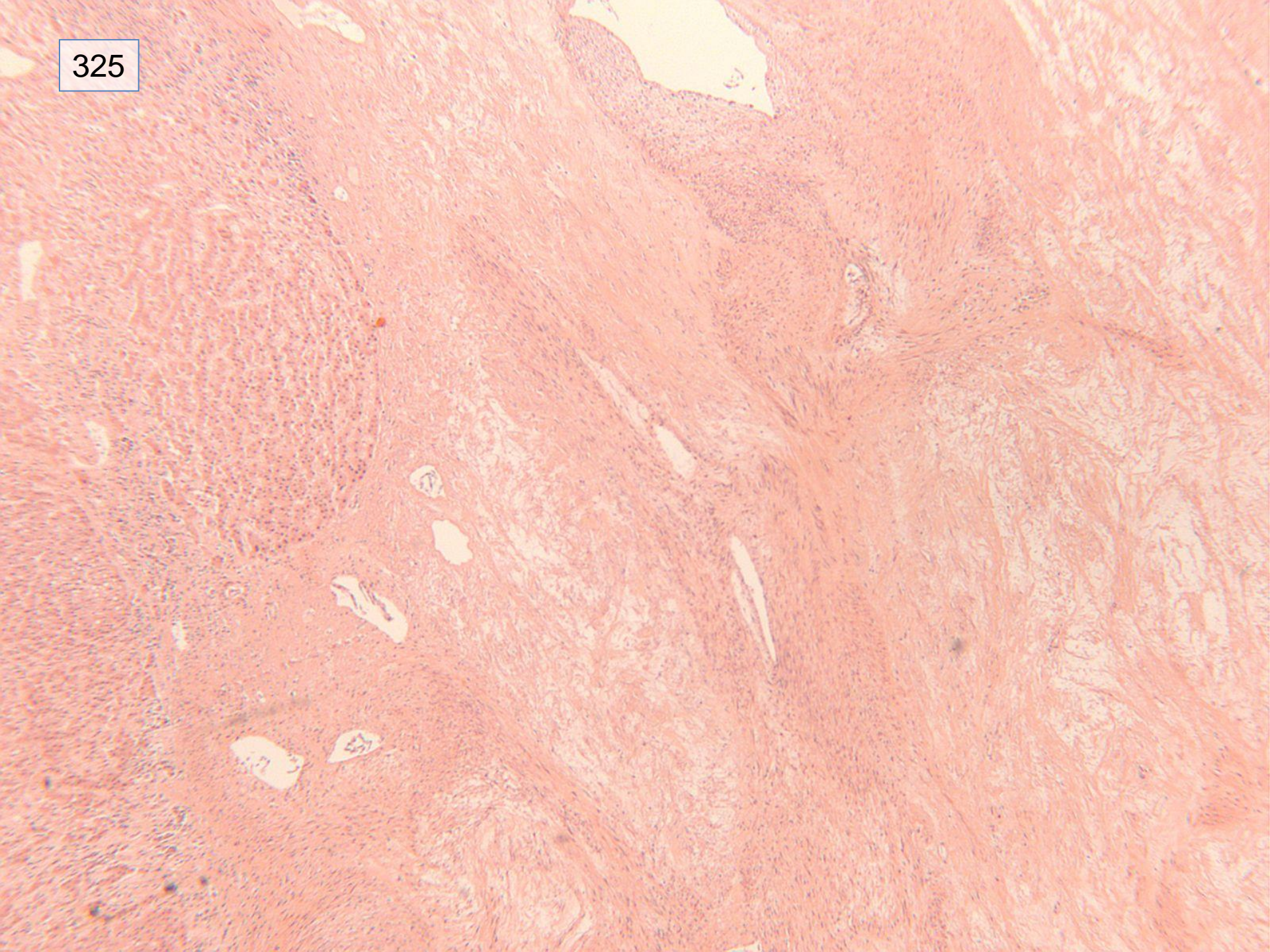




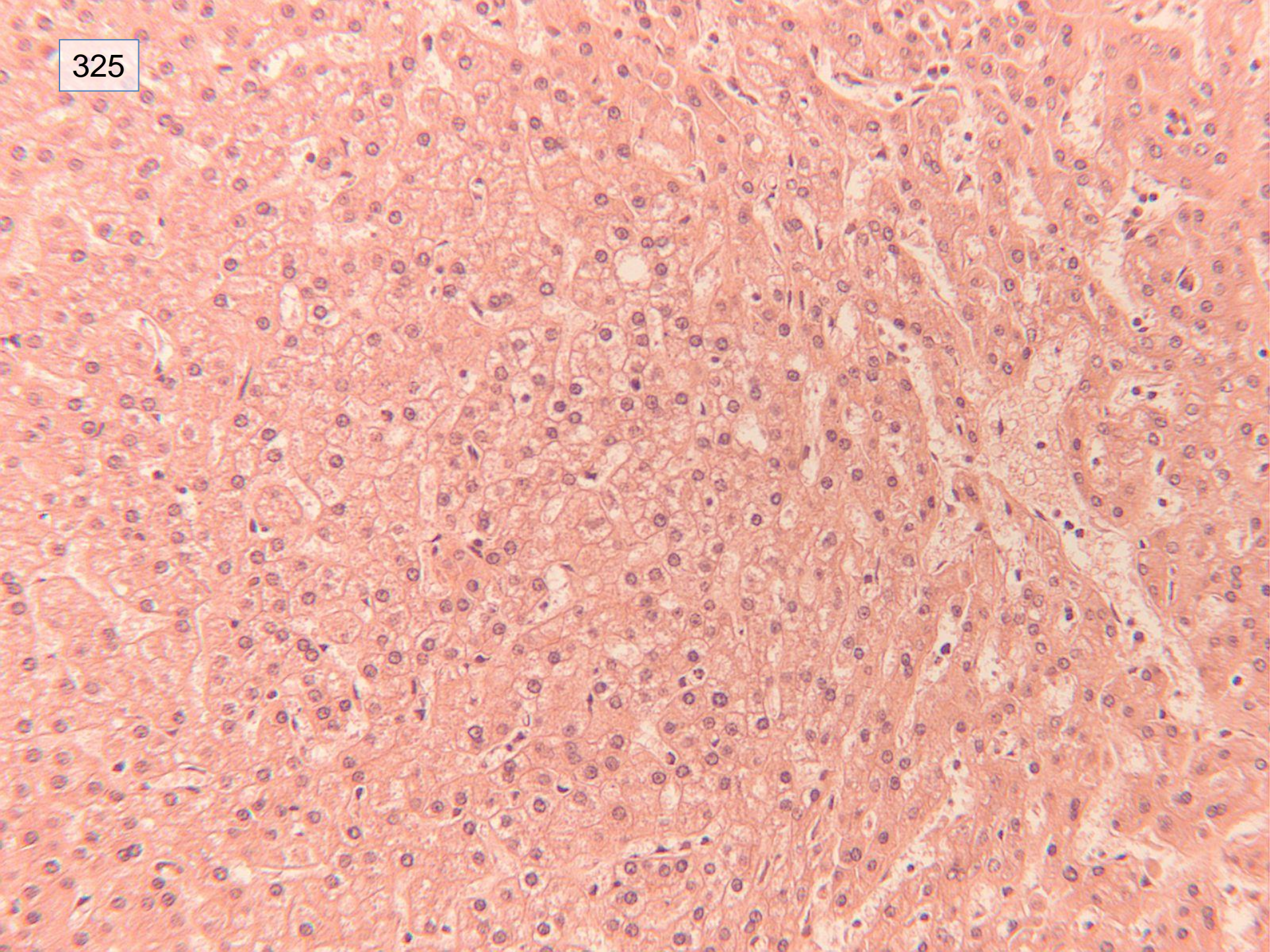
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325



325



## Case 325

### *Responses:*

57 focal nodular hyperplasia

1 cirrhotic changes; .....(illegible) await clinical correlation.

*Original diagnosis: focal nodular hyperplasia*

## Case 325 scoring and discussion

This shows characteristic features of focal nodular hyperplasia. Although there is no background liver in the submitted slide, the nature of this as a focal lesion is clear from the macro photograph, and the response 'cirrhotic changes' scores 0 marks.

The End

Circulation A1 – starts mid July

Next meeting December 10<sup>th</sup> 2009 in London.