National Liver EQA Scheme
Circulation S

March 21st 2006

Birmingham

Circulation S

Thanks to Anne, and to Schering Plough

Circulation ‘T’ – Pathological Society meeting July 5th, Manchester.

Circulation ‘S’: 56 responses / 72 members – consecutive non-responders will be contacted.

Images are on Virtualpathology@leeds.ac.uk

Web site – RCPath, members section, will have information on all EQA schemes – liver hopefully by April.

RCPath subcommittee for specialist areas in histopathology

Document: ‘The recognition and roles of specialist cellular pathologists’.
(Tim Helliwell)
recognised at Trust, Network, National and International levels.
Liver EQA scheme members include all of these.

Attributes of a specialist
- current science
- aware of clinicians’ needs
- self-critical
- time and willingness to help other pathologists

Experience = (years x volume of cases)

Liver pathology – subset of GI pathology, not a shortage, except of time
Autumn update meeting
- current science relevant to routine practice
- clinicians needs – reduce variation among pathologists

Case discussion:

Including results and discussion of open meeting:

Rejected diagnoses are shown in *italics.*

Basis for scoring in each case is shown in red.

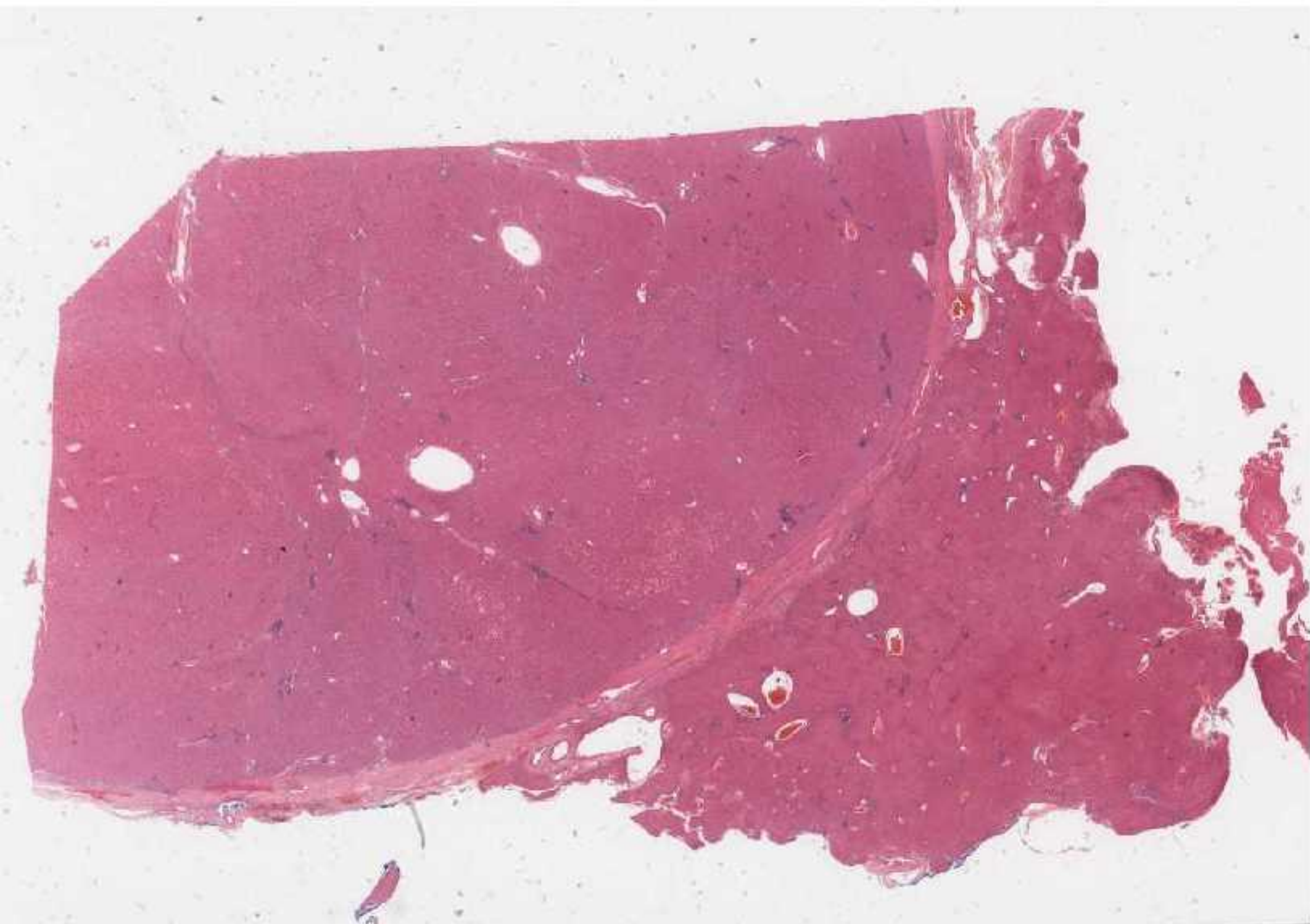
As a result of the discussion during the meeting,
4 of the cases (231,232, 233, 240) were deemed unsuitable for scoring.

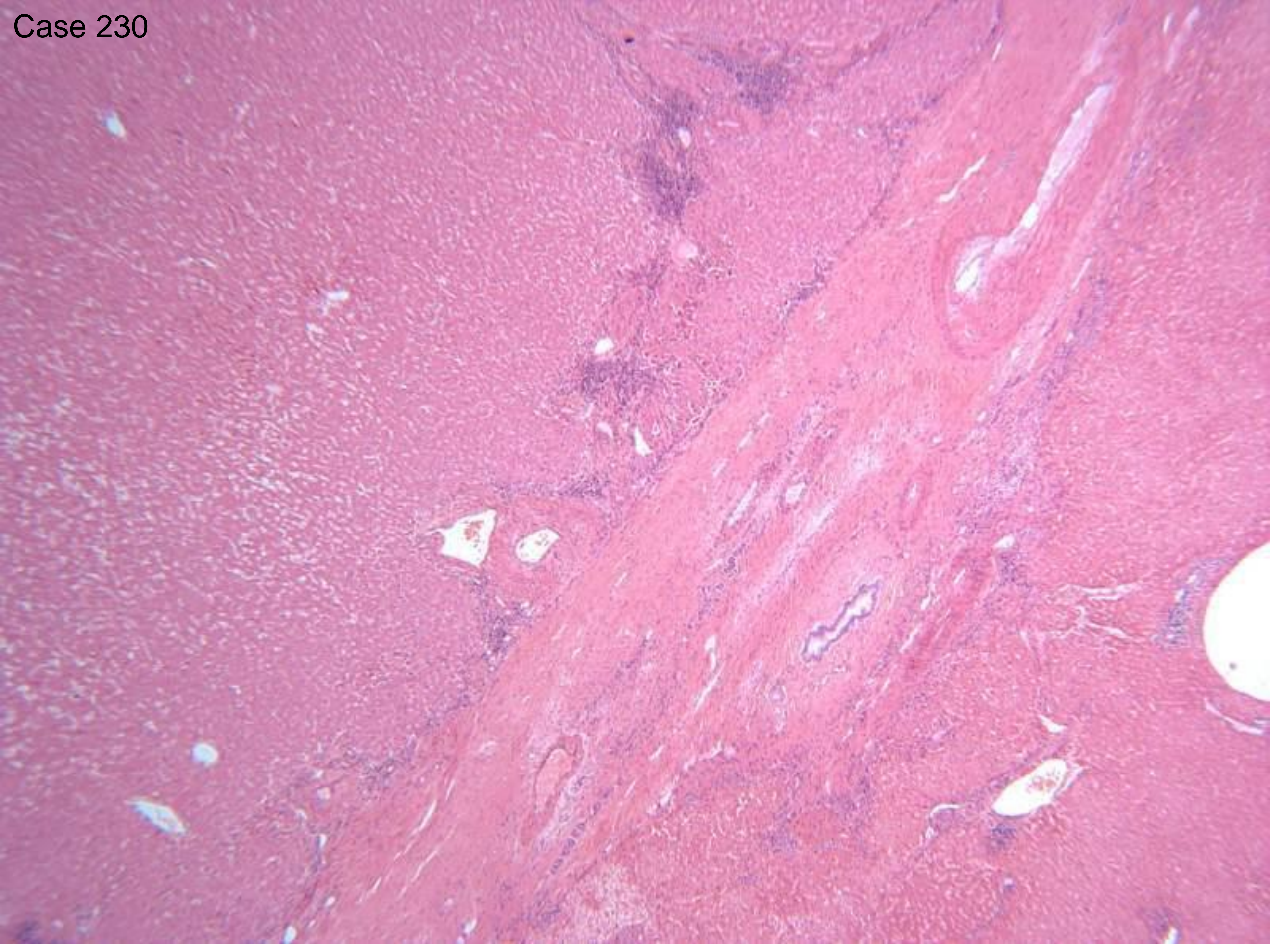
Case 230

55M. Mass found on US in his liver. Clinical diagnosis ‘fibrolamellar carcinoma or HCC’. Investigations: alpha FP negative. MiB1 less than 0.5% CK7 shows bile ductular reaction positivity within fibrovascular zones. Reticulin stain: normal pattern.

Hepatic resection: single mass 65x55x50mm. Well circumscribed with smooth cut surface. There is no evidence of necrosis or haemorrhage. The surrounding liver tissue was not cirrhotic or fibrotic.

Case 230

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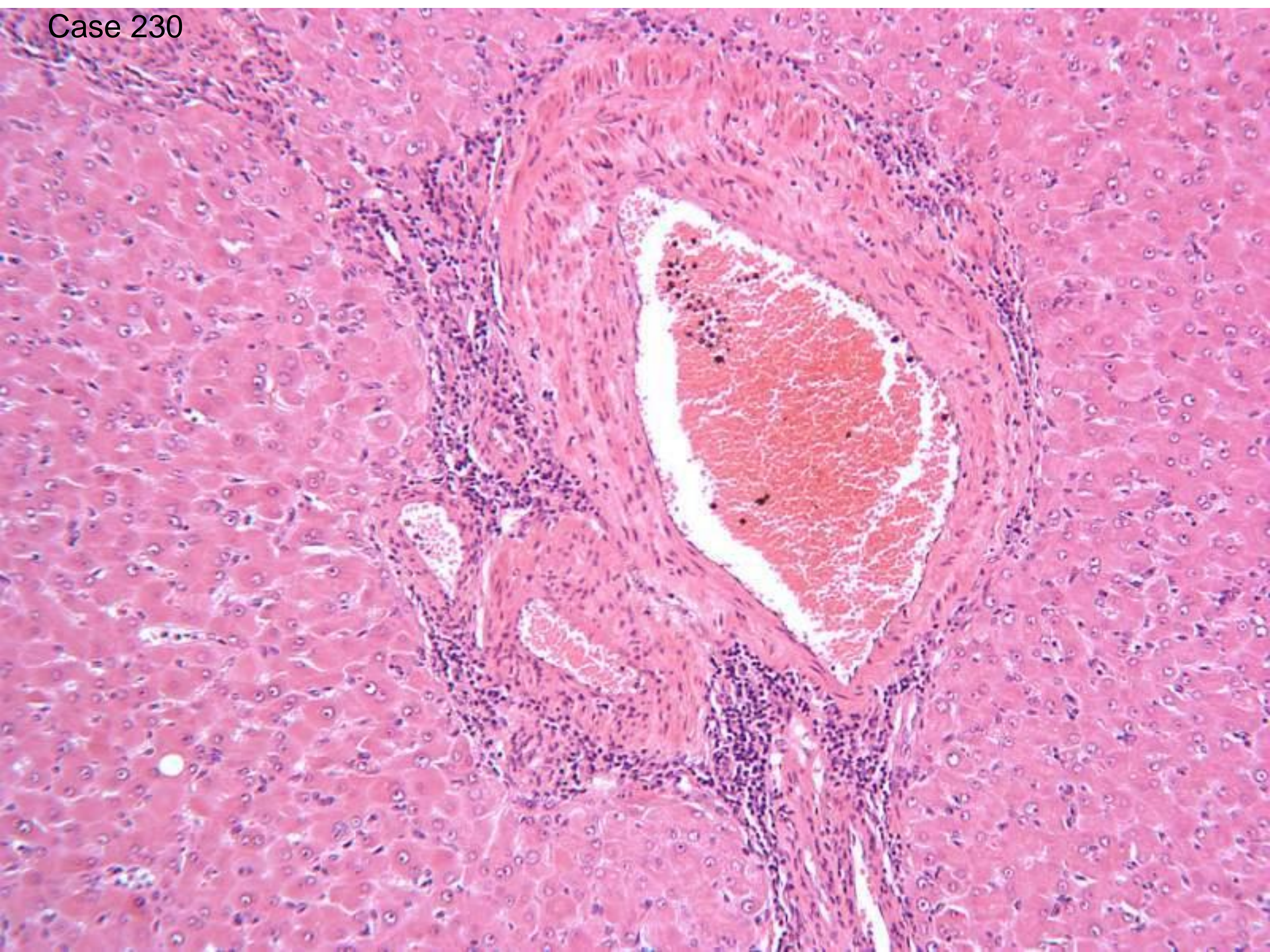
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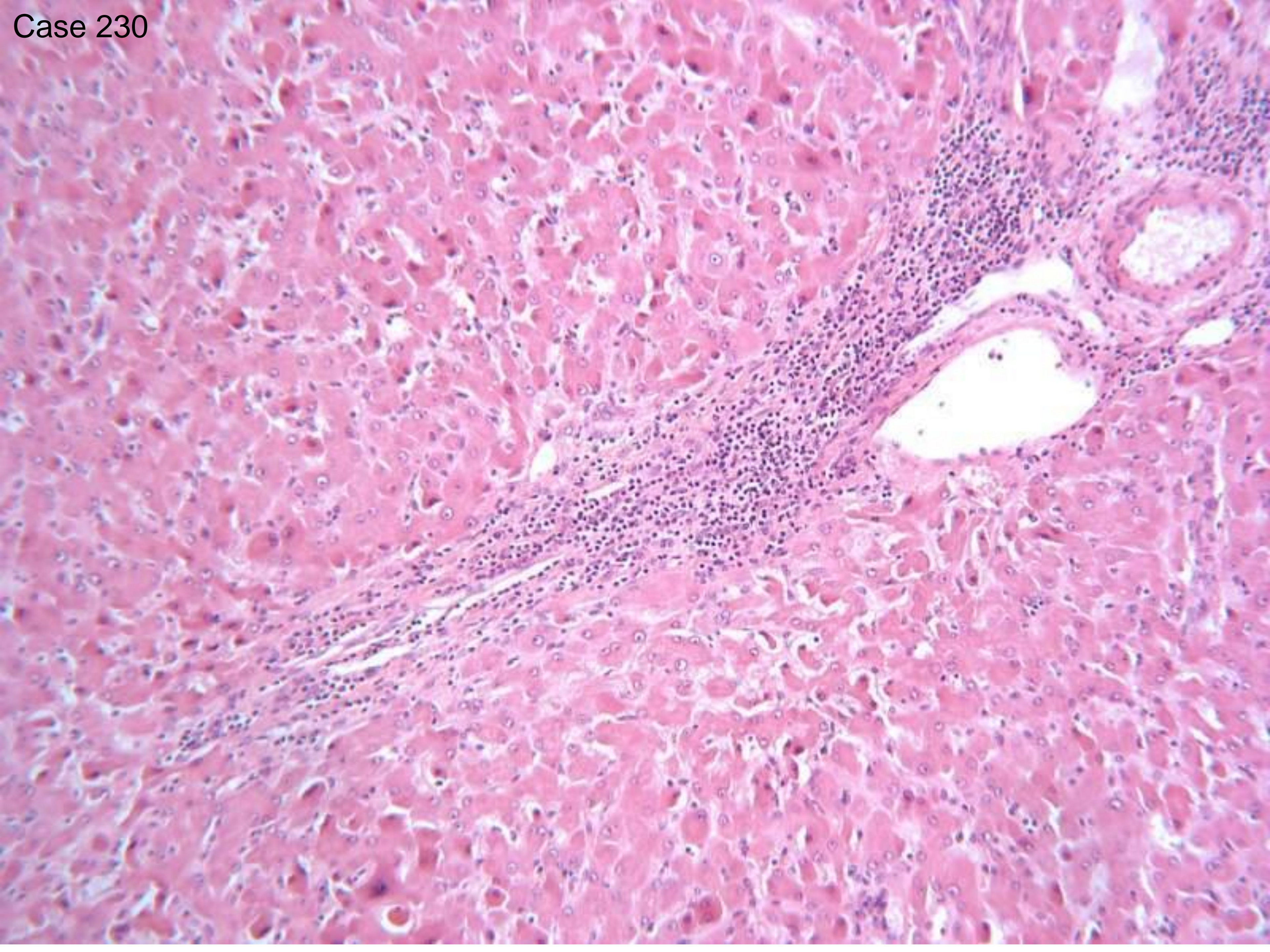
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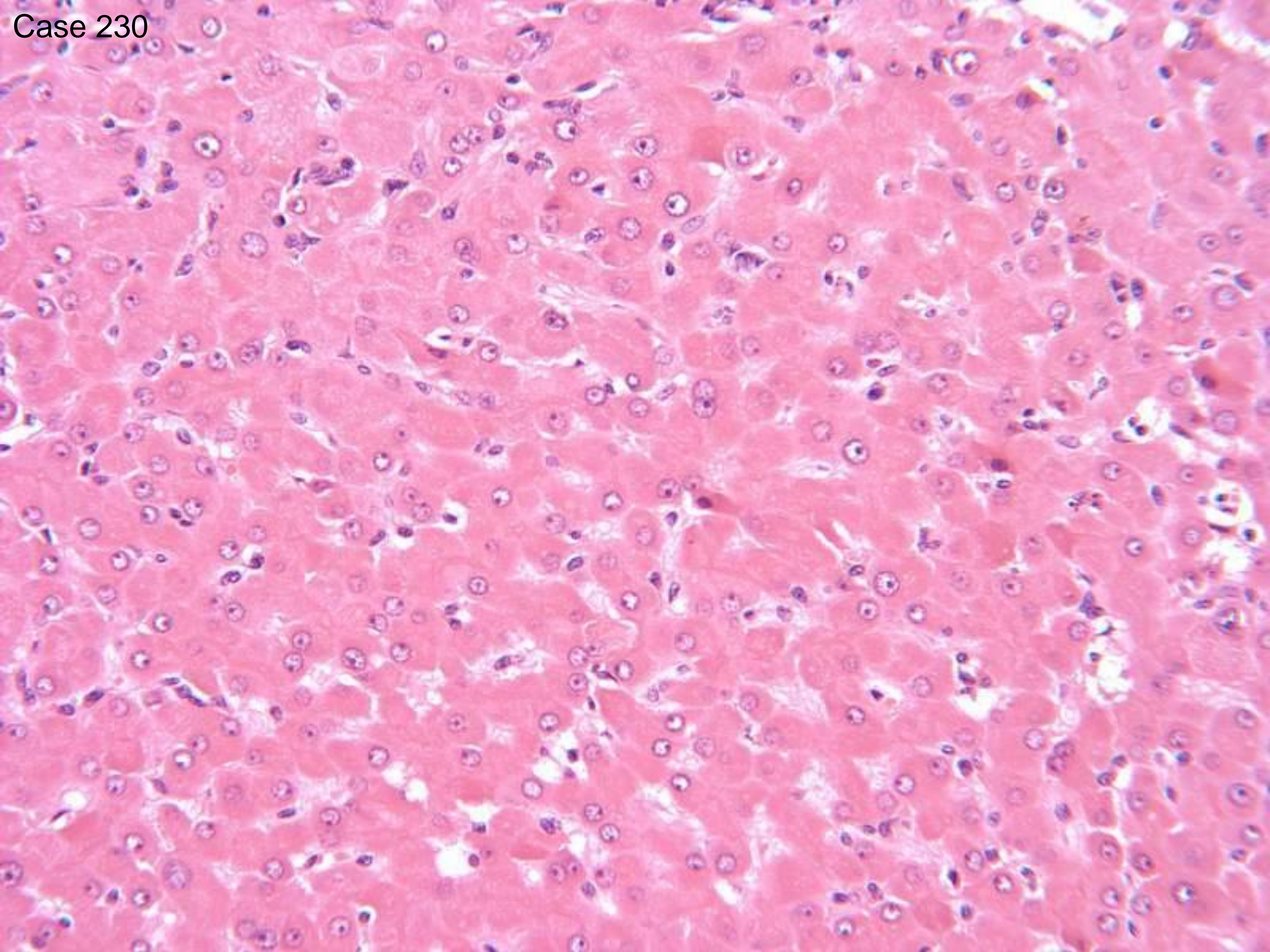

Case 230

Case 230

Results

23 focal nodular hyperplasia (includes those with comments about atypical FHN).

1 arterialised well differentiated hepatocellular lesion, ? FNH

1 macro-regenerative nodule

15 Liver cell adenoma

2 Well differentiated neoplasm, probably adenoma

1 telangiectatic adenoma (previously called FNH)

1 probably adenoma but considered well differentiated HCC

1 well differentiated HCC

3 fibrolamellar HCC,

2 differential FNH v. HCC v. adenoma

Scoring: Accept either adenoma or FNH;

reject macroregenerative nodule and HCC

Case 230

Comment: Discussion related to problem in distinguishing FNH from adenoma – ductular reaction was inconspicuous in this case, and for many the diagnosis on FNH depended on the description of the ductular reaction shown with CK7, rather than the features in the H&E slide. Oxyphyl change is conspicuous in hepatocytyes, and presumably accounts for the suggestions of fibrolamellar carcinoma.

Case 230

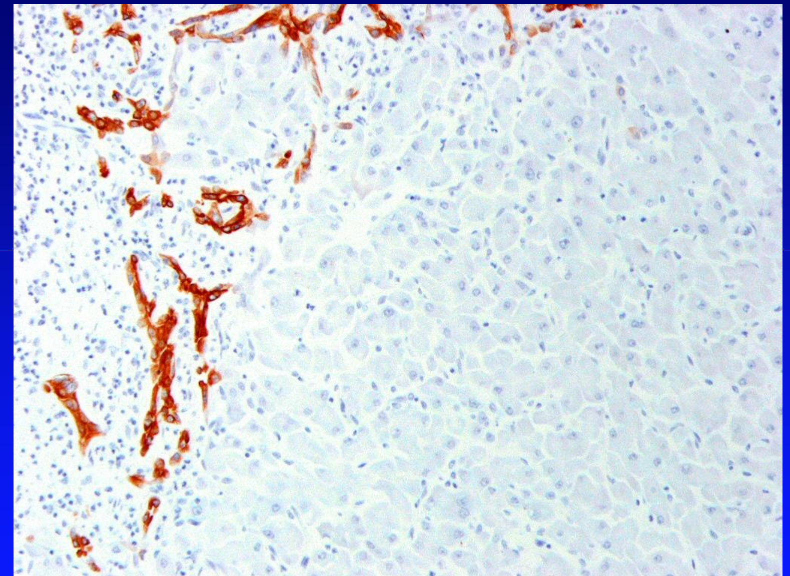
Follow up: Dr Zaitoun

Differential diagnosis between adenoma and FNH, with unusual oncocytic appearance of hepatocytes.

Sent to Prof. Anthony – diagnosed as FNH.

The ductular reaction is shown by CK7

We tend to see more atypical FNH these days, because these are the ones that get resected.



Case 231

65M. Abnormal LFTs/increased MCV, raised ferritin.

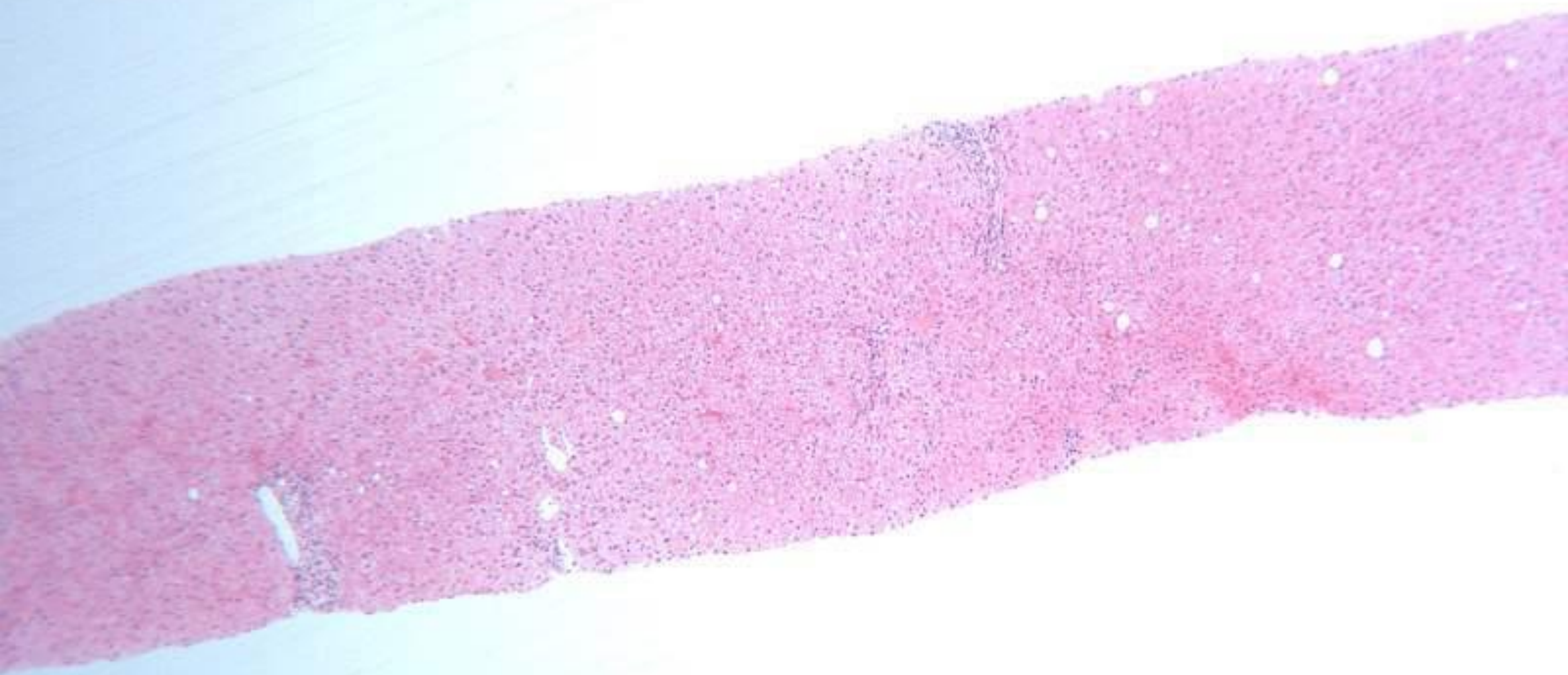
Perls:grade ½-1 out of 4,

alpha-1 antitrypsin PAS+/-.

No other clinical/immuno/serology results available.

Case 231

Case 231



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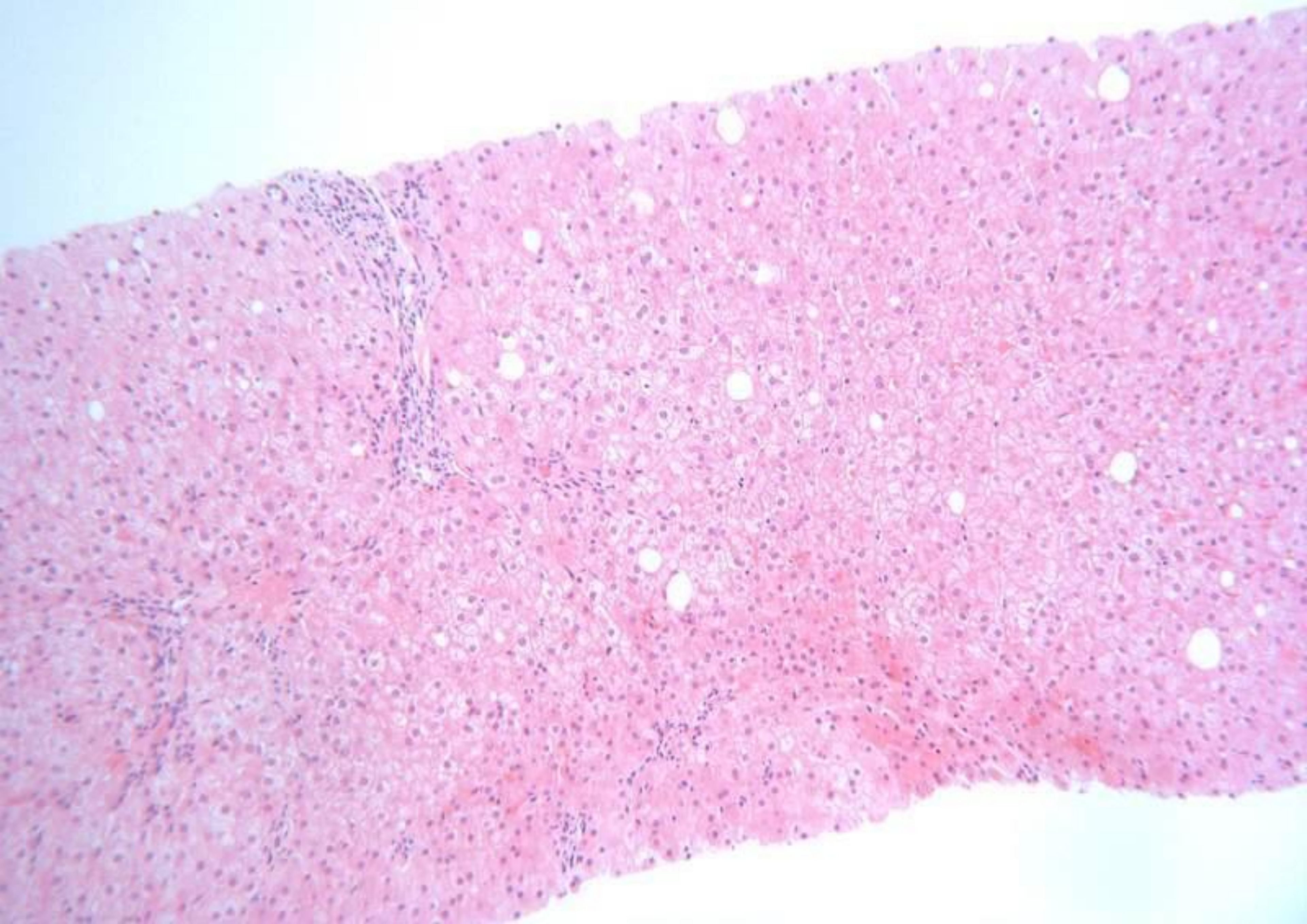

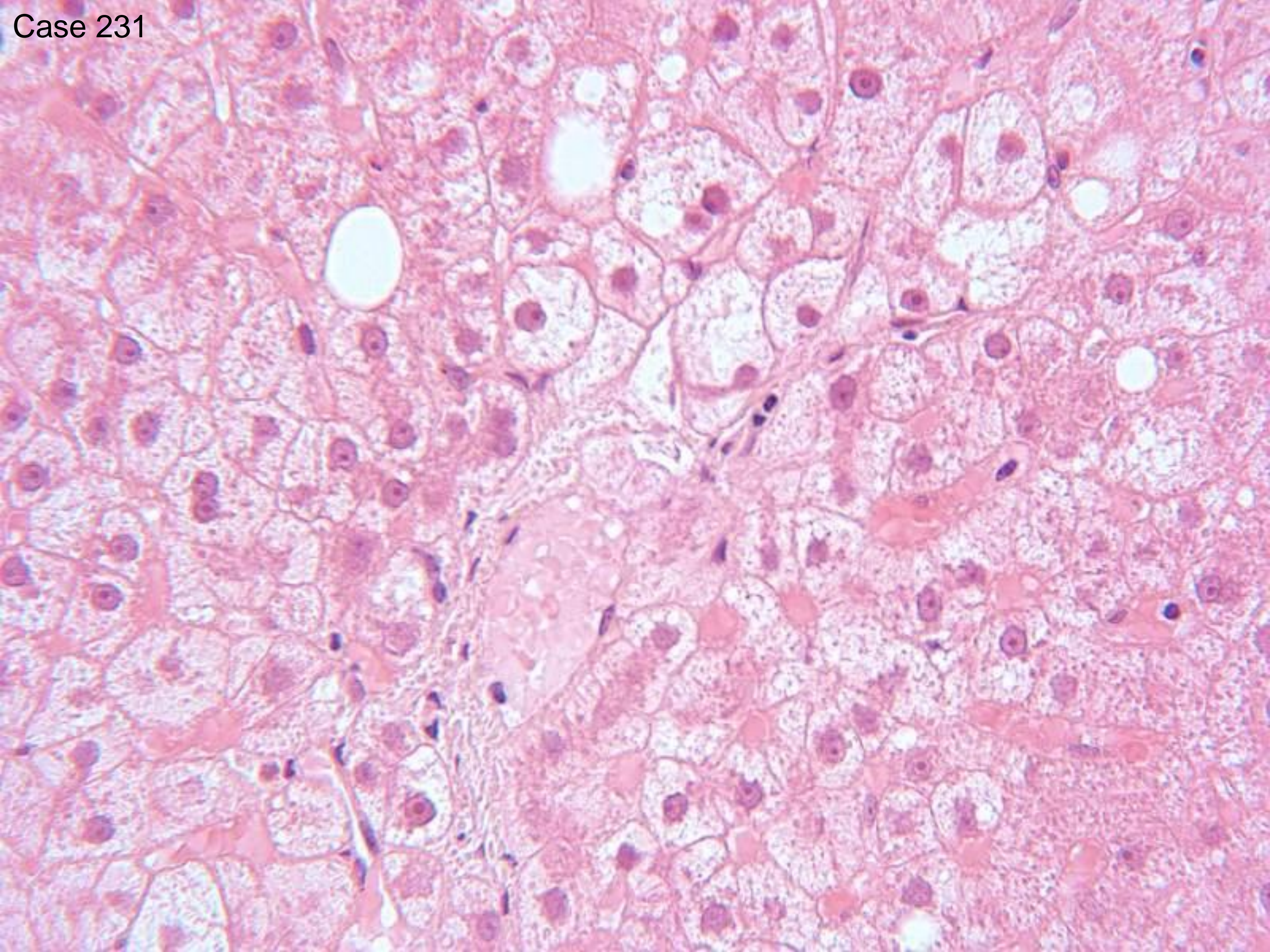
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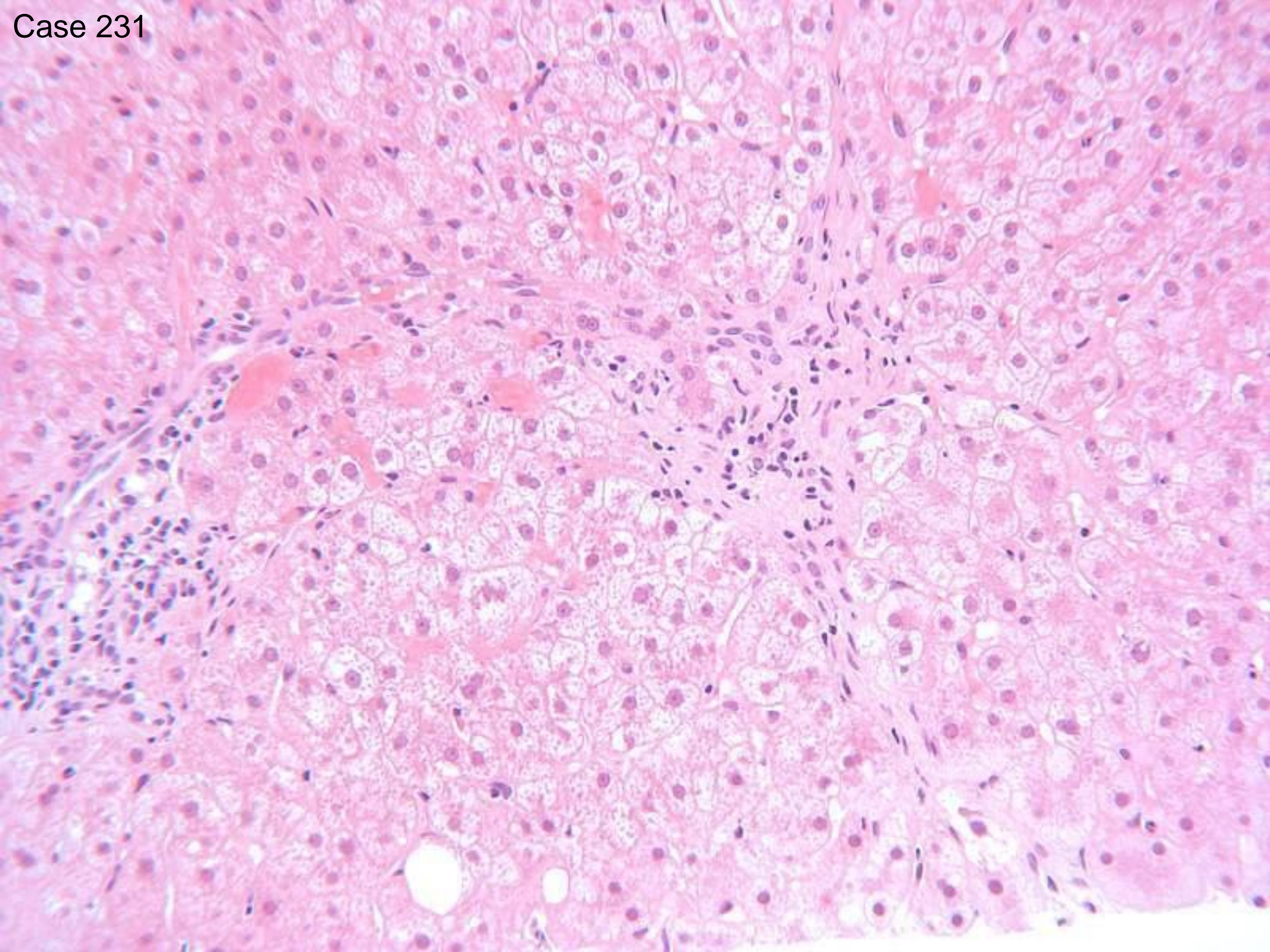
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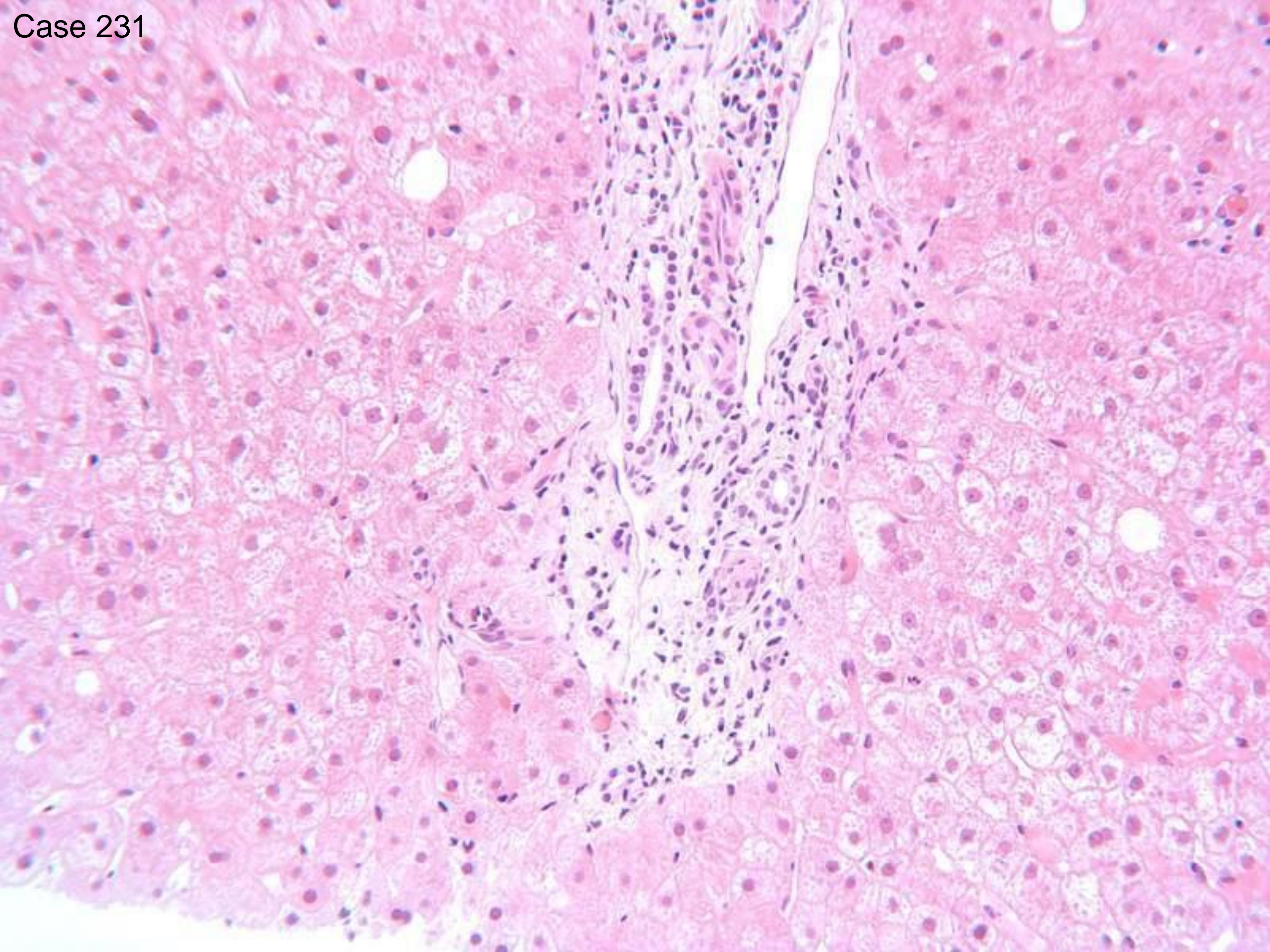
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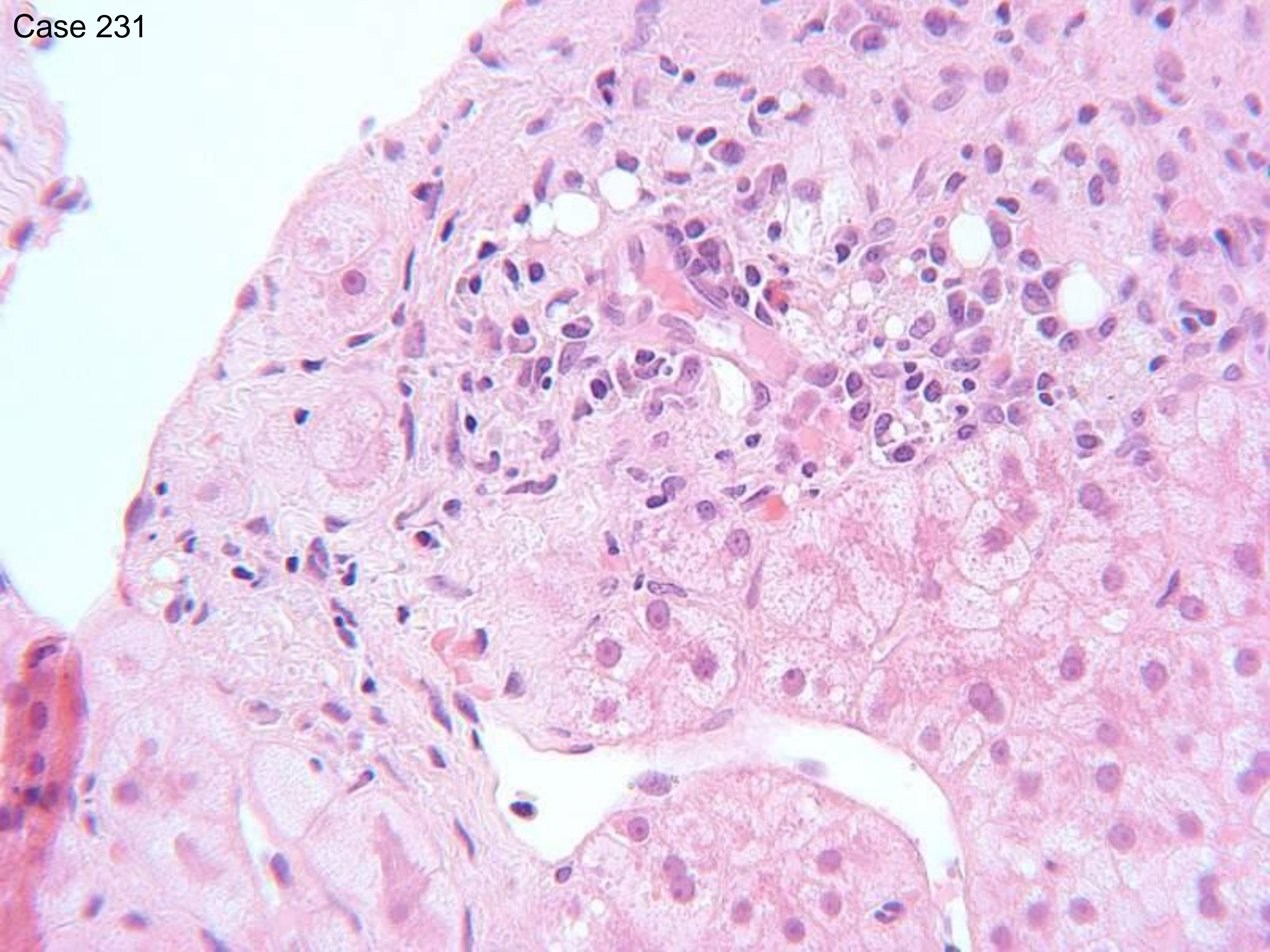

Case 231

Case 231

Results:

18 Mild steatohepatitis (need alcohol history)

1 mild steatosis (need alcohol history)

7 c/w alcohol (e.g. central hyaline necrosis, fibrosis+fatty change etc.)

5 drug reaction/alcoholic steatohepatitis

11 chronic portal hepatitis

1 chronic hepatitis, PCs++, no fatty change - ? autoimmune hepatitis

2 ?A1ATD

5 suggestive of biliary disease (2 with ductopaenia, ?PSC)

1 ? porphyria

1 non-specific inflammation

1 fatty change and ?abnormal vascular supply

Not suitable for scoring.

comments:11 not diagnostic; 2 not suitable for EQA

3 Granuloma; several – plasma cells

several ? what A1ATD comment means

18 alcohol history; 2 haemochromatosis features

Case 231

Comment: Biopsies like this are often encountered in routine practice, the pathologists cannot interpret the changes without additional clinical information.

It is quite common to see some portal inflammation in biopsies with steatohepatitis – in practice enquire whether there are alternative causes of portal inflammation (viral infection, drugs, autoantibodies) and in the absence of these assume that the portal inflammation is attributable to the fatty liver disease. Autoantibodies at low titre are relatively frequent in fatty liver disease, and as yet of no proven clinical significance.

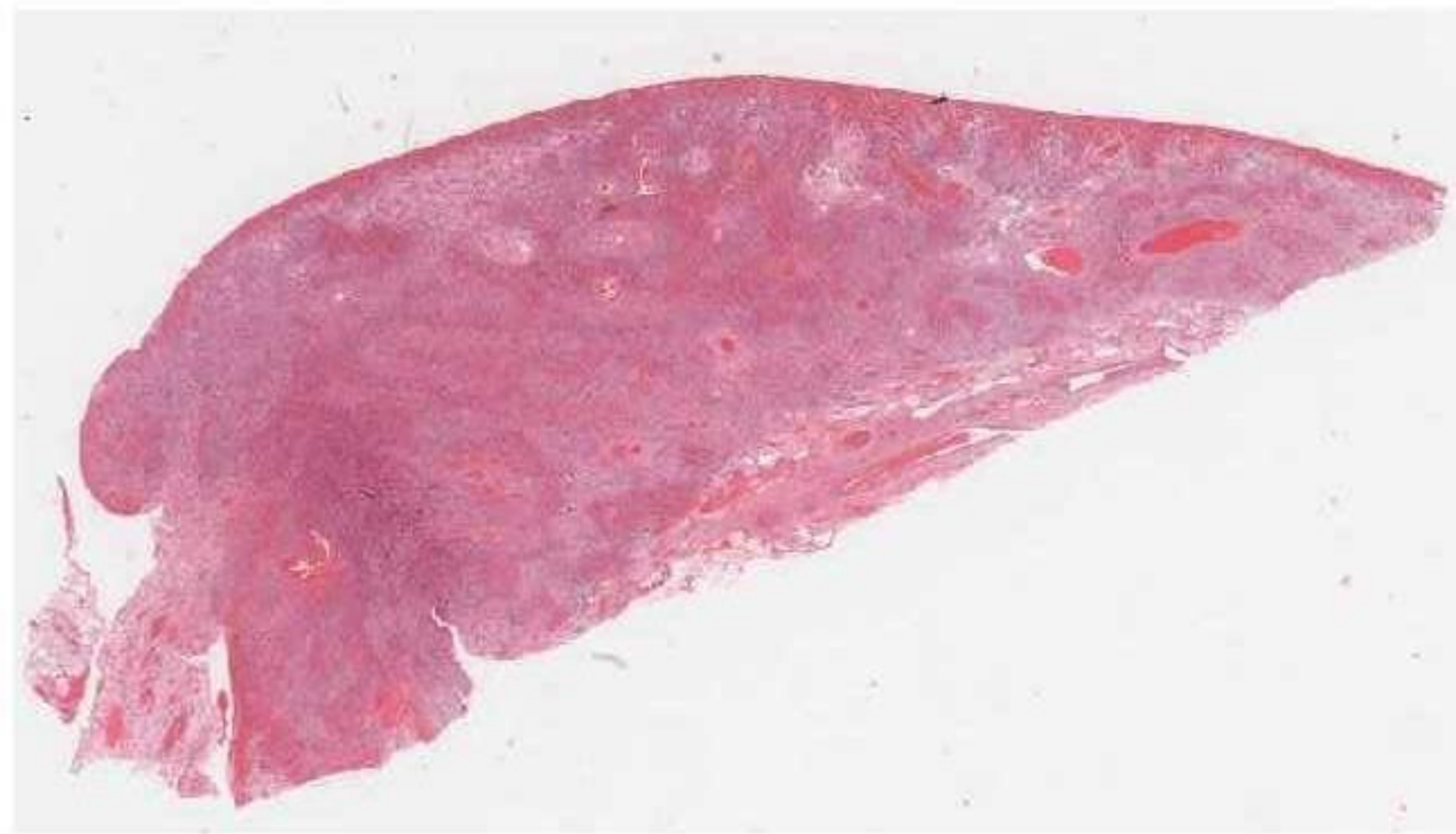
It is also quite common to see biliary features in biopsies of alcoholic steatohepatitis; this does not necessarily imply second diagnosis.

Case 232

4 day old female. Nodule stuck to side of diaphragm.

Crescent shaped piece of tan tissue, 23x8x8mm.

Case 232



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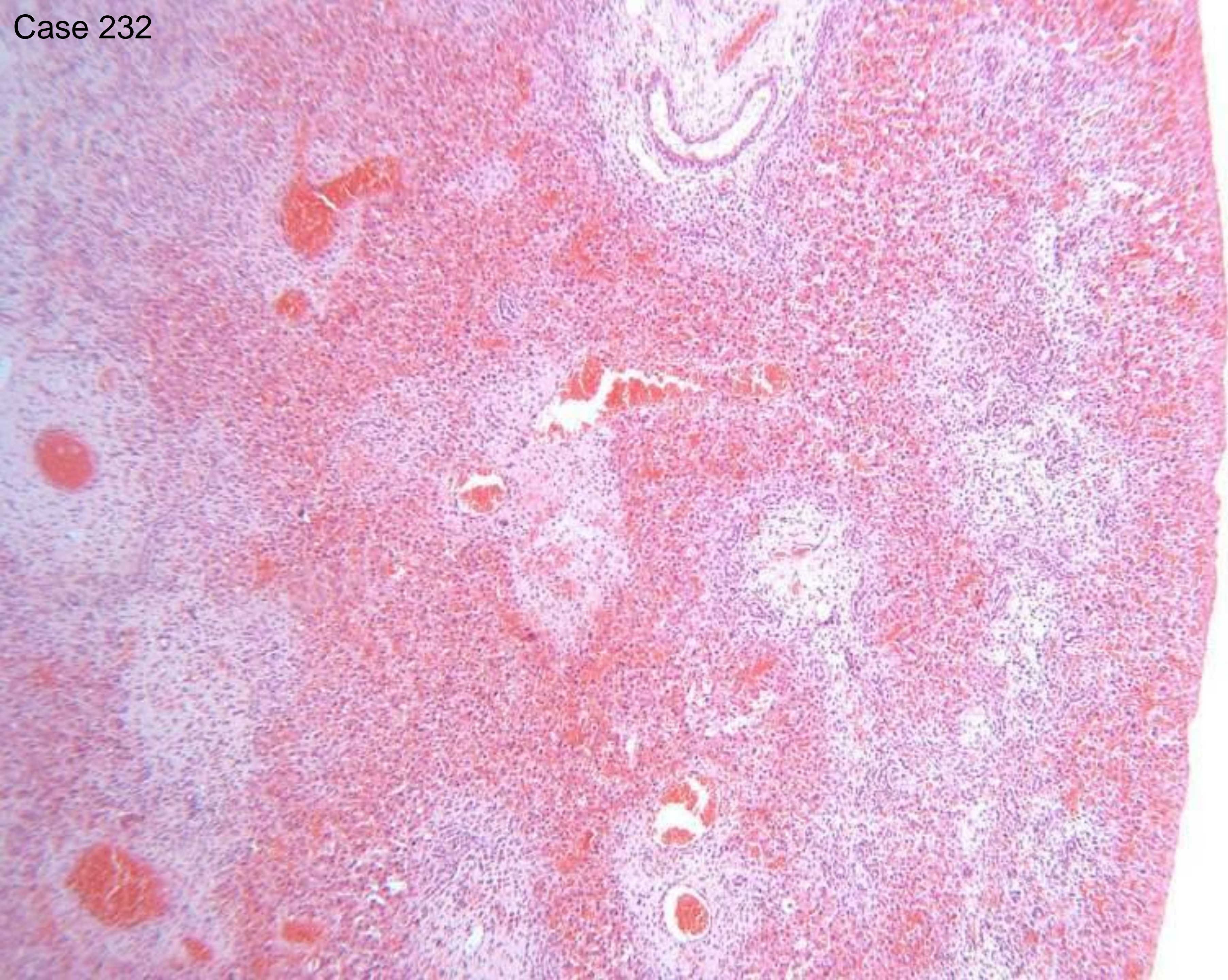

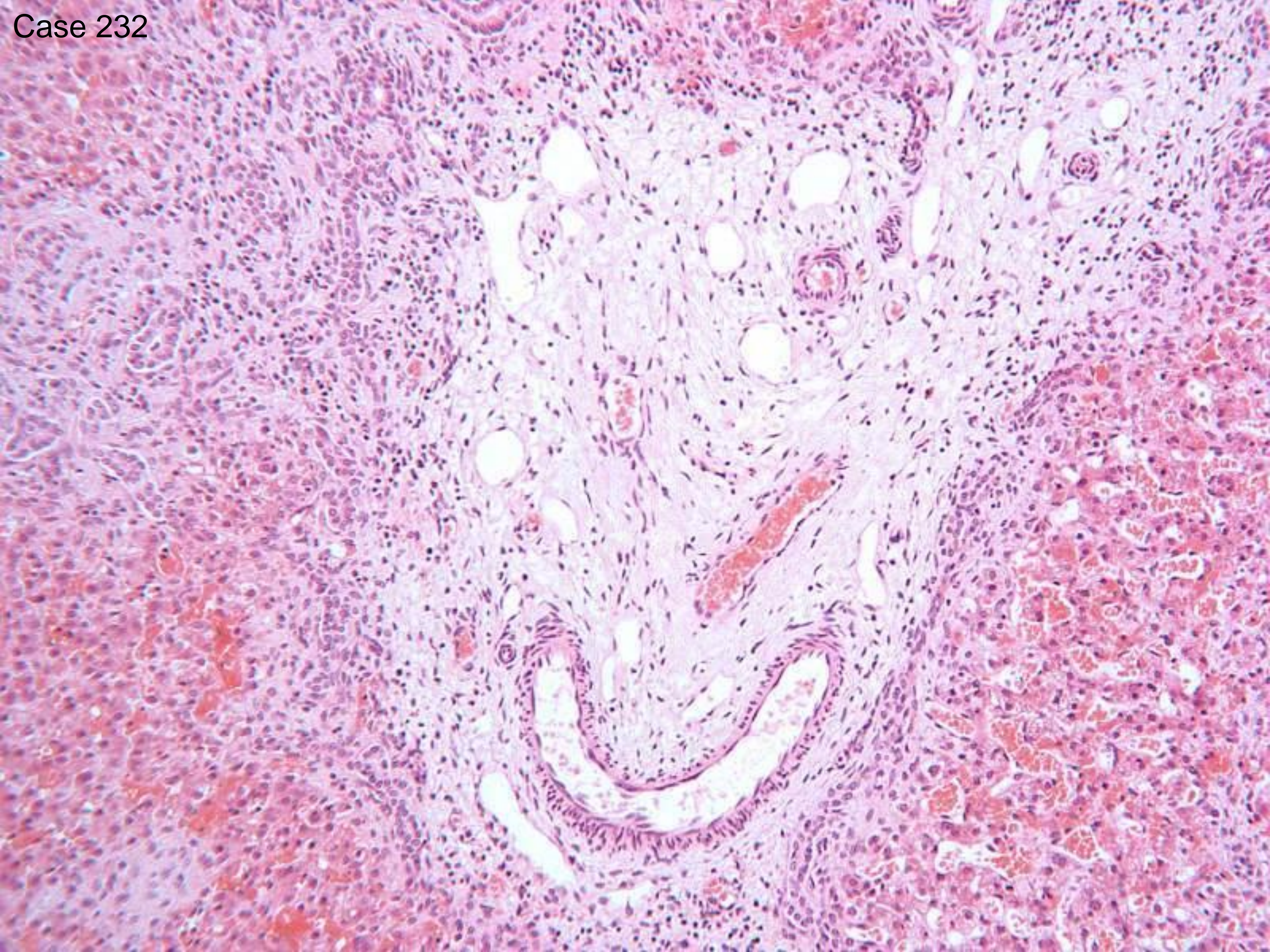
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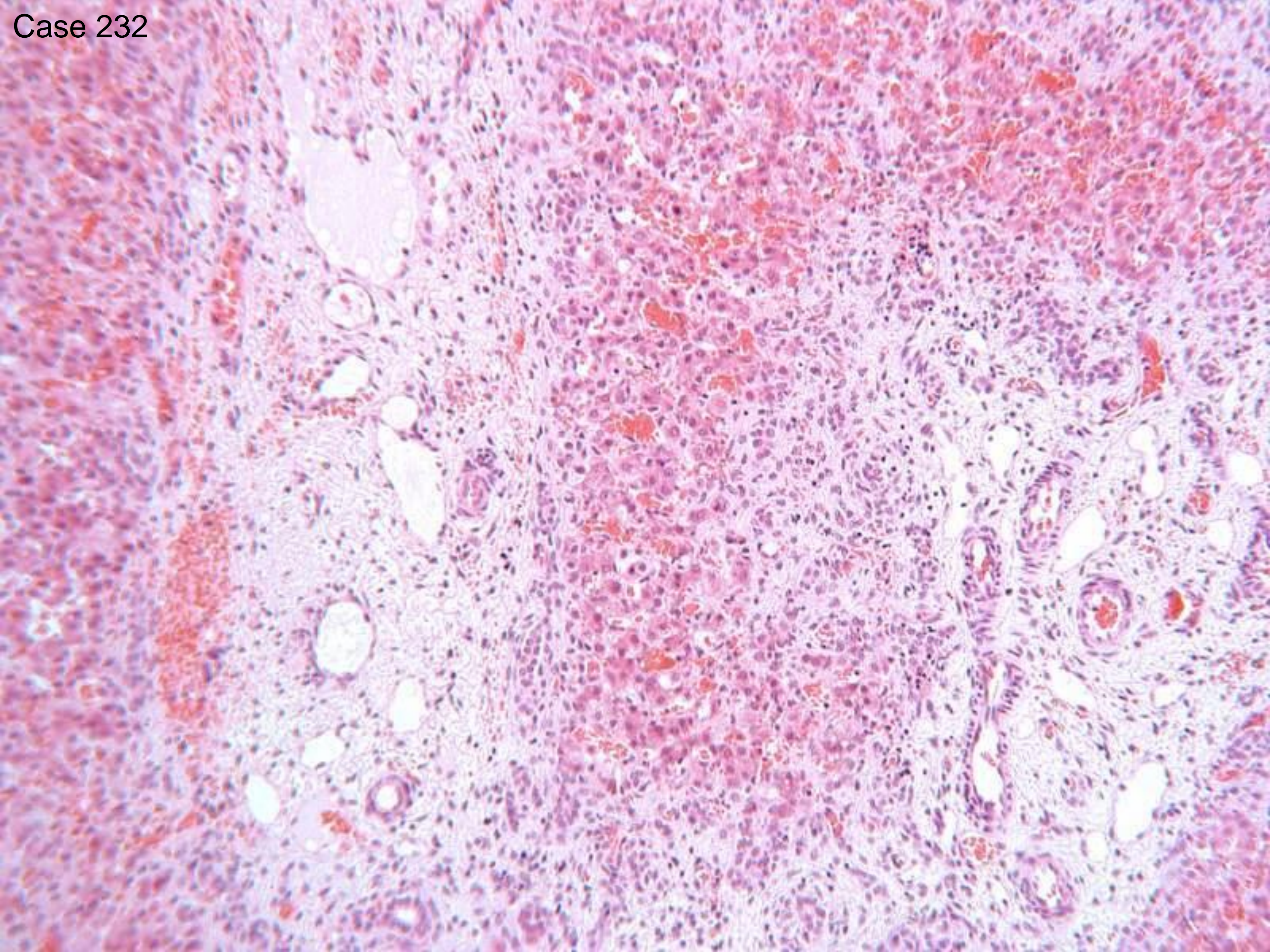
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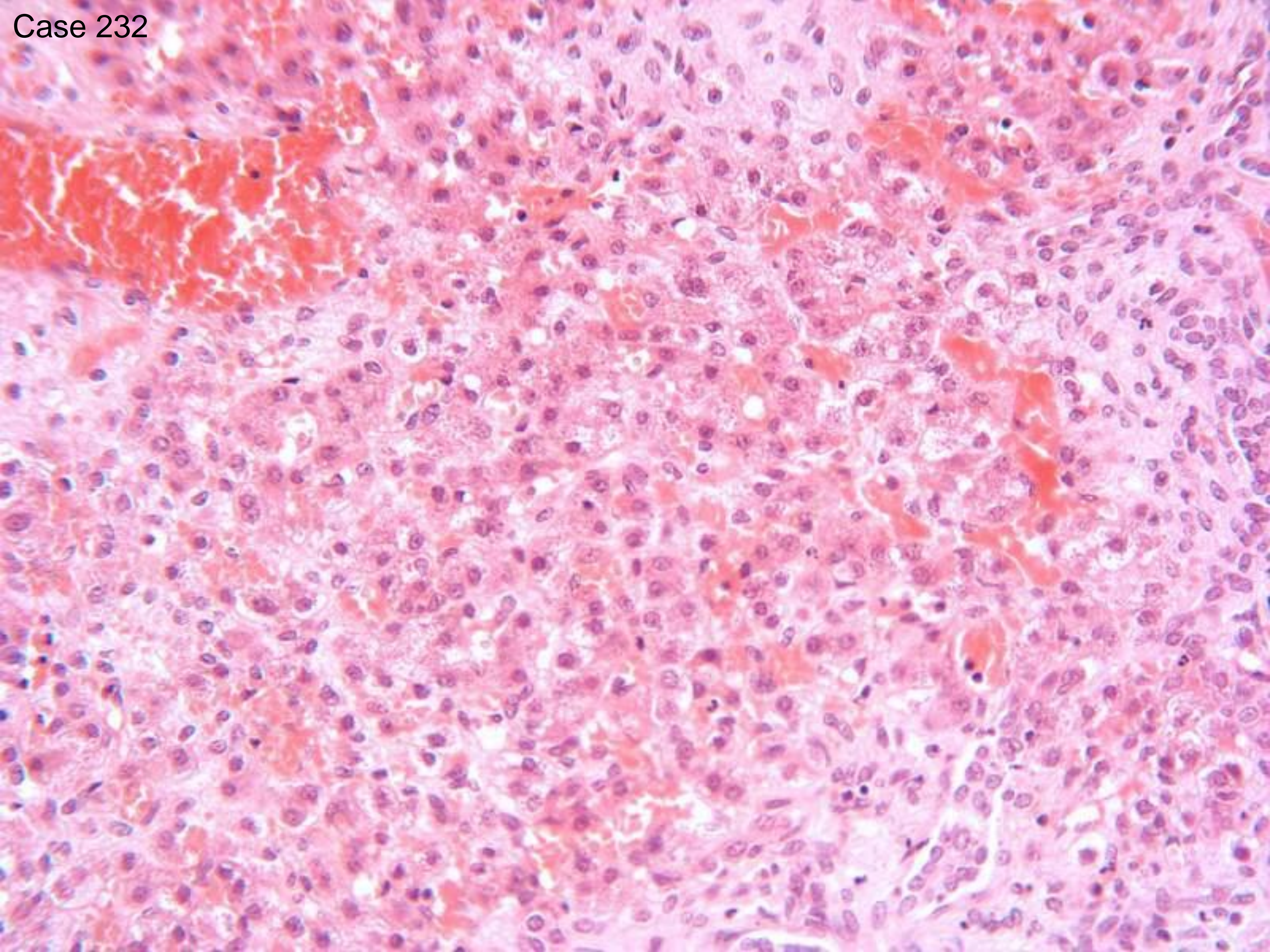

Case 232

Case 232

Results

36.5 Ectopic/heterotopic liver tissue/accessory lobe
+/- comment on biliary obstruction features

6.5 mesenchymal hamartoma
5 multiple VMCs/hamartomas

1 bile duct adenoma
1 congested liver with bile duct proliferation
1 angiomatous proliferation
1 haemangioma
1 pedunculated FNH
1 ductal plate malformation, CHF

Scoring:
Not suitable for scoring.

comments:
lots – inadequate details, where is this nodule/which side of diaphragm?
10 what is the rest of the liver like?
2 reason for surgery
1 illegible
4 don’t see paediatric cases

Case 232

Comment: It was not clear whether this tissue was above or below the diaphragm. We presume that the portal changes of ductopenia, oedema, and ductular proliferation are a reflection of the absence of biliary drainage in this heterotopic portion of liver.

There is not an 80% consensus on the result. Many participants do not see paediatric cases therefore excluded from scoring.

Case 232

Follow up: Dr Davies

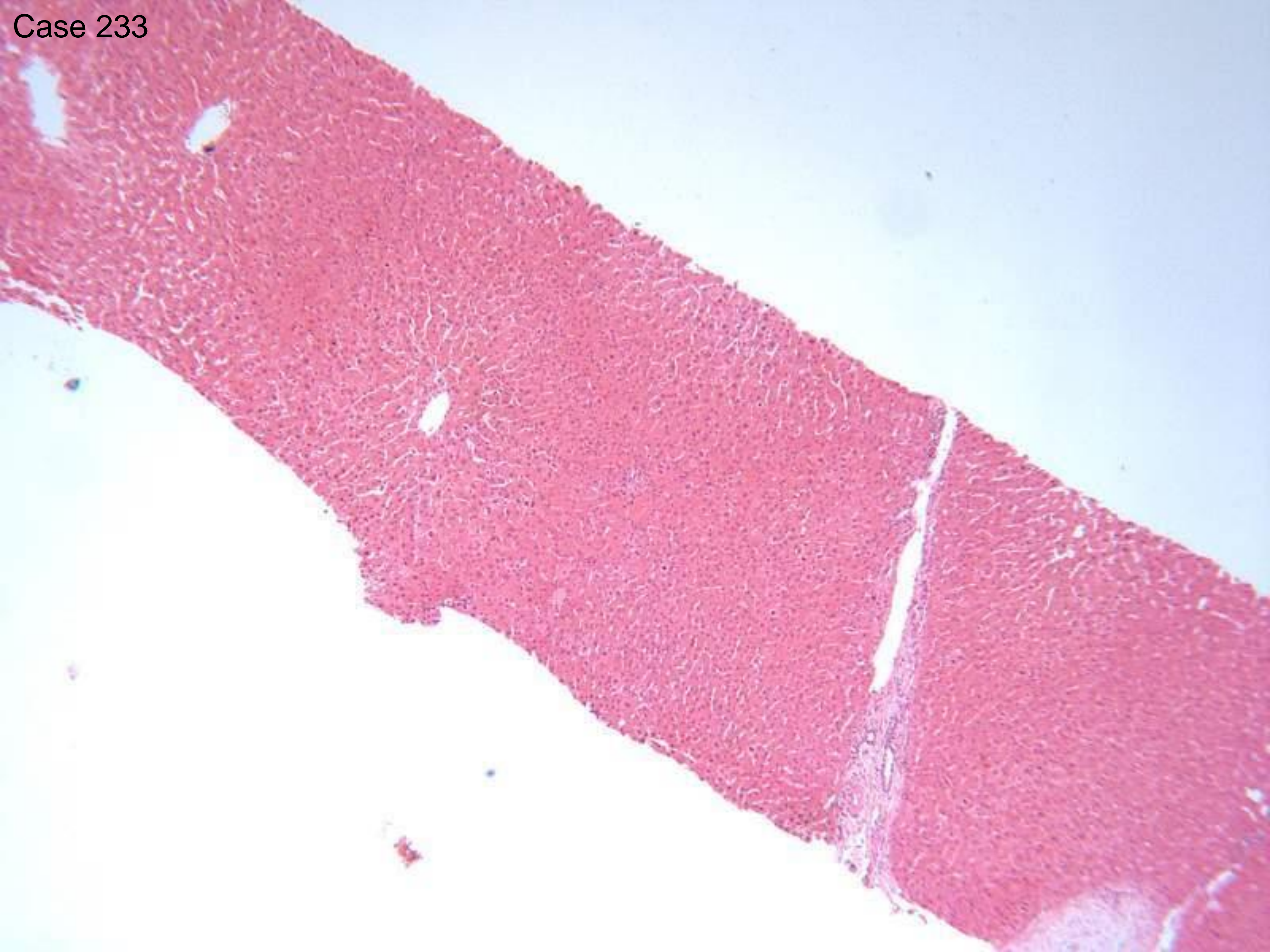
This tissue was discovered attached to the liver by a narrow pedicle during surgical repair of a diaphragmatic hernia. It was initially thought to be sequestration ? of lung but found to be attached to liver at surgery. As far as is known, there was no problem with the rest of the liver.

Case 233

53M. Liver mets and lung lesion.

Liver biopsy 20mm.

Case 233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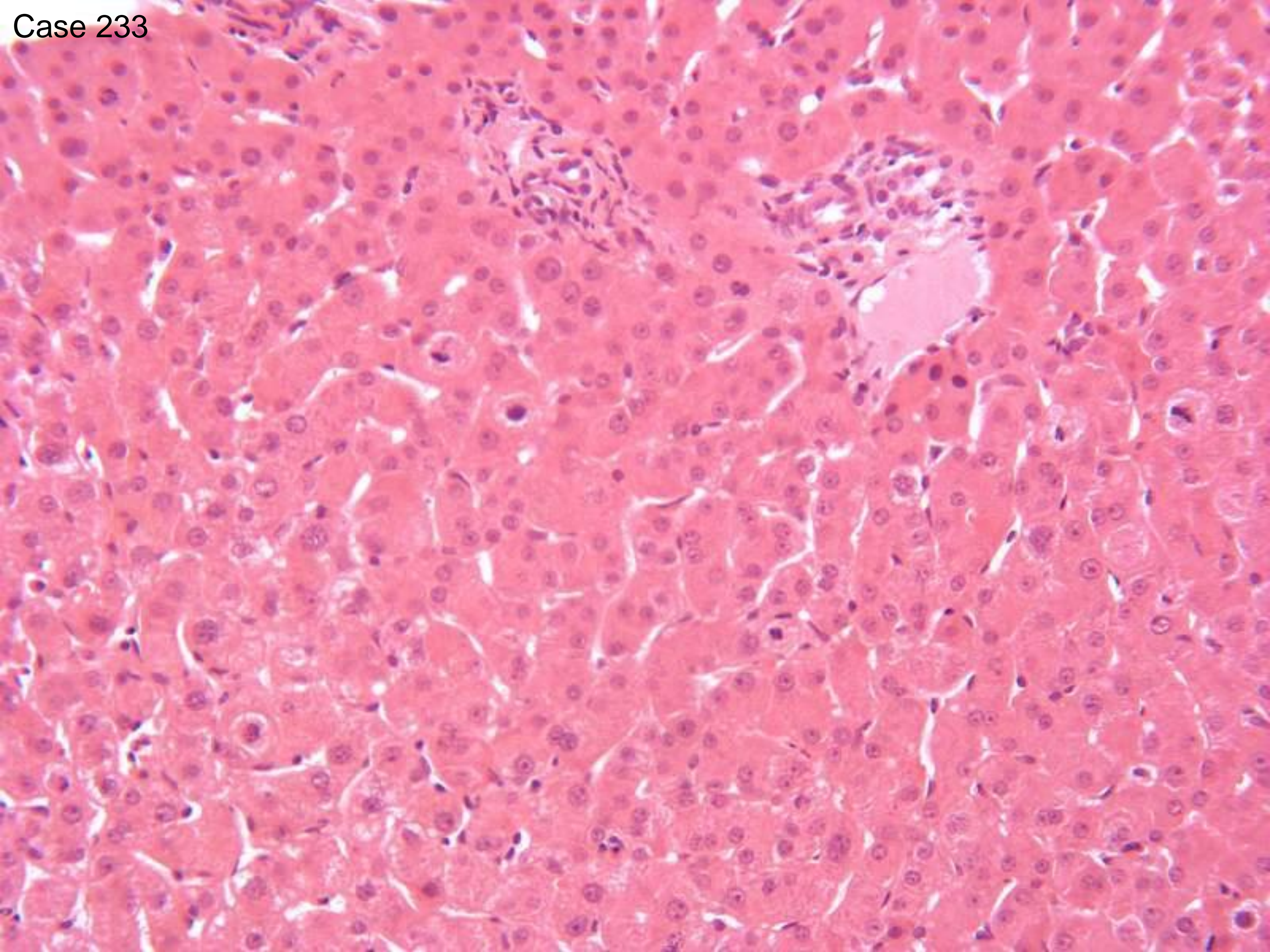
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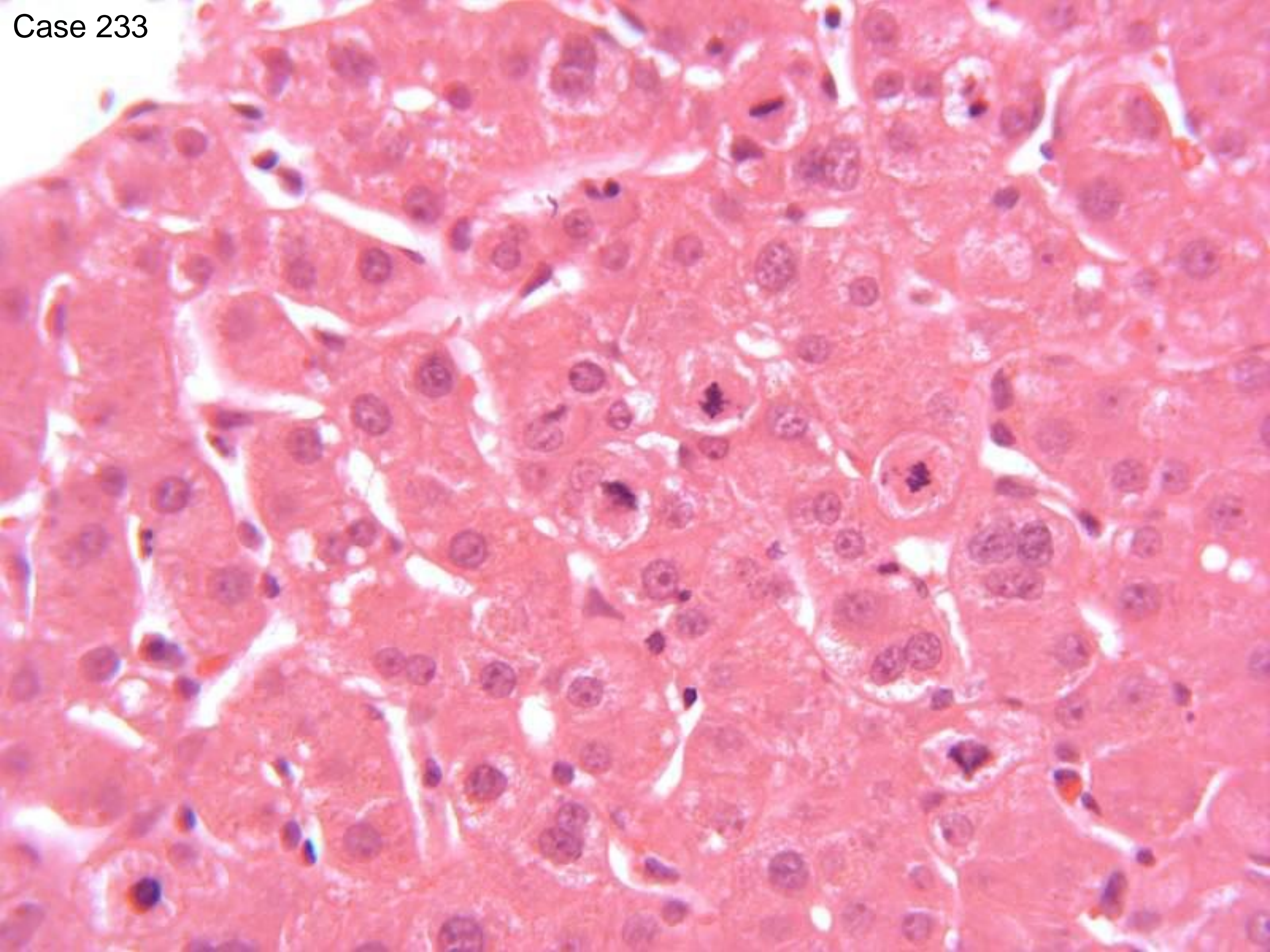
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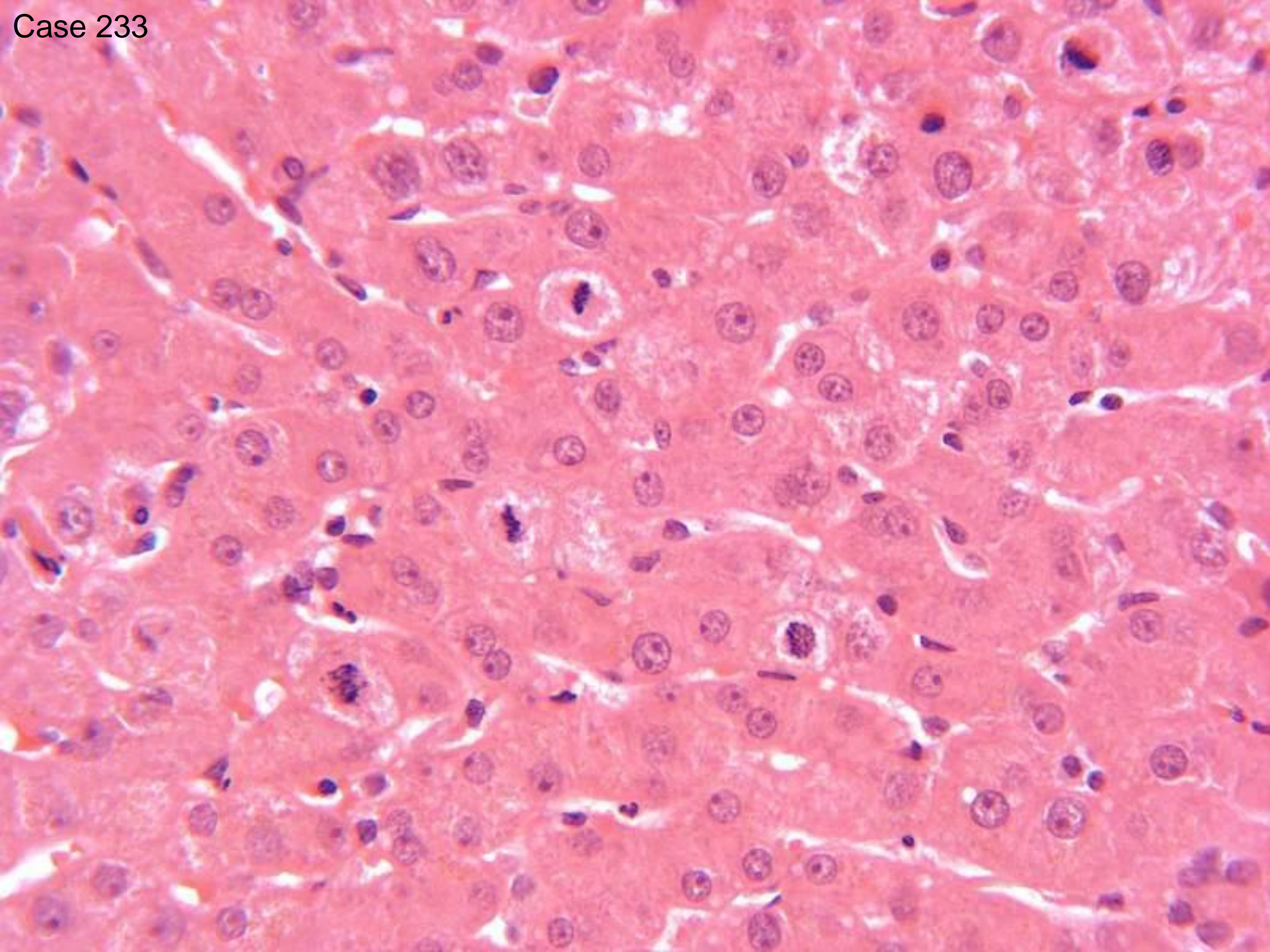
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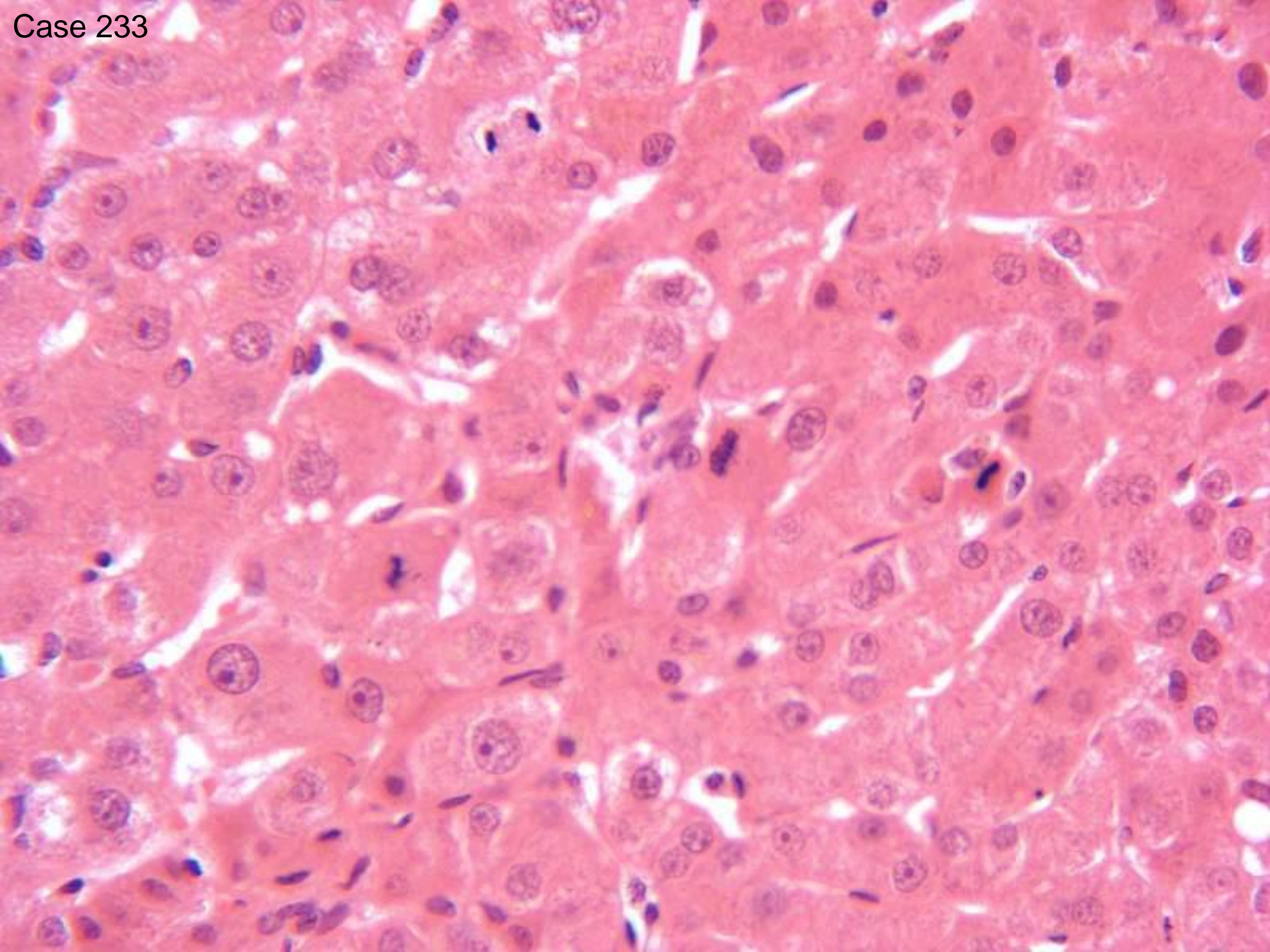

Case 233

Case 233: Results

28.5 reaction to chemotherapeutic drugs
3 chemotherapy induced metaphase arrest

5.5 regeneration/regenerative hyperplasia/macroregenerative nodule
5 non-specific ? adjacent to SOL
2 mild hepatitis
1 no firm diagnosis

1 malignant NOS
3 metastatic tumour growing in sinusoids
1 metastatic carcinoma (immunos for breast/gastric/melanoma)
3 probable well differentiated HCC
1 differential: HCC, dysplastic, drug reaction
2 dysplastic liver

Scoring: Excluded from scoring.

Comments:
Almost all - Numerous mitoses 3 mild cholestasis
2 not characteristic of changes adjacent to SOL
several? targeted biopsy 1 not suitable for EQA

Case 233

Comment; No one else had seen a reaction like this before.

This was excluded because the consensus diagnosis (reaction to chemotherapy) turned out to be incorrect!

Case 233

Follow-up: Dr Davies

This was more for interest – had other people seen this?

Possibly an unusual form of SOL effect or paraneopastic change – not on any chemotherapy.

The subsequent biopsy was of a typical metastatic adenocarcinoma, without a diffusely infiltrative pattern, and so the ? atypical sinusoidal cells are not believed to represent the tumour. The patient has since died, and no further clinical information is available.

Case 234

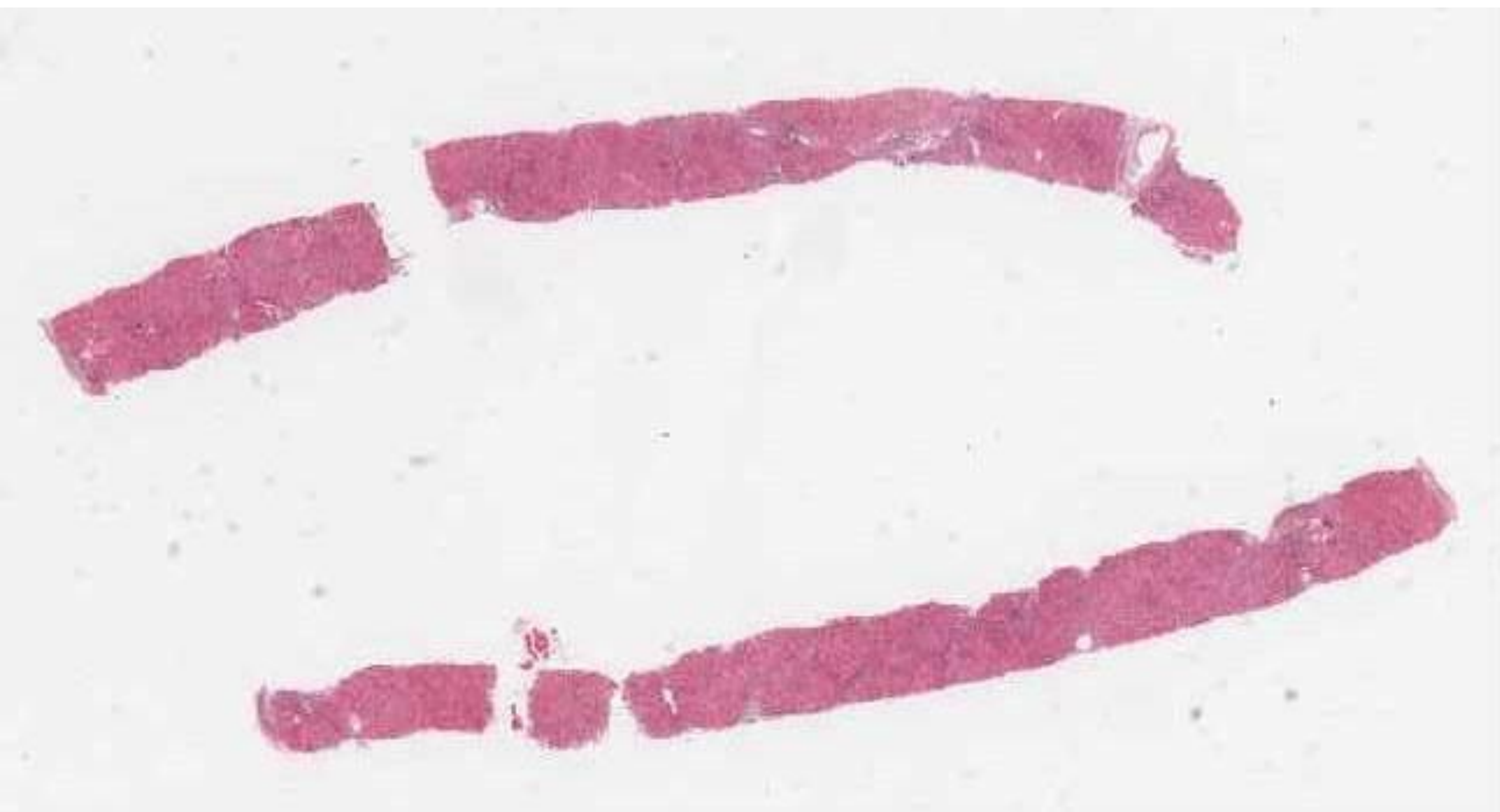
43F. ? PBC Investigations: Bili 54, ALP 344, ALT 183, Globs 36(+), Antimitochondrial Ab +ve 1/100.

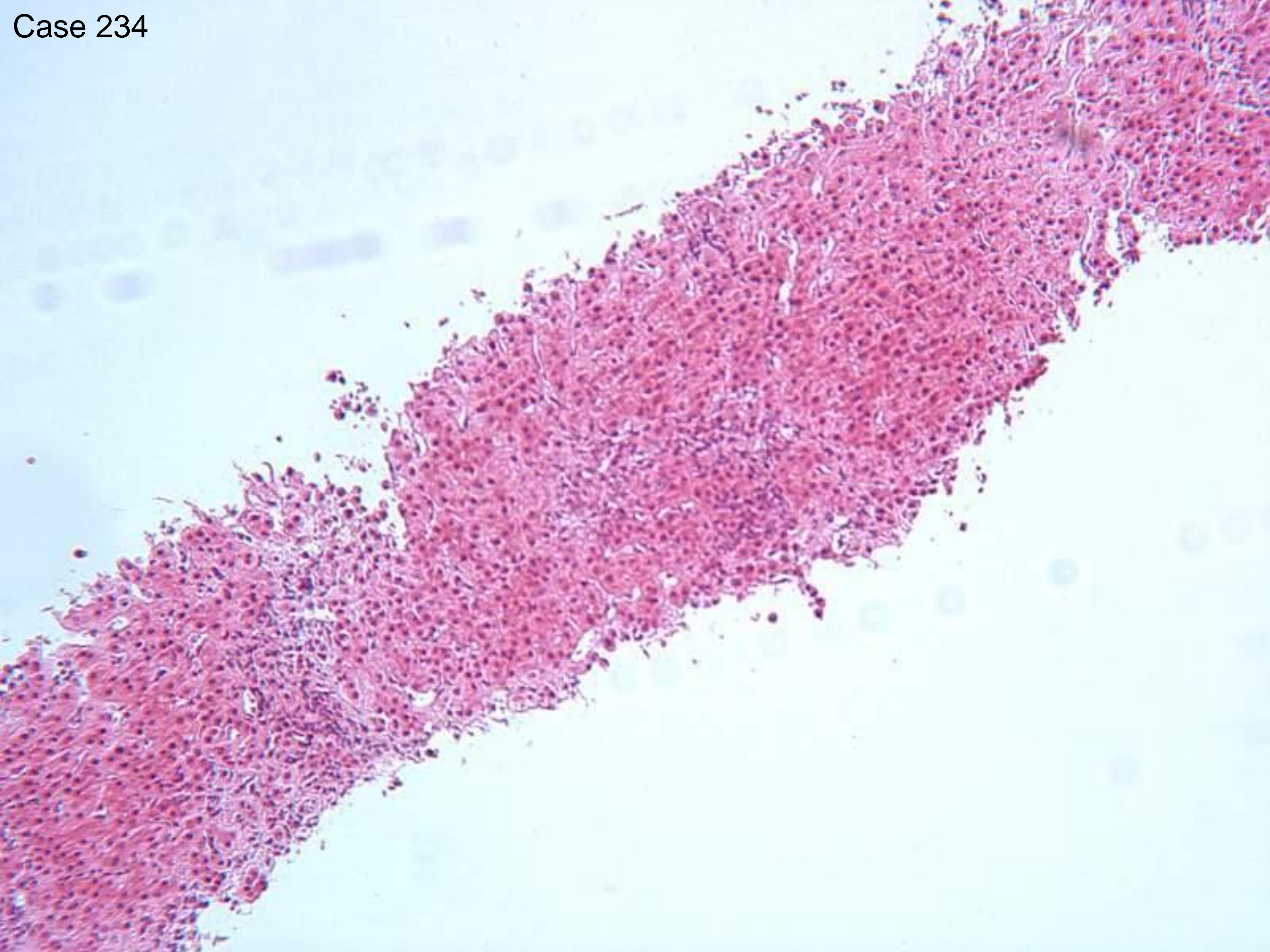
Orcein stain – abundant periportal copper associated protein.

EVG linking and bridging fibrosis.

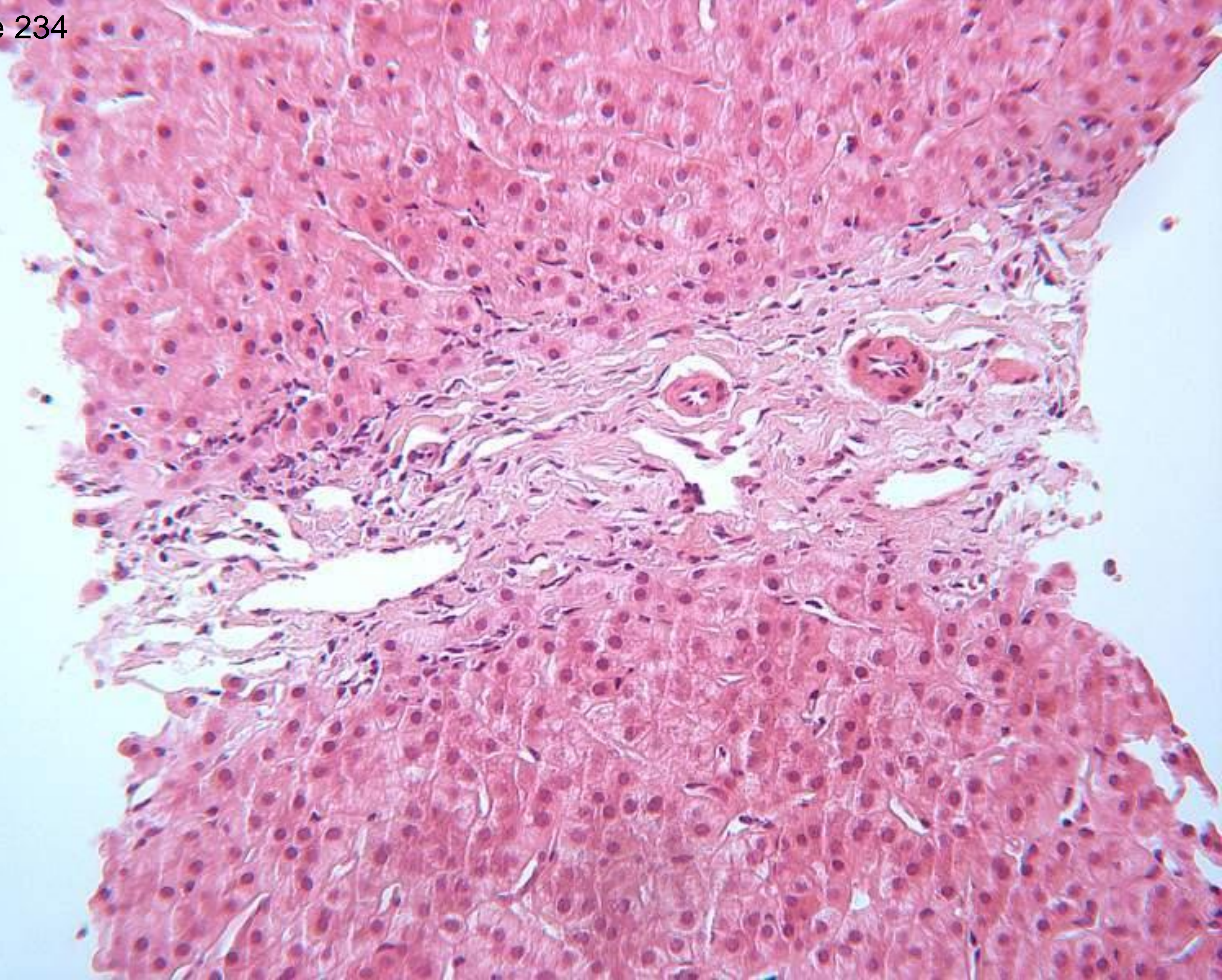
Liver biopsy – cores 12 &13mm.

Case 234




Case 234

Case 234



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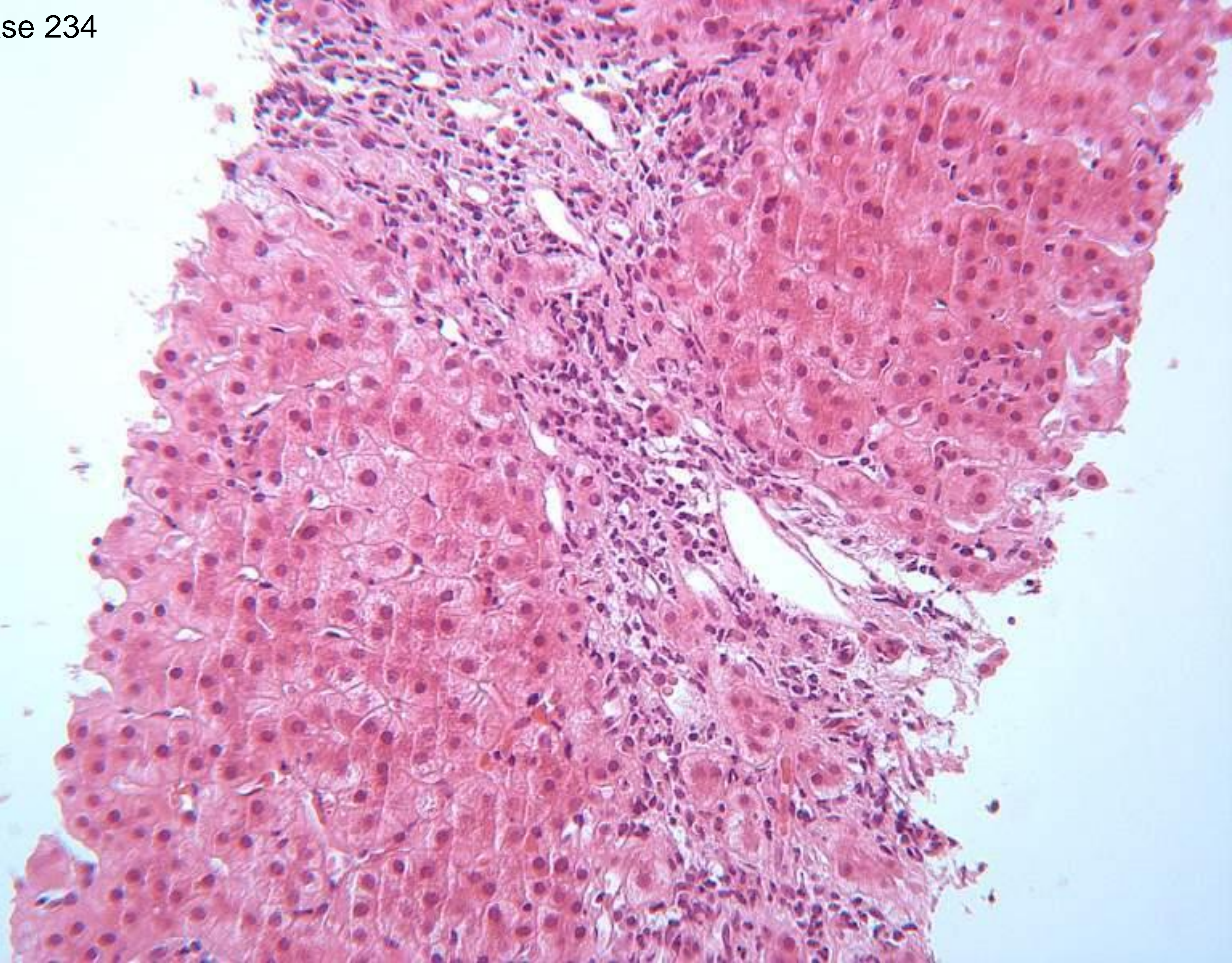
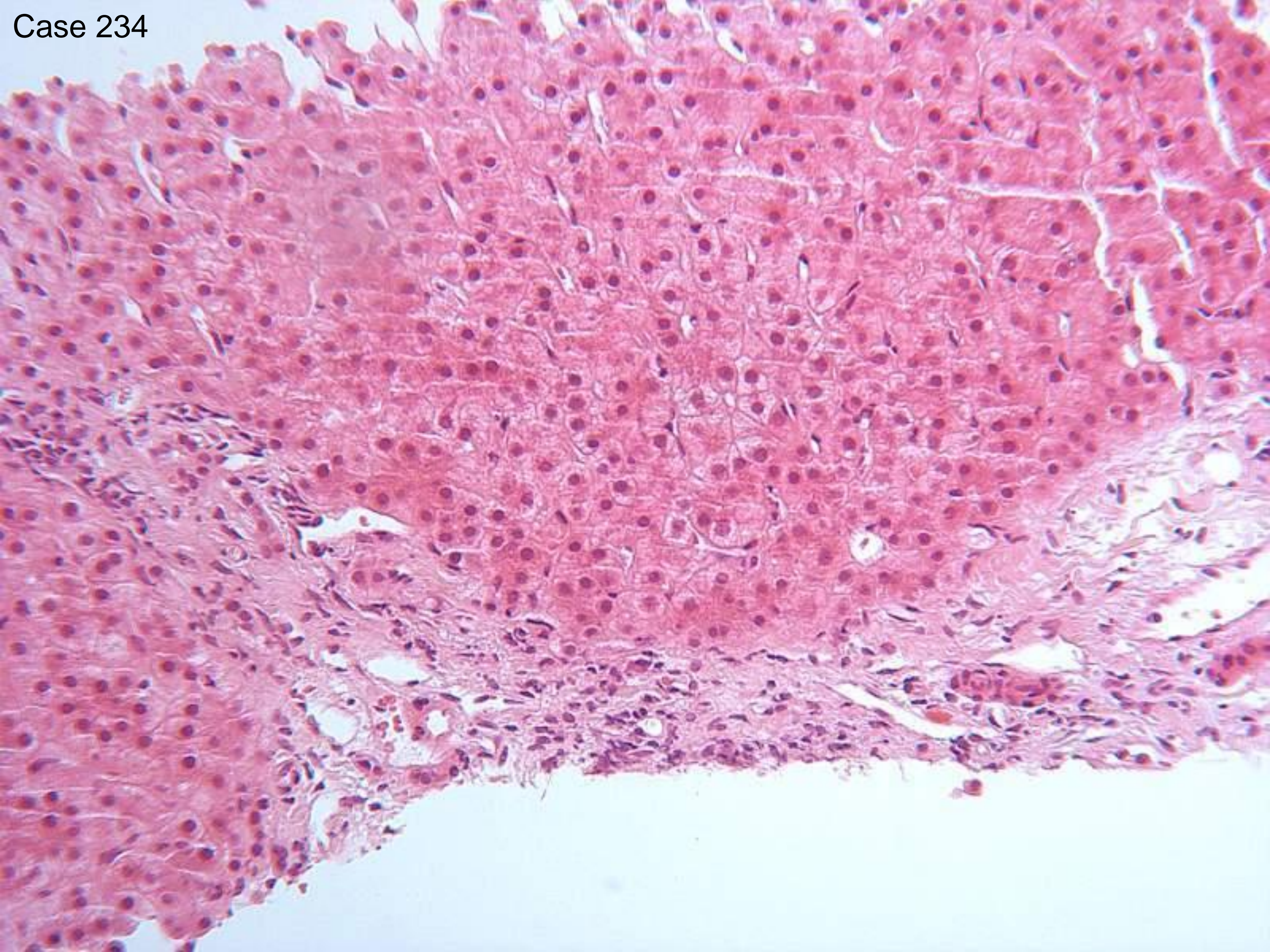



Case 234

Case 234: Results

33 PBC/consistent with PBC

15 stage 3 PBC/consistent with stage 3 PBC

1 PBC, cirrhosis

1 PBC, grade 3-4, stage 5

3 PBC/overlap syndrome

2 PBC, ? overlap syndrome

1 PBC and probable HBV, further investigations

comments:

2 overlap – Raised Ig, ALT

1 biopsy not suggestive of overlap

1 overlap not excluded

several – ? other autoantibodies

Scoring: Include all as correct.

Case 234

Comment: The discussion related to criteria for diagnosing overlap syndrome. There are no clearly defined criteria. In this case, the presence of raised immunoglobulins and raised ALT together with some interface hepatitis could be taken as grounds for diagnosing overlap syndrome. The proof will be in response to treatment – patients with possible overlap syndrome are treated initially with ursodeoxycholic acid, if insufficient response steroids are added, and a response to steroids would then support the diagnosis of overlap PBC/AIH.

There is no follow-up clinical information available in this case.

Case 234

Follow up: Dr Meehan

Biopsied because clinically poor control of liver disease, may require transplant. Now symptoms improved and liver function tests stable.

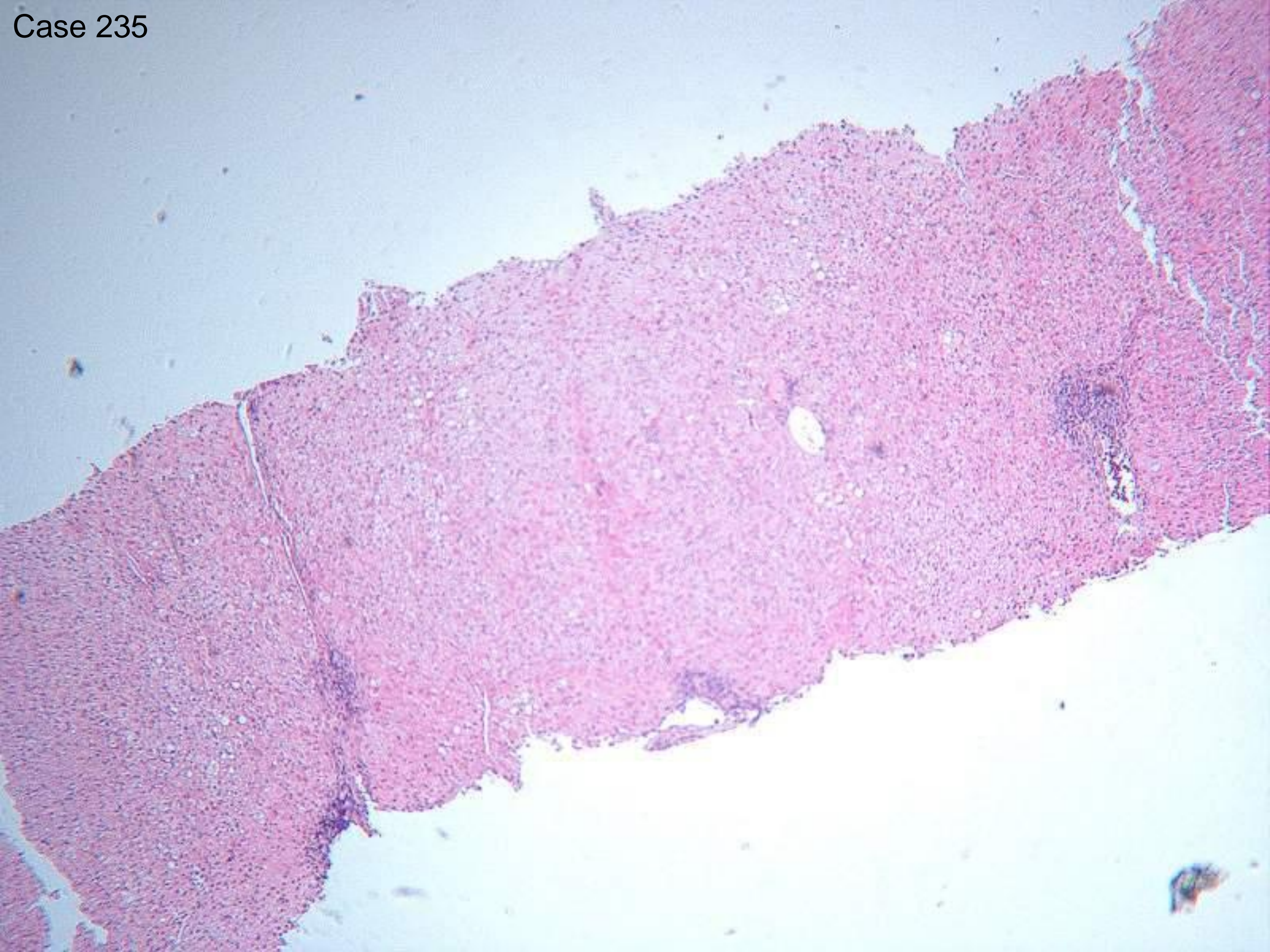
Also has Raynaud’s and hypothyroidism.

Case 235

24F. Liver biopsy – HBV infection to assess degree of liver damage.

19mm core biopsy.

Case 235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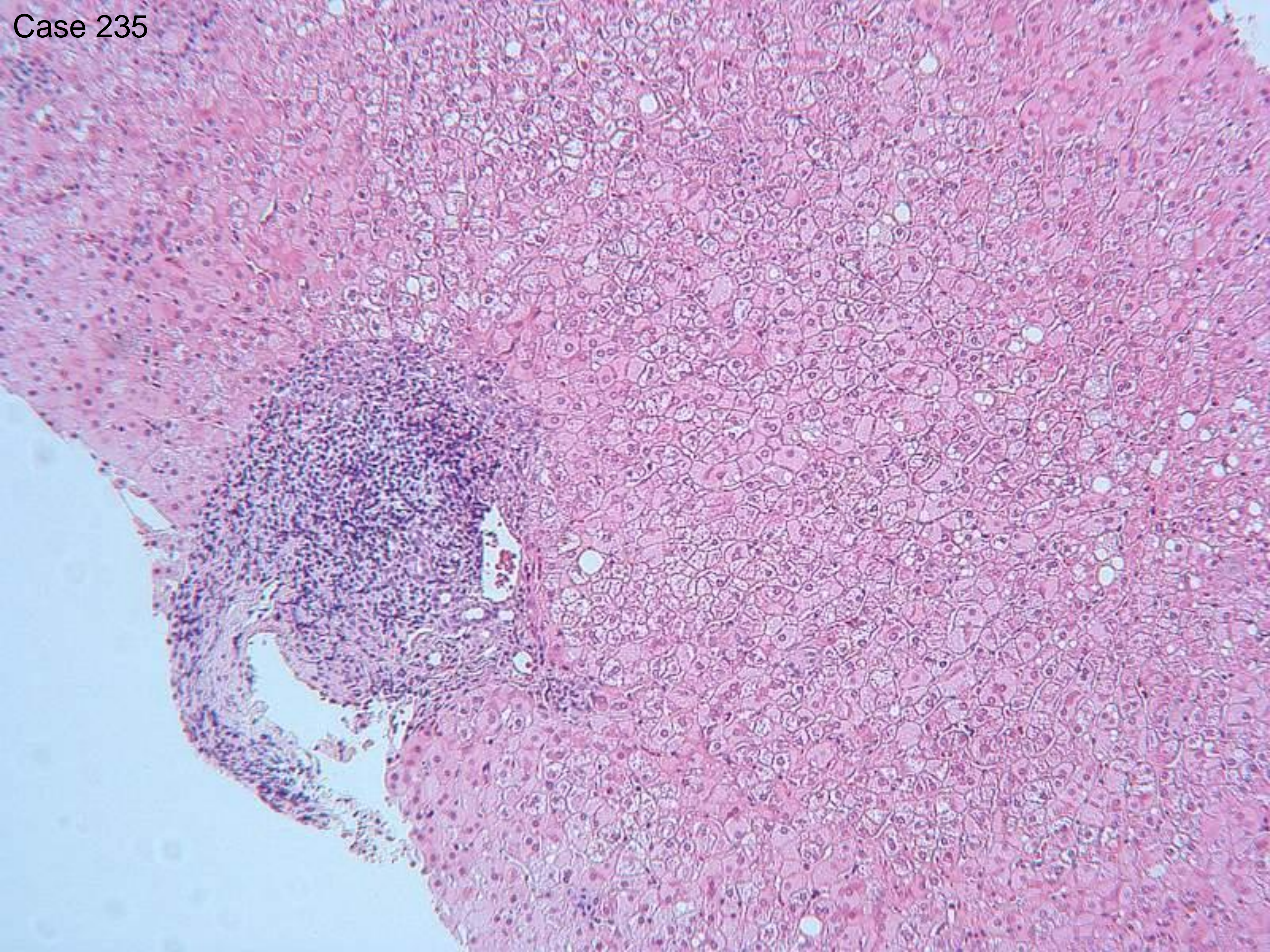
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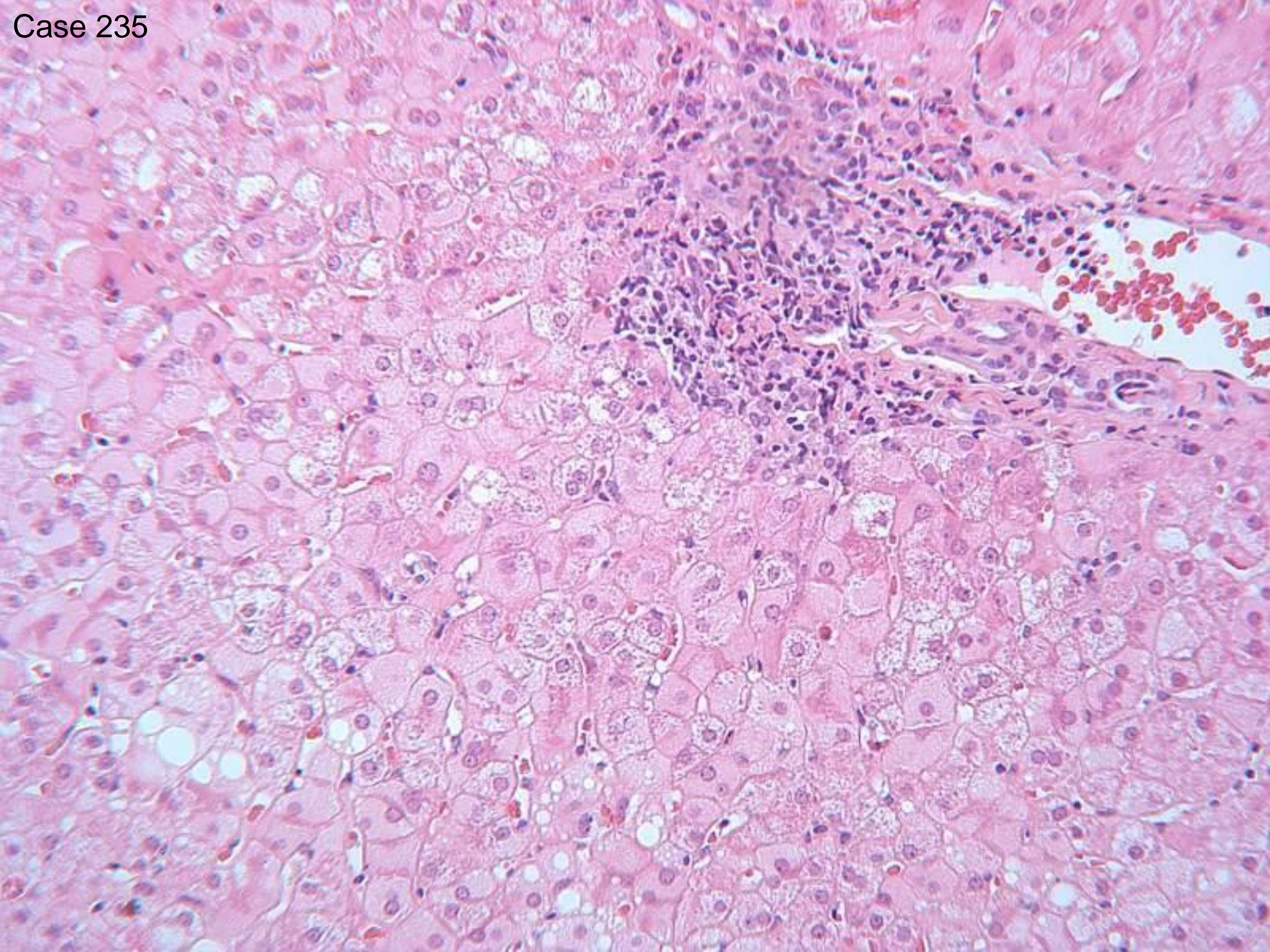
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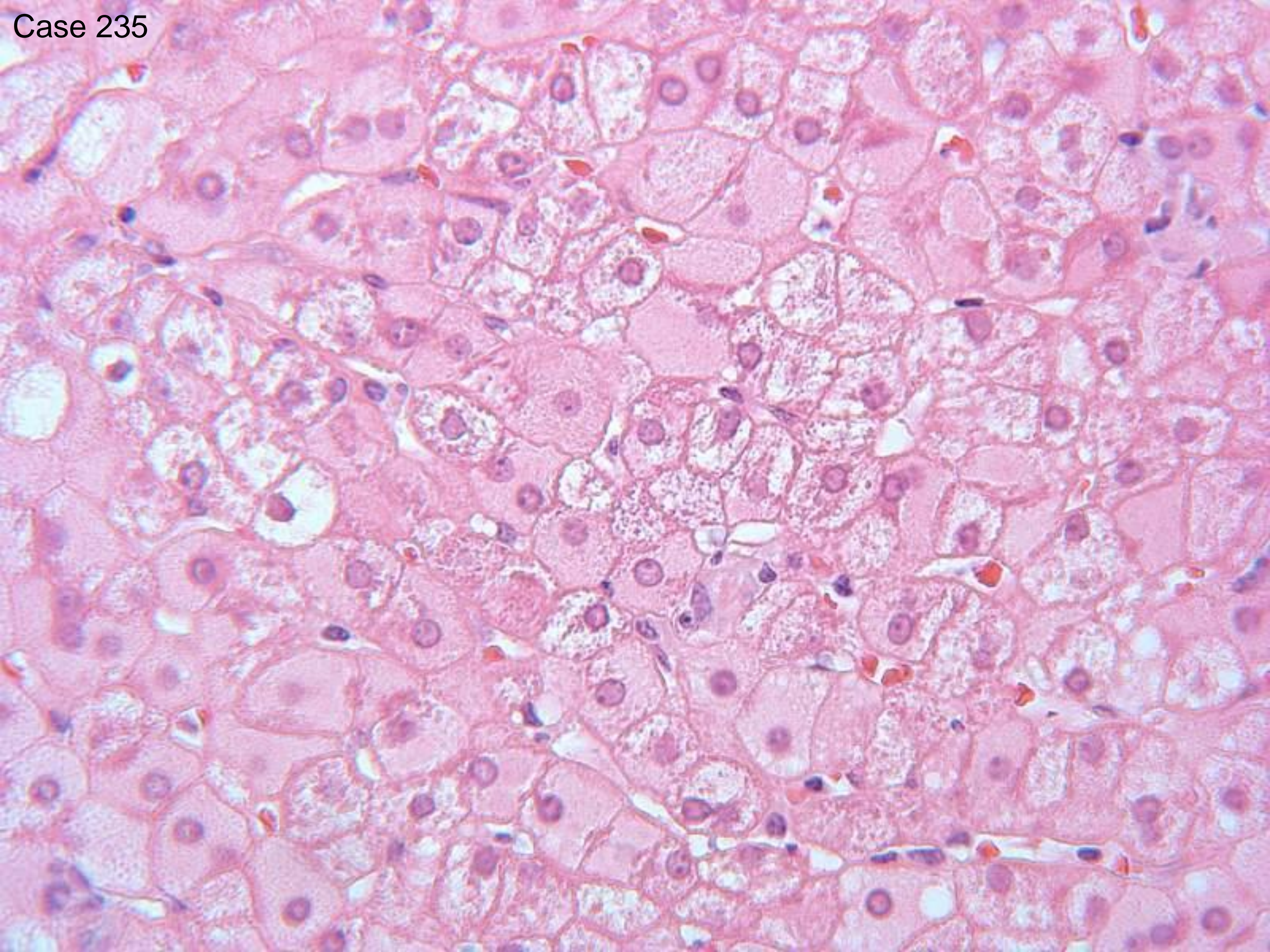
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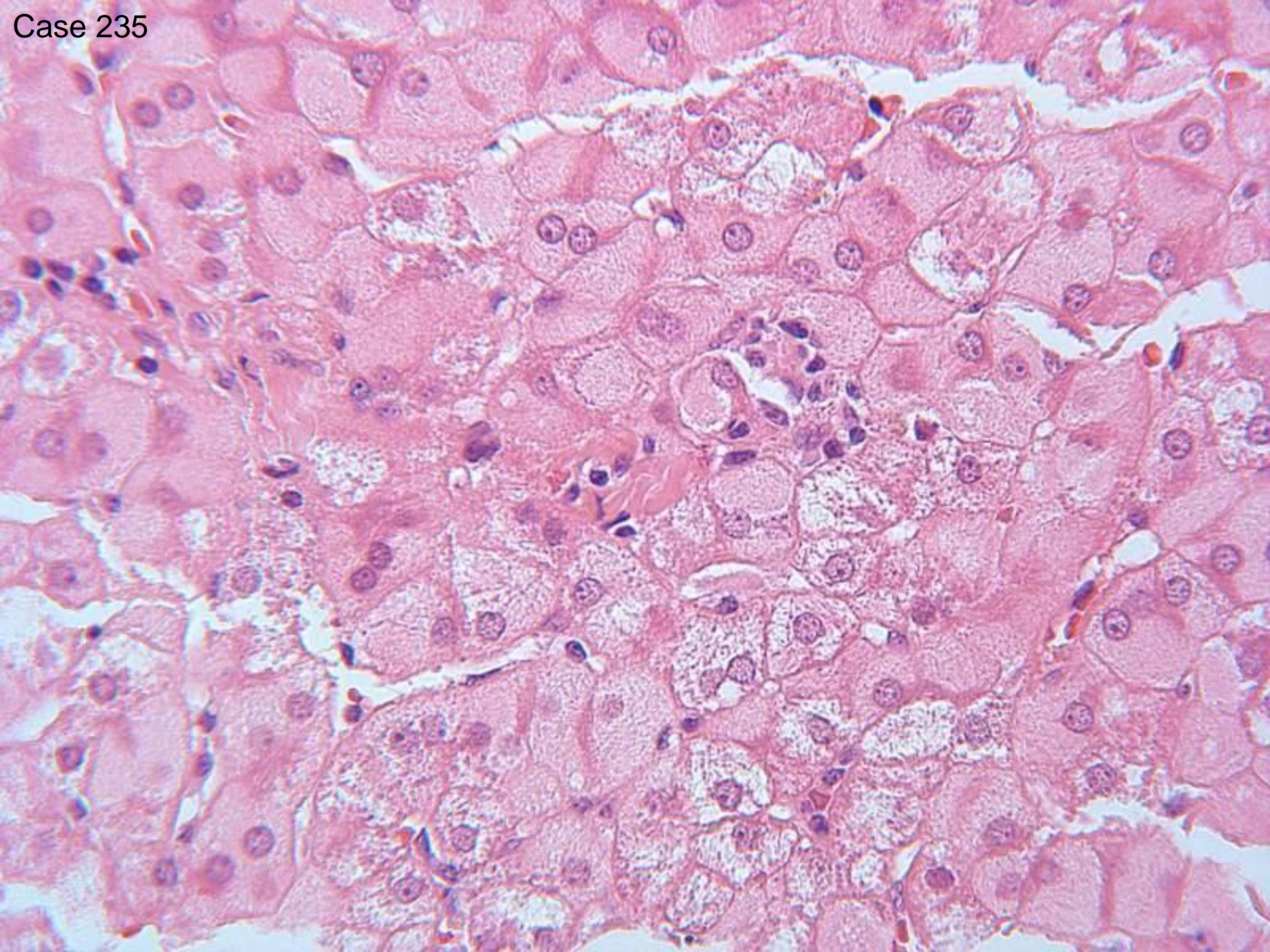
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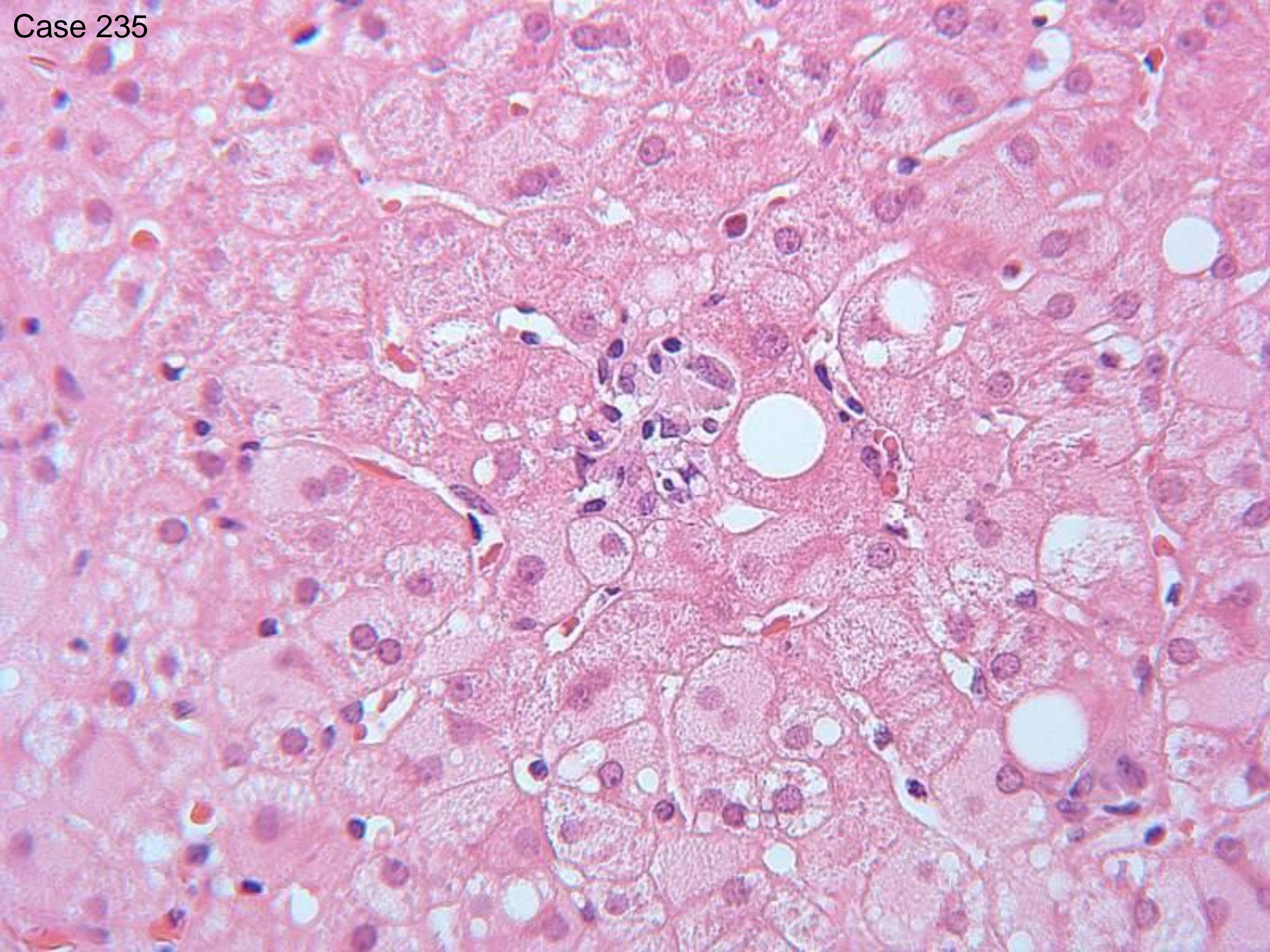

Case 235

Case 235

Results:

52 Hepatitis B

of which: 46 gave an indication of stage/grade (see below)

Half marks
- 4 no further comment on severity
- 1 Carrier HBV, nil else on severity
- 1 Drug induced granulomatous hepatitis complicating chronic HBV

3 hepatitis B implied but not specifically stated in response

1 chronic hepatitis C (but mentioned ground glass Hepatocytes)

Other comments:

Nearly all – ground glass Hepatocytes

16 – exclude HCV, portal lymphoid aggregates, steatosis

6 ? also steatohepatitis/NAFLD

several - ? cause of fatty change

Scoring – to follow ….

Case 235

Comments on severity:
Mild (stage/grade not distinguished) = 6

Stage of fibrosis:

None	1
Mild	8
0	5
1	9
1-2	1
2	3
2-3	1

Grade of necroinflammation:

Mild	13
Mild-mod	4
moderate	4
2	2
3	5
4	5
5	8

Case 235

Scoring; Full marks for responses giving hepatitis B with an indication of severity. Half marks for hepatitis B with no indication of severity.

No marks for those not specifically stating hepatitis B in the answer. For EQA purposes, the recognition that the morphological pattern of inflammation is attributable to hepatitis B should be clearly stated (this requirement to state aetiology of chronic hepatitis in the response has been previously discussed at liver EQA open meetings and is referred to on the answer sheets).

Case 235

Follow up: Dr Sherwood

The patient was born in Thailand. HBeAg +ve, high viral load and raised transaminases; she did not also have hepatitis C.

The steatosis can be attributed to a high BMI.

She has become HBeAg –ve following treatment.

Case 236

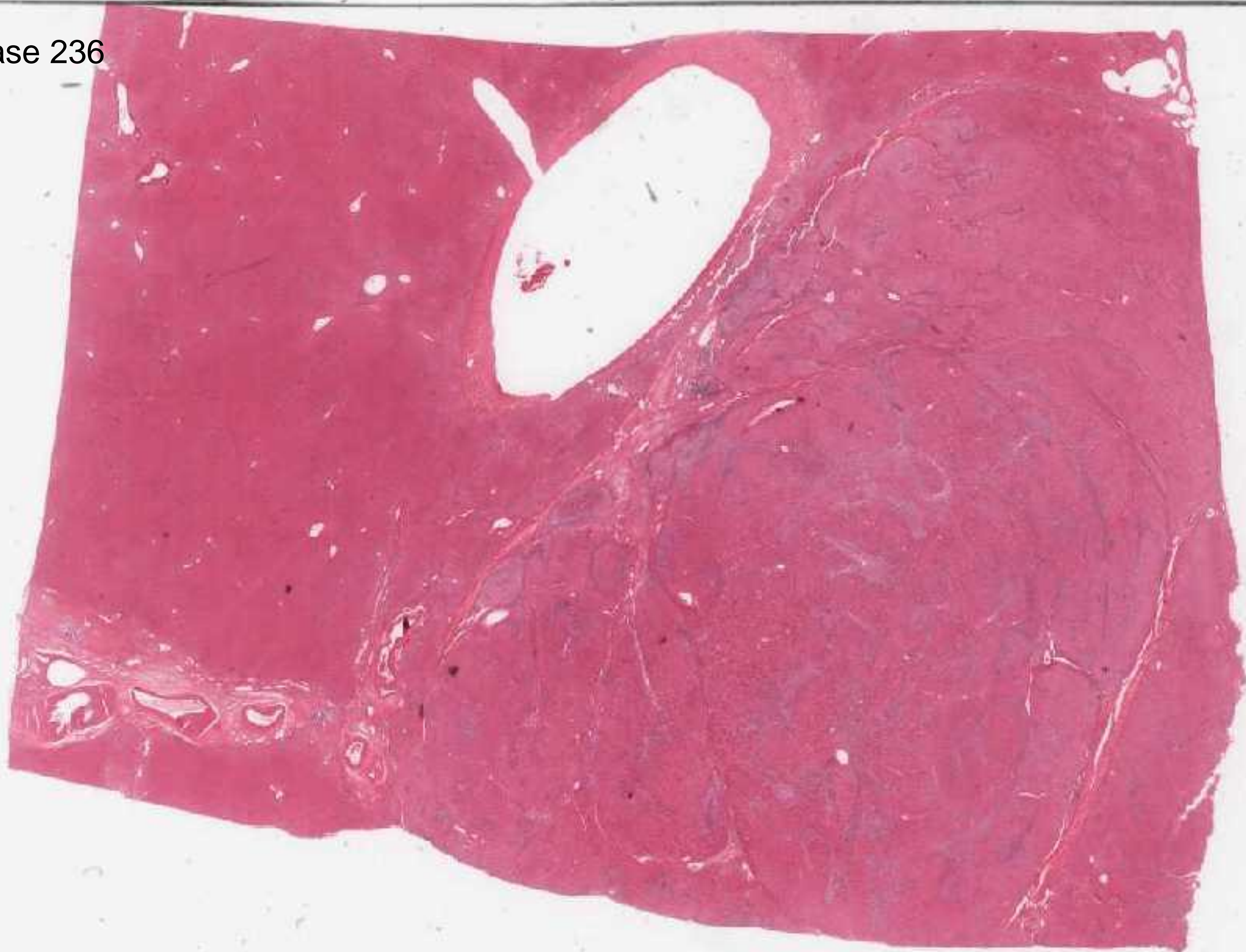
29F Abdominal pain investigation.

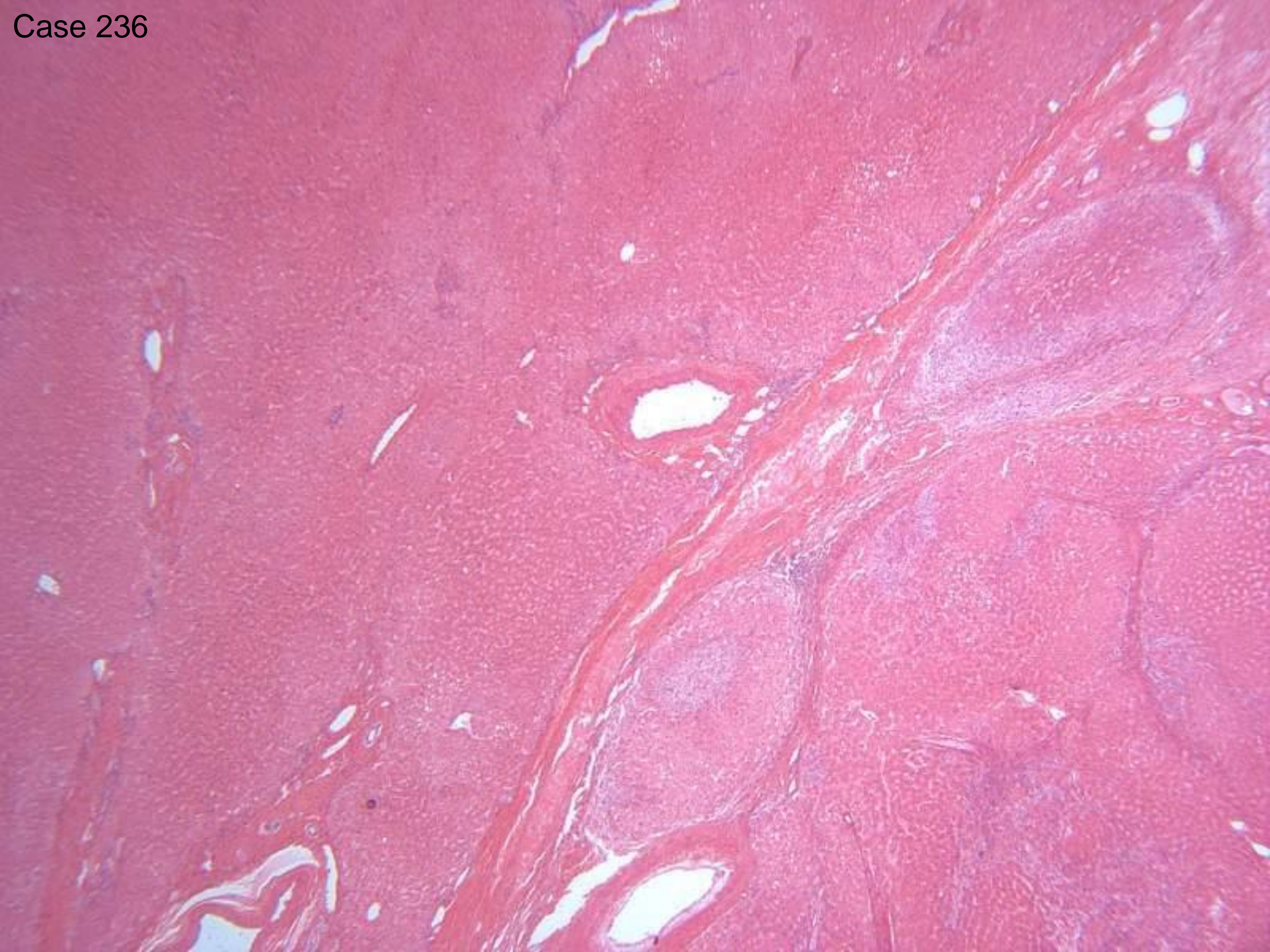
Liver tumour found clinically/imaging.

Clinically thought to be an adenoma. Resection carried out.

Right partial hepatectomy – 20x15x10cm liver resection specimen. Subcapsular well circumscribed nodule.   Brownish colour, 4.5cm max. diameter.

Case 236

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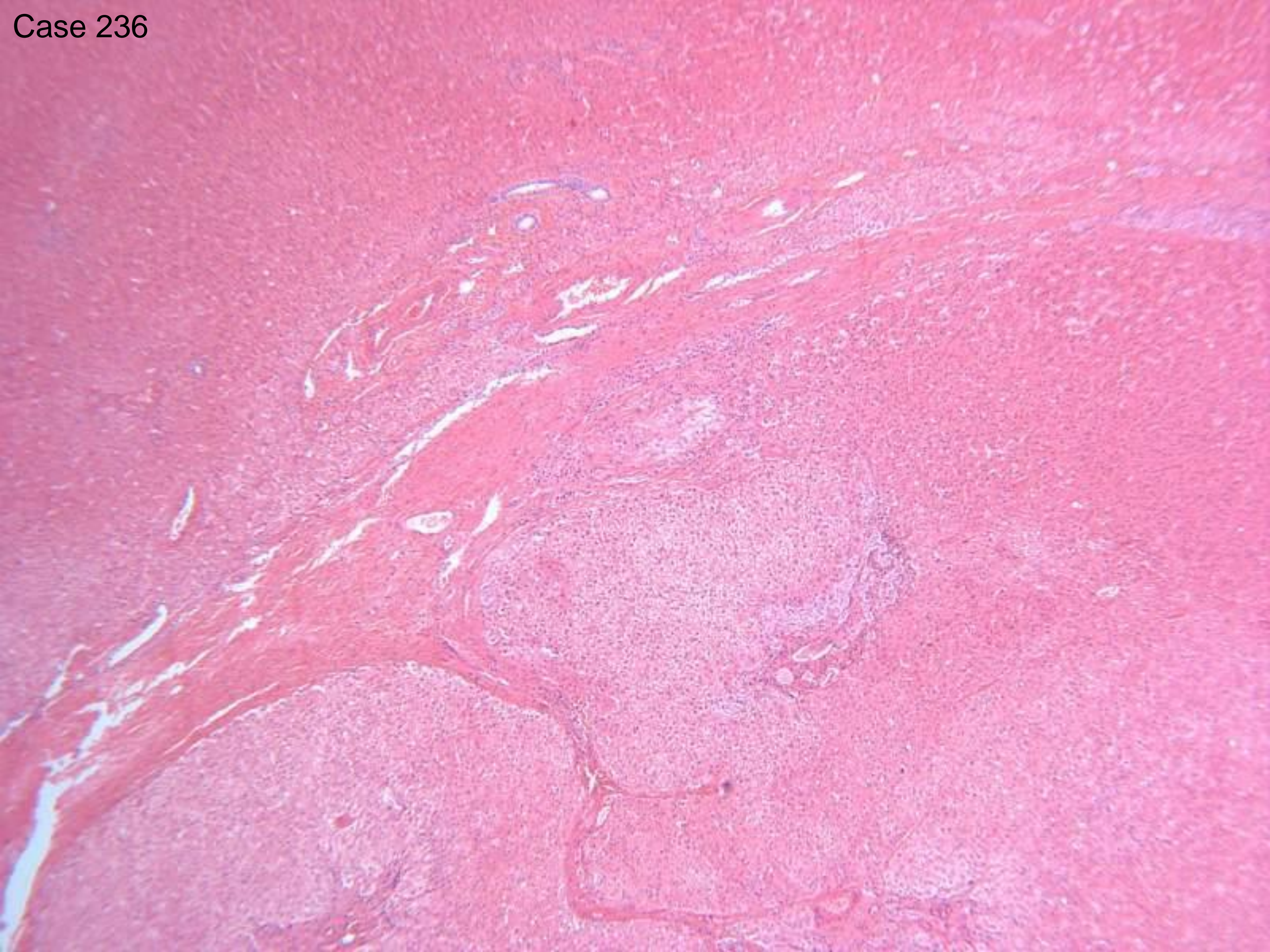
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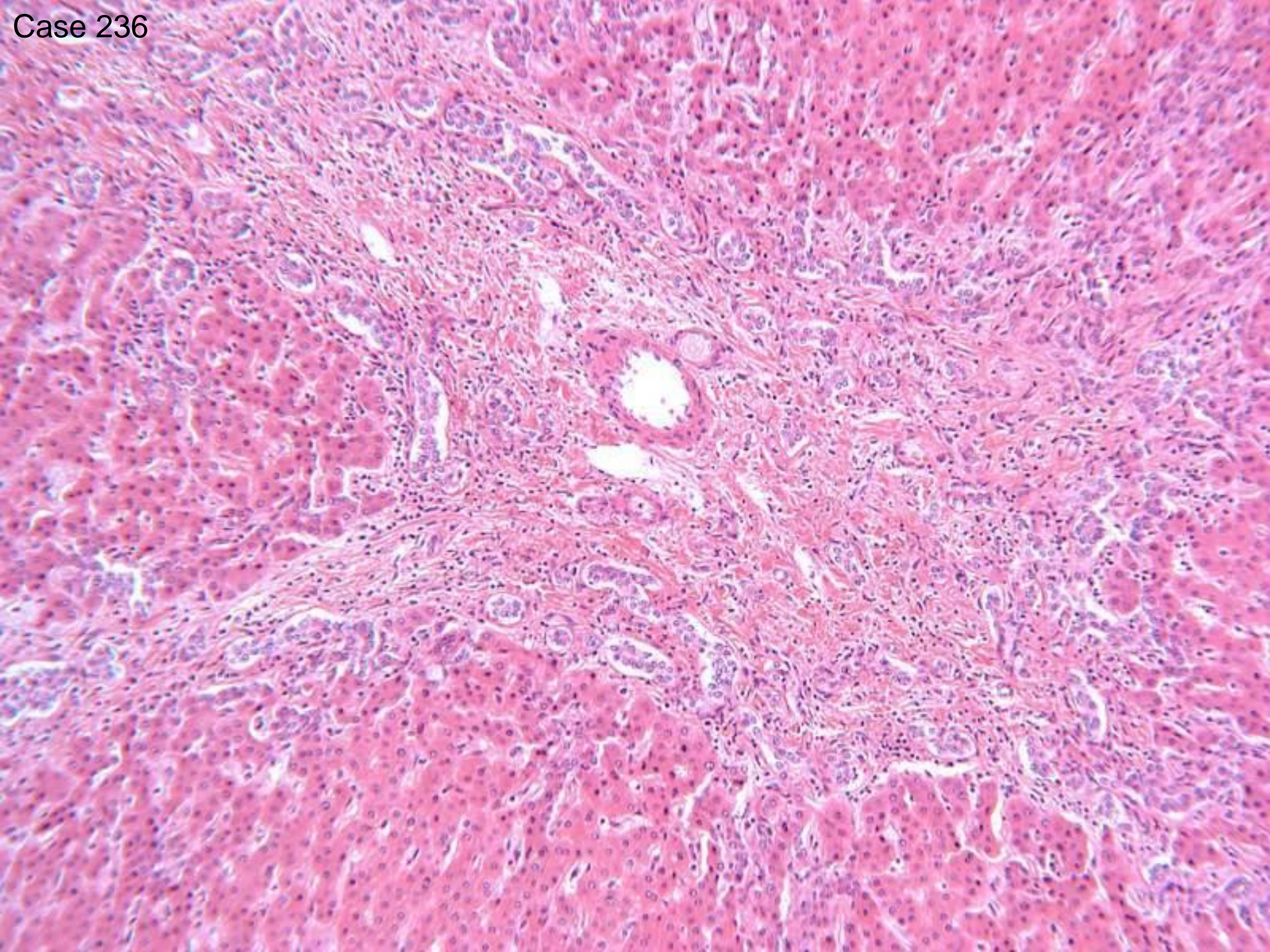
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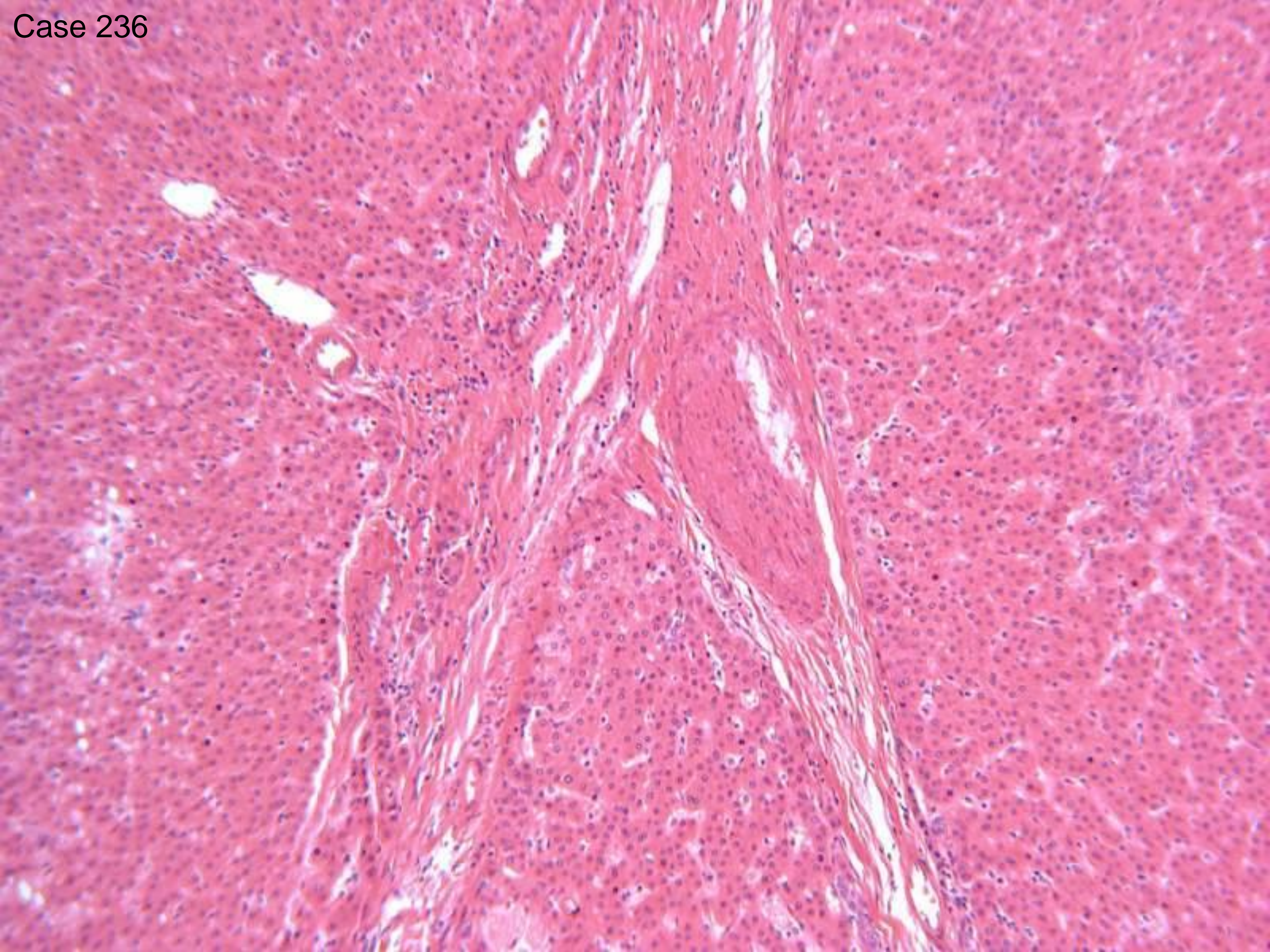

Case 236

Case 236: Results

52 Focal nodular hyperplasia

1 More like Focal nodular hyperplasia than adenoma

1 liver cell adenoma

1 ? nodular regenerative hyperplasia, no central scar, so not FNH

1 macro-regenerative nodule.

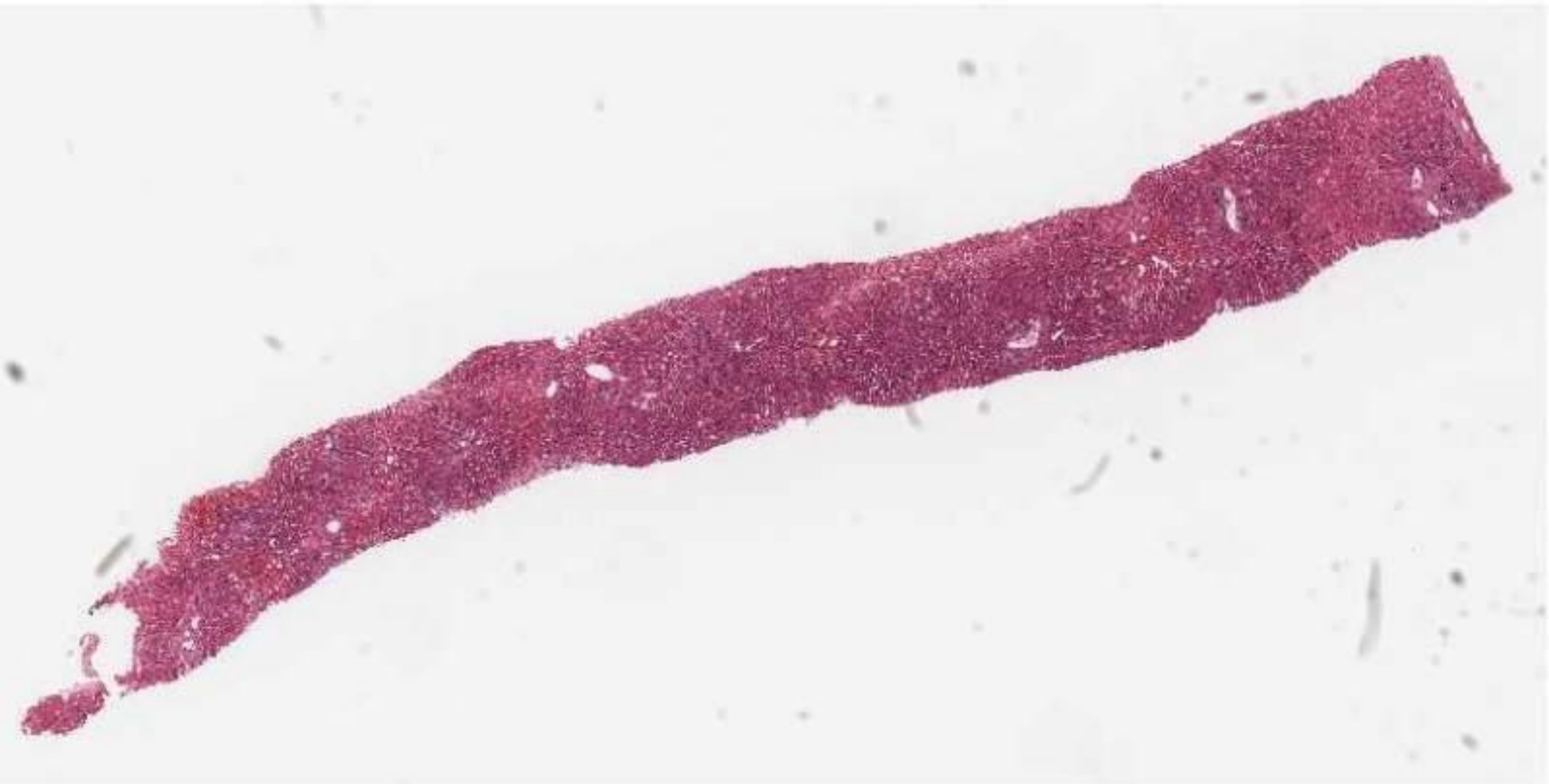
Scoring: clear example of FNH; rejected other diagnoses.

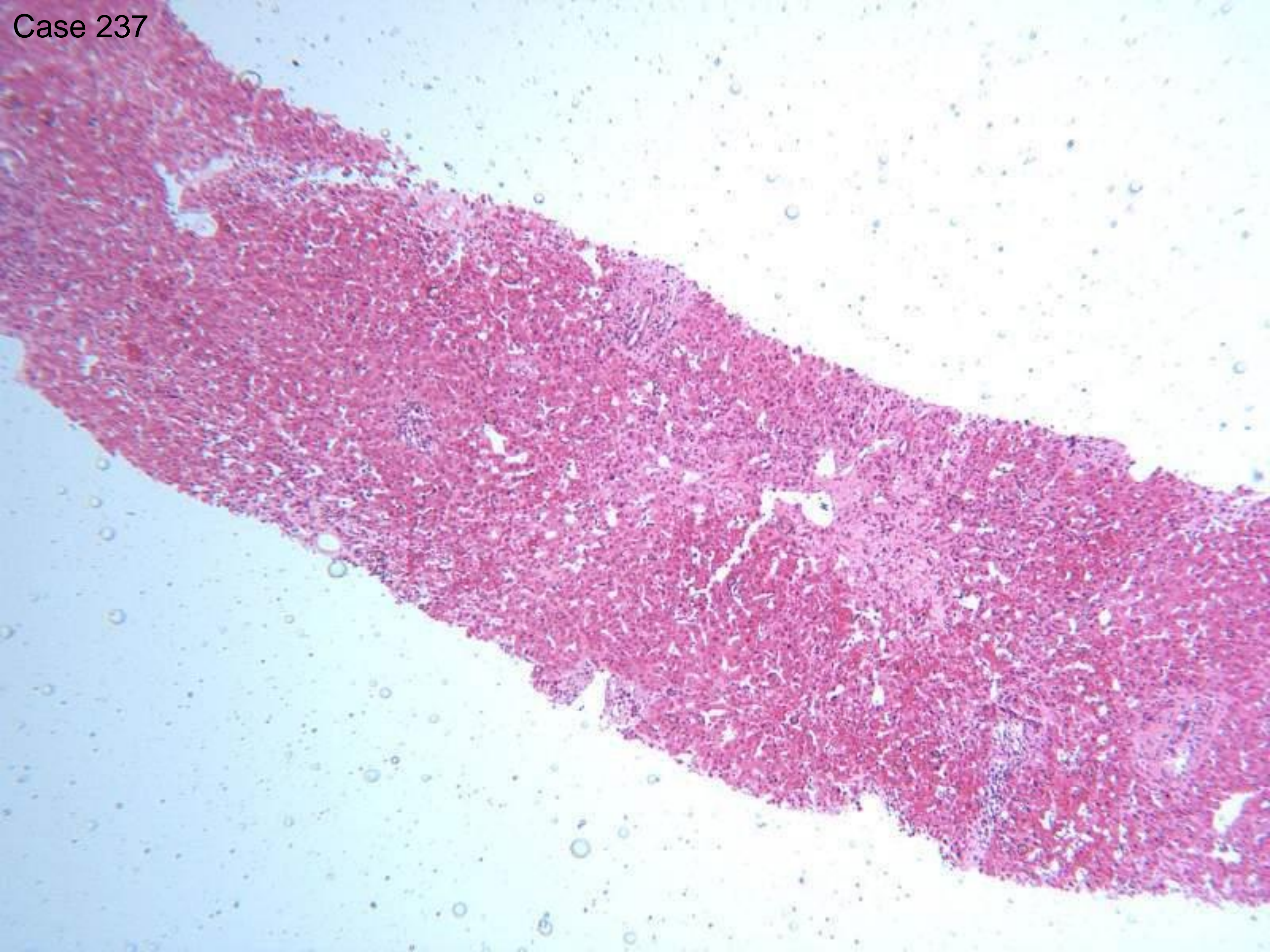
Case 237

55F. Abnormal liver function tests: GGT 400, ALT 25, Alk phos 167; Bili 27, hepatomegaly, ?chronic.

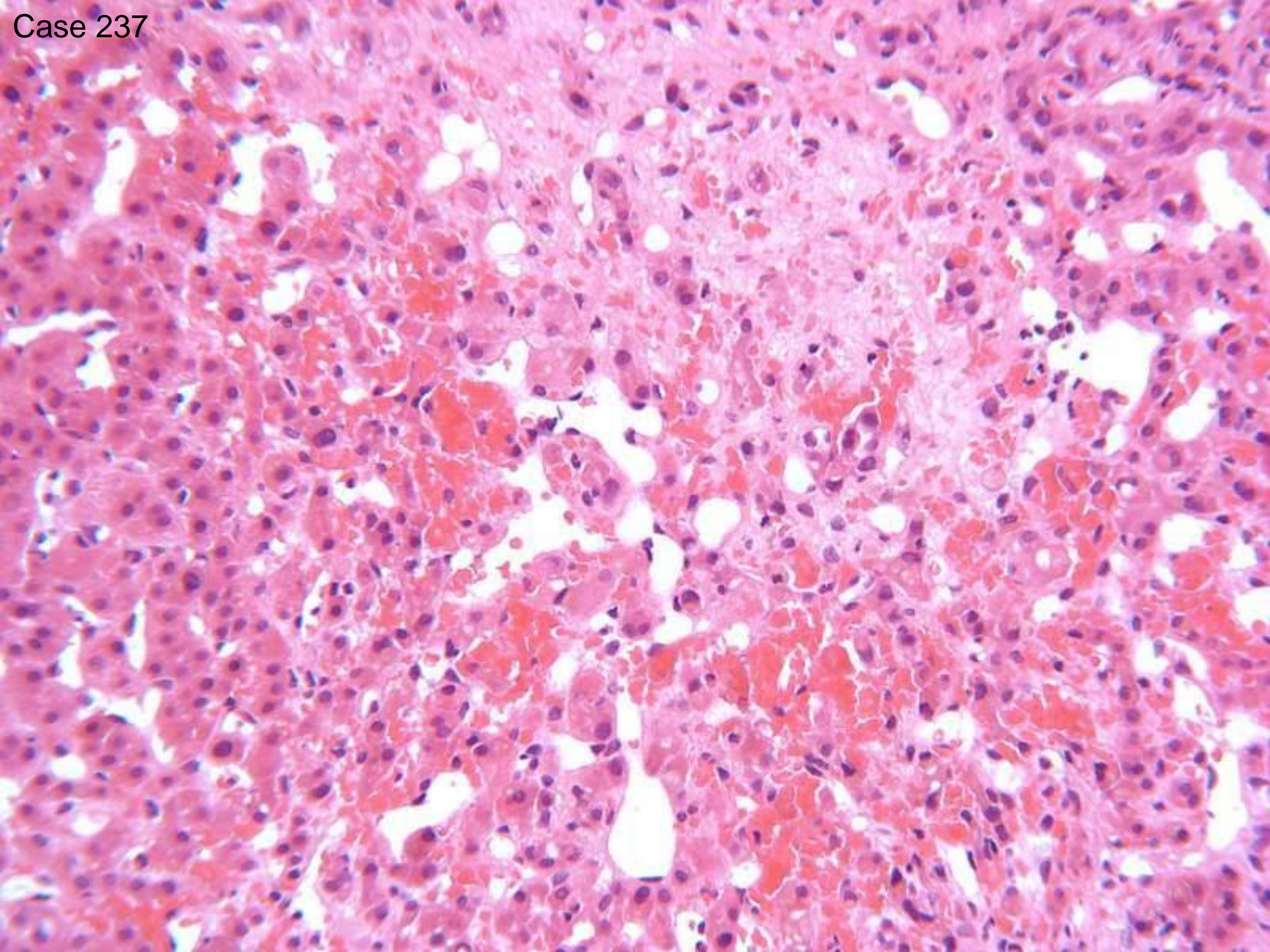
No serological clue as to cause… ultrasound: heterogeneous appearance but no obvious mass.

Case 237





Case 237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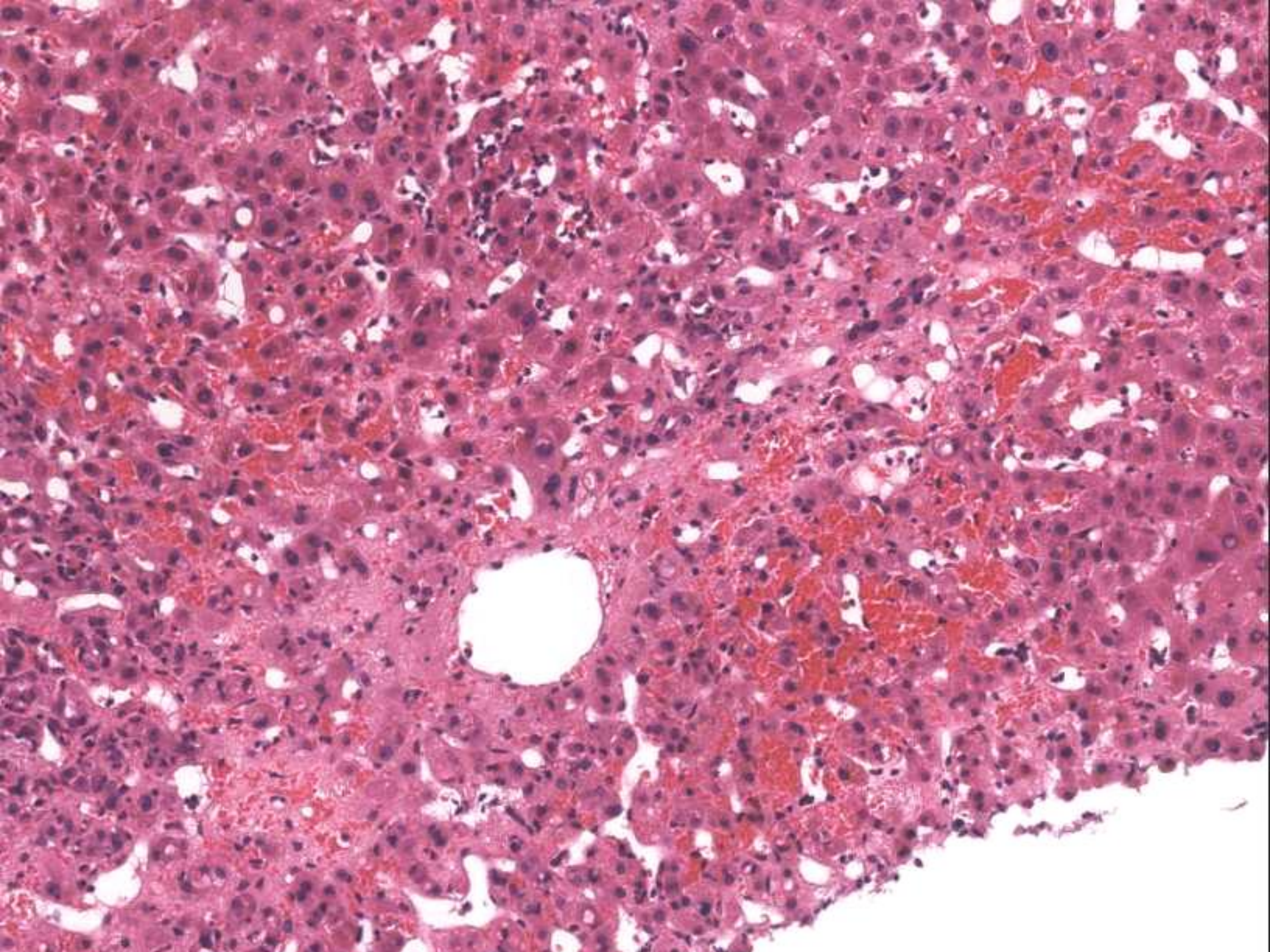

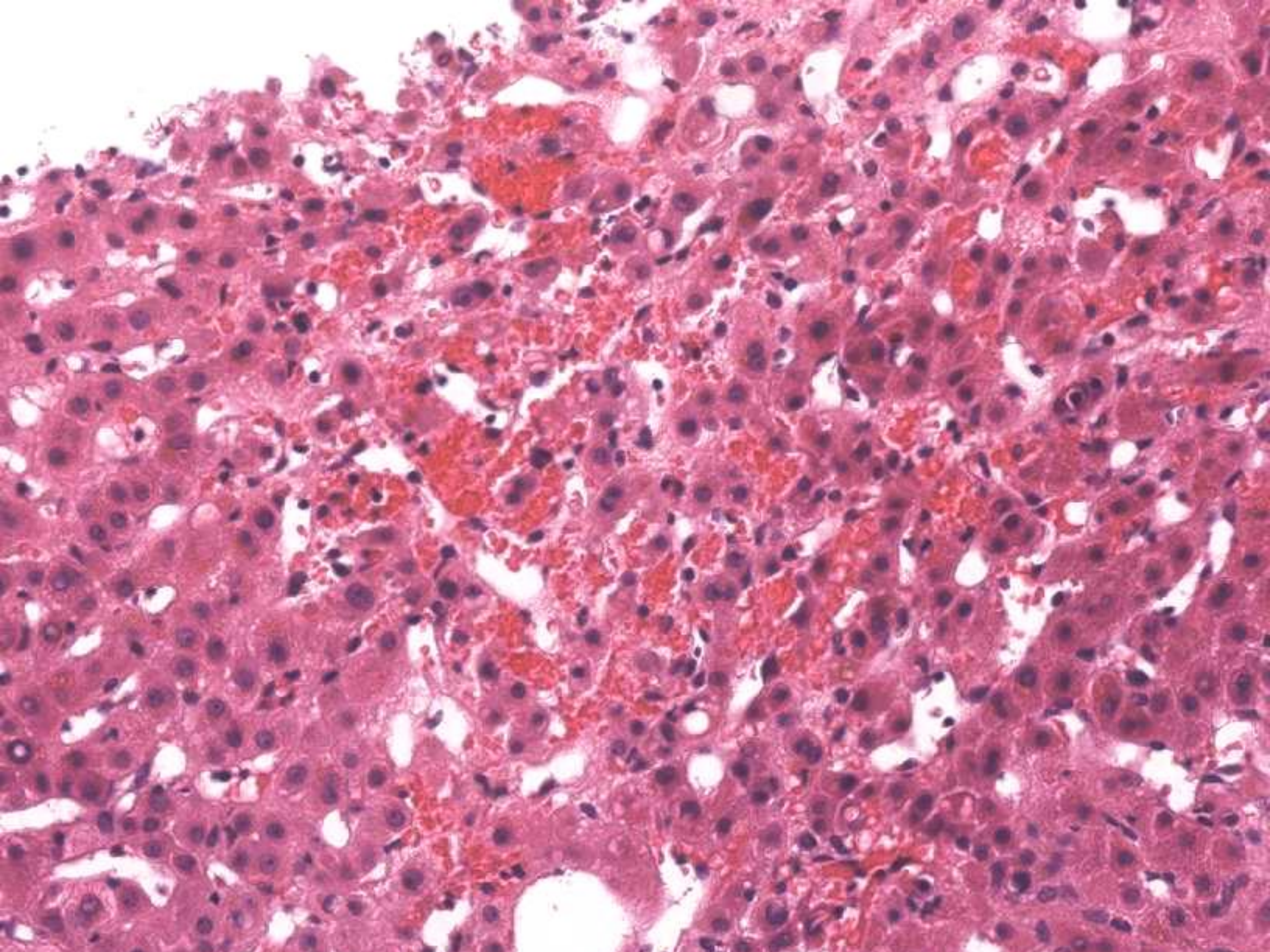

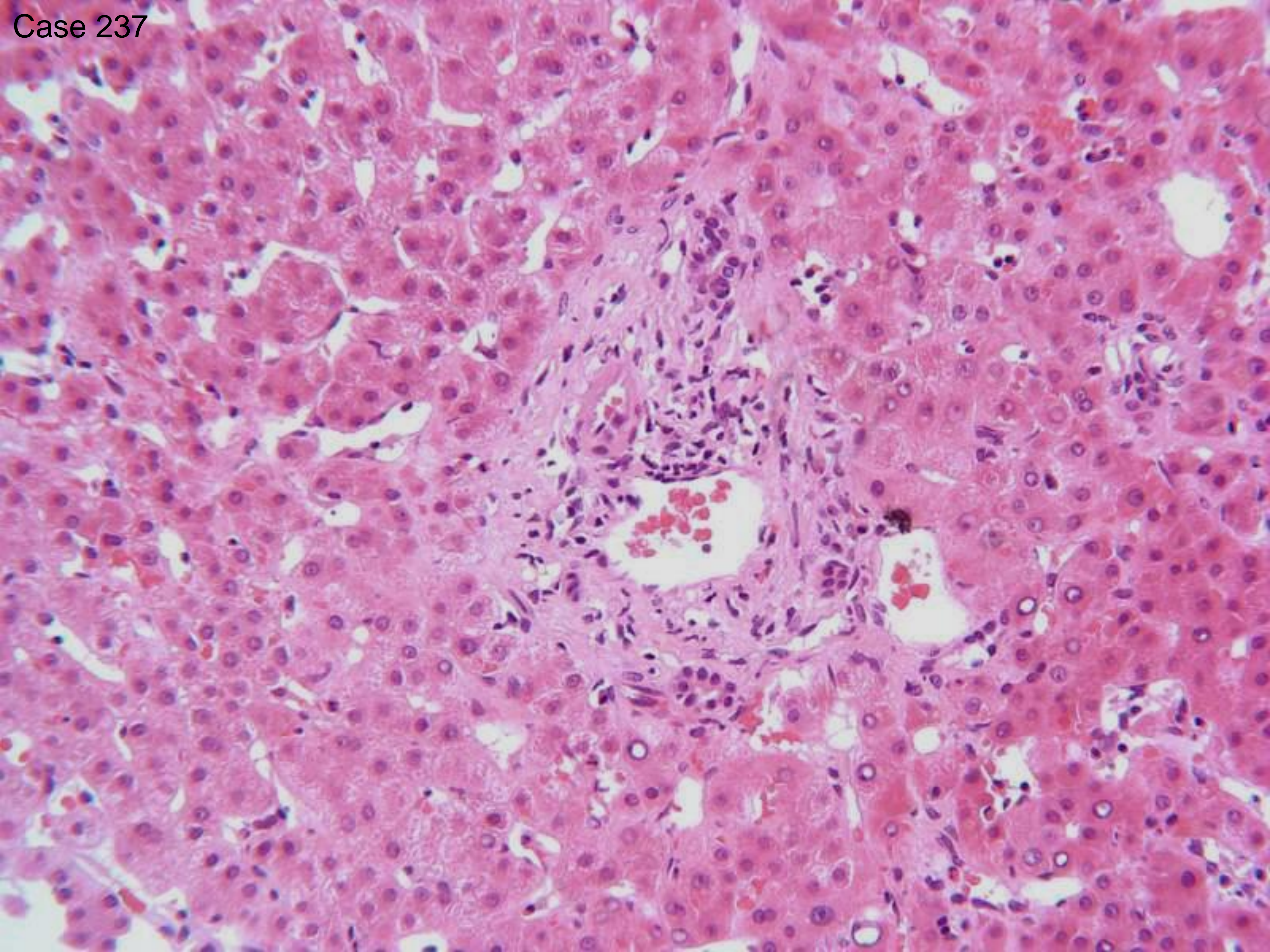
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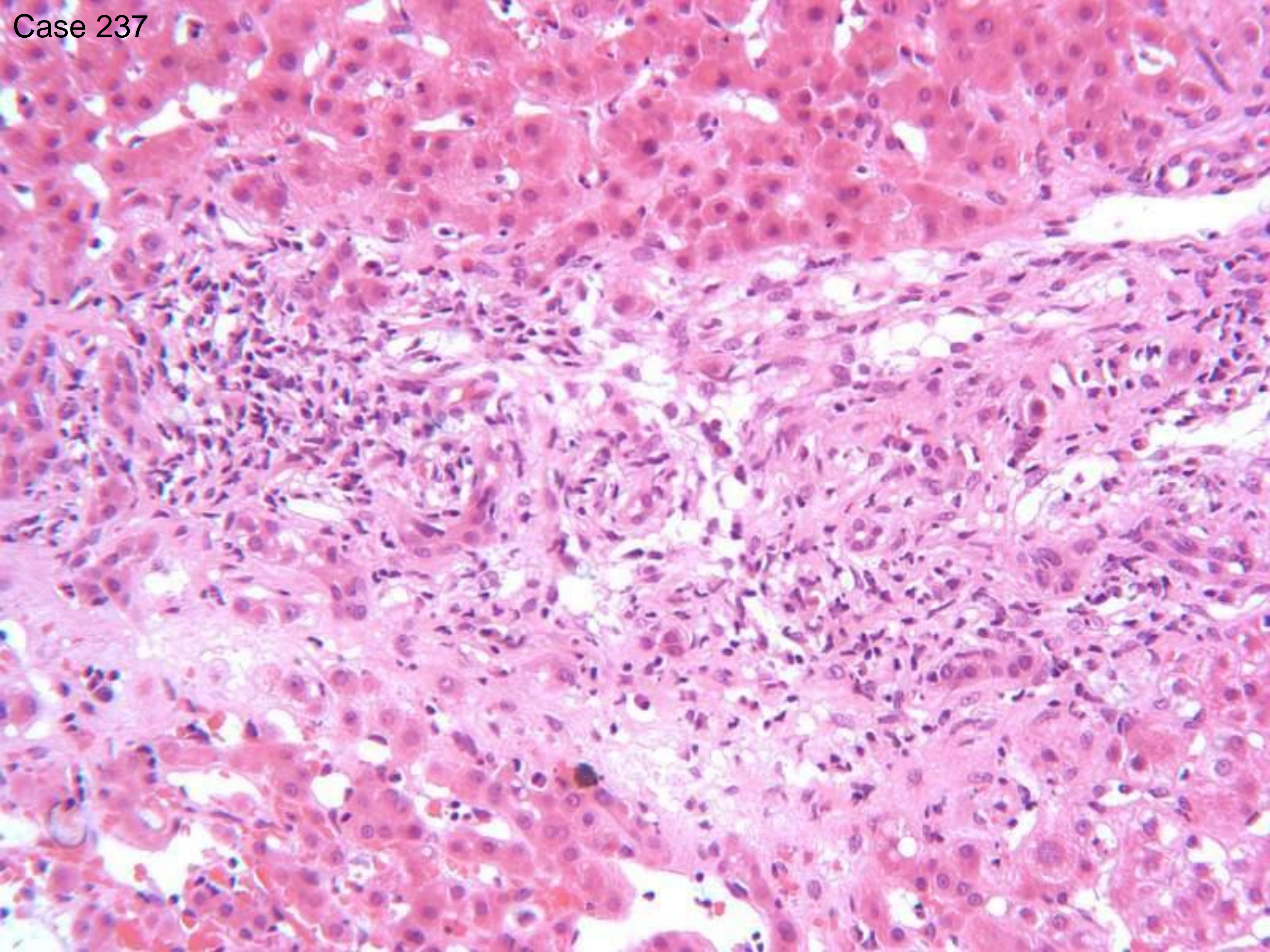
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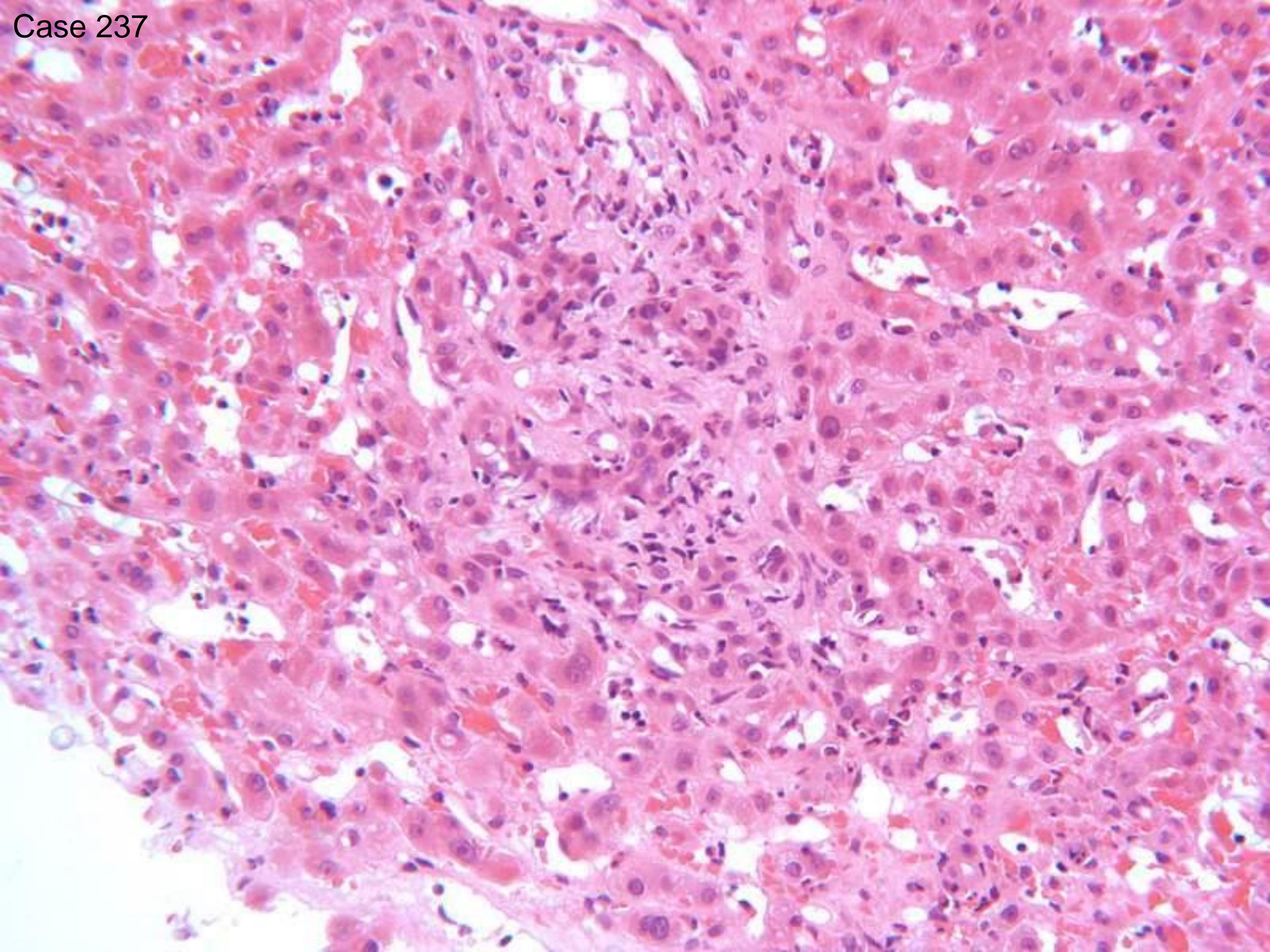

Case 237

Case 237: Results

47 venous outflow obstruction, alone or included in differential

1 submassive necrosis, ? drugs/circulatory failure

1 perivenular necrosis./congestion ?heart failure or POD

1 acute hepatitis with zone 1&3 necrosis

1 ischaemic hepatitis/drug related

1 centrivenular congestion (?right heart failure)

1 alcoholic hepatitis

1 obstructive features, with suspicious sinusoidal infiltrate, likely malignant

Scoring: Accept all where some form of venous outflow obstruction is indicated as the main pathology.

Case 237

Comment; The correct response should indicate the need for the clinicians to investigate for further evidence of venous outflow obstruction. Those answers that did not indicate the need for that investigation are rejected.

Case 237

Follow up: Dr Kaye

Hepatic vein obstruction due to large vascular mass involving IVC, hepatic veins, right and left hepatic arteries and right and left portal veins.

Biopsy of mass showed adenocarcinoma. Final diagnosis: large centrally situated cholangiocarcinoma.

Her main clinical problem was recurrent ascites due to hepatic venous outflow obstruction. Died 4 months later.

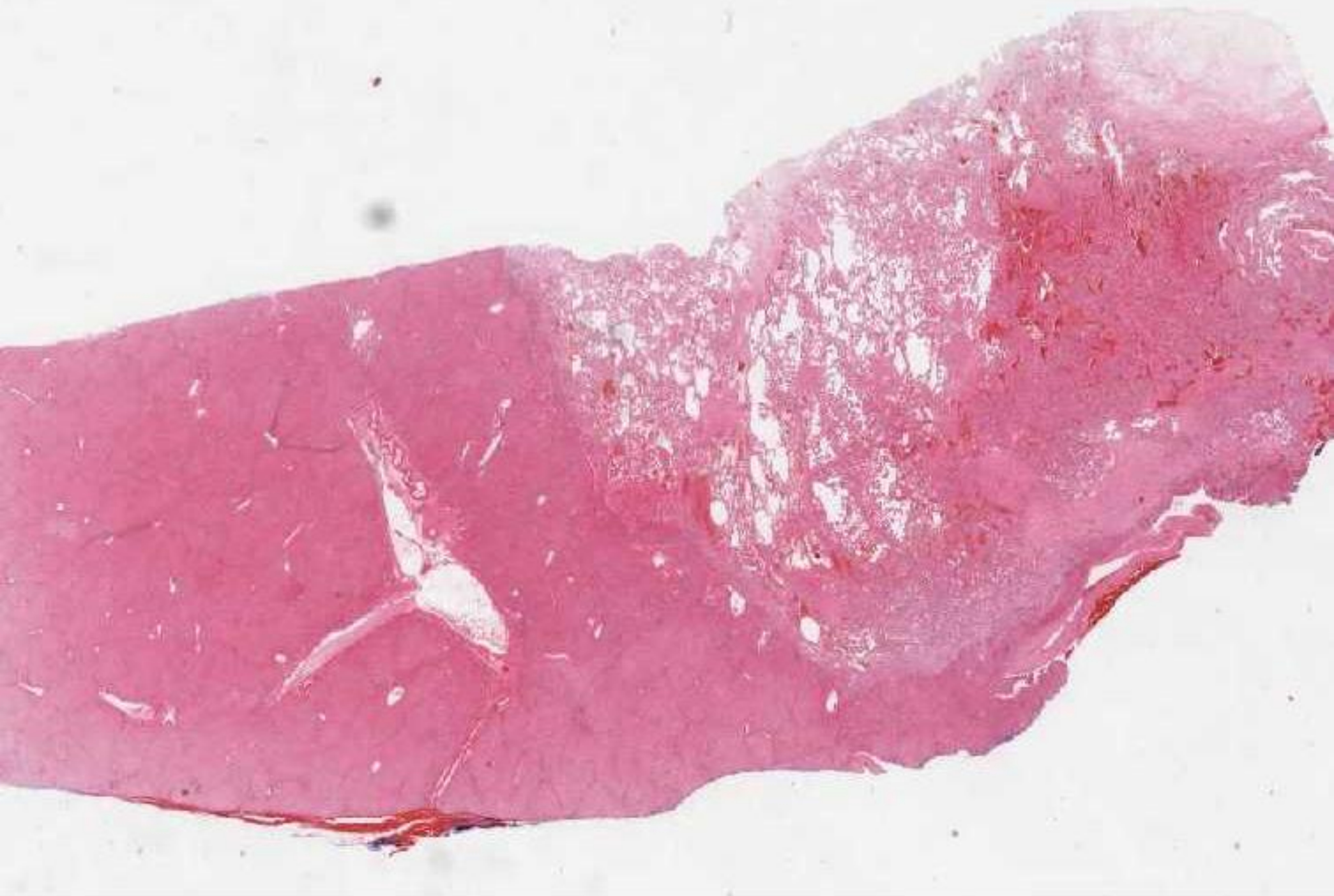
Case 238

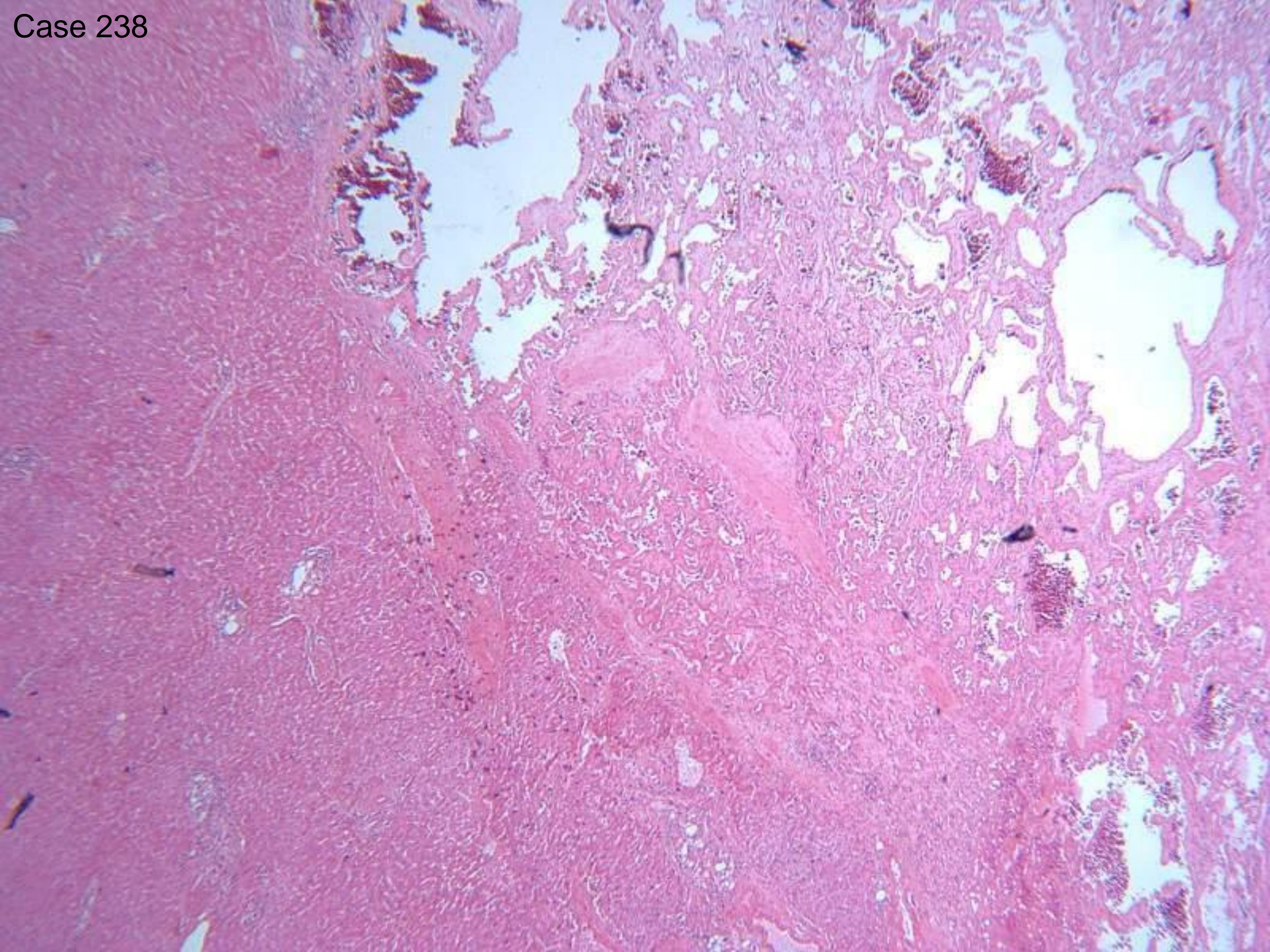
65F. No other clinical details supplied with specimen.

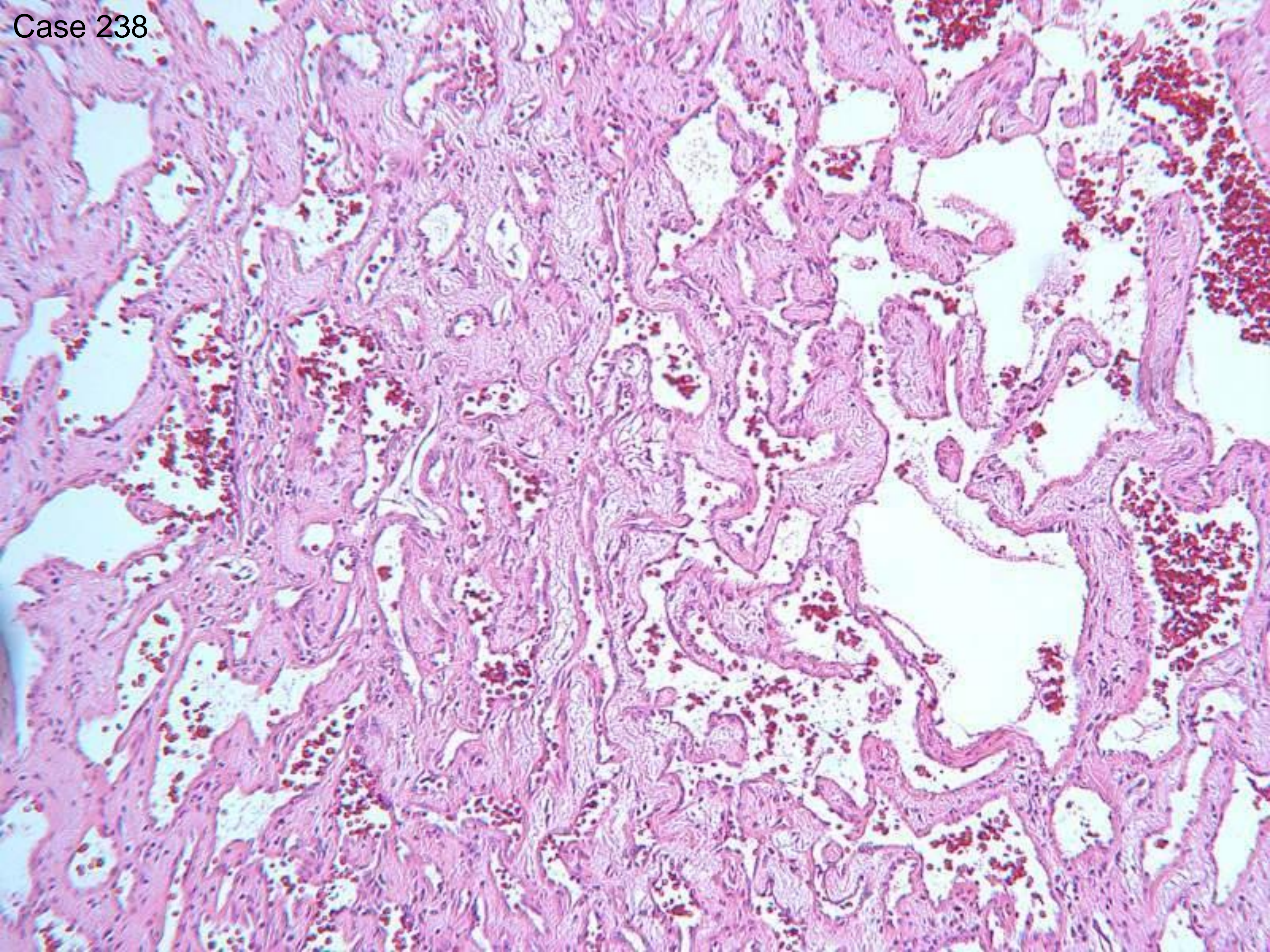
No special stains undertaken.

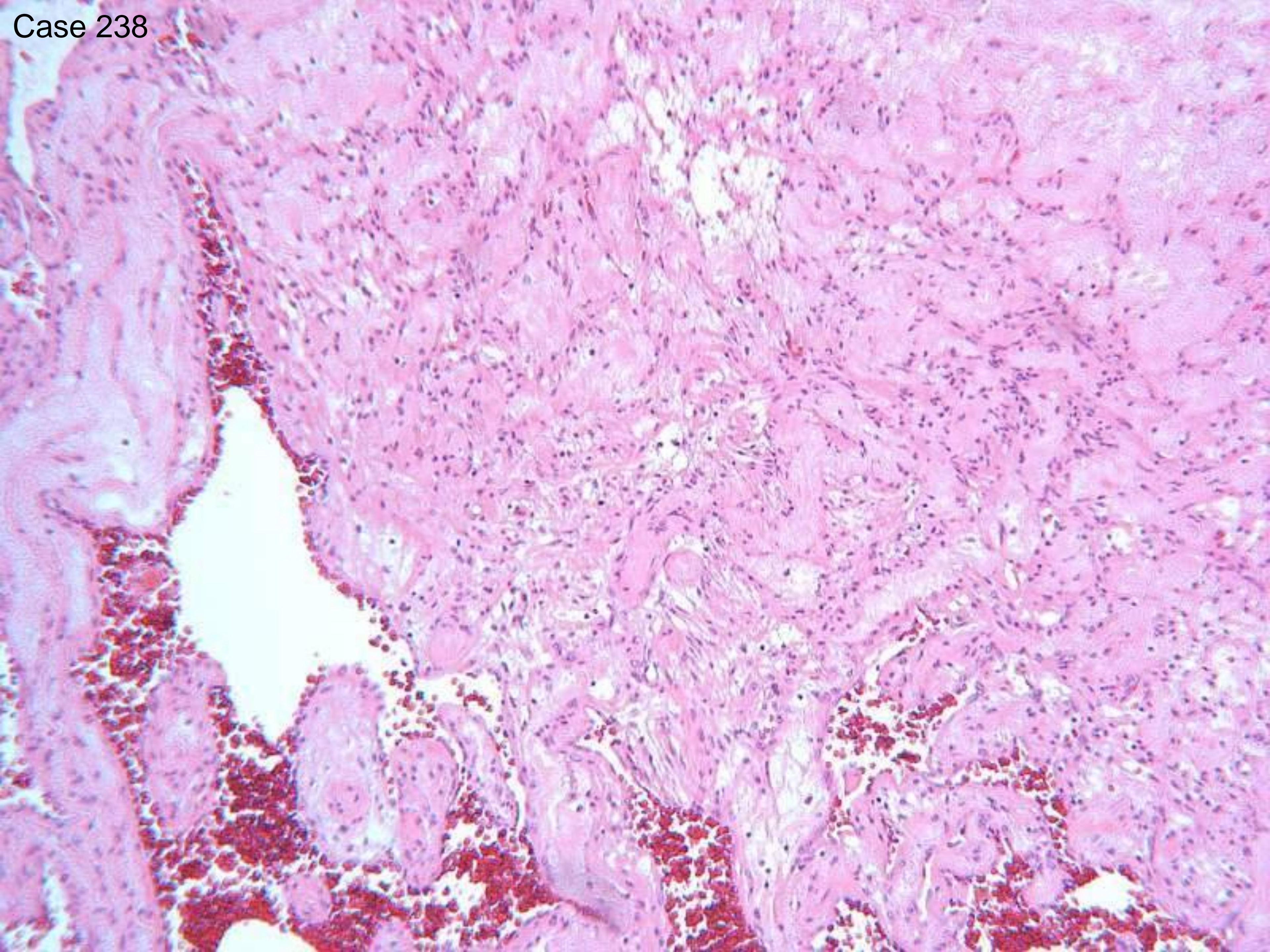
Liver resection = 164g wedge of liver with a haemorrhagic lesion visible on slicing.

Case 238




Case 238


Case 238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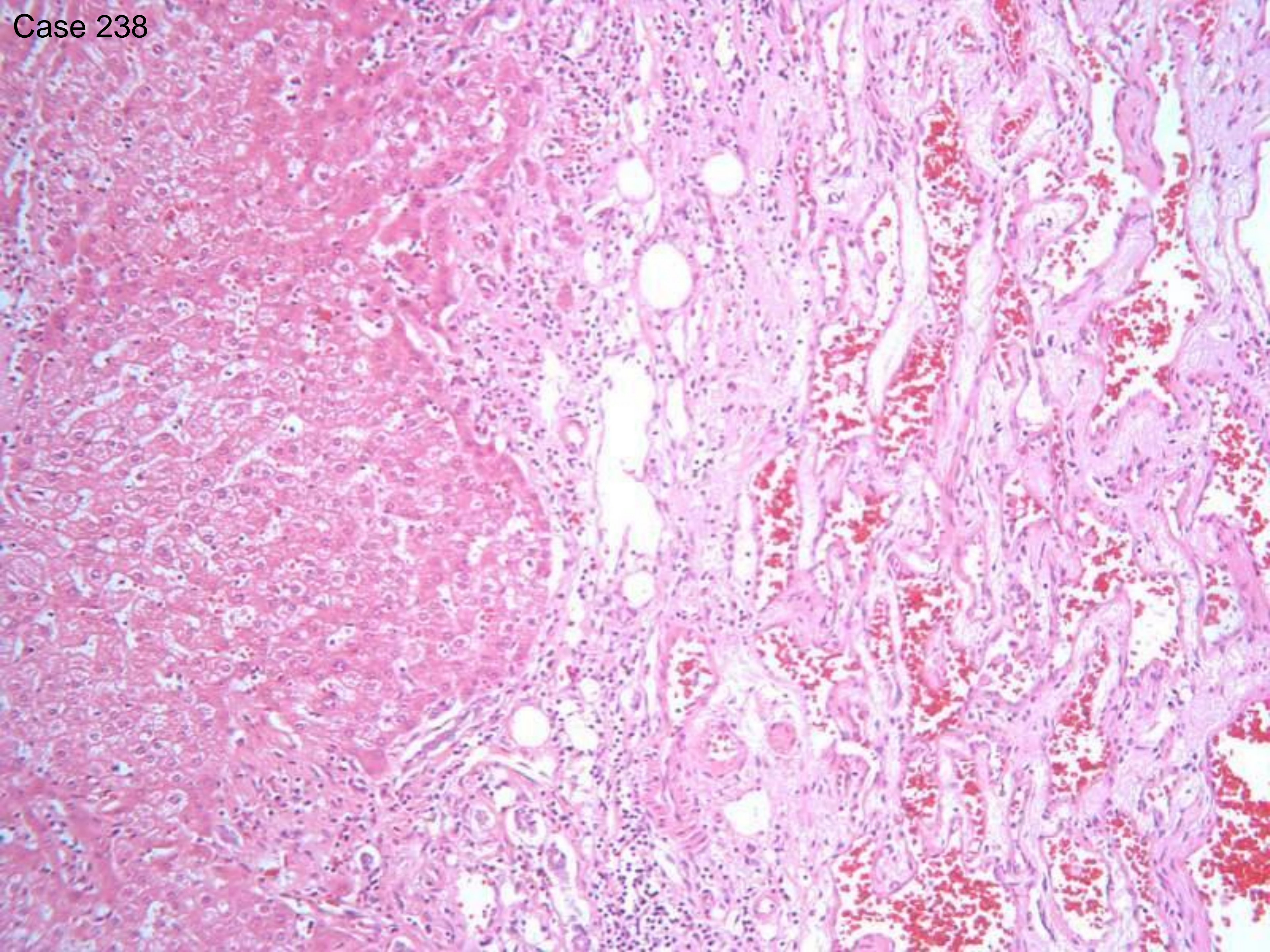

Case 238

Case 238: Results

54 haemangioma +/- cavernous

1 sclerosing haemangioma

1 sinusoidal haemangioma

Comments: why was it resected?

Not acceptable to have no clinical details.

Scoring: Accept all diagnoses

Case 238

Follow up: Dr Dube

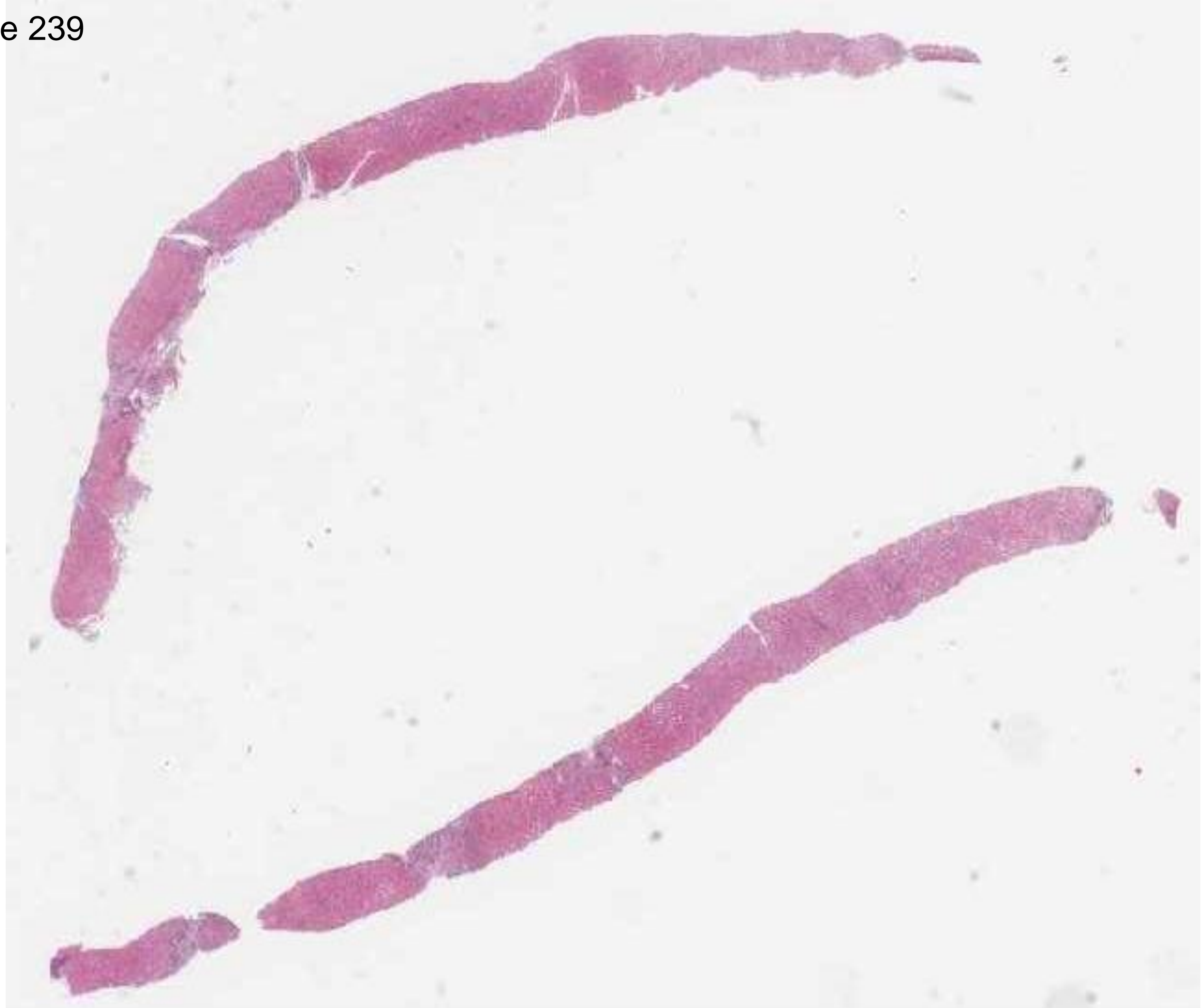
This woman had an incidental finding of 10cm haemangioma on USS for something else. It was removed because of the risk of bleeding. The surgeons shave off the resection margin, which was clear. She made a good recovery.

With large haemangiomas, our surgeons tend to remove them to reduce the risk of bleeding in case of trauma, especially if the lesion is growing or extends below the costal margin.

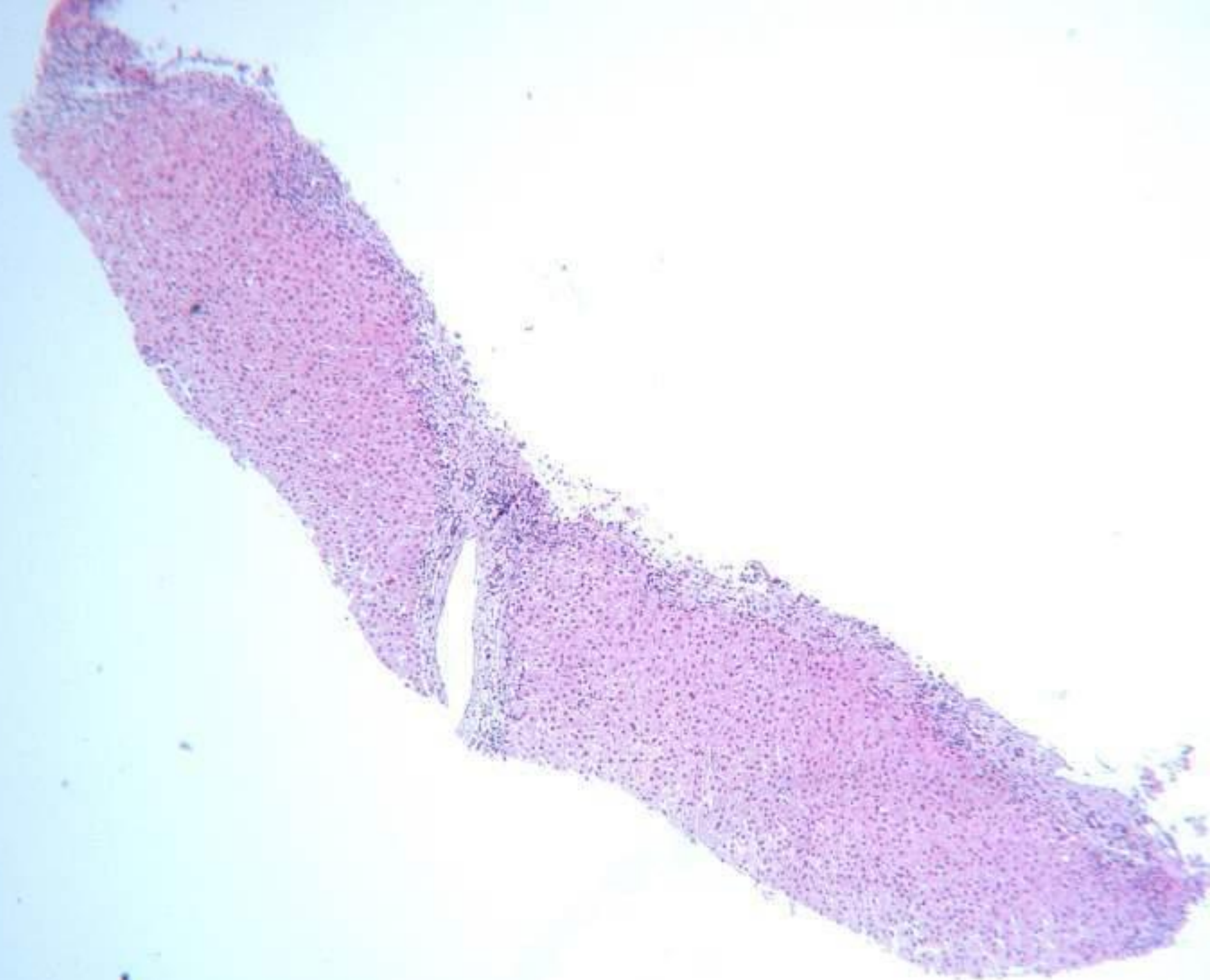
Case 239

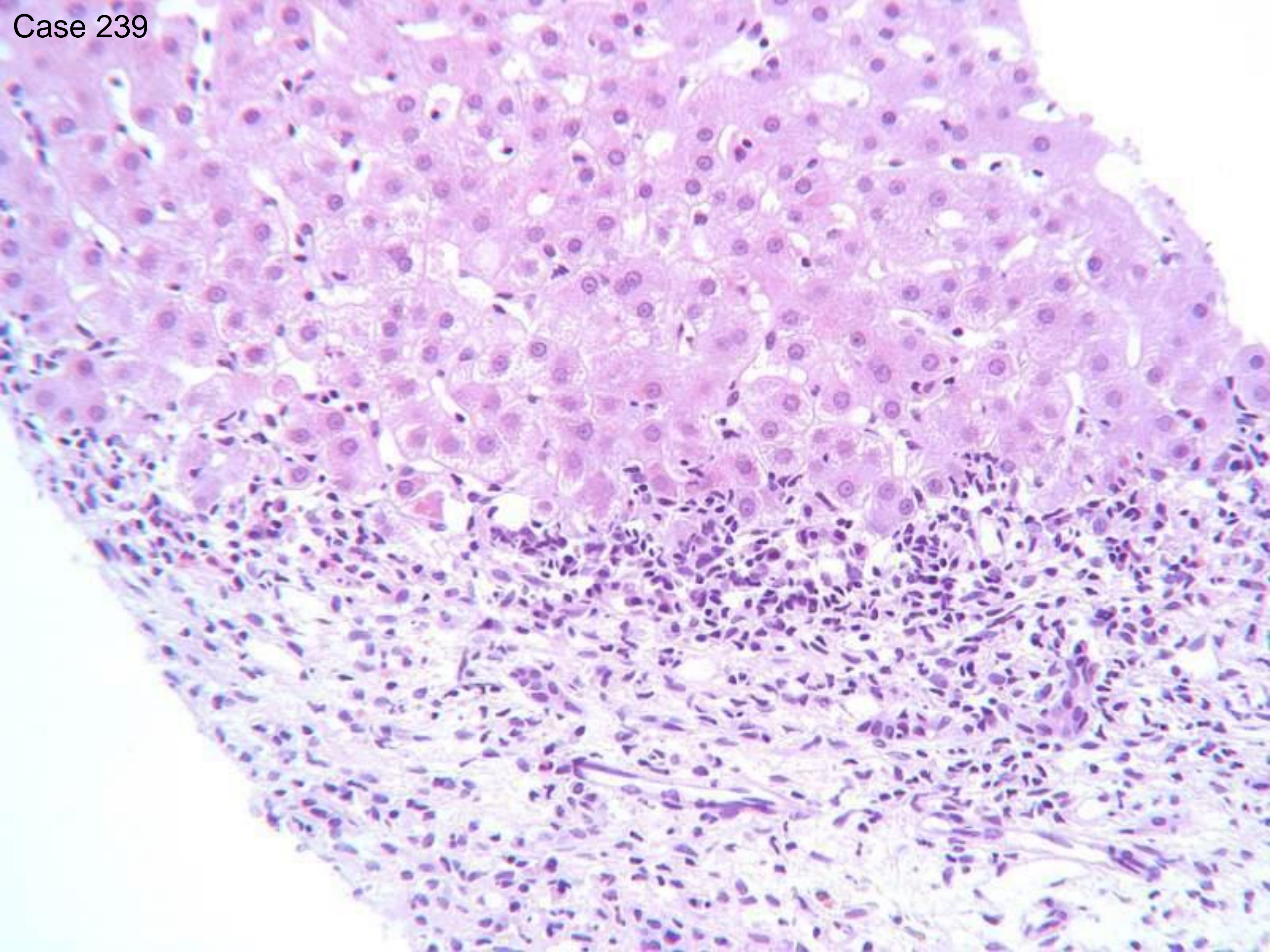
61M. Hepatitis B+ve, hep C –ve. IgG normal,
Antibodies negative. No drugs.
ALT 90-120. Bridging fibrosis on VG

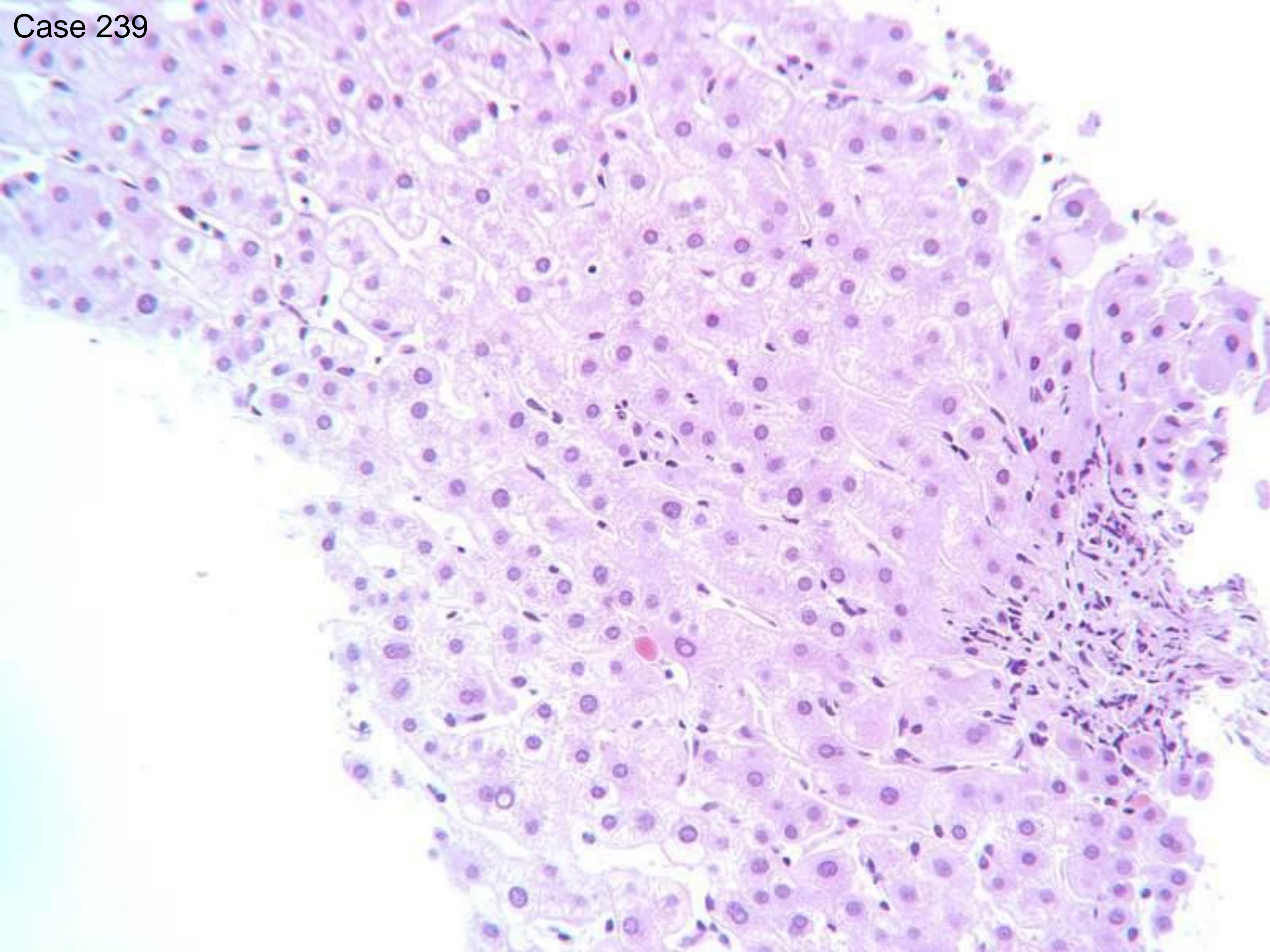
Case 239



Case 239




Case 239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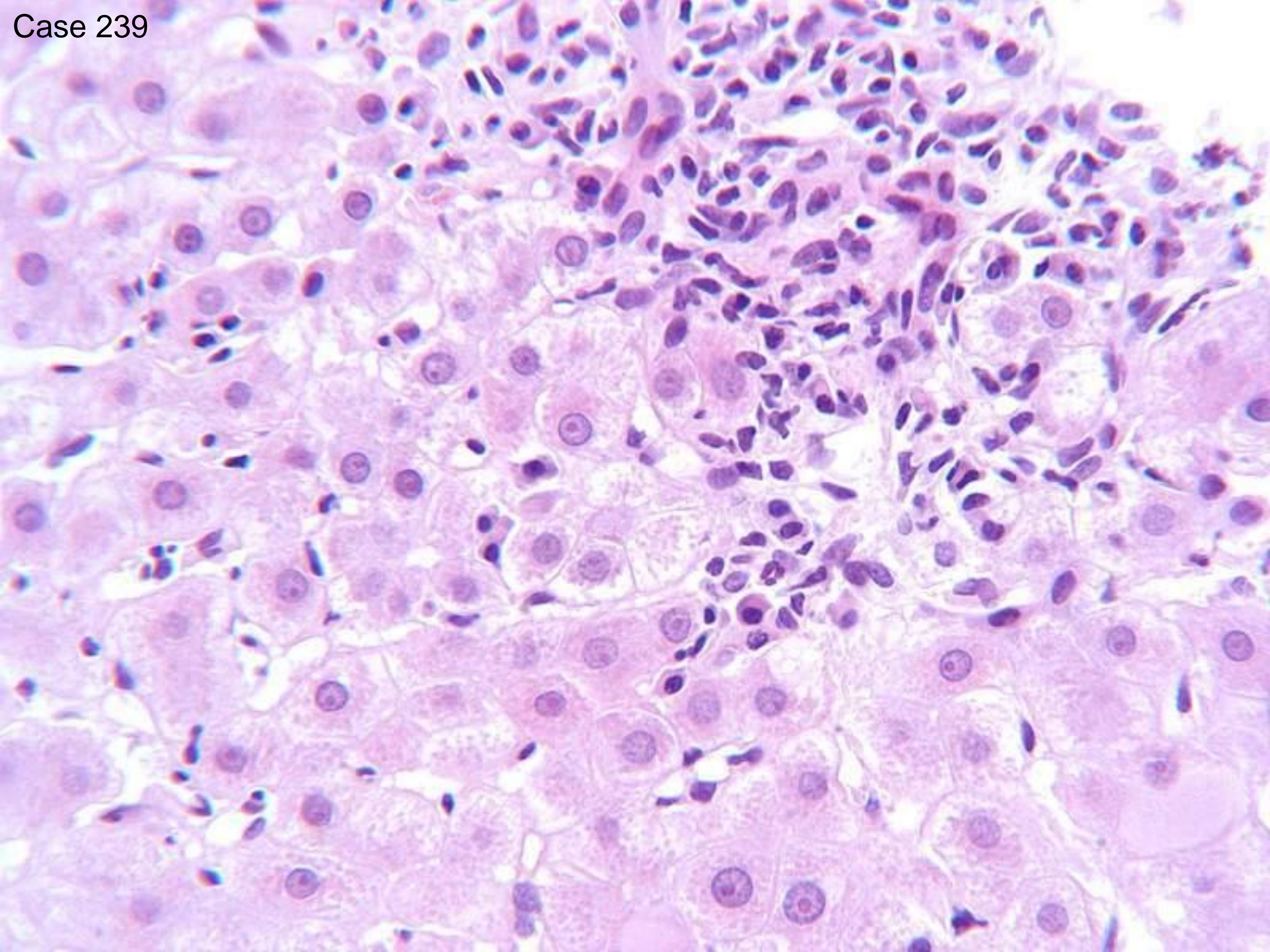
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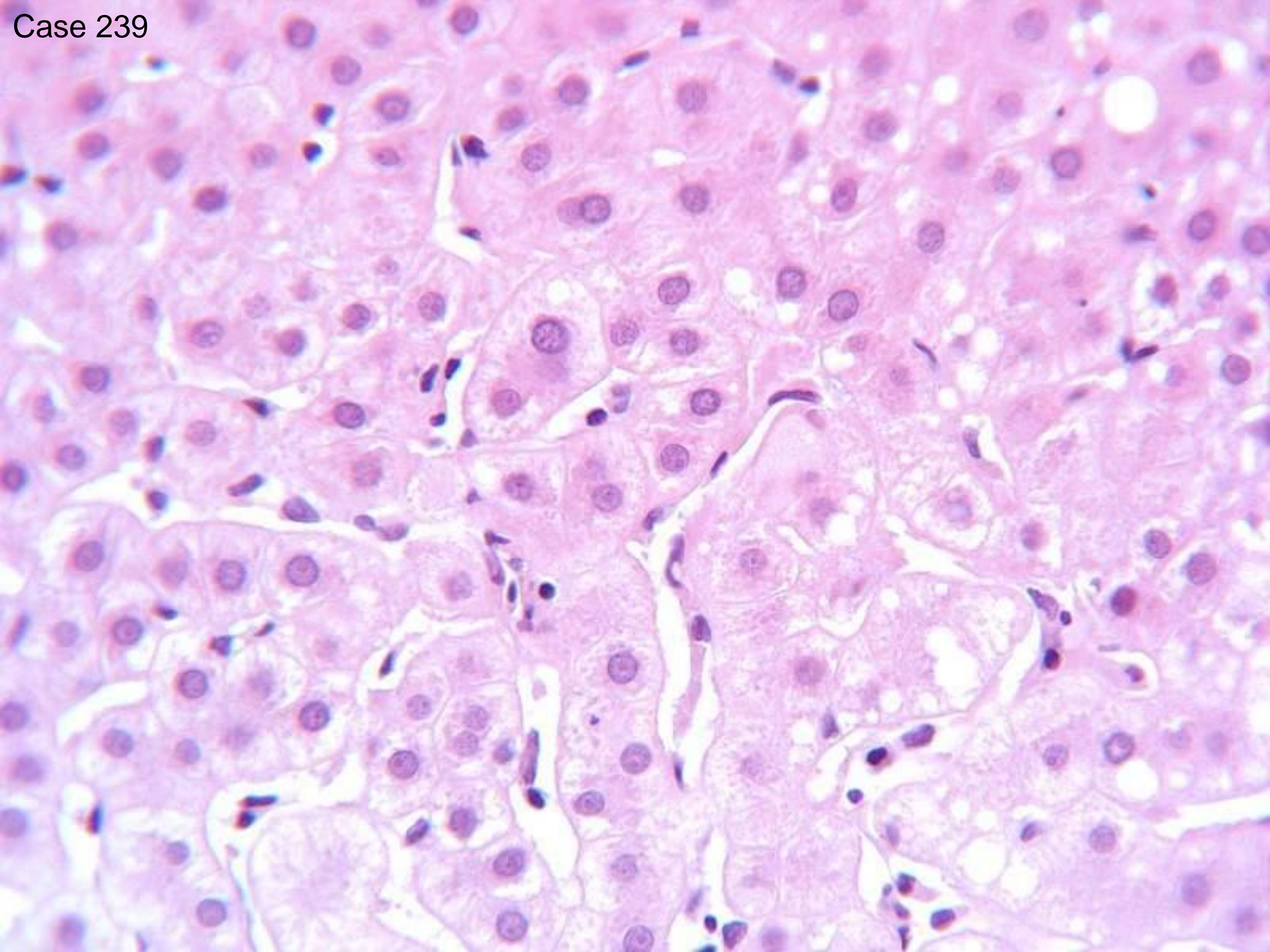

Case 239

Case 239: Results

48 chronic hepatitis B with comment on severity

1 chronic hepatitis B (no mention of severity) - *half marks*
1 hepatitis B/autoimmune/drugs – could all be hep B
2 chronic hepatitis (no mention of B or ground glass cells)
1 chronic hepatitis, occasional ground glass hepatocyte (Hep B not mentioned)
1 viral hepatitis and cirrhosis (ground glass Hepatocytes, Hep B not mentioned)
1 hepatitis B and C

Comments:
Several exclude drugs
1 exclude delta infection
1 ? alcohol too
1 inadequate for assessment

Scoring: Accept hepatitis B with comment on severity. Half marks if no comment on severity, and reject those that do not specifically state hepatitis B.

Stage of fibrosis:

Moderate	7
Bridging	8
3	5
4	7
5	9
6	1

Grade of necroinflammation:

Mild	3
Mild-mod	1
moderate	11
severe	1
2	1
4	1
5	3
6	8
7	6
8	1

Case 239

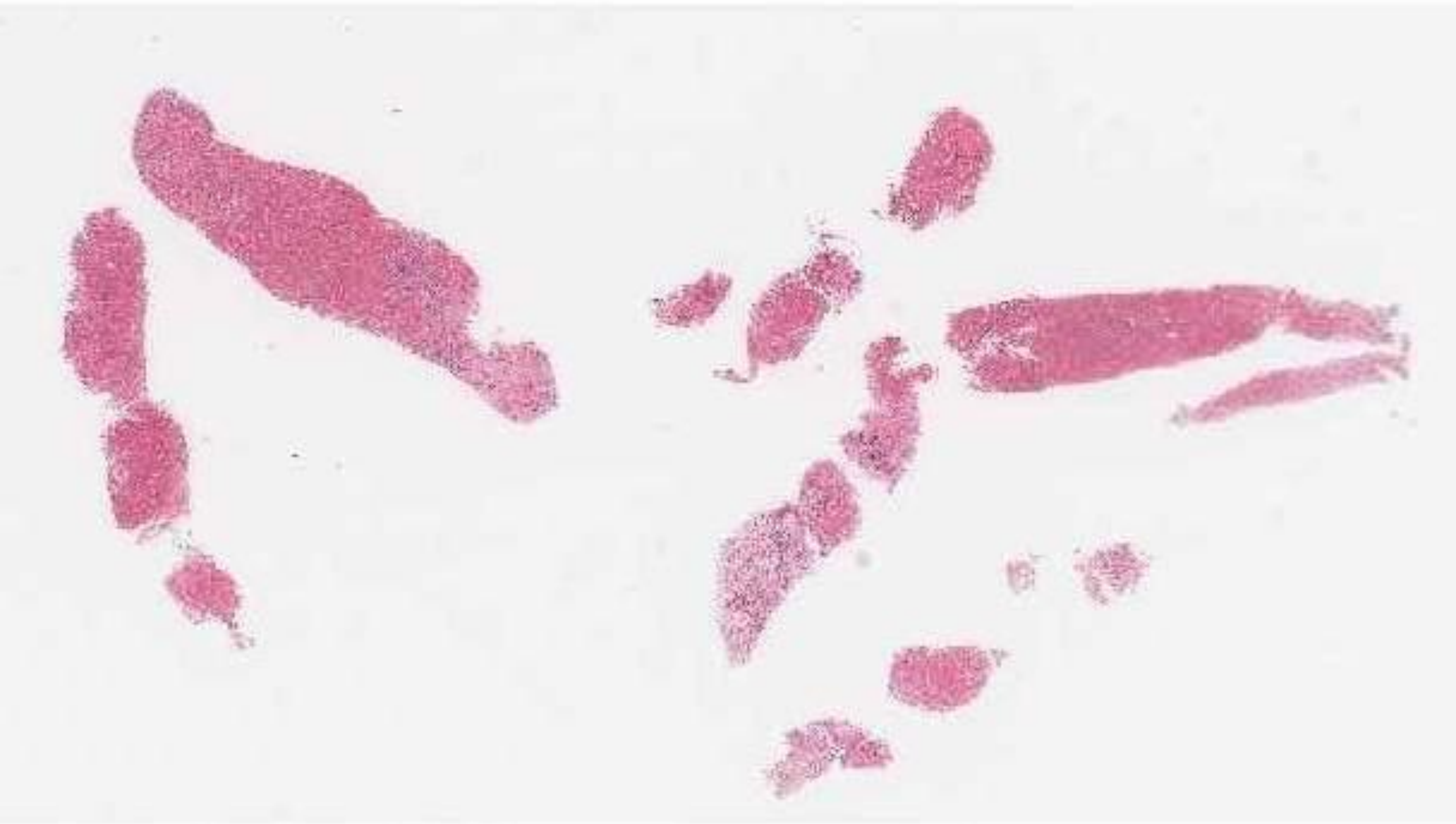
Follow up: Dr McGregor

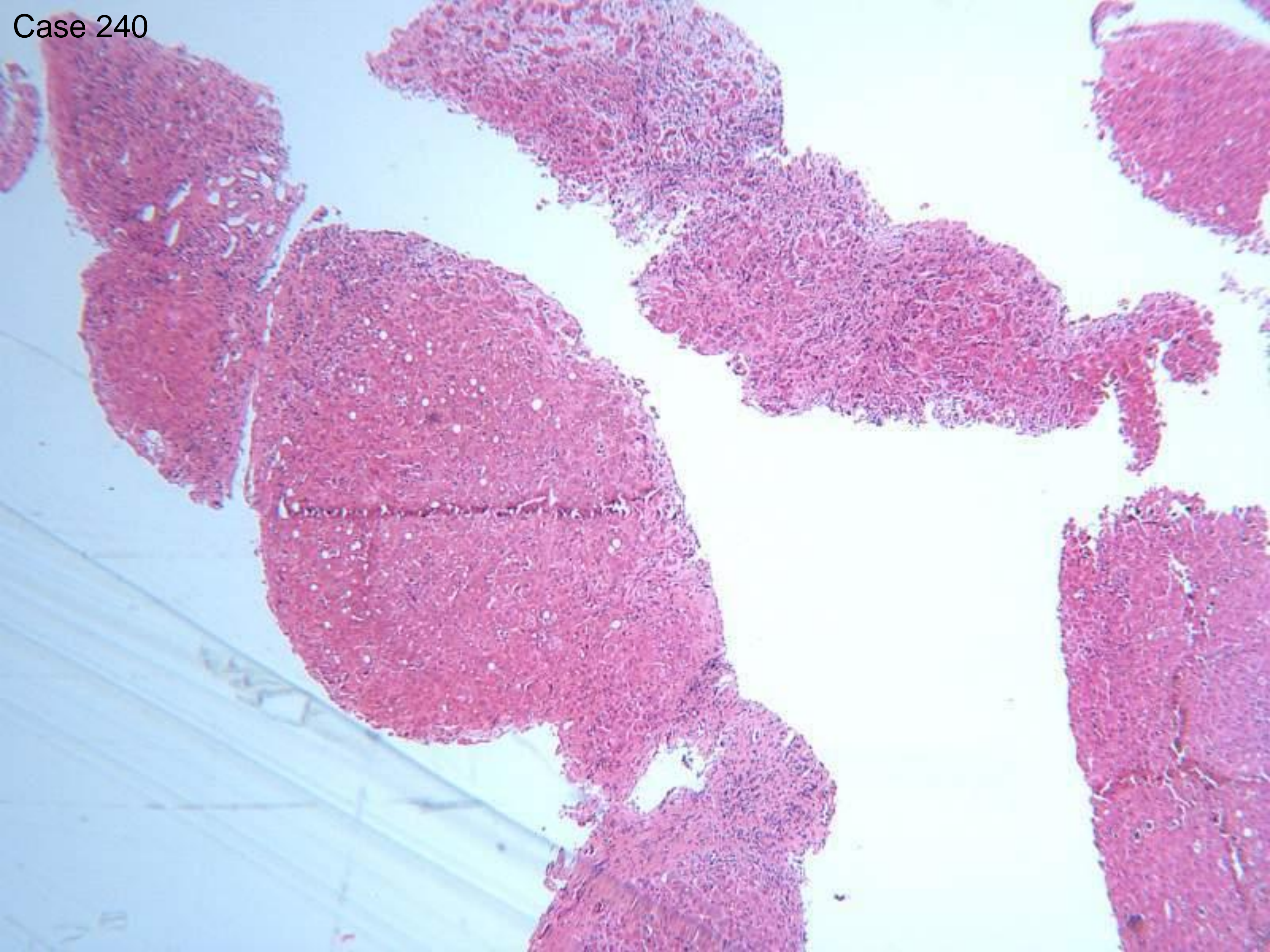
Biopsy done for staging of disease – diagnosed as bridging fibrosis but not cirrhosis.

Case 240

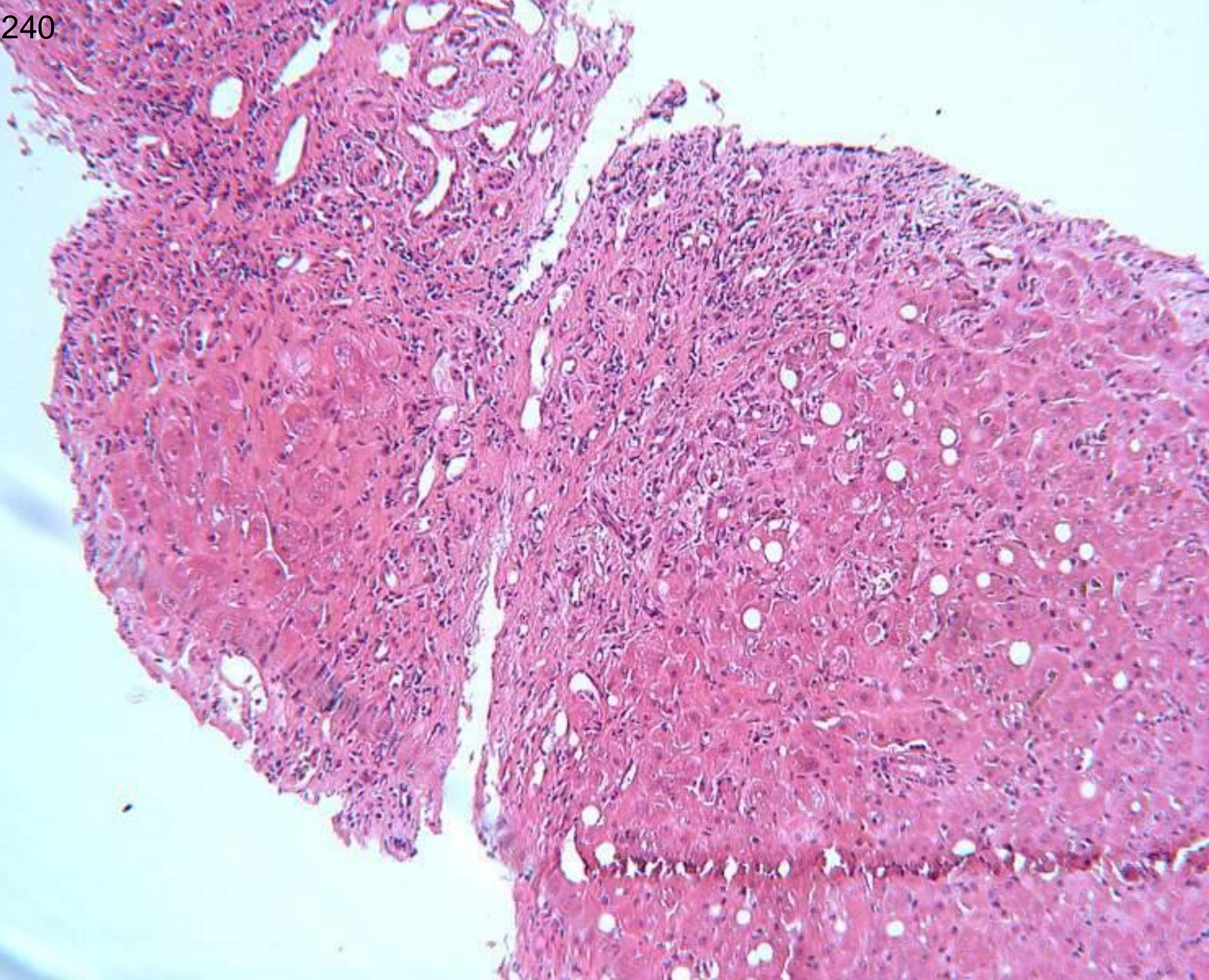
44M. Jaundice, Ascites, abnormal clotting, suspected ALD, ?alcoholic hepatitis, ?cirrhosis.

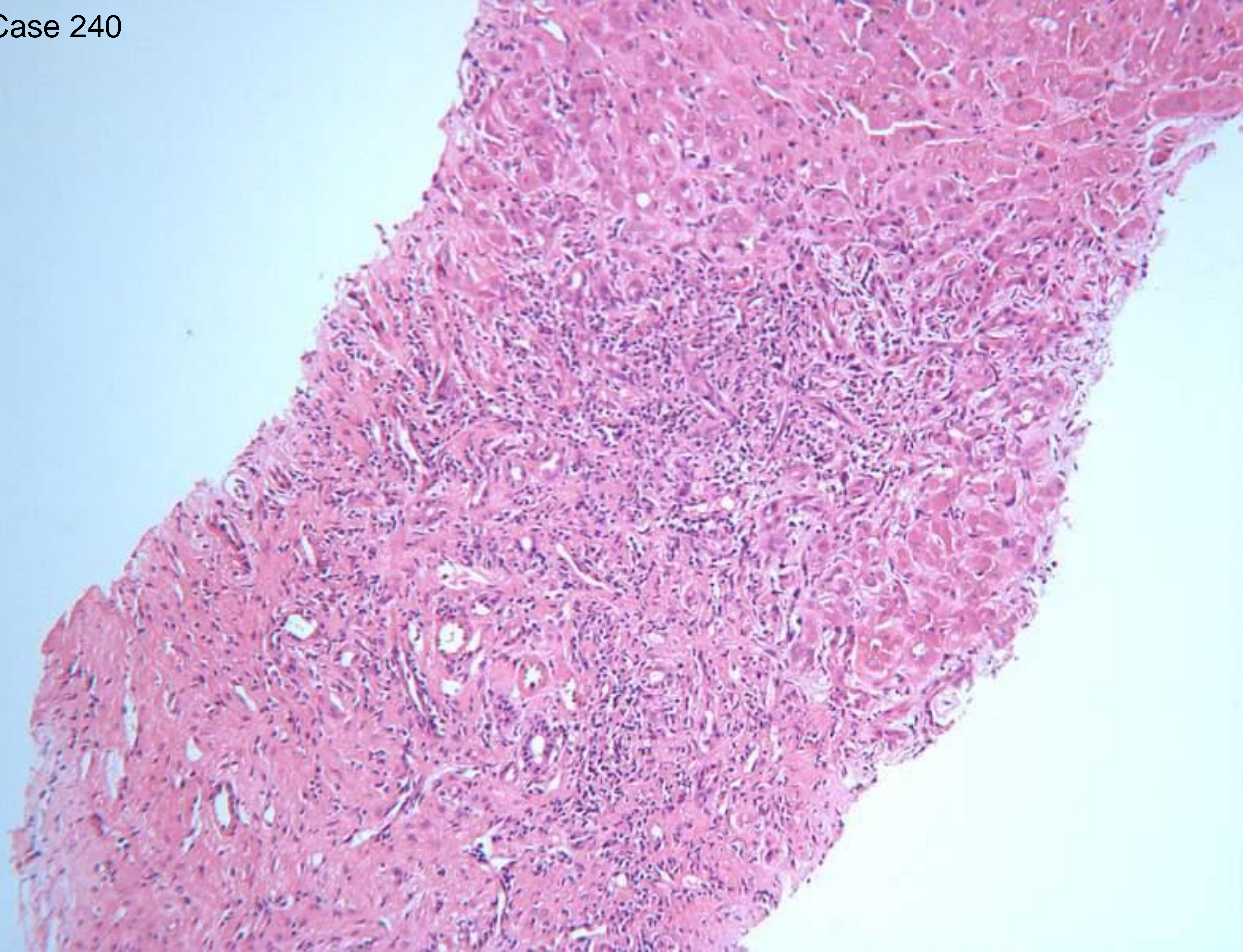
Case 240




Case 240

Case 240

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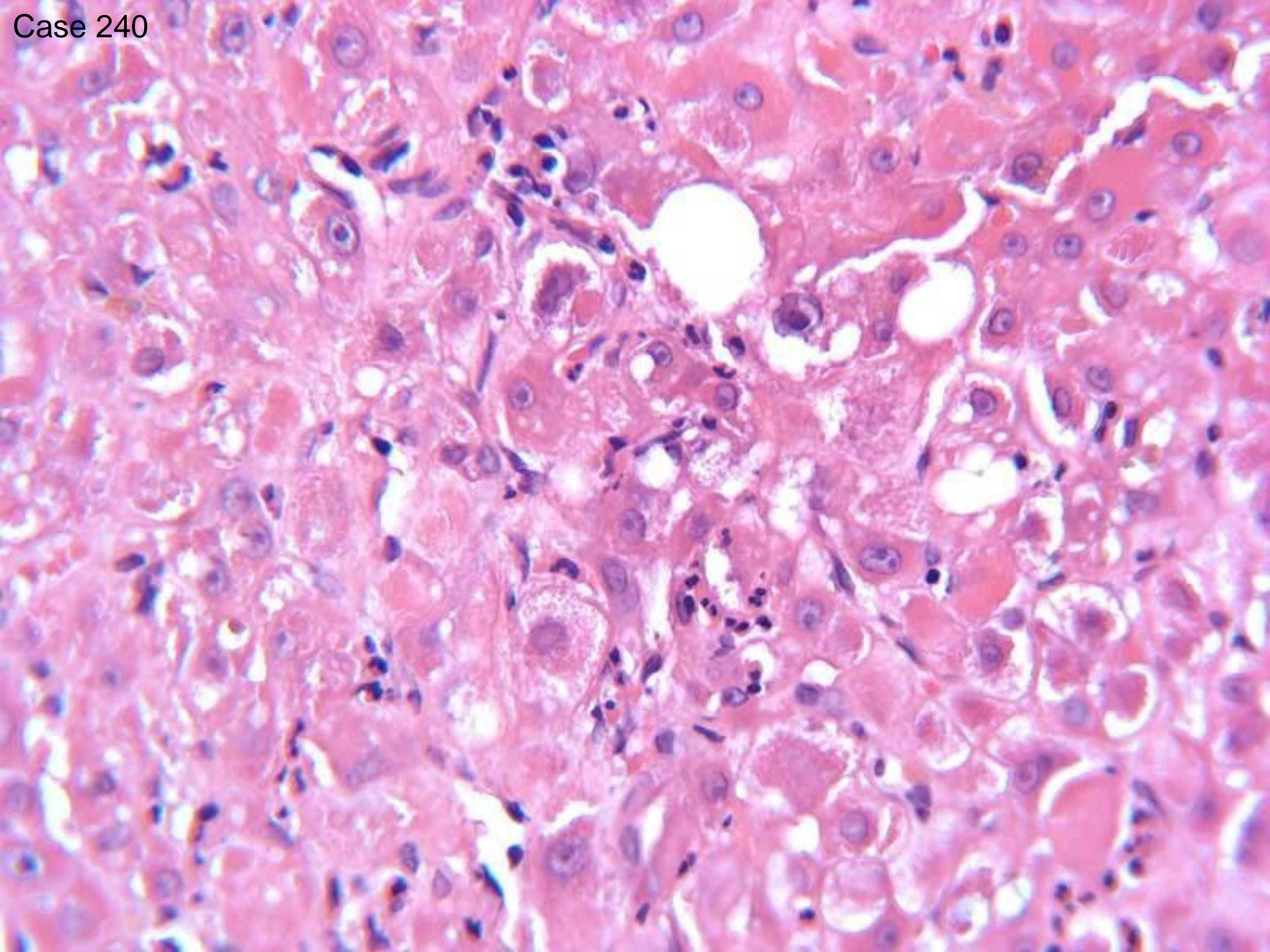
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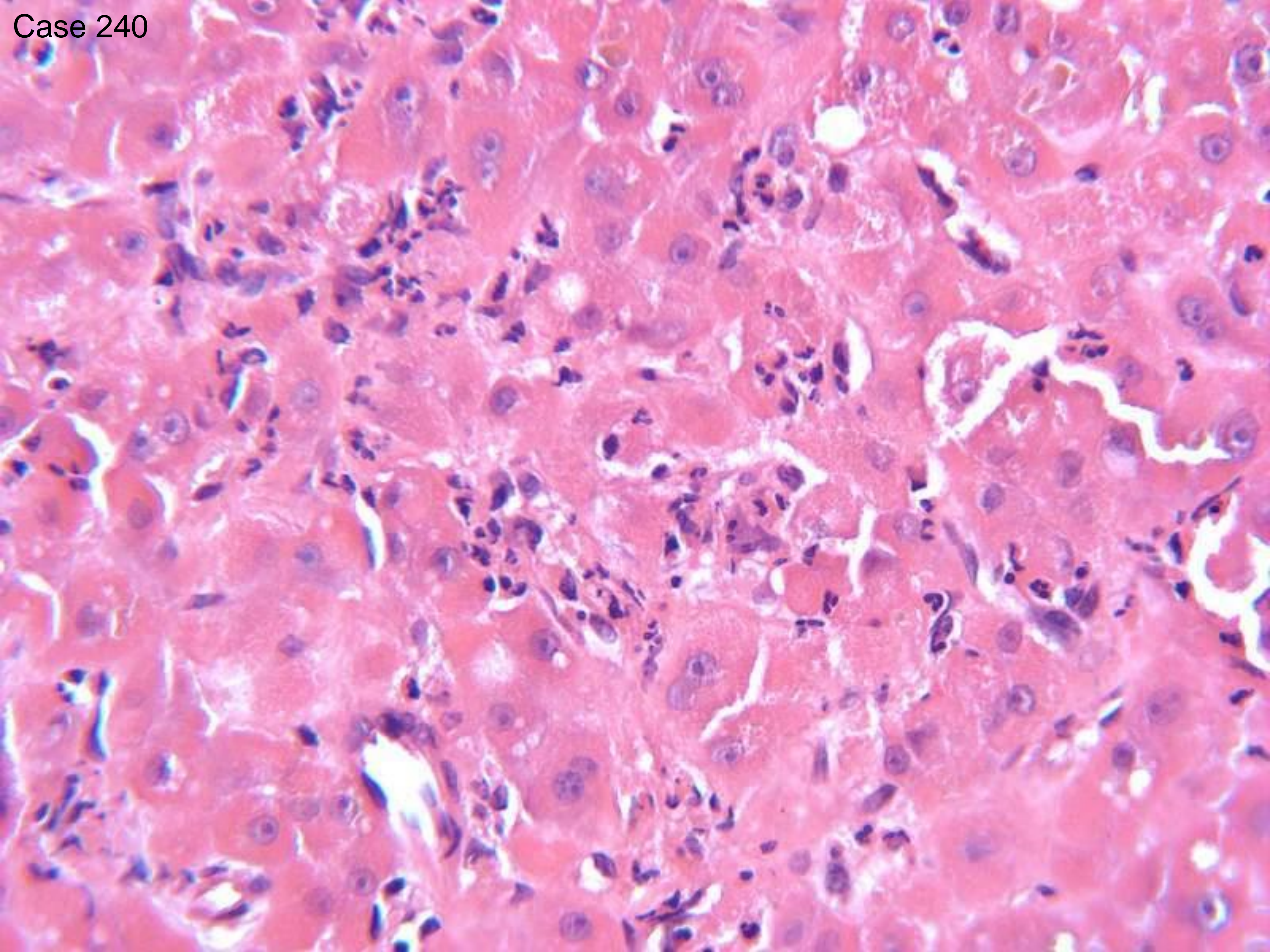
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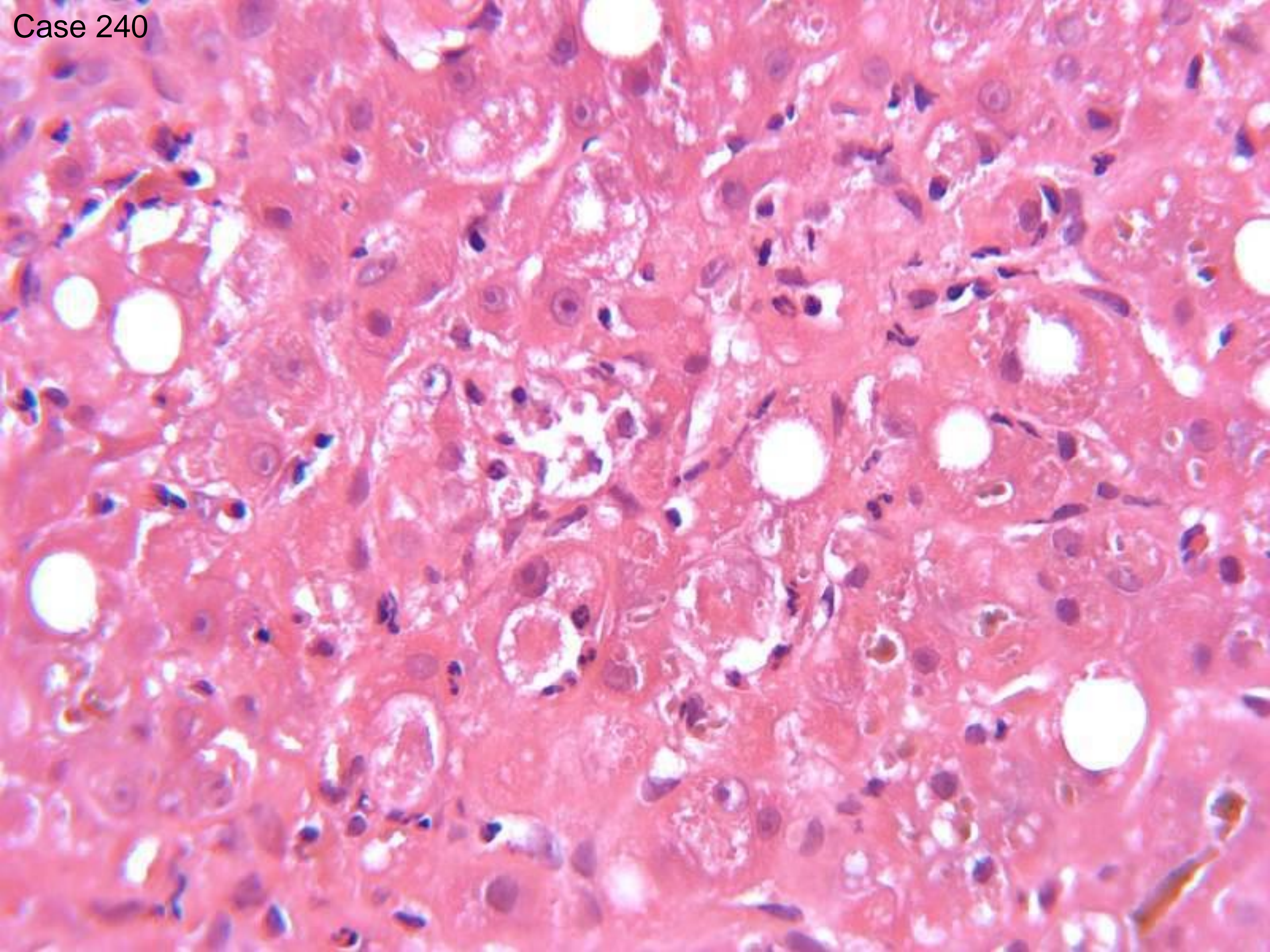
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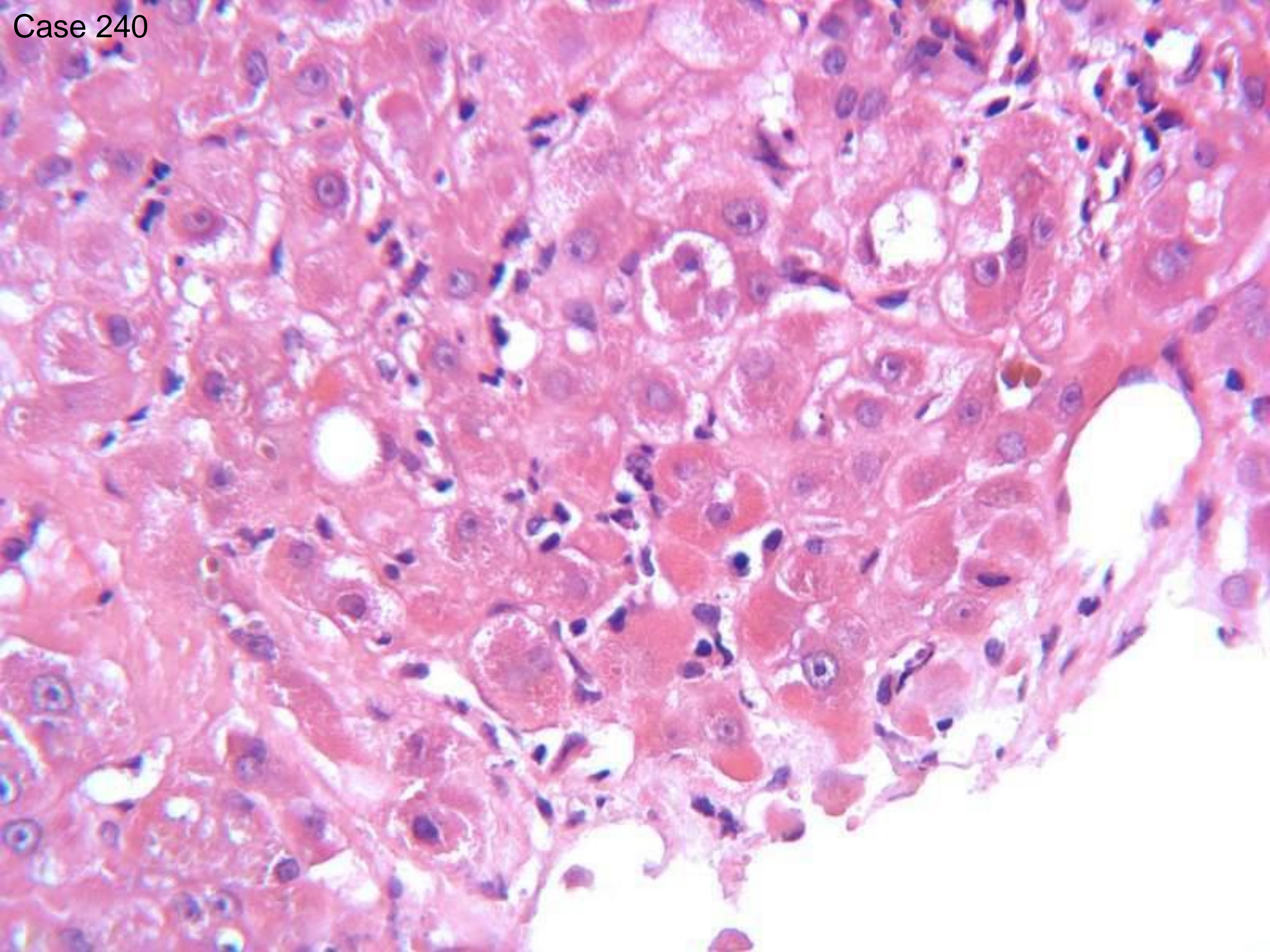
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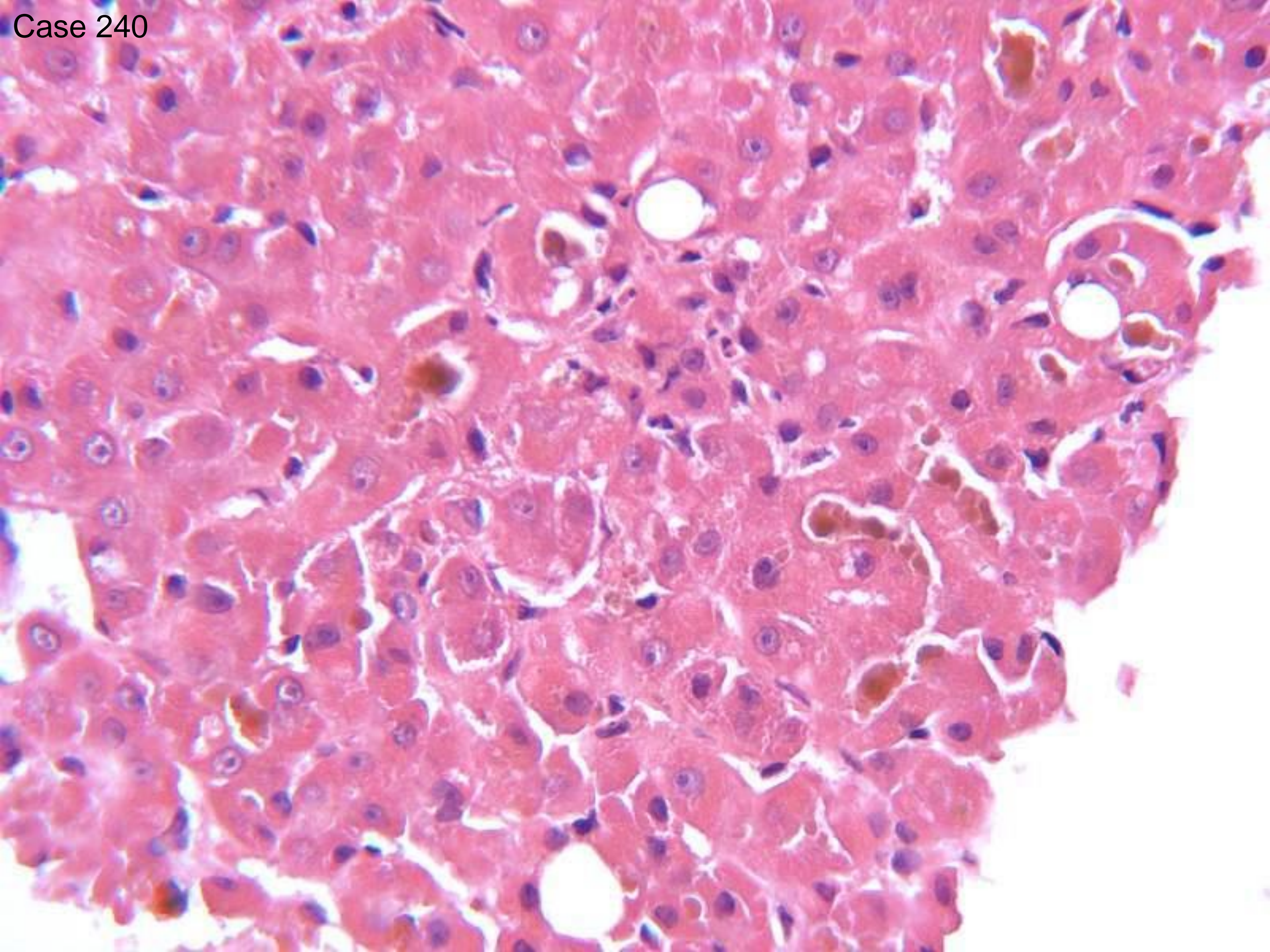
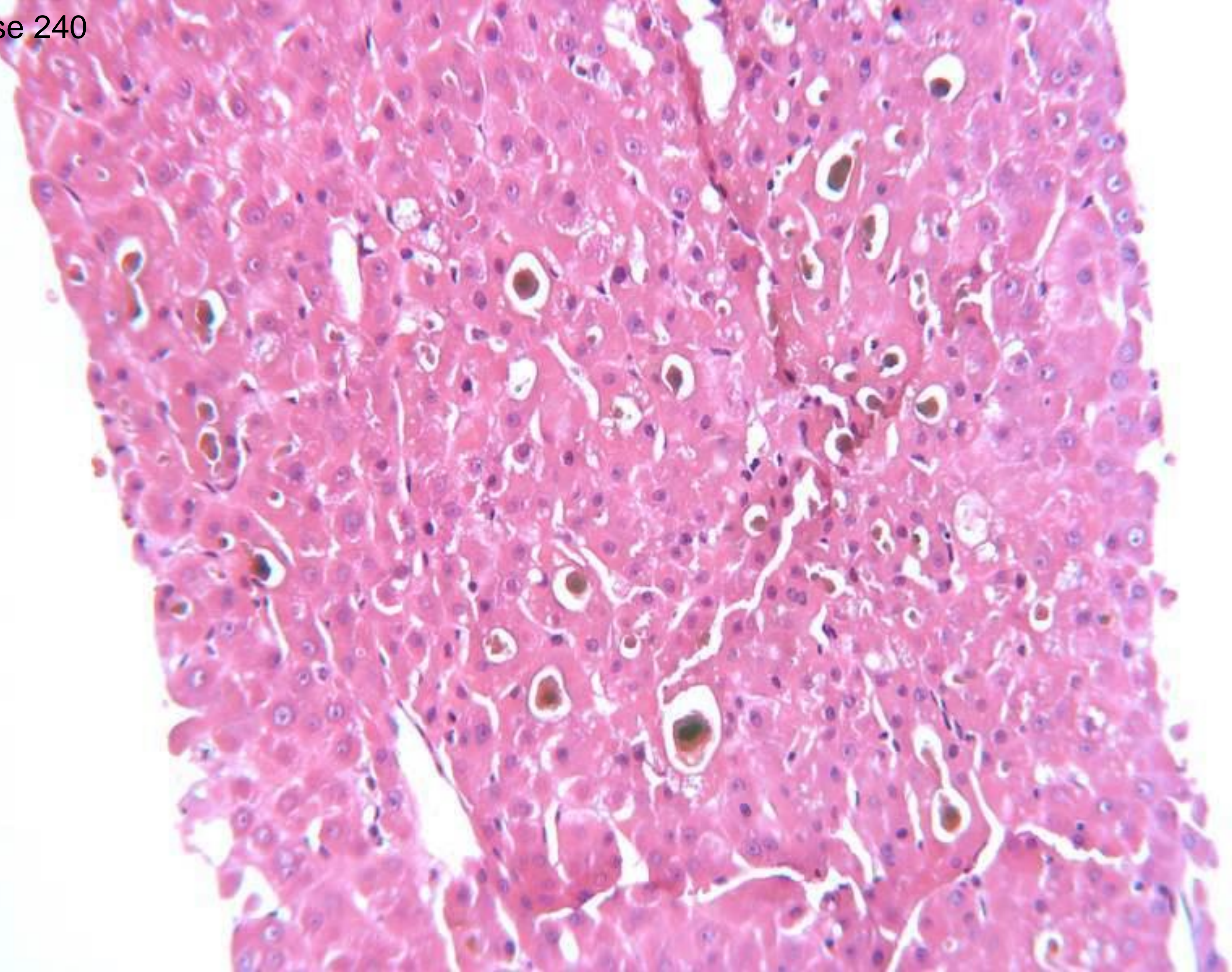
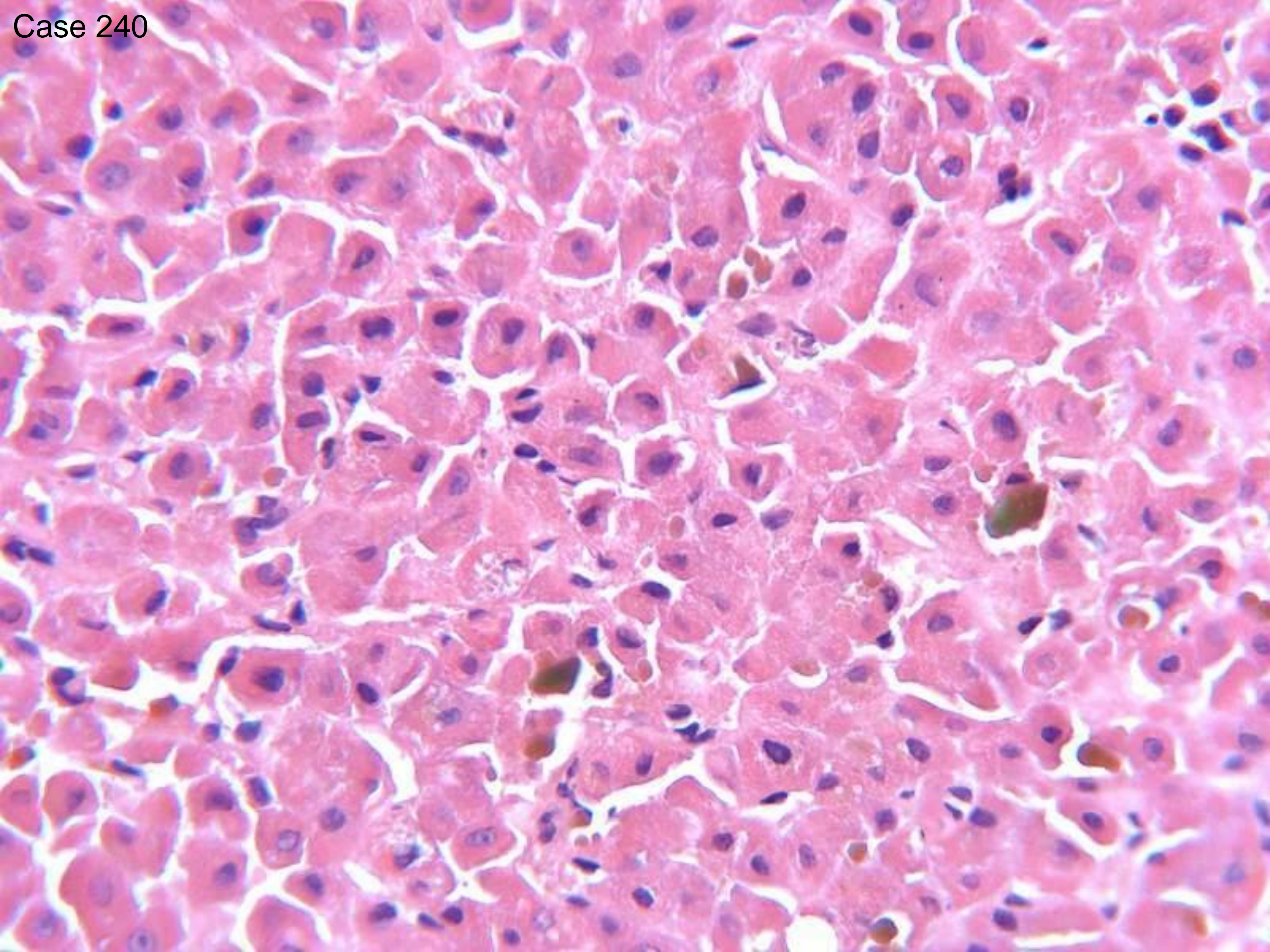

Case 240

Case 240

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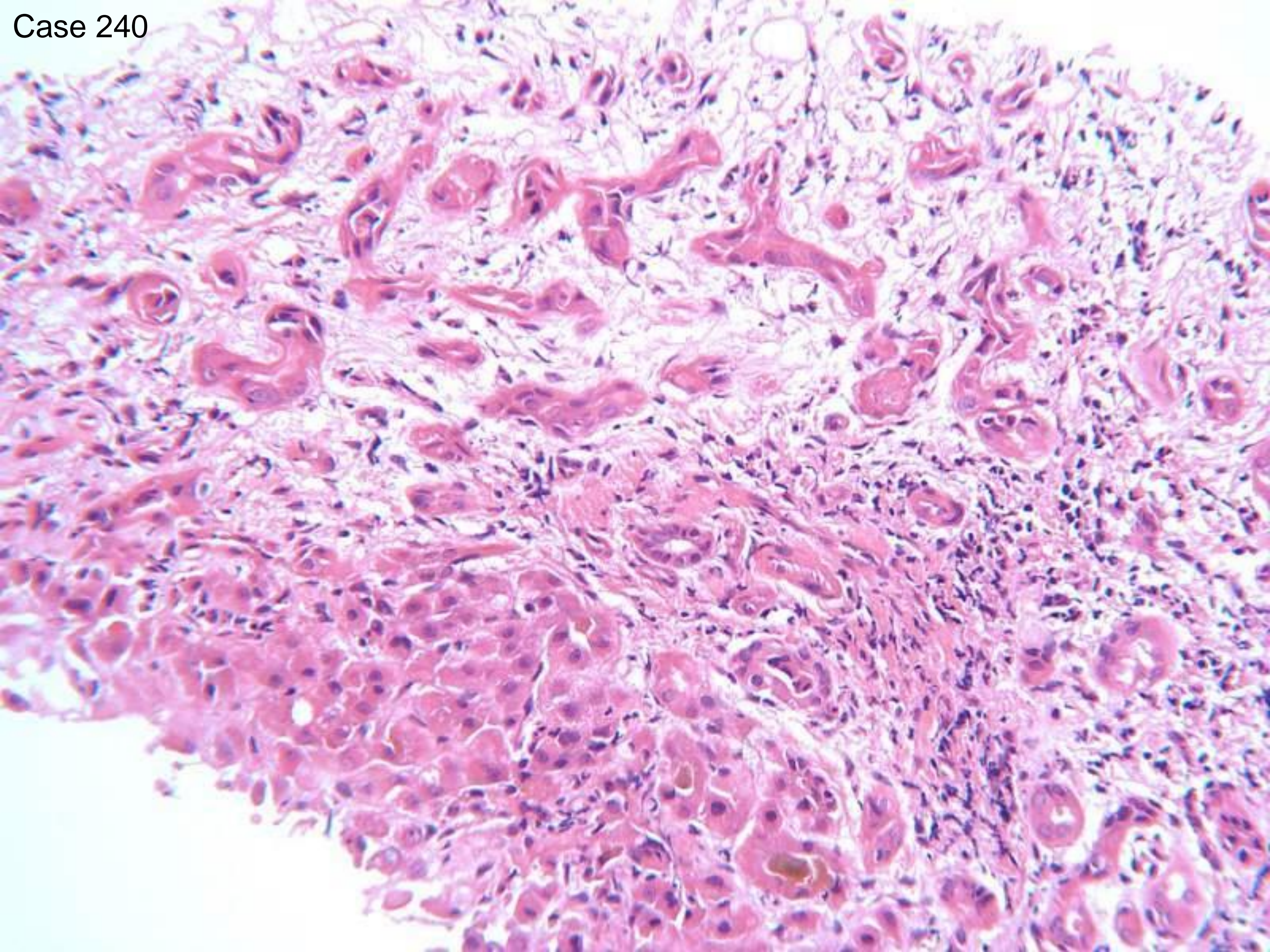

Case 240

Case 240: Results

21 alcoholic hepatitis and cirrhosis
6 alcoholic hepatitis
9 cirrhosis (probable or definite)
3 ALD + additional cause for cholestasis
1 cholestatic ALD

4 chronic biliary disease
1 suspect PSC
1 acute cholestasis ? cause – drugs,
2 drug related cholestasis,
1 cholestasis, not typical of alcohol

1 drug reaction, d/d viral, alcohol, sepsis, LBDO.
1 A1ATD
1 ? Wilson's
2 HCC and cirrhosis
5 suspect HCC
1 ? cholangiocarcinoma

Scoring:
Not suitable for scoring.

Comments:
2 ?Sepsis to account for decompensation

Case 240

Follow up: Dr Neil

No positive microbiology

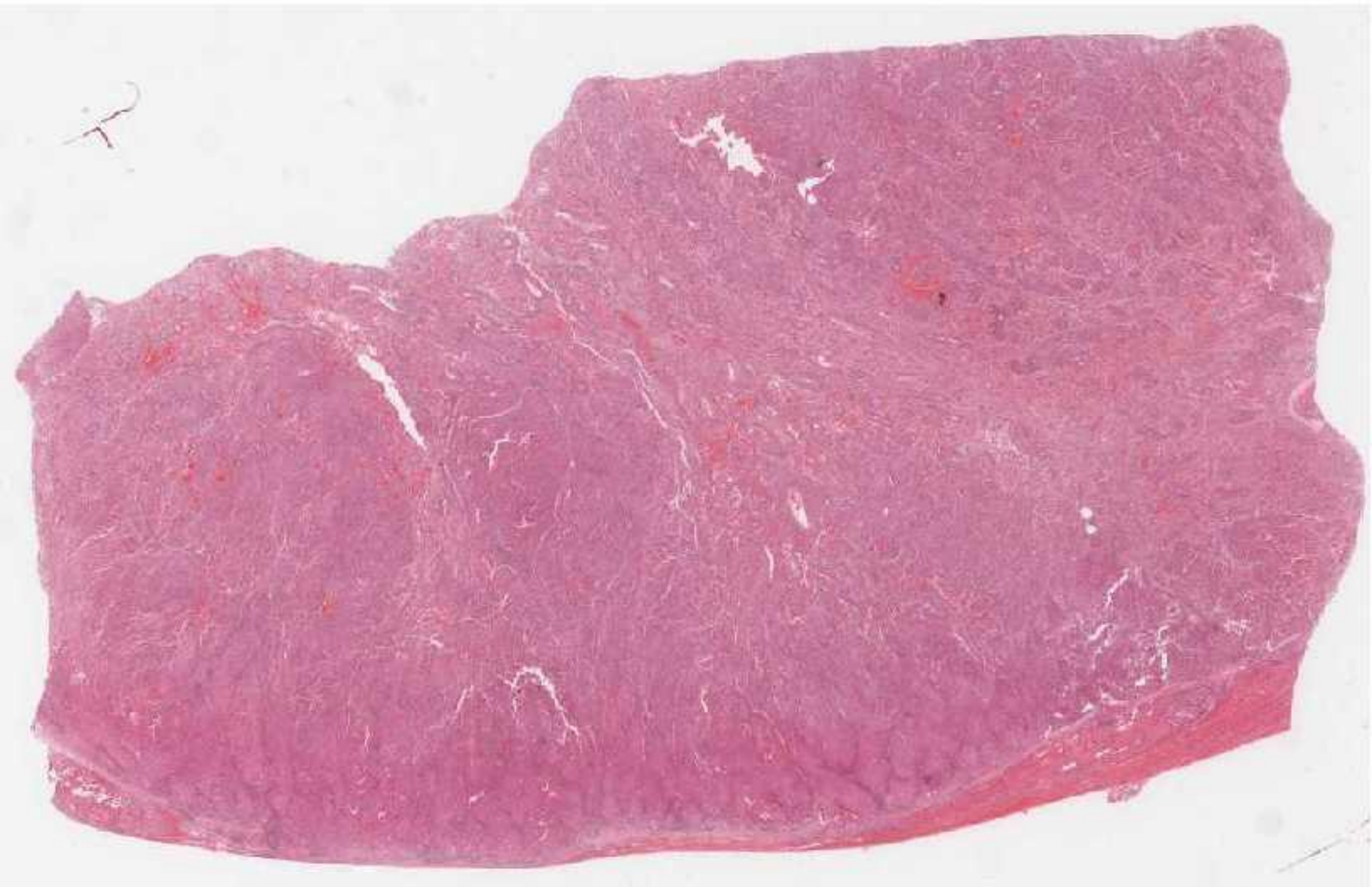
? Details of alcohol and drug history at EQA meeting

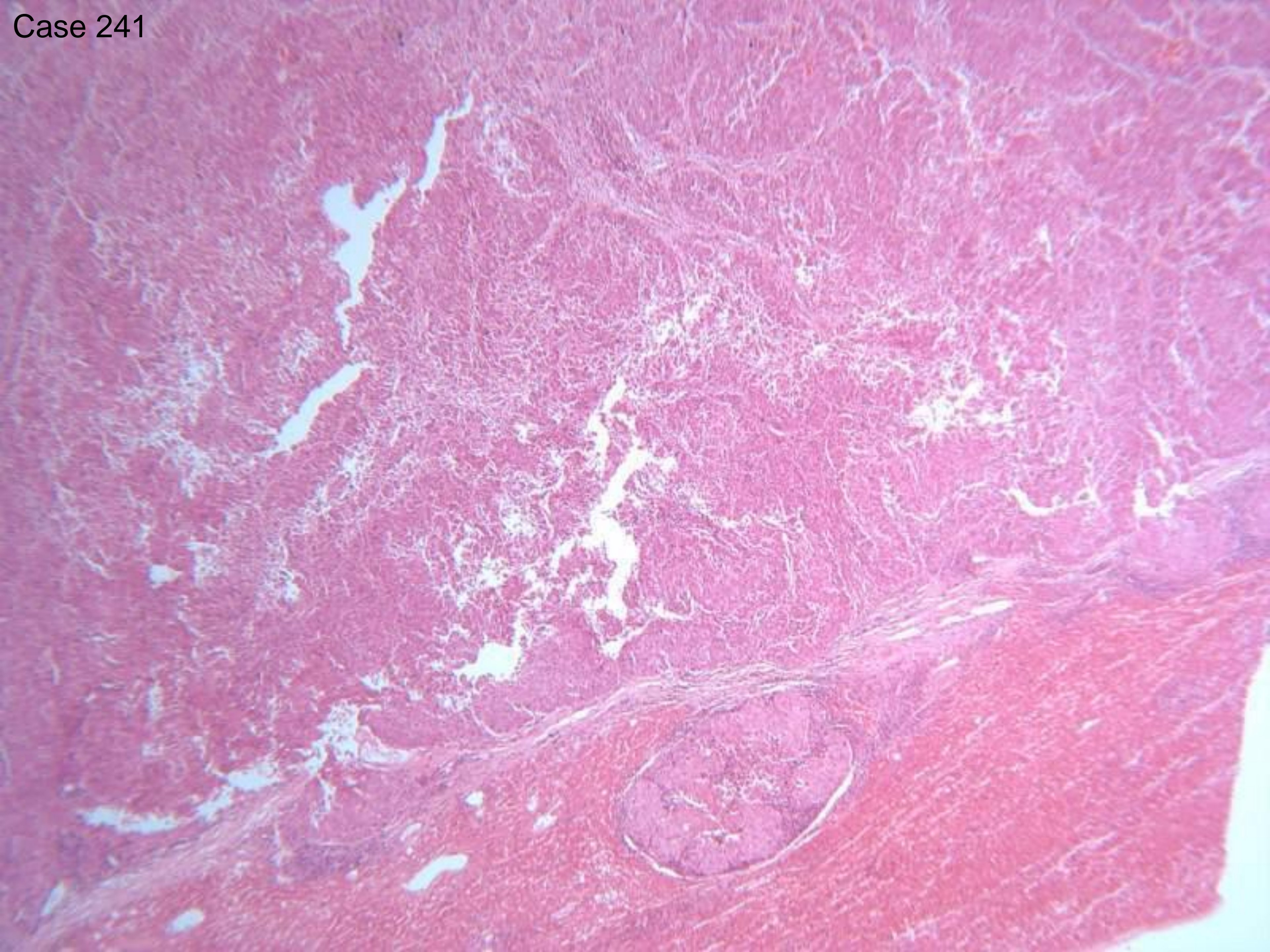
Case 241

54M Right hepatectomy for ??? metastasis.

Right hepatectomy; 2 nodules. The larger nodule is greyish and the smaller nodule black.

Case 241

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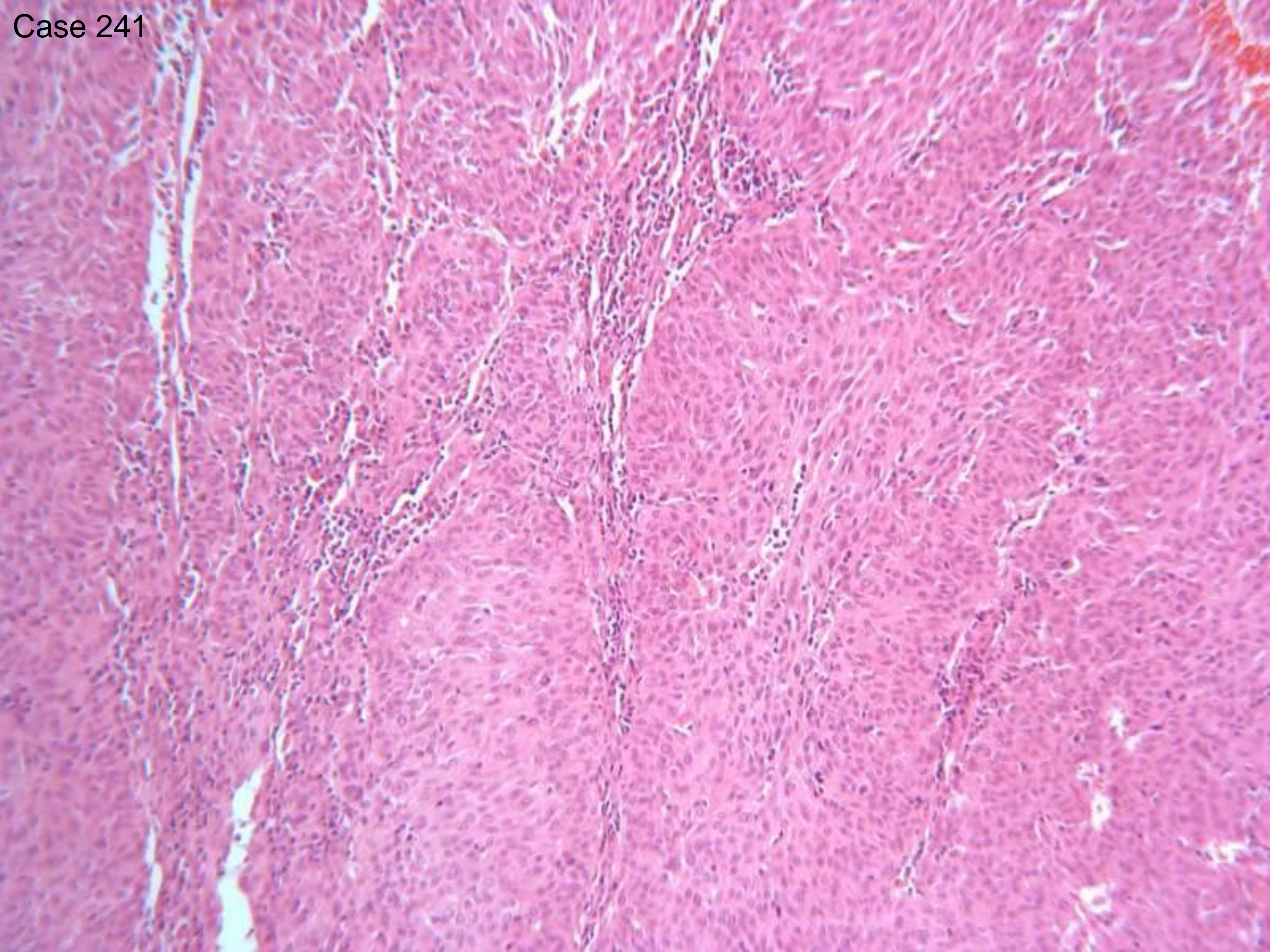
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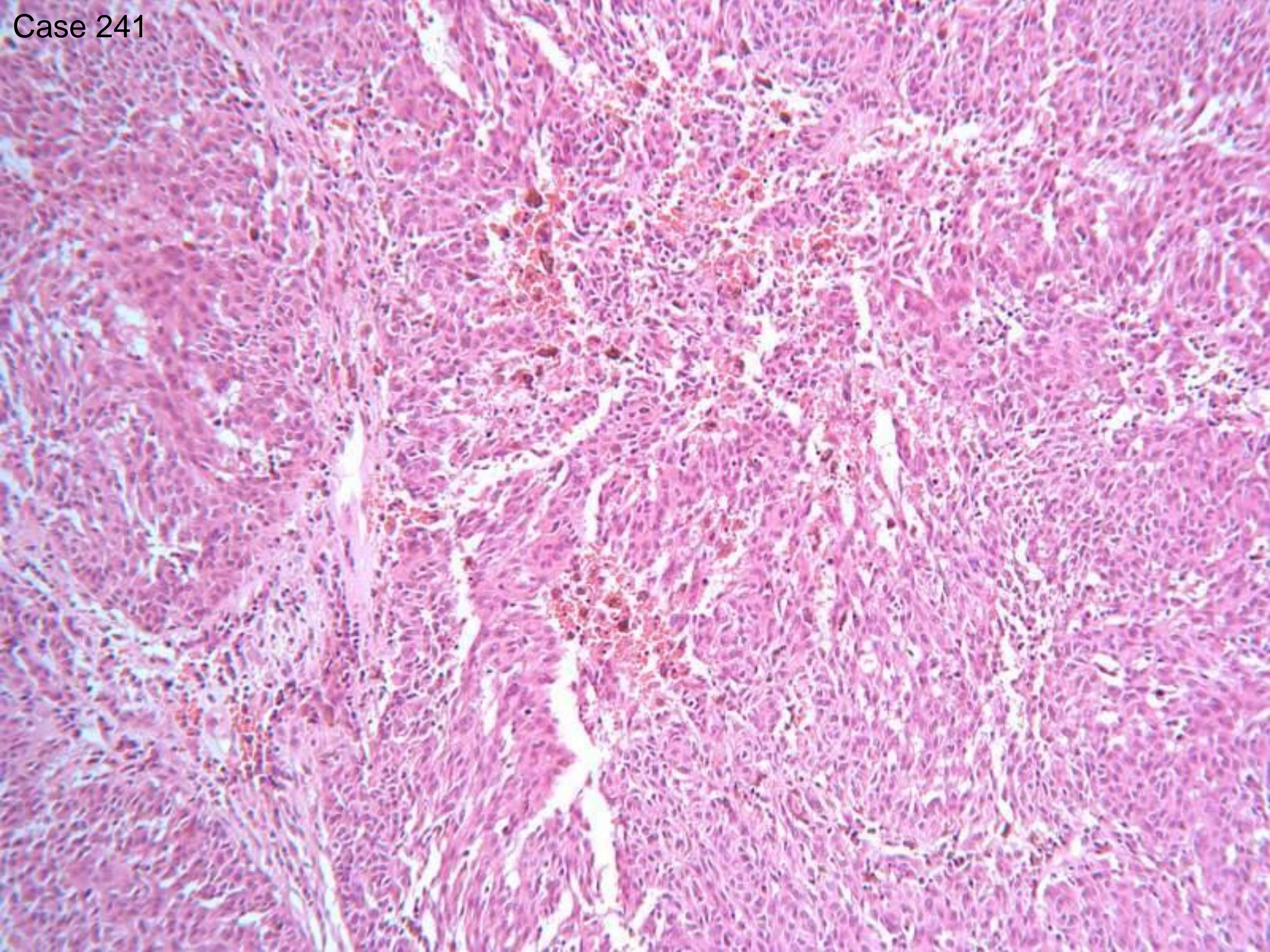
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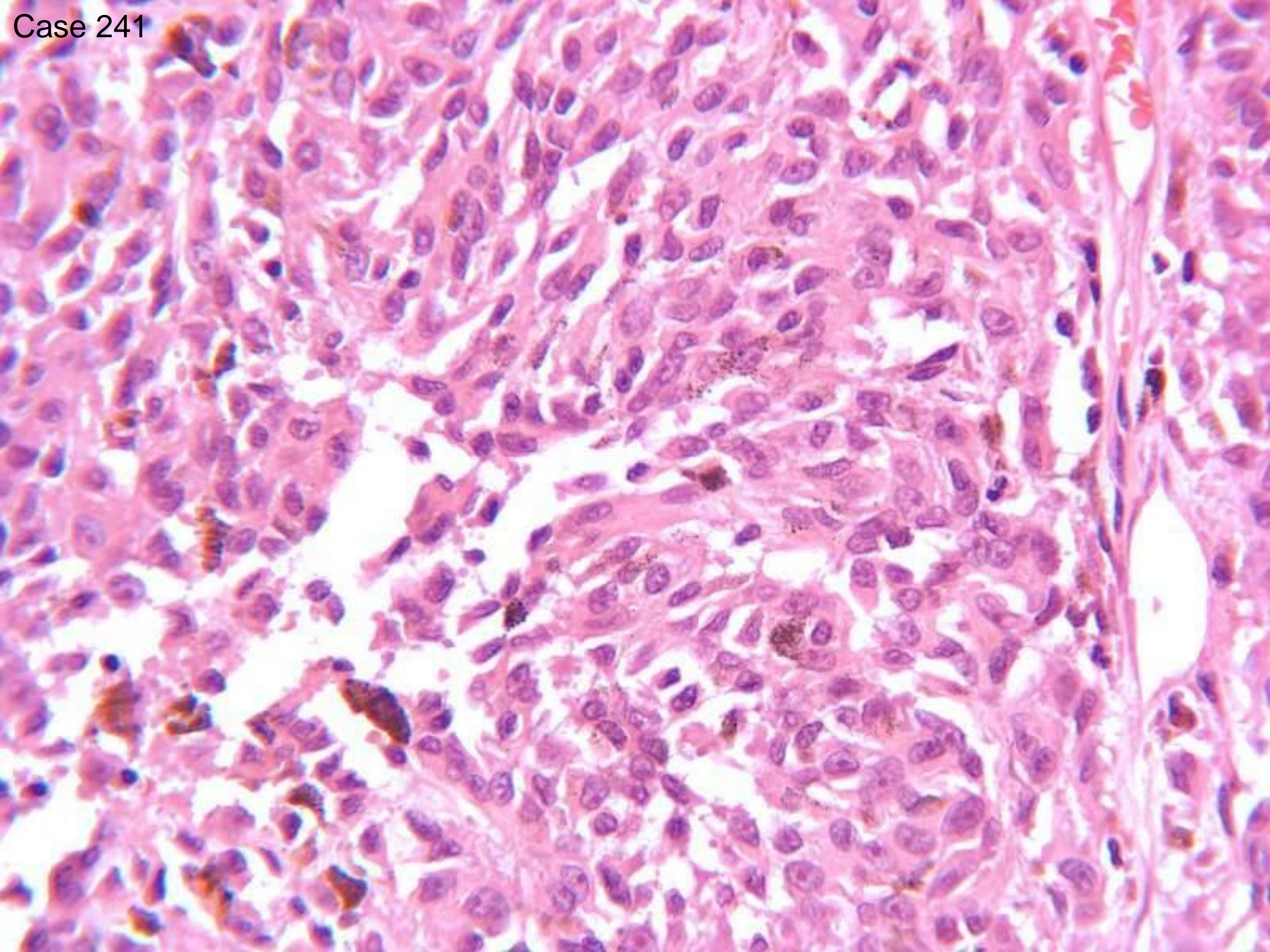
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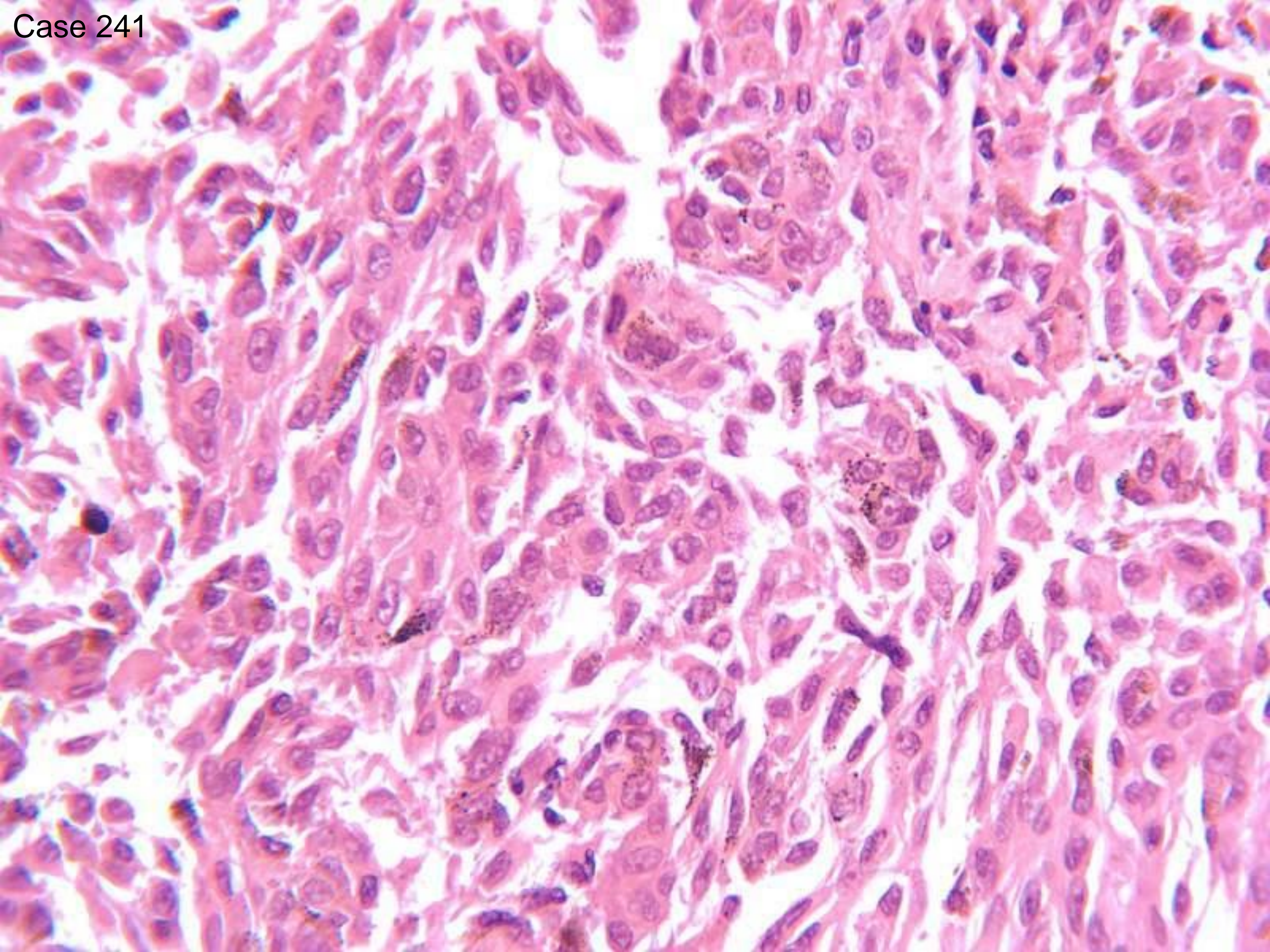
Case 241

Case 241

<u>Results</u>

51 metastatic malignant melanoma

1 angiomyolipoma (PEComa), exclude other spindle tumours
1 metastatic neurendocrine tumour, ?phaeo, ?melanoma
1 HCC
1 HCC > Melanoma
1 metastatic carcinoma/melanoma.

Comments:
12 ? a known primary
22 HMB45/S100
1 ? a glass eye
5 other immunos

Scoring: The H & E morphology should be sufficient to diagnosis metastatic melanoma unless proved otherwise with immunohistochemistry. The five alternative diagnoses were therefore rejected for EQA purposes.

Case 241

Follow up; Dr Quaglia

Left ocular melanoma enucleation 1998

Liver lesion S100 +ve