National Liver EQA Scheme Circulation U

Glasgow March 27th 2007

Business meeting

Increasing membership – increase number of cells, 6 per cell

Second class post – increase circulation interval to 3 weeks from autumn 2007

No action points, but 1 person no response for 3 circulations, will be removed,

1 person no response to 2 circulations – letter

Update meeting Thursday December 6th Lancaster, followed by hollow GI meeting on 7th – topic MDTs

CPA accreditation – not at present, but reviewing documents and will circulate a questionnaire

Documents – dataset for liver tumours – primary and secondary, at RCPath, will be in consultation process shortly

Tissue pathways – completed version circulated to EQA members last autumn – submission due May 2007

HRGs re-scheduled for pathology, work in progress on assigning bands to specimens – ?informed by data from Carter pilot sites

National Group representing Liver Pathology

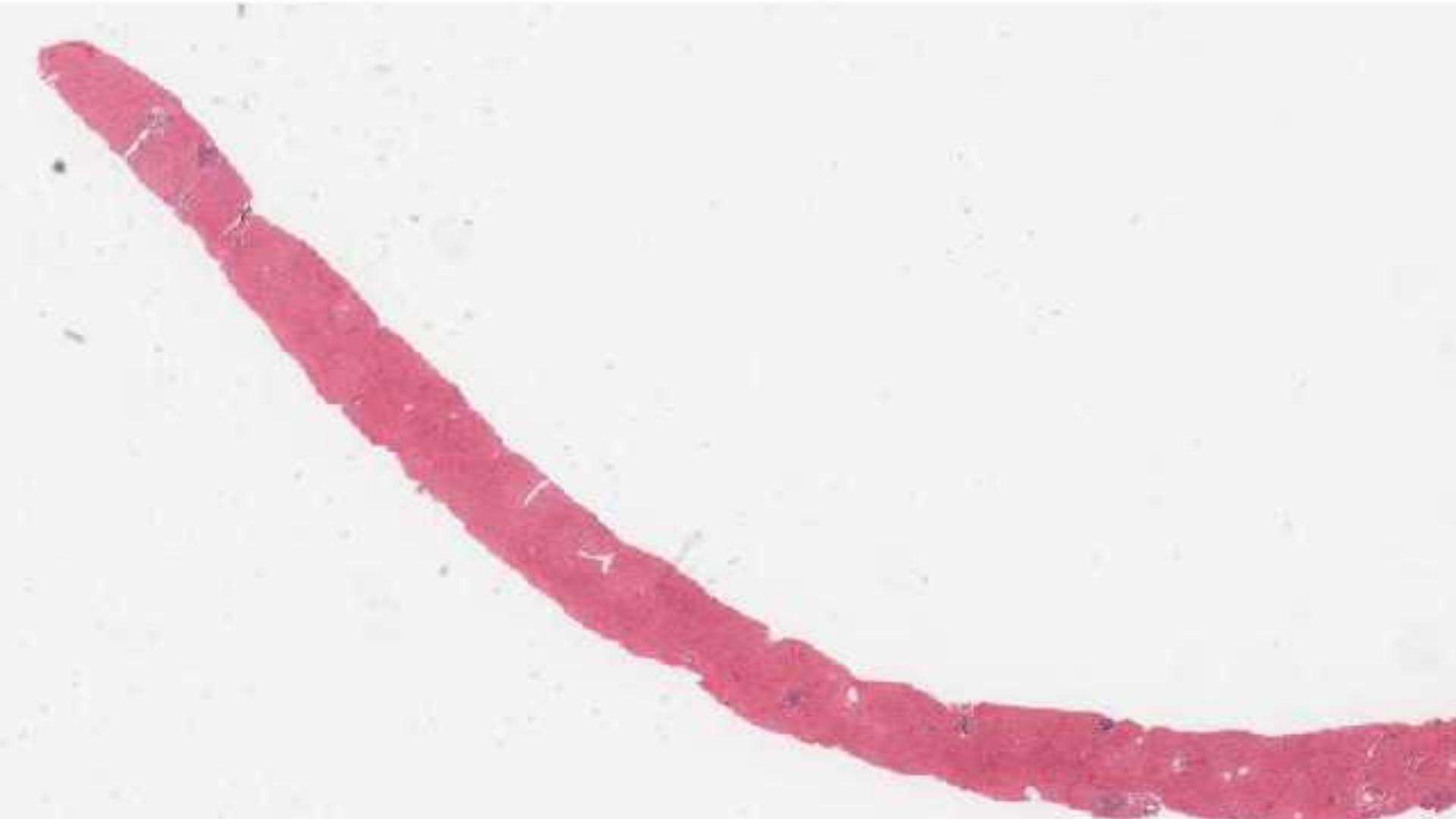
- sub-committee of BSG Pathology section – to be discussed in committee meeting on Thursday 29th March

Case 254

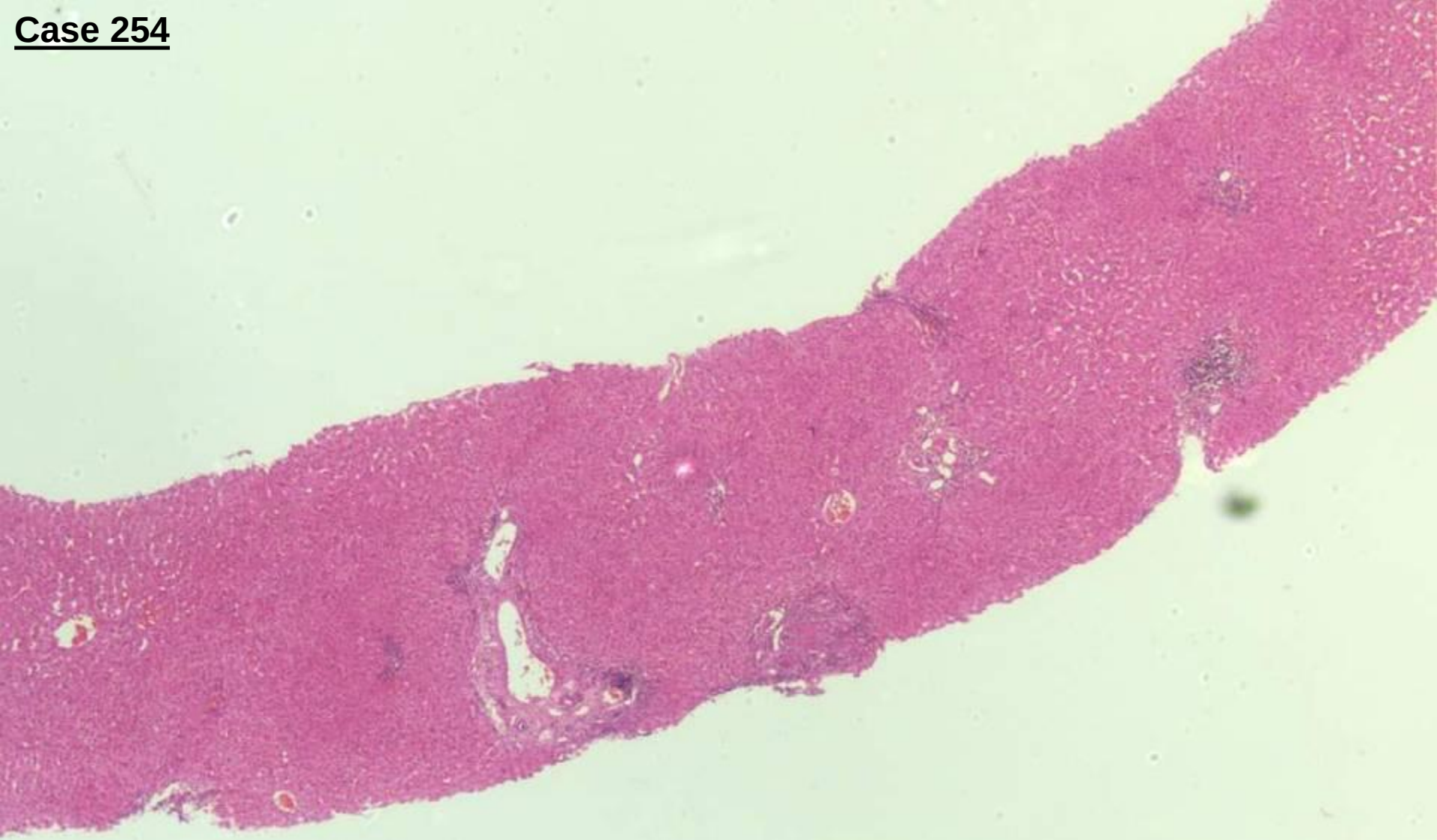
47 F

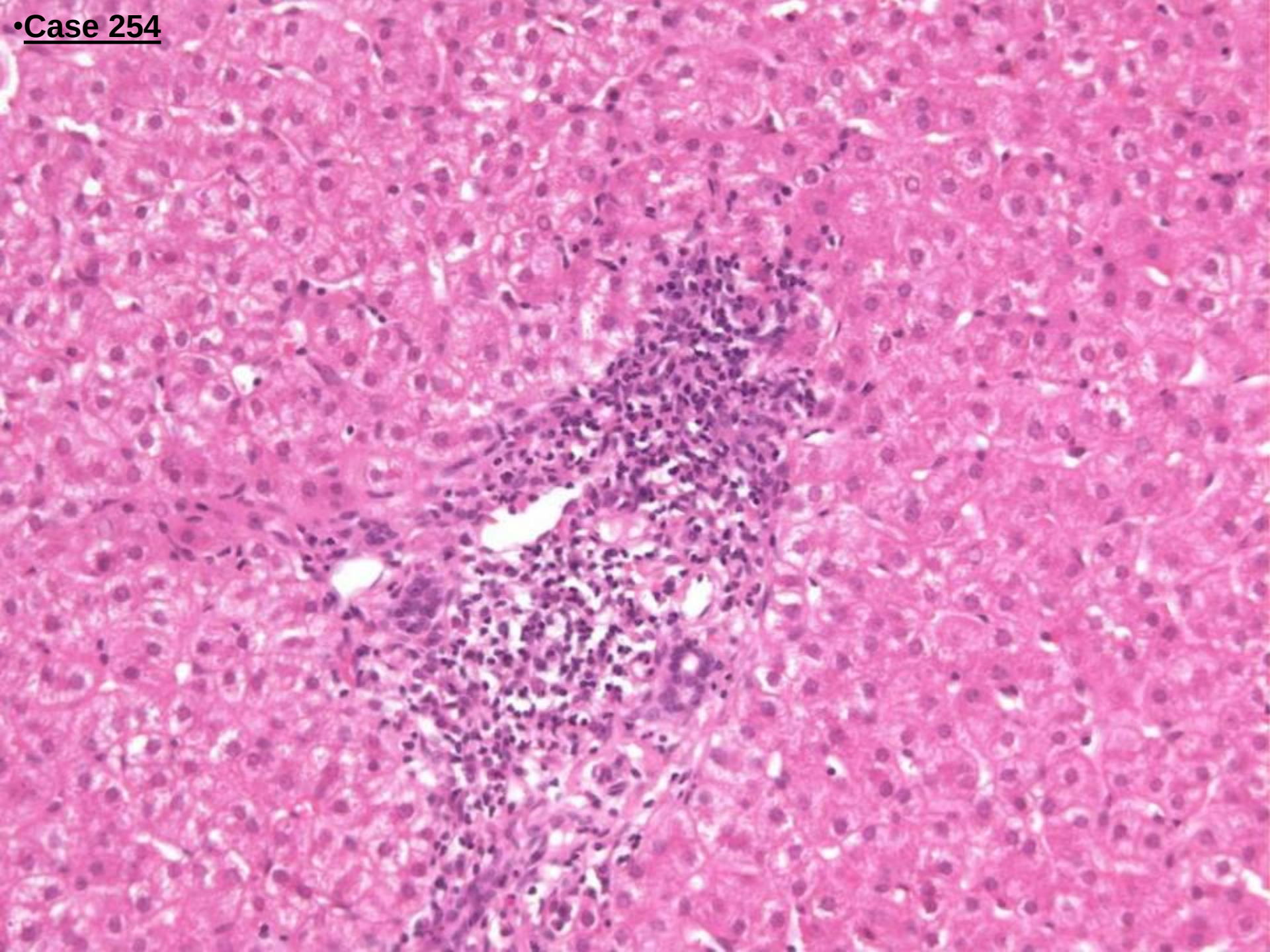
HCV infection. Genotype 1. Prior biopsy in 1998 Ishak 2 fibrosis. ? progression . ALT 1.5x normal. No IV drug history. No treatment.

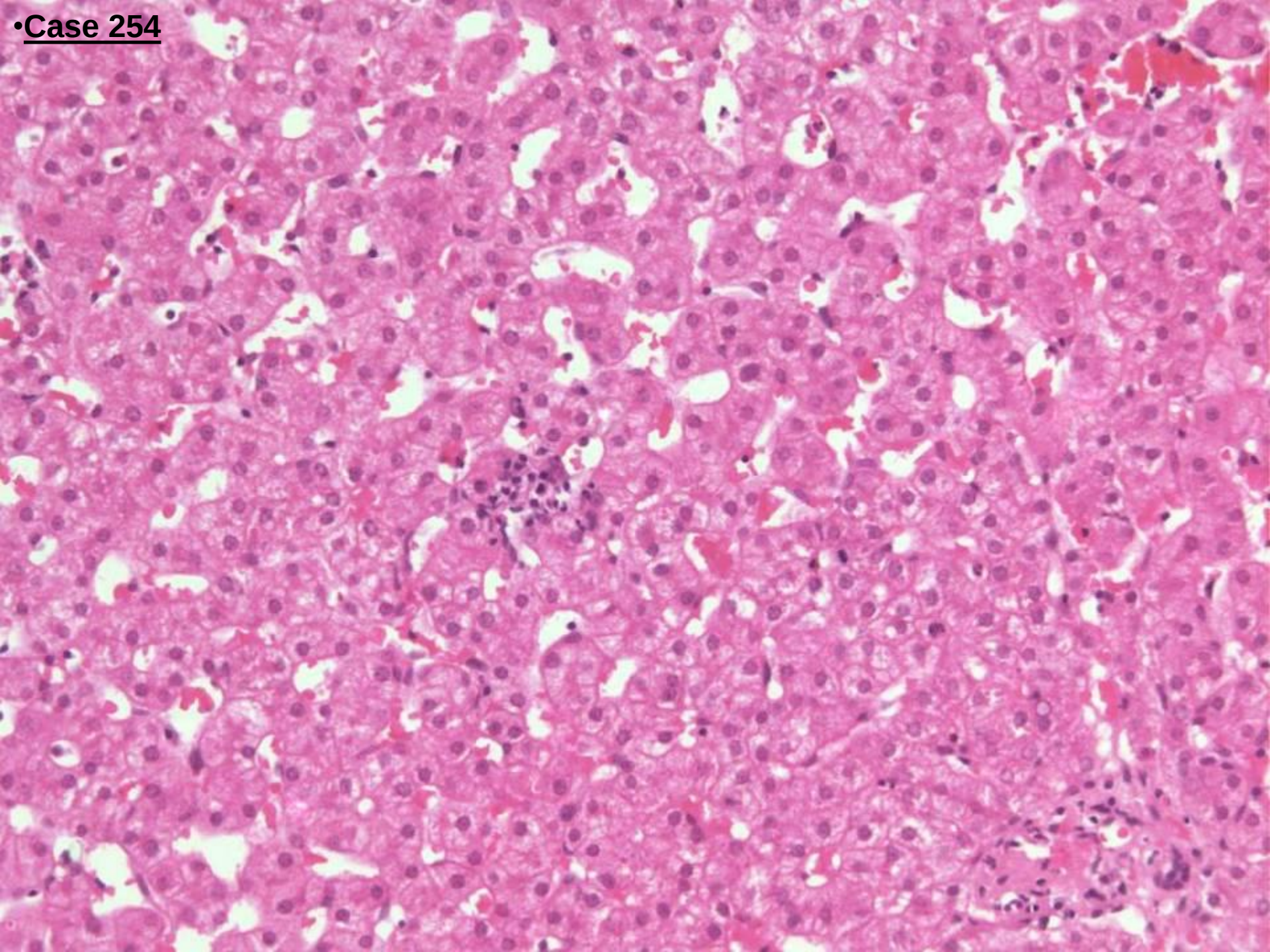
Case 254



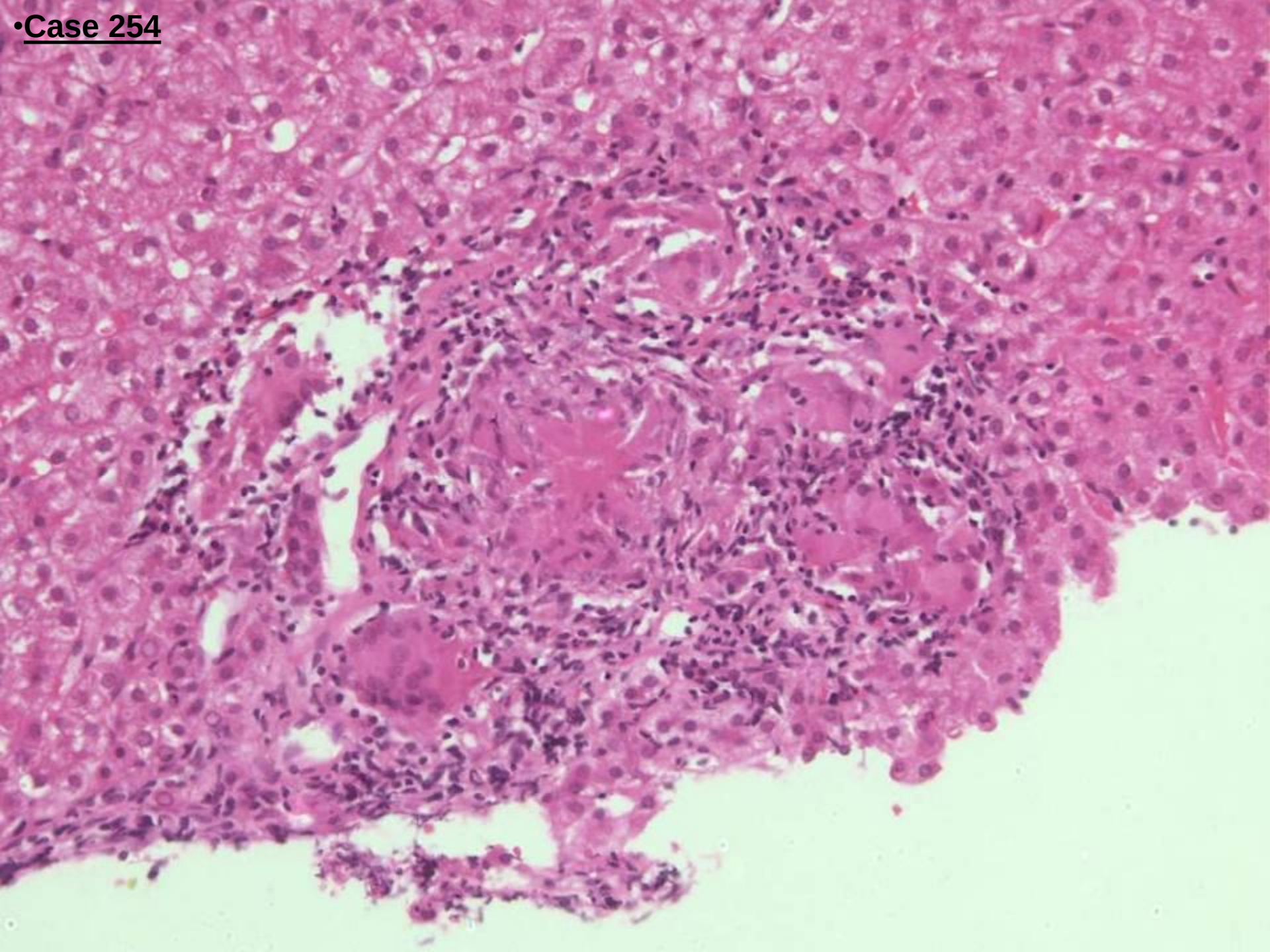
Case 254




•Case 254


•Case 254

•**Case 254**



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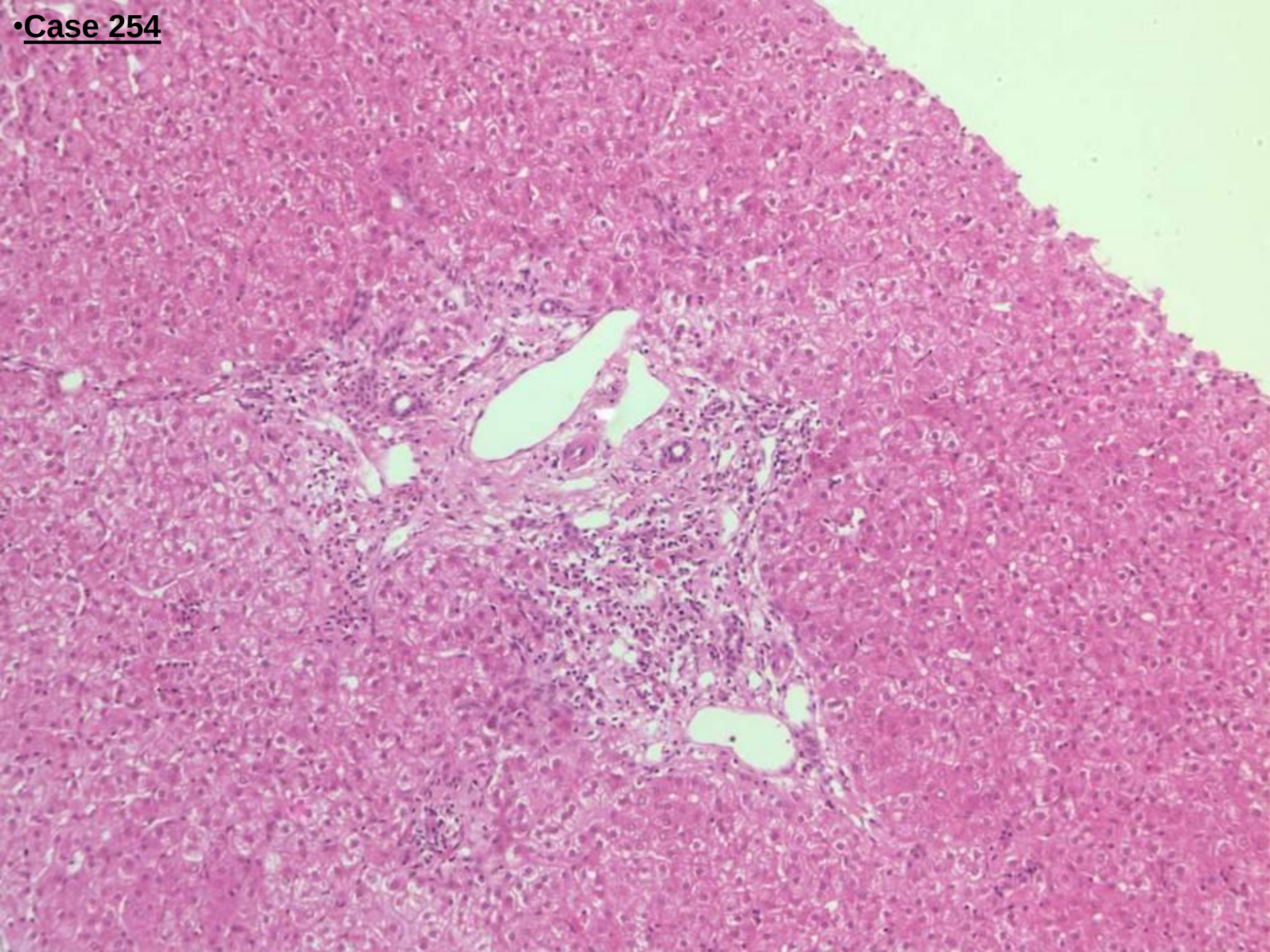


Case 254

59 HCV + granulomas; of which:

8	no comment on HCV severity
39	mild HCV + granulomas
10	moderate HCV + granulomas
2	HCV with bridging fibrosis + granulomas

2 mild HCV, no granulomas mentioned
1 moderate HCV, no granulomas mentioned
1 portal inflammation, ? sarcoid, no mention of HCV

comments on investigation of granulomas necessary?

Of 59 mentioning granulomas and HCV:

50	some indication of differential diagnosis of granulomas
7	gave one cause for granulomas (3 PBC, 2 TB, 2 sarcoidosis)
2	no mention of cause/investigation of granulomas

Case 254

Original diagnosis: Hepatitis C with granulomas.

Ishak grade 1, stage 2,

Exclude underlying PBC

Follow up information:

AMA –ve

No cause for granulomas found

(not sure how hard they looked)

Case 254

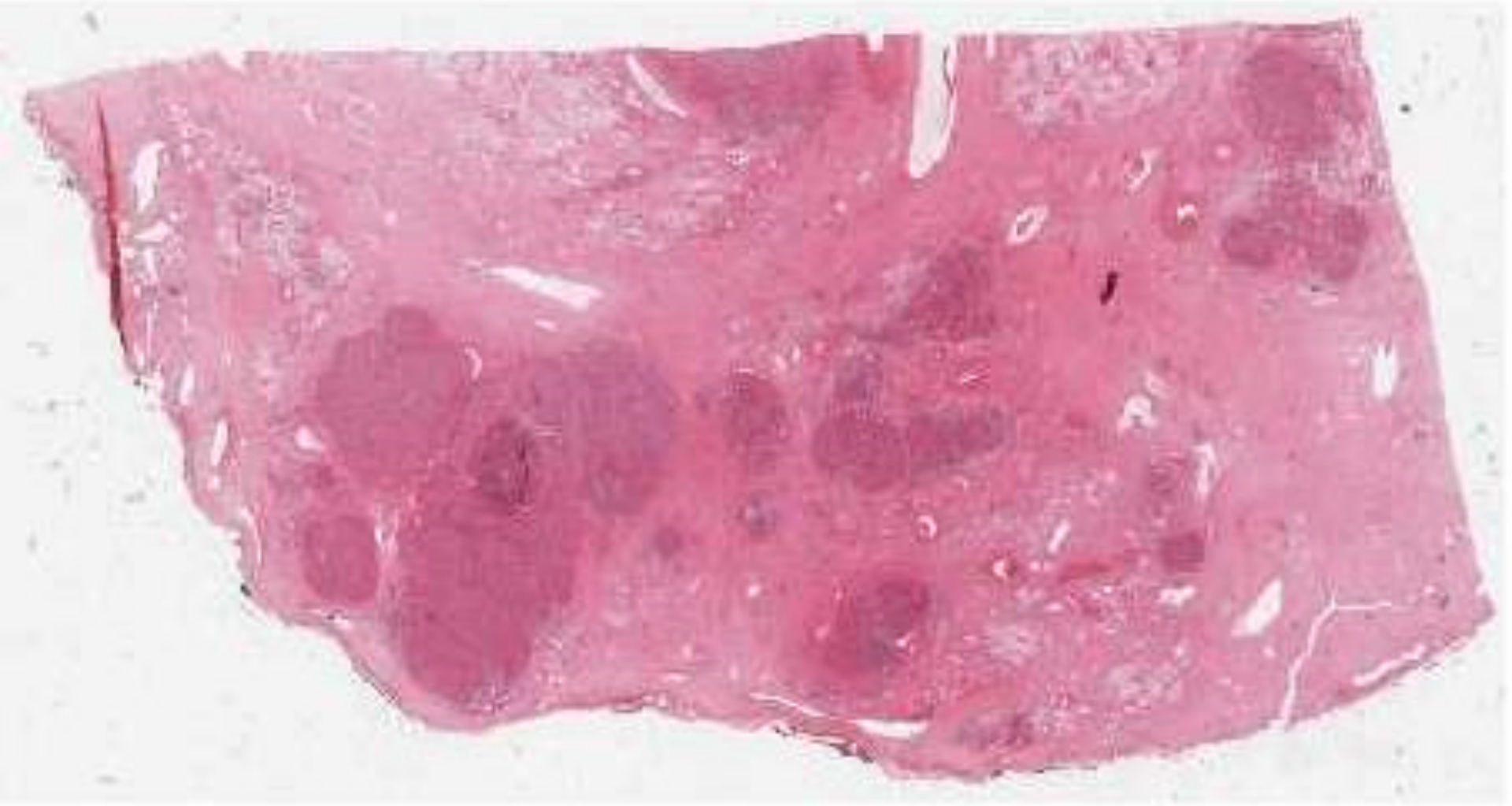
Scoring: Score full marks for including HCV with a comment on severity, no marks if omitted granulomas or HCV; half marks if no comment on HCV severity.

Case 255

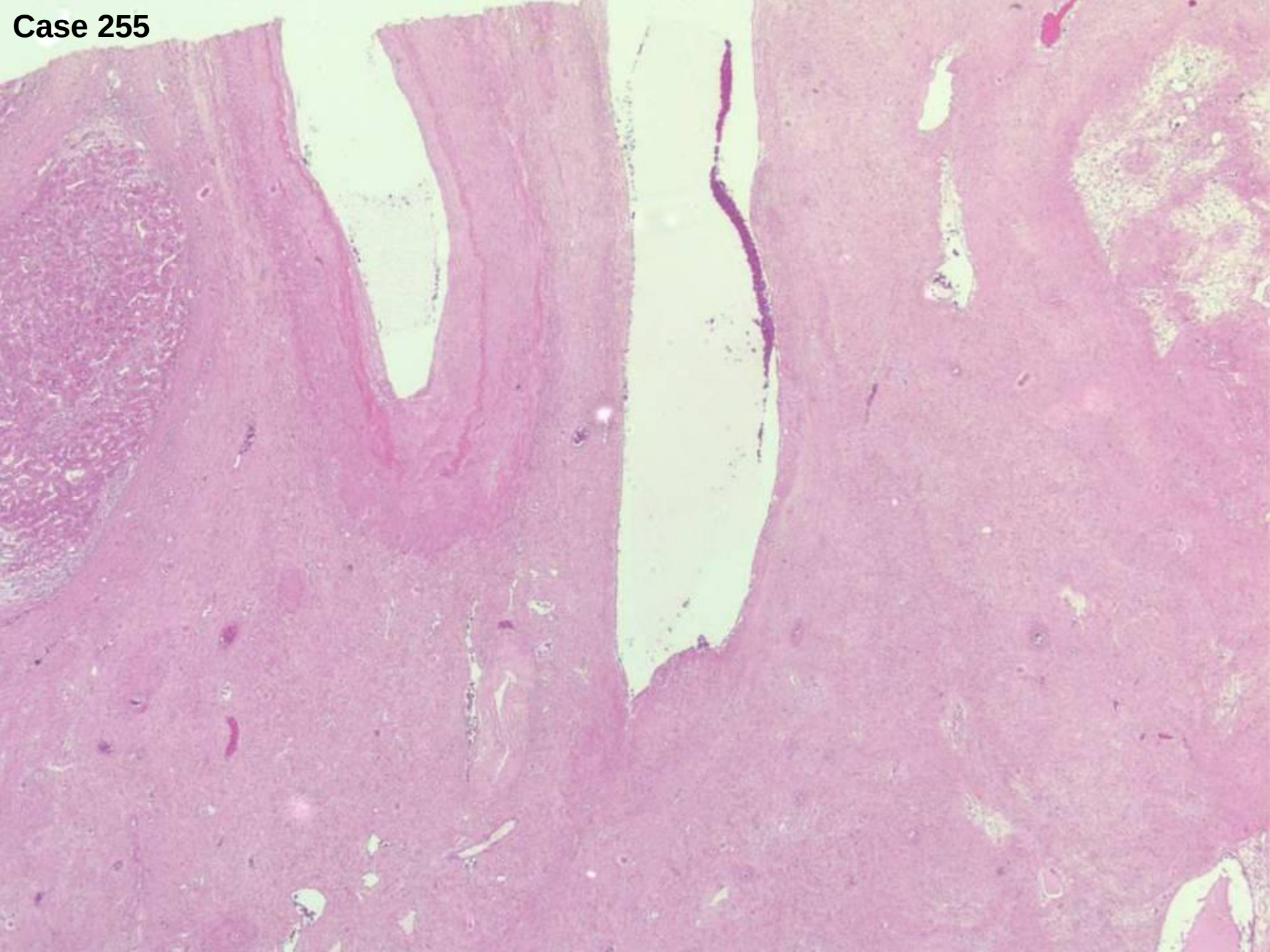
36 M

Previous history of testicular teratoma 5 years earlier; (no record of any chemotherapy). ?adenoma, ? metastatic teratoma.

Case 255



Case 255



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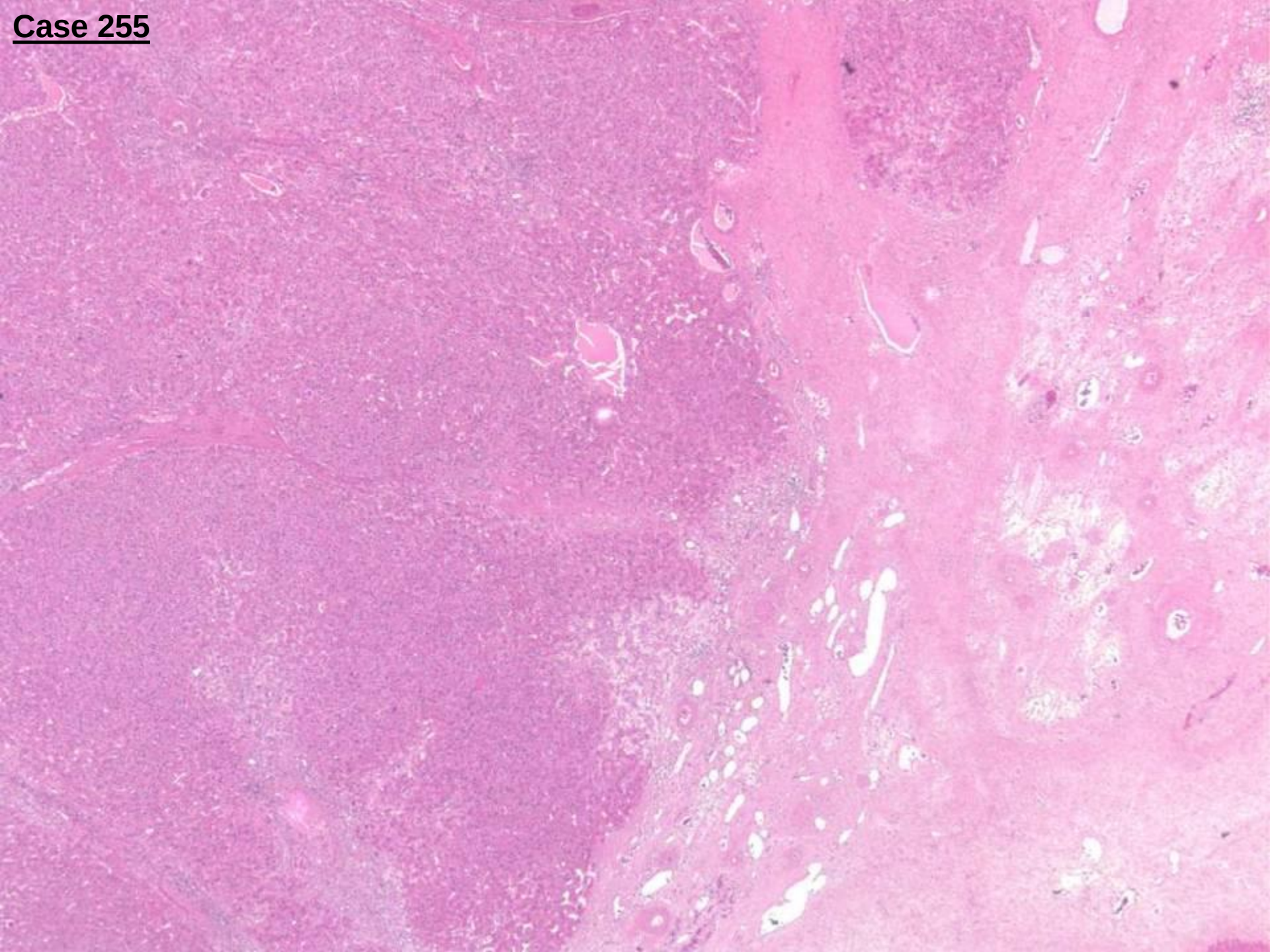

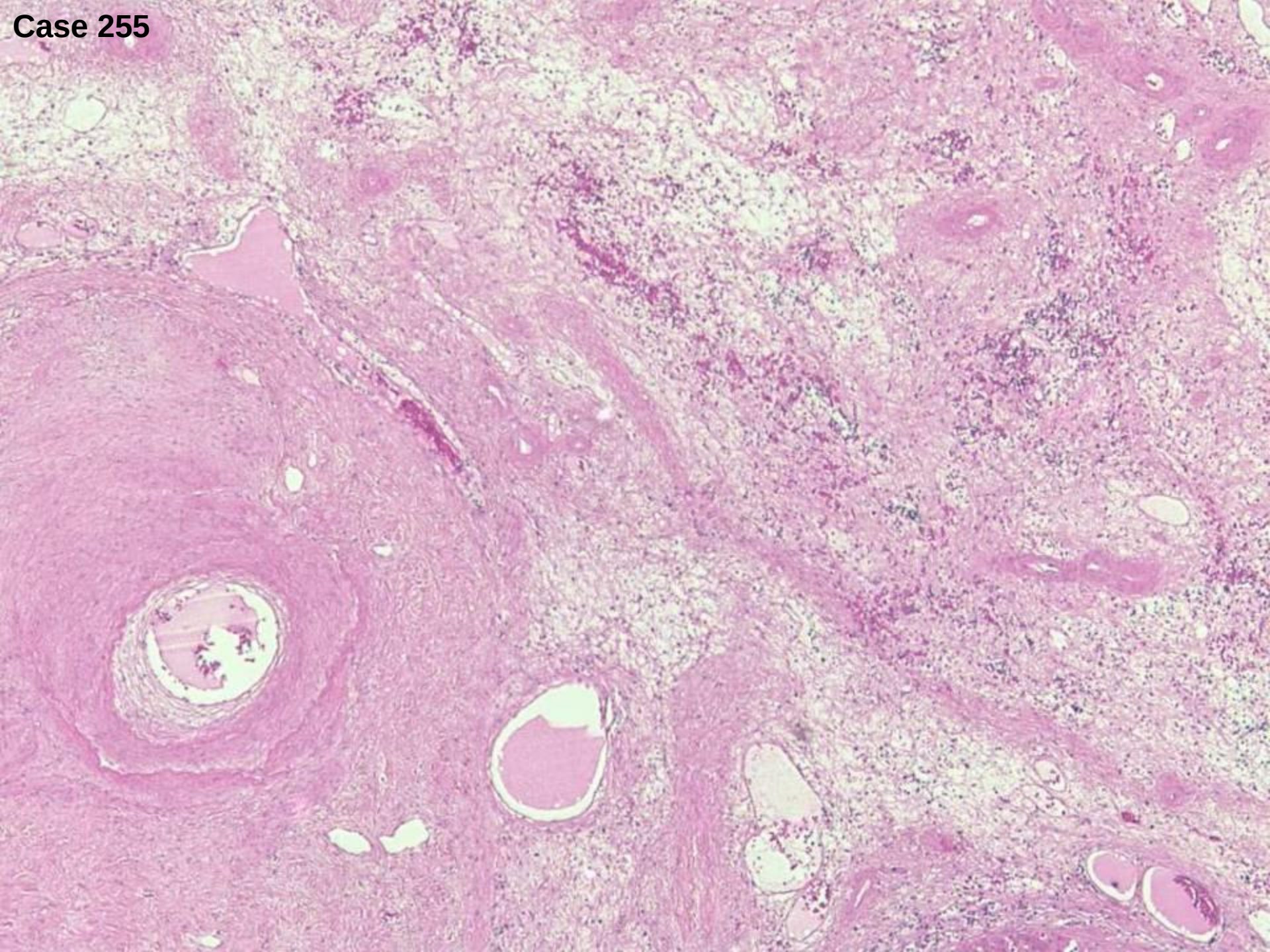
Case 255

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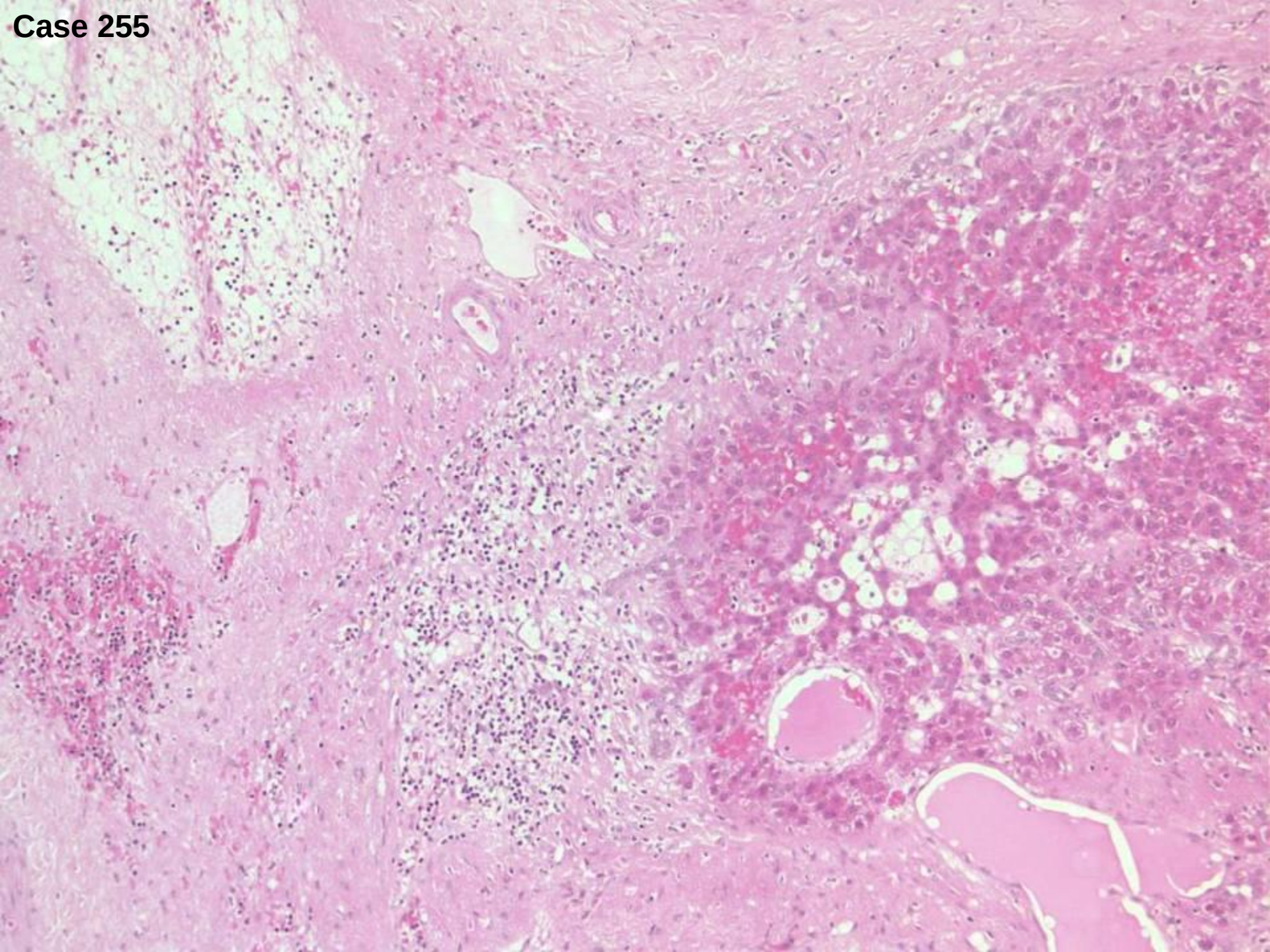

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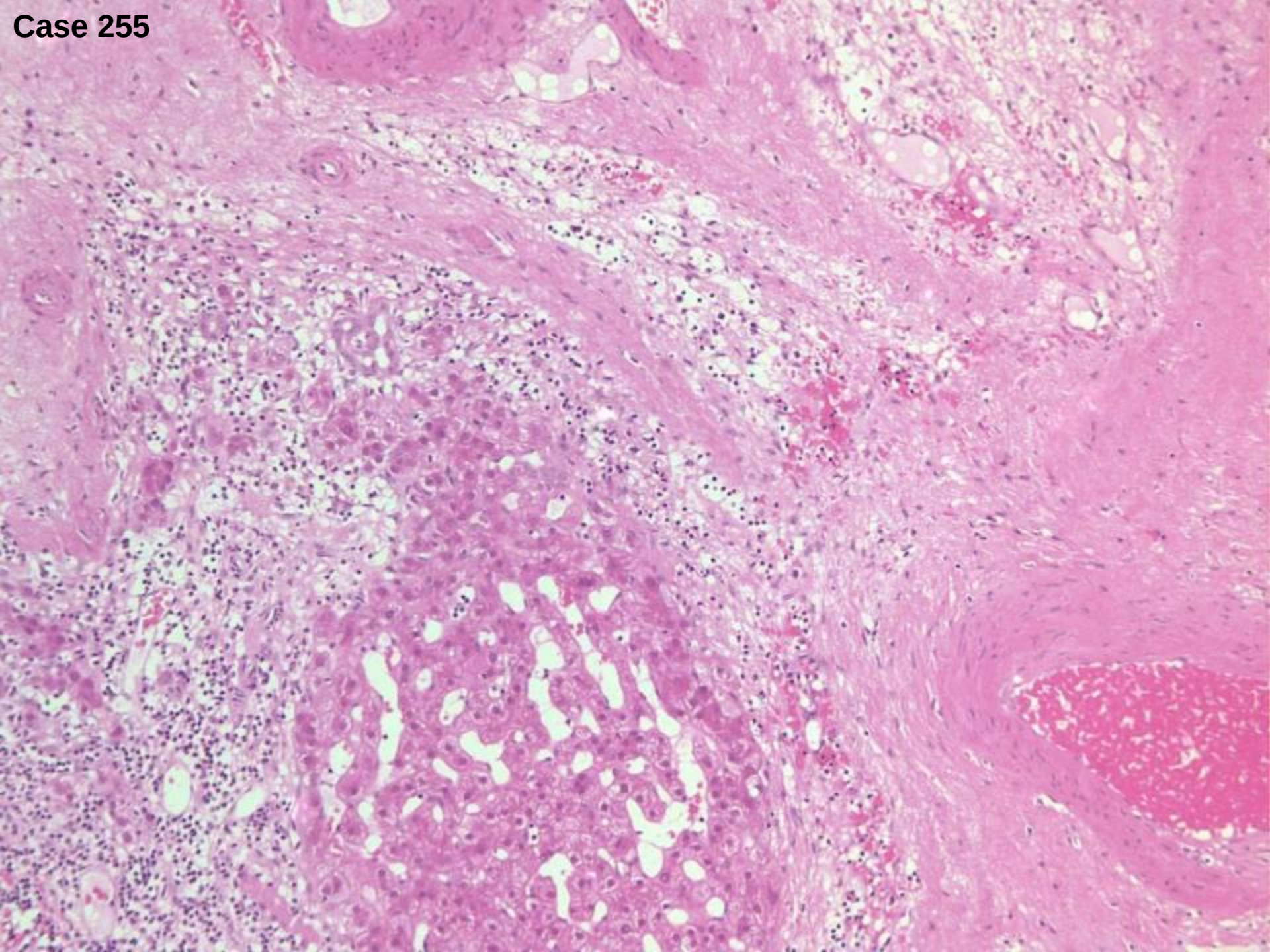

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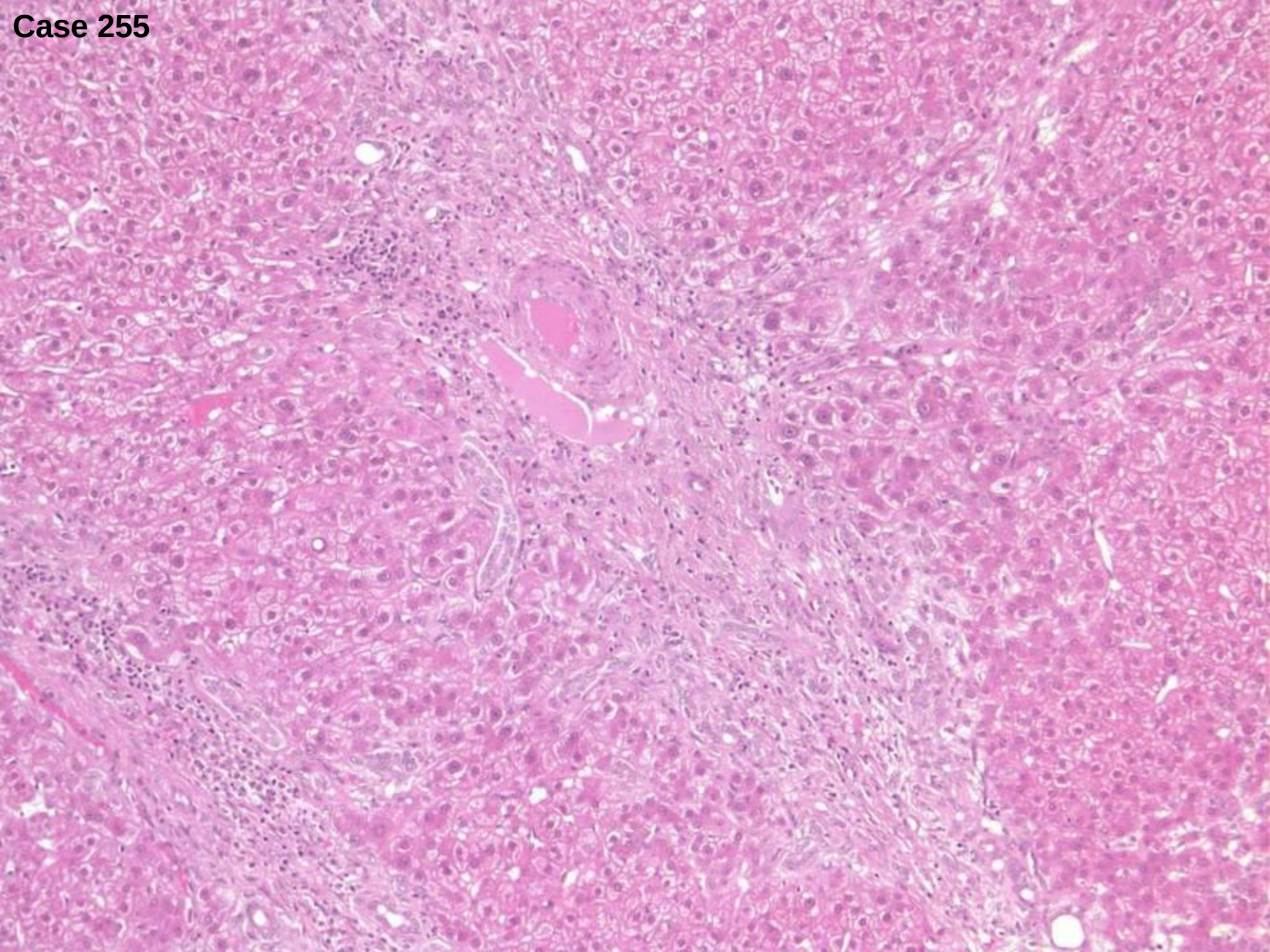

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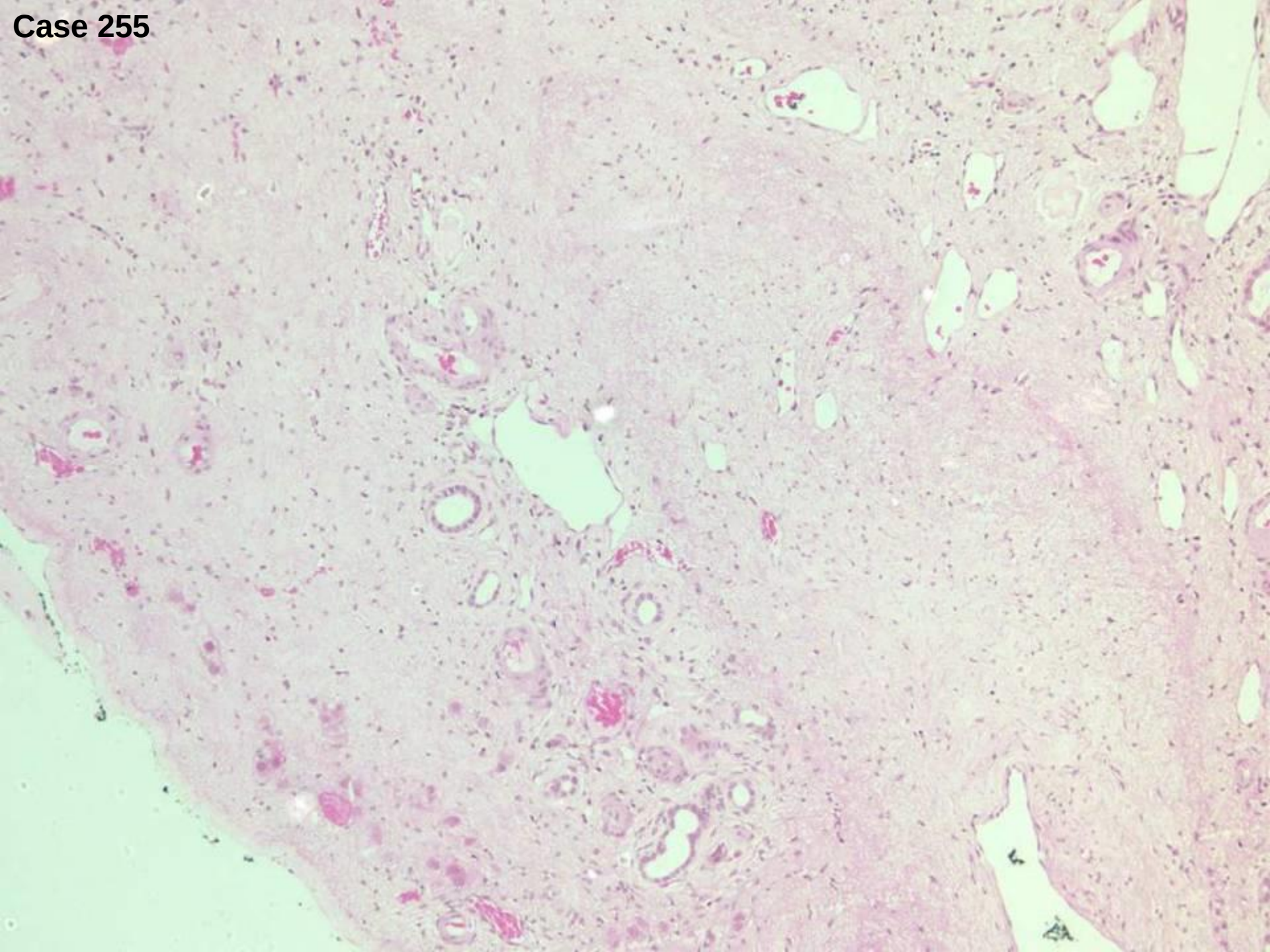


Case 255

35 focal nodular hyperplasia
6 vascular malformation
4 mesenchymal hamartoma (only diagnosis)
3 mesenchymal hamartoma + differential
1 sclerosed haemangioma
parenchymal extinction/fibrosis due to chemotherapy/radiation

4 metastatic teratoma with regression
1 metastatic seminoma with regression
2 probable treated teratoma
infarction ? of tumour tissue

1 angiomyolipoma (no differential)
1 ?hepar lobatum

Case 255

Scoring: no clear diagnosis, not suitable for scoring

Case 255

Original diagnosis: mesenchymal hamartoma.

Follow up information:

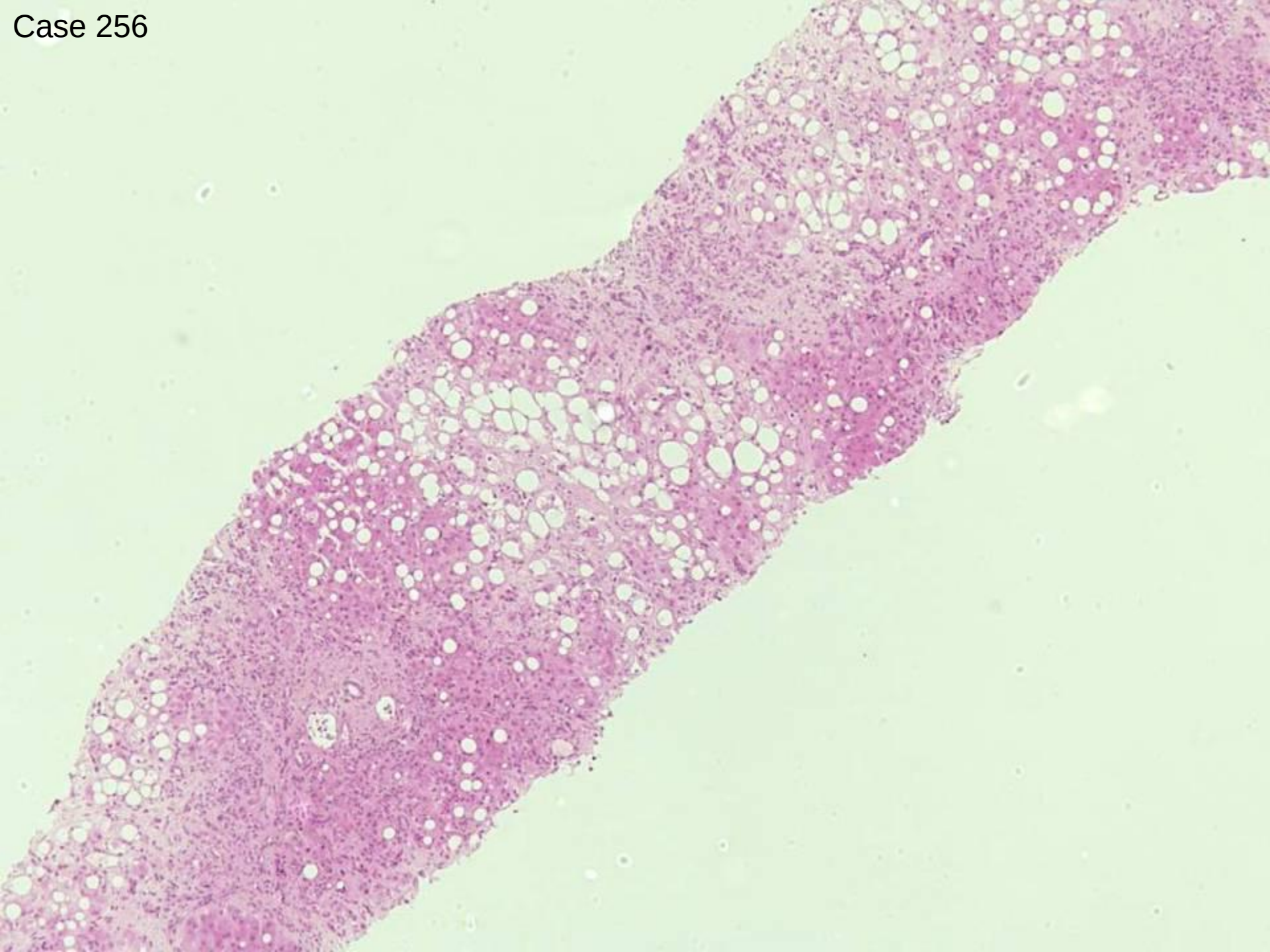
‘I have personally looked at his hospital notes’. Left orchidectomy for testicular teratoma 1998. No mention of any chemotherapy. Liver resection in 2004, uneventful recovery. Believed to remain well since.

Case 256

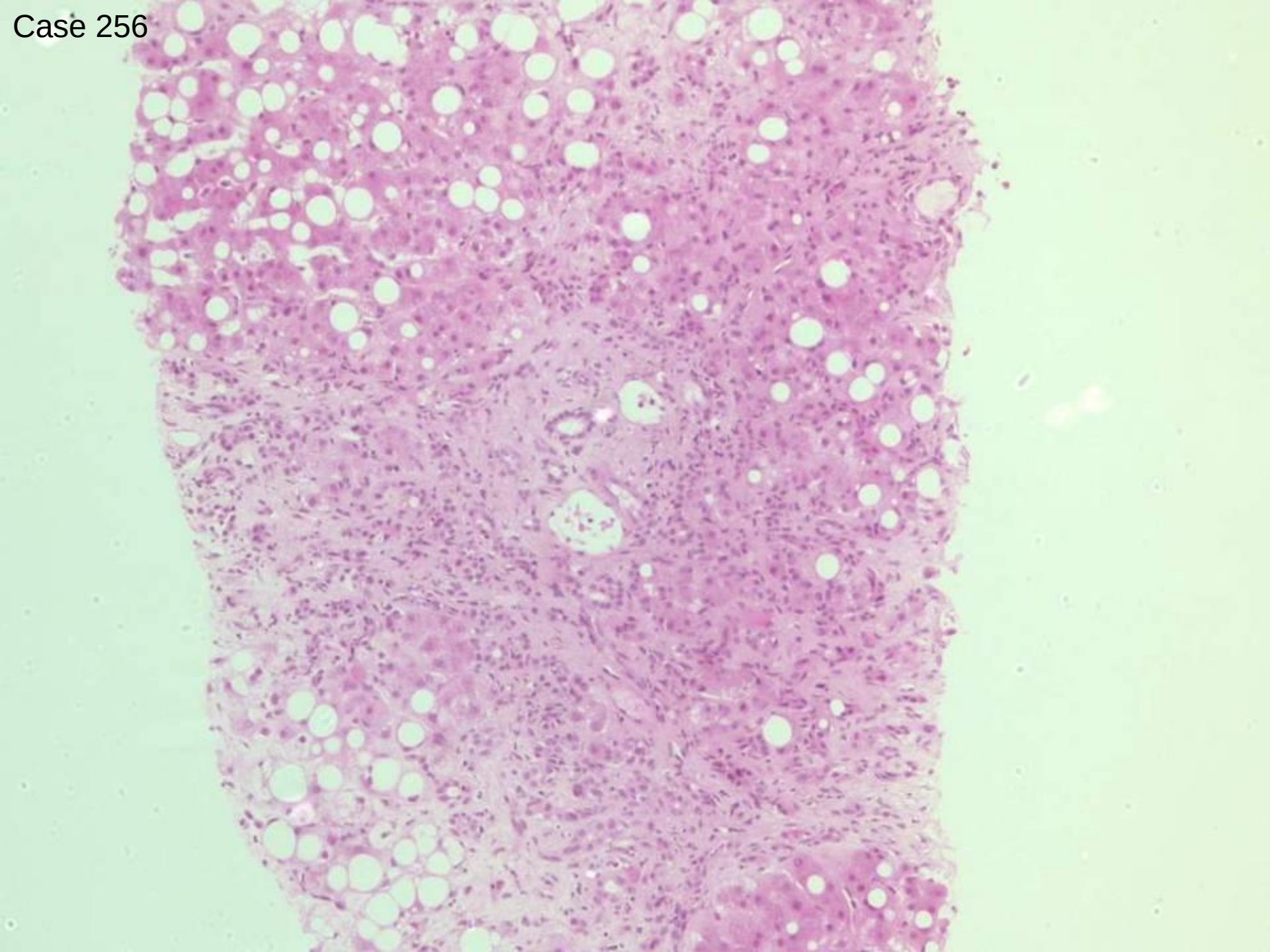
57 F

Weight loss and jaundice. Positive SMA. ? autoimmune hepatitis. Bili 20, ALP 199, AST 243, Glob 32, SMA +ve

Case 256



Case 256



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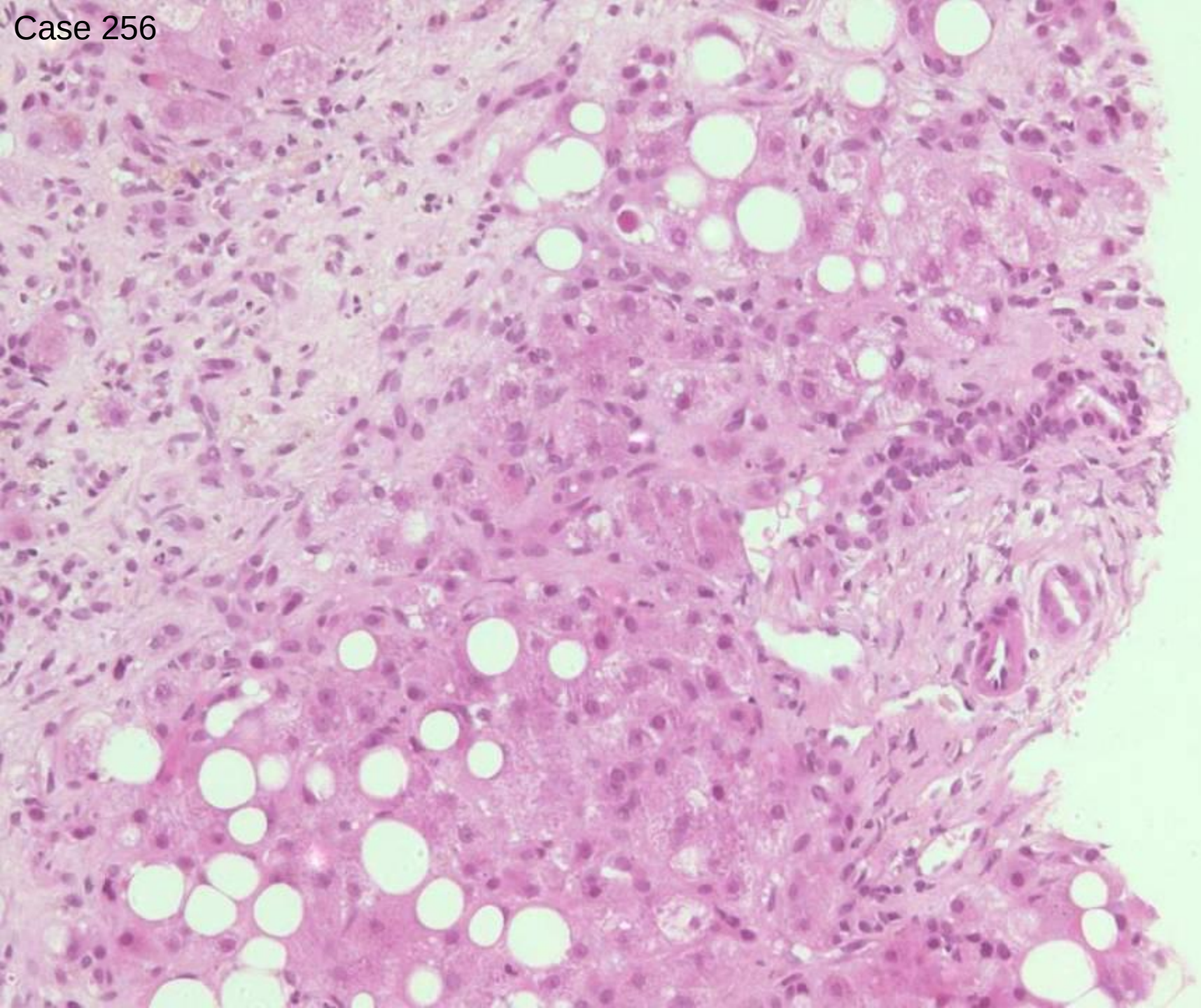

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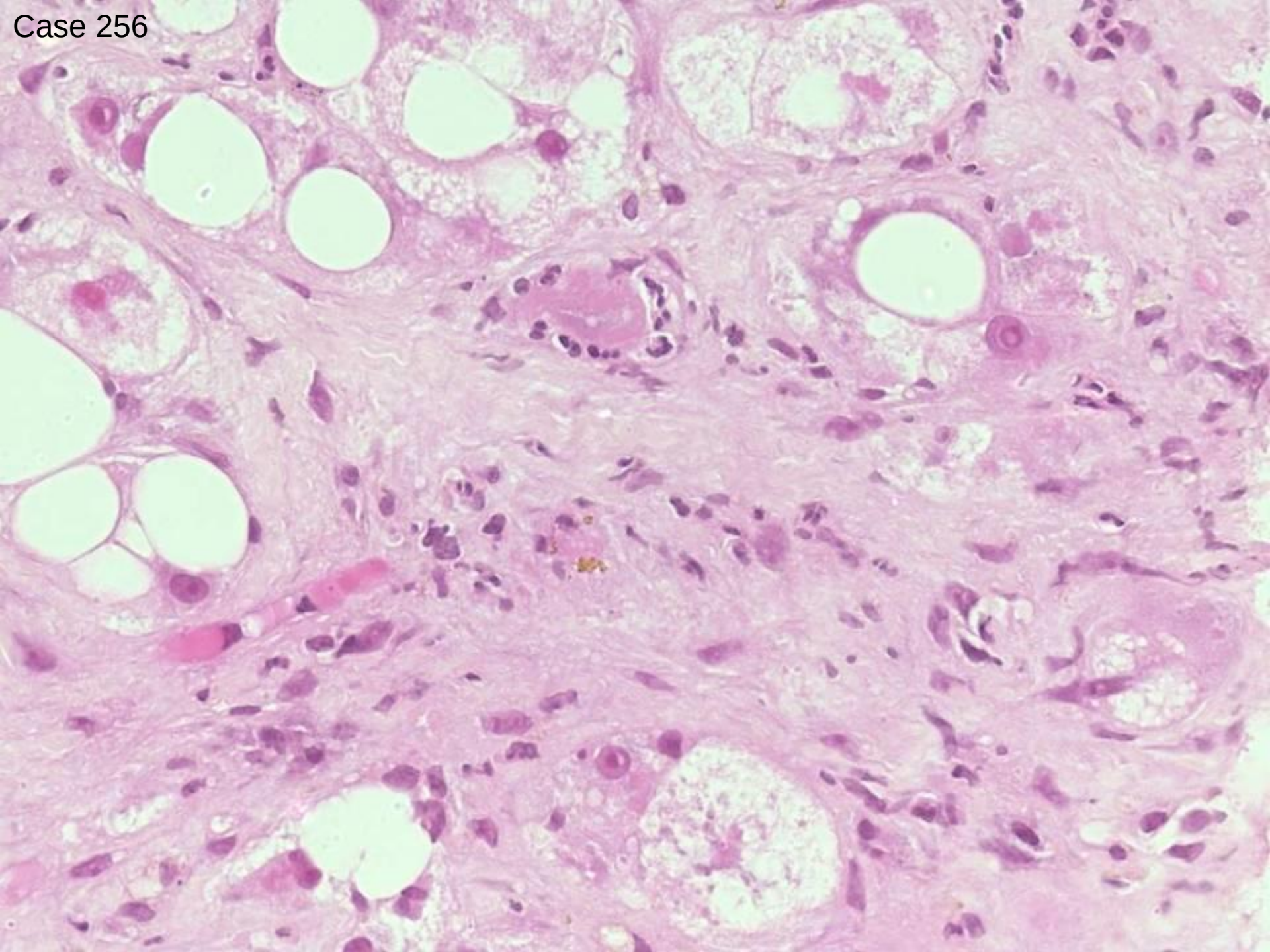

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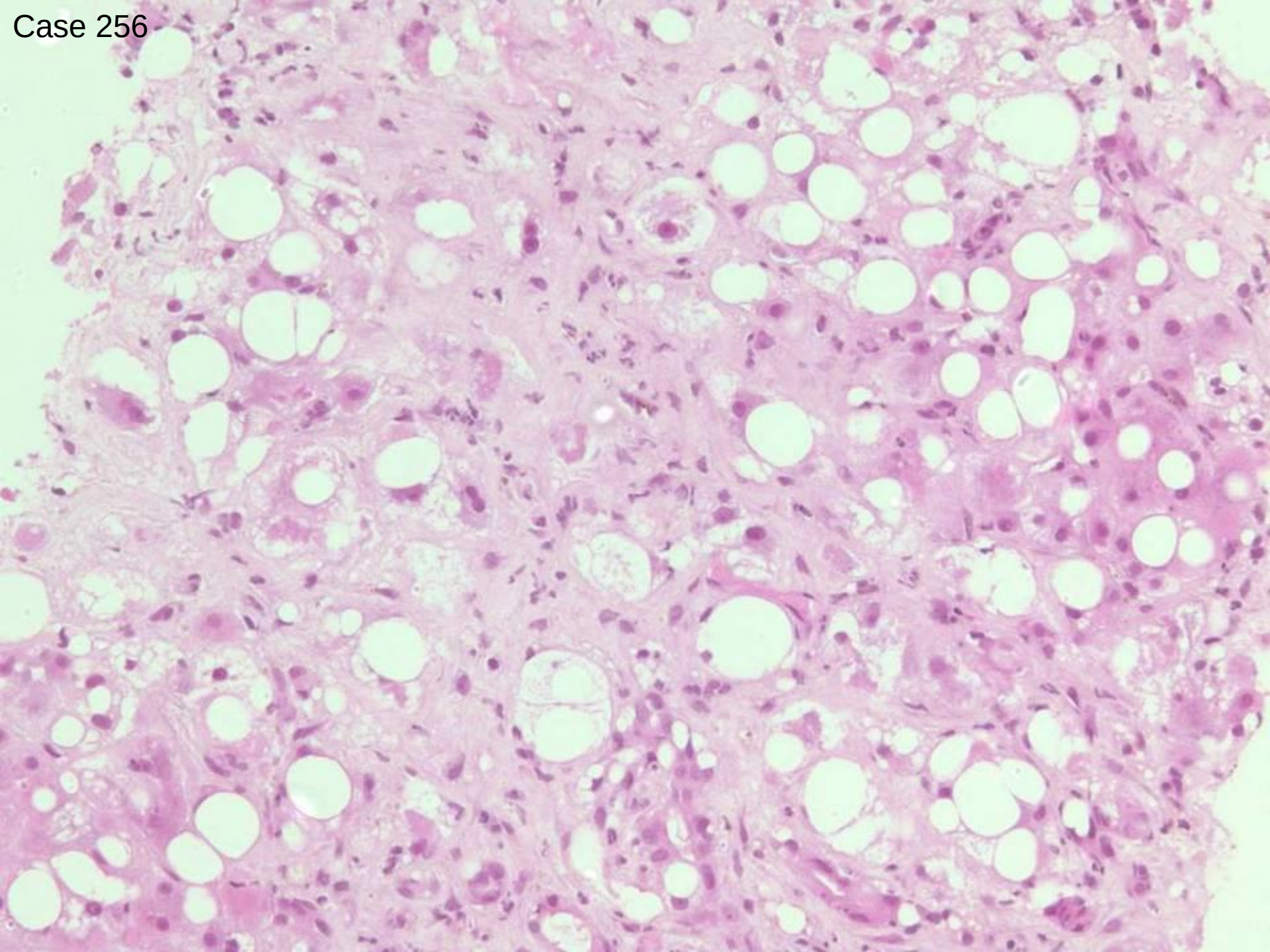

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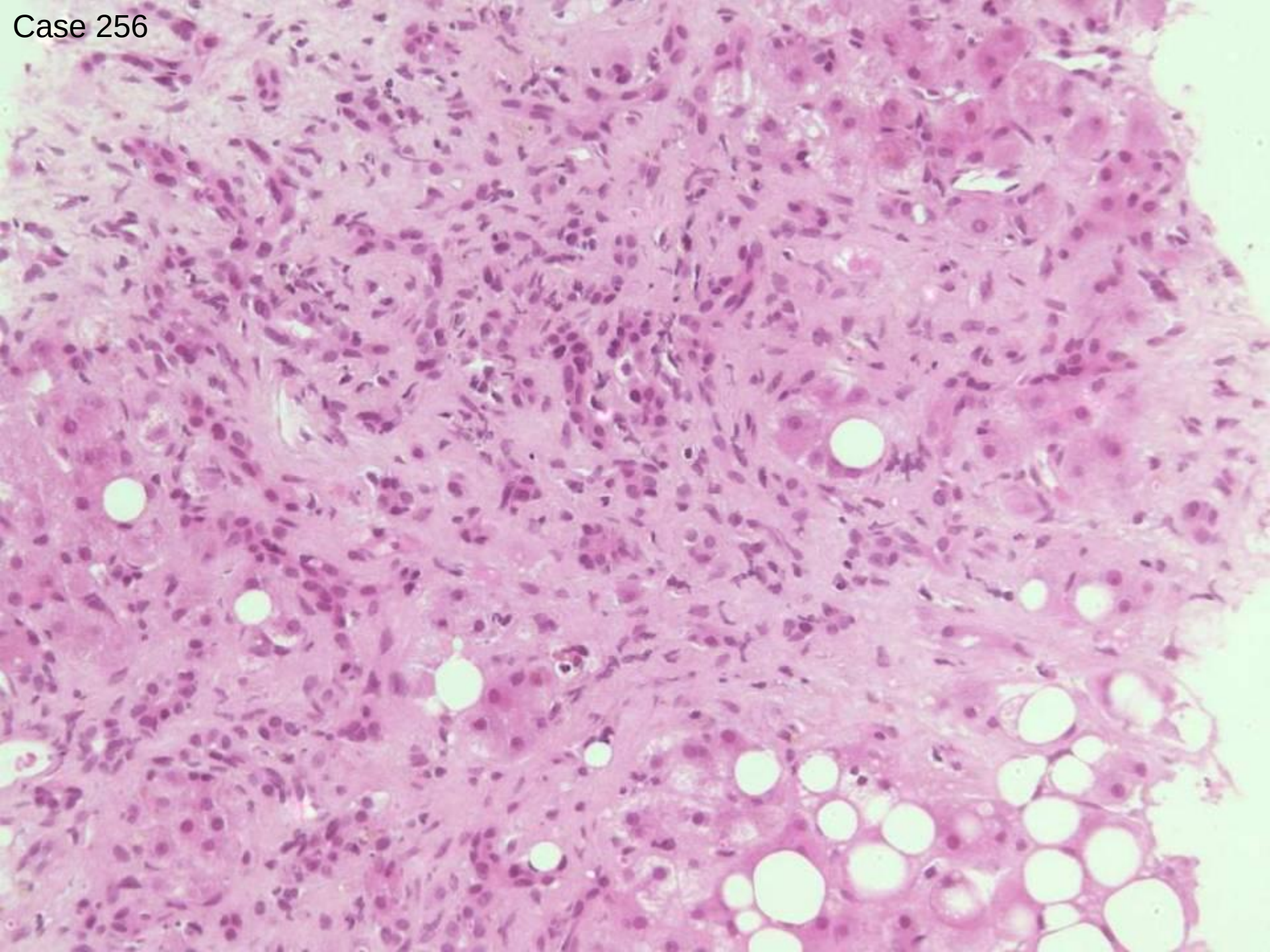


Case 256

37 steatohepatitis + fibrosis/cirrhosis, ? alcohol, not histological features of AIH

19 steatohepatitis + fibrosis/cirrhosis, ? alchohol, no mention of AIH

1 steatohepatitis rather than AIH, no mention of cause/alcohol
1 steatohepatitis, PBC not excluded, no mention of AIH

1 steatohepatitis with submassive necrosis or cirrhosis ? cause not diagnostic of AIH
1 severe chronic hepatitis + cirrhosis, likely autoimmune
1 hepatitic + biliary features, may be a variant syndrome

Case 256

Scoring: Reject answers with no mention of steatohepatitis.

Responses with no mention of AIH score 5

Discussion: Correct answers identified the diagnosis of steatohepatitis, and commented on the likely cause – in this case the marked degree of Mallory bodies and pericellular fibrosis makes alcohol extremely likely – these features of ‘central sclerosing hyaline necrosis’ are not seen to this degree in NASH.

Responses should include reference to the absence of histological features of autoimmune hepatitis, despite presence of smooth muscle antibodies – this was the clinical suspicion prompting the biopsy. Smooth muscle antibodies, like anti nuclear antibodies, are not uncommon in patients with alcoholic liver disease.

Case 256

Original diagnosis: steatohepatitis with cirrhosis

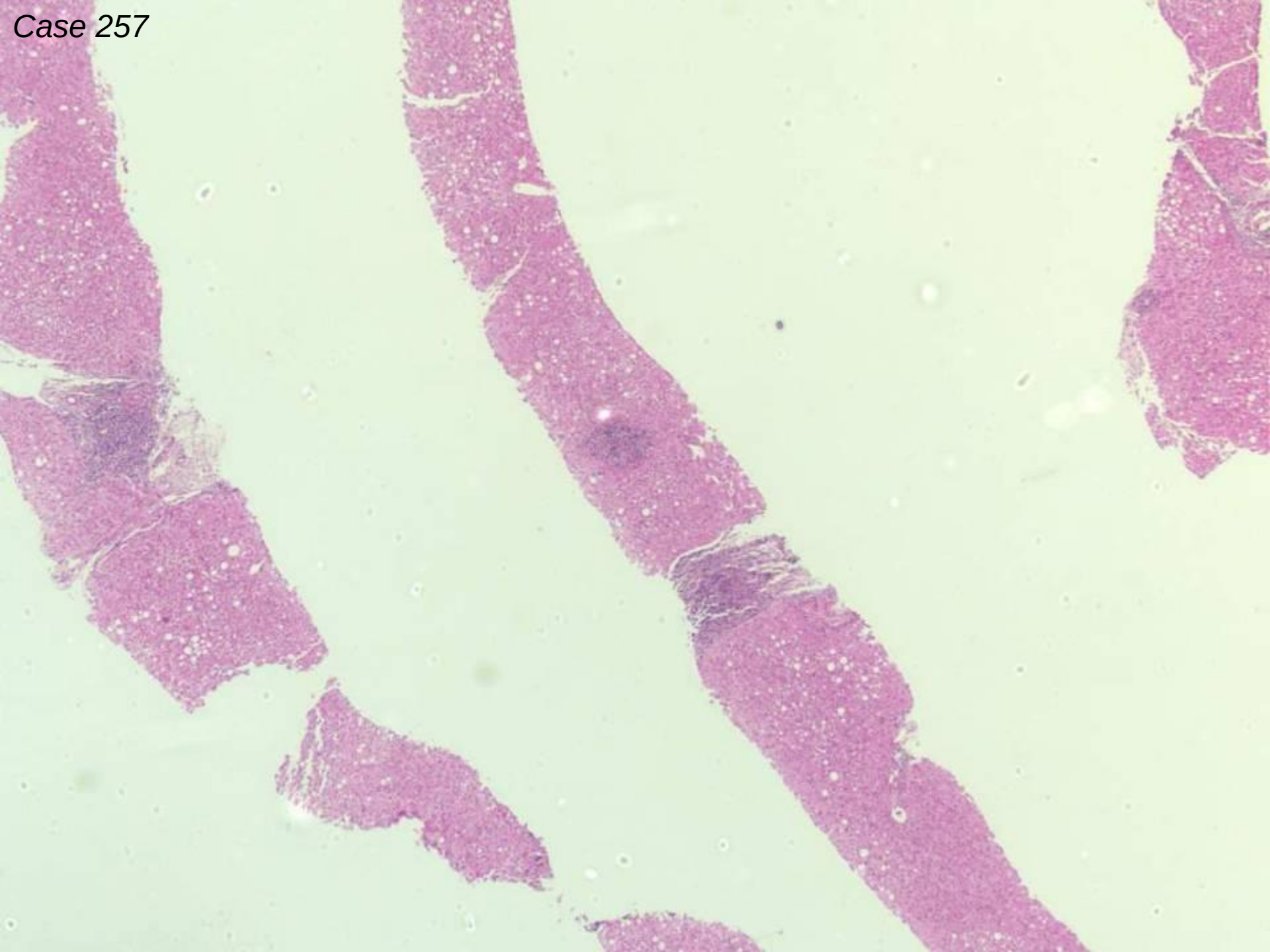
Subsequent history of alcohol abuse obtained.

Case 257

57 M

Hepatitis C positive, ? for viral therapy. Reticulin stain shows portal expansion with fibrous septa, without linkage

Case 257


Case 257

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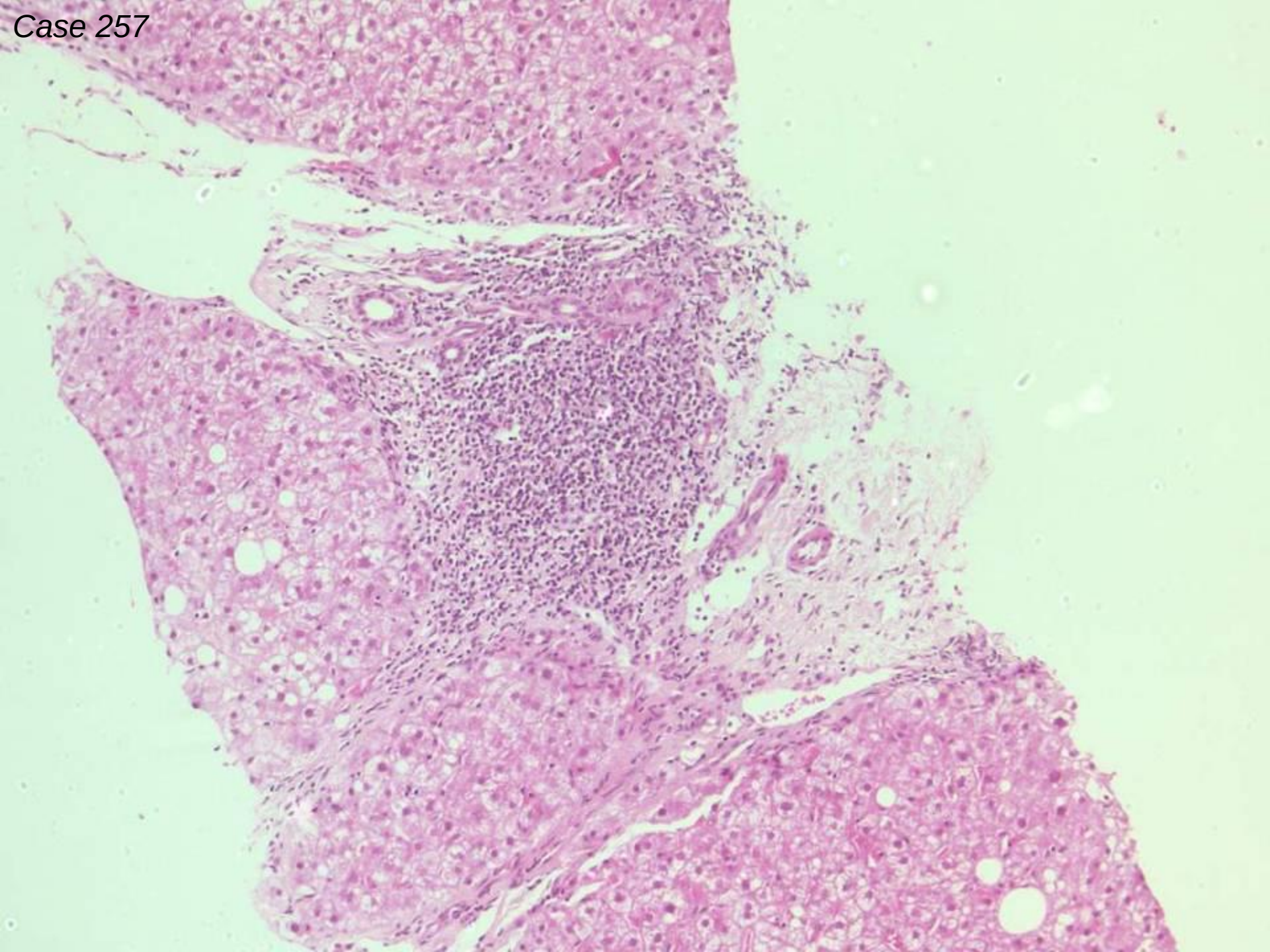
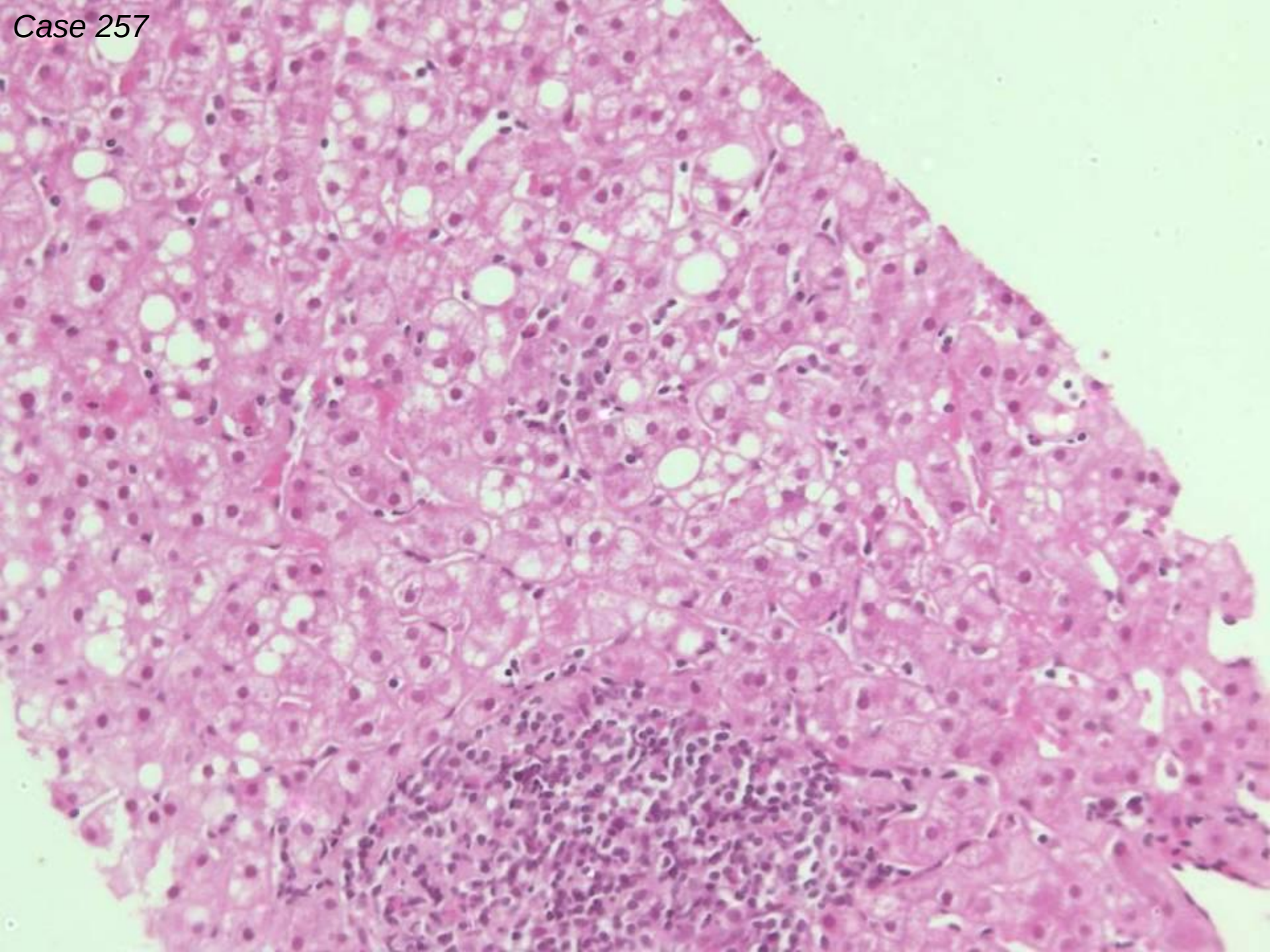
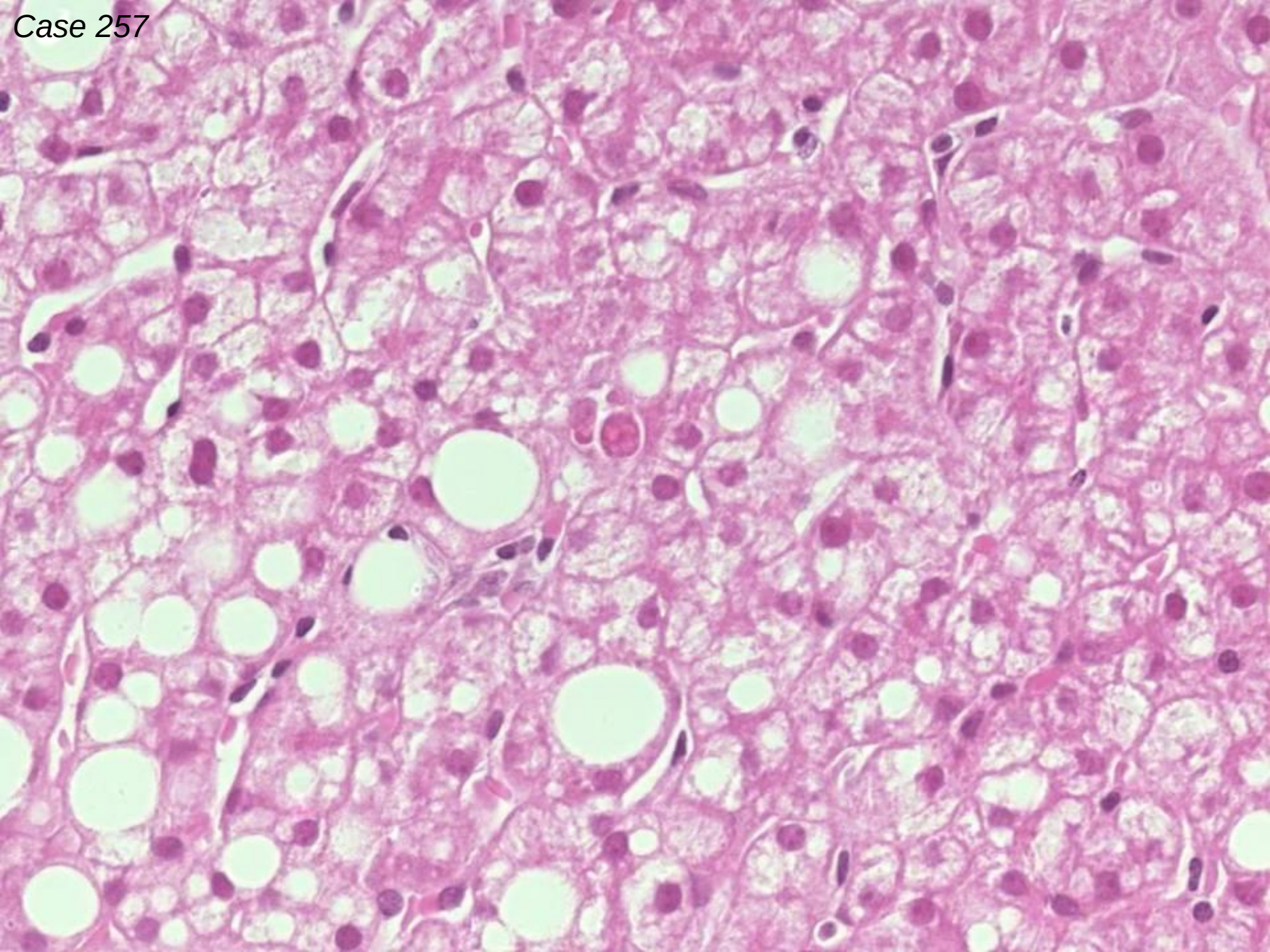



Case 257


Case 257

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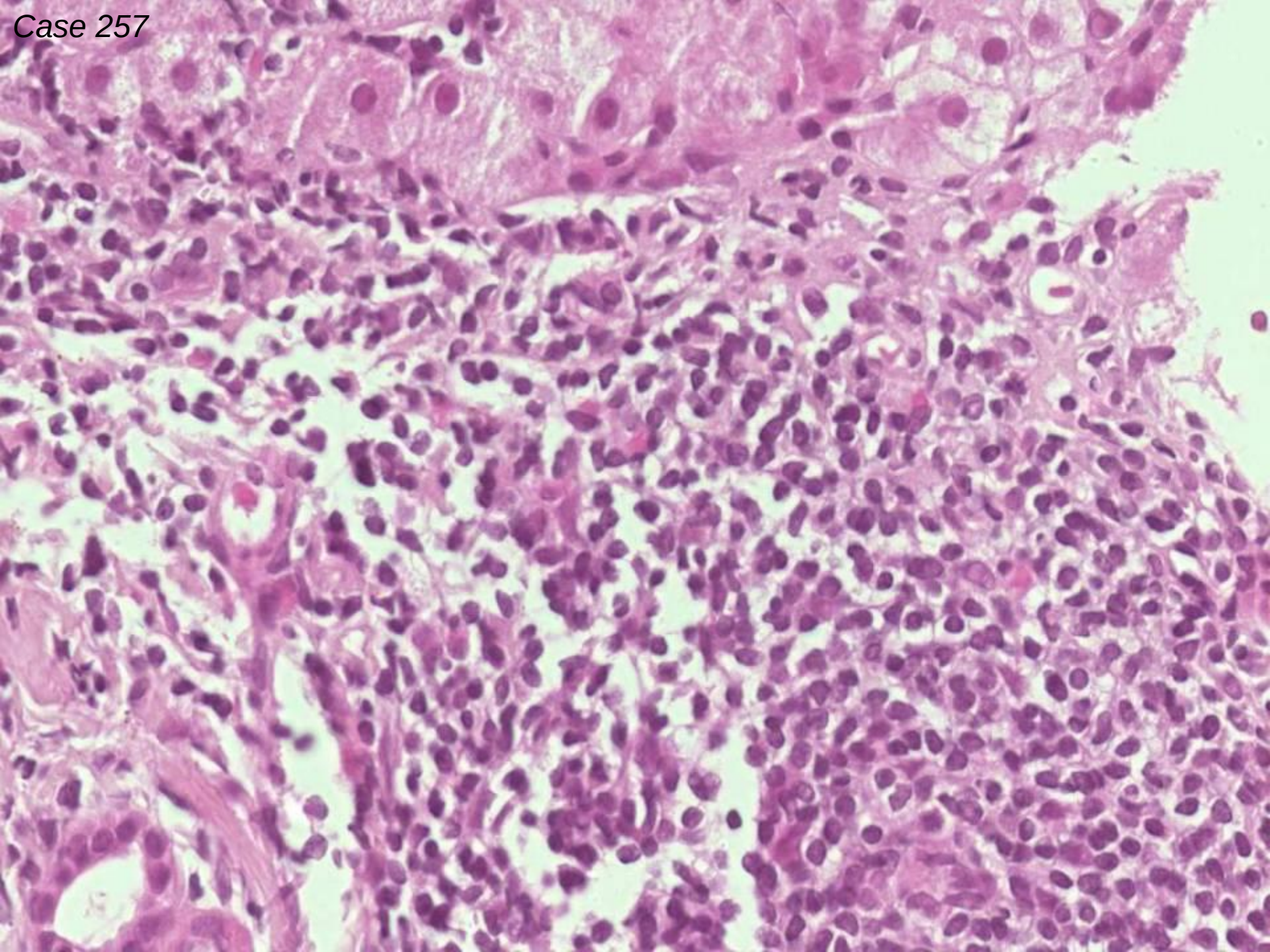


Case 257

62 hepatitis C, of which:

- 3 consistent with hepatitis C, no severity included
- 18 mild chronic hepatitis C
- 34 moderate chronic hepatitis C

- 5 minimal or mild chronic hepatitis C with bridging
- 1 moderate chronic hepatitis C with bridging
- 1 ?chronic hepatitis C, ? low grade lymphoma, needs immunos

1 chronic hepatitis but must exclude lymphoma

Case 257

Scoring: Score full marks for hepatitis C with comment on severity. Half marks for no comment on severity, no marks if hepatitis C not mentioned.

Discussion: actual assessment of stage is not possible without a connective tissue stain; the description of portal expansion with fibrous septa, without linkage, implies there is not bridging fibrosis. The current NICE appraisal for hepatitis C management includes recommendation of combination therapy for patients with mild chronic hepatitis C, and therefore no longer requires biopsy demonstration of disease severity.

Case 257

Original diagnosis:

Chronic hepatitis consistent with HCV

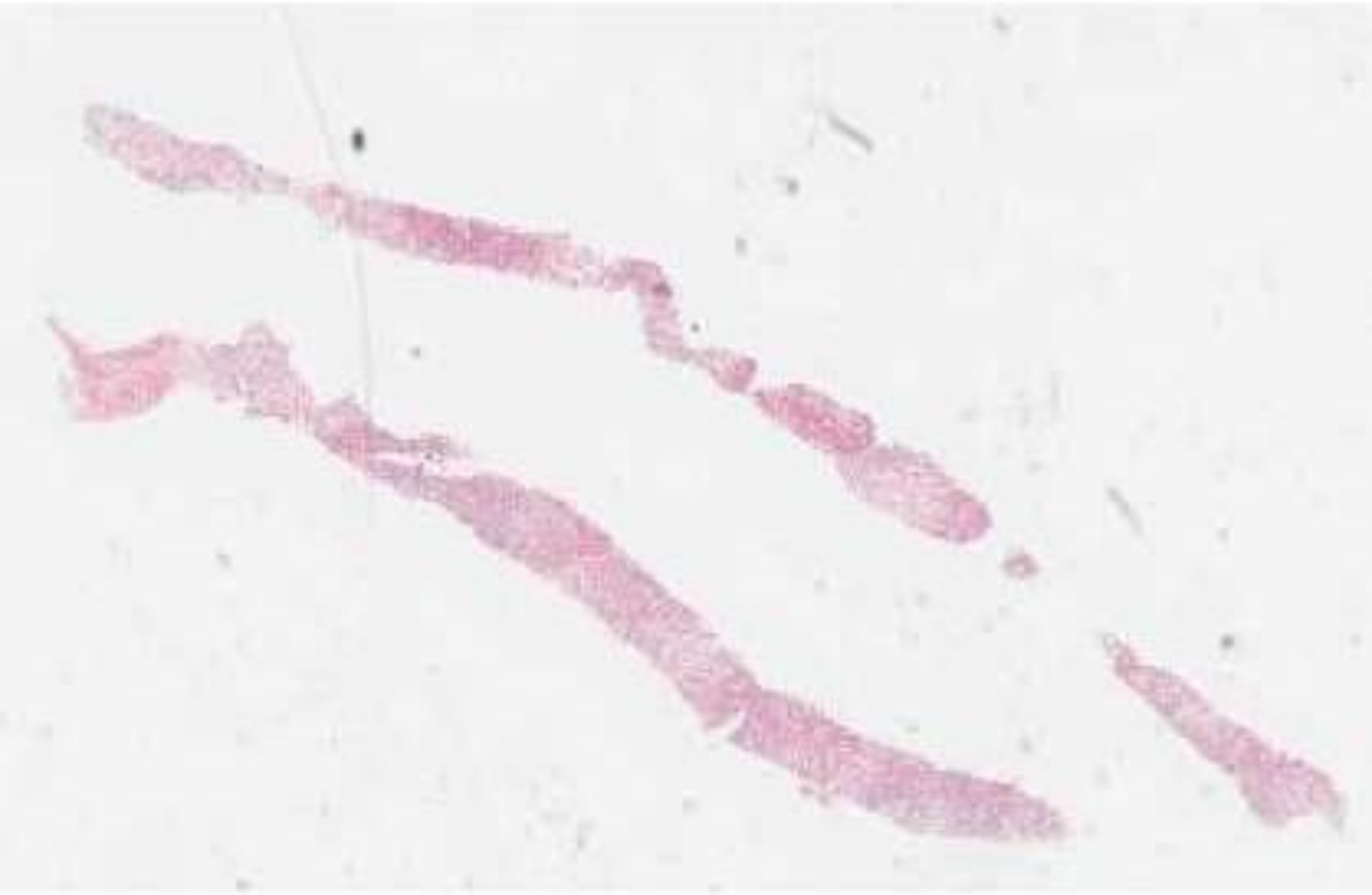
Moderate inflammatory activity.

Case 258

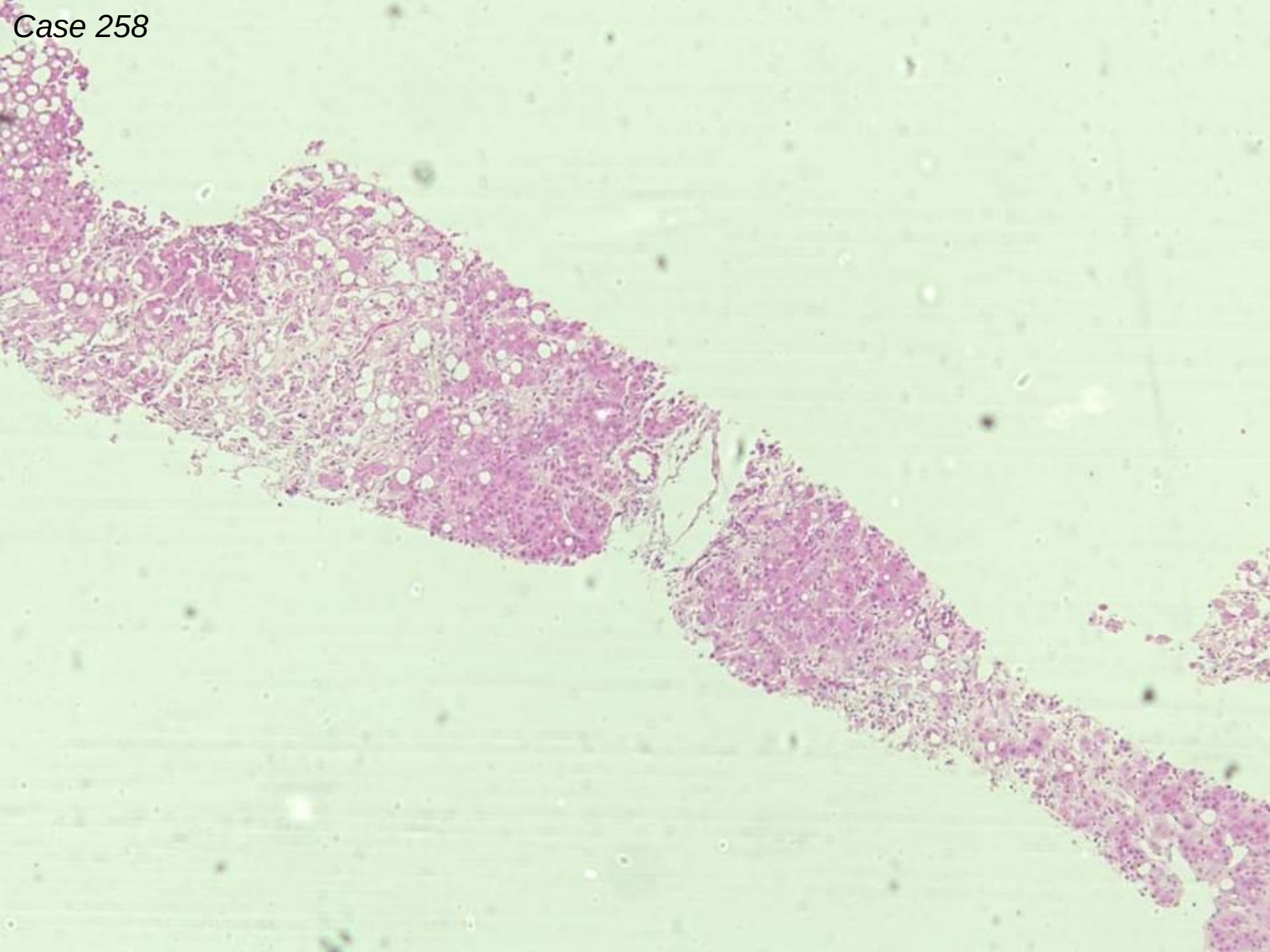
42 F

Transjugular liver biopsy - ? aetiology

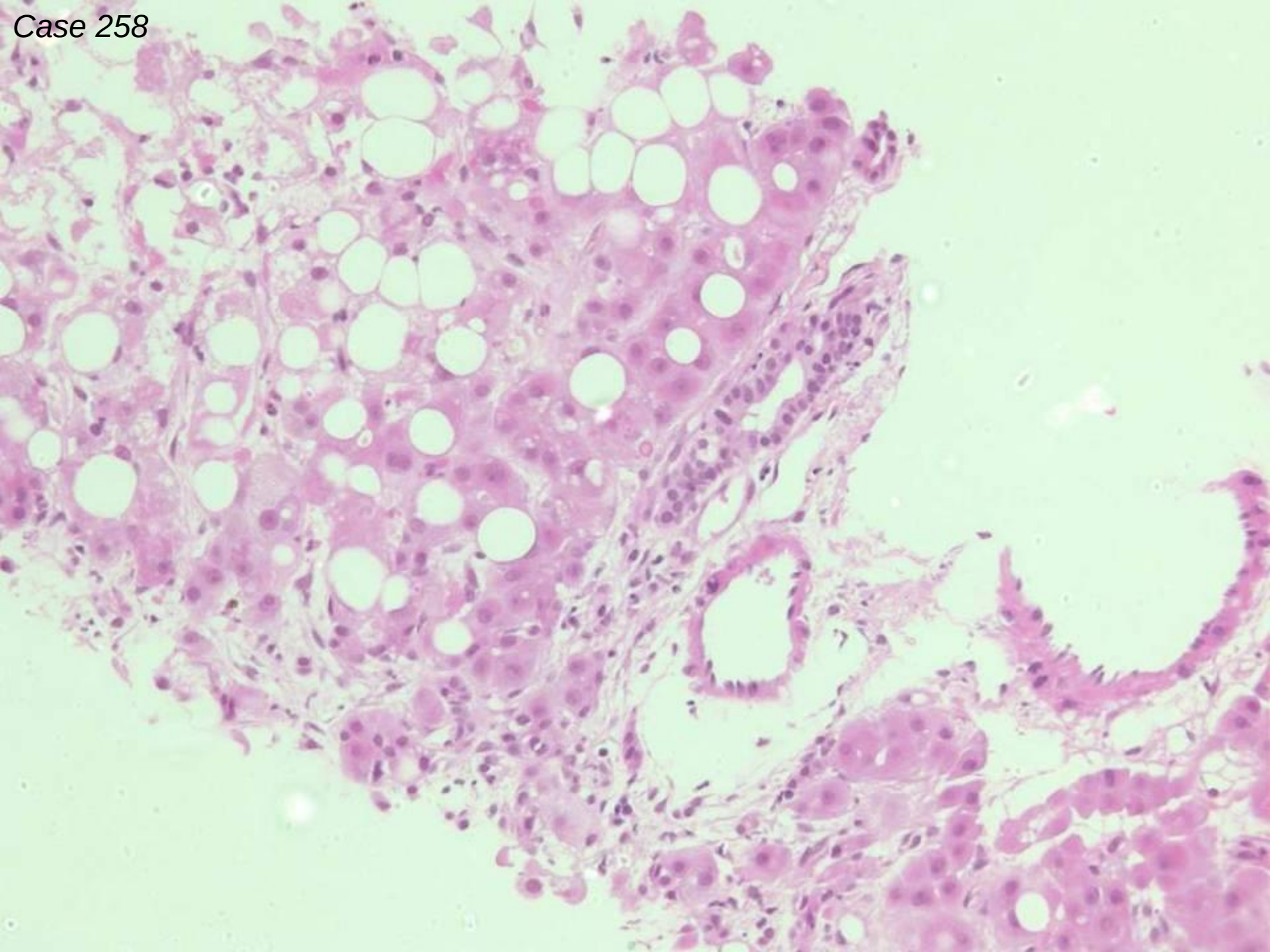
Case 258



Case 258



Case 258



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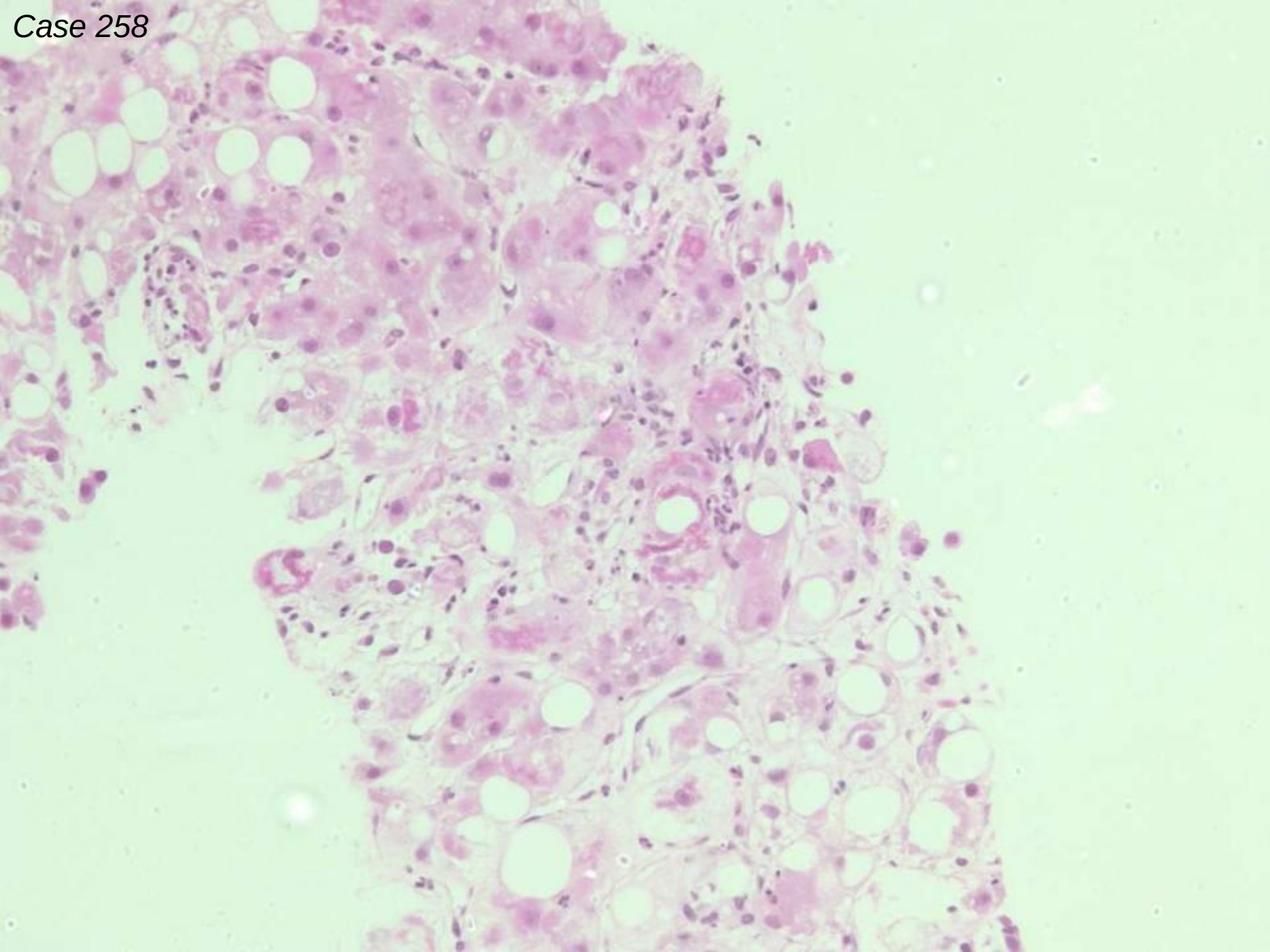

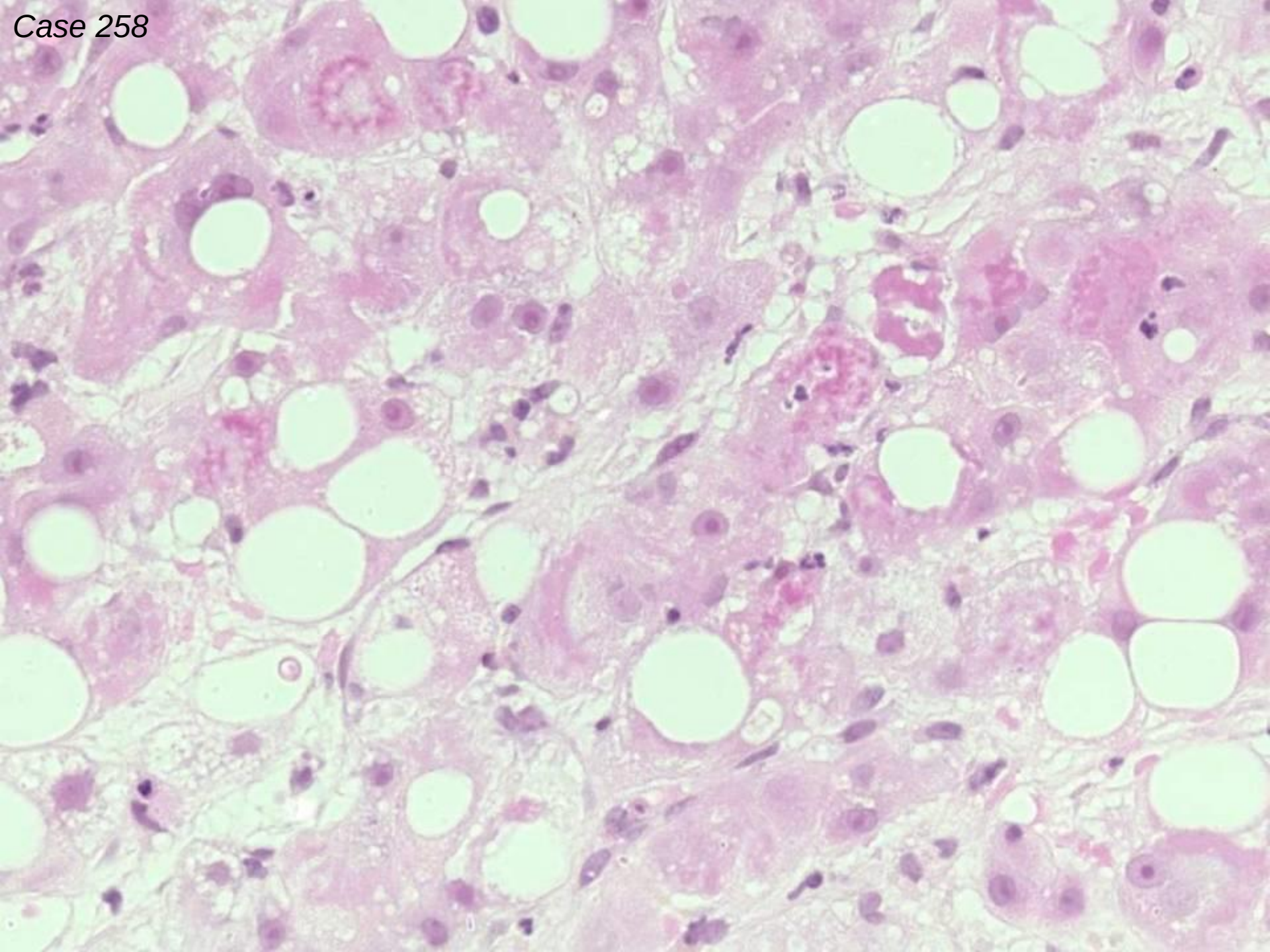
Case 258

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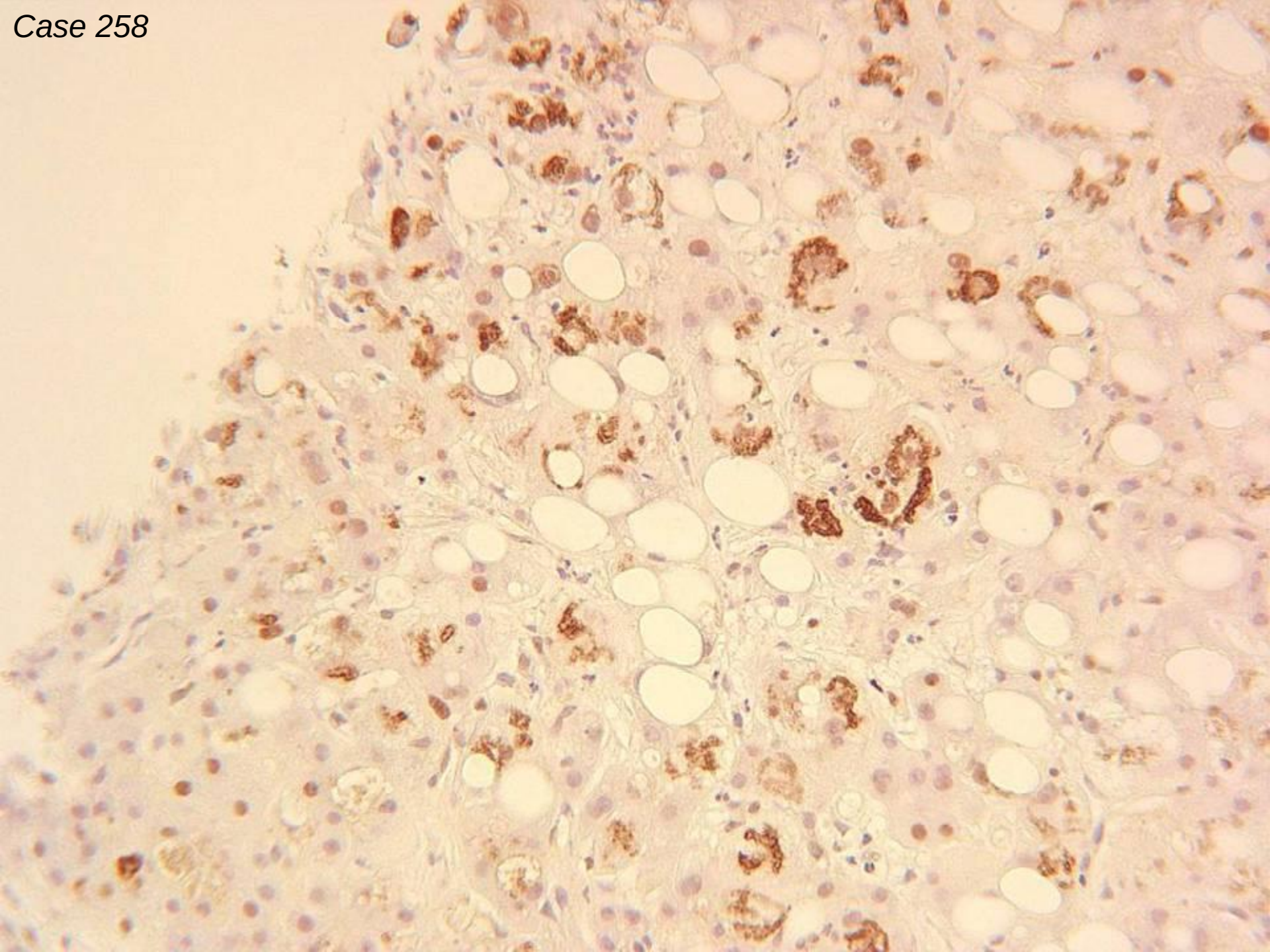


Case 258

59 steatohepatitis – text implies likely due to alcohol

1 alcoholic type hepatitis

3 steatohepatitis – no mention of aetiology

Case 258

Scoring: score full marks for steatohepatitis with likelihood of alcohol (includes alcoholic type hepatitis); during the discussion responses with no mention of aetiology were accepted – although on previous occasions the members present had awarded half marks in this situation.

Case 258

Original diagnosis:

Severe alcoholic liver disease with fibrosis

Follow up information

History of alcohol +++++ not supplied with the original clinical information

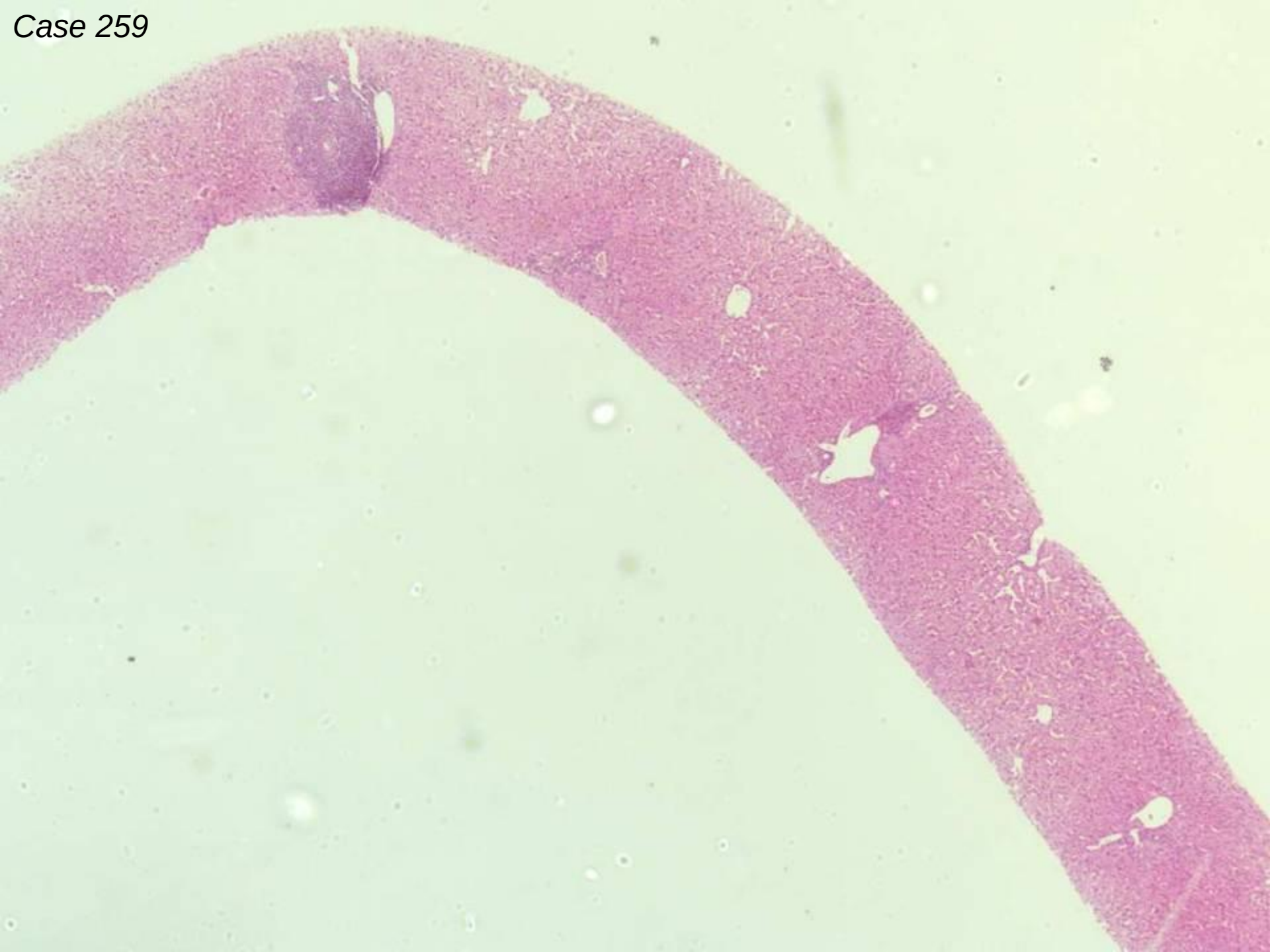
Case 259

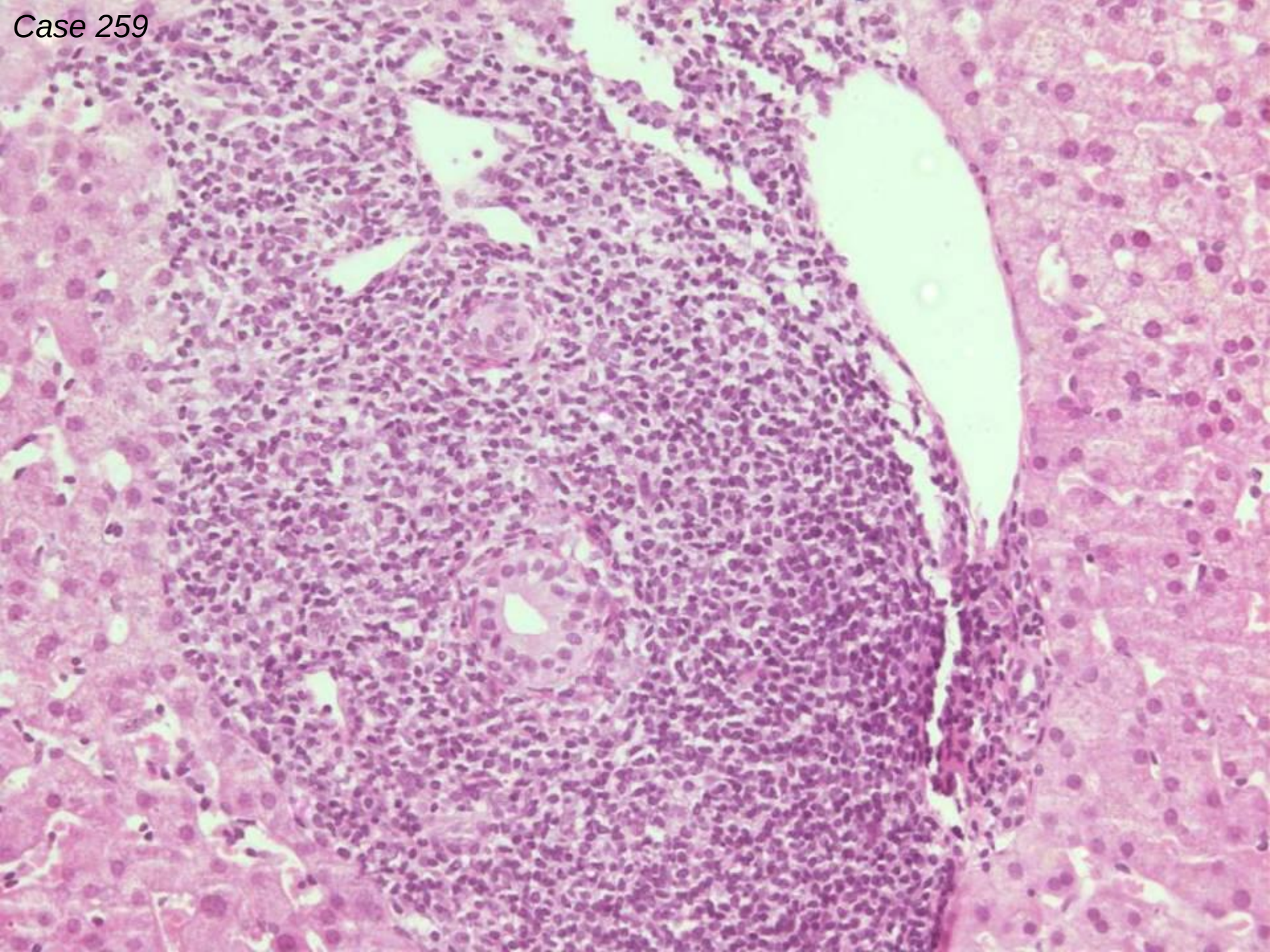
39 F

Anti-mitochondrial antibody strongly positive

Case 259

Case 259




Case 259

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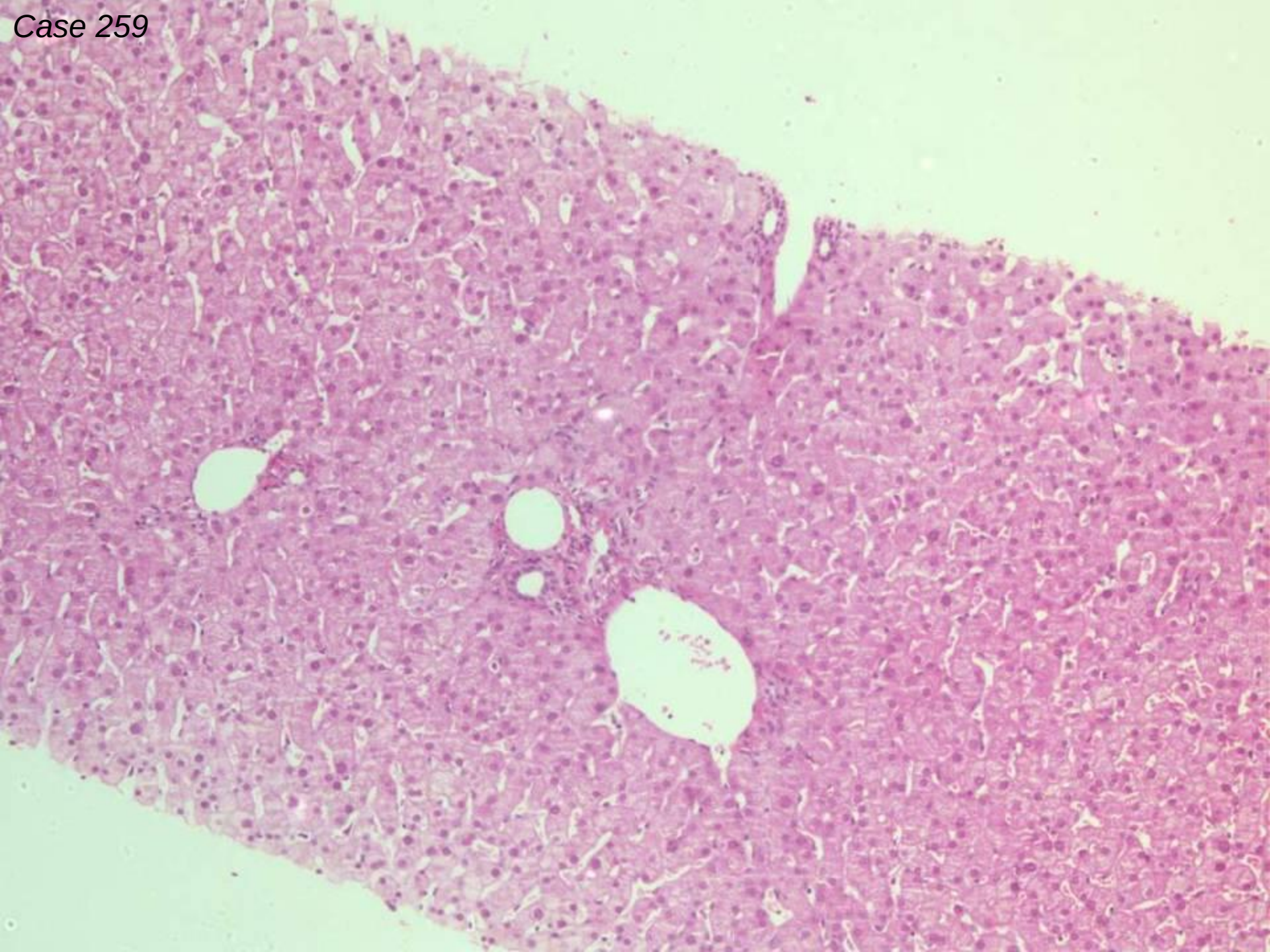

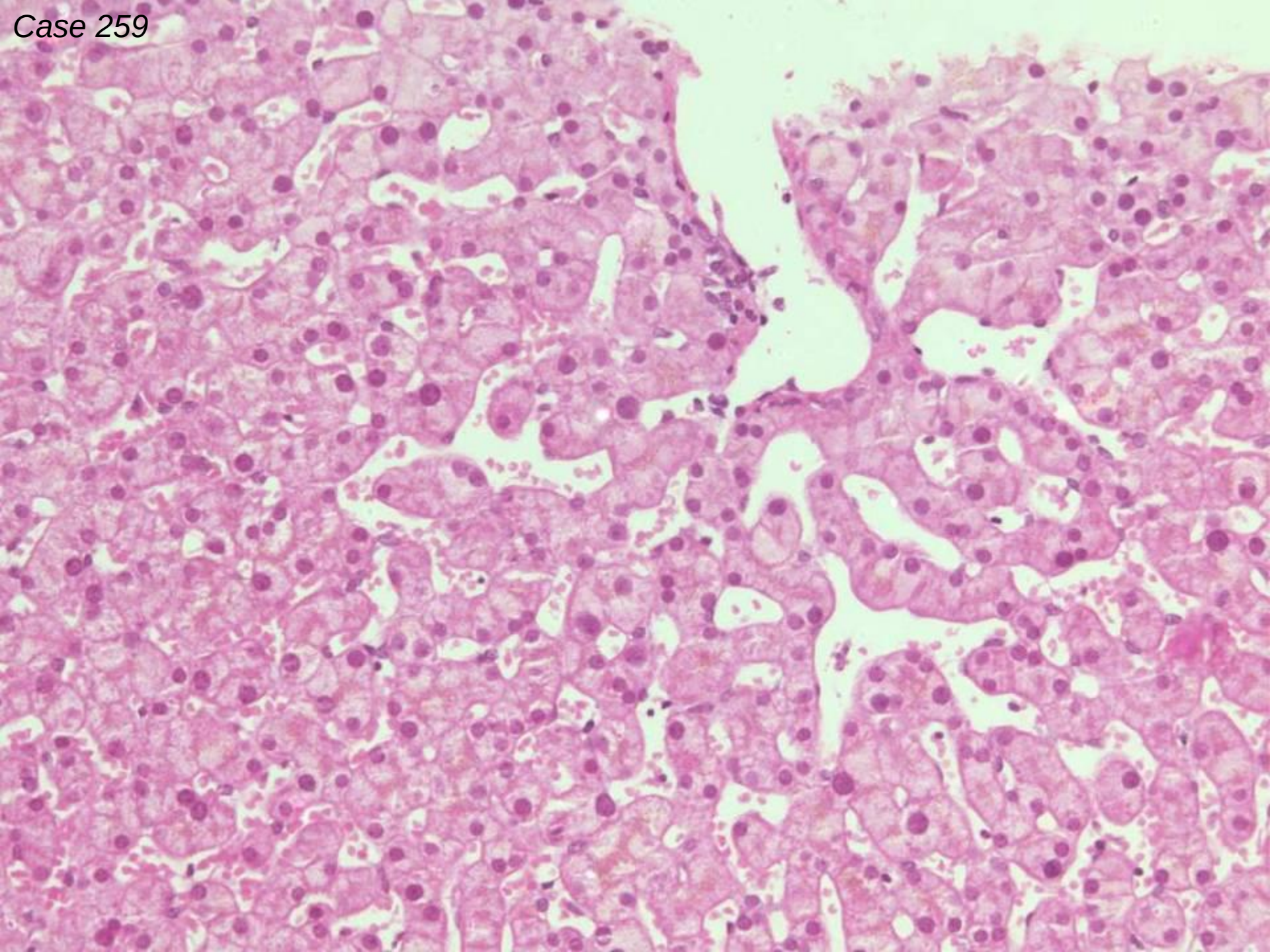
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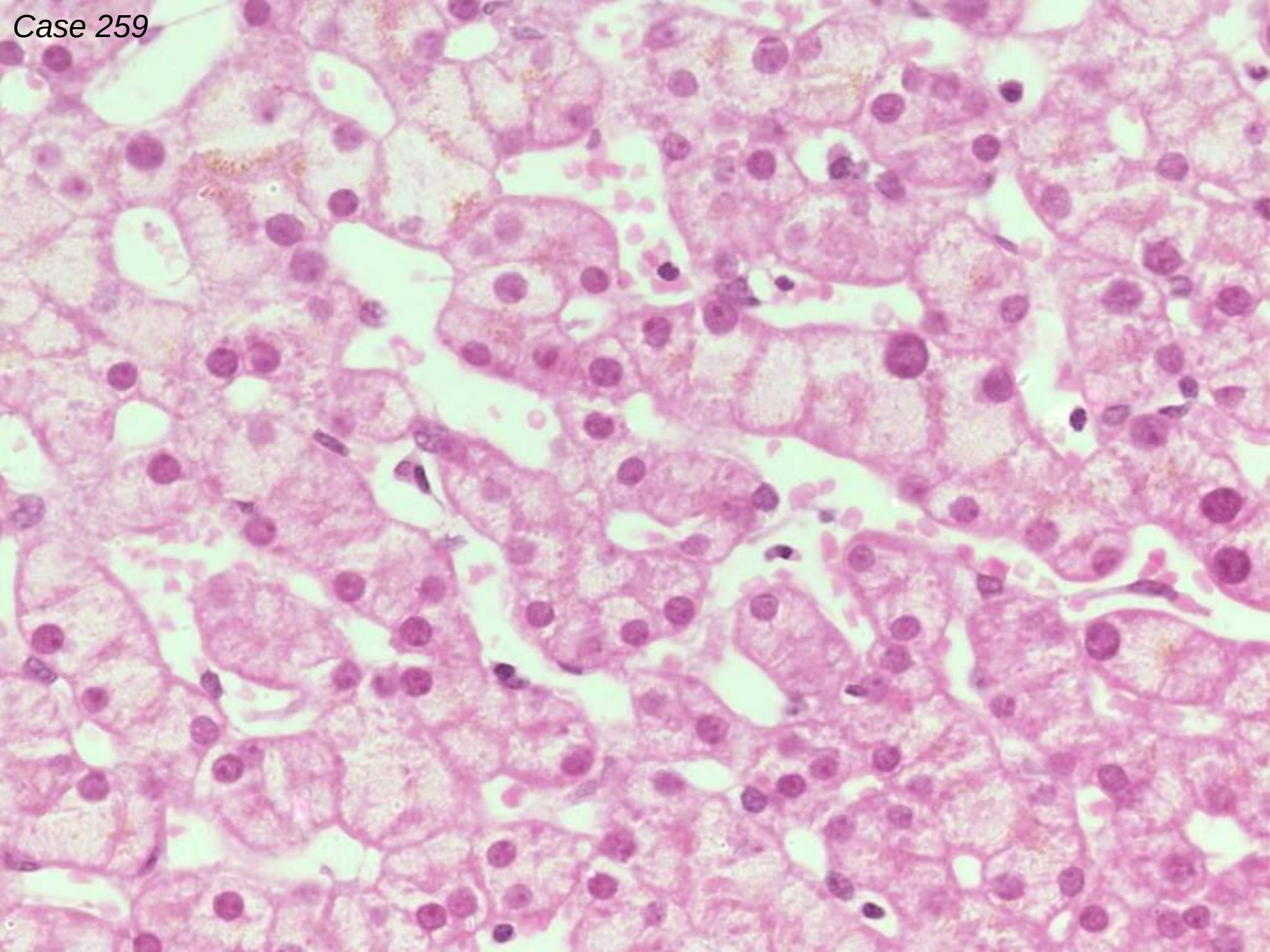

Case 259

Case 259

56 primary biliary cirrhosis, of which:
- 2 PBC (nothing else)
- 50 consistent with PBC (+/- early stage)
- 4 consistent with PBC but exclude hepatitis C

1 can't exclude the possibility of PBC (no alternatives)

4 not typical of PBC – 3 give more likely alternatives:
- 1 ? adjacent to a SOL
- 1 VOD
- 1 ? chronic hepatitis B

2 morphological description only, no mention of PBC

comments: ? significance of sinusoidal dilatation

Case 259

Scoring: reject responses with morphological description only, no mention of PBC

Discussion: the histology of a single tract with marked inflammation surrounding the duct, but with no granulomas, is consistent with PBC because of the information on anti-mitochondrial antibodies. Caution was expressed by the clinicians present on putting too much reliance on mitochondrial antibodies, and the biopsy findings were not typical of PBC.

Case 259

Original diagnosis:

Consistent with PBC

Case 260

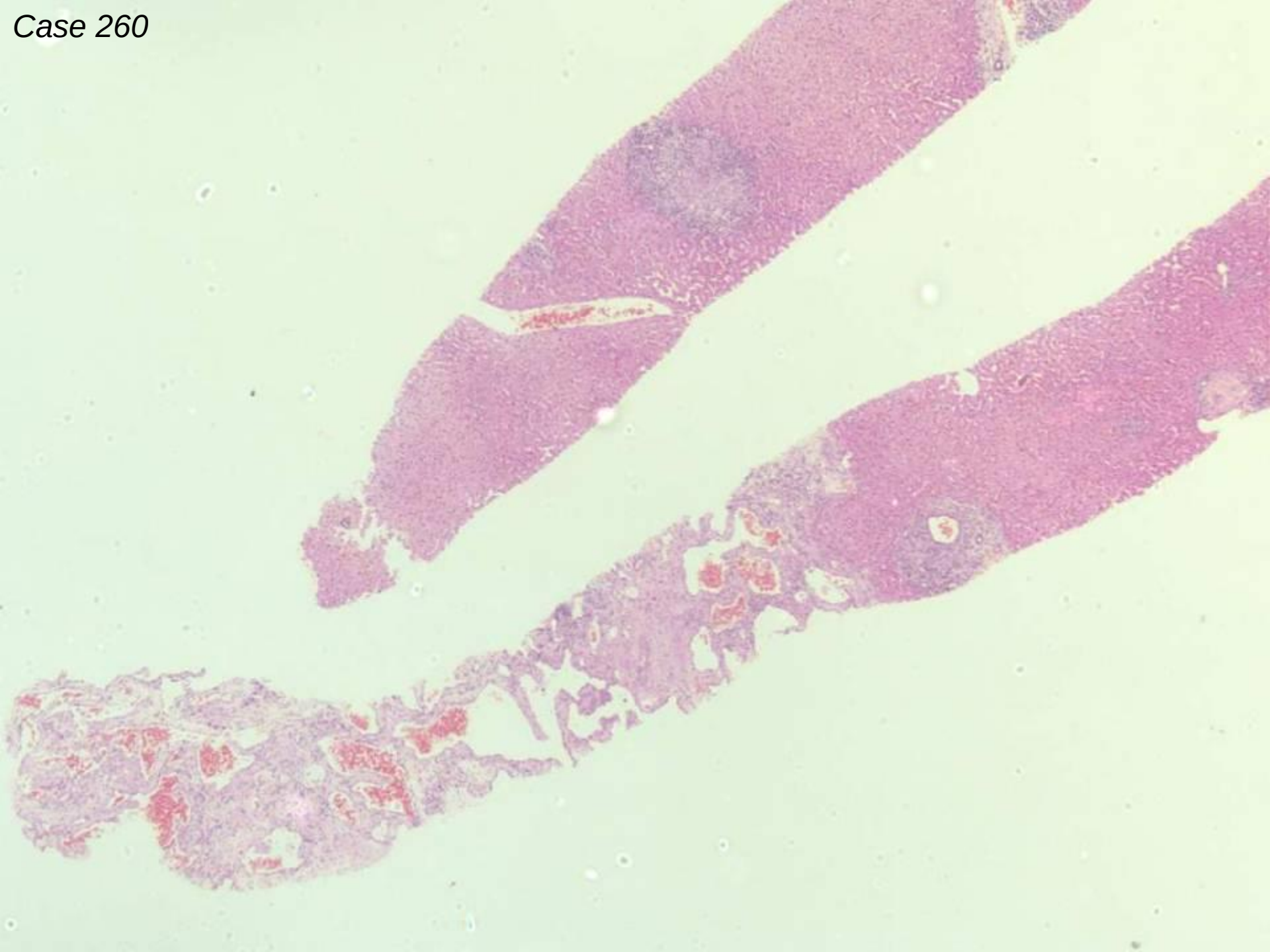
50 F

? Primary biliary cirrhosis. AMA positive (>1:640) M2 positive, bilirubin 7,

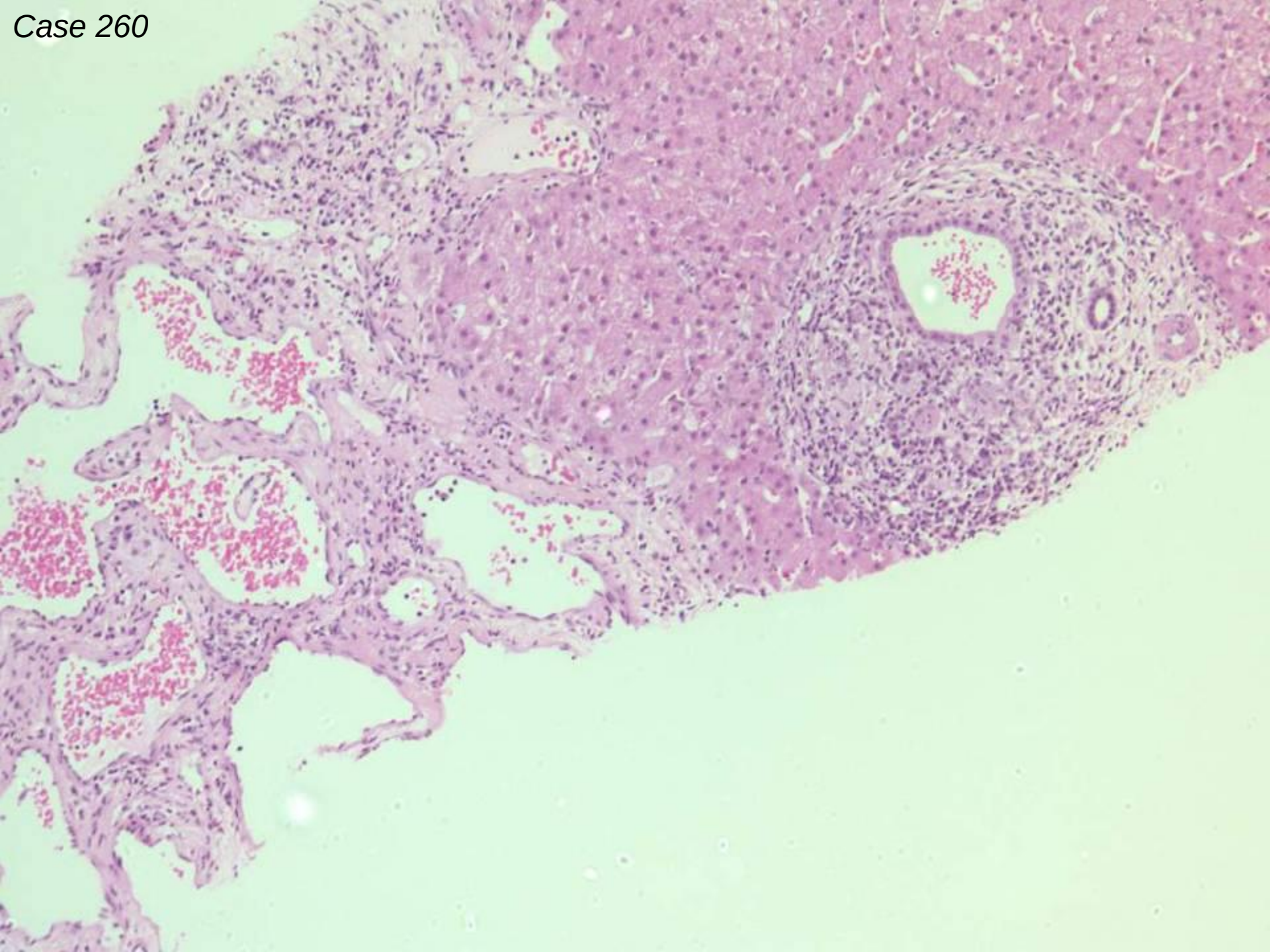
Alk phos 106, WVG =- mild fibrous expansion of some portal areas only.

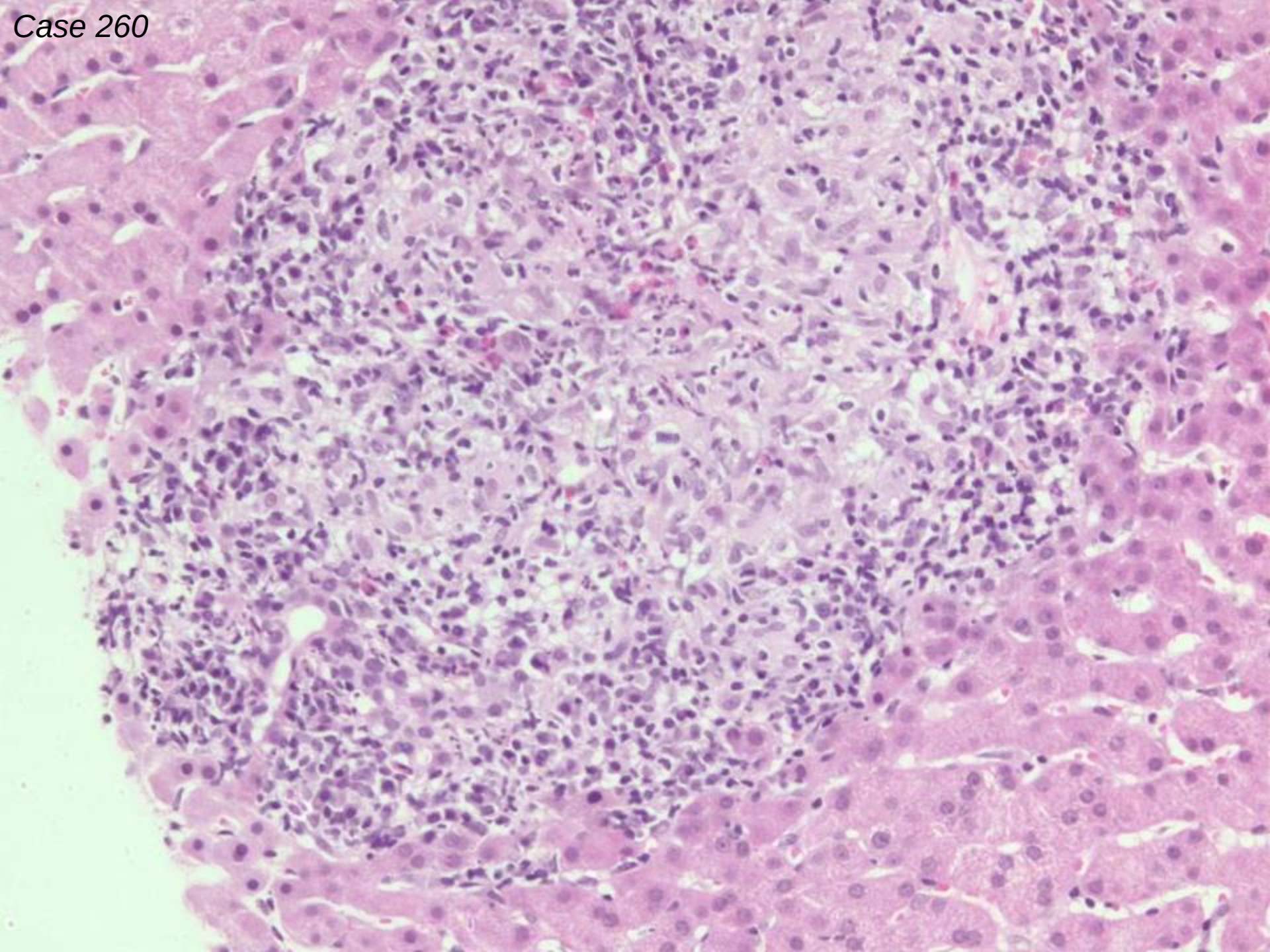
Case 260

Case 260



Case 260




Case 260

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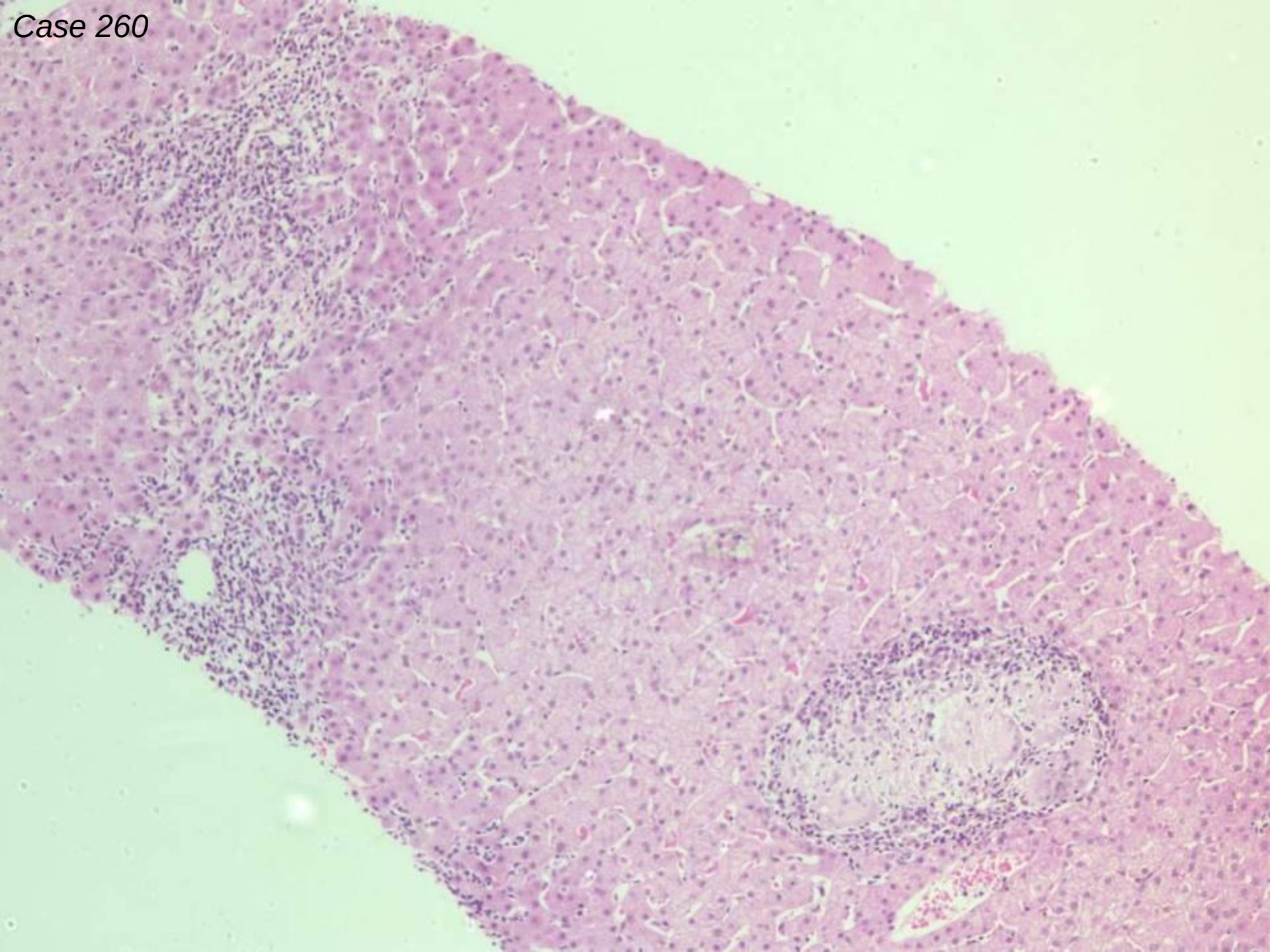
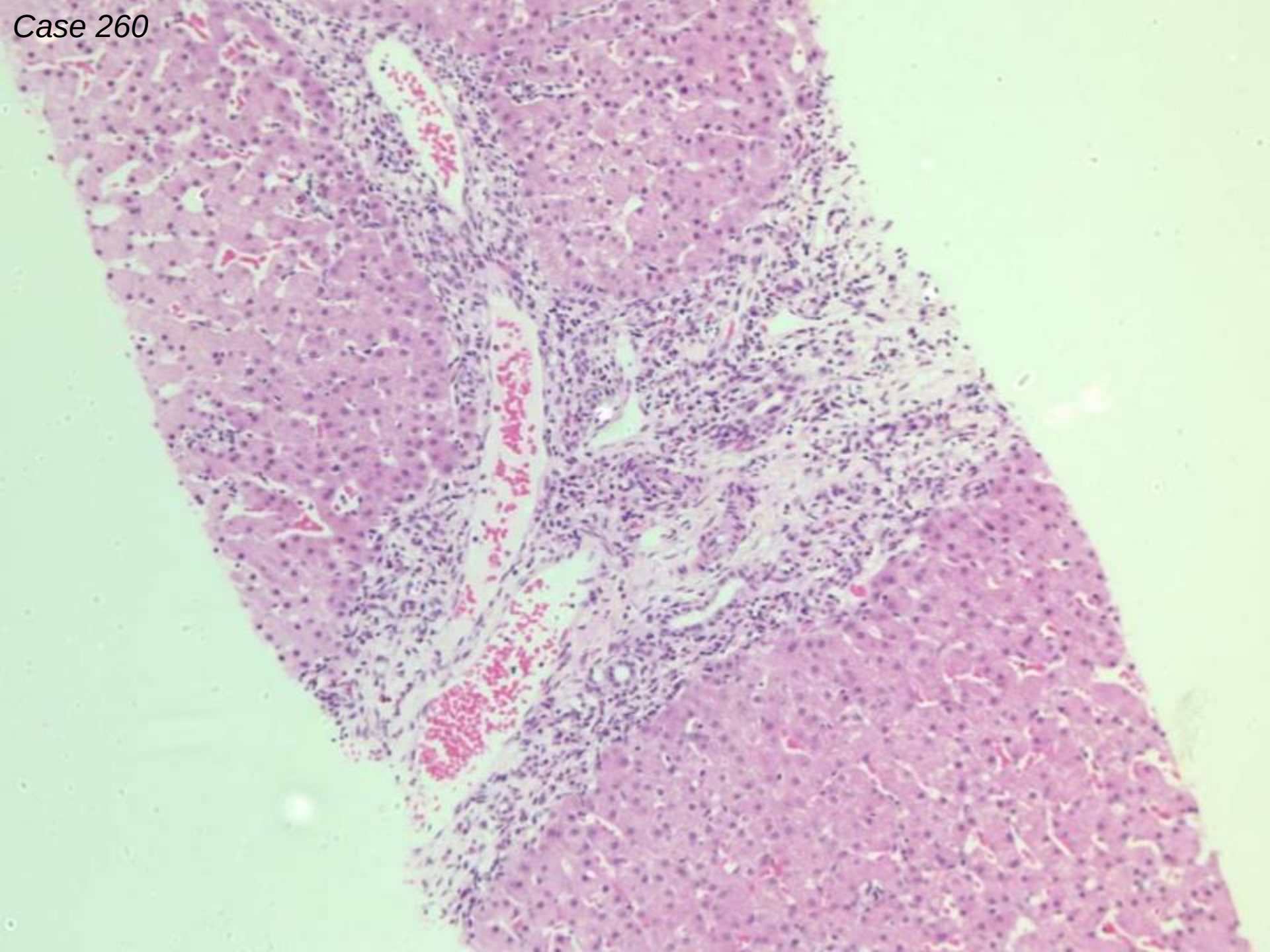


Case 260



Case 260

43 PBC + haemangioma

14 PBC, no mention of haemangioma

4 unusual for PBC, - ?drug ? AIH, + haemangioma

2 consistent with PBC but ?AIH/Drugs, no mention of haemangioma

1 morphology and serology (mimic that of PBC) suggest type 3 AIH, and haemangioma

Case 260

Scoring: Score full marks for including PBC and haemangioma. Score half marks if no mention of haemangioma, or if response indicated this was unusual for PBC. No marks for response suggesting that diagnosis was not PBC.

Discussion: There were some responses including the haemangioma from every cell in the circulation, confirming that it was present on all slides, although the amount may have varied. The bile duct granulomas in this case were so typical of PBC that responses implying a differential were marked down.

Case 260

Original diagnosis:

Consistent with early stage PBC

+ haemangioma

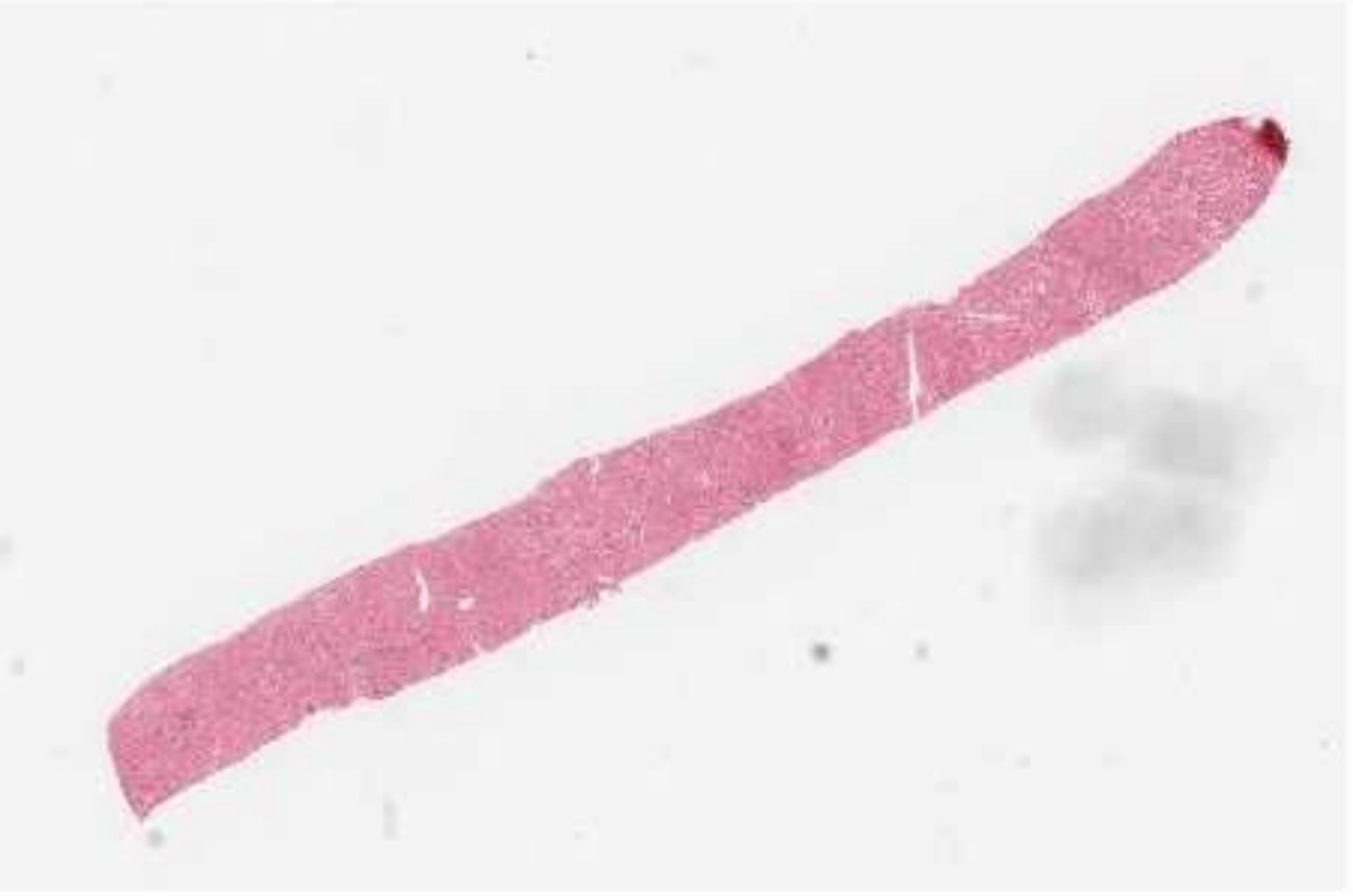
Case 261

53 M

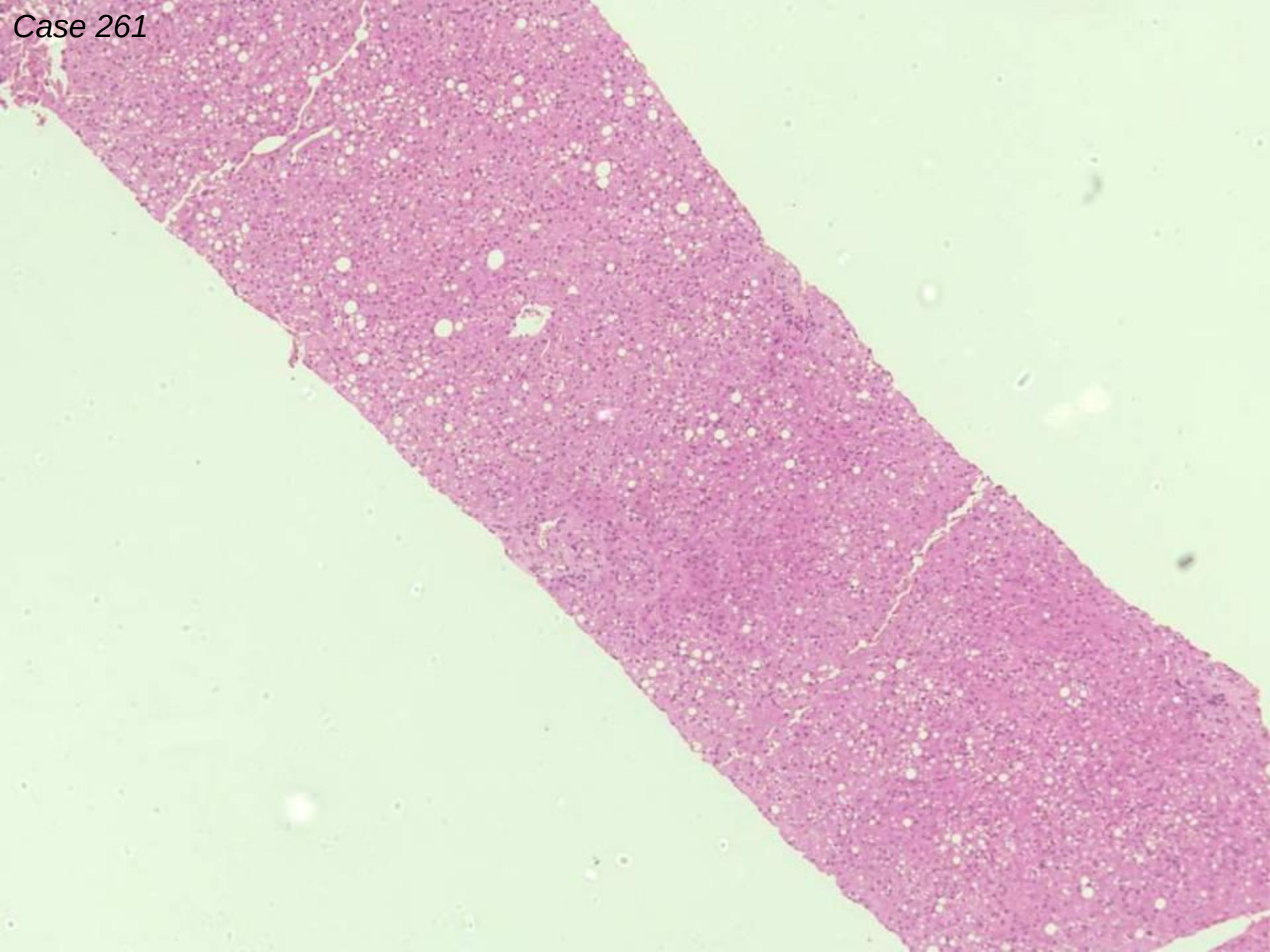
Abnormal LFTs

Core of tissue measuring 8mm in length (perivenular and pericellular fibrosis)

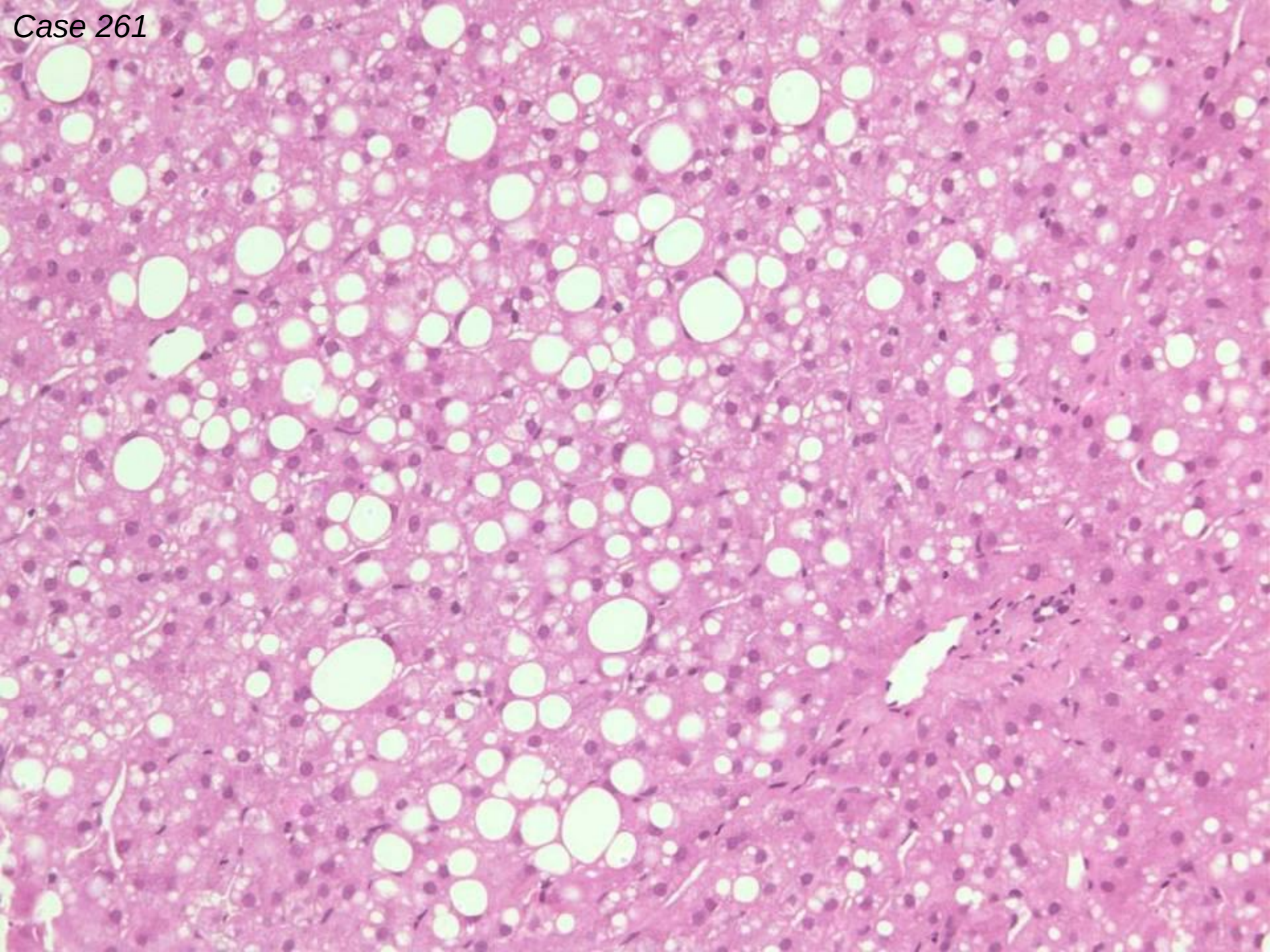
Case 261

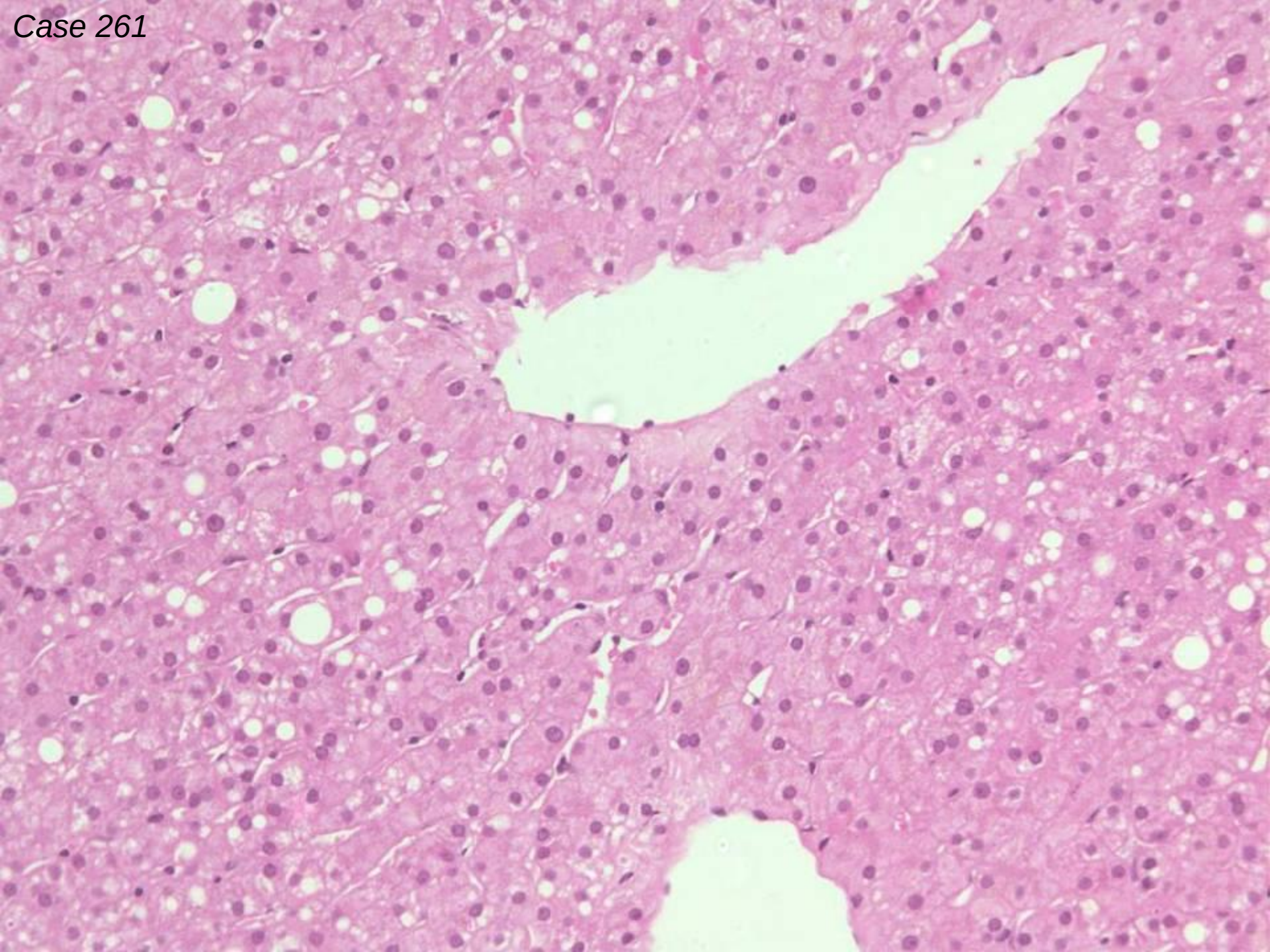


Case 261



Case 261

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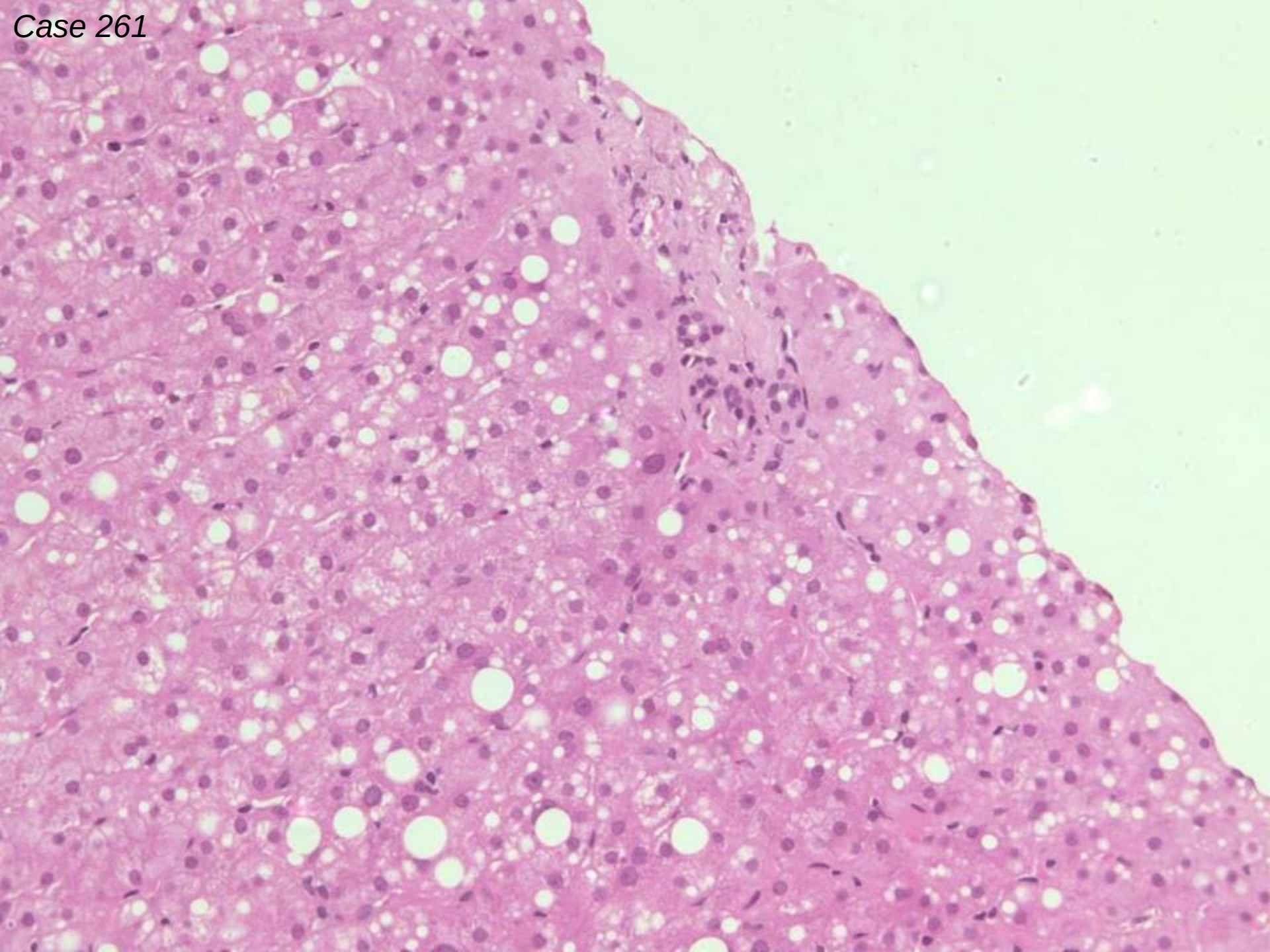
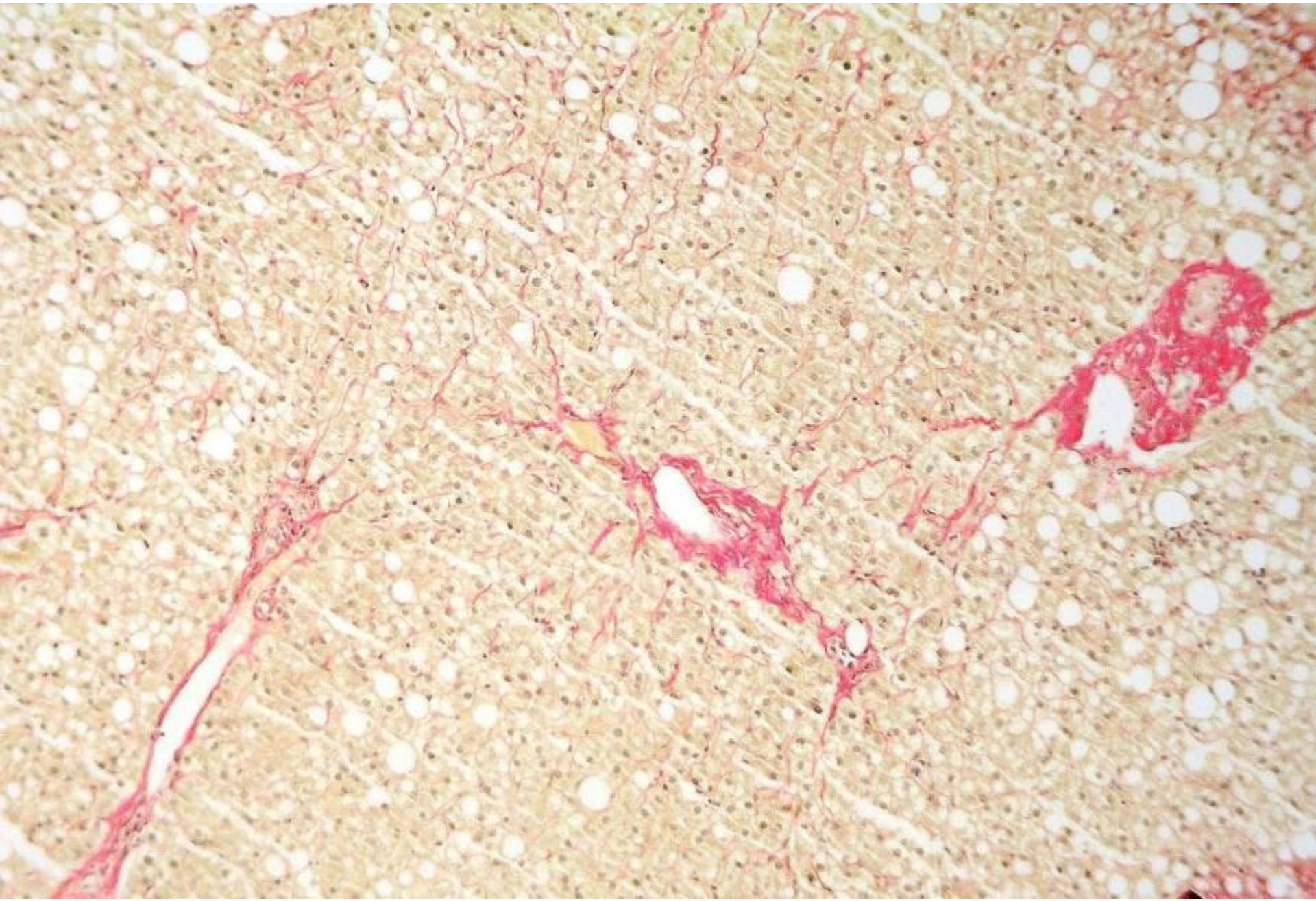

Case 261

Case 261



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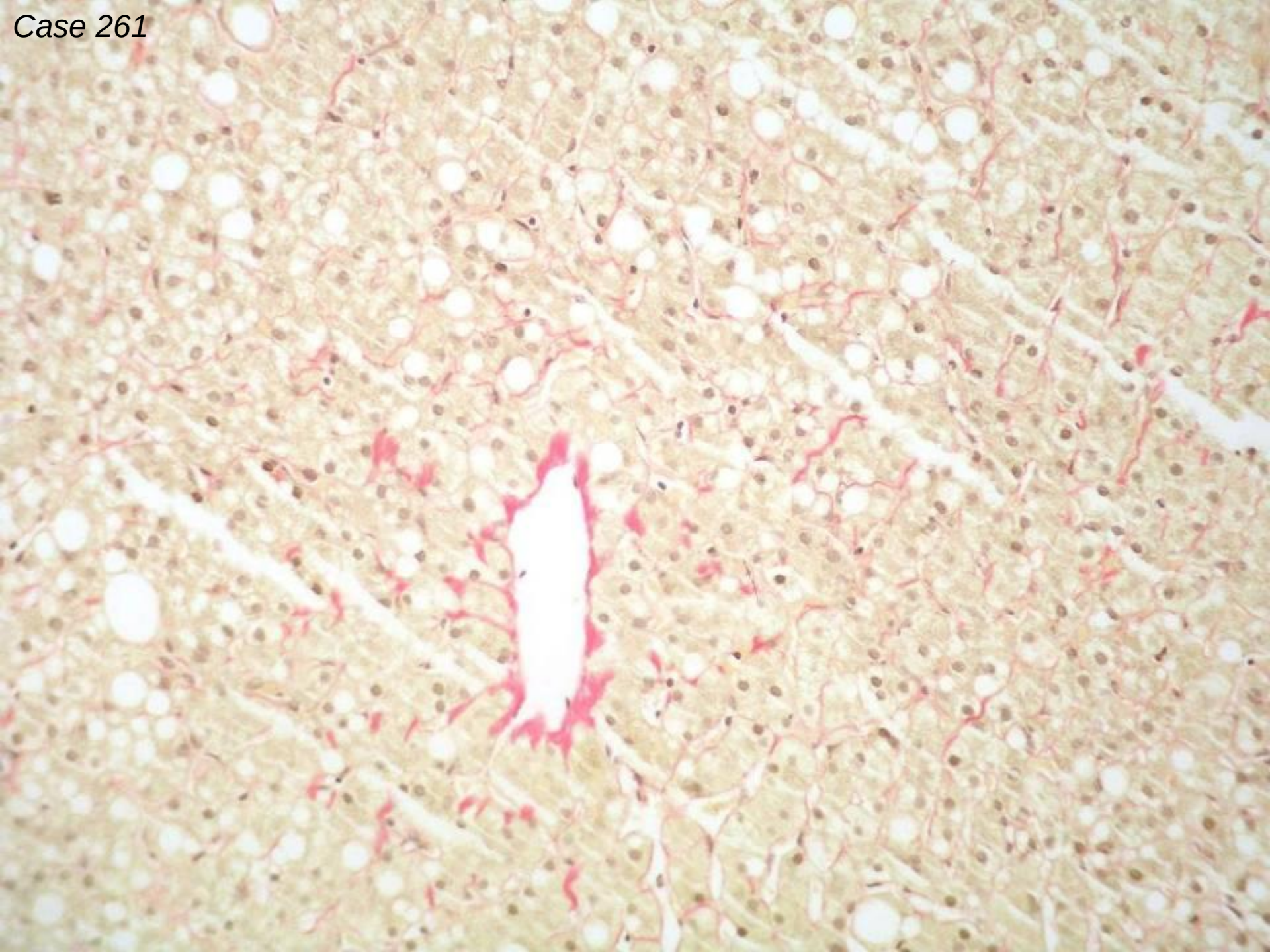


Case 261

Morphology:

16 steatosis
31 steatosis and fibrosis
14 steatohepatitis
1 steatosis and central hyaline sclerosis

Aetiology:

37 alcohol or NAFLD
7 alcohol only
3 NAFLD only (alcohol not mentioned)
1 drugs/NAFLD (alcohol not mentioned)

11 no aetiology mentioned
1 exclude venous outflow obstruction, as only aetiology
1 aetiology not clear. Possible PVF
1 'fine and large vacuole steatosis (of acquired mitochondriopathy/HAART?)
? ground glass cells of hepatitis B. Serology/orcein/drug history'

comment: 7/14 steatohepatitis - steatosis and fibrosis implies diagnosis of steatohepatitis

Case 261

Scoring: Reject 'steatosis and central hyaline sclerosis' and 'fine and large vacuole steatosis (of acquired mitochondriopathy/HAART?) ; full marks for the others.

Discussion: There was discussion about whether the sinusoidal fibrosis illustrated by the van Gieson stain should be considered pathological, and if it was, whether this would be sufficient for a diagnosis of steatohepatitis.

The fibrosis was slight, discontinuous, along the space of Disse. Comments were that this can be seen in biopsies which are otherwise normal, and the degree to which this is seen is dependent on the stain used. It increases in various situations, including venous outflow obstruction, perhaps portal vein obstruction, and in previous hepatitis, as well as in fatty liver disease. The small amount in this case is of doubtful significance, and perhaps represents regressing fibrosis. This should be distinguished from pericellular fibrosis, where collagen surrounds the circumference of a ballooned hepatocyte – as characteristically occurs in steatohepatitis.

Case 261

Discussion contd.

The terminology of fatty liver disease – when to use steatohepatitis v. steatosis was discussed. Fibrosis can be seen in fatty liver disease without other features of steatohepatitis, and is of clinical importance since it implies progressive chronic liver disease. The features of hepatocyte injury in steatohepatitis (i.e. ballooning, Mallory bodies, parenchymal inflammation) can be focal in a fatty liver biopsy and can vary with time, leaving fibrosis. It is possible (based on animal models) that fibrosis in fatty liver disease can develop independently without steatohepatitis. Therefore steatosis and fibrosis would be more appropriate than steatohepatitis.

Case 261

Original diagnosis:

Steatofibrosis

Clinically NAFLD

Case 262

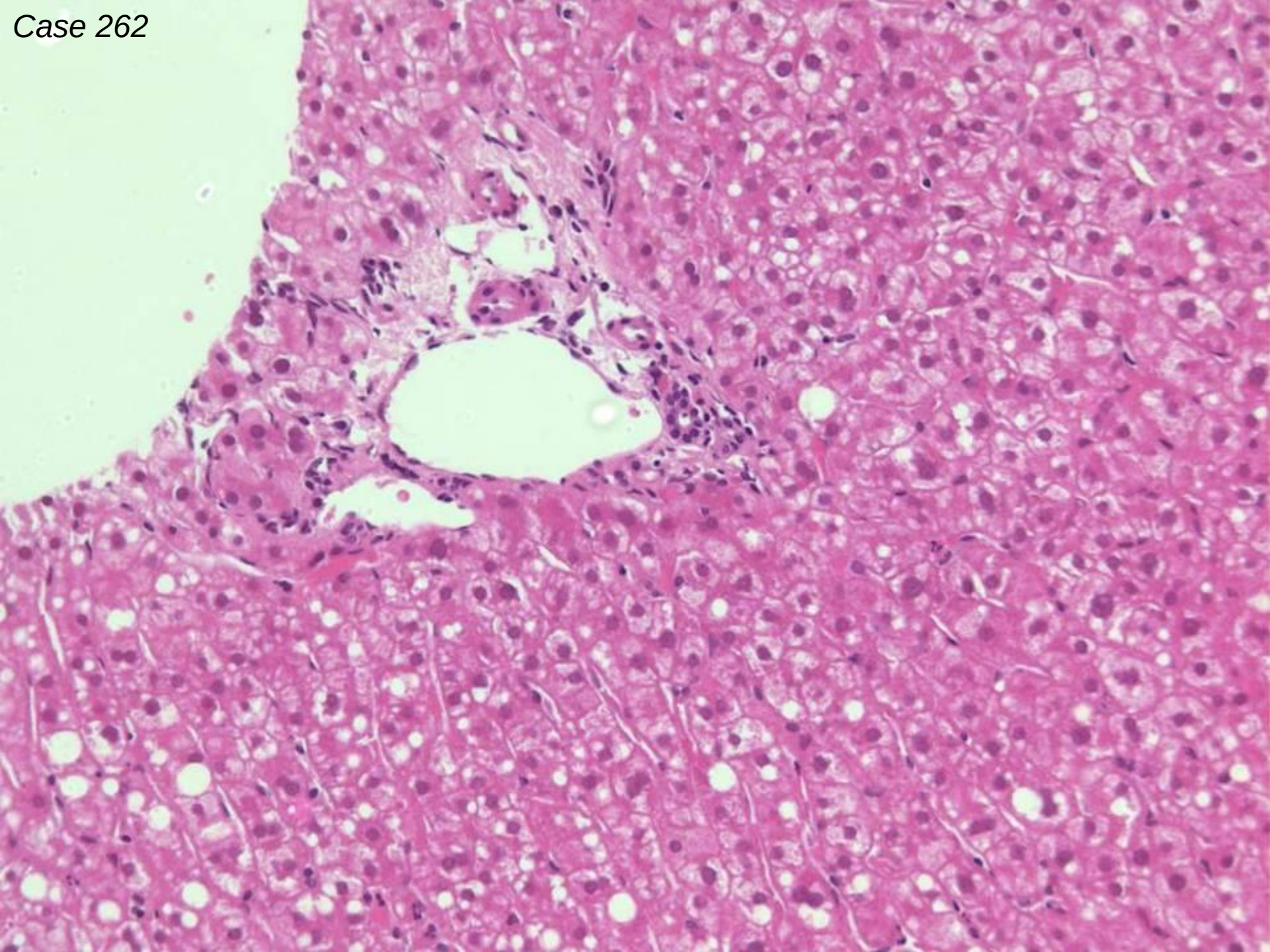
51 M

Gilbert's syndrome and sarcoidosis on steroids. Abnormal LFTs

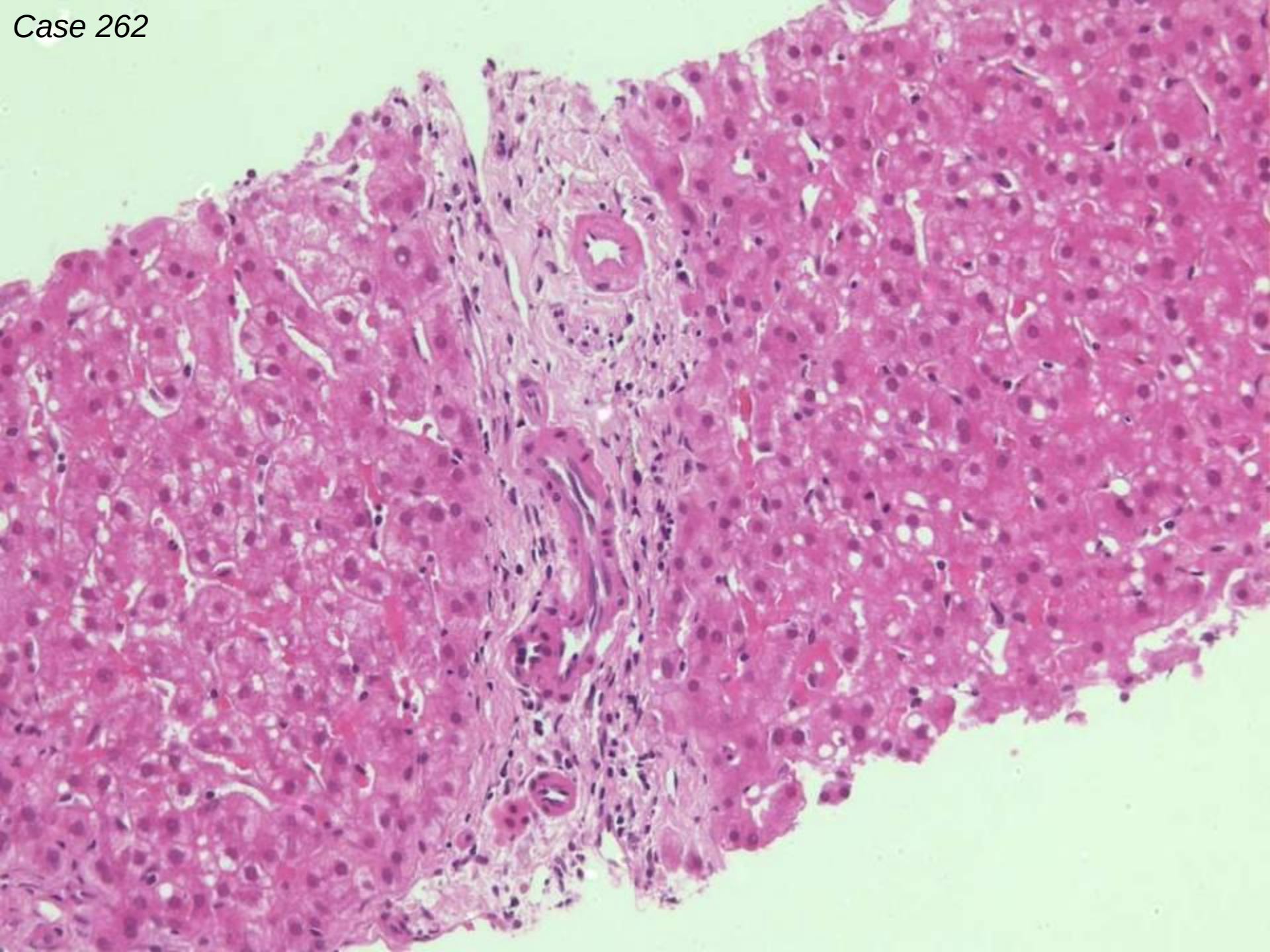
special stains: Perl's shows increased iron in hepatocytes.

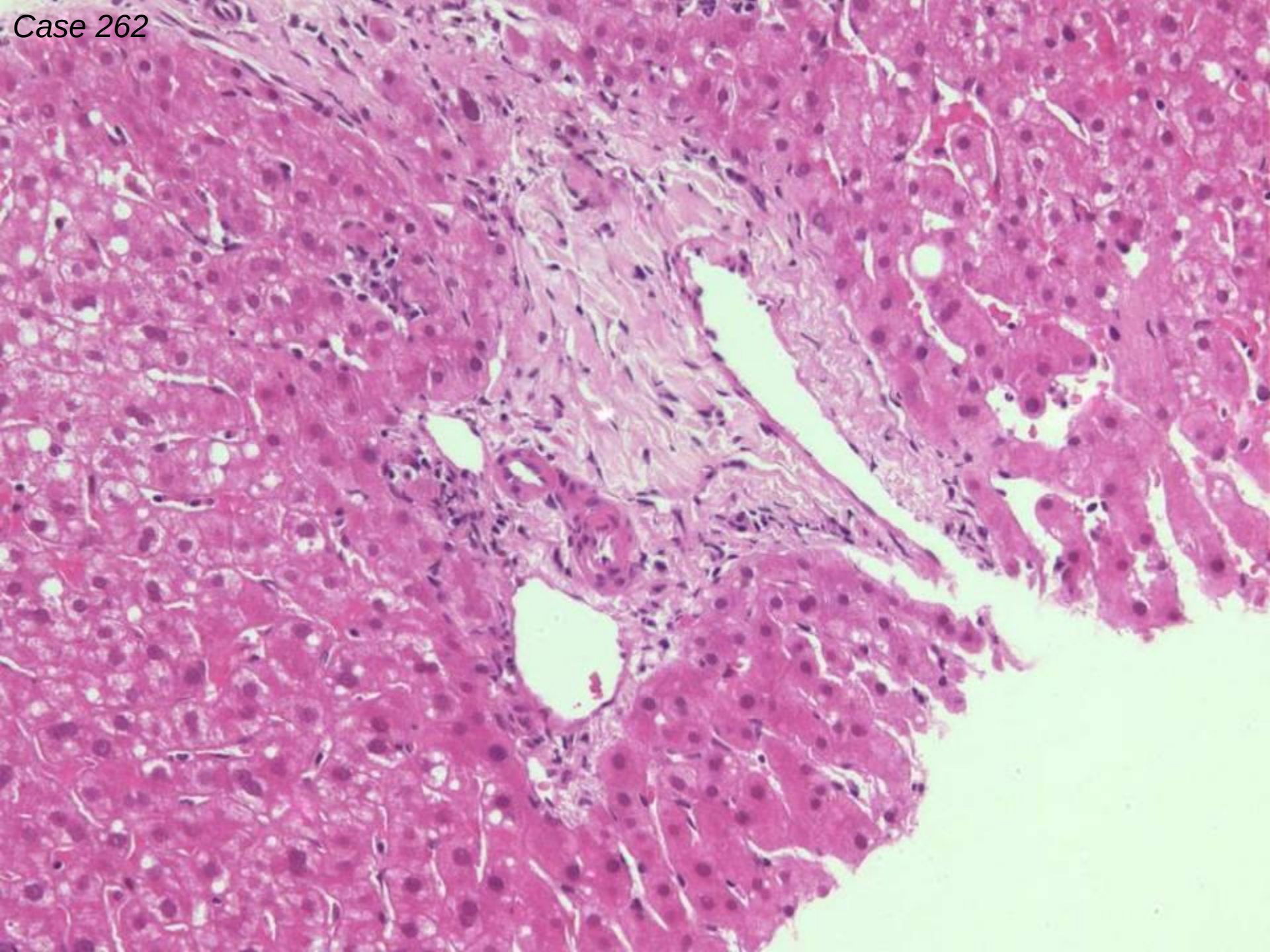
Case 262

Case 262

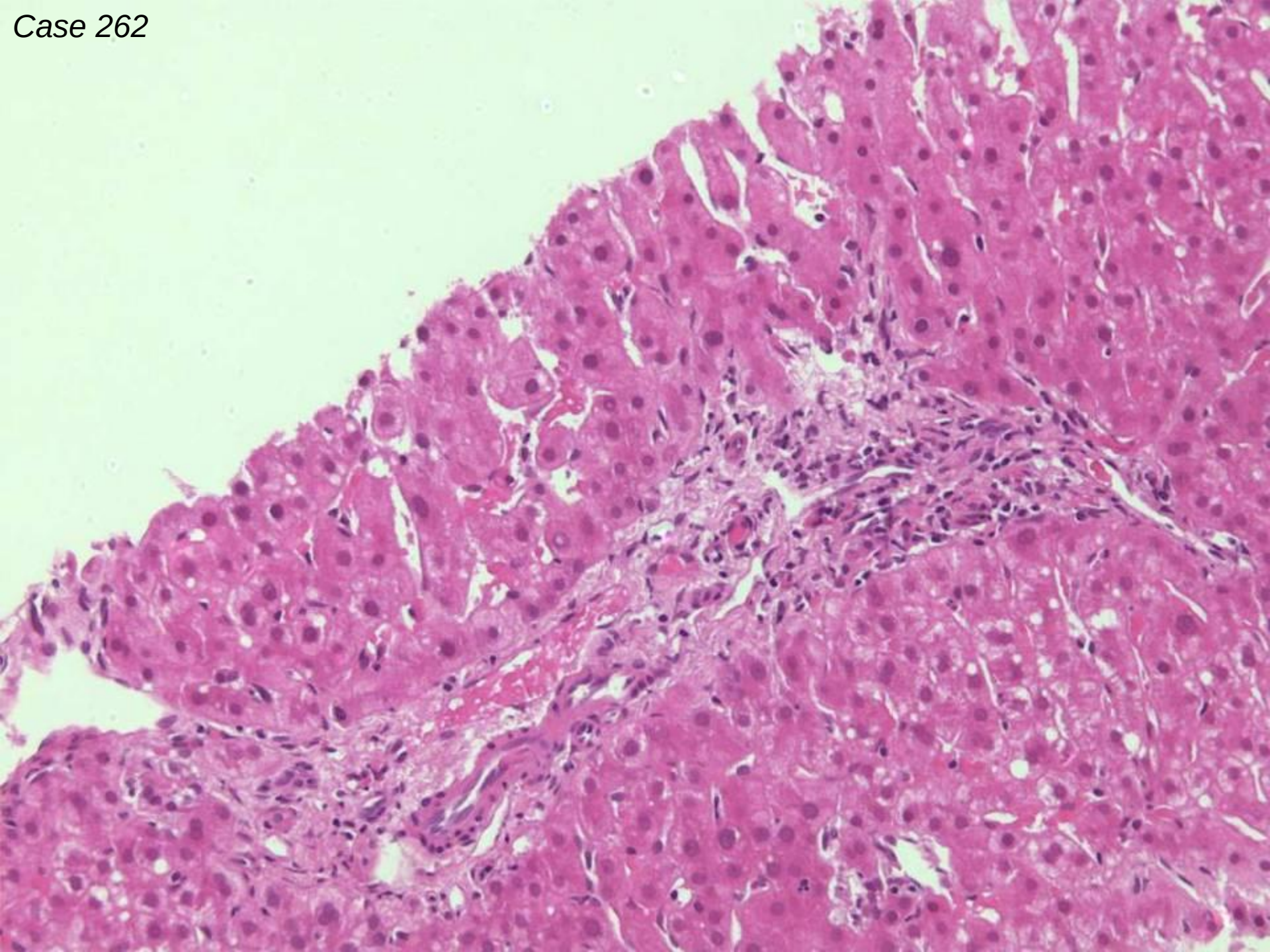


Case 262




Case 262

Case 262



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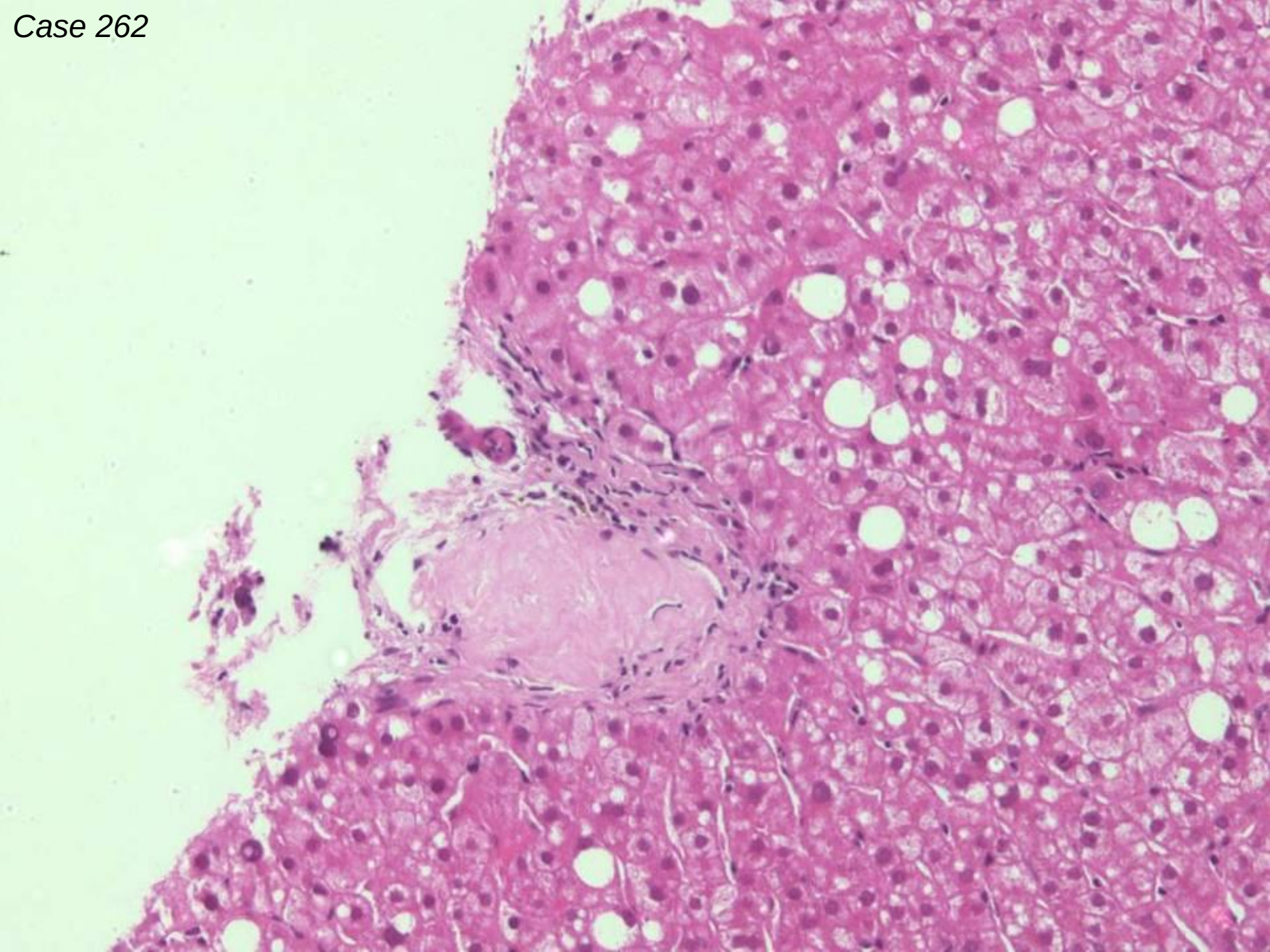
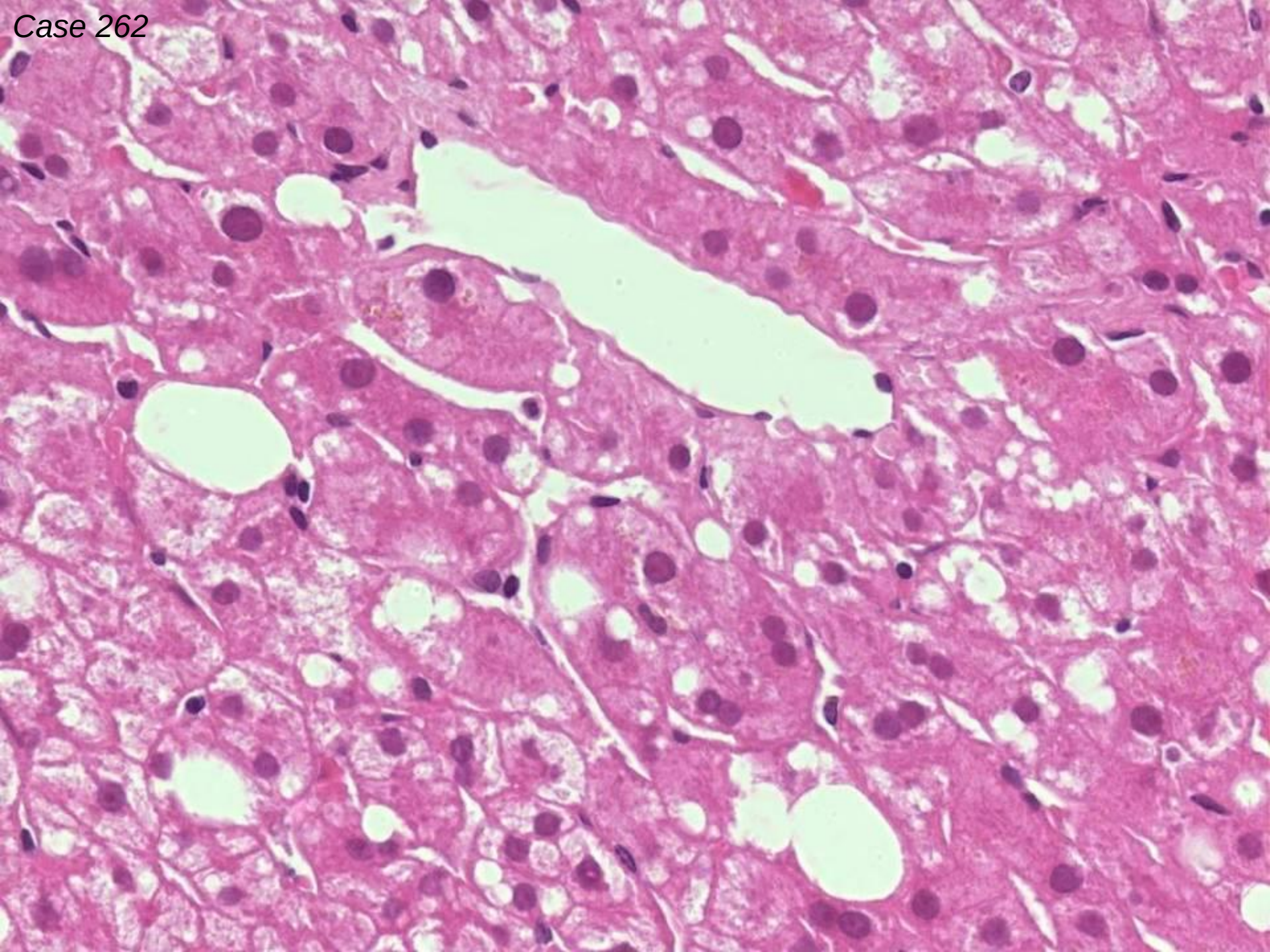



Case 262

Case 262

43 probably or consistent with sarcoidosis
3 not related to sarcoidosis
17 no mention of sarcoidosis

13 non specific changes, steatosis,

Diagnosis of sarcoid related to:-
nodular scars probably of previous granulomas,
and/or ductopaenia.

Diagnosis	Ductopaenia	No comment on ductopaenia
Probably or c/w sarcoidosis	37	6
Not sarcoidosis	-	3
Sarcoid not mentioned	7	10

Other comments:
16 differential diagnosis – exclude PSC
15 investigate for haemochromatosis
7 exclude amyloid

2 drug induced steatosis due to steroids
2 Gilbert's

Case 262

Other comments:

16 differential diagnosis – exclude PSC

15 investigate for haemochromatosis

7 exclude amyloid

2 drug induced steatosis due to steroids

2 Gilbert's

Case 262

Scoring: no consensus diagnosis – this case not included in scoring.

Discussion: this was of educational interest, as an example of ductopaenia in a patient with sarcoidosis. With the clinical history of sarcoidosis, it is likely that the rounded fibrous scar represents a healed granuloma, although its resemblance to the scarring of PSC was noted. The tendency of granulomas to heal with fibrosis can point to sarcoidosis in the differential diagnosis of granulomas in liver biopsies.

Ductopaenia occurs in some patients with sarcoidosis (37% in the study from AFIP, Am J Surg Pathol 1993;17;1272-80) although usually associated with portal fibrosis and ductular reaction, not seen in this case. Chronic biliary disease in patients can mimic either PBC or PSC, and the diagnosis of sarcoidosis depends on the clinical history of sarcoidosis involving other organs, unless other features of sarcoidosis (extent of granulomas with healing by fibrosis) are prominent in the liver biopsy.

Case 262

Original diagnosis:

Mild reactive hepatitis, fatty change and scarred granuloma associated with sarcoidosis

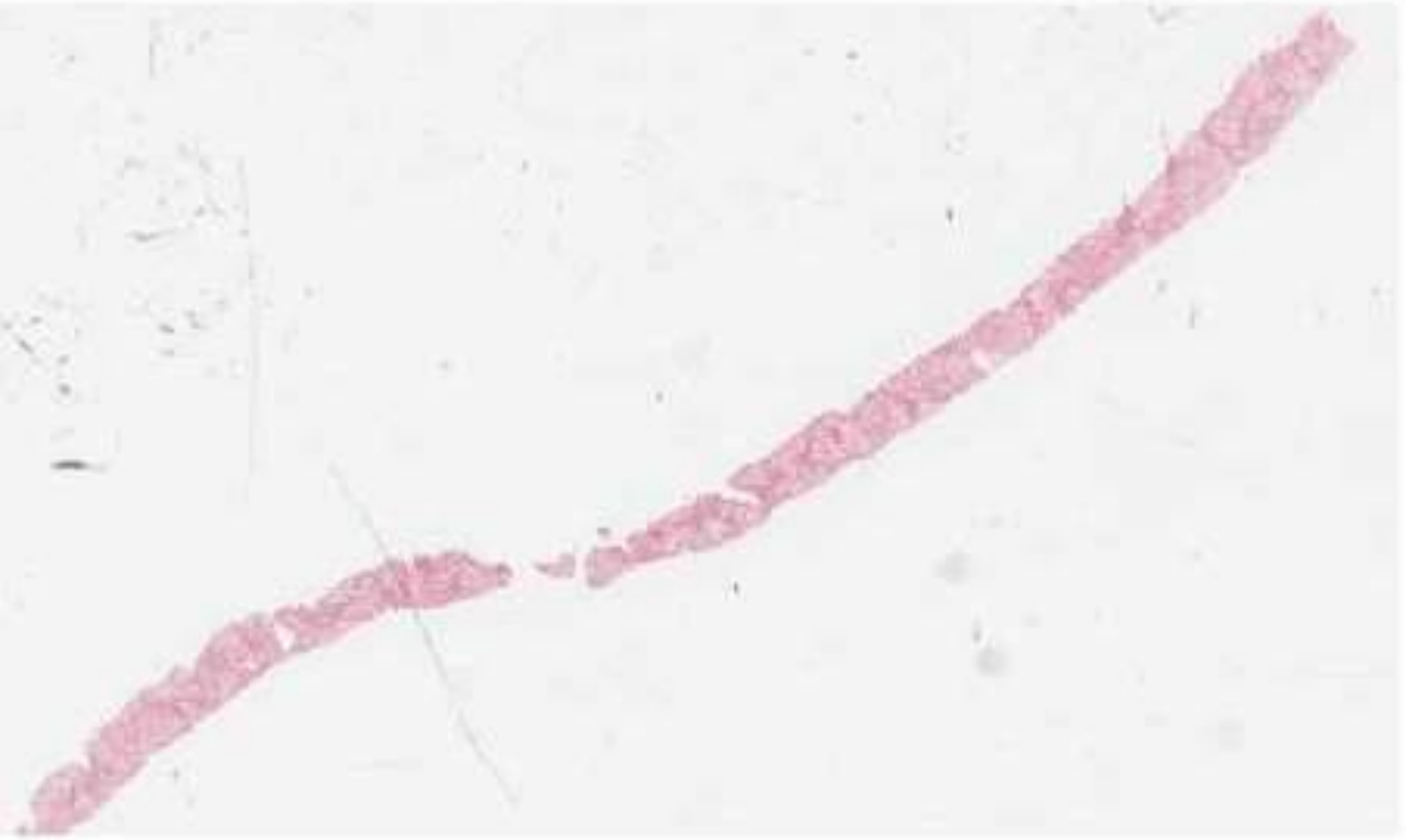
Increased iron in hepatocytes consistent with Gilbert’s disease.

Case 263

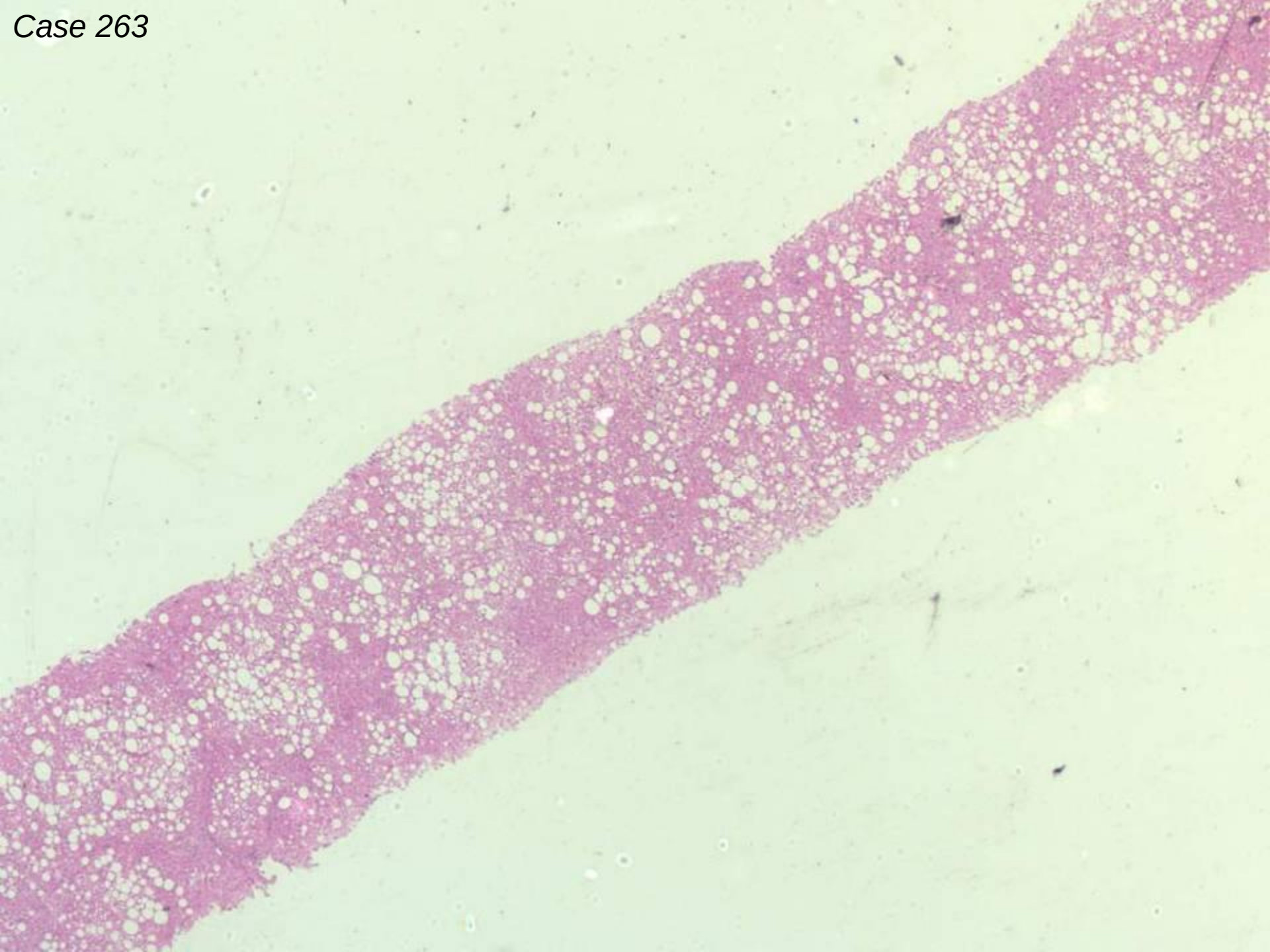
50 M

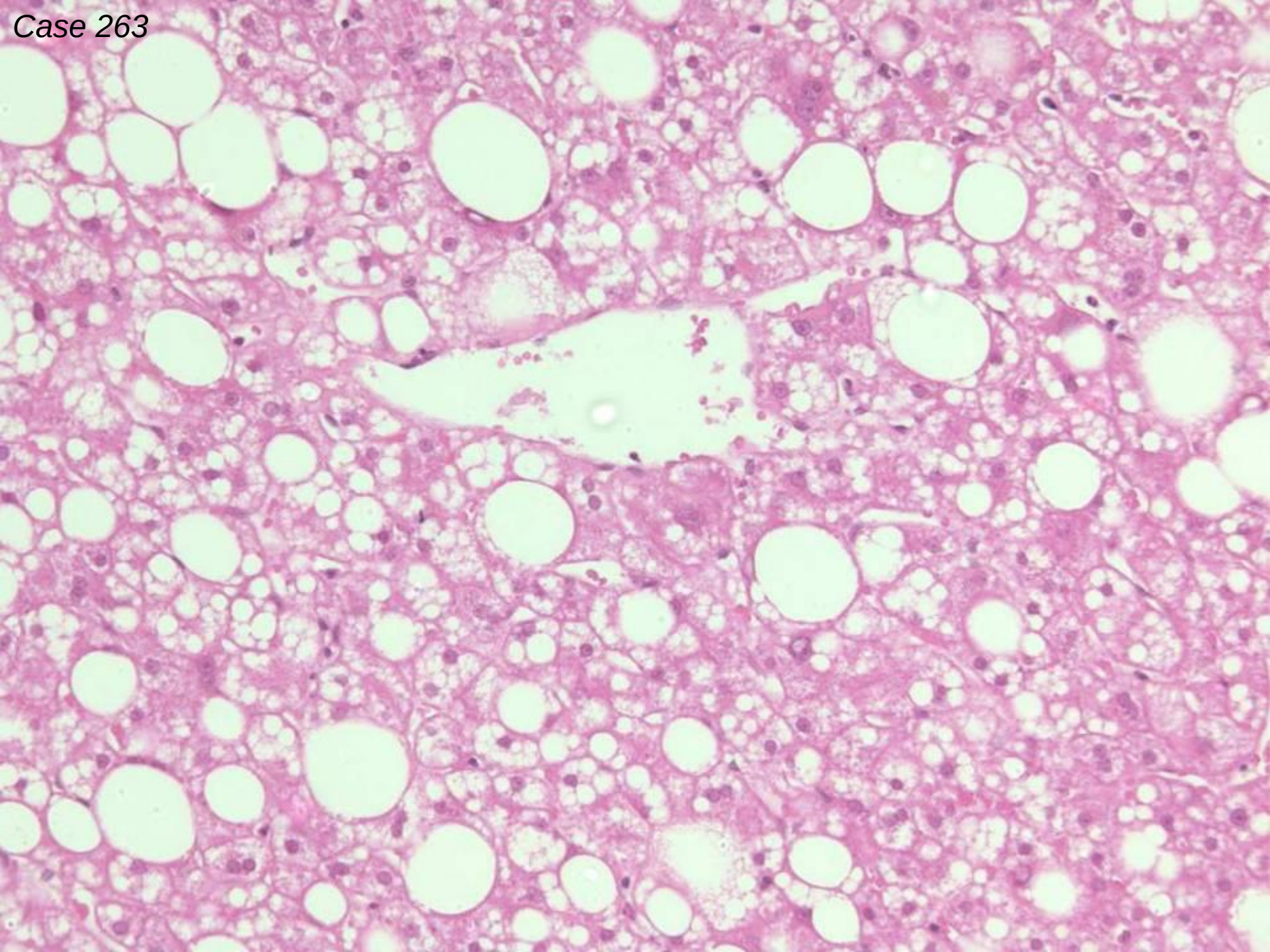
? methotrexate fibrosis. Increasing procollagen 3

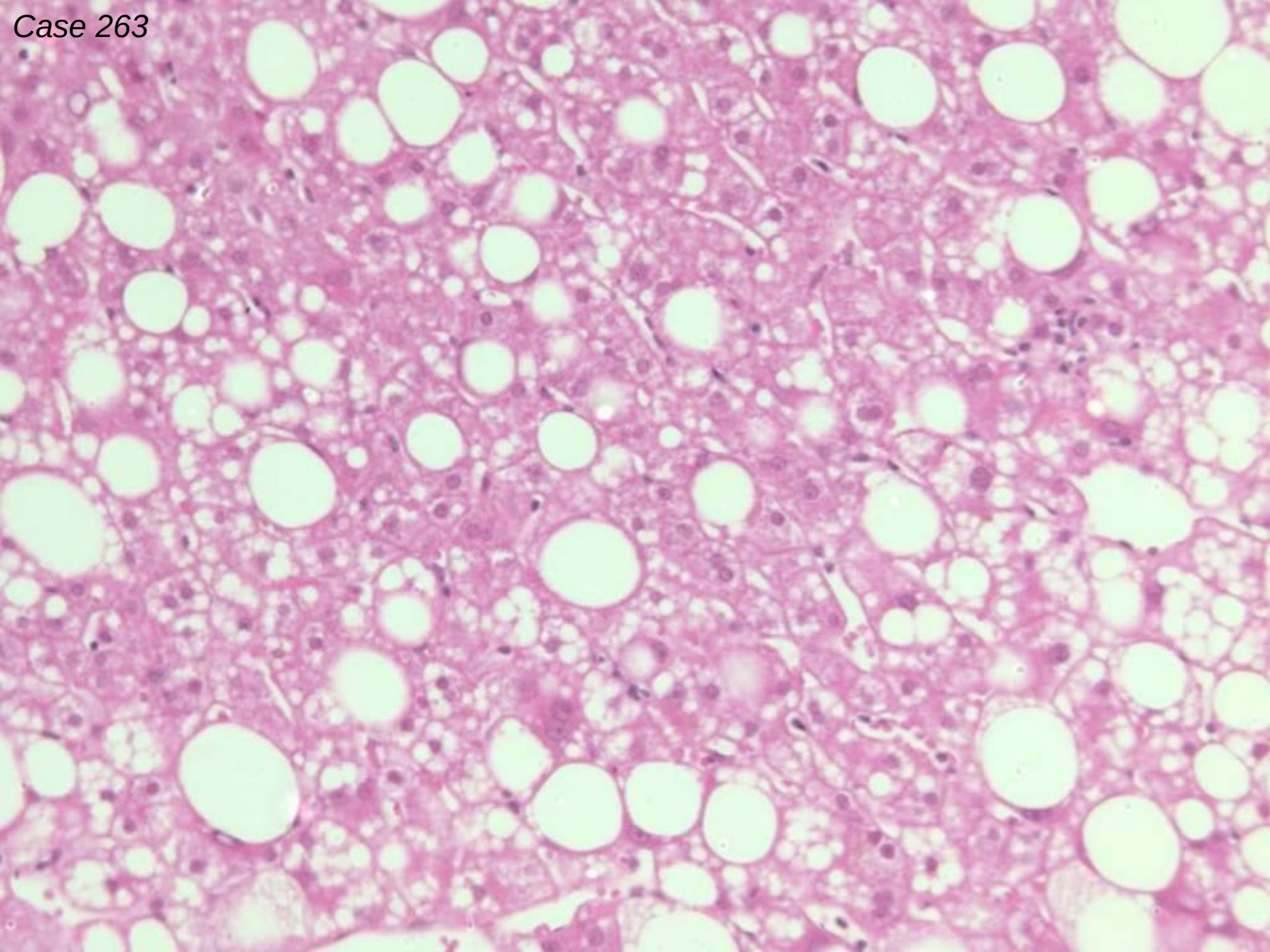
Case 263

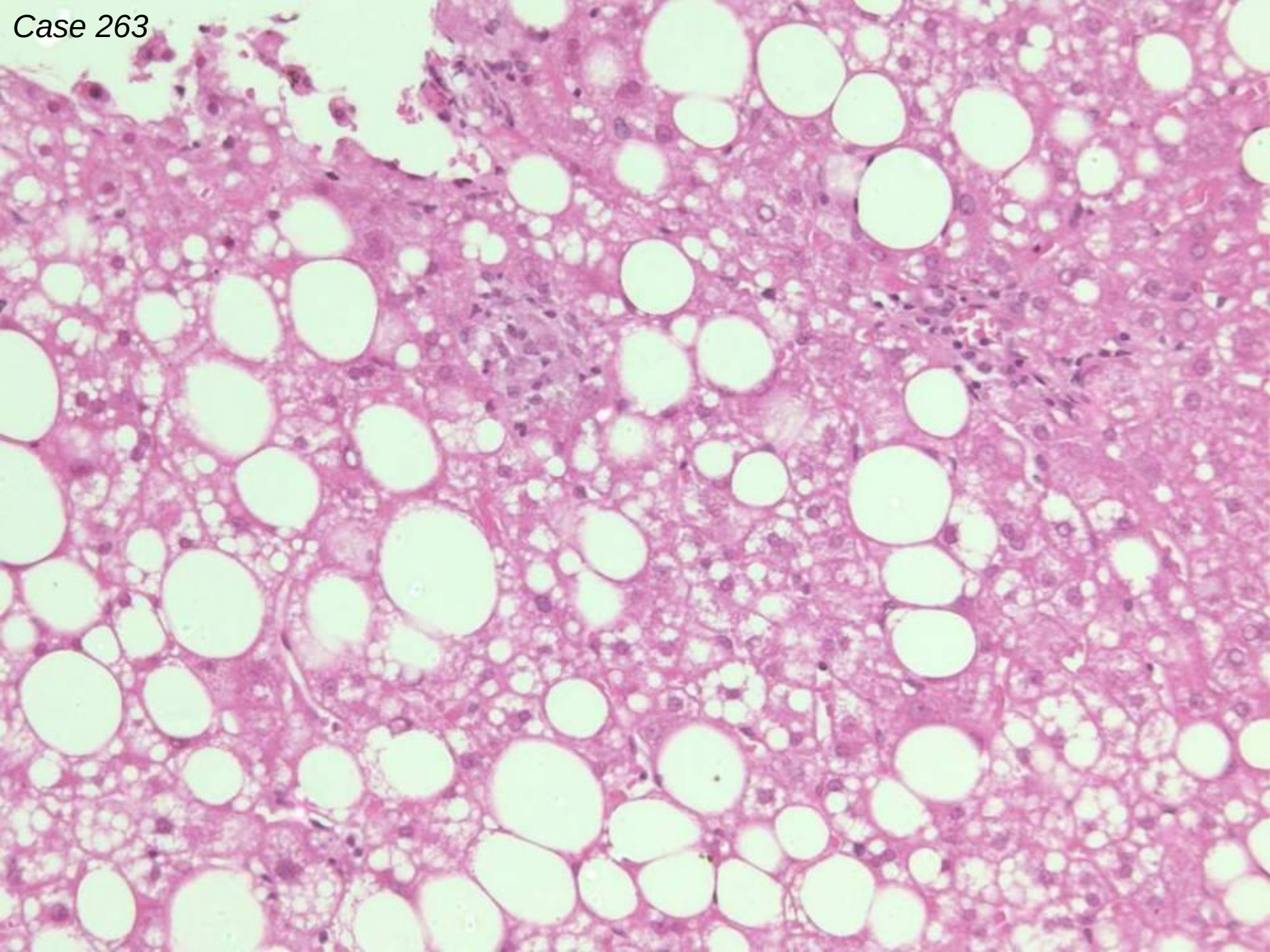


Case 263




Case 263


Case 263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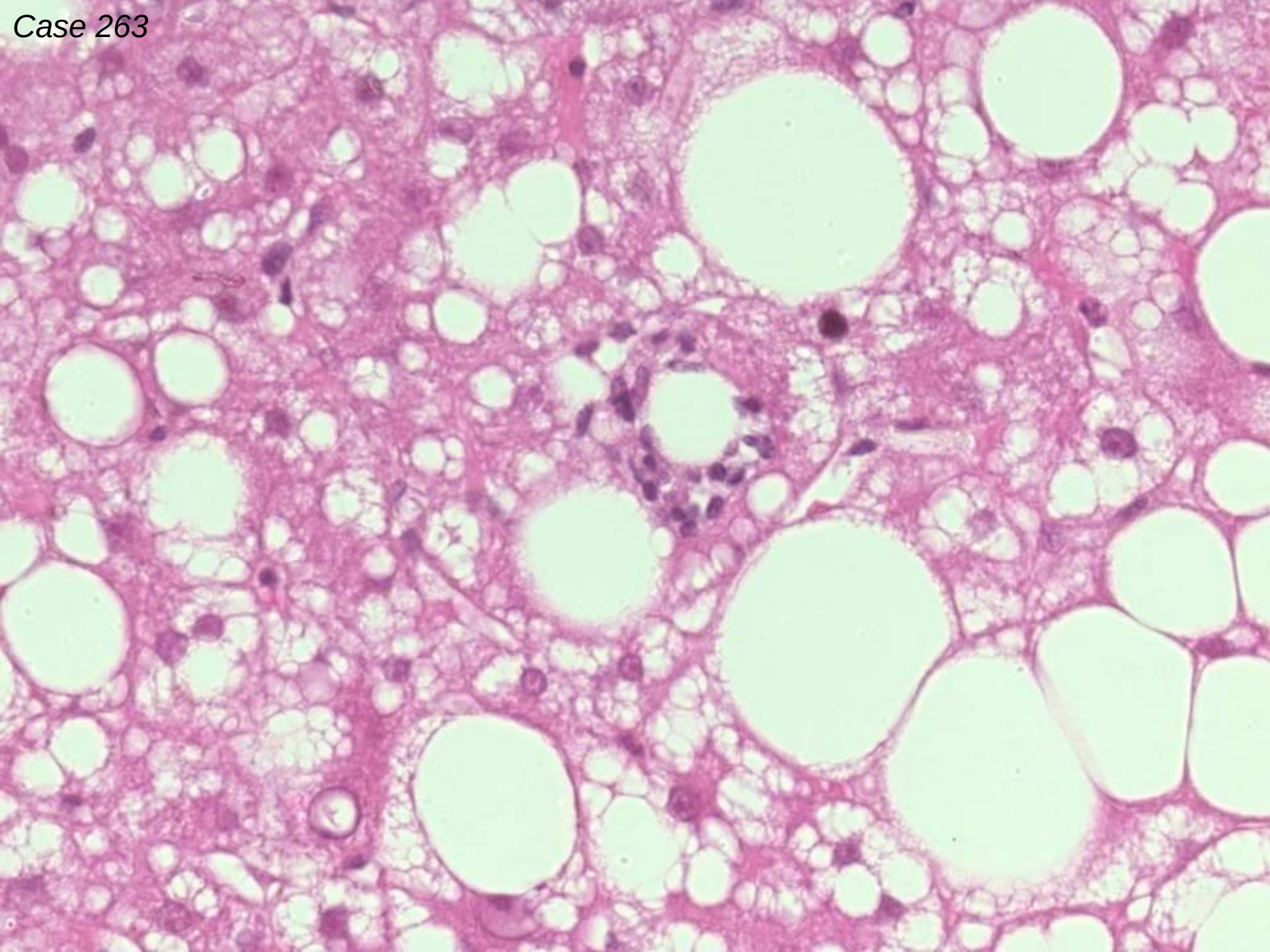

Case 263

Case 263

morphology

14 fatty change
26 fatty change and mild fibrosis
1 fatty change and ? bridging fibrosis
20 Steatohepatitis

1 ‘methotrexate hepatopathy’ as only diagnosis
1 ‘fine and large vacuole steatosis (of acquired mitochondriopathy/HAART?) connective tissue stain and infection/serologic history, drug history required’

aetiology

51 consistent with methotrexate
3 no comment on methotrexate
2 no comment on any aetiology
36 consider ASH/NASH, or history of ? alcohol, ?obesity

comments: Several very impressed by size of this biopsy!
2 May/recommend stop methotrexate
those who diagnosed steatohepatitis were more likely to ask about alcohol/obesity

Case 263

Scoring; Accept all responses of fatty change/steatohepatitis. Reject the last 2 diagnosis – methotrexate hepatopathy and fine and large vacuole steatosis (of acquired mitochondriopathy/HAART).

Discussion: Optimal answers suggest an additional cause for the fatty change here – alcohol or obesity – in view of the severity of the steatosis. There is no further clinical information available in this case. The impressively large biopsy was obtained with a Menghini needle.

Case 263

Original diagnosis:

Mild fibrosis and severe macrovesicular steatosis

Follow up information:

Rising procollagen 3 after 4 years on methotrexate. Enlarged, echobright liver on US, normal LFTs (alk phos, ALT, albumin). Biopsy report ? Alcohol – but patient followed up at another hospital, and both consultants have left.

Magnificent biopsies – thanks to Menghini needle, consultant took his needles with him.

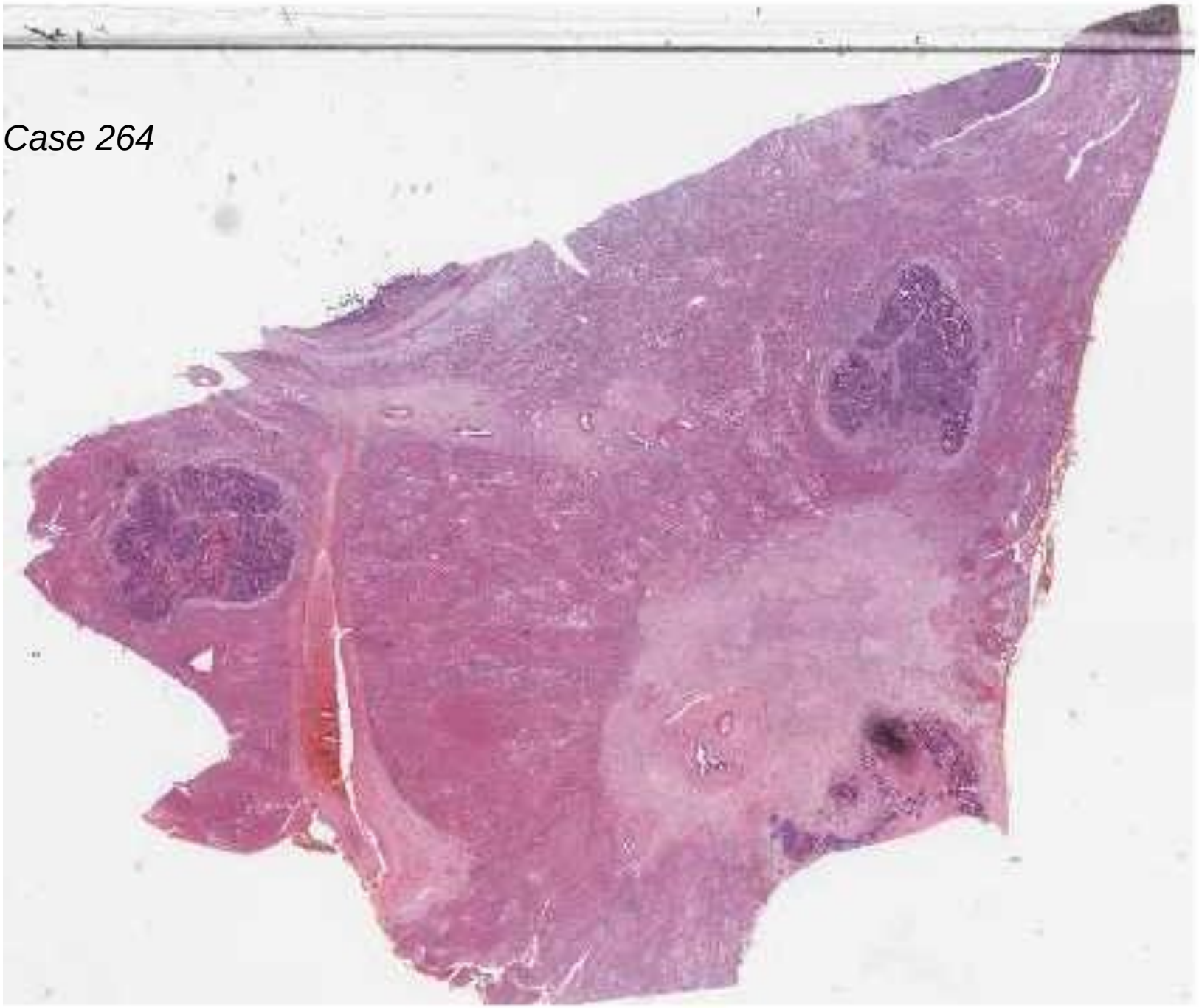
Recent biopsies use very delicate needles

Case 264

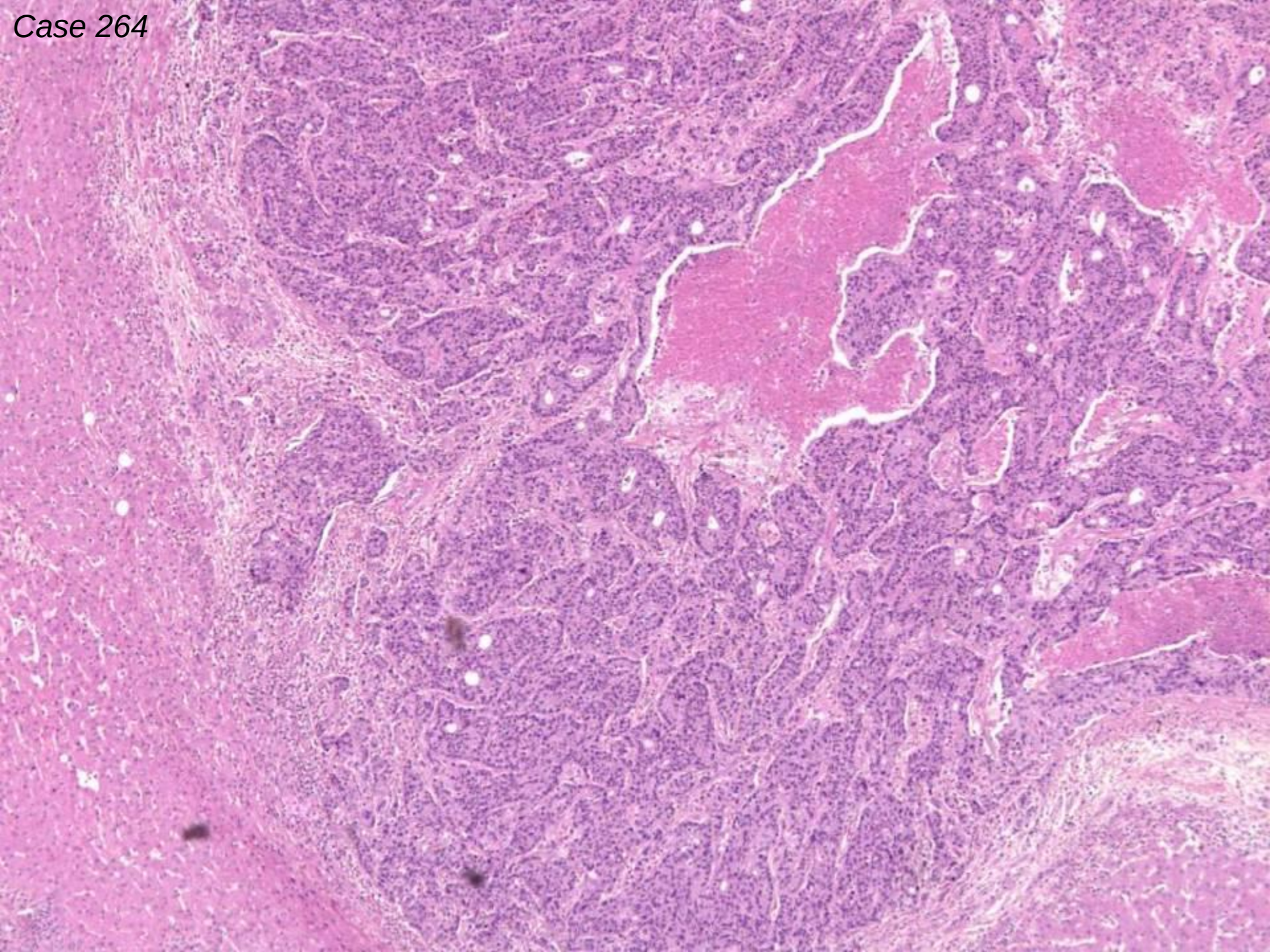
57 M

Liver resection for metastatic colorectal cancer following oxaliplatin and 5FU chemotherapy.

Tumours in segments 5 & 8, plus segments 2 & 3, as separate wedge resections. (2x H&E slides)


Case 264

Case 264



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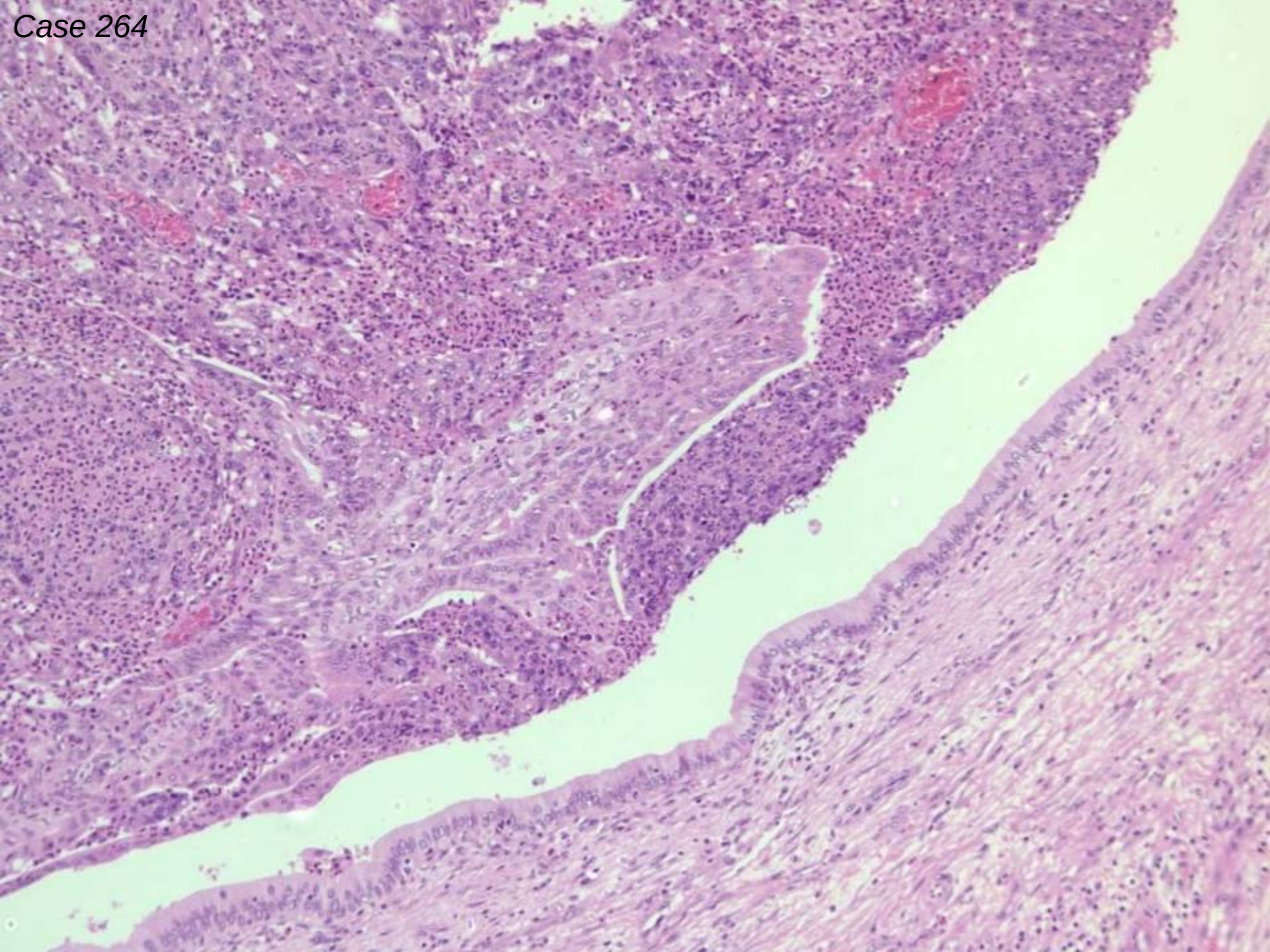

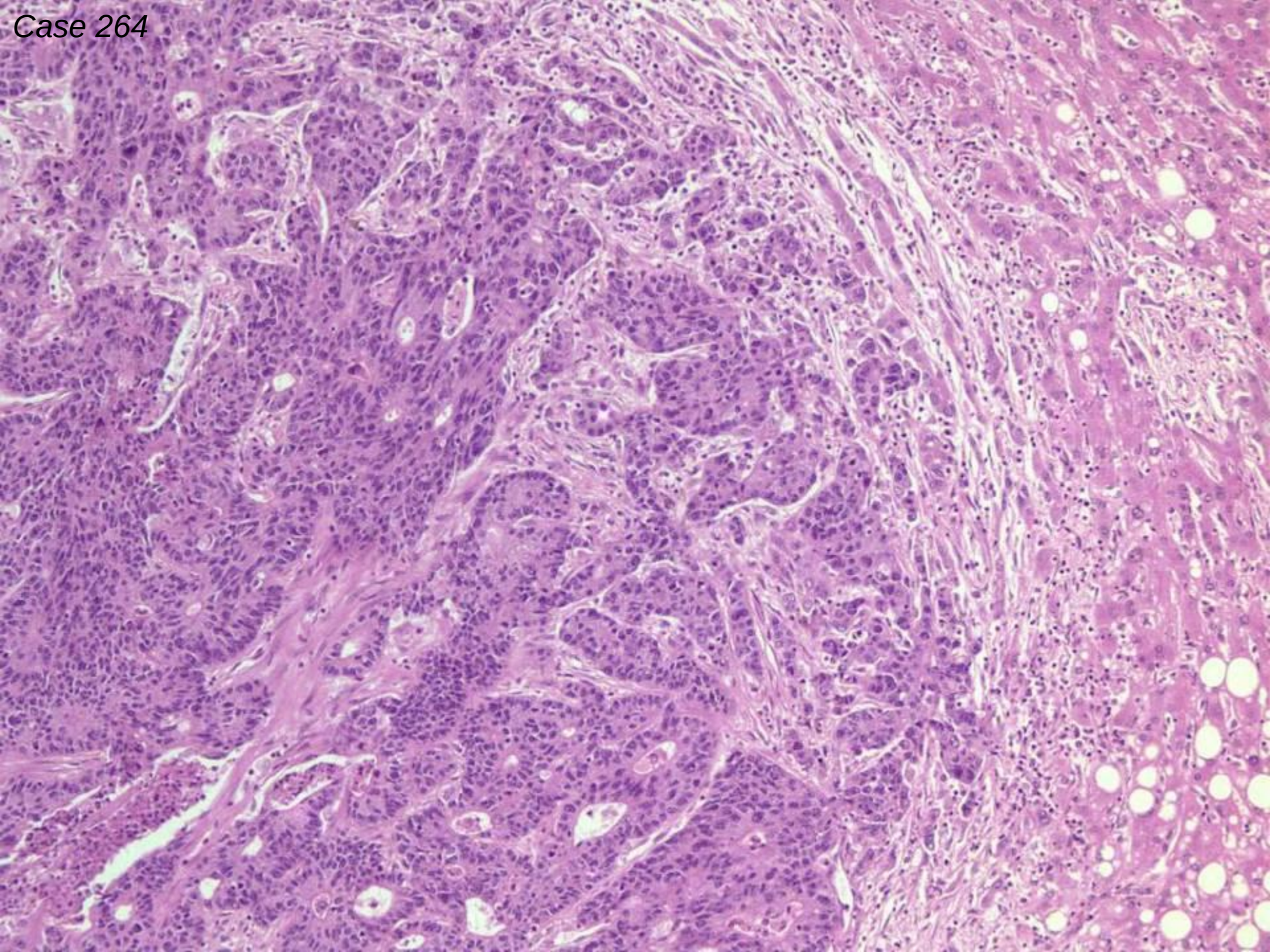
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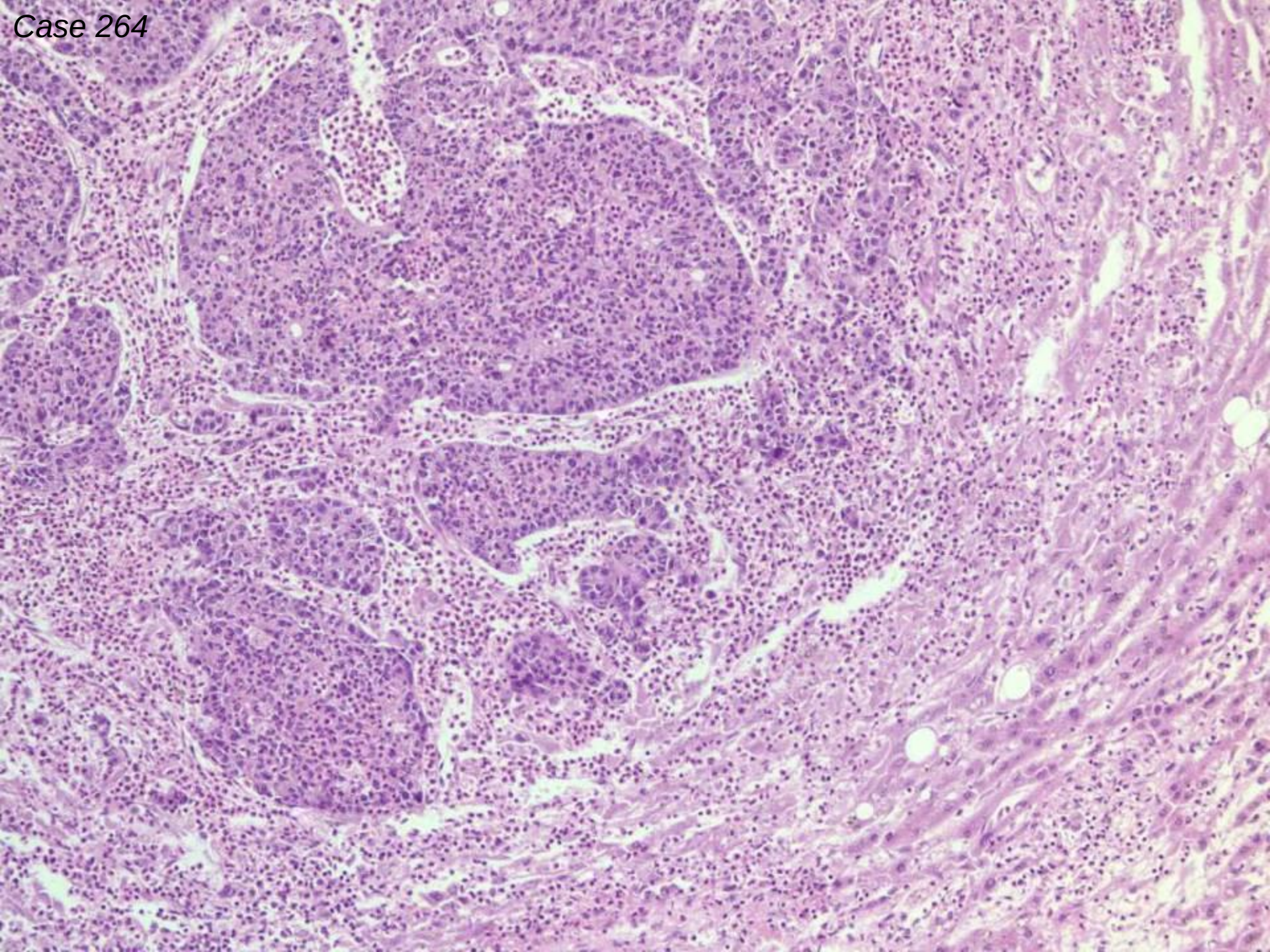
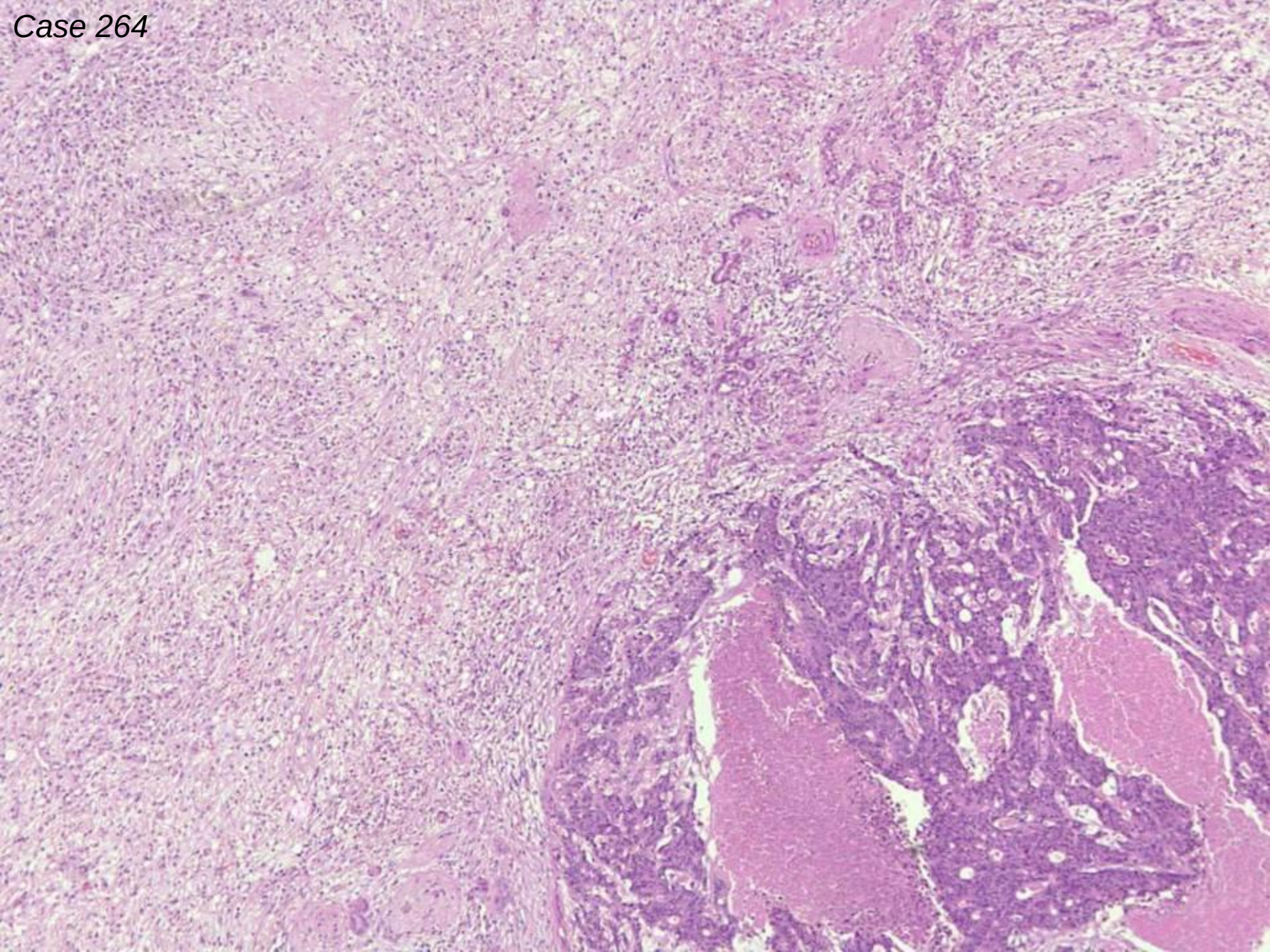

Case 264

Case 264



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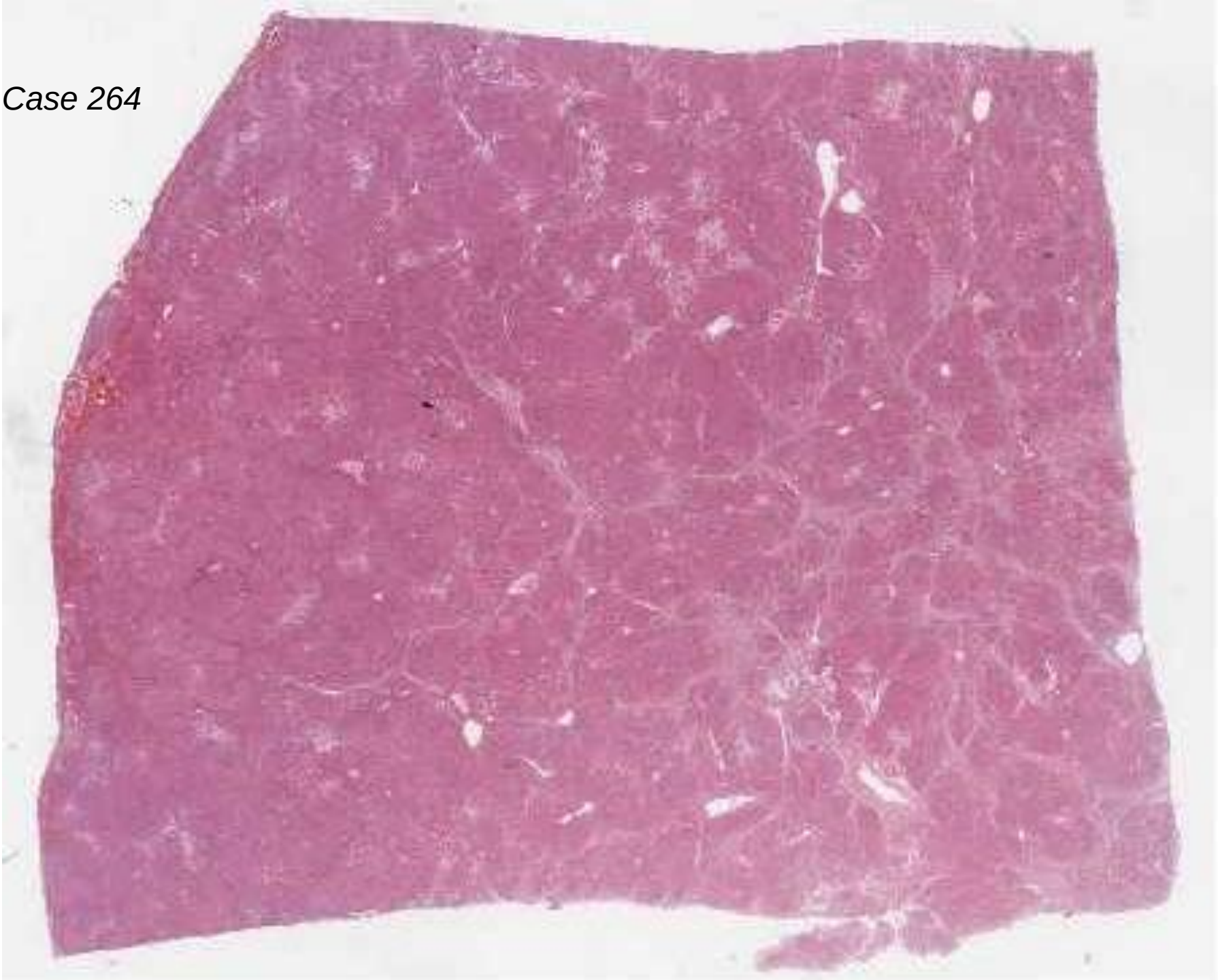

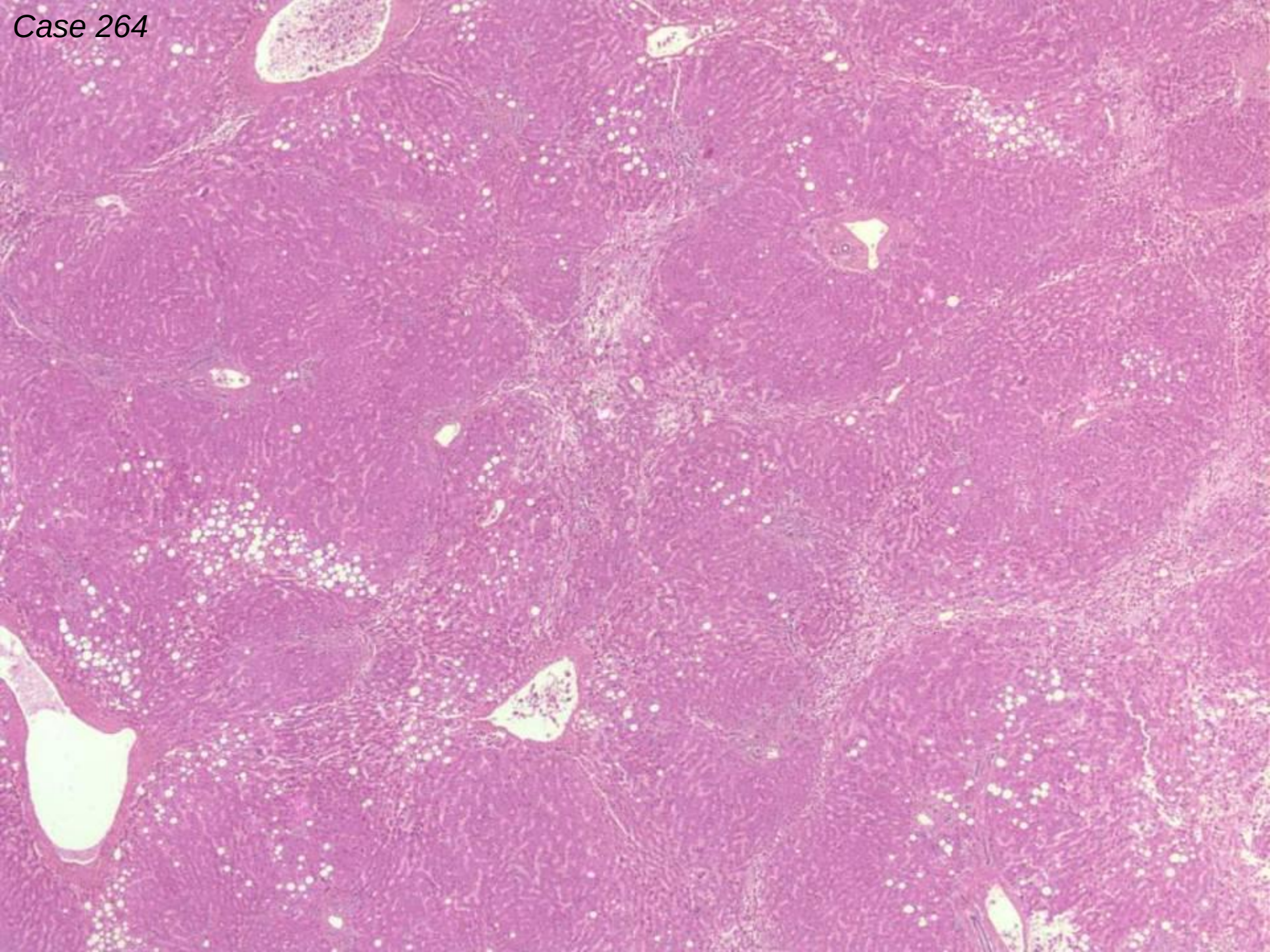
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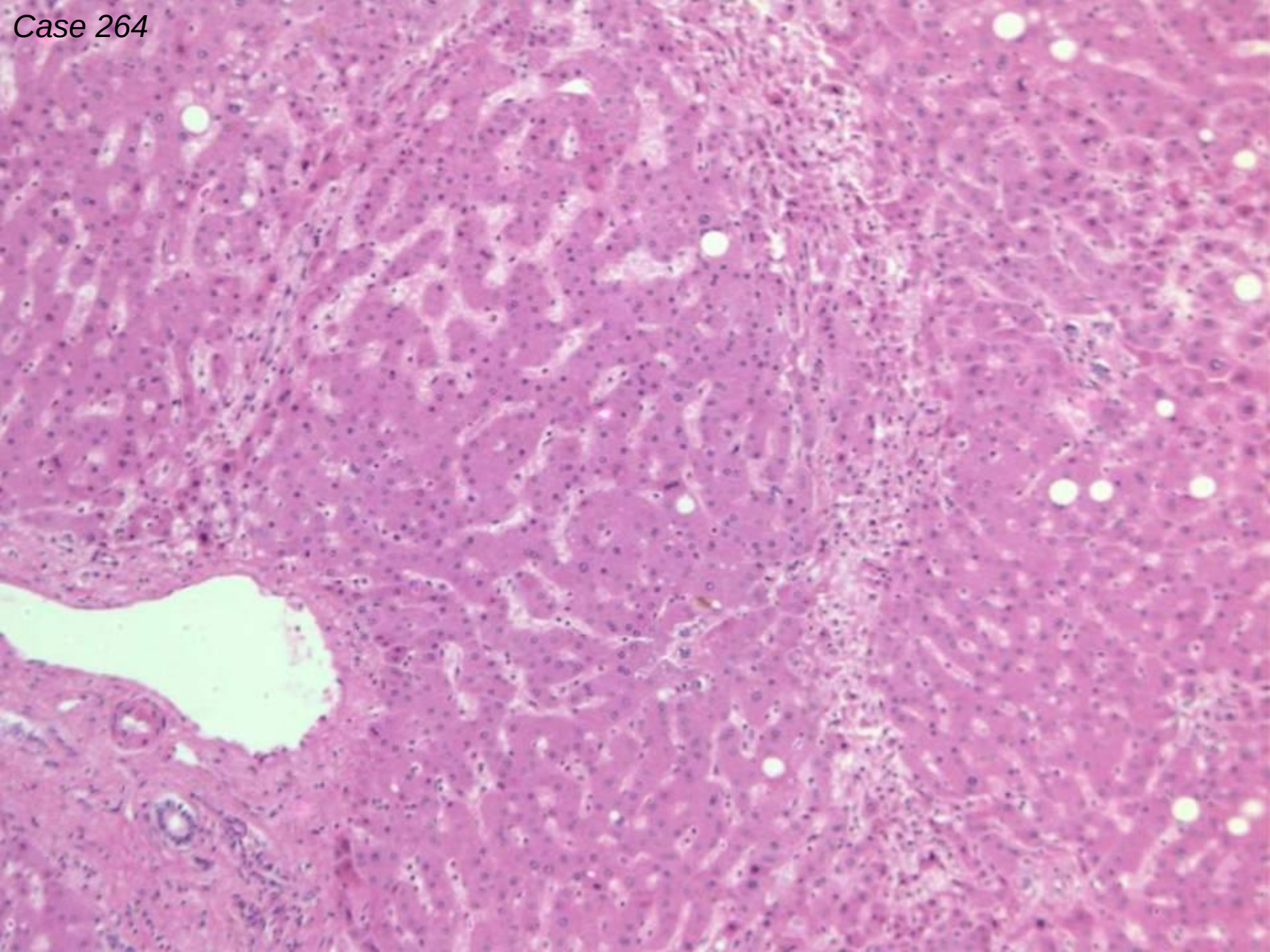
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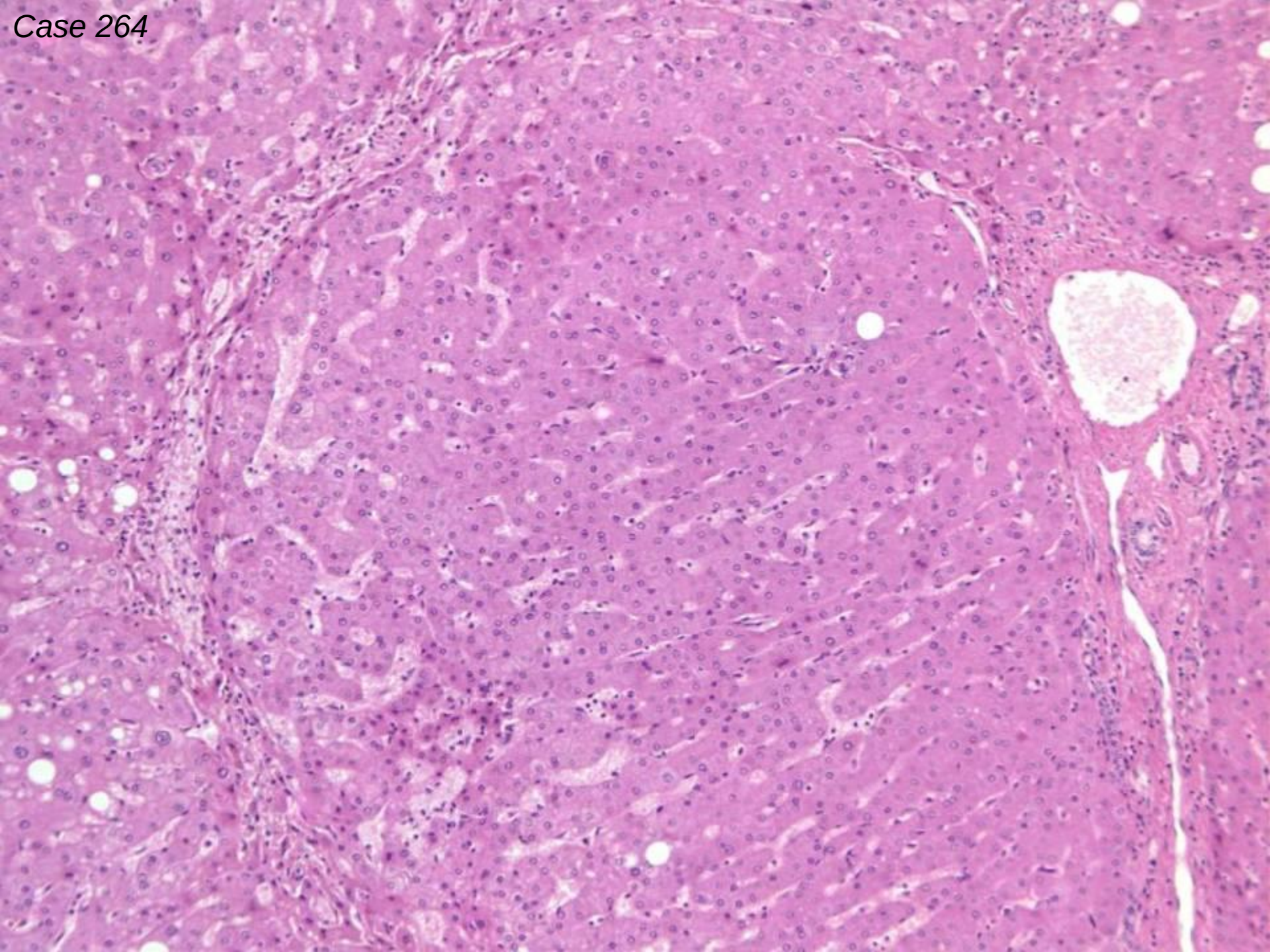
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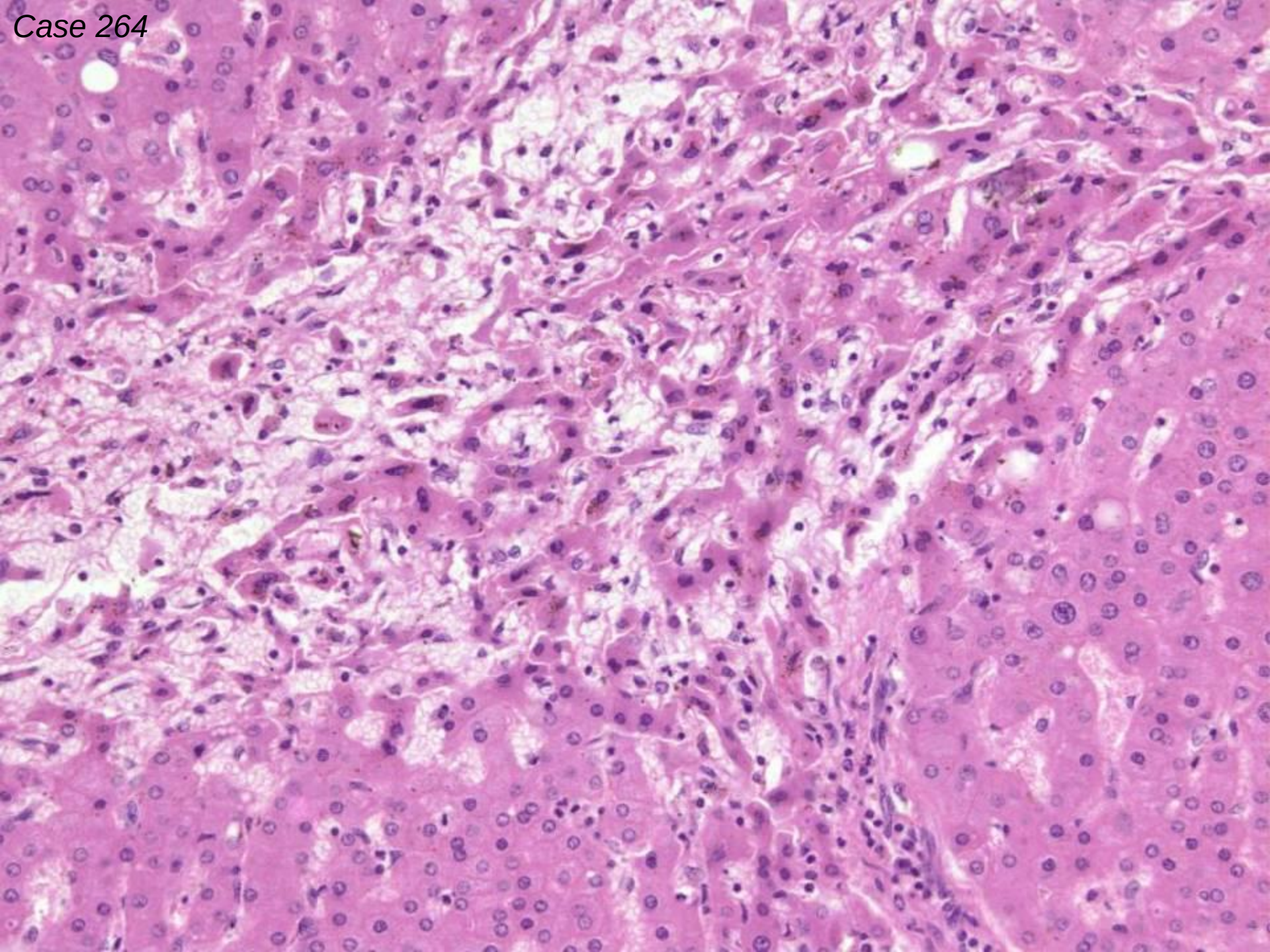

Case 264

Case 264

40 metastatic adenocarcinoma, c/w colorectal primary
18 metastatic adenocarcinoma, with effects of chemotherapy
2 metastatic neuroendocrine carcinoma
1 metastatic adenocarcinoma, requires immunos for primary site
1 adenocarcinoma, probably pancreaticobiliary, for immunos

3 No mention of background liver
27 fatty change

52 some comment on sinusoidal congestion/zonal changes, of which
- 25 nodular regenerative hyperplasia
- 2 sinusoidal obstruction
- 9 sinusoidal congestion
- 13 zone 3 necrosis
- 4 fibrosis

41 comment that changes in background liver may be related to chemotherapy

Case 264

Scoring: All responses accepted – either metastatic colorectal adenocarcinoma, or investigations leading to that conclusion.

Discussion: this case included for educational interest – an example of the regenerative hyperplasia/sinusoidal obstruction changes associated with chemotherapy, recently described as frequently present following neo-adjuvent chemotherapy, particularly oxaliplatin, for colorectal metastases. ***Rubbia-Brandt, et al*** *Annals of Oncology* 2004;15:460-466.

Immunohistchemical markers for neurendocrine differentiation were negative in this case.

Case 264

Original diagnosis:

Metastatic colorectal adenocarcinoma,

Chemotherapy effect in tumour and in background liver.

Severe hepatic sinusoidal obstruction associated with oxaliplatin-based chemotherapy in patients with metastatic colorectal cancer.

Rubbia-Brandt, et al *Annals of Oncology* 15:460-466, 2004

153 resections for metatatic colorectal cancer, 87 neoadjuvent chemotherapy

Sinusoidal dilatation, +/- fibrosis, irregular distribution, often with nodular hyperplasia, occasionally with veno-occlusive lesions

Seen in 44/87 with chemotherapy

(34/43 included oxaliplatin, 10/44 didn't)

And in 0/66 resection without chemotherapy

Steatosis 50% both groups

Case 265

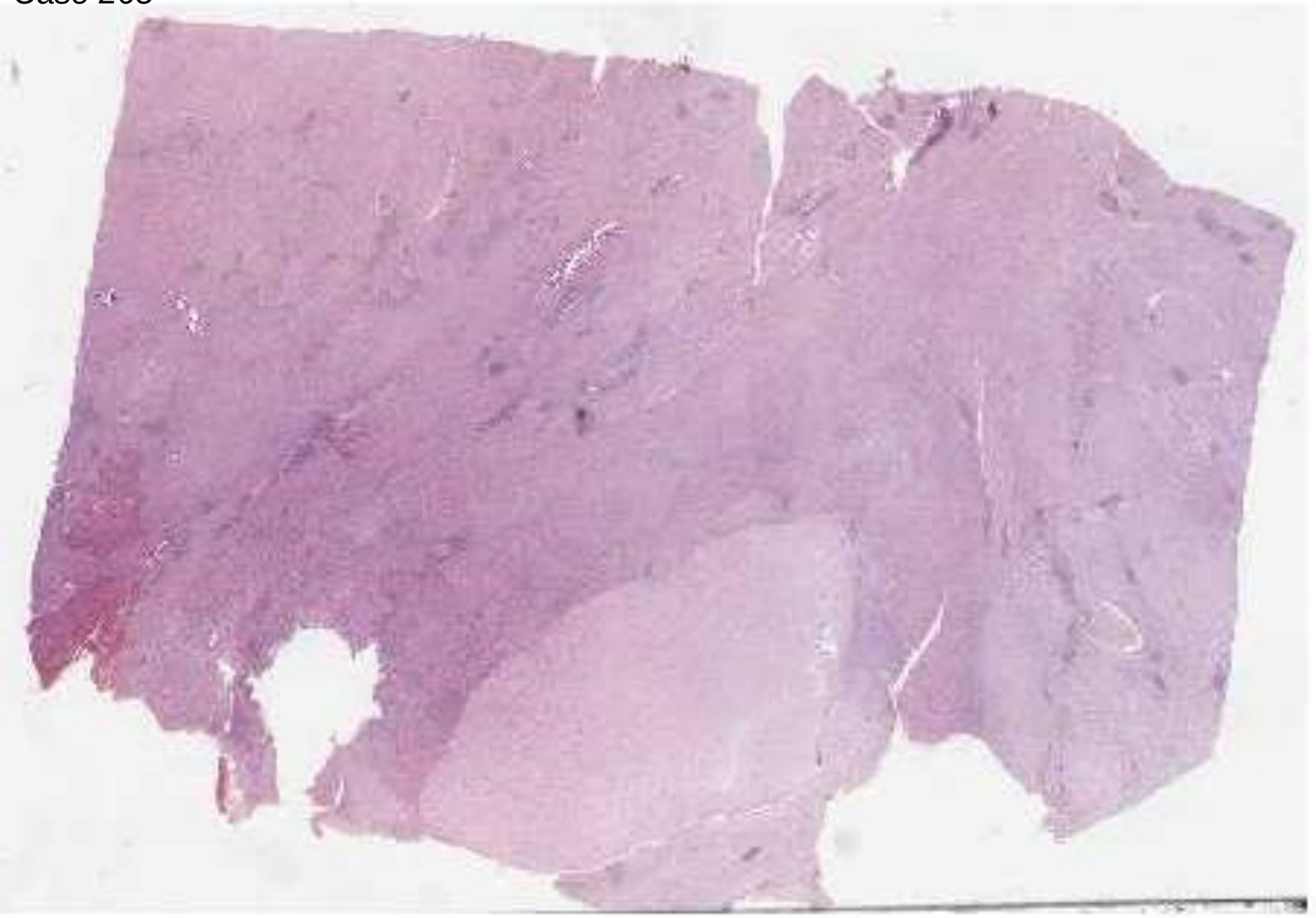
8 M

Investigated for weight loss and abnormal LFTs.

Imaging showed mass at porta hepatis.

Left trisectionectomy – 2.5cm white mass at porta hepatis, obstructing portal vein which is thrombosed.

Case 265



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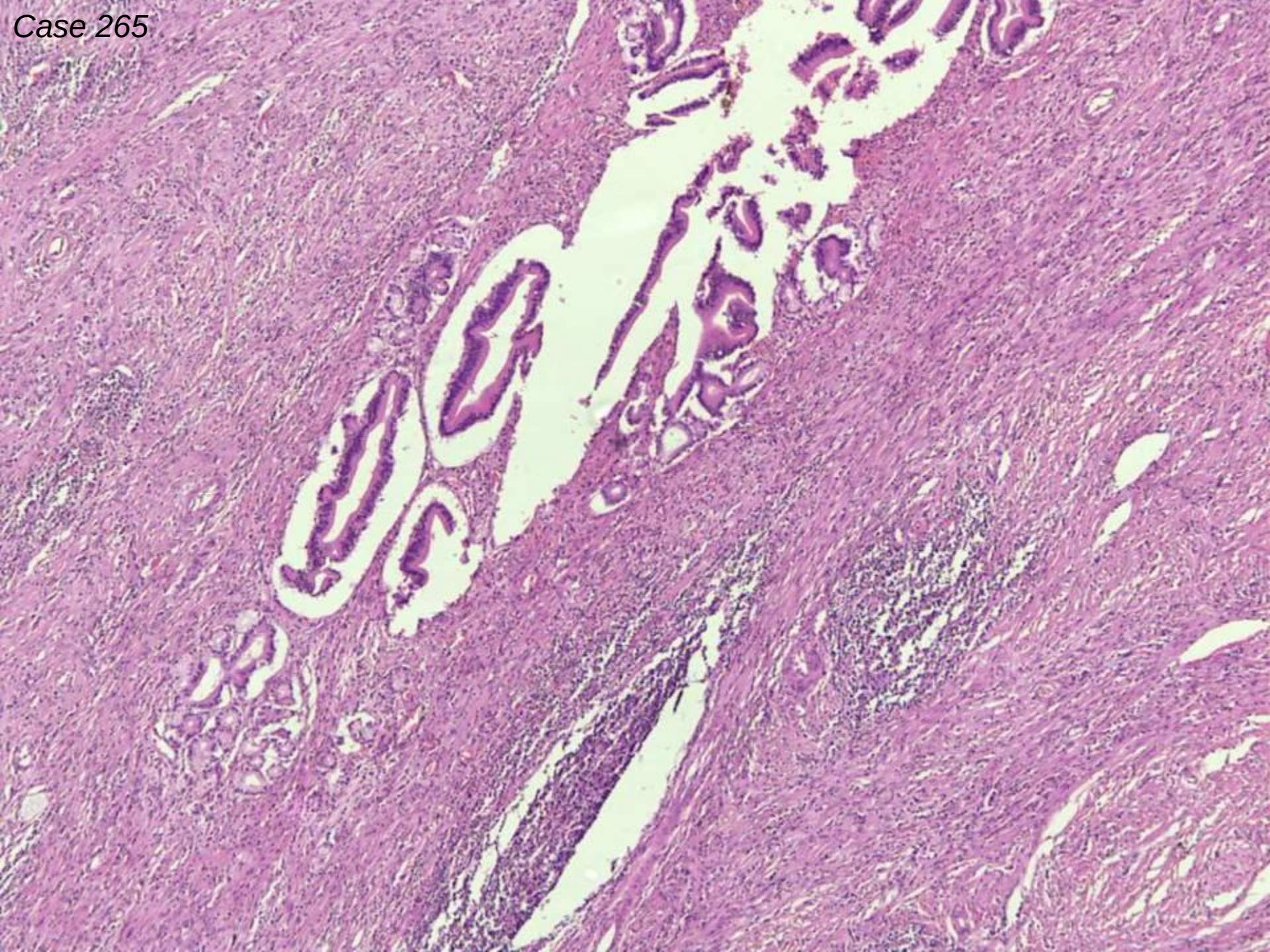

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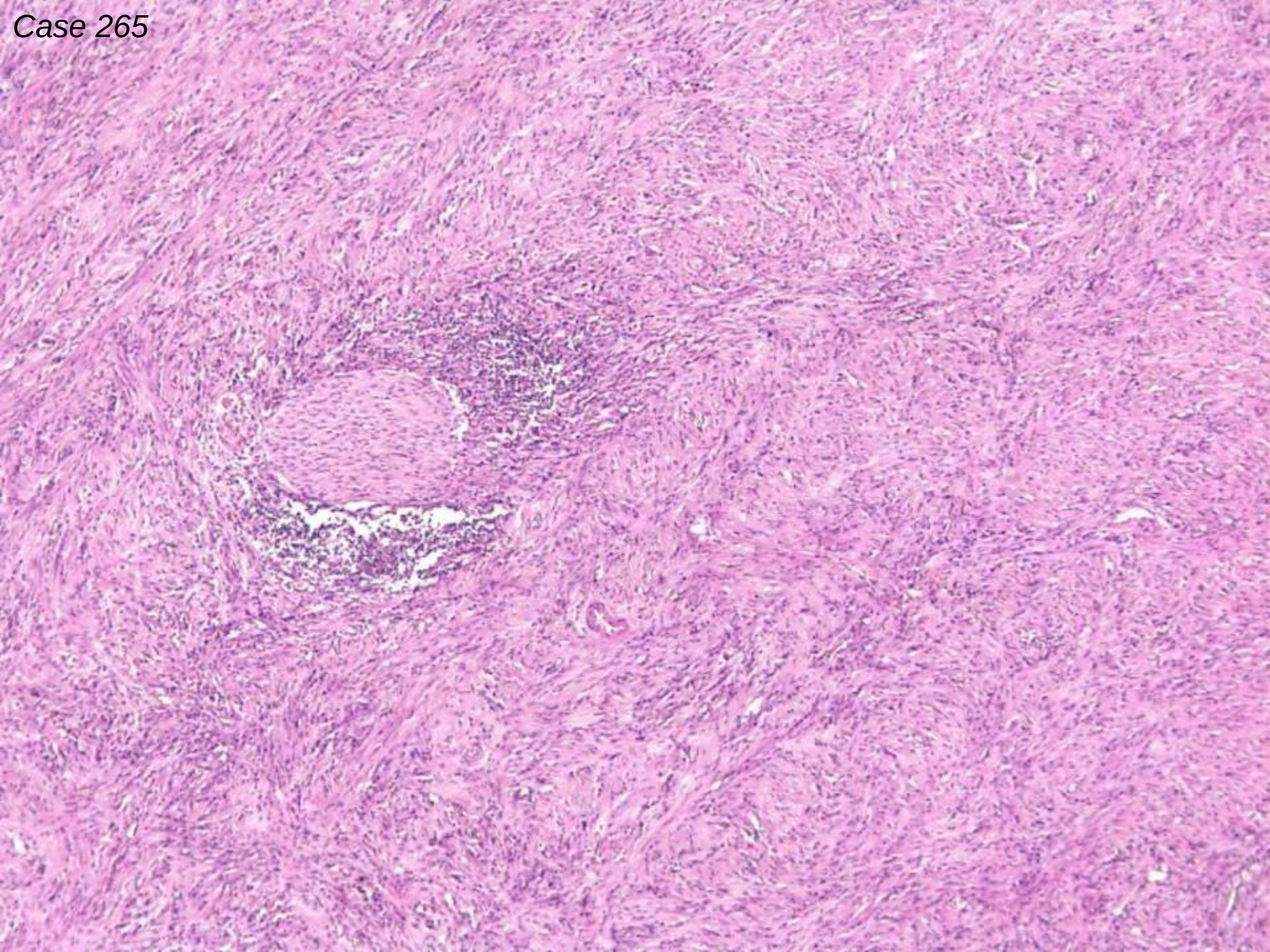

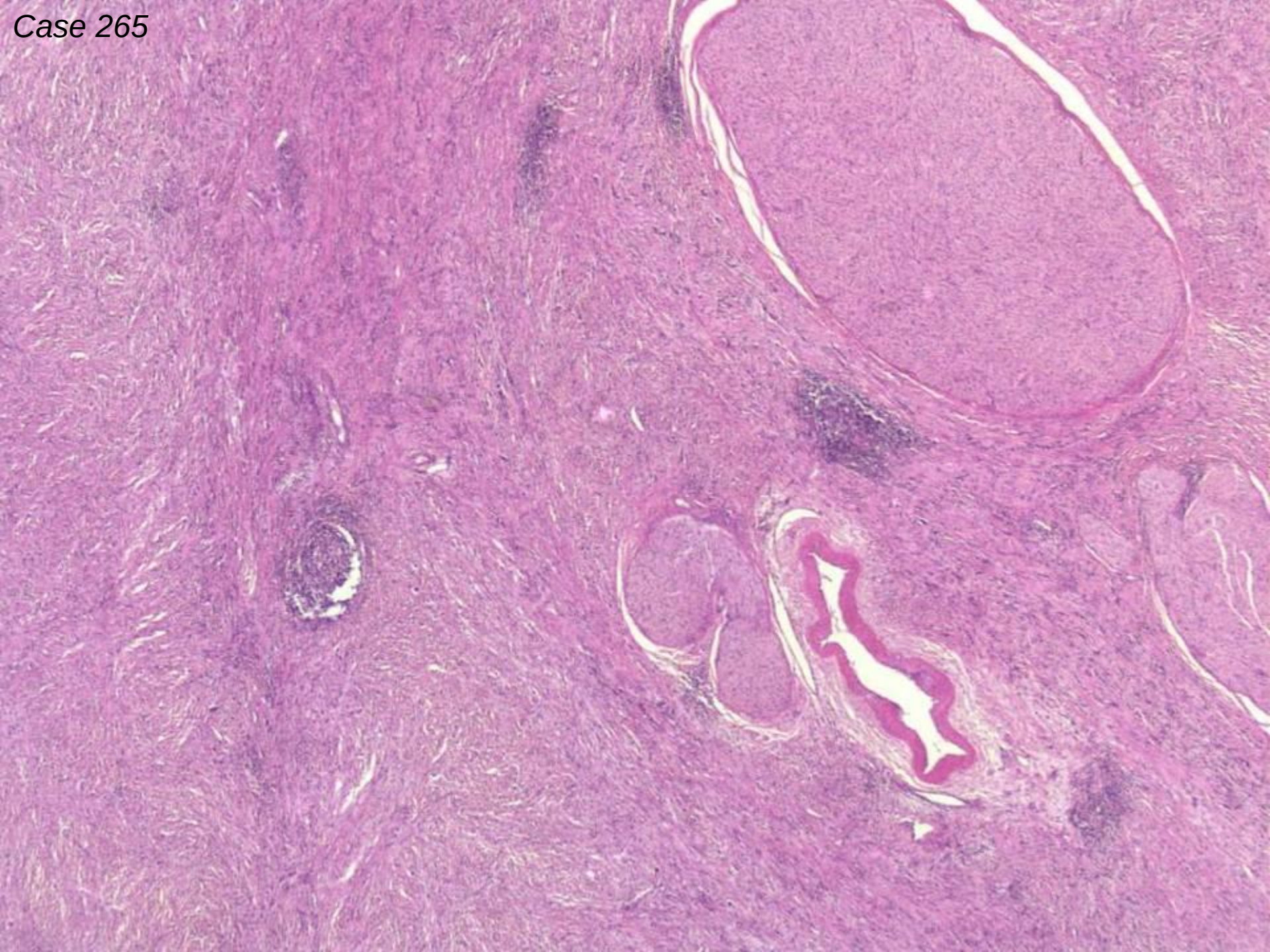
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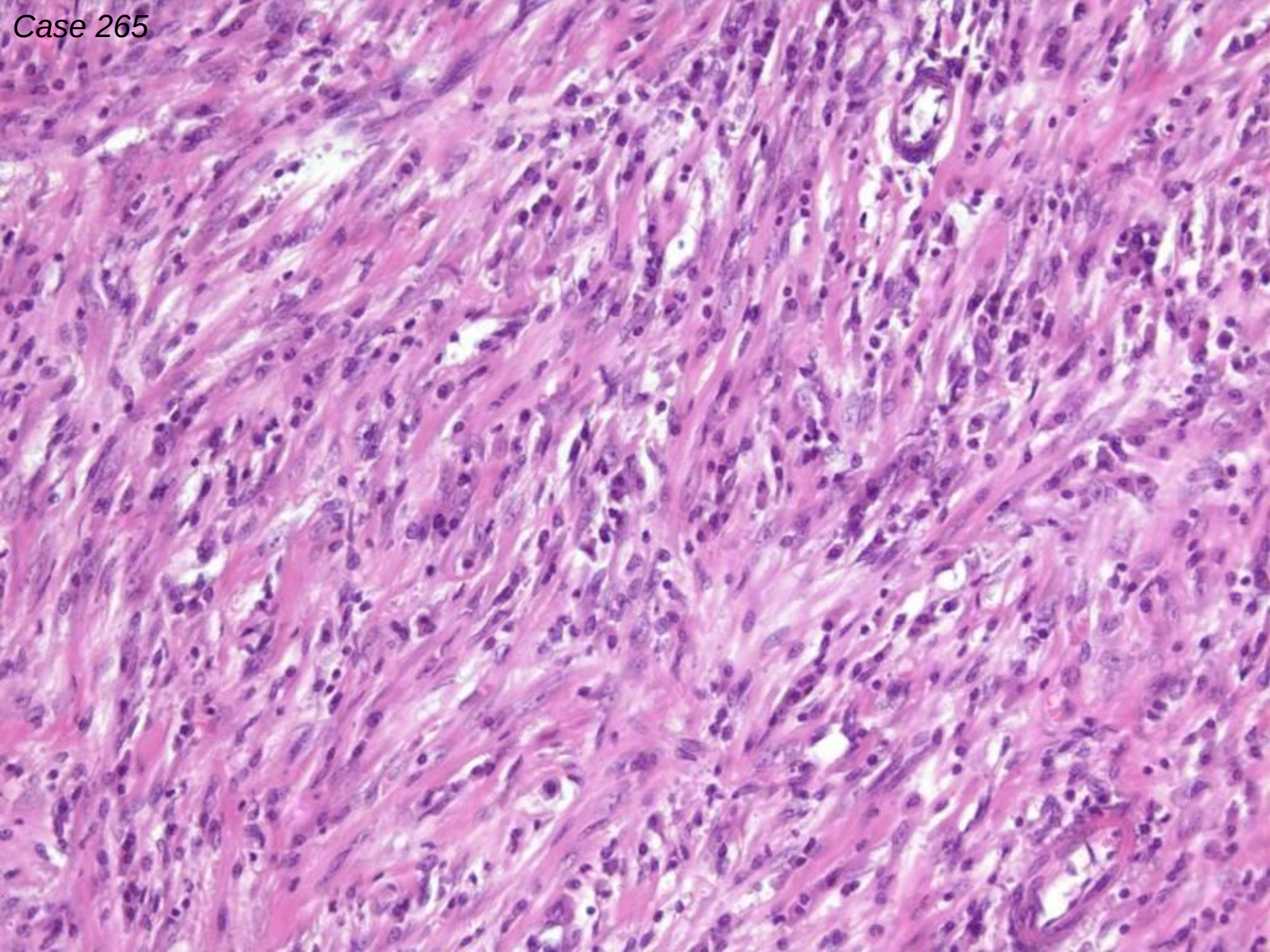
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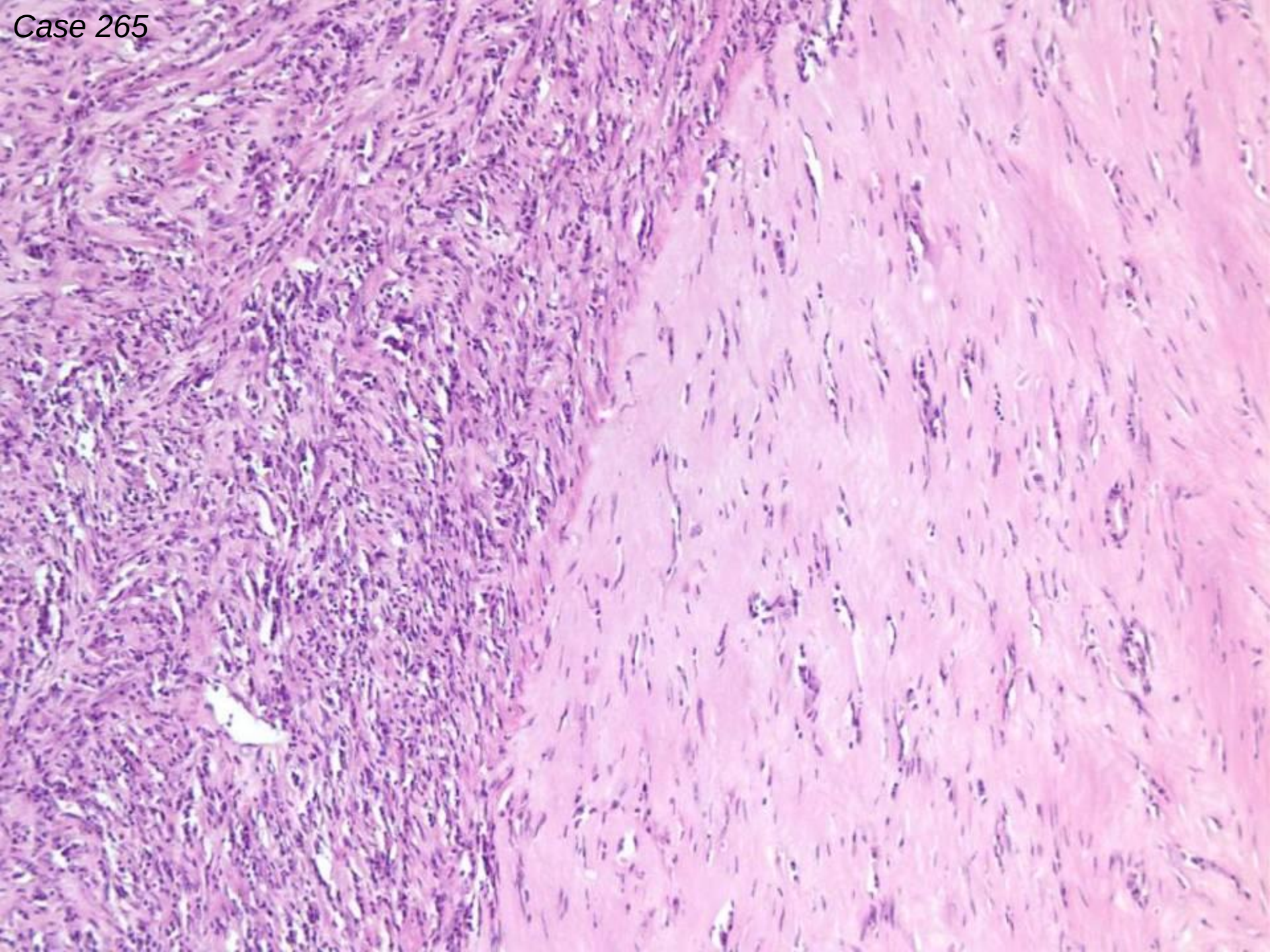
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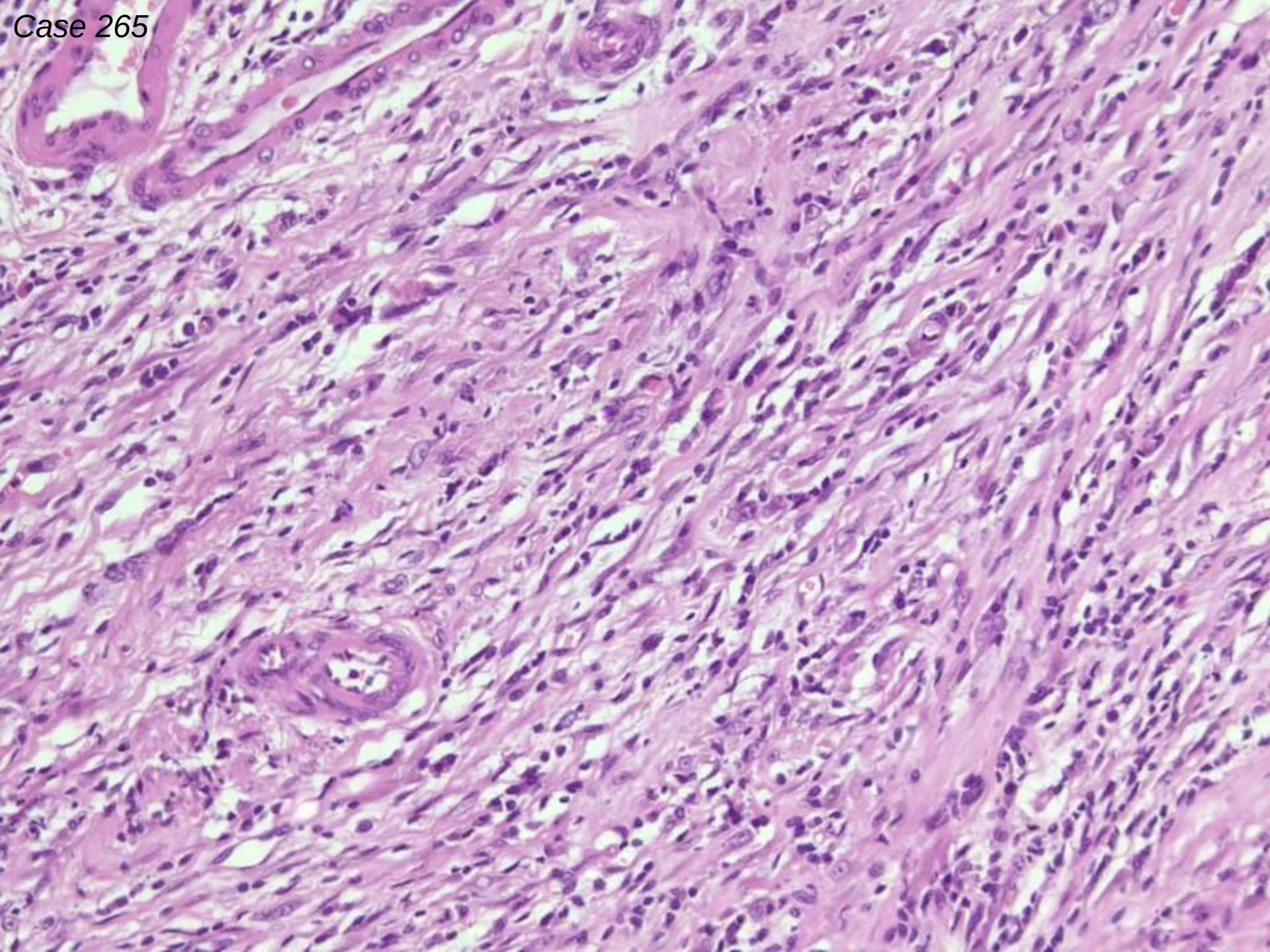
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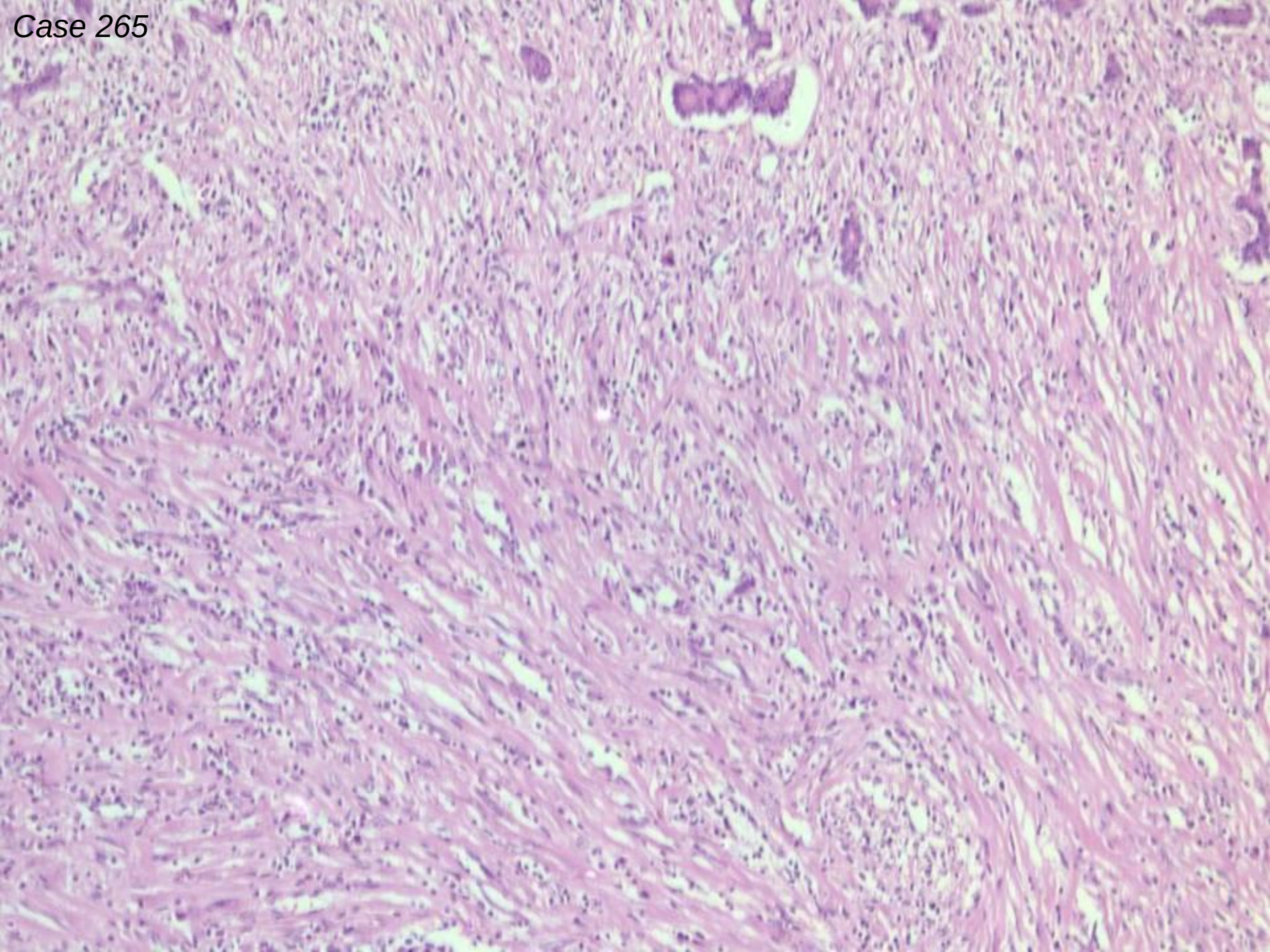
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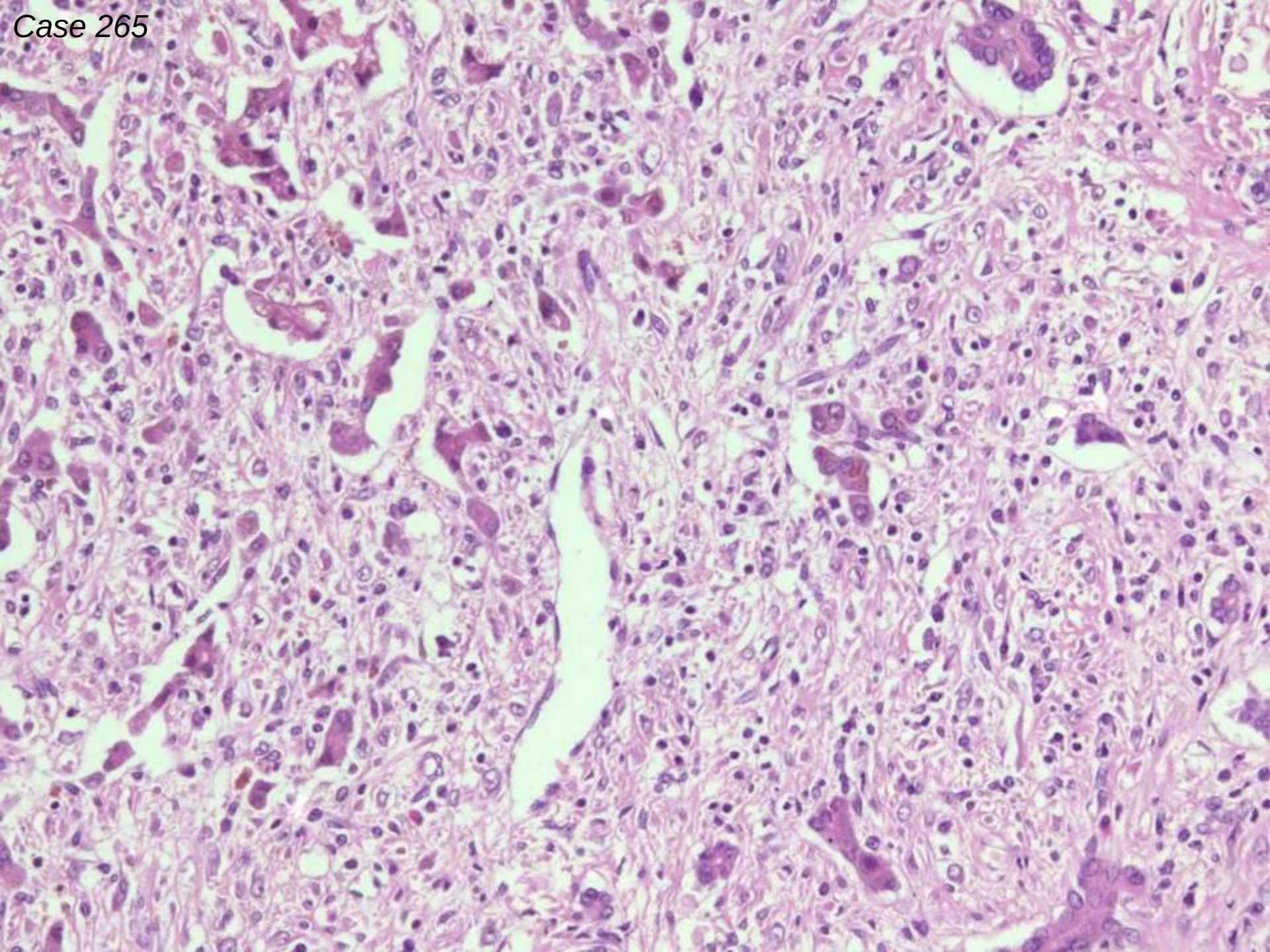
Case 265

Case 265

27 Inflammatory pseudotumour

27 Inflammatory myofibroblastic tumour (+/- pseudotumour)

1 spindle cell tumour, needs immunos
1 inflammatory pseudotumour + neurofibroma
1 inflammatory myofibroblastic lesion, ?autoimmune pancreatitis/Inflammatory pseudotumour /PSC
1 ?hamartoma/neural tumour/inflammatory pseudotumour
1 mesenchymal hamartoma

1 congenital hepatic fibrosis + PV thrombosis
1 extrahepatic biliary atresia/organising thrombus

Case 265

Scoring: Reject congenital hepatic fibrosis and extrahepatic biliary atresia; accept all the others.

Discussion: this case was included largely for educational interest – there have been several previous cases circulated in the liver EQA scheme with a proffered diagnosis of inflammatory pseudotumour. The terminology for inflammatory pseudotumour in the liver is unclear - in other sites, lesions which in the past were diagnosed as inflammatory pseudotumour are now considered usually to be cases of inflammatory myofibroblastic tumour.

This case is an example of an inflammatory myofibroblastic tumour in a child, confirmed by Alk-1 positivity (Pediatr Transplant. 2004 Oct;8(5):517-21). However, previous cases discussed in the liver EQA have been in adults, and probably represented unresolving inflammatory masses rather than neoplastic proliferations. These occur predominantly around bile ducts in patients with PSC, and also in patients with autoimmune pancreatitis (associated with predominance of IgG4 plasma cells). Others appear to represent delayed resolution of inflammation associated with liver abscesses.

Case 265

Original diagnosis:

Inflammatory myofibroblastic tumour

Immunos: +ve actin, vimentin

-ve S100, desmin, myogenin

+ve Alk-1

Case included for educational interest

discuss inflammatory myofibroblastic tumour

- true neoplasm, Alk 1 +ve in children

inflammatory pseudotumour

parenchymal ? Abscess

around bile ducts – associated with PSC

- associated with autoimmune sclerosing pancreatitis

Case 265

Follow up information: Extensive liver resection followed by liver failure due to portal vein thrombosis of reconstructed right portal vein.

Emergency liver transplantation, primary non-function and re-transplant.

Now very well (4½ years later) no recurrence.

Dasgupta et al. ***Pediatr Transplant. 2004 Oct;8(5):517-21.***
Liver transplantation for a hilar inflammatory myofibroblastic tumor