Liver EQA Scheme, Circulation W

Birmingham BSG

March 2008

Open meeting 11.03.08, Birmingham

There were 11 members and 9 guests.

Slides discussed had been in circulation since September 2007, forwarded after 3 weeks, in view of use of second class post by trusts.

Virtual slides could be reviewed on the web – in cases where the biopsy was small the best sections were selected for scanning.

The next meeting (circulation X, already started) will be during the Pathological Society meeting in Leeds, in early July.

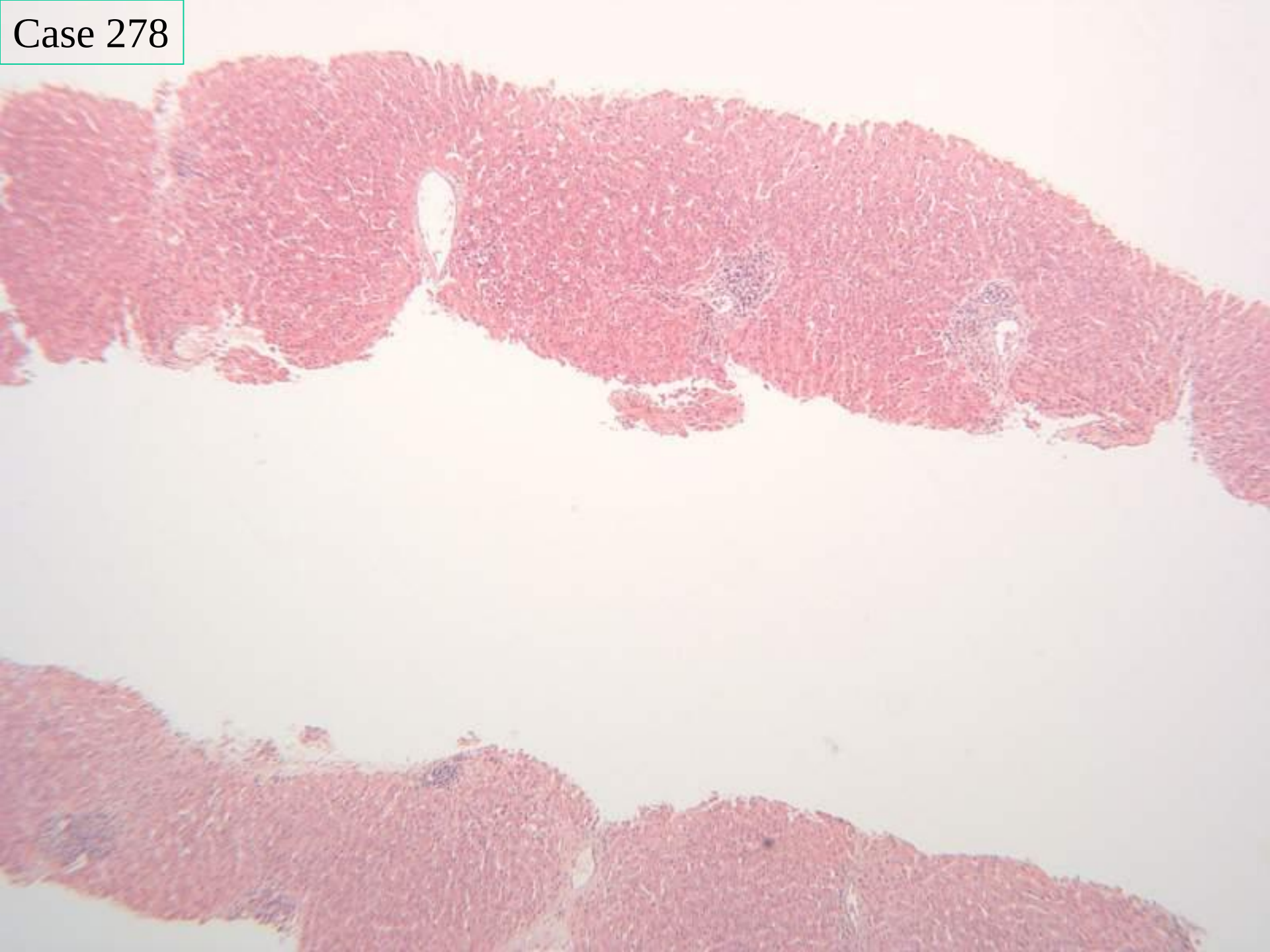
No other issues relating to the organisation of the scheme were raised by members.

In the results below, diagnoses scoring less than full marks are italicised in brown, and the discussion will explain the bases for marking agreed during the open meeting. Several cases have more than one diagnosis.

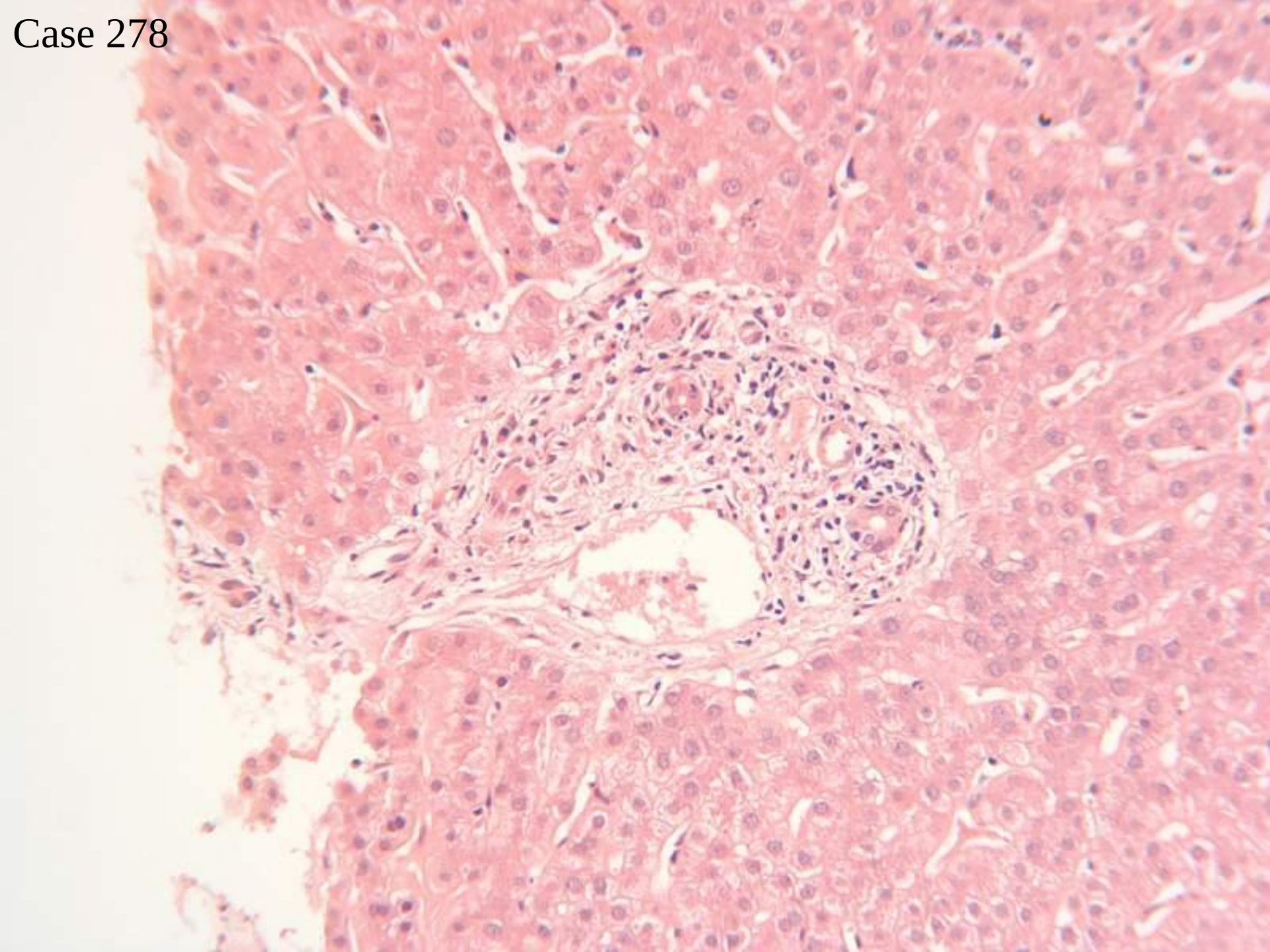
Case 278

- 50/female.
- Liver transplant for autoimmune hepatitis in 1995. Been taken off Cyclosporin for nephrotoxicity.
- Developed abnormal LFTs. Bilirubin 295, alk phos 2467, AST 150, ?acute rejection.

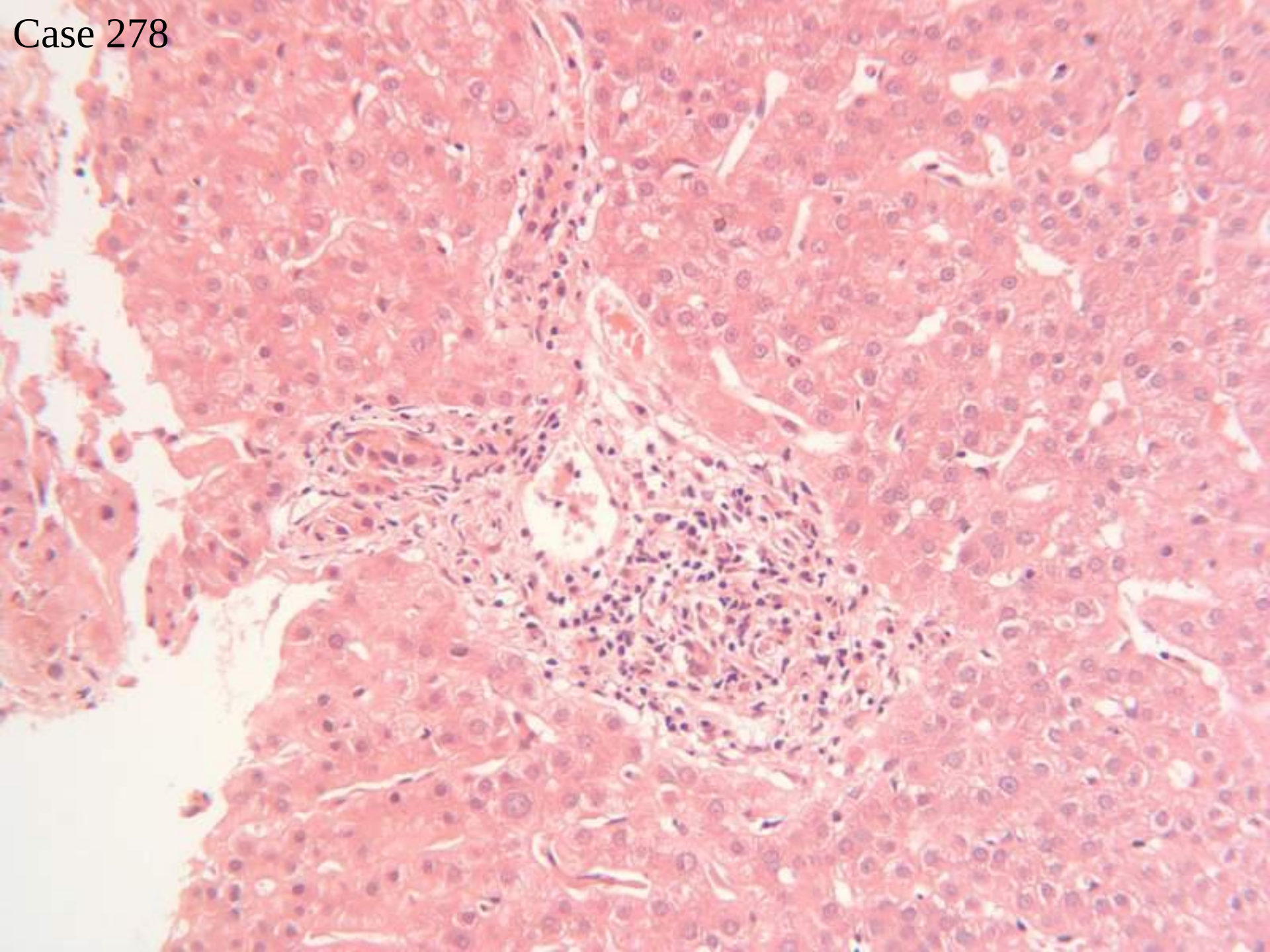
Case 278



Case 278



Case 278



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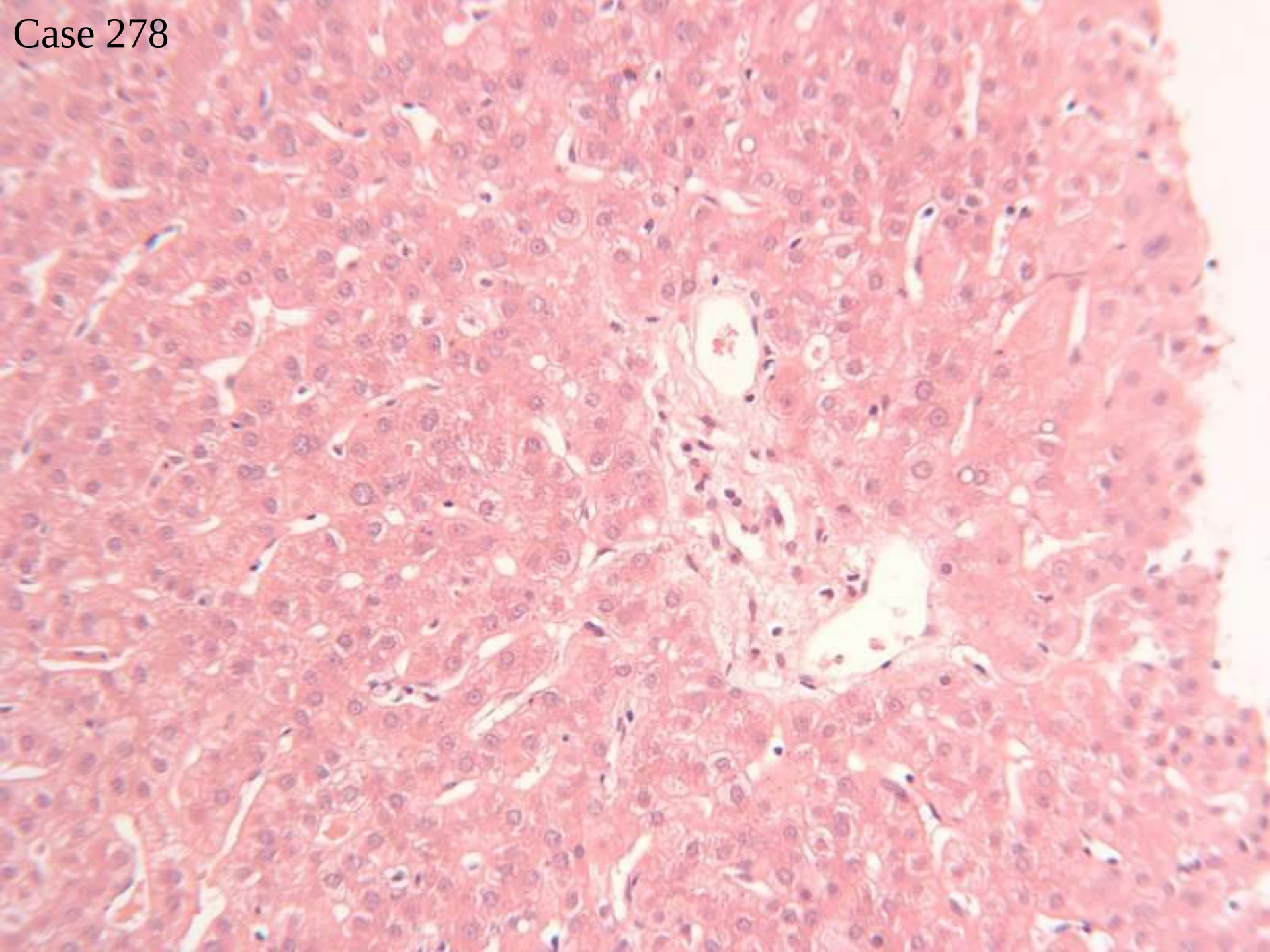

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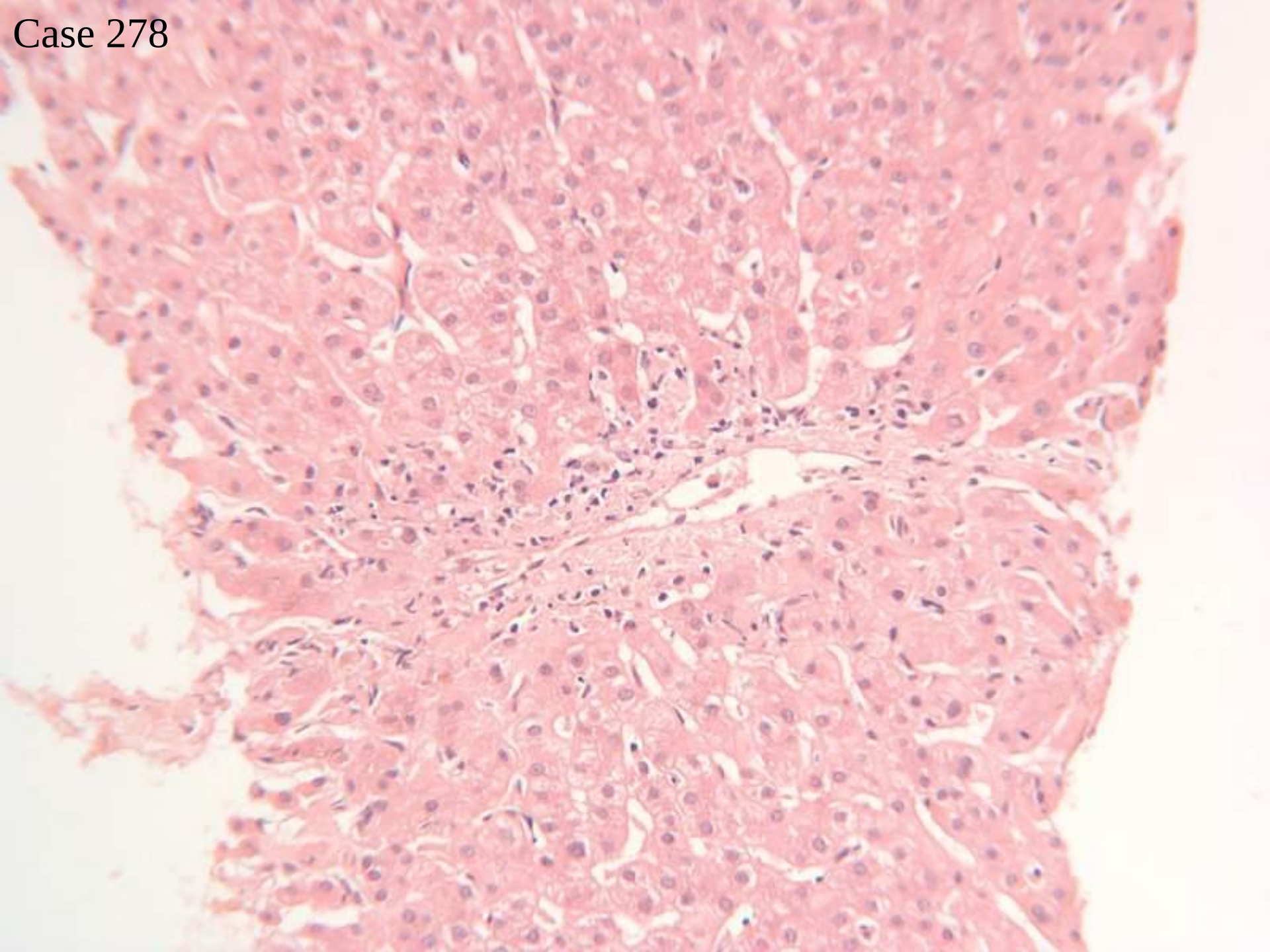

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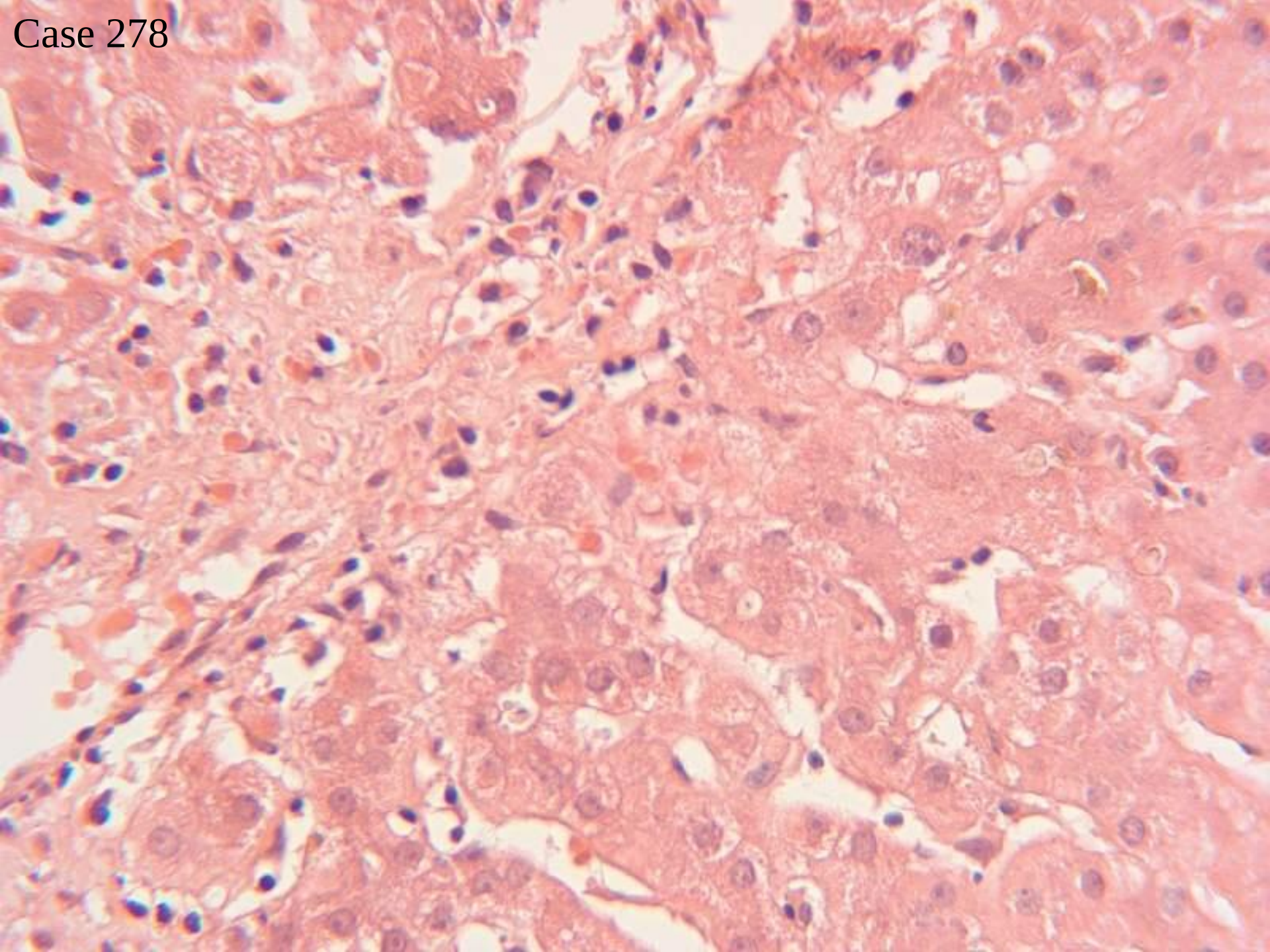


Case 278

Responses:

61 rejection, of which

- 4 rejection NOS
- 22 acute rejection
- 4 acute and chronic rejection
- 31 chronic rejection

1 chronic rejection and AIH recurrence

1 chronic rejection and cyclosporin A cholestasis

1 hepatitic, not rejection

1 Large bile duct obstruction pattern (? Drug)

1 don't do transplant biopsies

Scoring:

All diagnoses of rejection accepted. Although it is recommended that post transplant biopsies are also sent to the transplant centre for review, an initial local assessment, in this case to allow treatment for rejection to be commenced, should be possible.

Discussion:

This was the first transplant biopsy to be included in the liver EQA. It was felt appropriate to include late post transplant biopsies, since these may be received outside transplant centres.

There is an element of acute (reversible) rejection in this case – duct inflammation and perivenulitis – and in addition senescent changes in duct epithelium, some ductopaenia and bilirubinostasis, which indicate early chronic rejection.

Acinar inflammation from early recurrent autoimmune hepatitis is in the differential, but would not explain the rejection changes. The terminology and concepts of immune mediated graft injury (alloimmune in rejection v. autoimmune) is confusing, and clinical management is the same.

Case 278

Submitting pathologist diagnosis:

Moderate to severe acute rejection

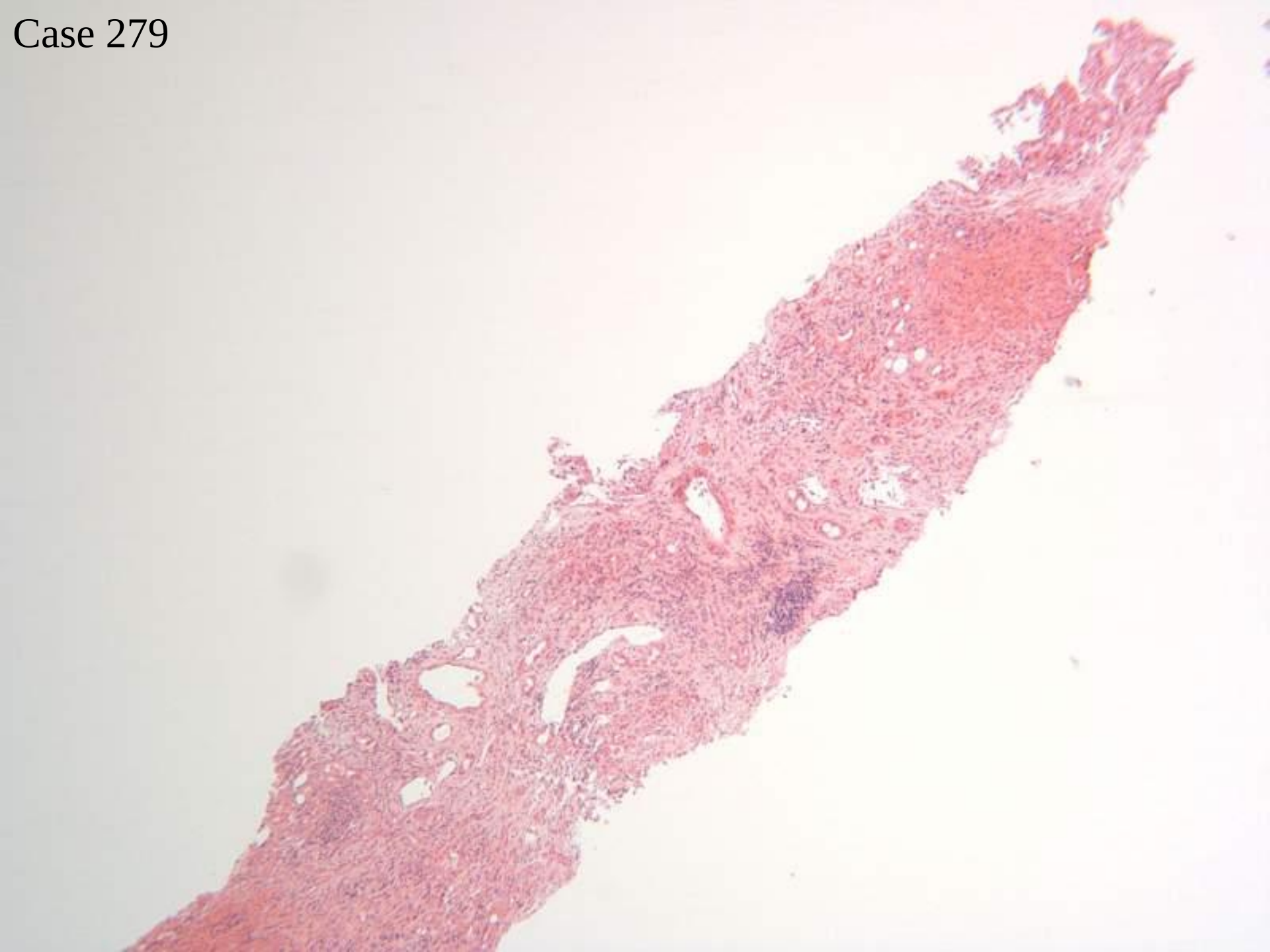
+/- evolving chronic rejection

+ chronic hepatitis

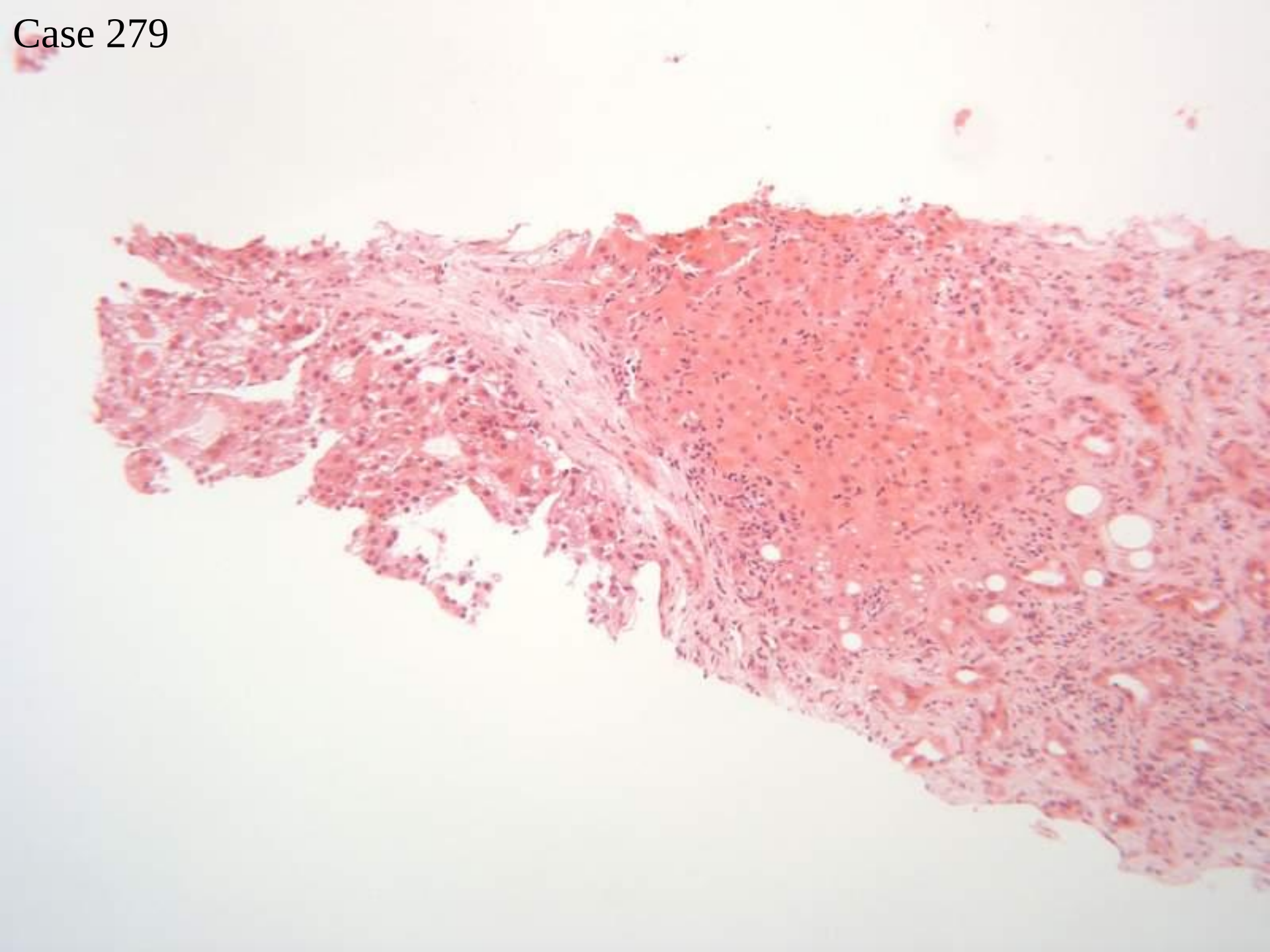
Case 279

60/Male Jaundice, no focal lesion on ultrasound

Case 279



Case 279



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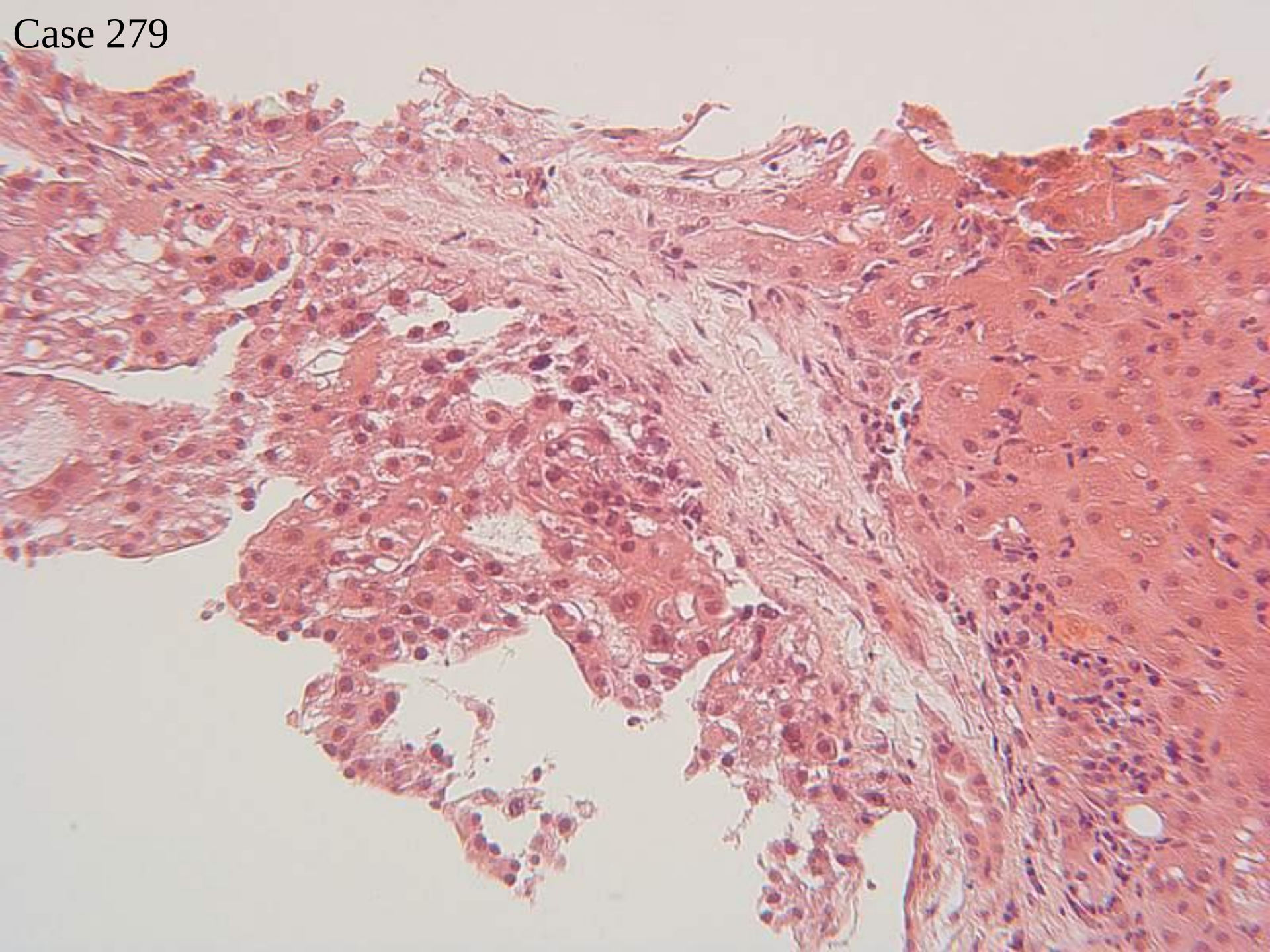

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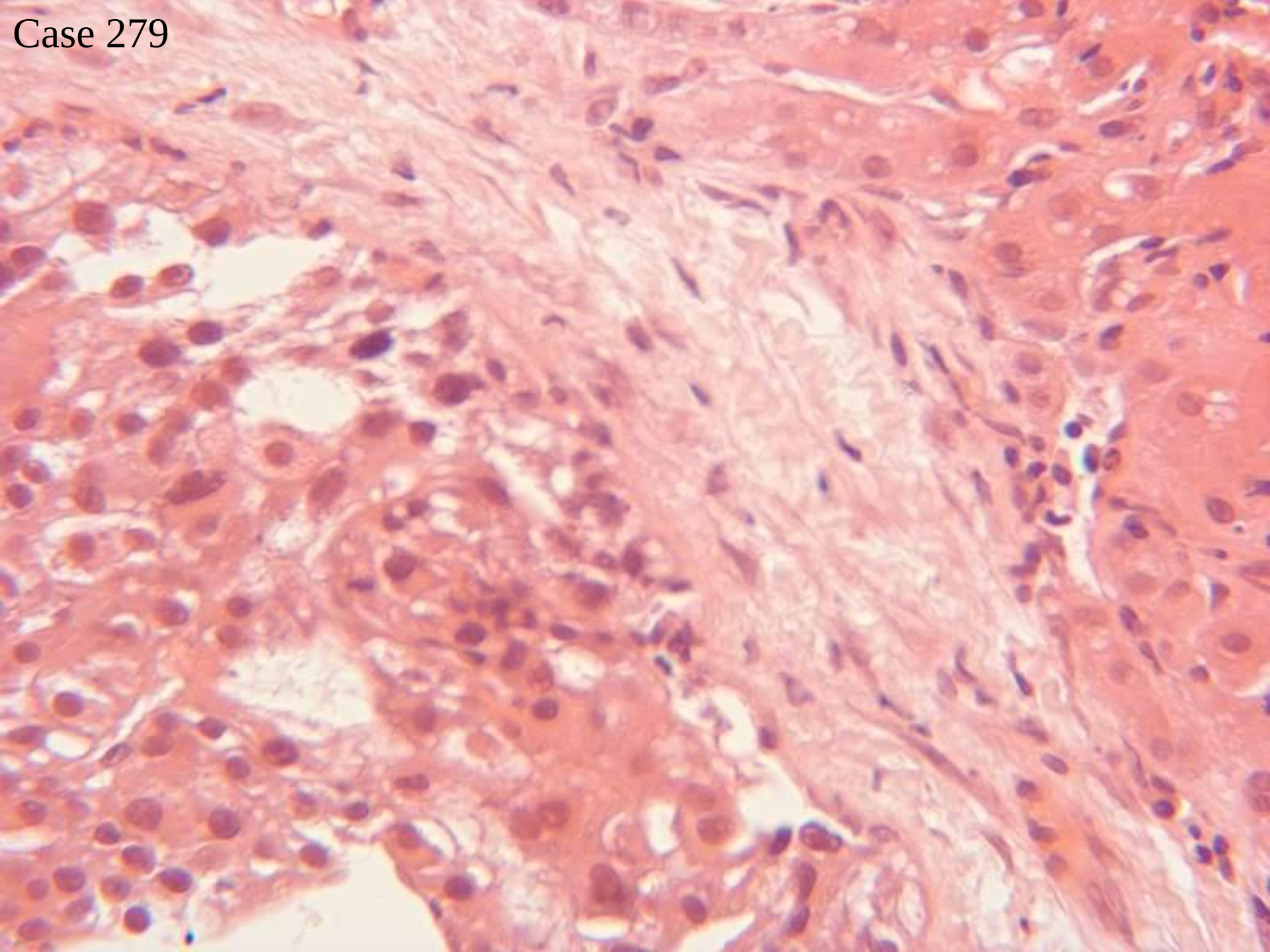

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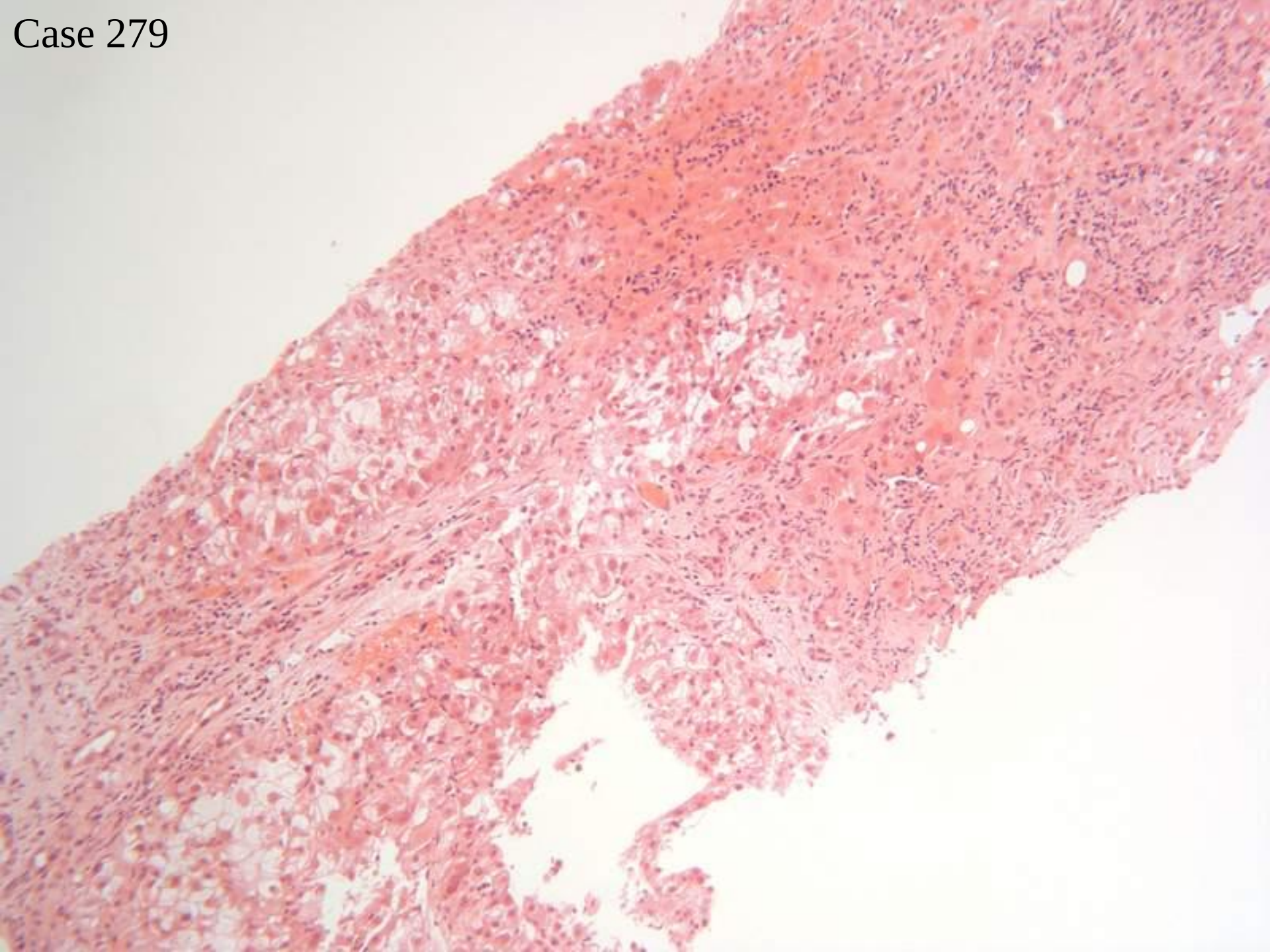

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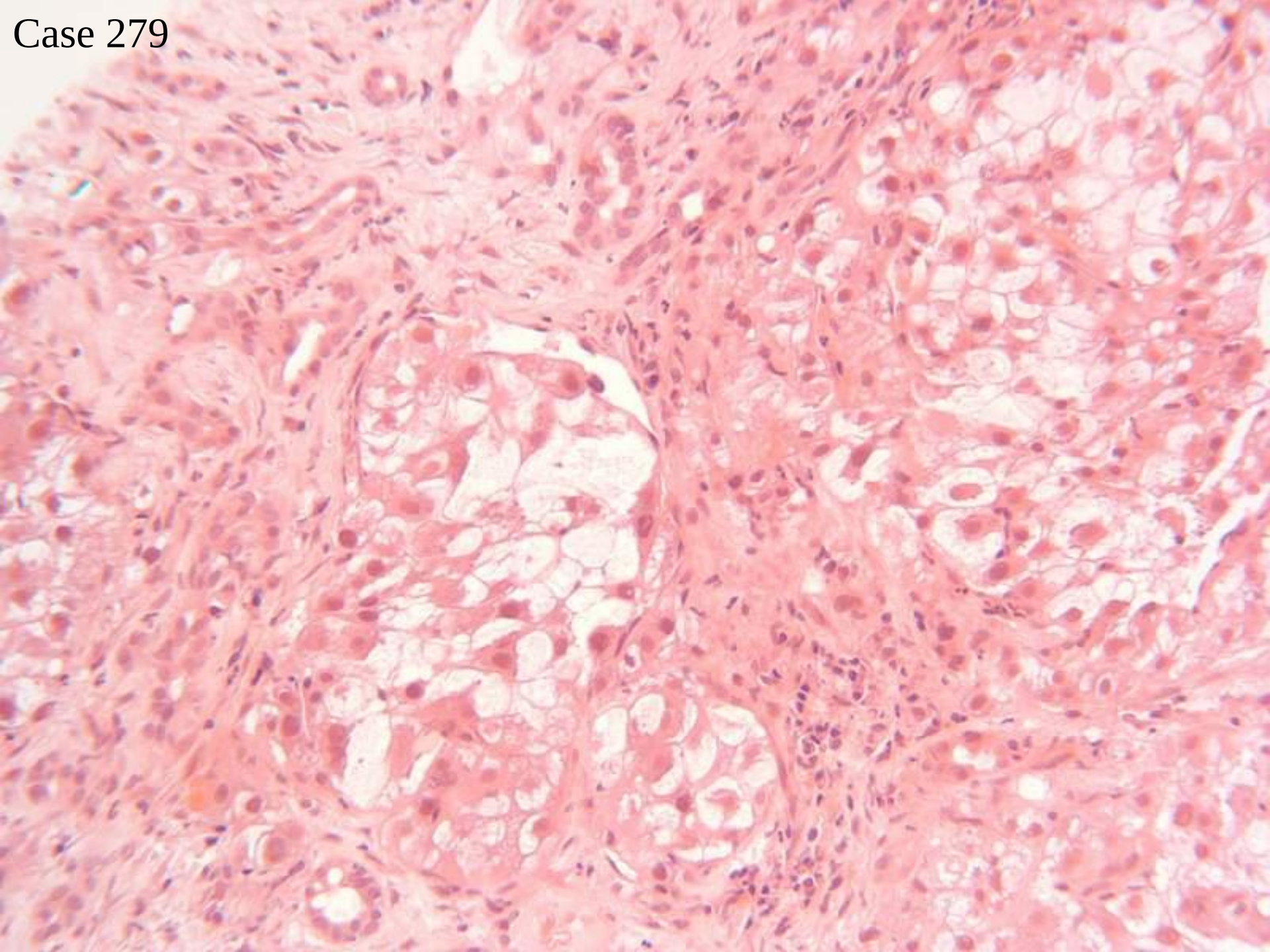

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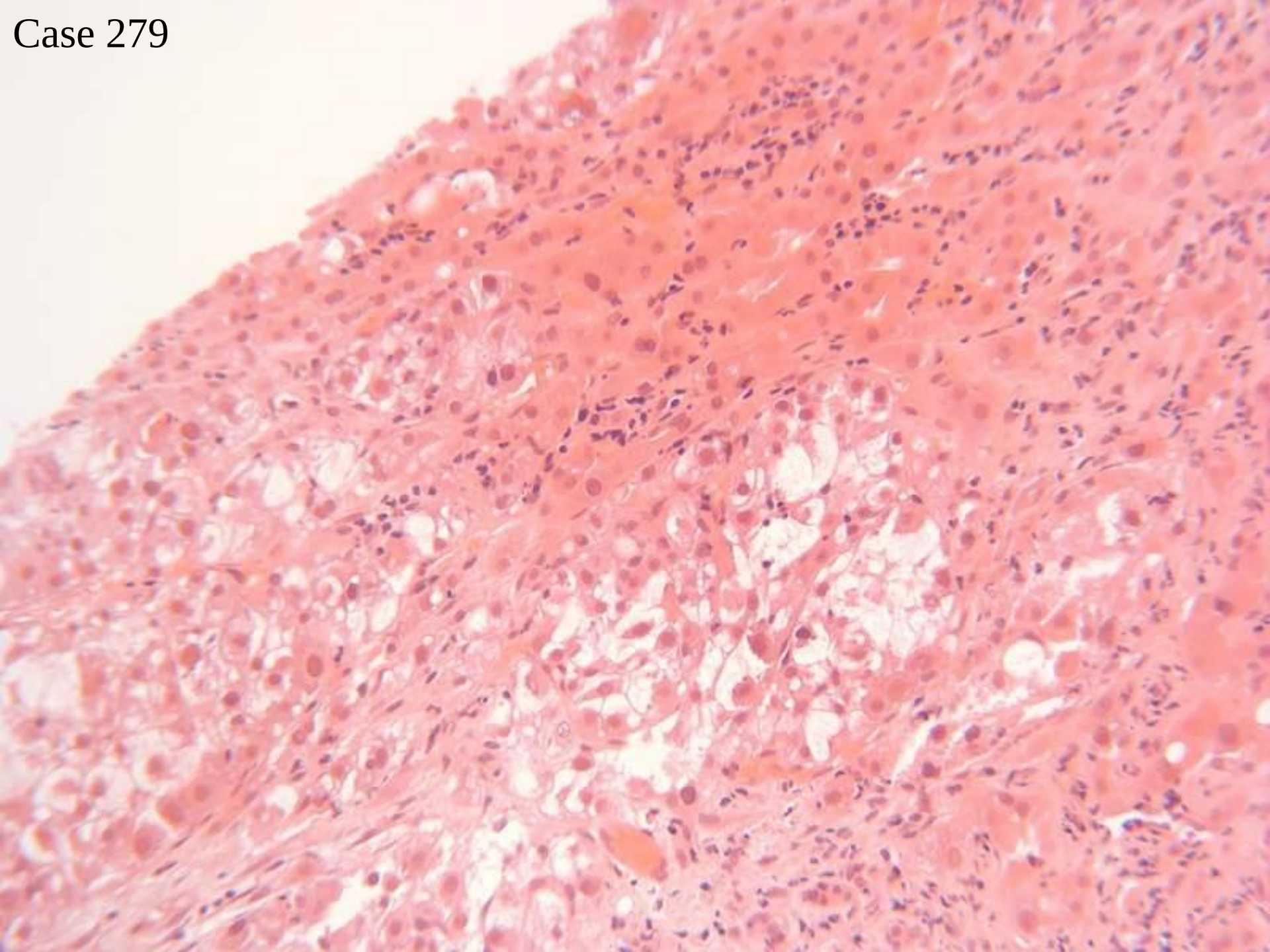


Case 279

Responses:

42 Neoplasm:

17 confident diagnosis of HCC

11 probable HCC (clear cell)

5 possible HCC

4 mixed HCC/ cholangiocarcinoma

1 cholangiocarcinoma

3 cirrhosis or AIH + dysplasia

1 angiomyolipoma

23 not neoplastic

9 cirrhosis

5 acute hepatitis

2 subfulminant, massive necrosis

1 steatohepatitis

1 herpes hepatitis

1 acute liver injury ? alcohol

1 toxic liver injury

1 chronic hepatitis

1 large bile duct obstruction

1 description only

Case 279

Scoring: not suitable for scoring

Discussion: This was a small biopsy, but all sections circulated included diagnostic material, and the best section is on the web.

Recognition of HCC in small biopsies can be difficult – comparison with background non-neoplastic liver is helpful. It is very unusual for HCC to be present in non-targeted biopsies, but does occasionally happen.

Follow up from Dr Sidky.....

Case 279

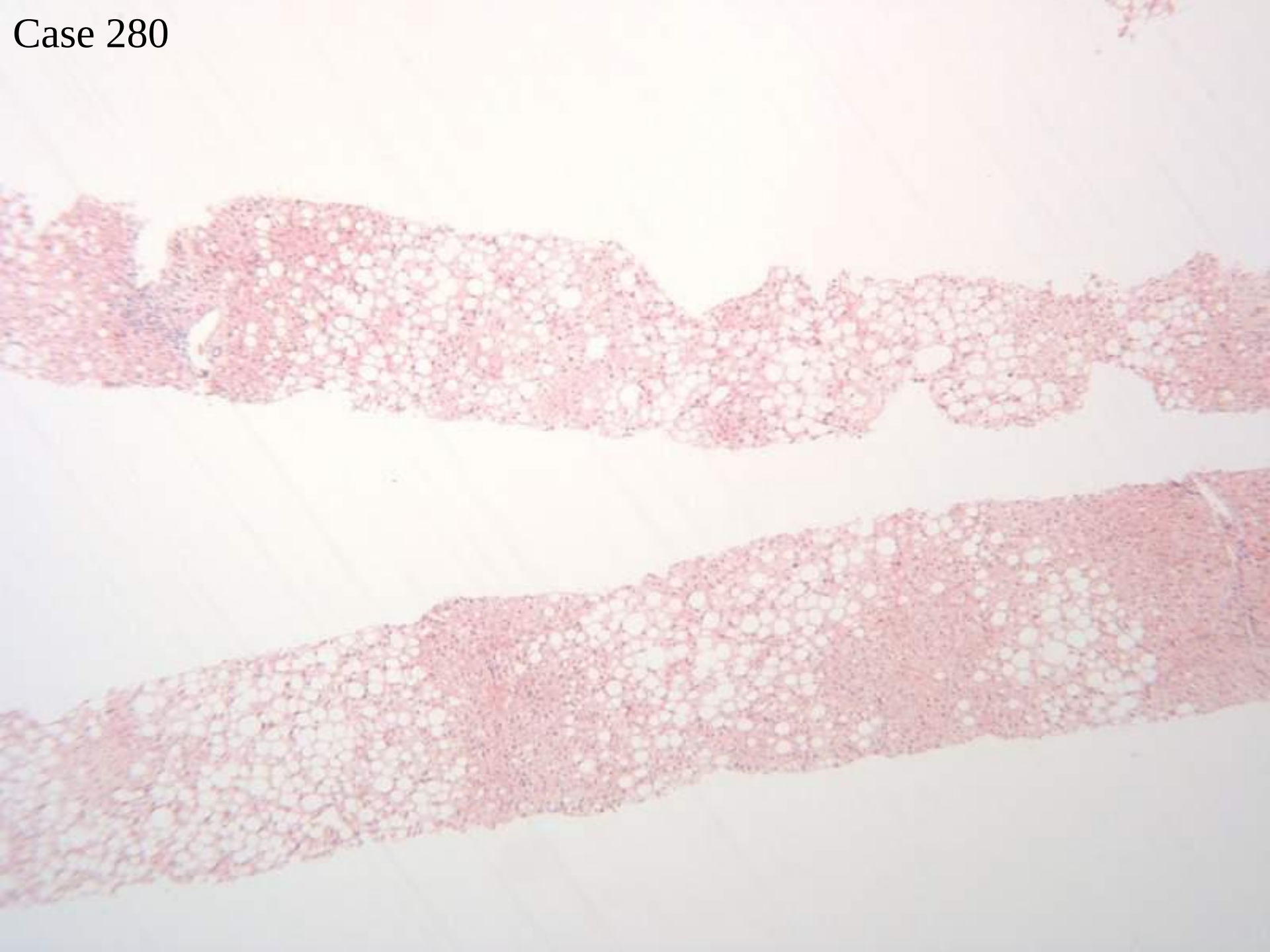
Submitting Pathologist's diagnosis:

Well differentiated hepatocellular carcinoma arising in cirrhotic liver

Case 280

62/Female. Abnormal LFTs. Raised Ferritin. 62 years, ?haemochromatosis

Case 280



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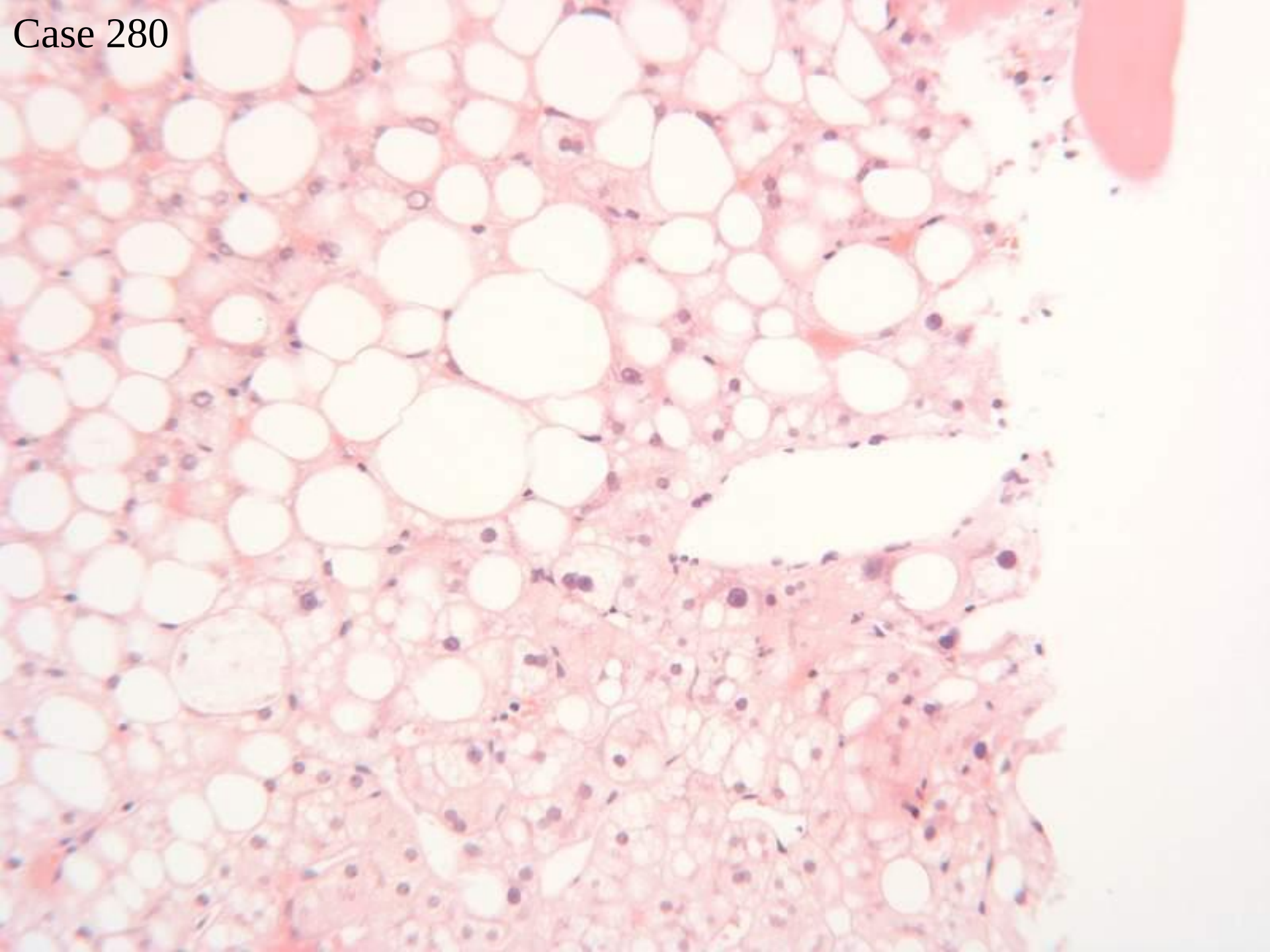

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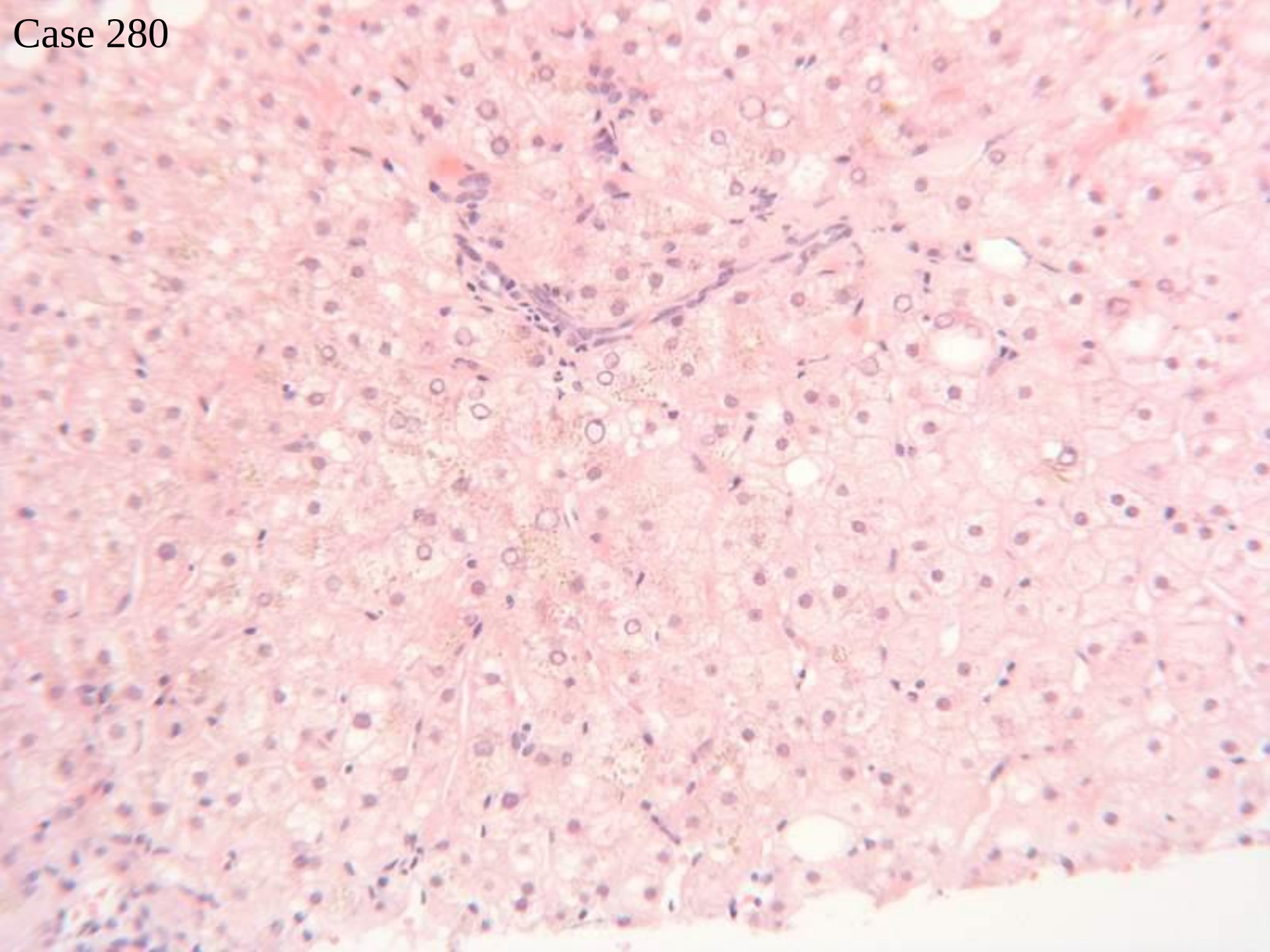

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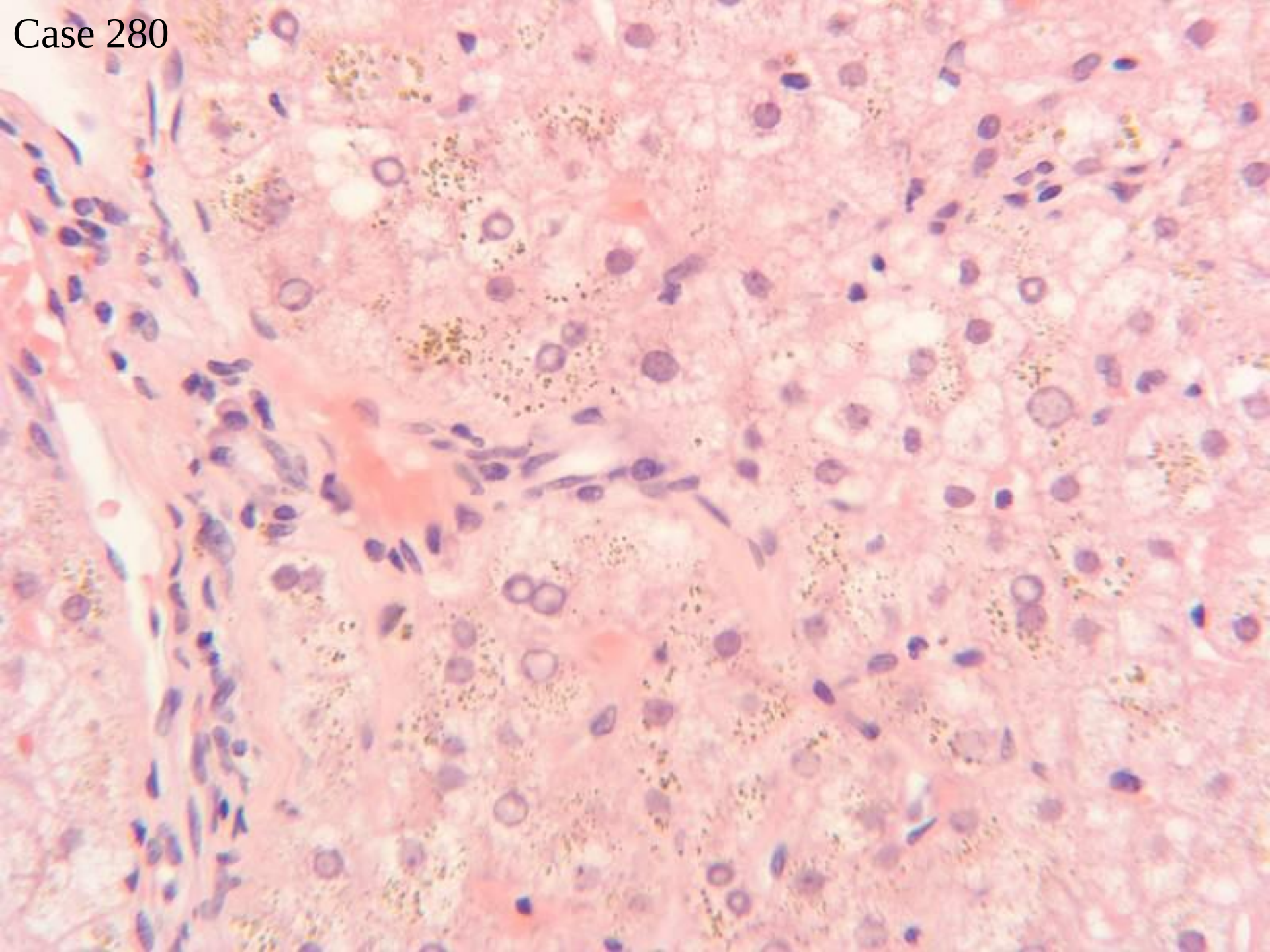

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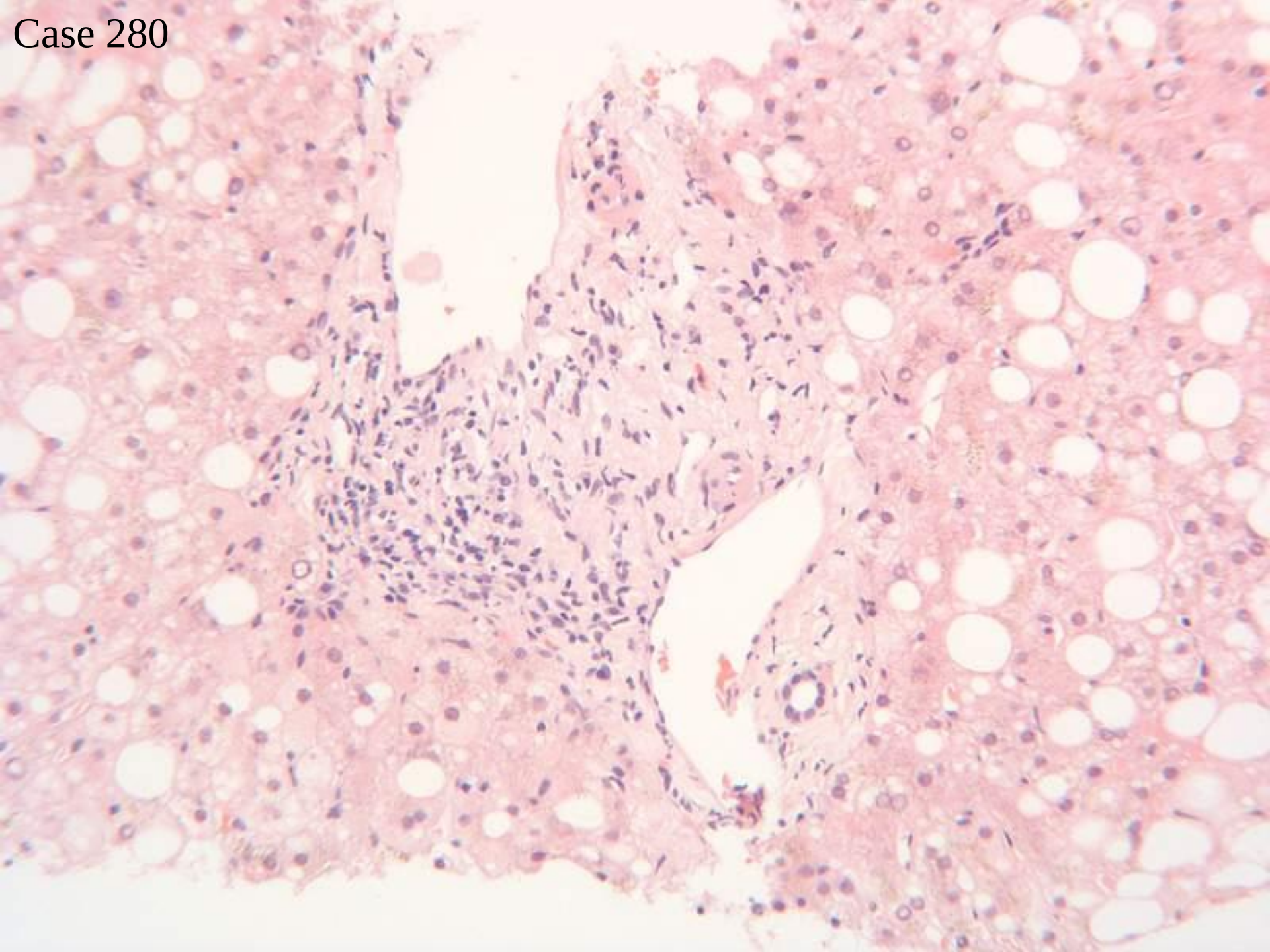

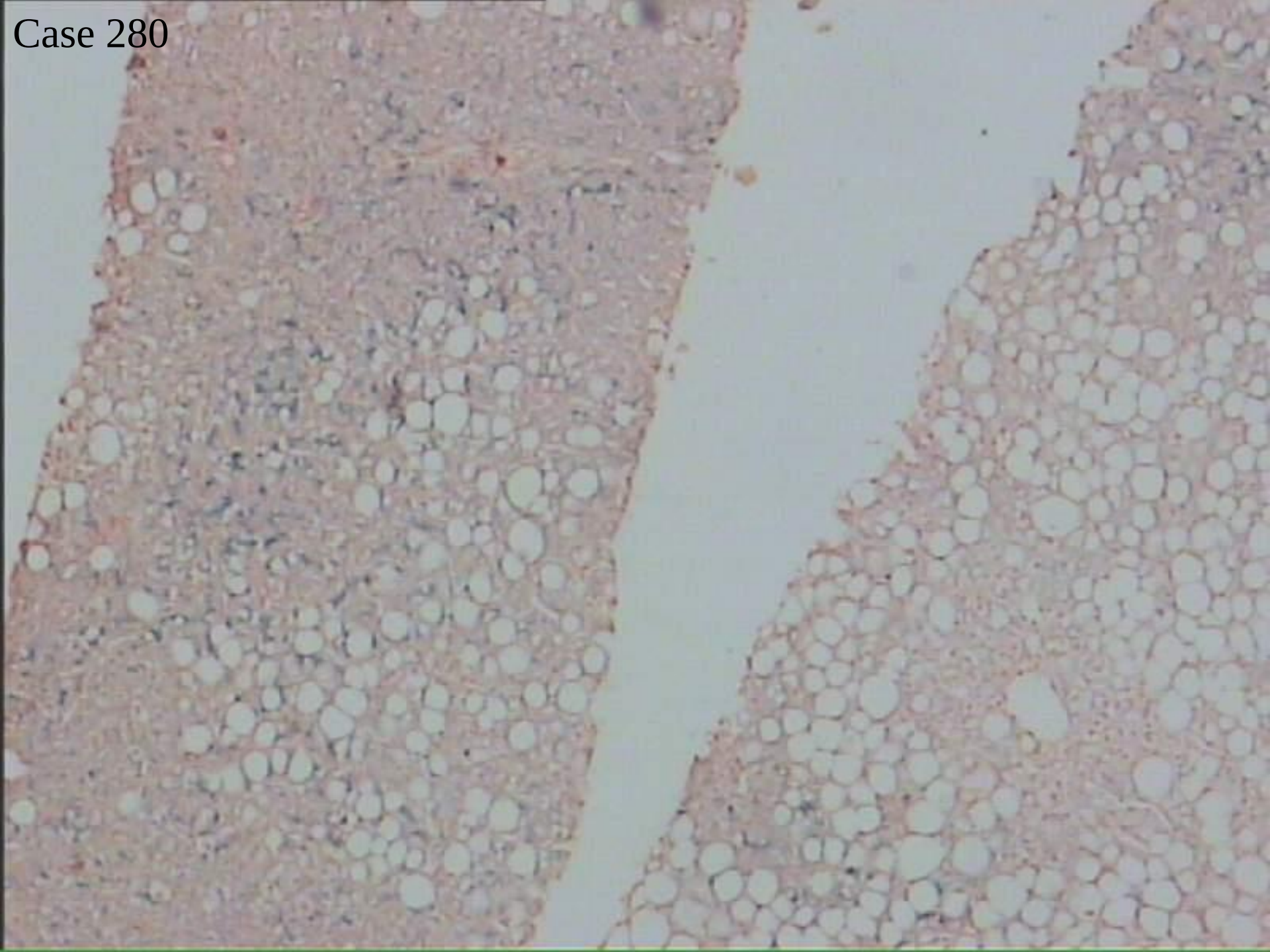
Case 280

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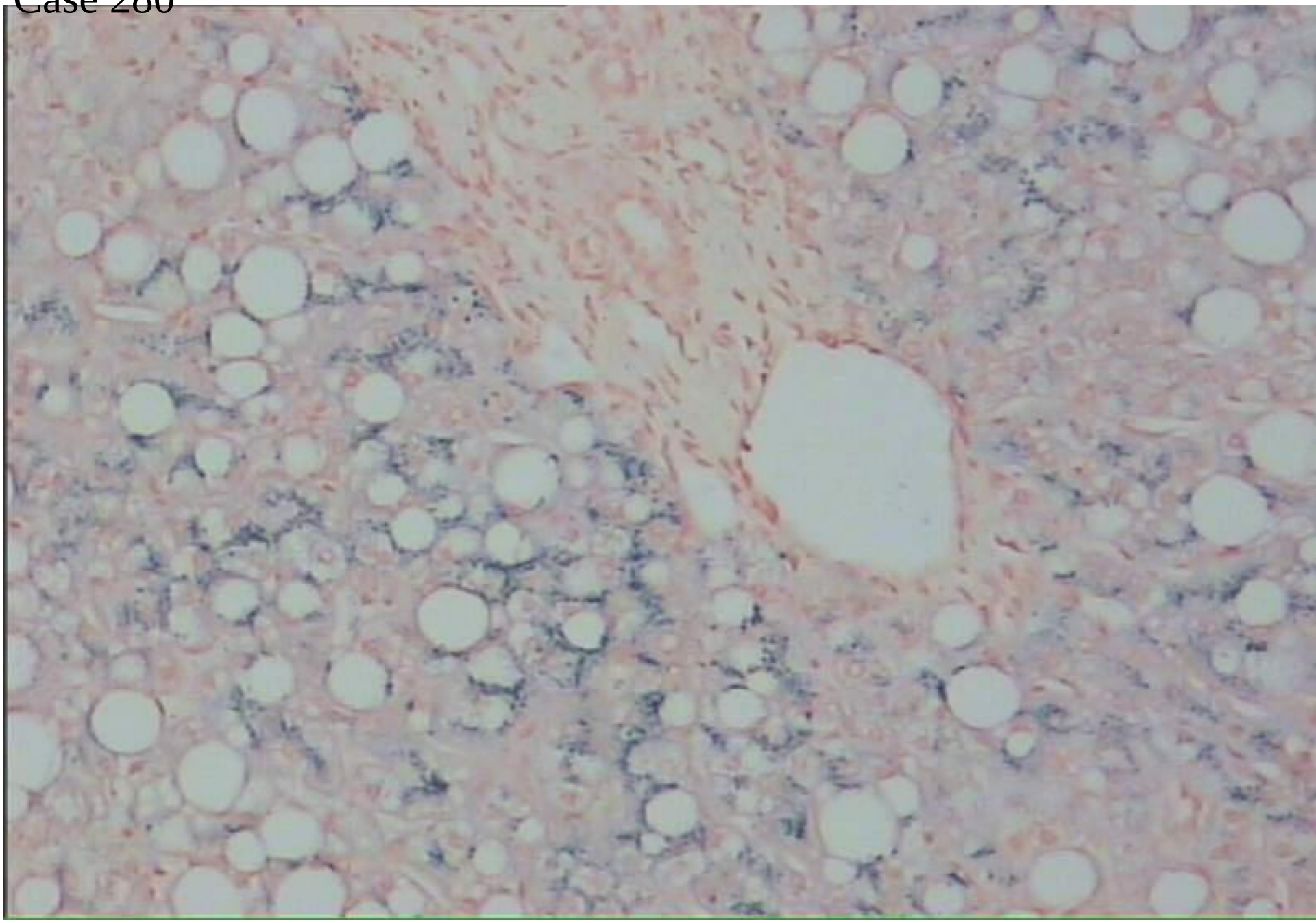


Case 280

Responses:

33 steatosis and any suggestion of haemochromatosis

20 steatohepatitis and haemochromatosis

3 steatosis/mild steatohepatitis and haemochromatosis

7 fatty liver disease and haemochromatosis

1 steatosis/steatohepatiits + grade 2-3 iron, but no further comment

1 ASH/NASH probably not haemochromatosis

1 steatohepatitis and mild iron, not primary haemochromatosis

1 Steatosis and granular pigment, ? Perls

Of the above, 27 suggested genetic testing for haemochromatosis

Case 280

Scoring: full marks for answers including fatty liver disease and haemochromatosis. Half marks for fatty liver disease without diagnosing (probable) haemochromatosis.

Reporting biopsies with fatty liver disease which are borderline for steatohepatitis - sampling error and problem with diagnostic criteria is acknowledged – the text of the report should include a description of the features on which the diagnosis is made. Some places include a steatohepatitis score (e.g Kleiner, *Hepatology. 2005;41:1313-21)* .

Case 280

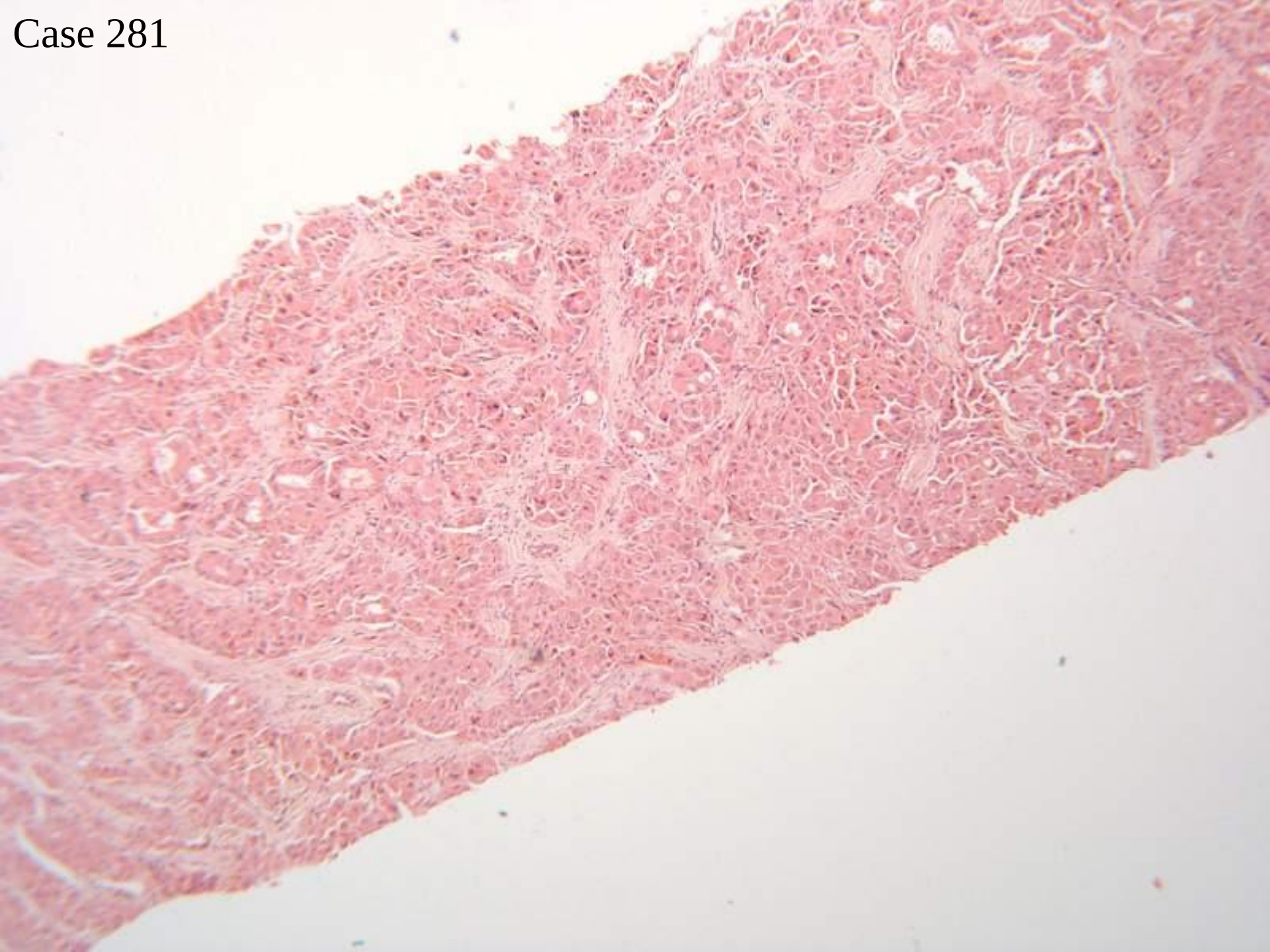
Submitting pathologist's diagnosis:

NASH and siderosis, in keeping with genetic haemochromatosis

Case 281

37/F Previous hemihepatectomy. Coeliac lymph node

Case 281



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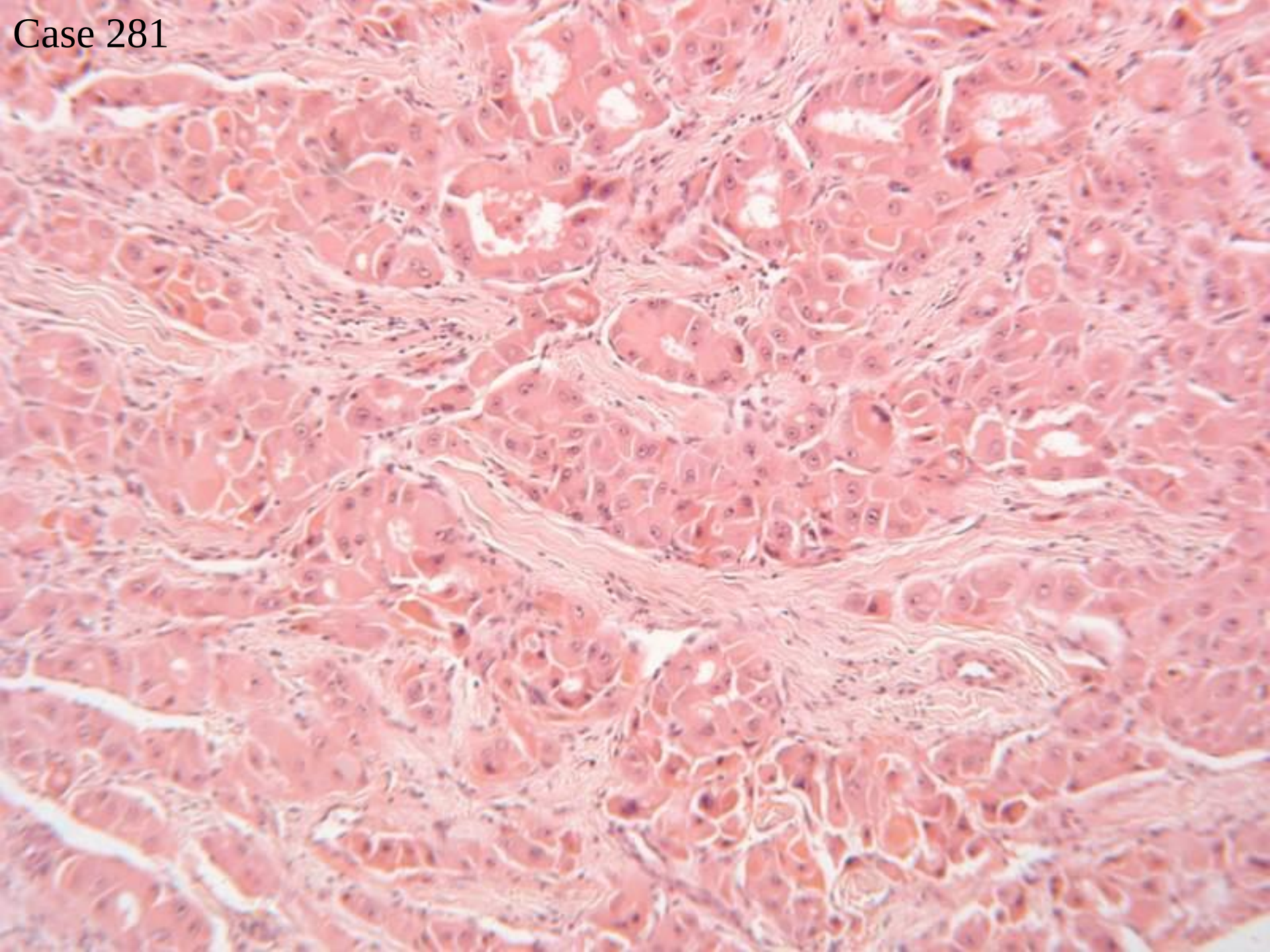

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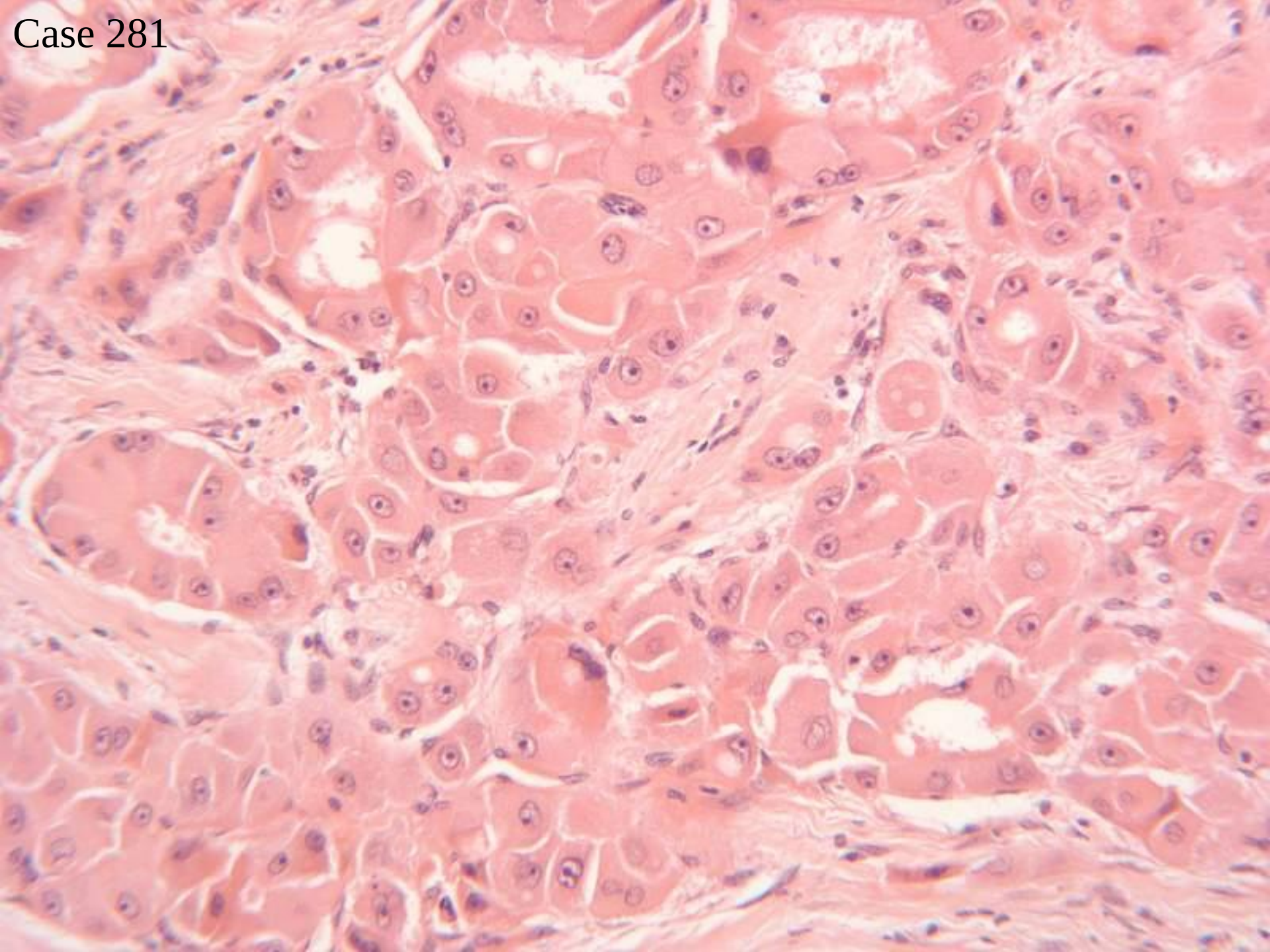


Case 281

Responses:

53 metastatic fibrolamellar carcinoma

13 metastatic hepatocellular carcinoma

Scoring: it was felt that the features of fibrolamellar carcinoma were well illustrated by this case, and marks were reduced for answers that did not suggest it – even though in this case it would not affect further patient management. In practice FLC commonly spreads to nodes, whereas metastases of conventional HCC in hilar nodes is very unusual.

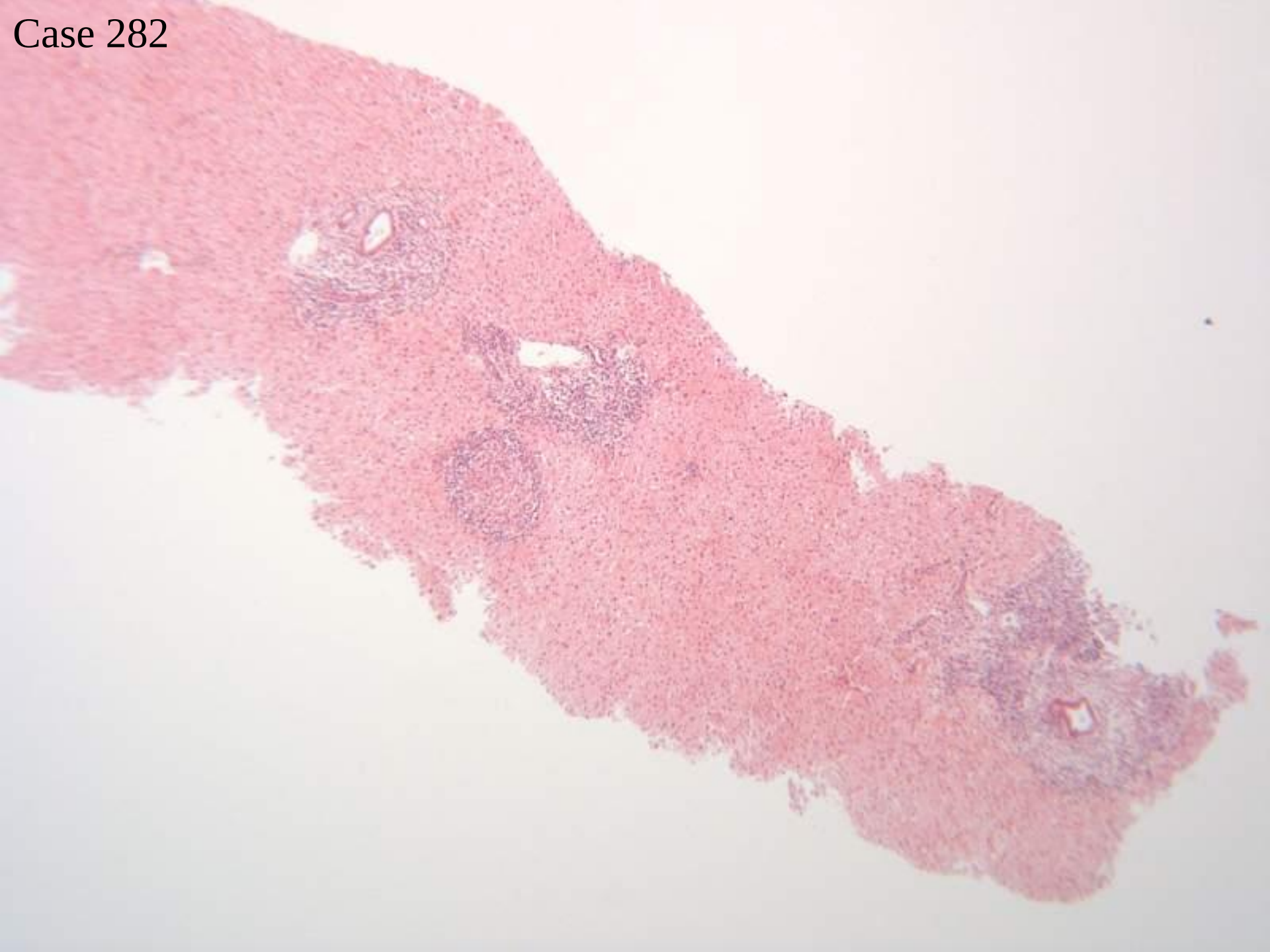
Submitting pathologist's diagnosis:

metastatic fibrolamellar HCC

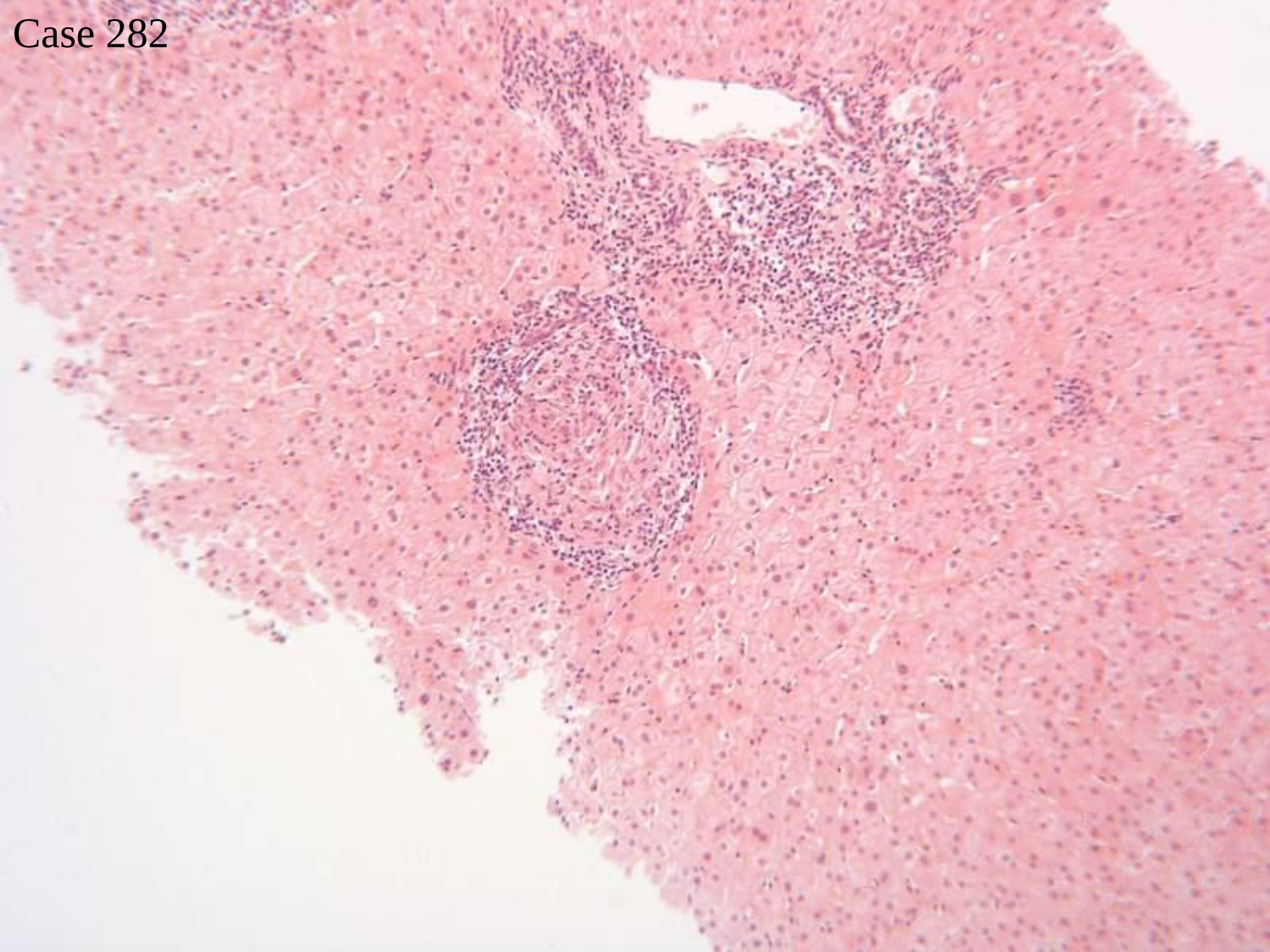
Case 282

46/F ? PBC. Positive M2 antibody. Normal LFTs, normal IgM

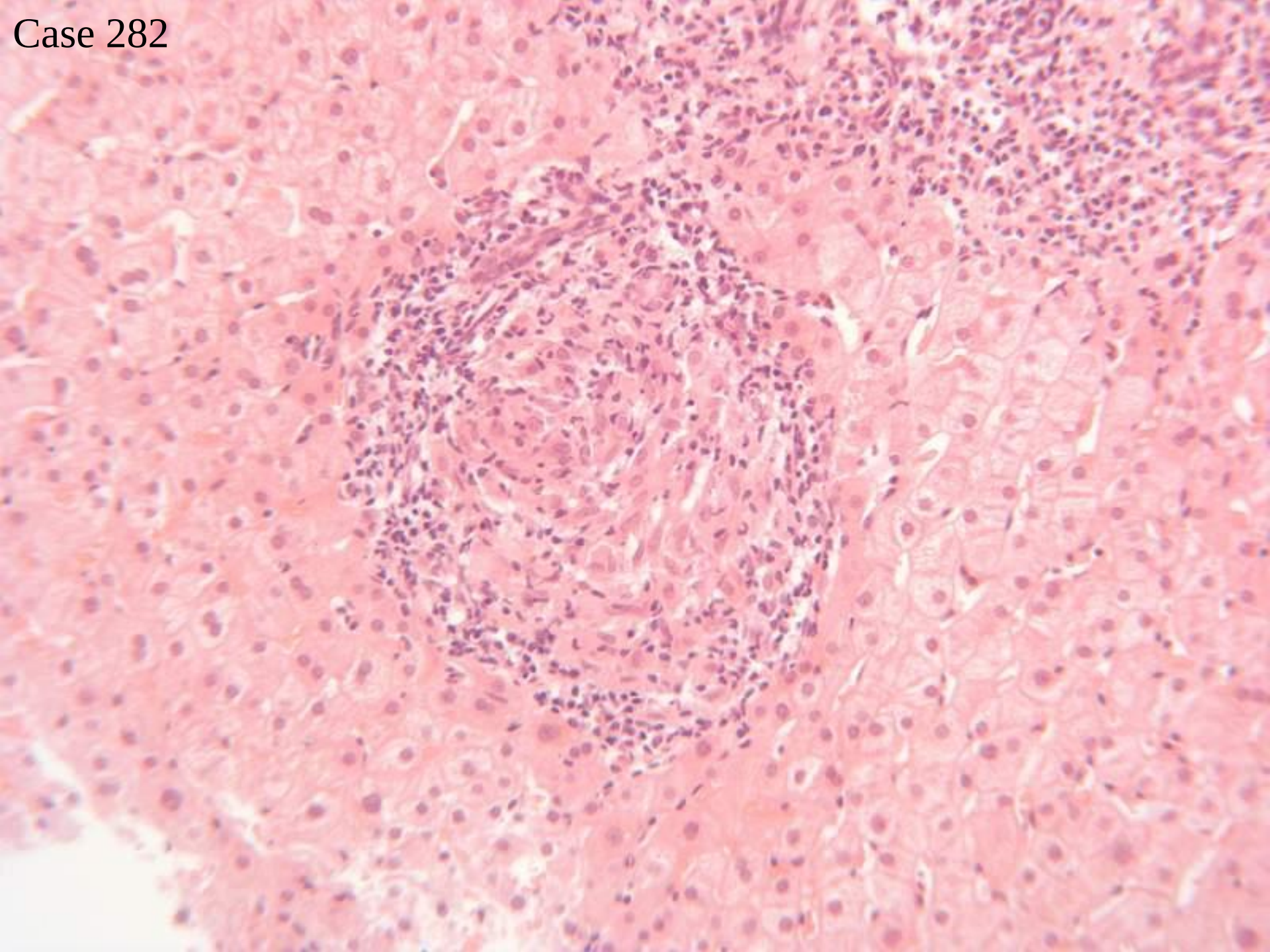
Case 282



Case 282



Case 282



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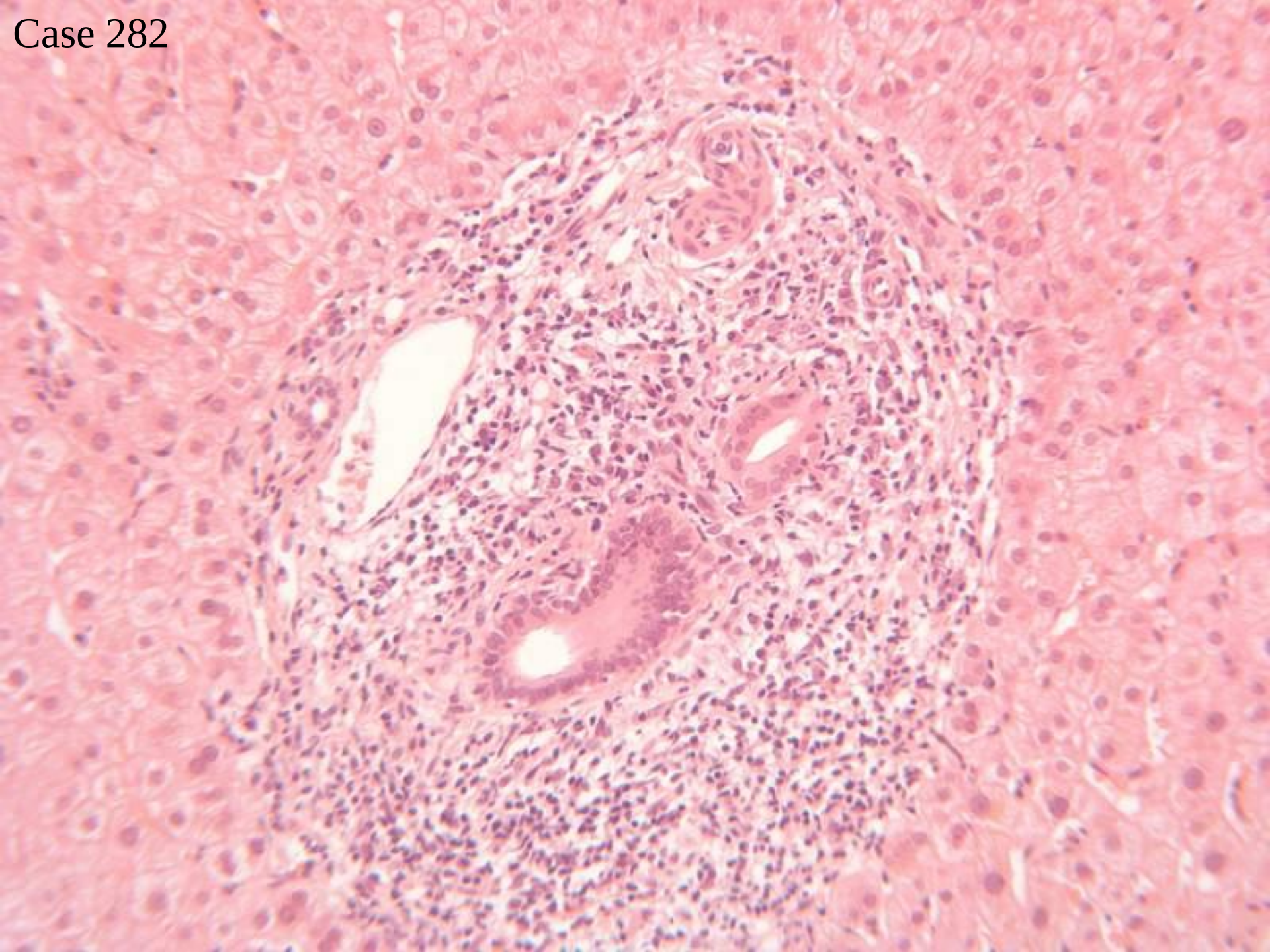

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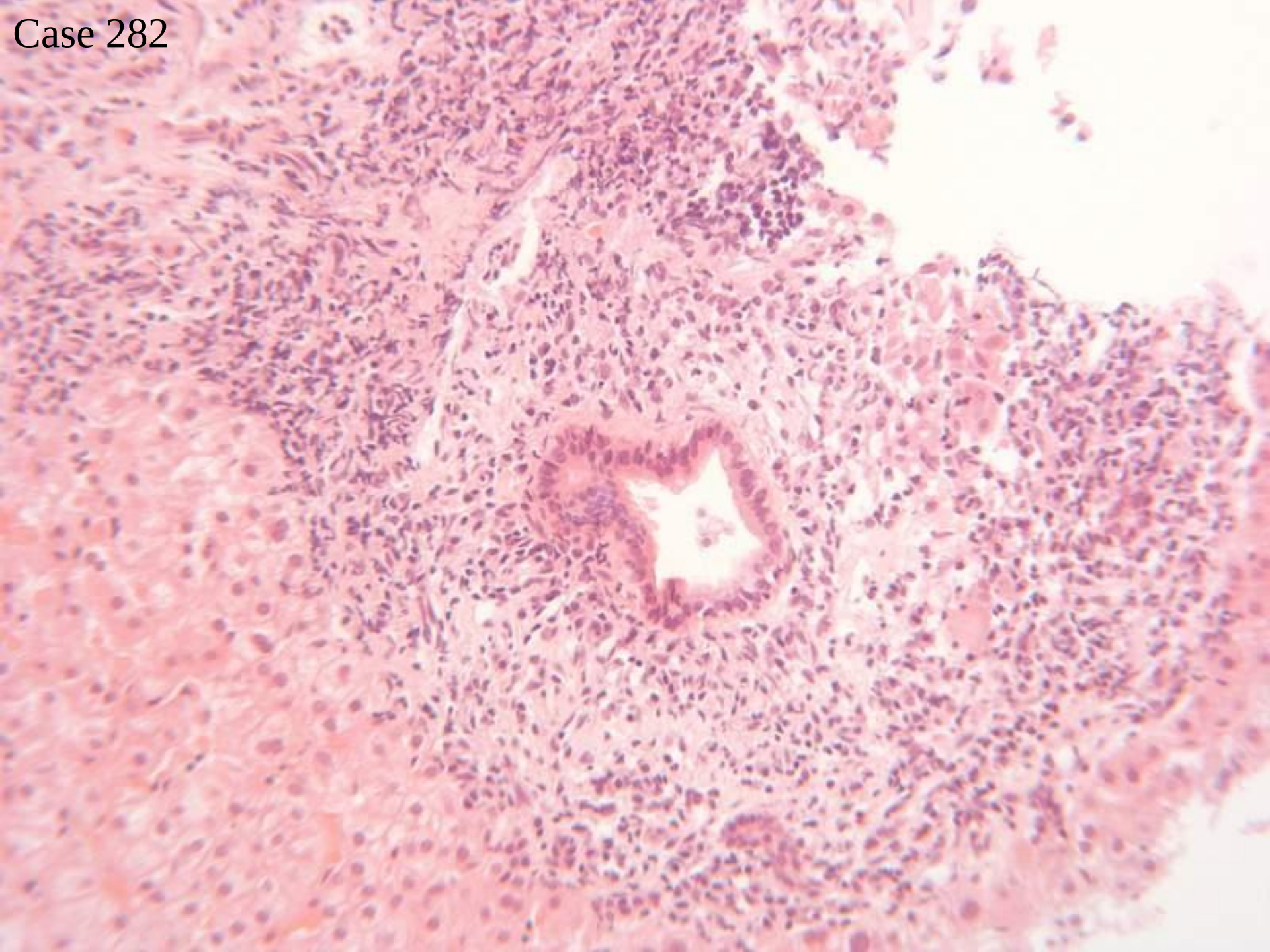

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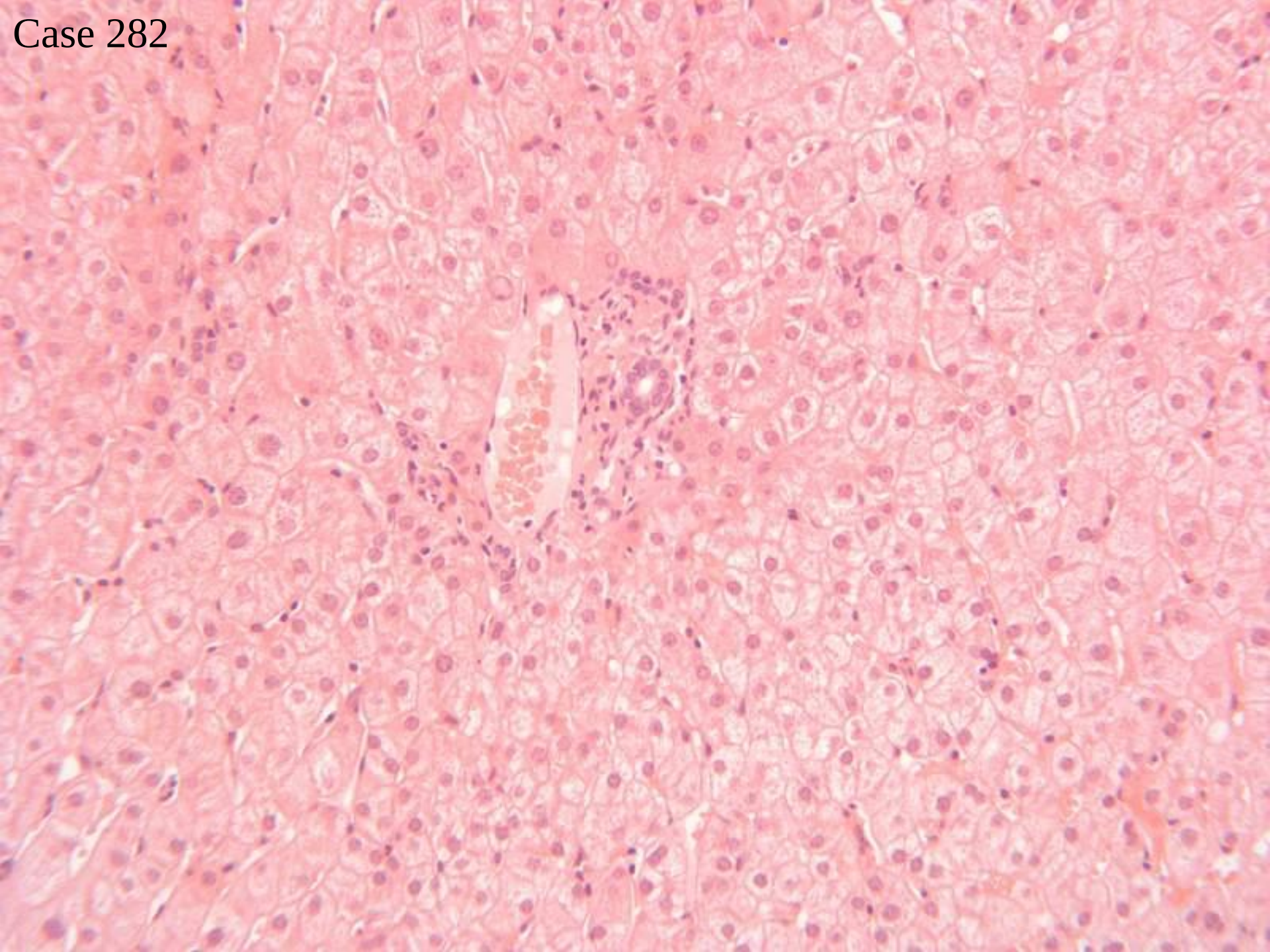

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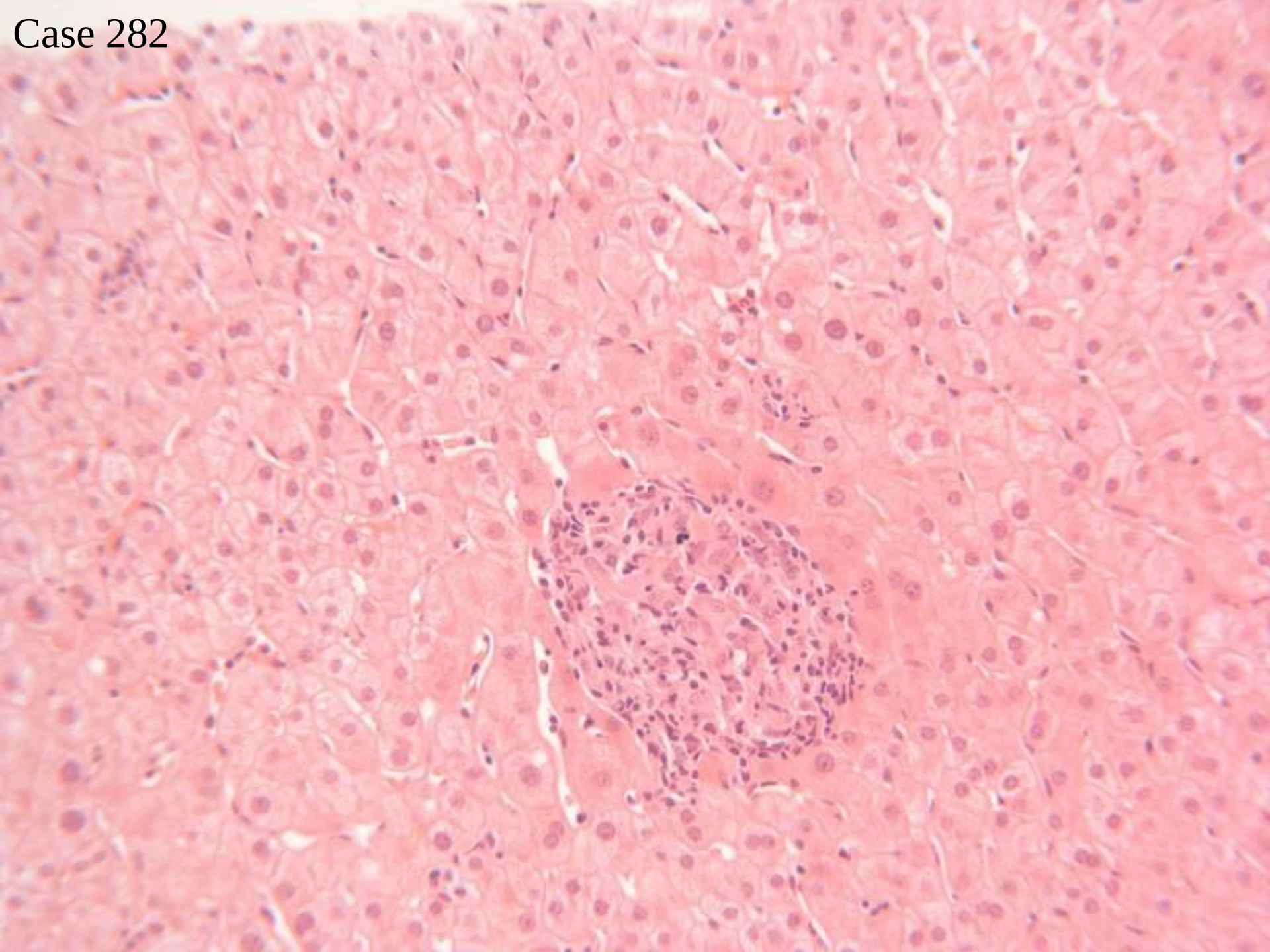


Case 282

Responses:

34 PBC, NOS

24 PBC, early stage

3 PBC ?AIH overlap

2 PBC ?PSC overlap

1 consistent with PBC, chest X-ray to exclude sarcoid and TB

1 PBC with differential of granulomas in liver

1 chronic hepatitis (PBC)

Scoring: all responses score 10.

Submitting pathologist's diagnosis: Primary biliary cirrhosis

Case 283

58/M 6 cm mass periphery in right lobe of liver, ?primary or secondary malignancy.

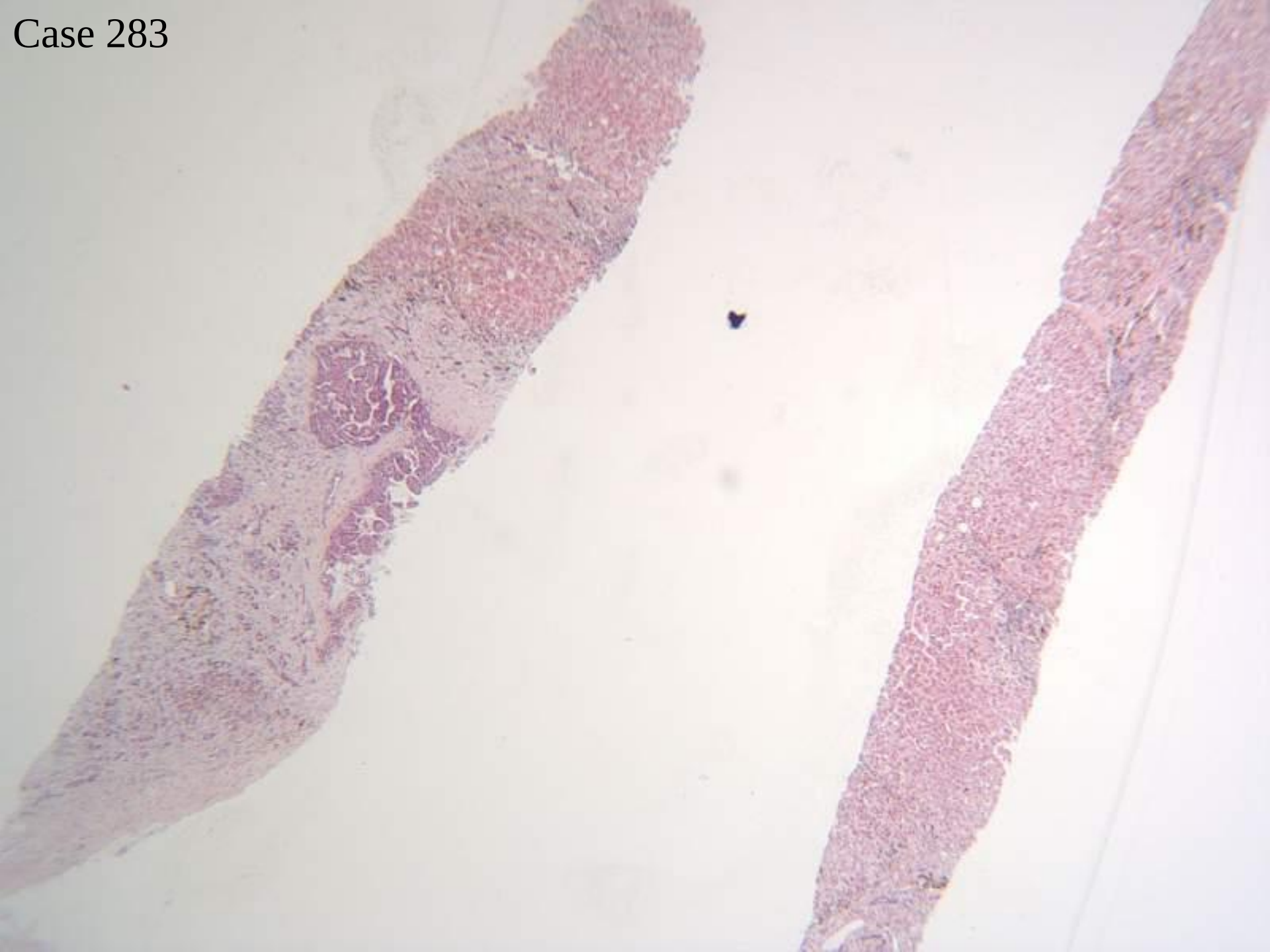
Further information – two liver masses on CT scan – 1 in segment 4 suggestive of a haemangioma,

the other in segment 8. Also a 5 cm mass in adrenal.

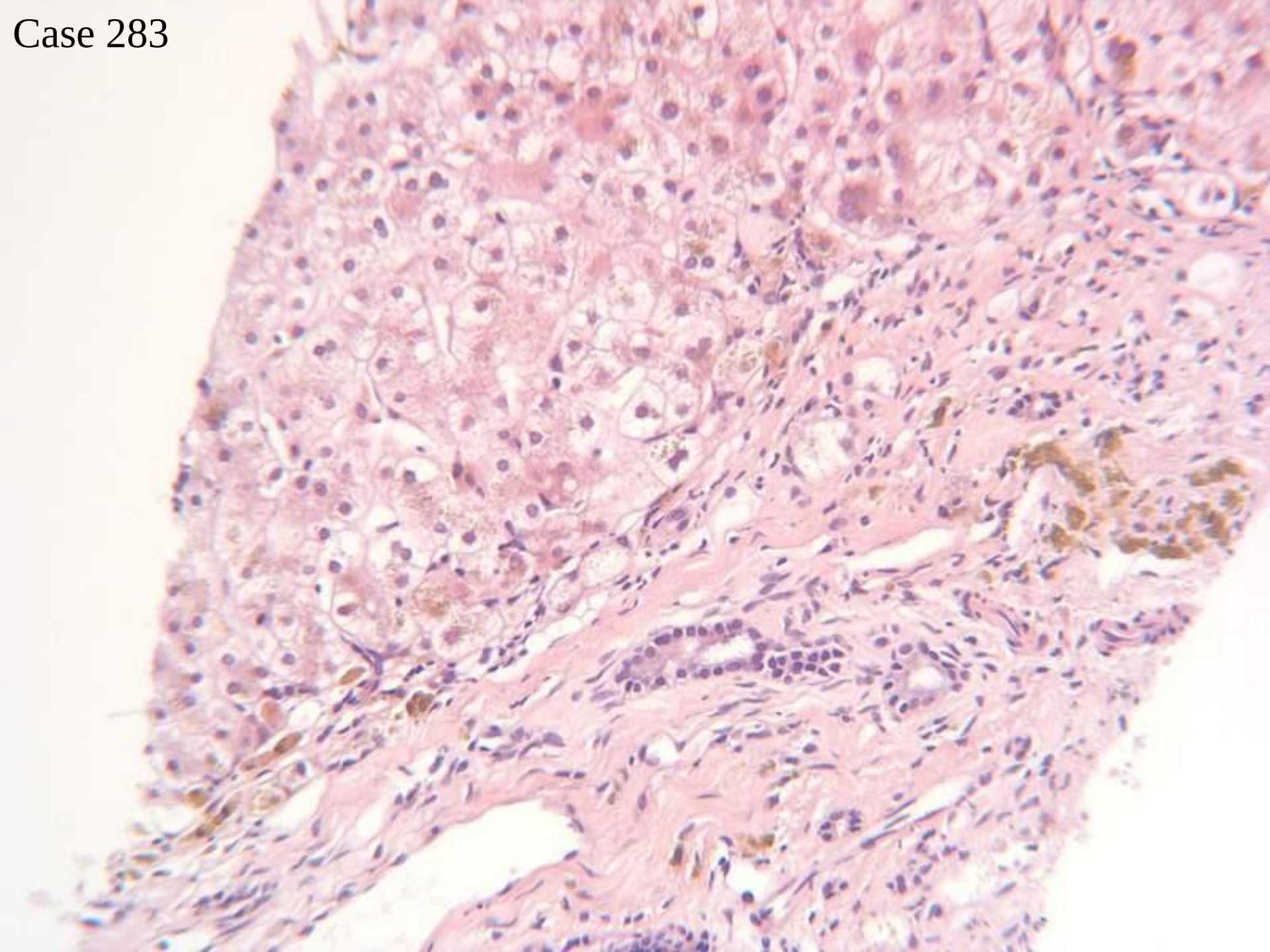
Review of laboratory investigations –

hCG, AFP, CA19.9, CEA, PSA all normal

Case 283



Case 283



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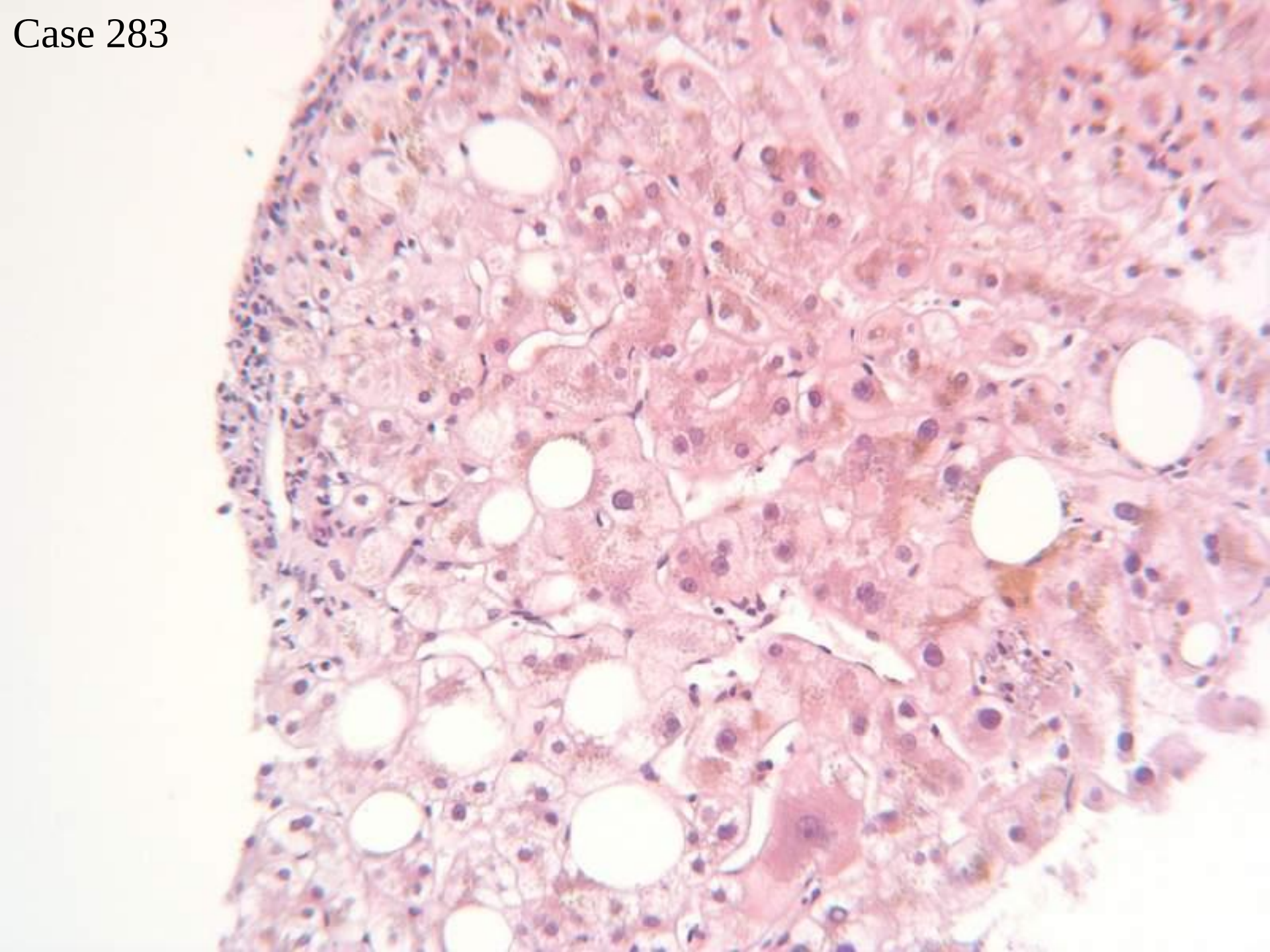

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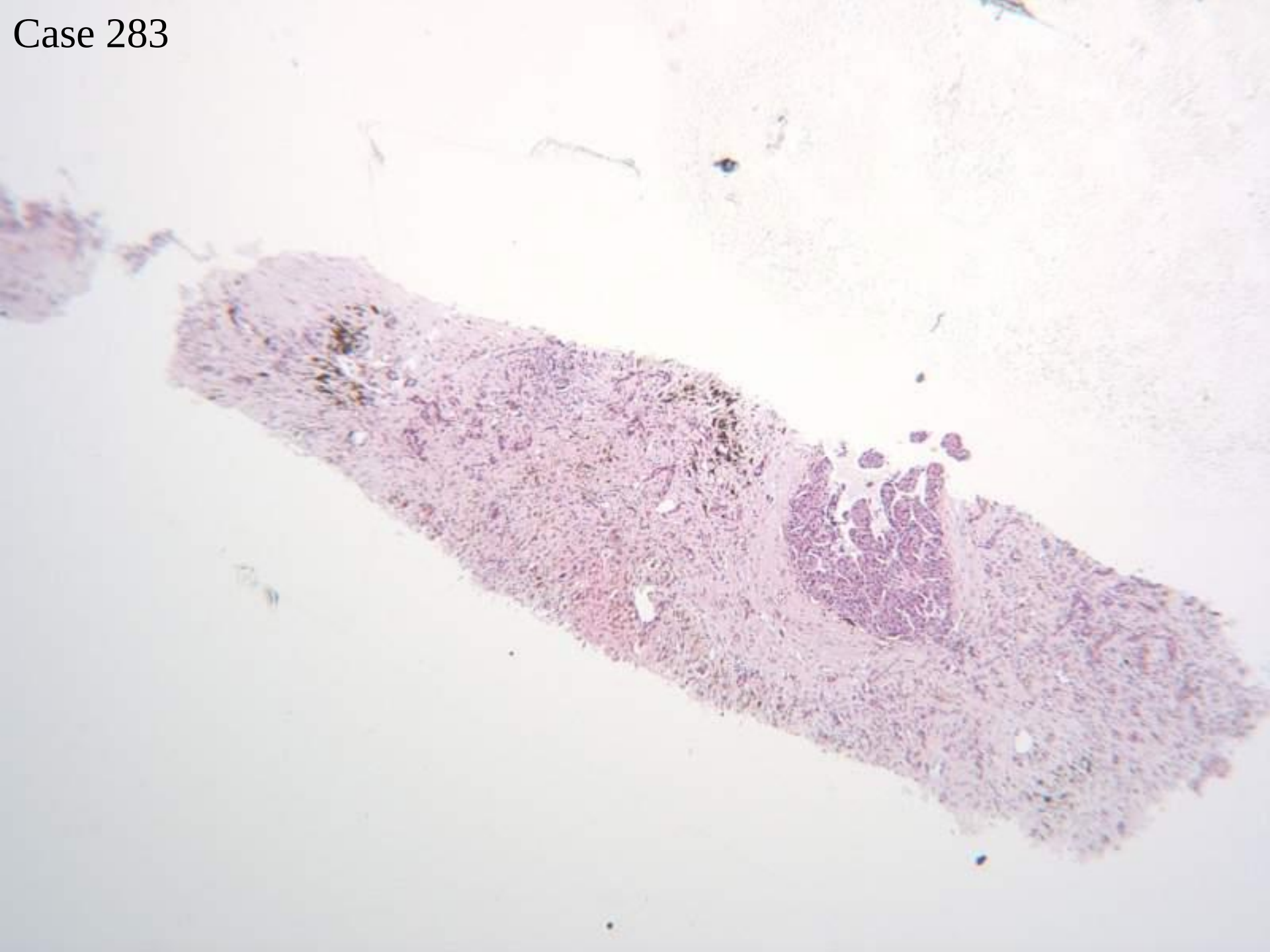

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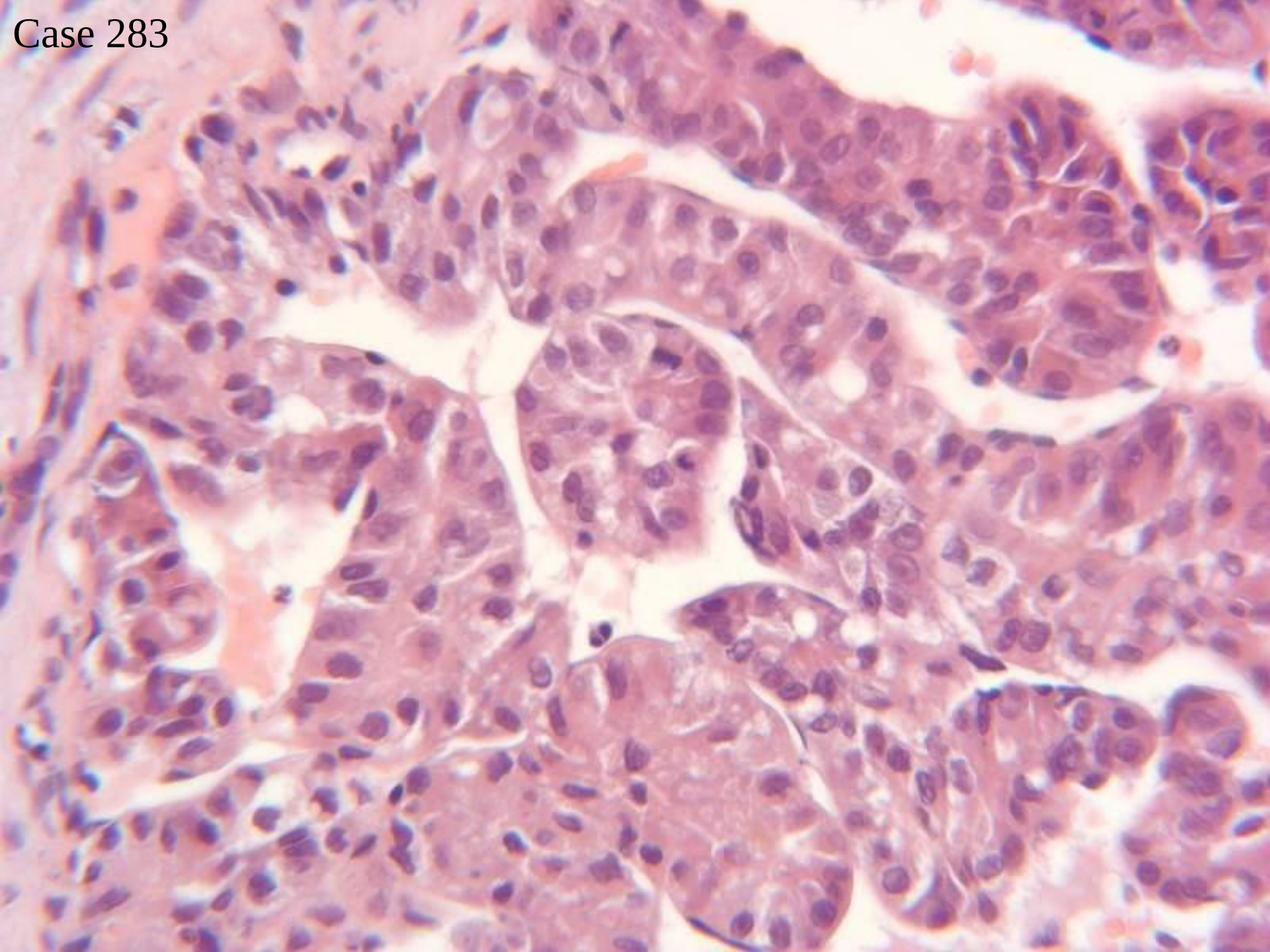

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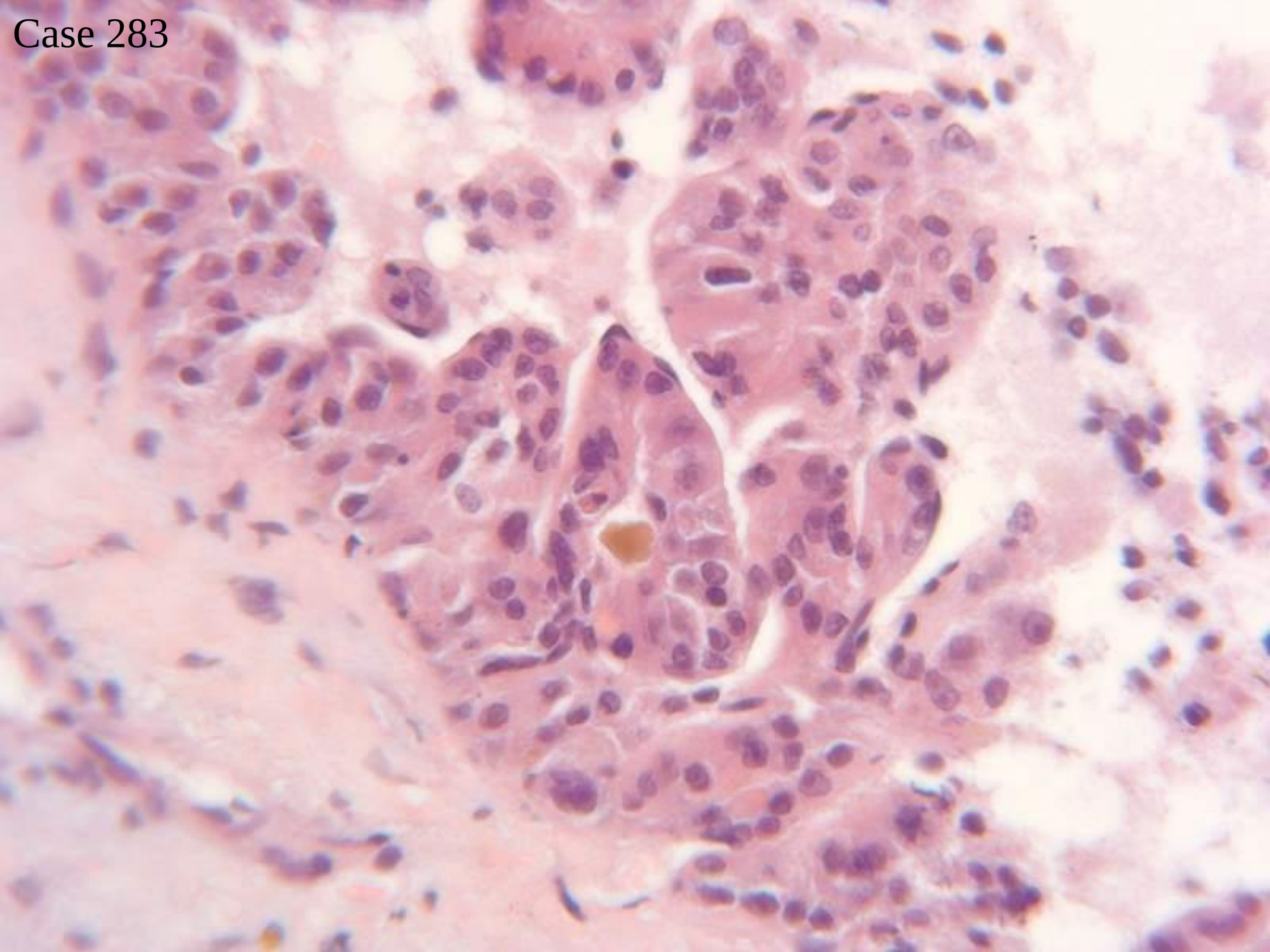


Case 283

Responses:

46 HCC, fibrosis/cirrhosis and haemochromatosis

4 carcinoma and cirrhosis, iron not mentioned

1 HCC, Background liver not mentioned

2 HCC, cholestatic liver

2 HCC/angiosarcoma

2 cirrhosis, haemochromatosis and tumour ? primary/secondary

1 cholangio carcinoma + pigment

1 adenocarcinoma, background not mentioned

1 cholangio/HCC/adrenal metastasis, background not mentioned

1 favour metastases (adeno/carcinoid)

1 papillary carcinoma, probably metastatic

1 carcinoma ? adeno

1 metastasis, ? carcinoid

1 cholangiocarcioma + ?thorotrast

1 description, no clear diagnosis

21 would do immunohistochemistry.

Case 283

Scoring: For full marks – both a clear diagnosis of HCC and a comment about the background liver disease, fibrosis/cirrhosis. Half marks if the differential includes HCC, none if HCC not mentioned.

A further 50% marks deducted if there is no mention of background liver disease, which should included some comment about both fibrosis and iron, ?haemochromatosis.

Discussion: This case had very characteristic features of HCC, including bile production, and therefore firm diagnosis was felt to be achievable on the basis of H&E. The use of immunohistochemistry in diagnosis of HCC was discussed – used more in departments seeing fewer cases, where H&E characteristics are less familiar to pathologists. From responses in the EQA, use and selection of immunostains varies a lot between individuals.

Case 283

Submitting pathologist's diagnosis:

Cirrhosis, likely haemochromatosis,

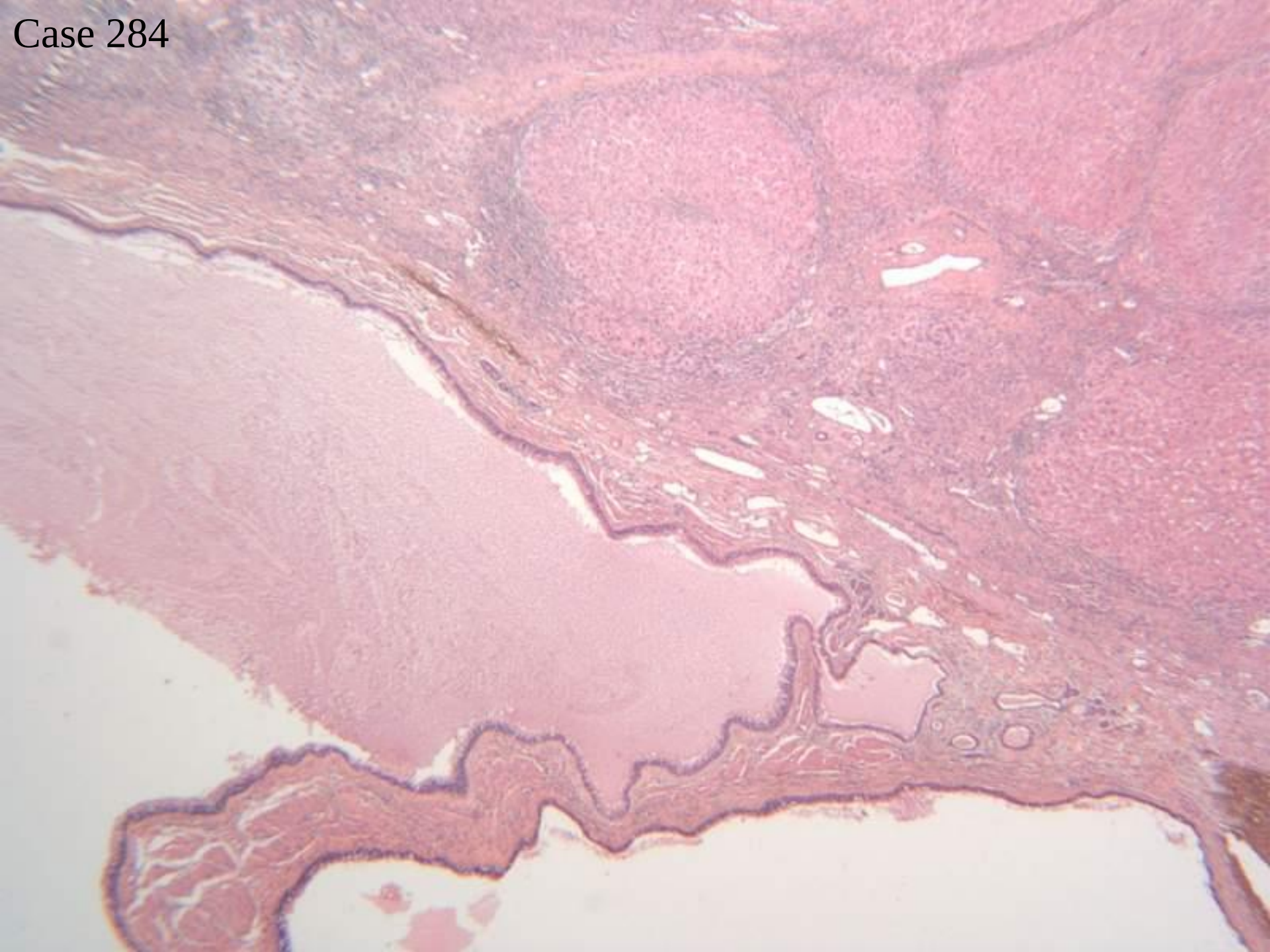
HCC

Case 284

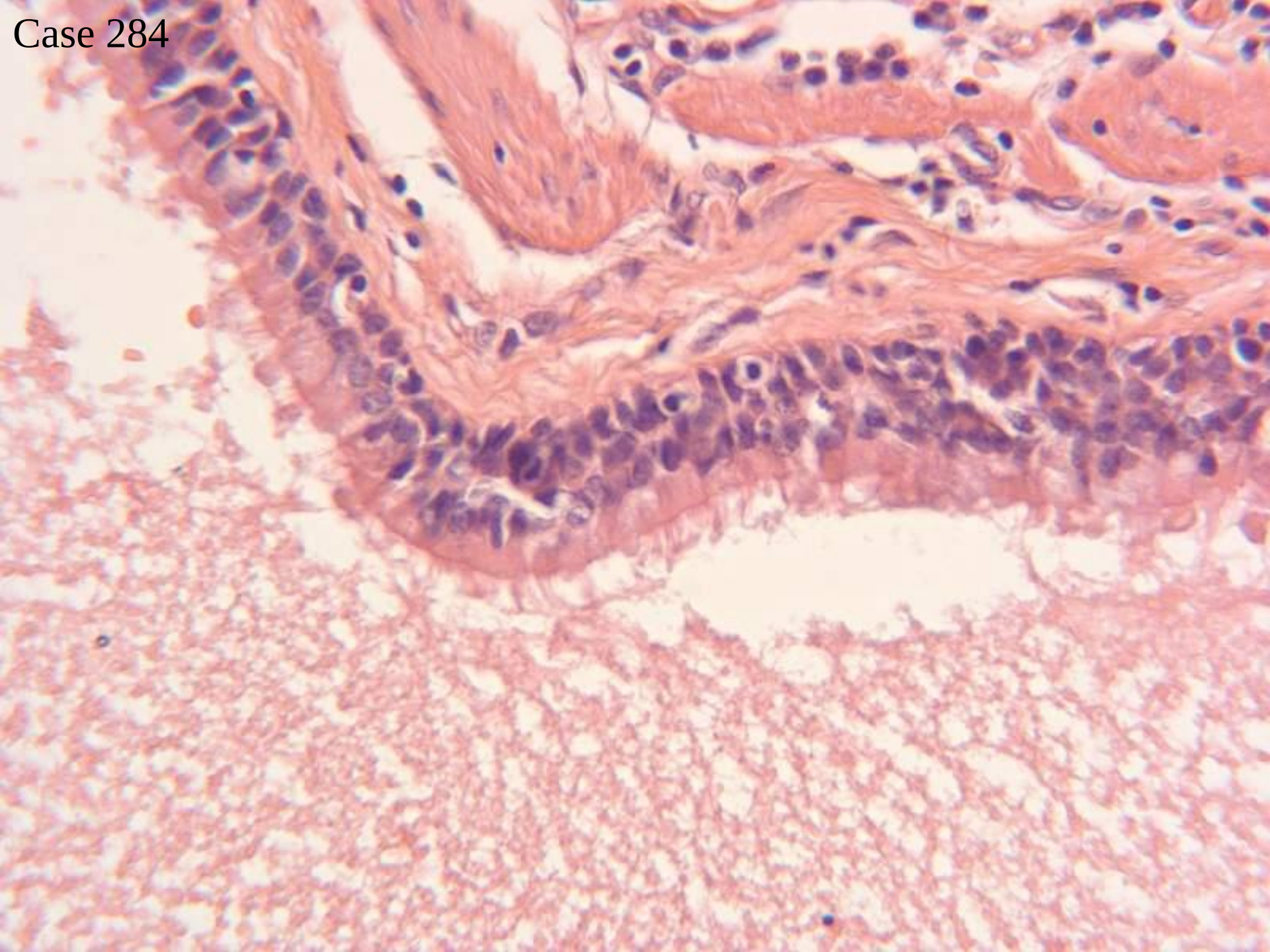
51/Male ALD and alpha-1 antitrypsin deficiency.
Liver removed at time of OLTx.

Incidental cyst

Case 284



Case 284



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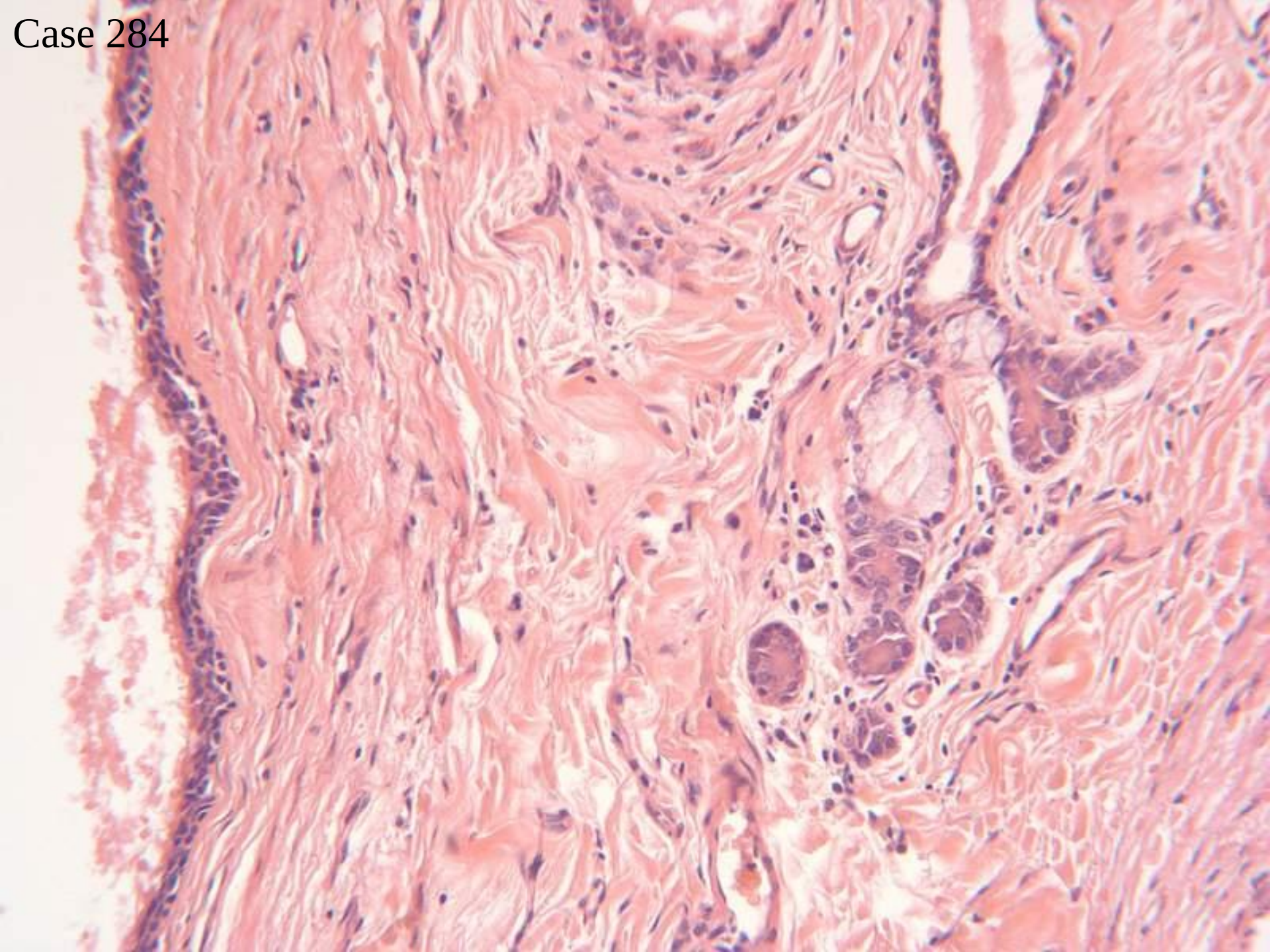
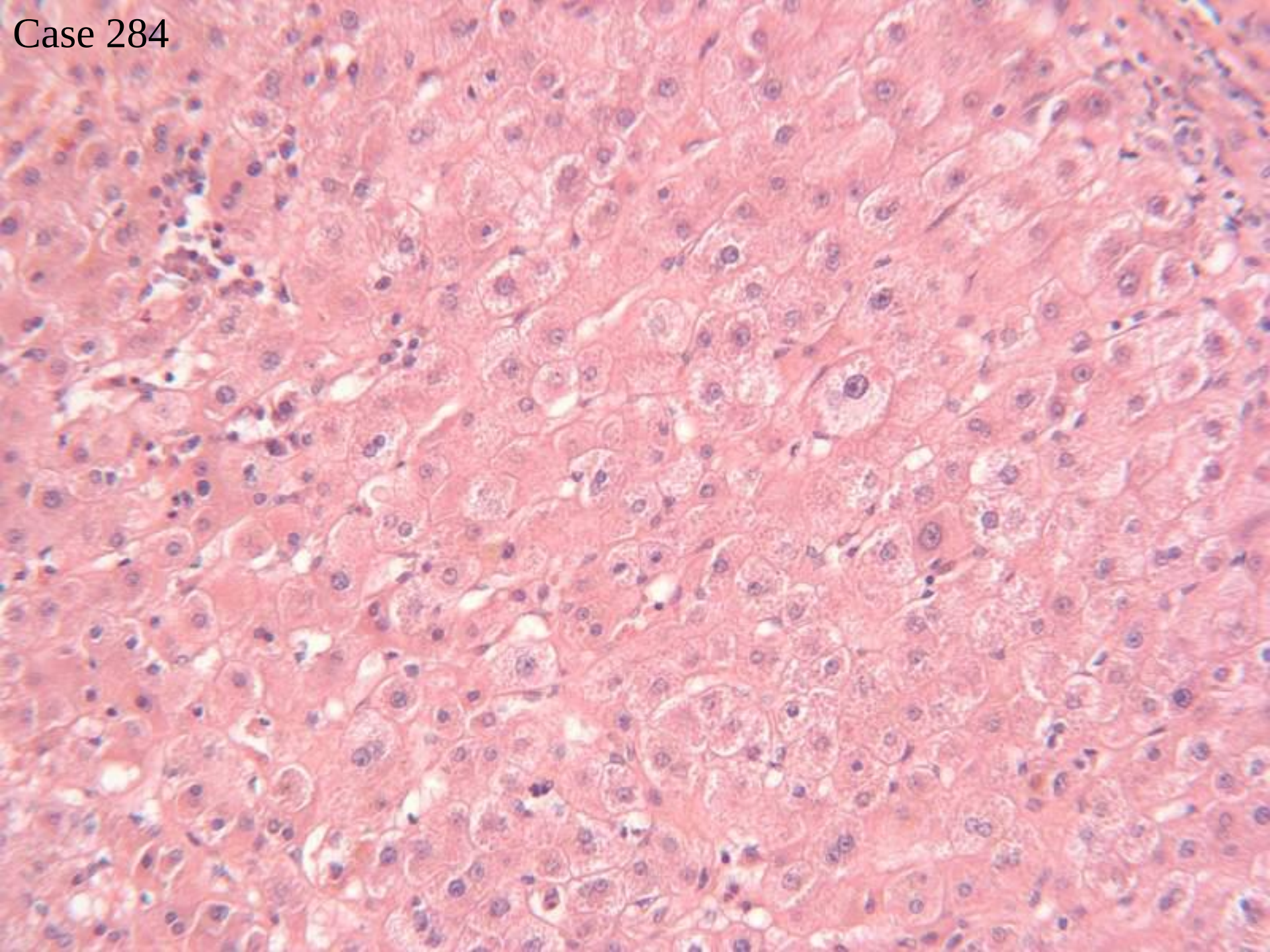


Case 284



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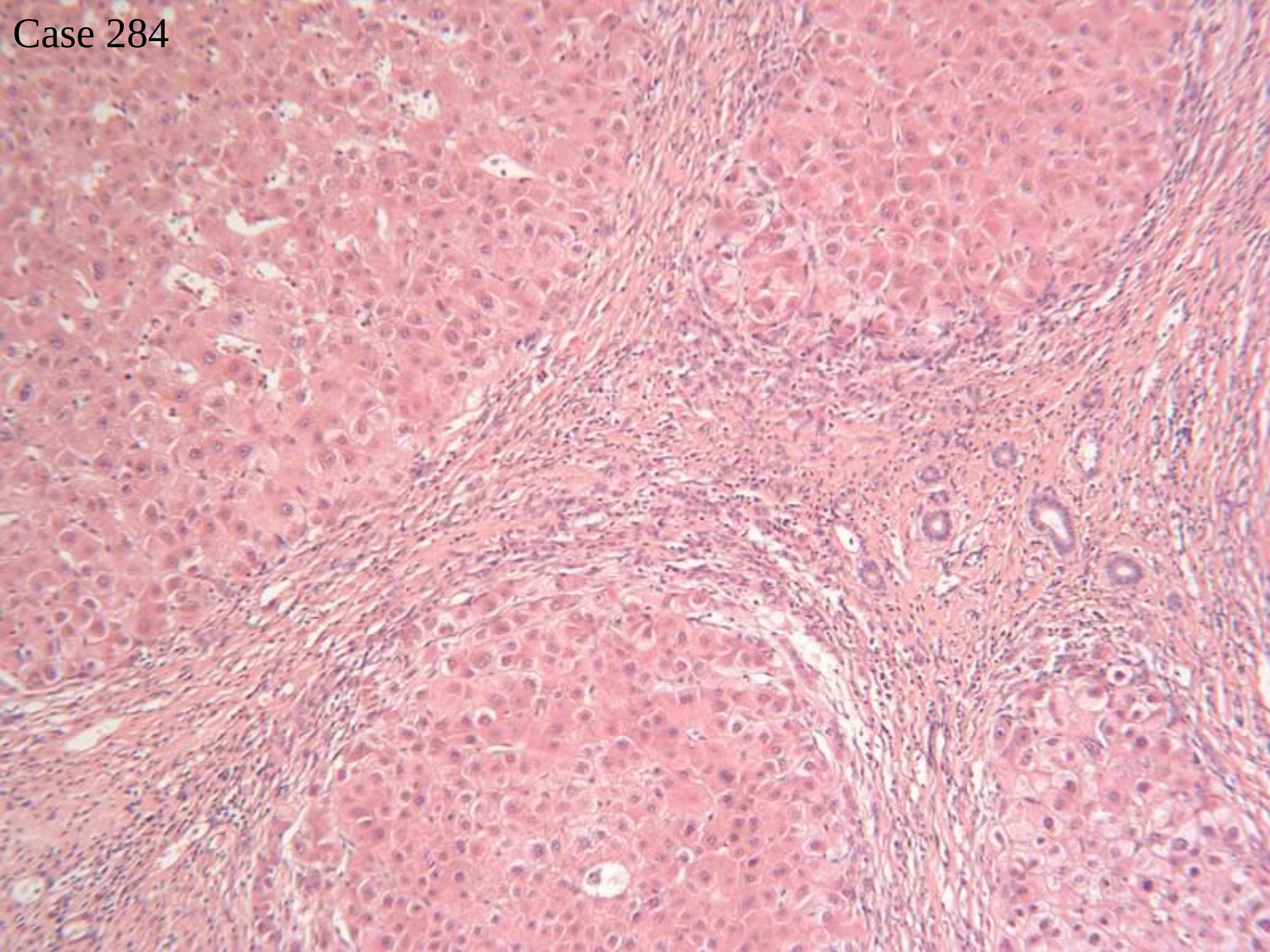

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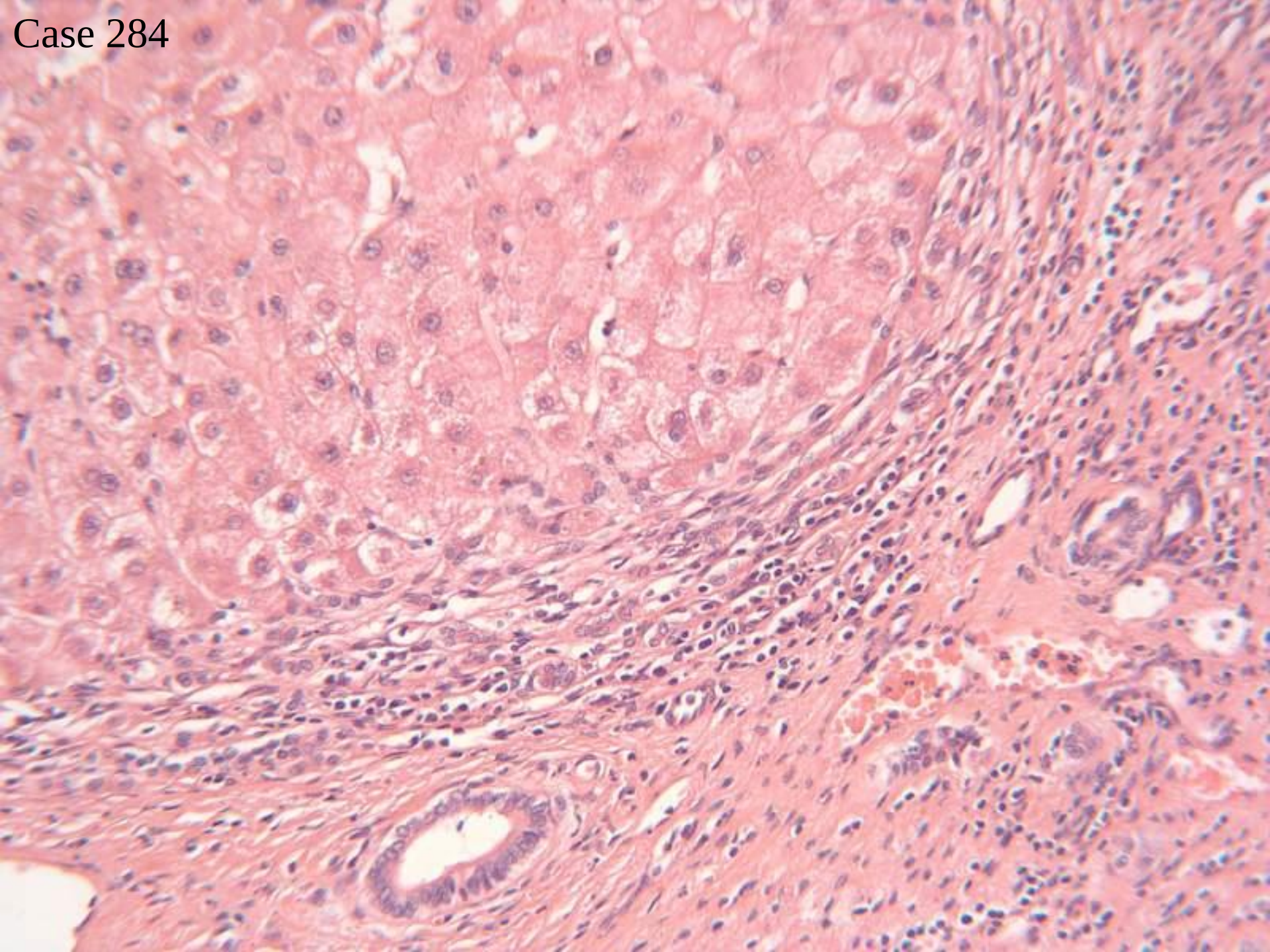

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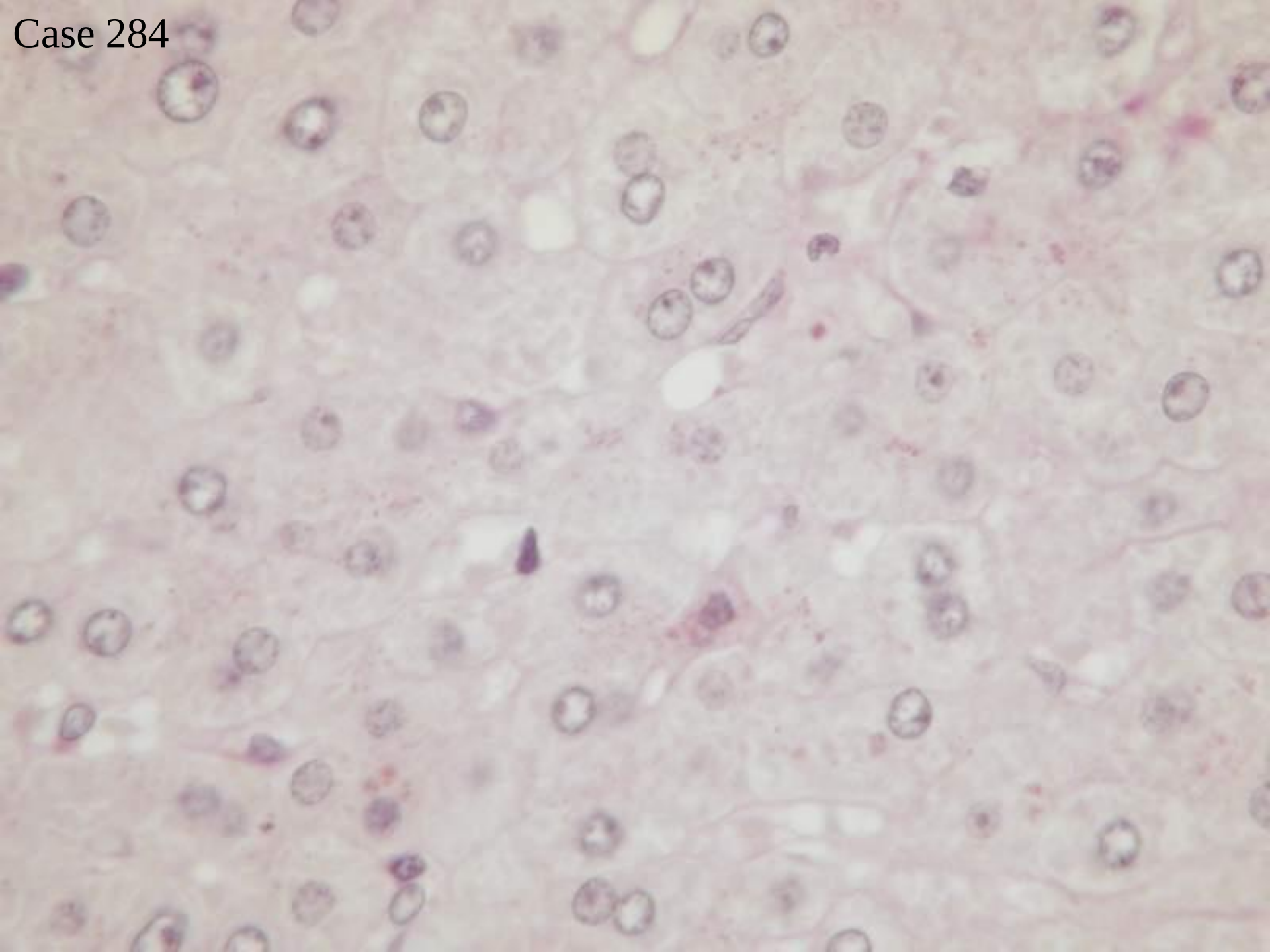

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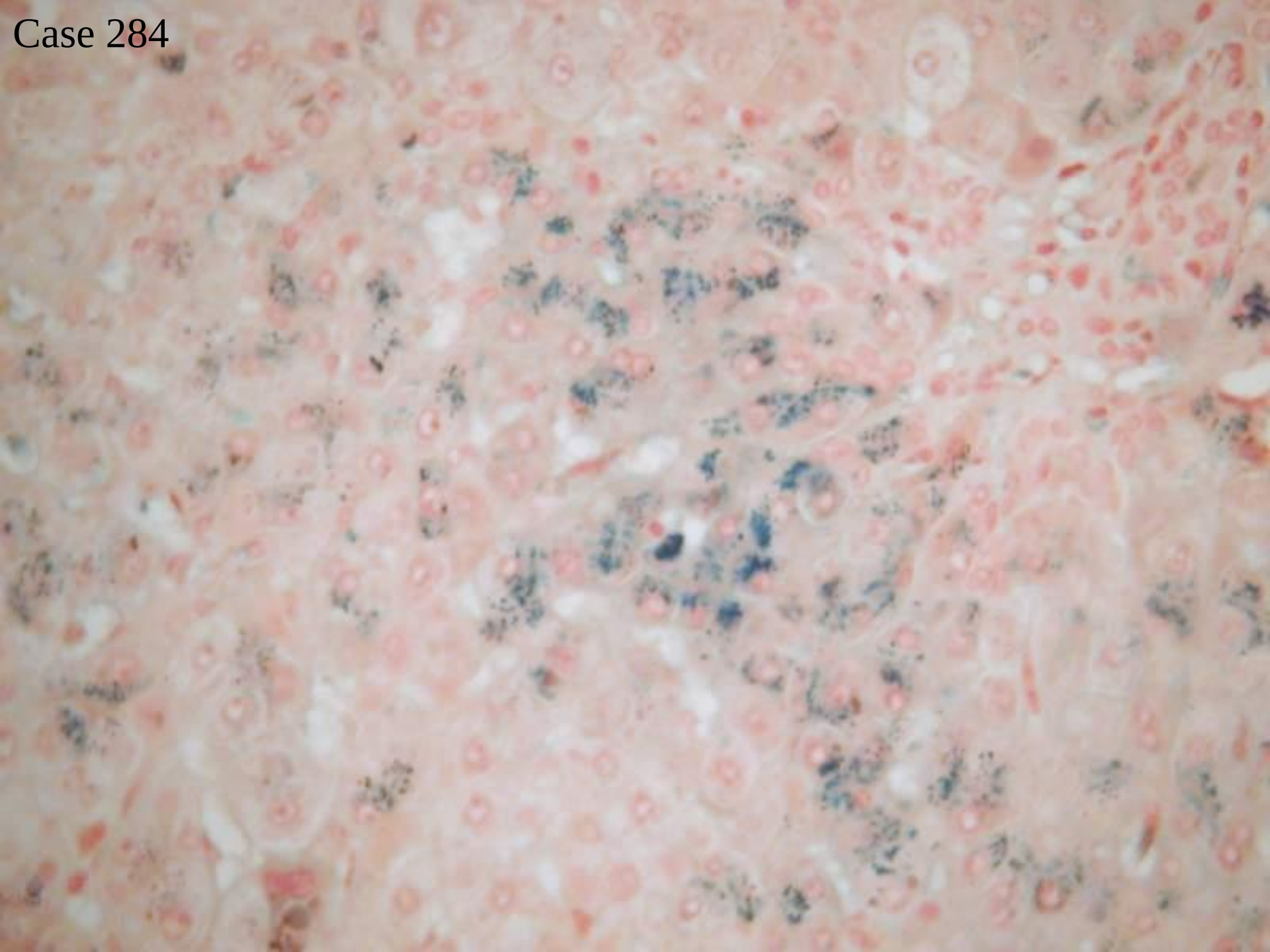


Case 284

Cyst:

47 ciliated foregut cyst

10 biliary cyst

3 simple cyst

1 von Meyenberg complex

5 cystadenoma (biliary, mucinous)

Siderosis:

14 possible haemochromatosis

13 siderosis NOS

10 siderosis, c/w alcohol

6 no mention of siderosis

(4 photos missing)

Background liver:

65 cirrhosis, of which:

19 cirrhosis NOS

16 cirrhosis c/w ALD +/- possible A1ATD

10 cirrhosis c/w ALD + A1ATD

11 cirrhosis c/w A1ATD

5 cirrhosis, haemochromatosis

1 cirrhosis, steatohepatitis

1 biliary cirrhosis

2 cirrhosis, multifactorial

4 cirrhosis, cause not clear

1 ALD, cirrhosis not stated

Case 284

Scoring: score 5 marks for correctly identifying the cyst, and 5 marks for background of cirrhosis, although the aetiology of the cirrhosis could not be determined.

Discussion: The features of the ciliated foregut cyst are so distinctive that it was considered diagnosable even by those who had not encountered this entity before – should be easy to look up in a text book. It is not related to a Biliary cyst.

Mention of the cirrhosis was important in the diagnosis, although the cause could not be ascertained. It is not clear why A1ATD was stated in the history – the patient's serum A1AT was normal, and the PASD did not show convincing globules.

There was a discussion of reporting siderosis in patients with cirrhosis – the possibility of haemochromatosis can be raised in cases with lower grades of iron positivity, since it is known that homozygous patients can have a wide range of severity of iron deposition. While alcohol increases iron absorption, histology cannot reliably distinguish primary/secondary iron excess – very heavy (grade 4) iron overload is likely to indicate haemochromatosis unless there is a haematological cause.

Case 284

Submitting pathologist's diagnosis:

Ciliated hepatic foregut cyst

Cirrosis (ALD)

Ubiquitin confirms Malory's hyaline

No PASD positive globules

Mild (grade 1-2) siderosis of hepatocytes

Case 285

66/Male

Shrunken left lobe, ?malignant, cholangiocarcinoma.

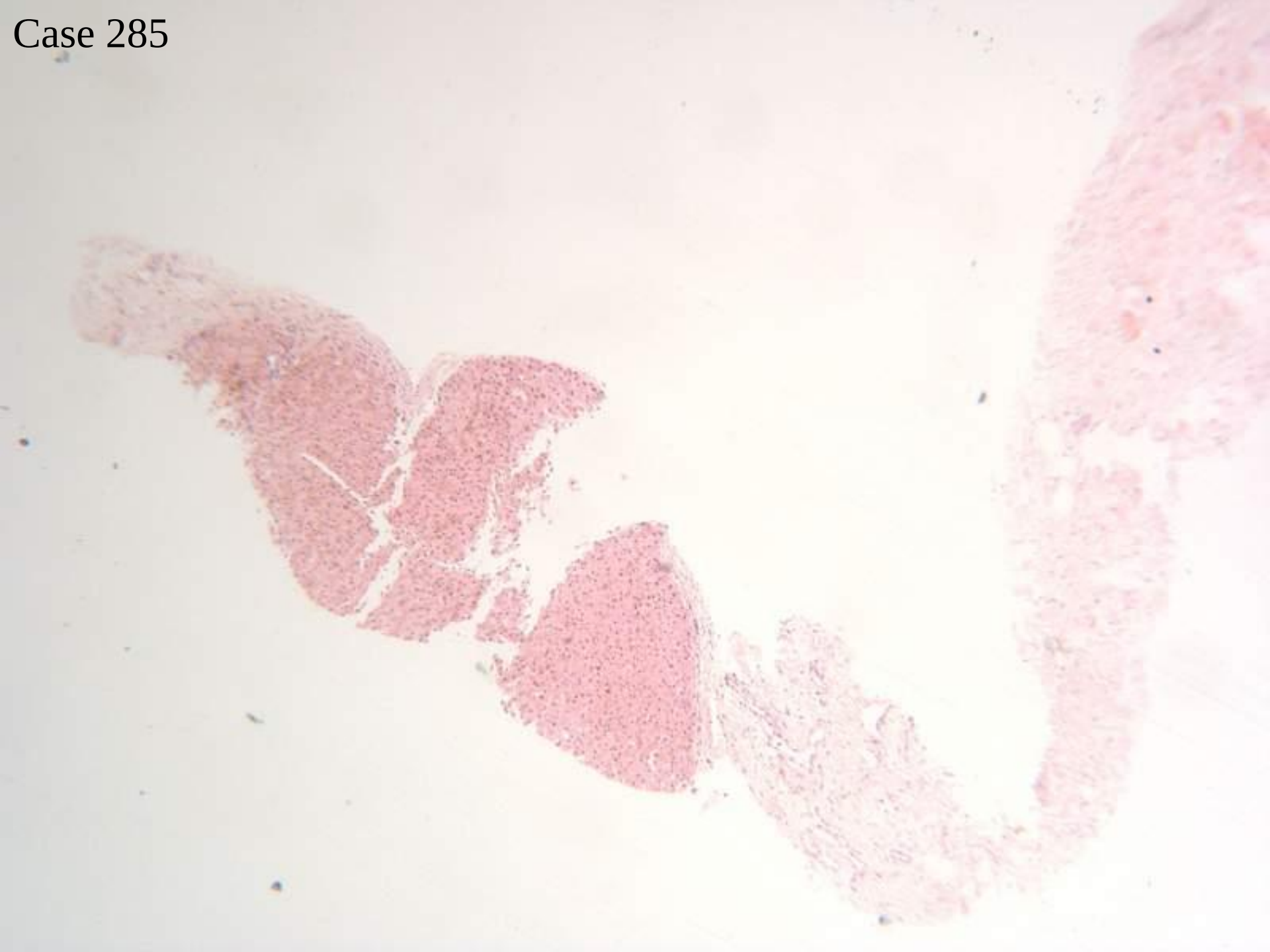
Left nephrectomy for renal cancer 6 years previously.

Weight loss and abnormal LFTs. ALT 140, BR 10, ALP 294.

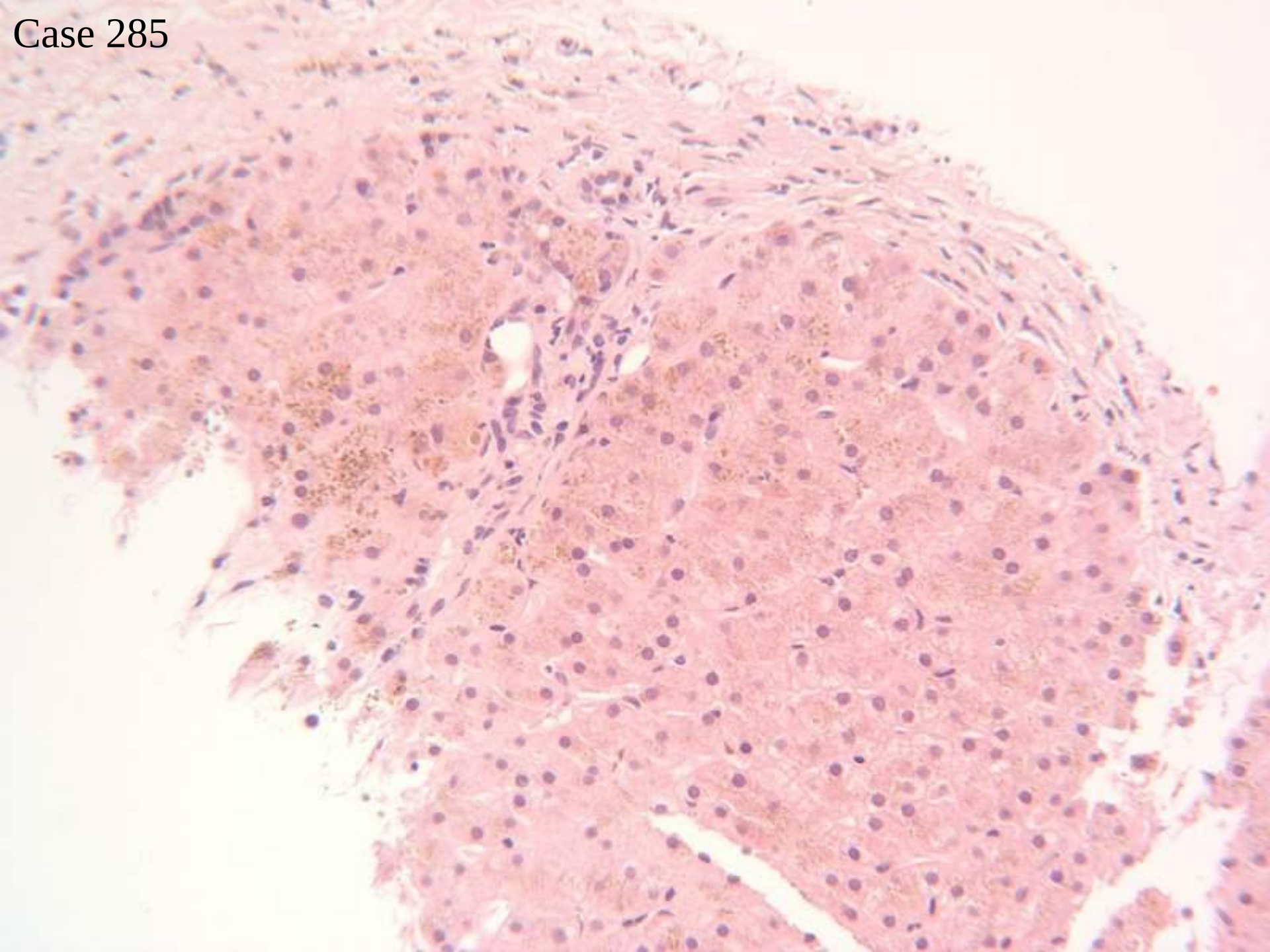
MRCP - NAD, ERCP – failed.

Biopsy -Perls - iron encrusted collagen and heavy iron deposition within biliary epithelium and hepatocytes.

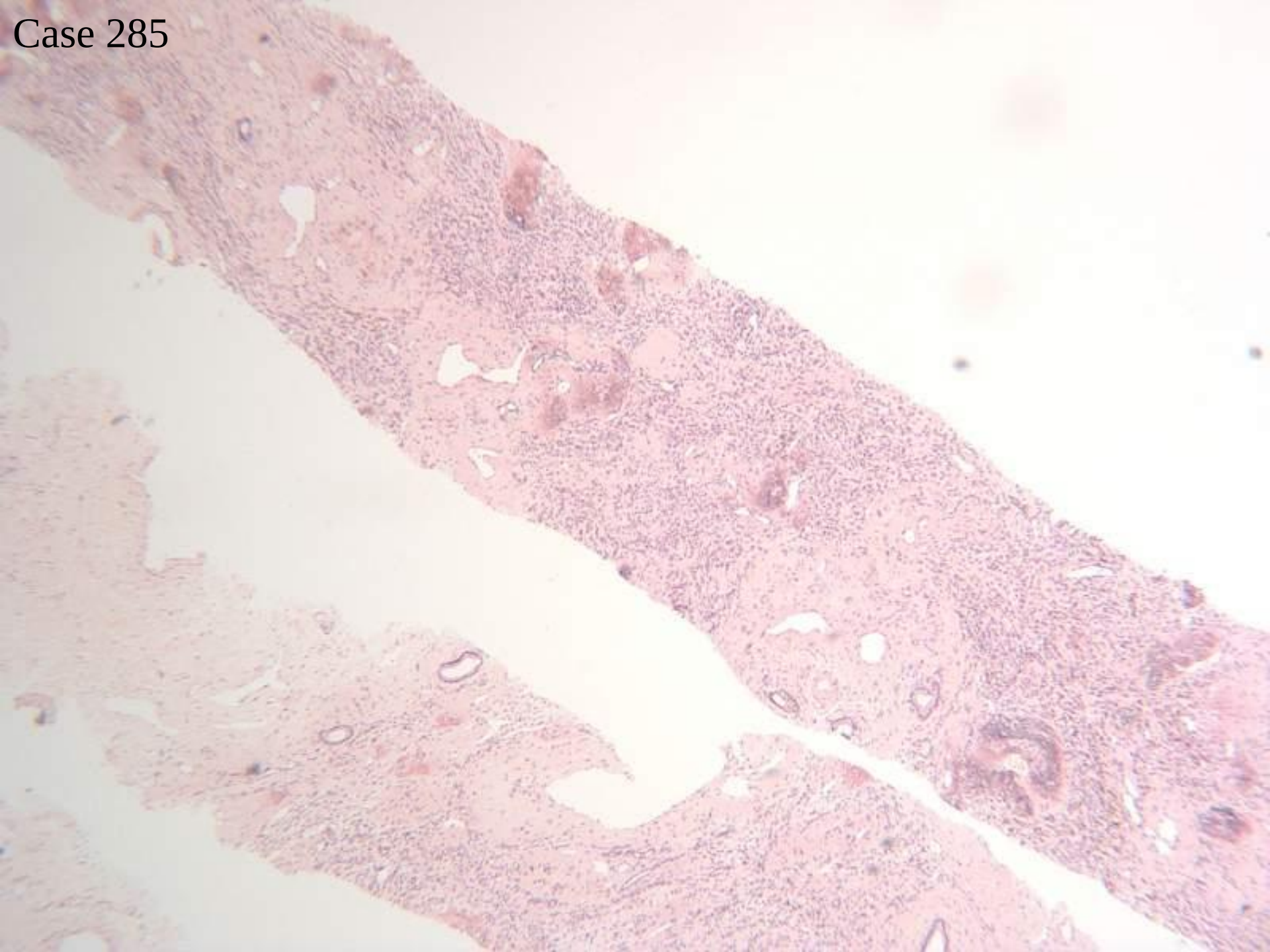
Case 285



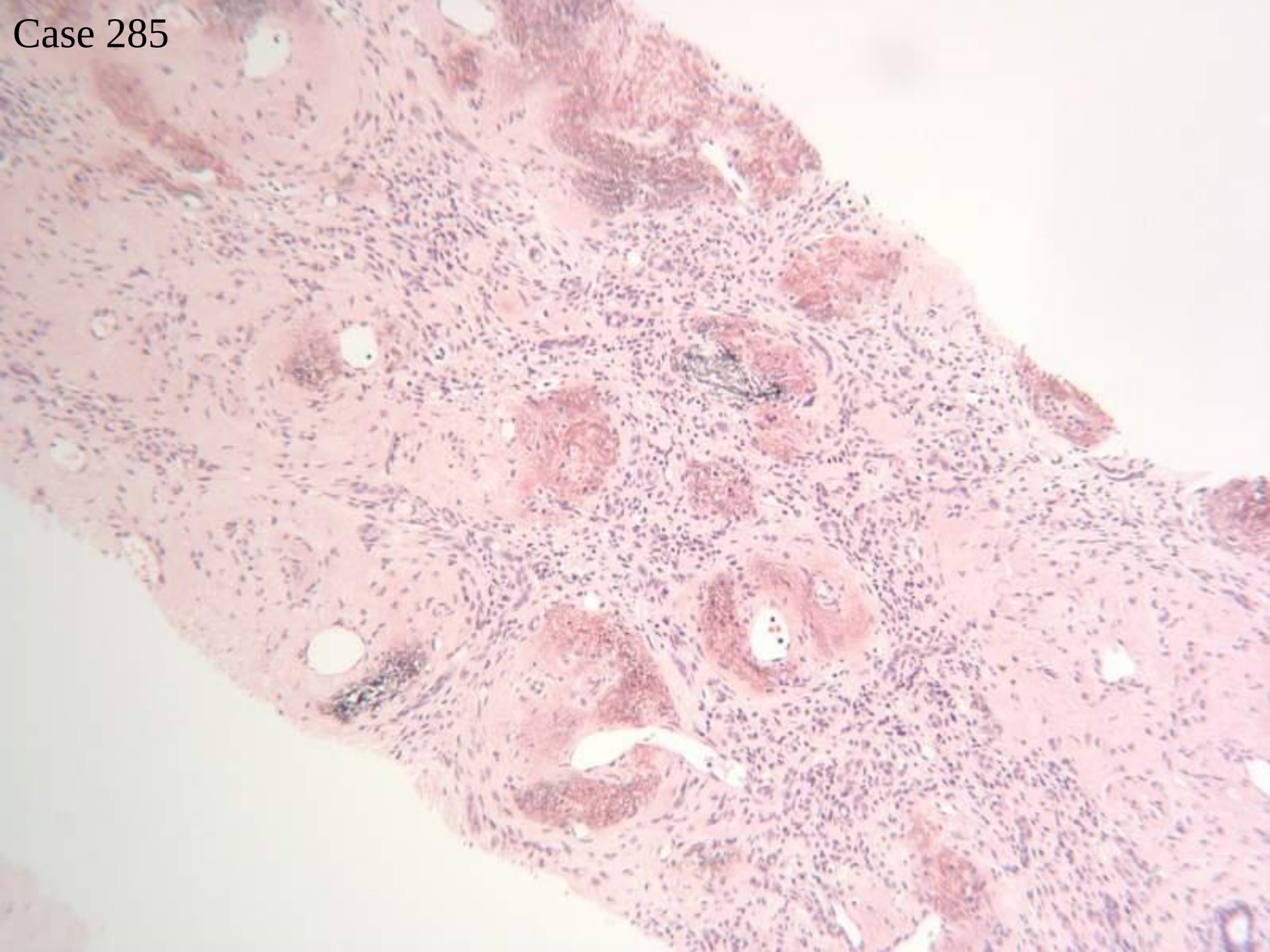
Case 285



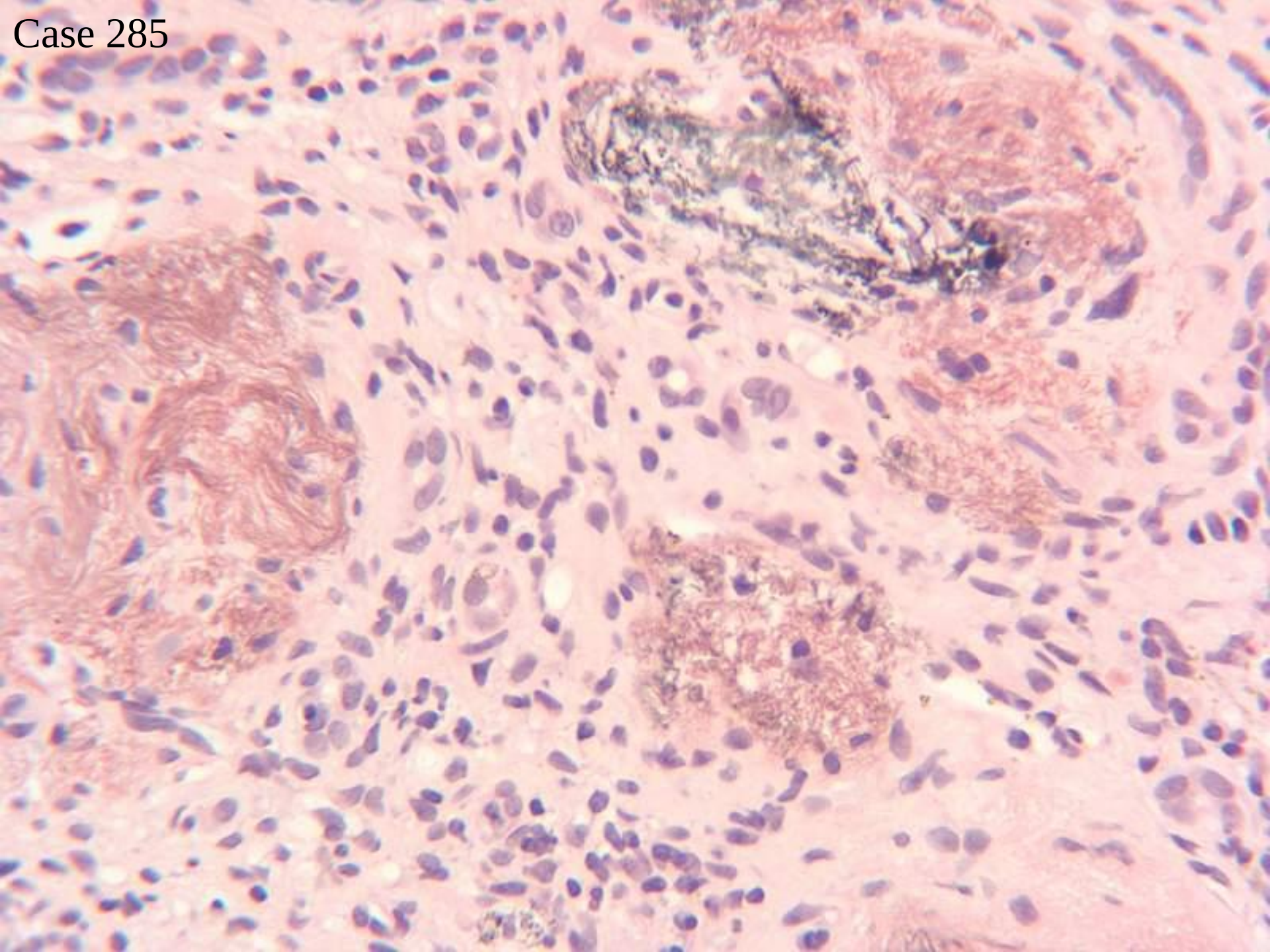
Case 285

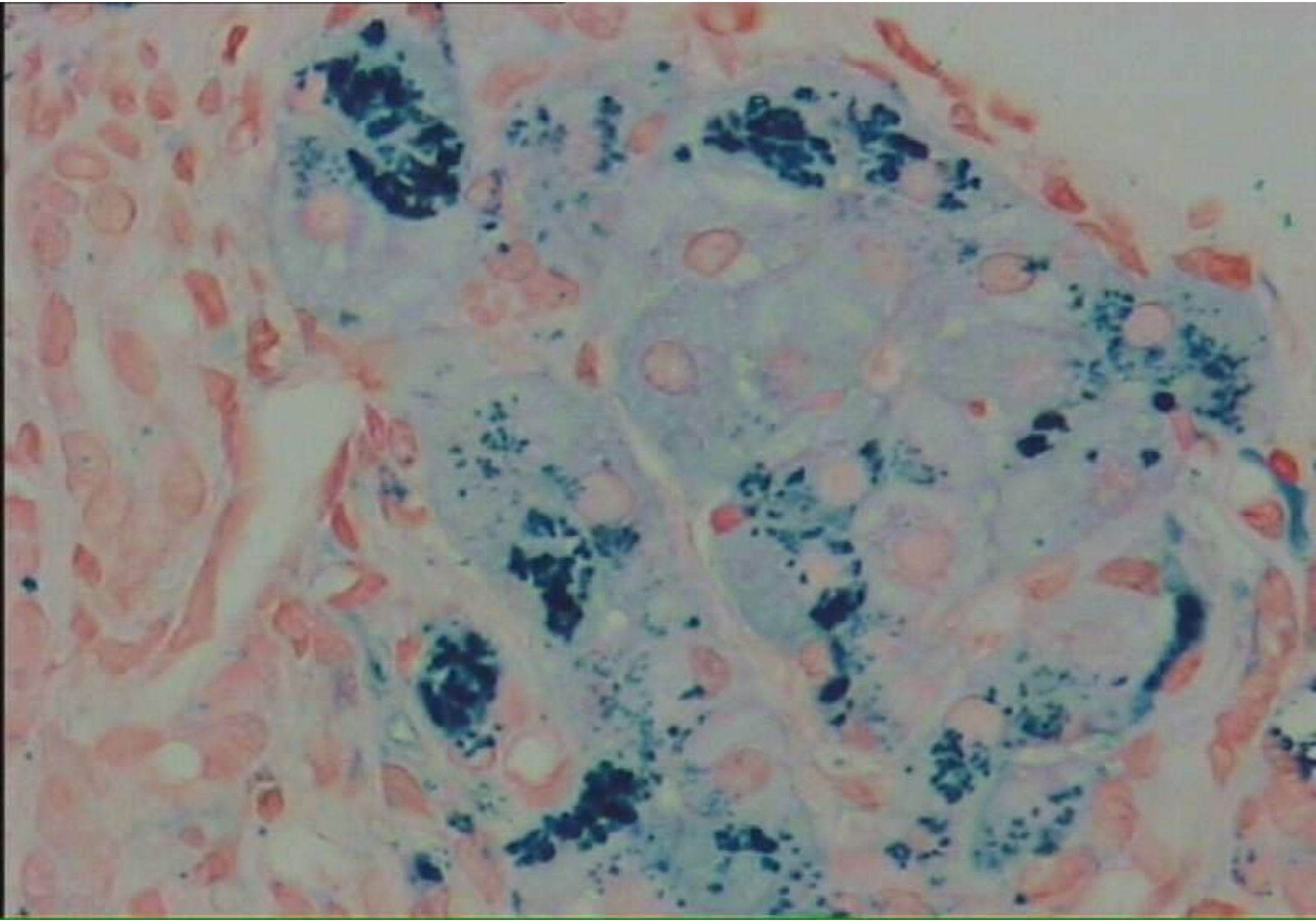


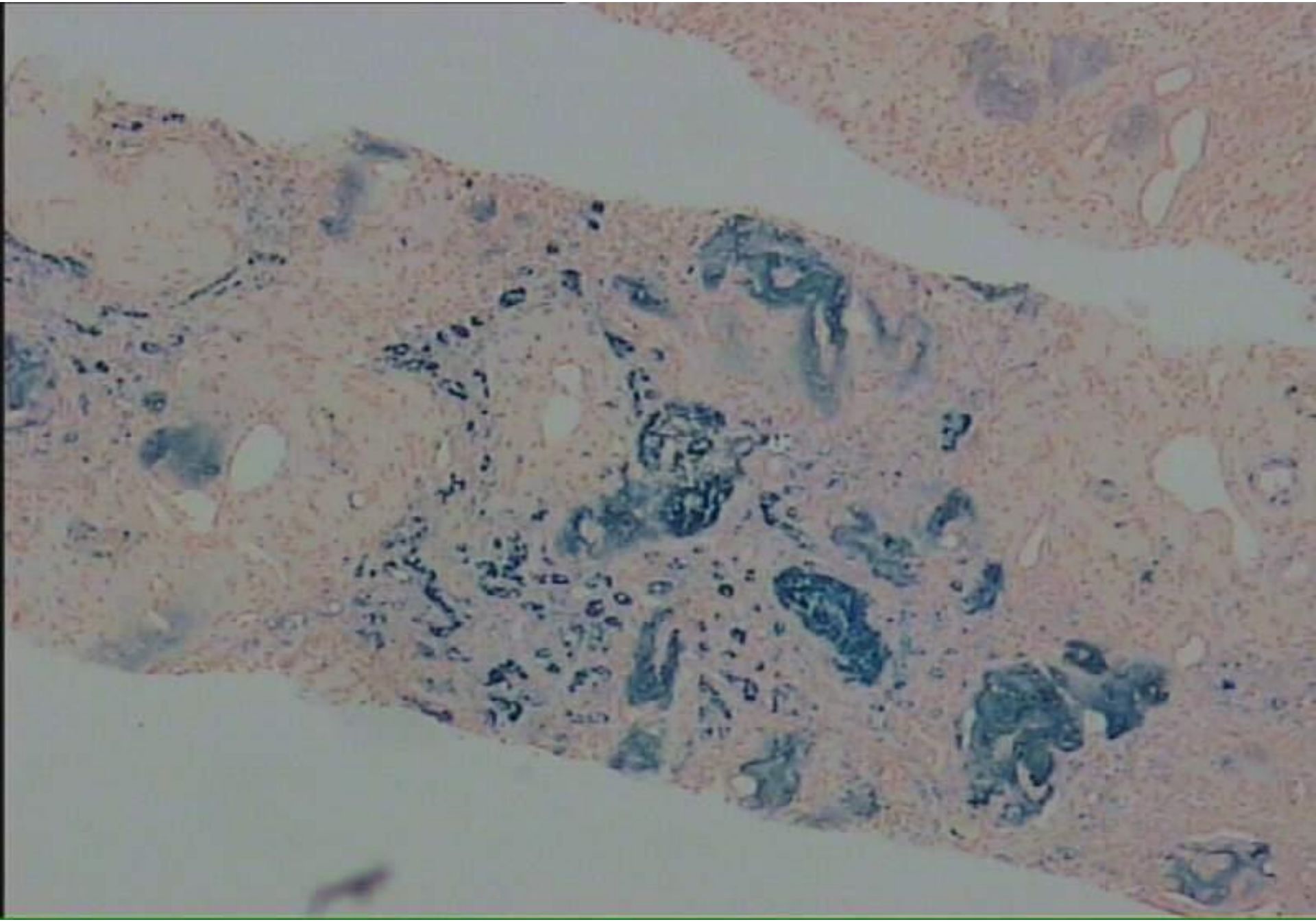
Case 285



Case 285







Case 285

Responses

Morphology

22 cirrhosis

18 atrophic

6 fibrotic

6 parenchymal extinction

4 massive necrosis/lobar collapse

6 scarring after vascular event/infarct

6 haemangioma/vascular anomaly

3 hamartoma, mesenchymal hamartoma

1 radiation induced damage (no other comments)

1 polycystic liver disease with haemosiderin deposition

1 ?hepatic vein obstructed by HCC in IVC

1 burnt out granulomas

Comment on iron:

25 definite or probable haemochromatosis

26 secondary iron deposition/encrustation

8 iron not mentioned anywhere

Other comments:

15 ? previous surgery with vascular injury

9 ? intravascular chemotherapy and/or radiotherapy

3 amyloid stains.

Case 285

Scoring: this case is unsuitable for scoring.

Discussion: Unilateral lobar atrophy can occur as a result of a main (left or right) bile duct or portal vein occlusion in a non-cirrhotic liver. Most often seen in patients with PSC and a dominant stricture that was present early in the course of the disease. The cause of the parenchymal extinction in this case is not clear. In view of the elastosis, ? radiotherapy affecting left lobe. Get further history.

Case 285

Submitting pathologist's diagnosis:

Parenchymal extinction/lobular atrophy with siderosis grade 4.

(homozygous HFE gene mutation C282Y)

Underlying cause of lobular atropy unclear

? vascular catastrophy

? secondary to cirrhosis

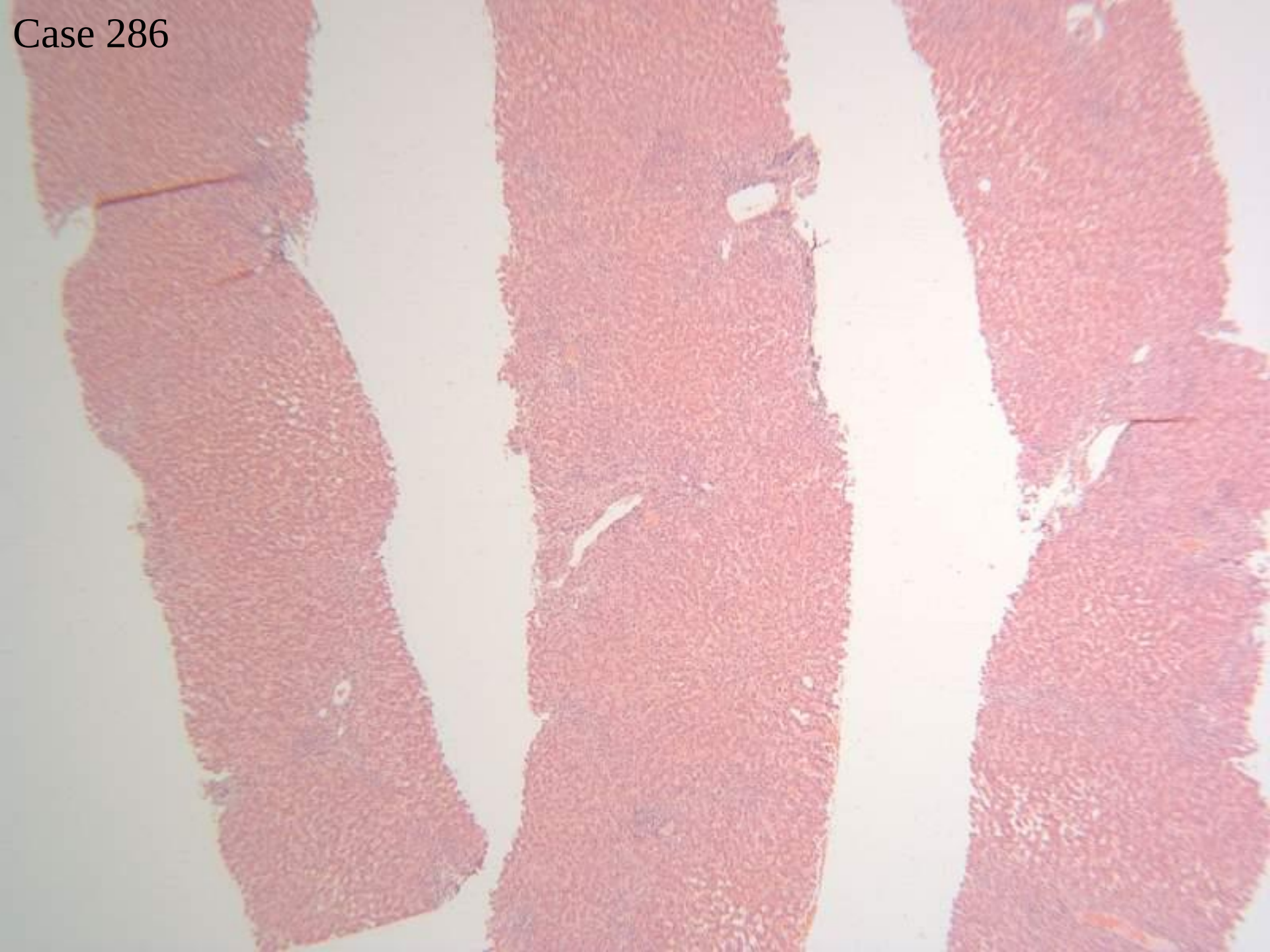
Case 286

25/Male. Two week history of cholestatic jaundice.

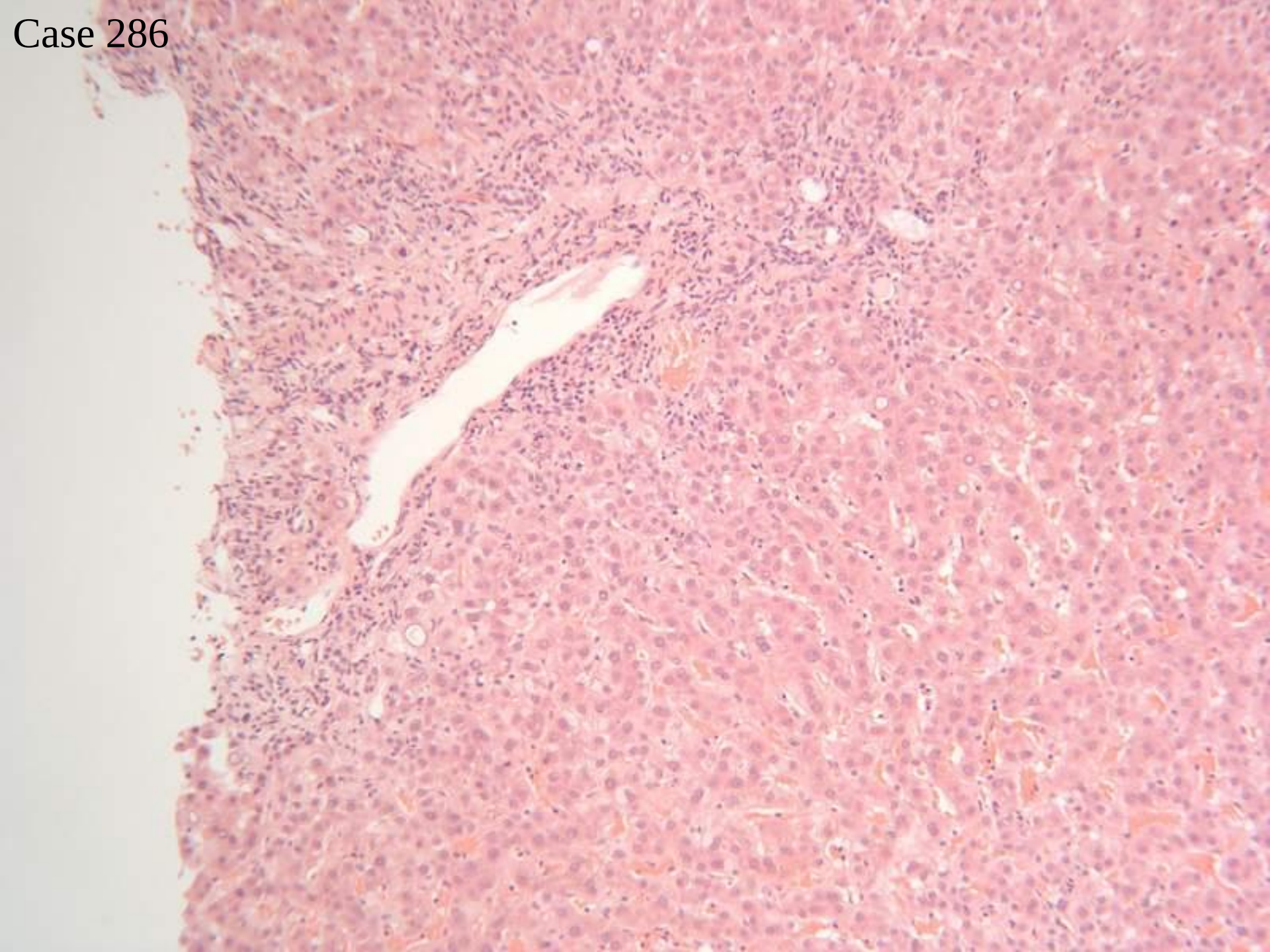
Chronic liver screen negative.

BR550. AP276. ALT 76.

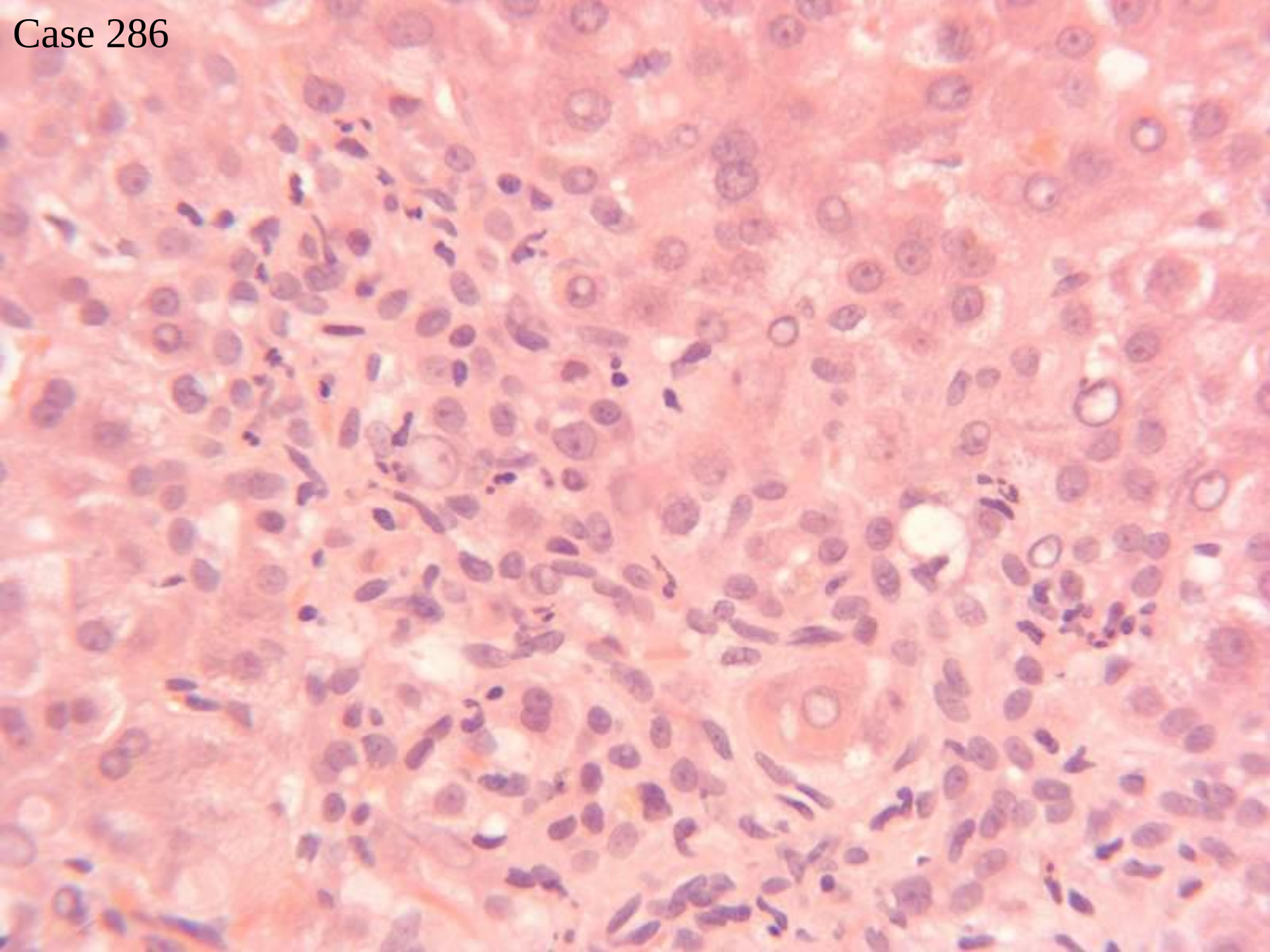
Case 286



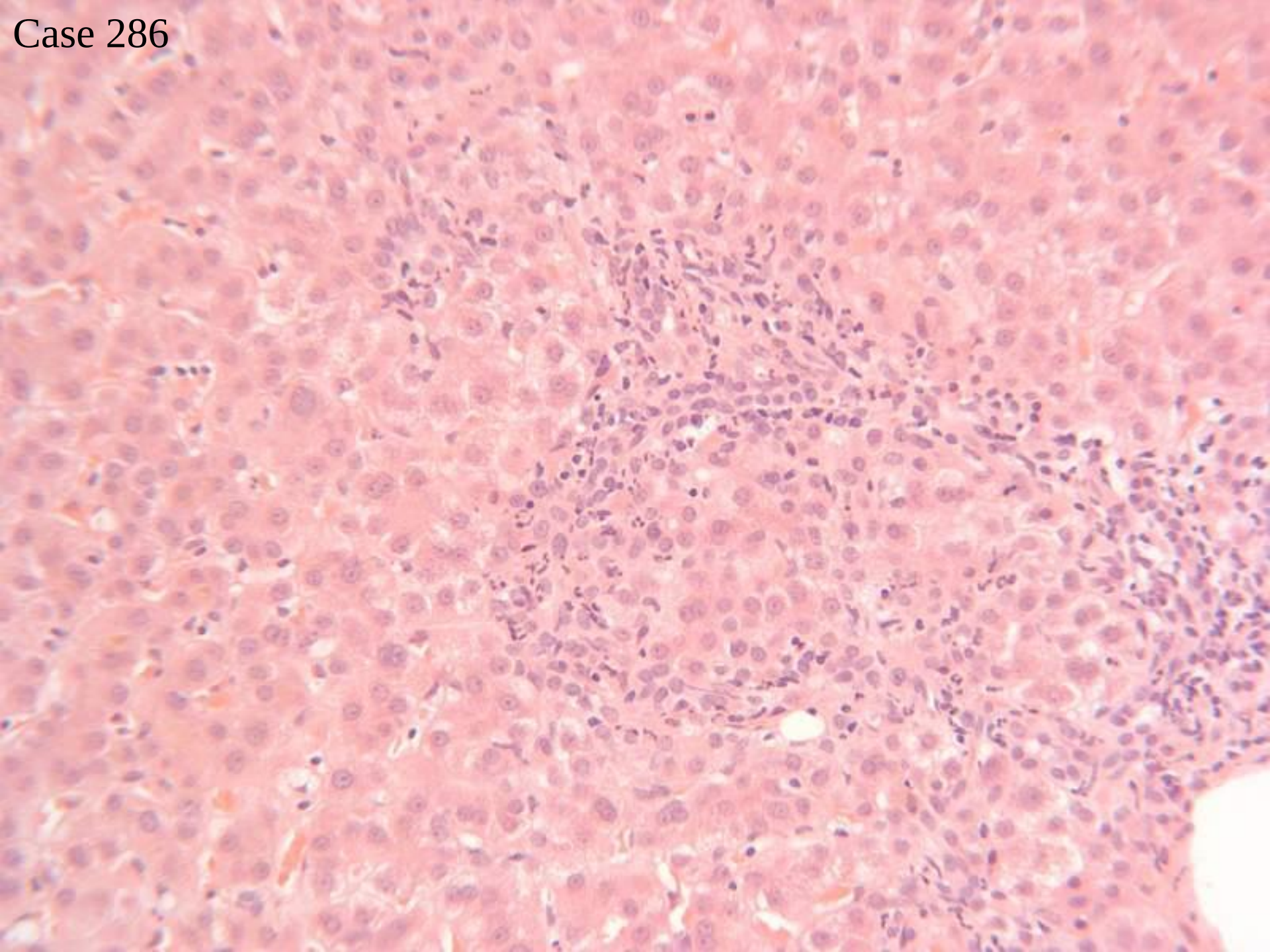
Case 286



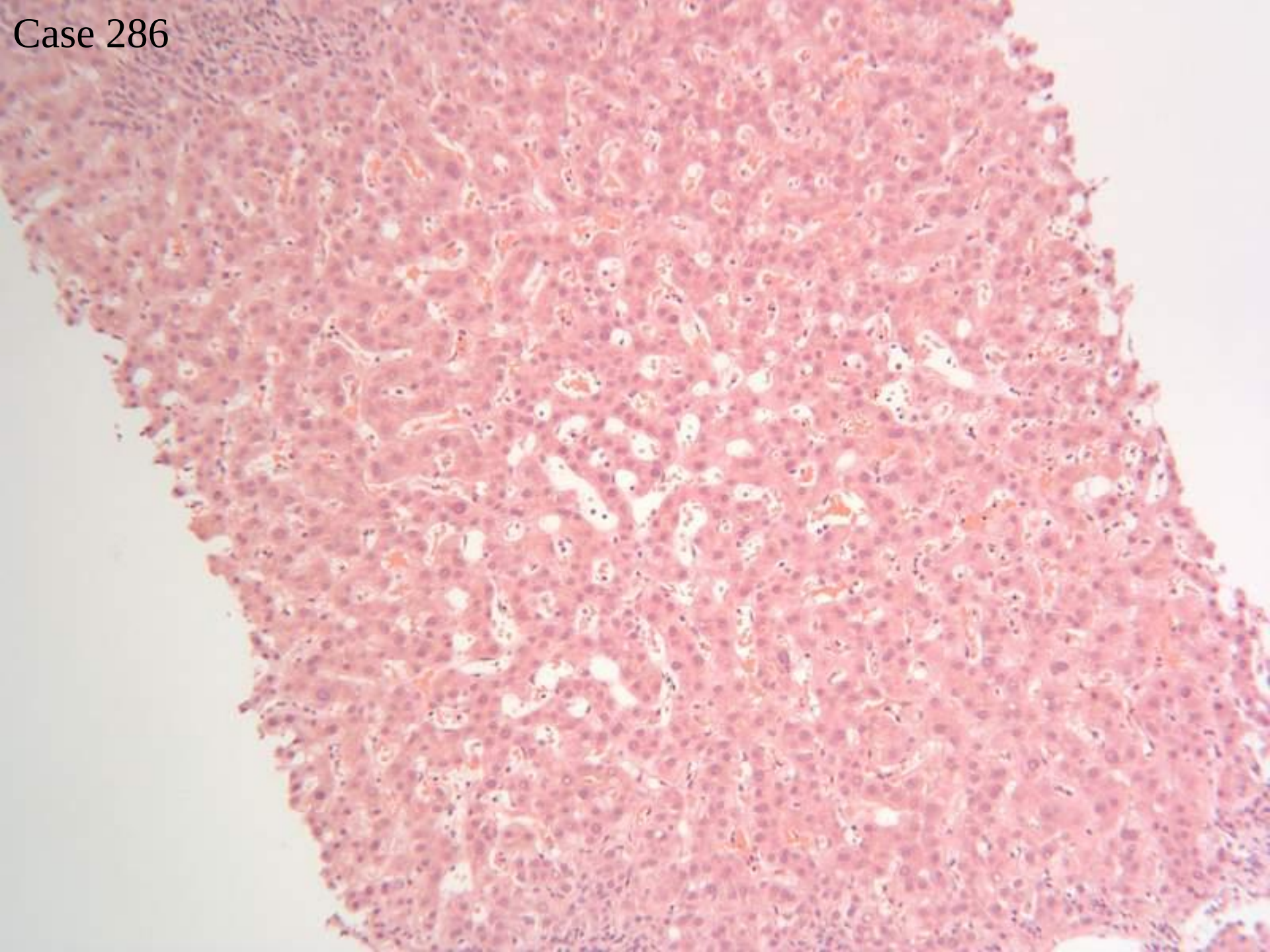
Case 286



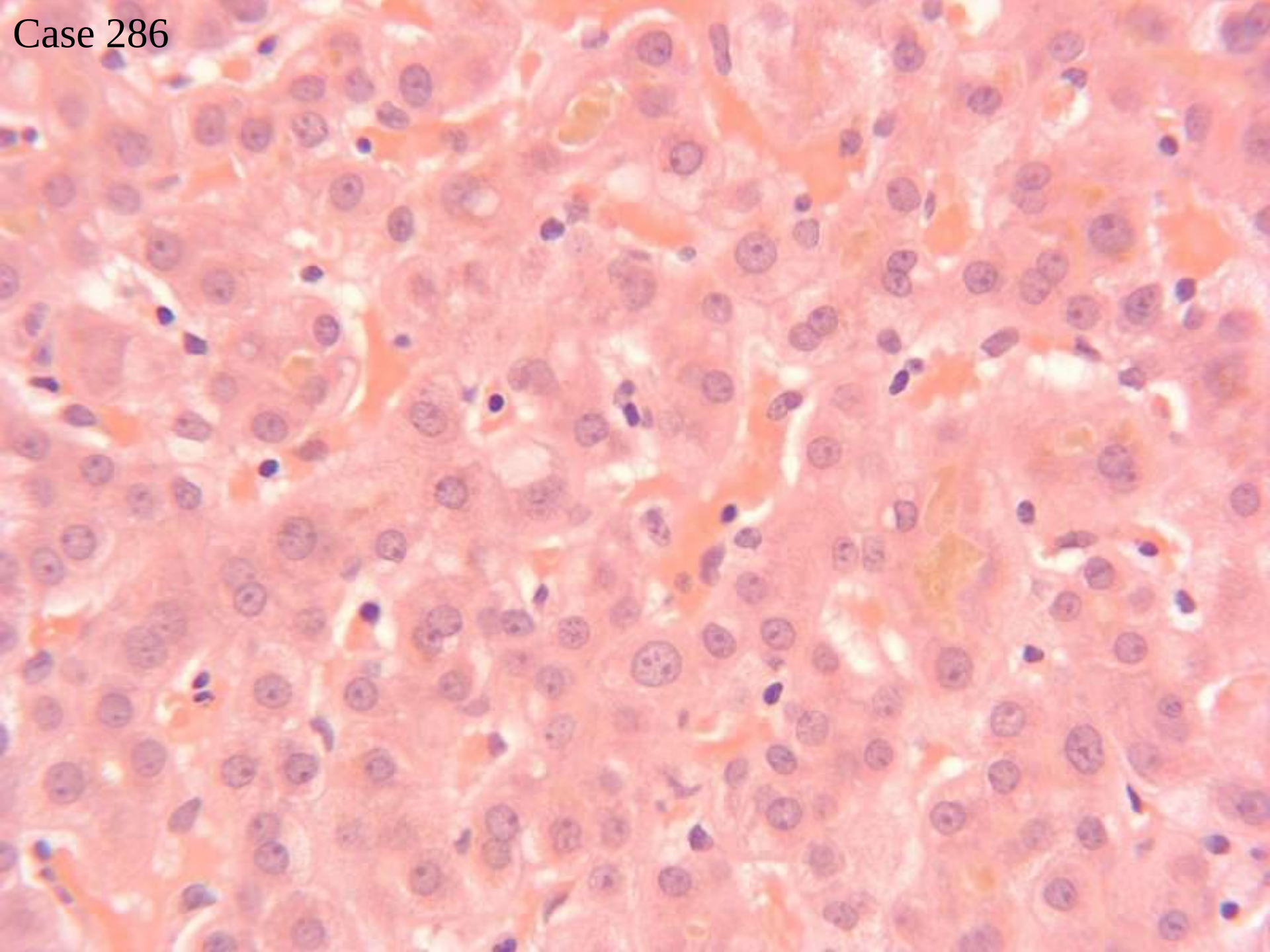
Case 286



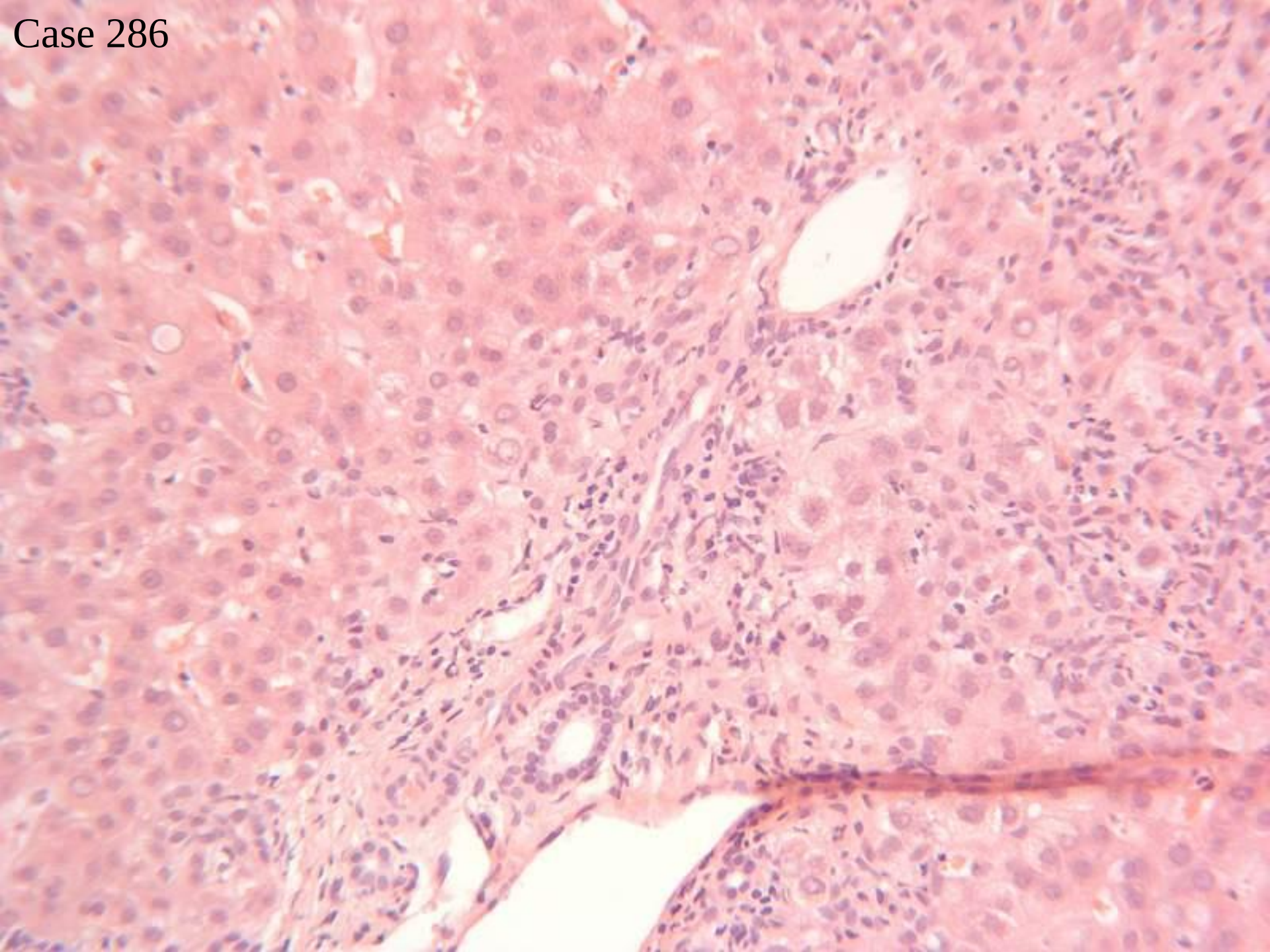
Case 286



Case 286



Case 286



Case 286

Responses:

Morphology:

49 cholestasis

7 cholestasis not mentioned anywhere

10 cholangiolitis

15 cholestatic hepatitis

10 acute hepatitis

13 ductular proliferation/reaction

5 ductopaenia

15 sinusoidal dilatation

(=133)

Aetiology:

55 drug - mentioned somewhere

7 no mention of drugs

32 biliary obstruction – need to exclude

6 acute hepatitis, ? viral

2 ? hepatitis E

3 ? sepsis

2 ? PSC

2 ? AIH

1 chronic hepatitis with biliary features

Other diagnoses:

2 combined venous and biliary outflow obstruction, ? SOL

1 portal and lobular mixed inflammation, ? acute alcoholic hepatitis, ? drug/toxin, ??? acute viral hepatitis

1 features of cholangiopathy with granuloma, ? sickle cells

1 hepatitis +/- cholangitis (non-ABCD)

Case 286

Scoring: Required both mention of cholestasis/Biliary pathology and of drugs for full marks – 5 marks awarded for each component.

Discussion:

Aetiology: Consideration of drugs is important in any patient presenting with cholestasis, and the report should steer the clinician to a full drug history.

Morphology: The biopsy showed bilirubinostasis and a marked ductular reaction with cholangiolitis although not portal oedema. The differential of large duct obstruction is relevant, although in early stages oedema is usually more obvious than ductular reaction. The cholangiolitis is not unusual in drug related cholestasis. There was little evidence of hepatitis changes in this case and a diagnosis of hepatitis without mention of cholestatis was rejected.

Case 286

Submitting pathologist's diagnosis:

Bland cholestasis: slight peliosis.

Patient was on anabolic steroids – also milk thistle and n-acetyl cysteine and tamoxifen

Further information, Sue Davies:

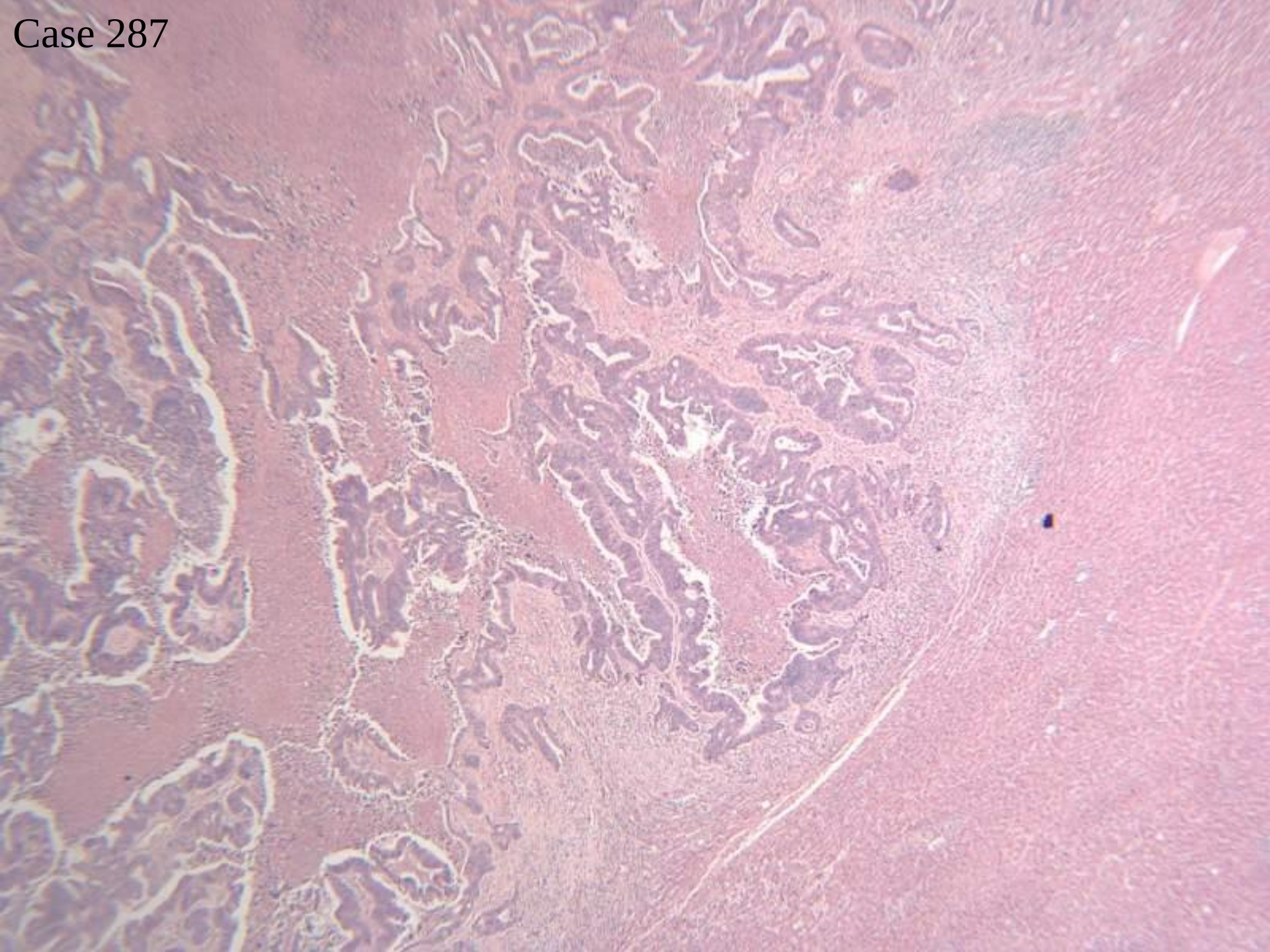
Patient is a member of the British Association of Doormen (BAD) and was using a drug combination called 'Juggernaut' obtained over the internet.

Case 287

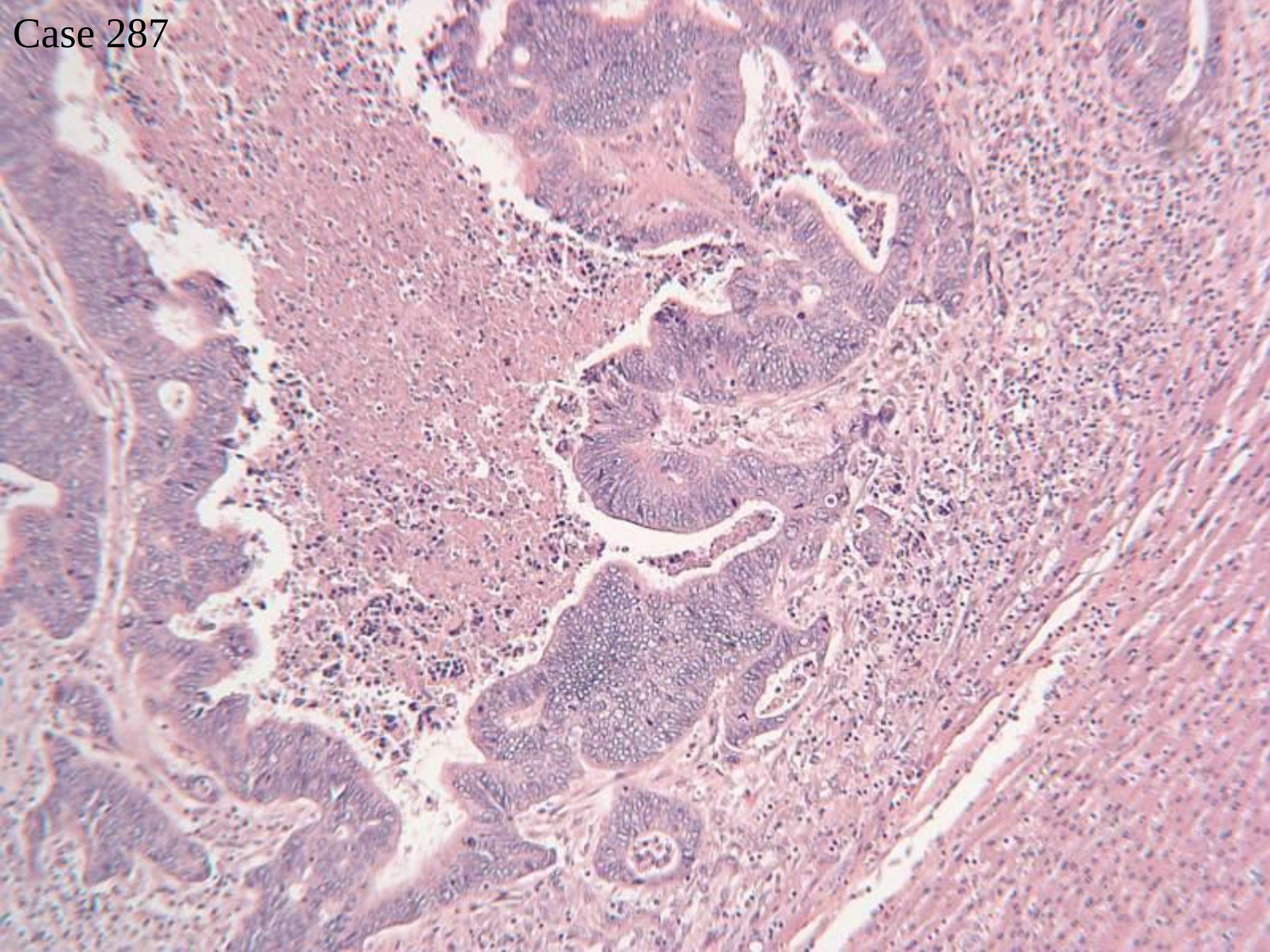
65/Male. Previous Duke's A colorectal cancer 2004. AP resection. Liver mets at the time treated by embolisation.

Now recurrent liver lesions.

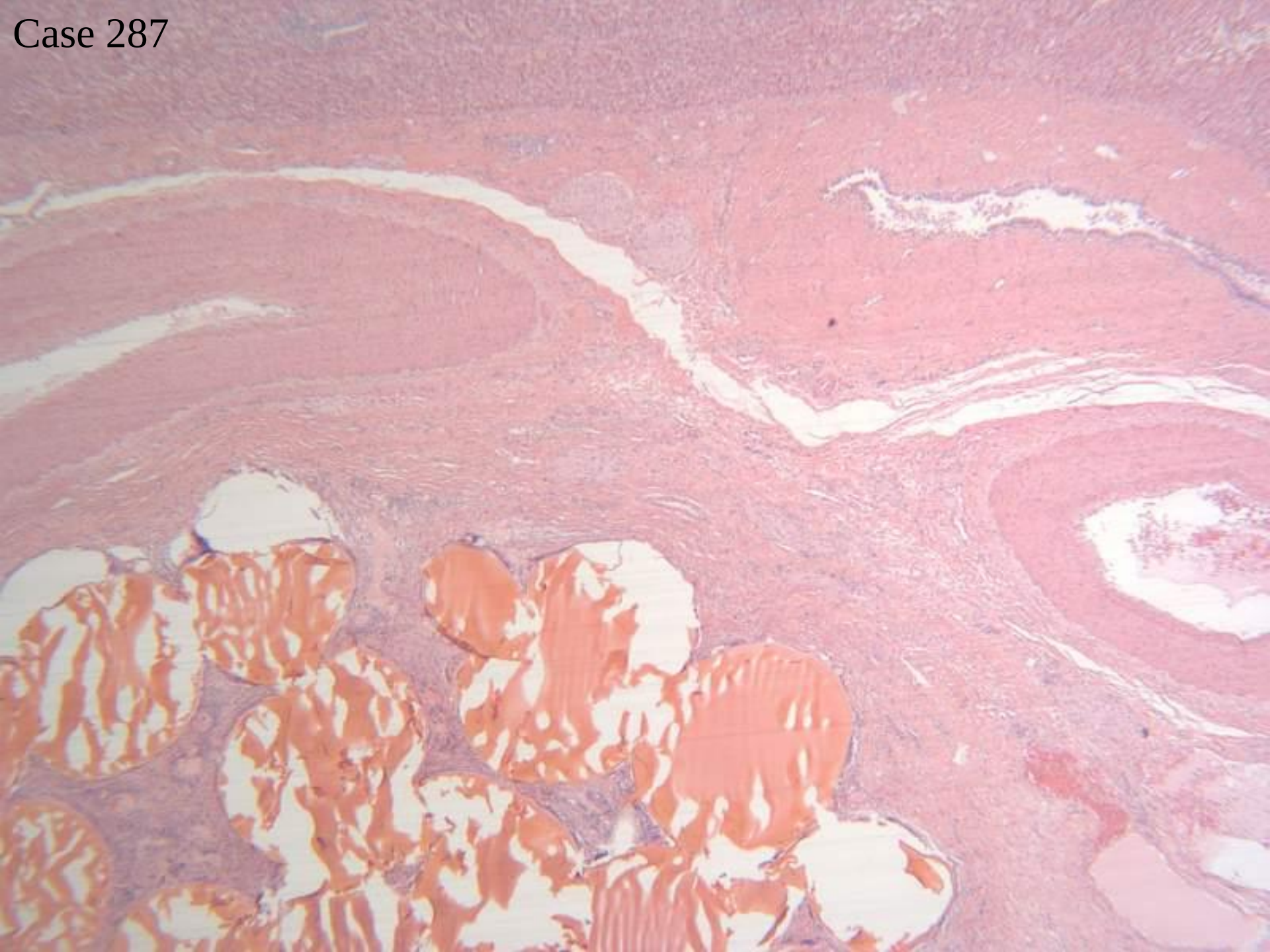
Case 287



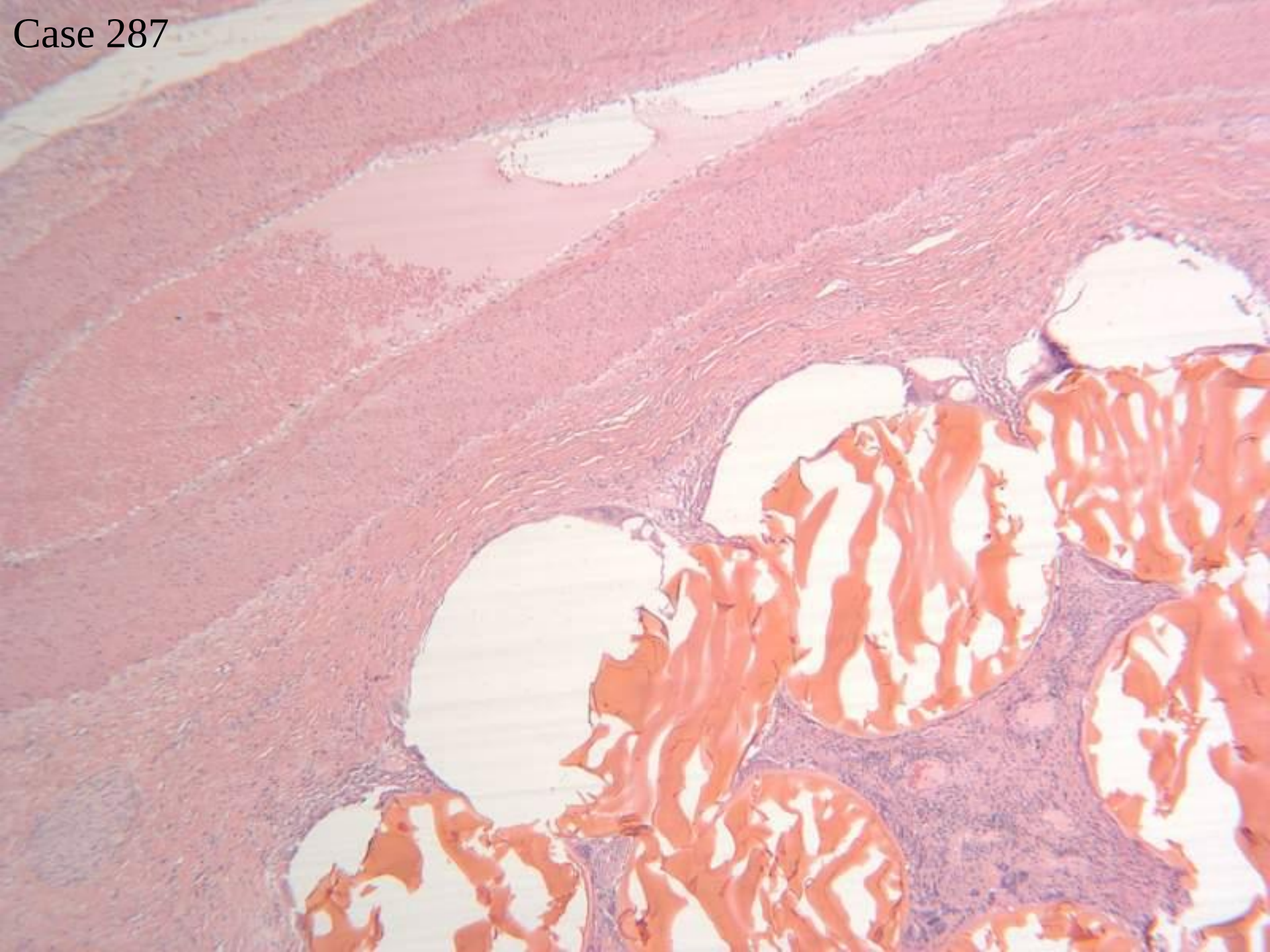
Case 287



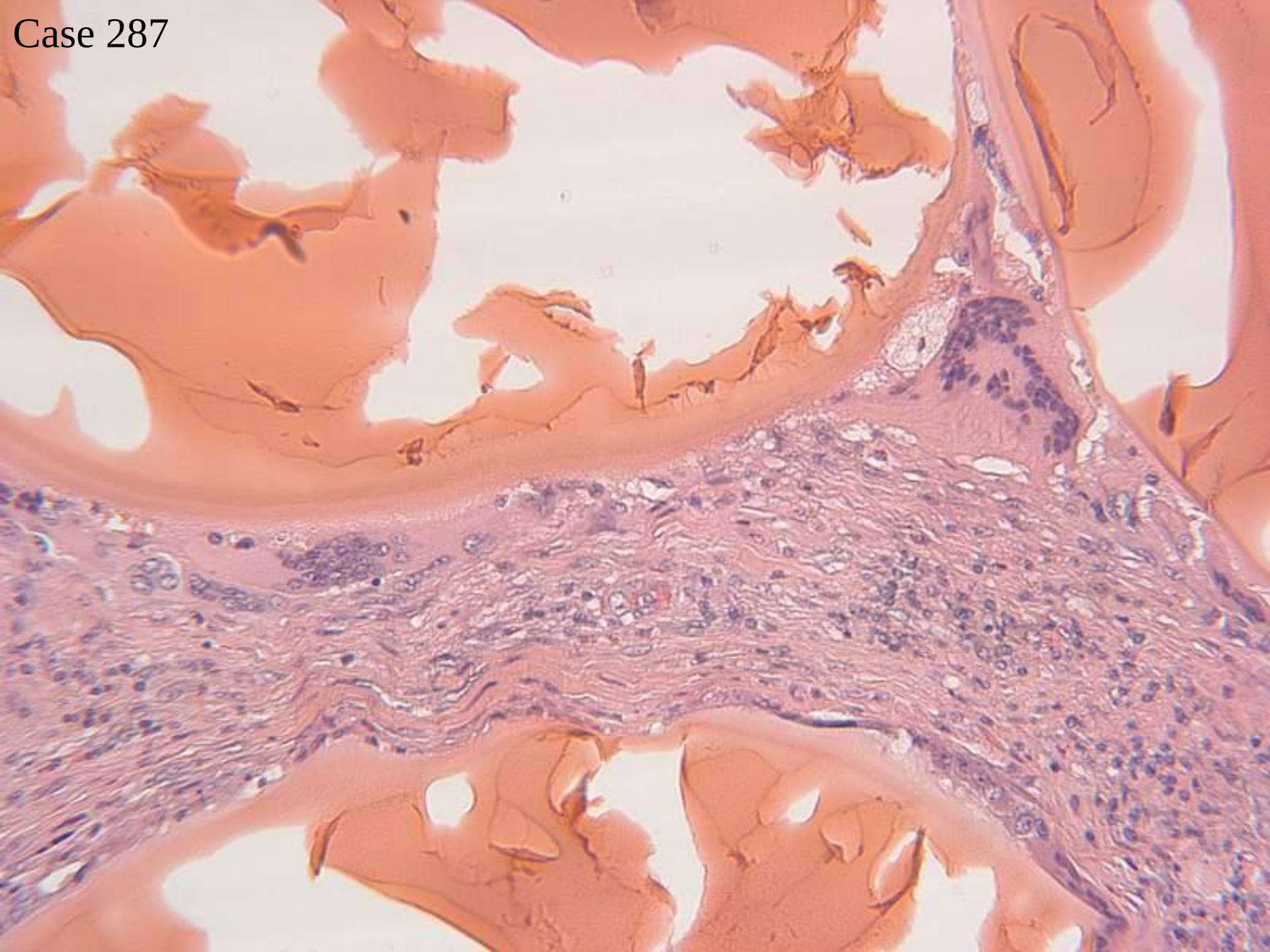
Case 287



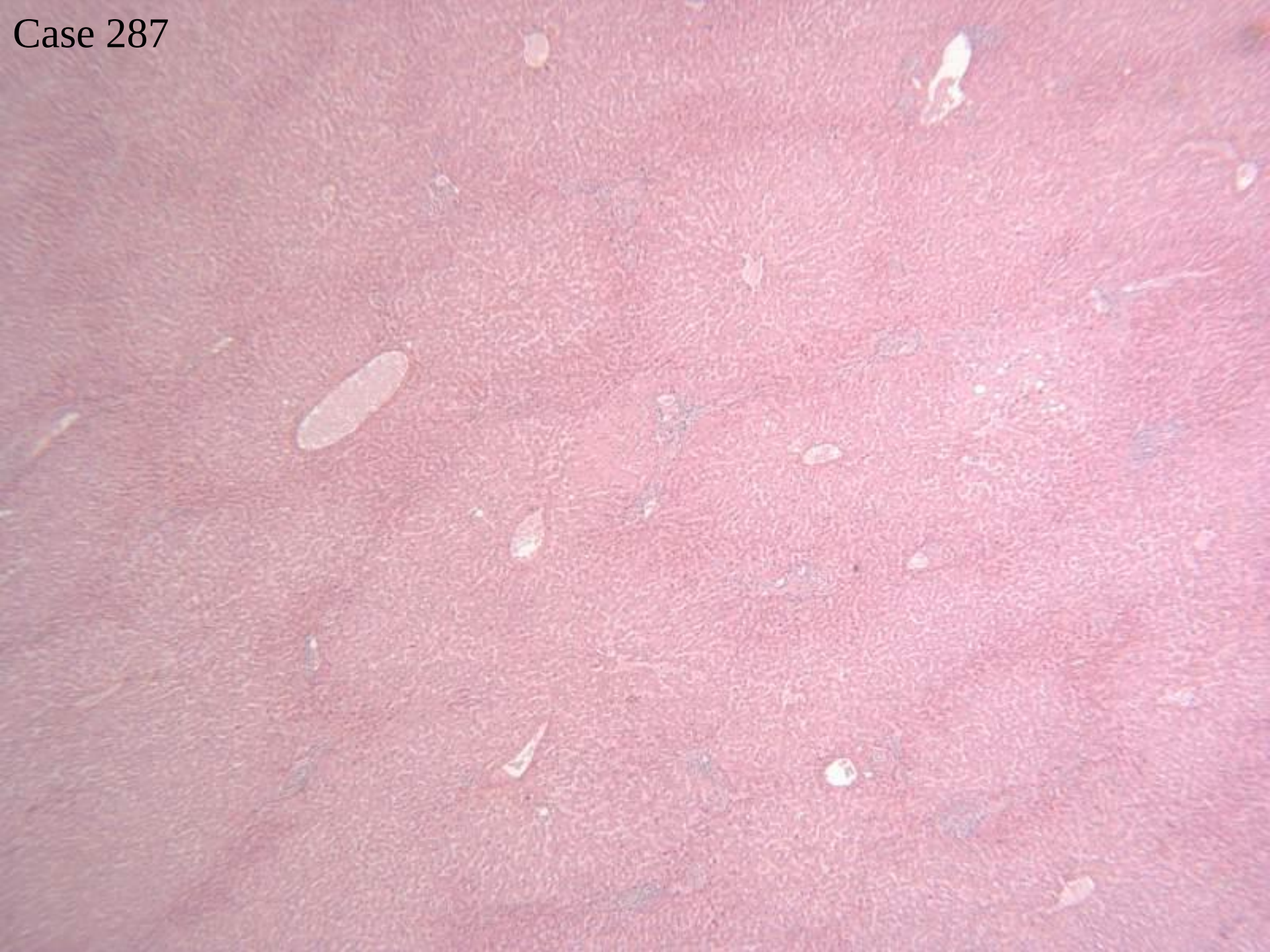
Case 287



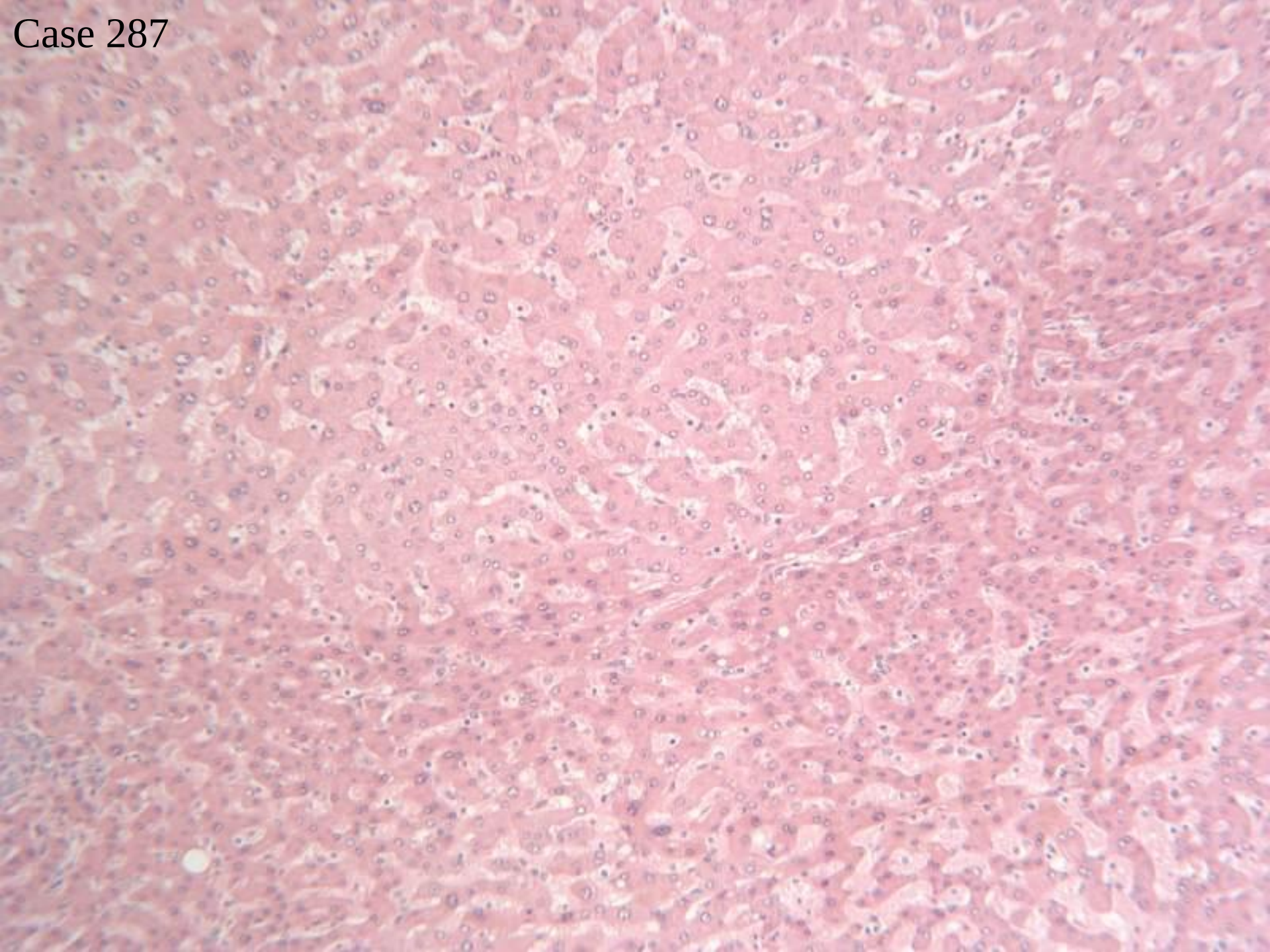
Case 287



Case 287



Case 287



Case 287

Responses:

60 metastatic adenocarcinoma, consistent with colorectal primary

6 metastatic adenocarcinoma, no comment about origin

59 foreign body reaction, consistent with embolic material

1 funny lesion = mucin with foreigh nody reaction, due to treatment of previous metastatic carcinoma nodule

6 embolic material reaction not mentioned

Other comments;

10 NRH or background changes due to chemotherapy

7 would do immunohistochemistry.

Case 287

Scoring: For full marks, require mention of colorectal carcinoma metastasis and of embolic material – 5 marks awarded for each.

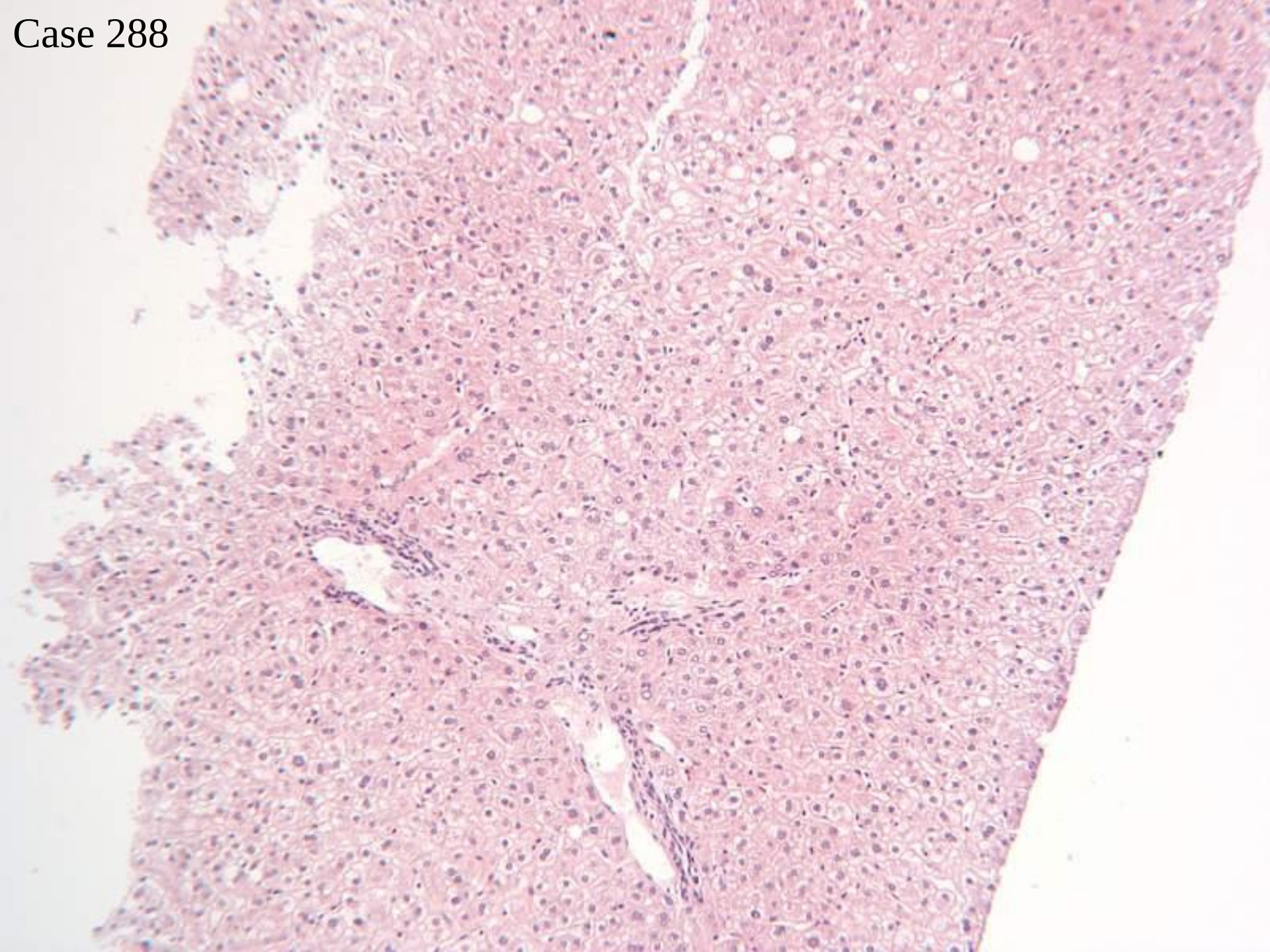
Discussion: The characteristics of metastatic CRC are well seen in this case (circumscribed margin, dirty necrosis surrounded by garland of adenocarcinoma) and in a patient with previous history of CRC most would not do immunohistochemistry.

Case 288

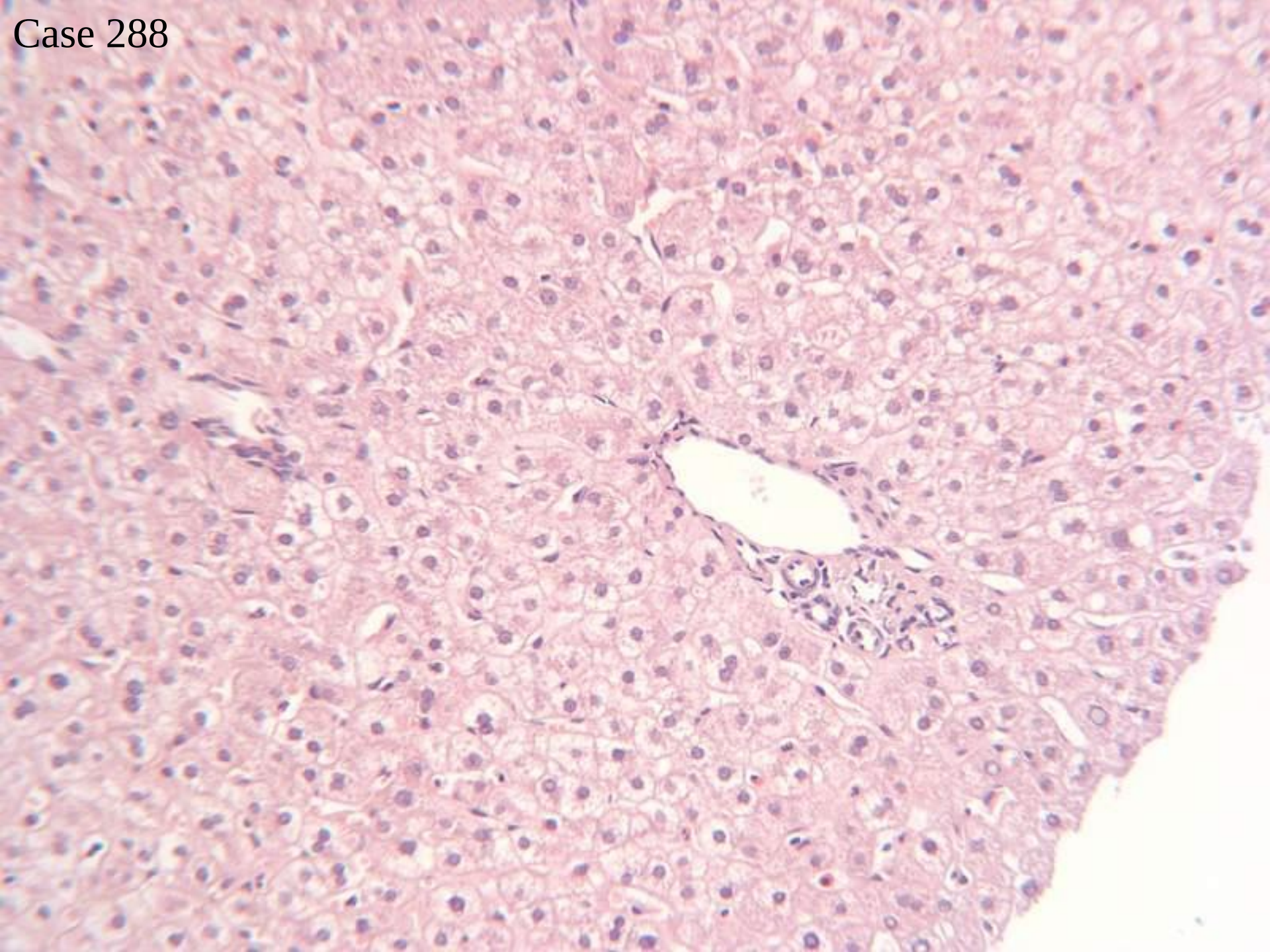
28/female Abnormal LFTs, ?PBC. Autoantibody screen including AMA is negative.

Alk phos 1936 iU/l, ALT 114.

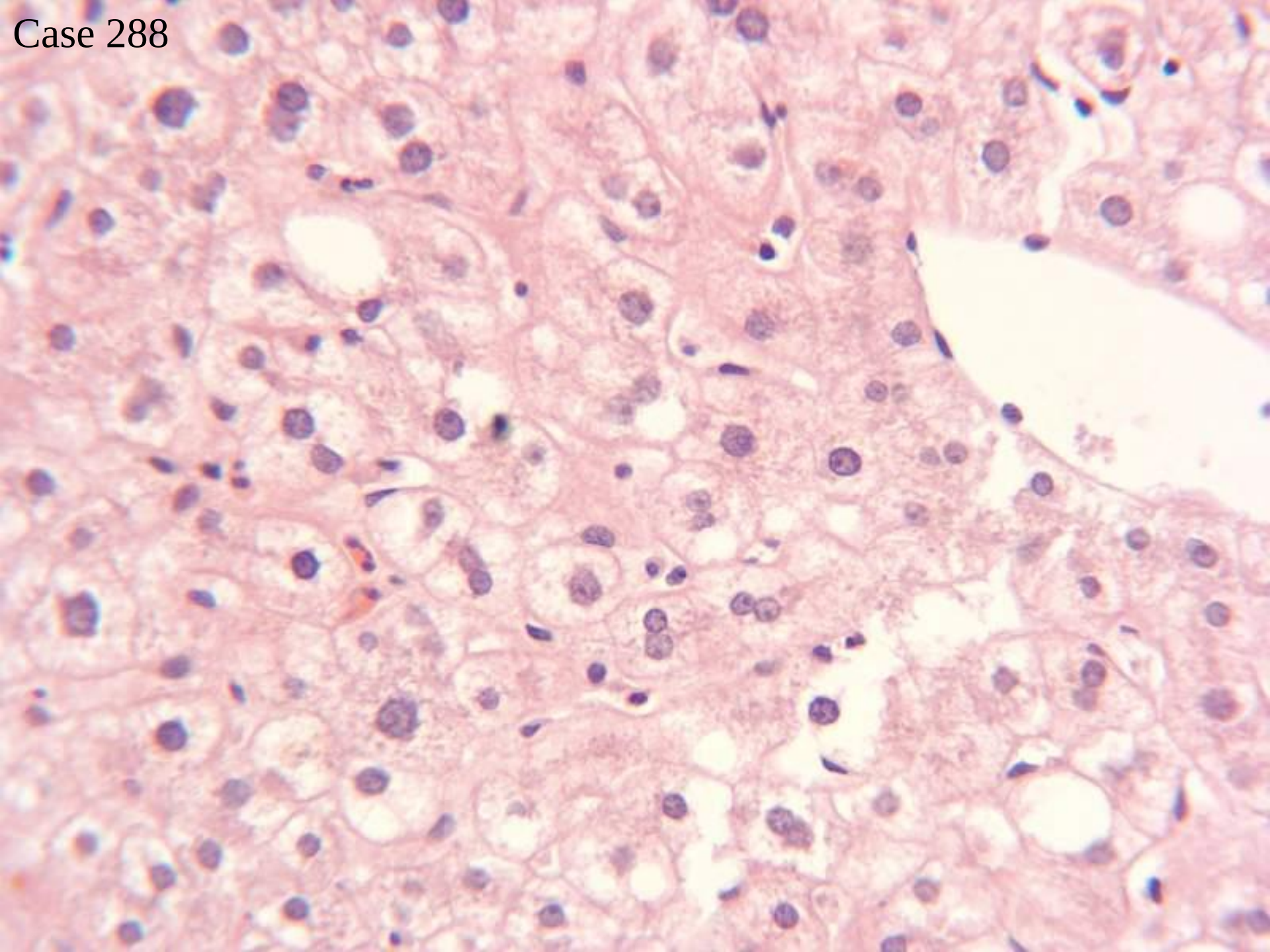
Case 288



Case 288



Case 288



Case 288

Responses: No concensus! Responses include:

15 mild steatosis

9 sinusoidal eosinophilia

10 nuclear vacuolation

3 mild lobular inflammation

3 non-specific inflammation

4 ductopaenia

10 insufficient for diagnosis

15 no features of PBC

14 no significant abnormality

5 biopsy does not explain abnormal LFTs

4 ? isoenzymes of alkaline phosphatise

Case 288

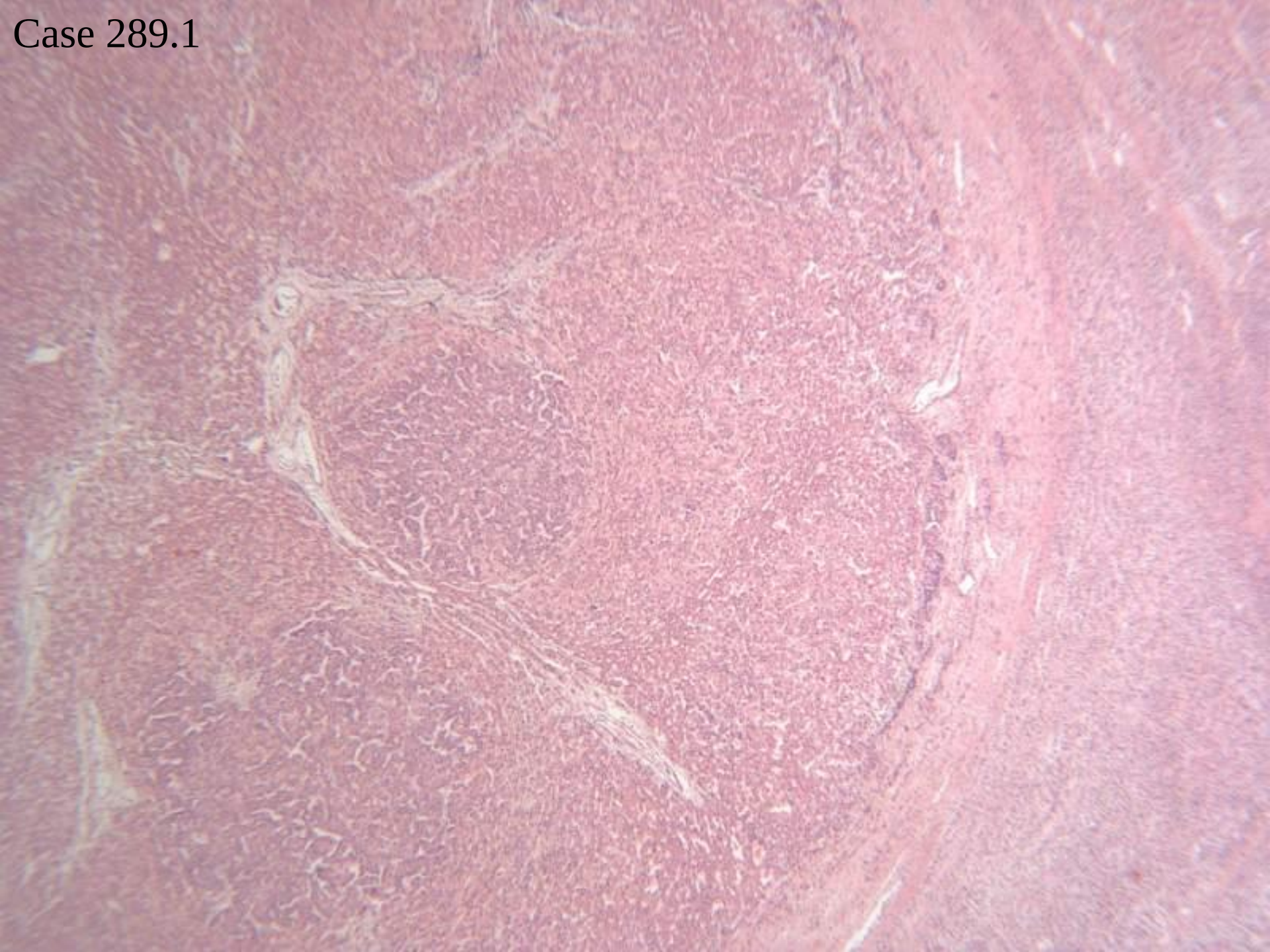
Scoring: unsuitable for scoring

Discussion: This biopsy is within normal limits but small, and may be insufficient to exclude early biliary disease. The high alk phos is not explained by the biopsy – which should prompt discussion with the clinicians to consider other causes for the high alk phos, or whether further biliary investigation is indicated.

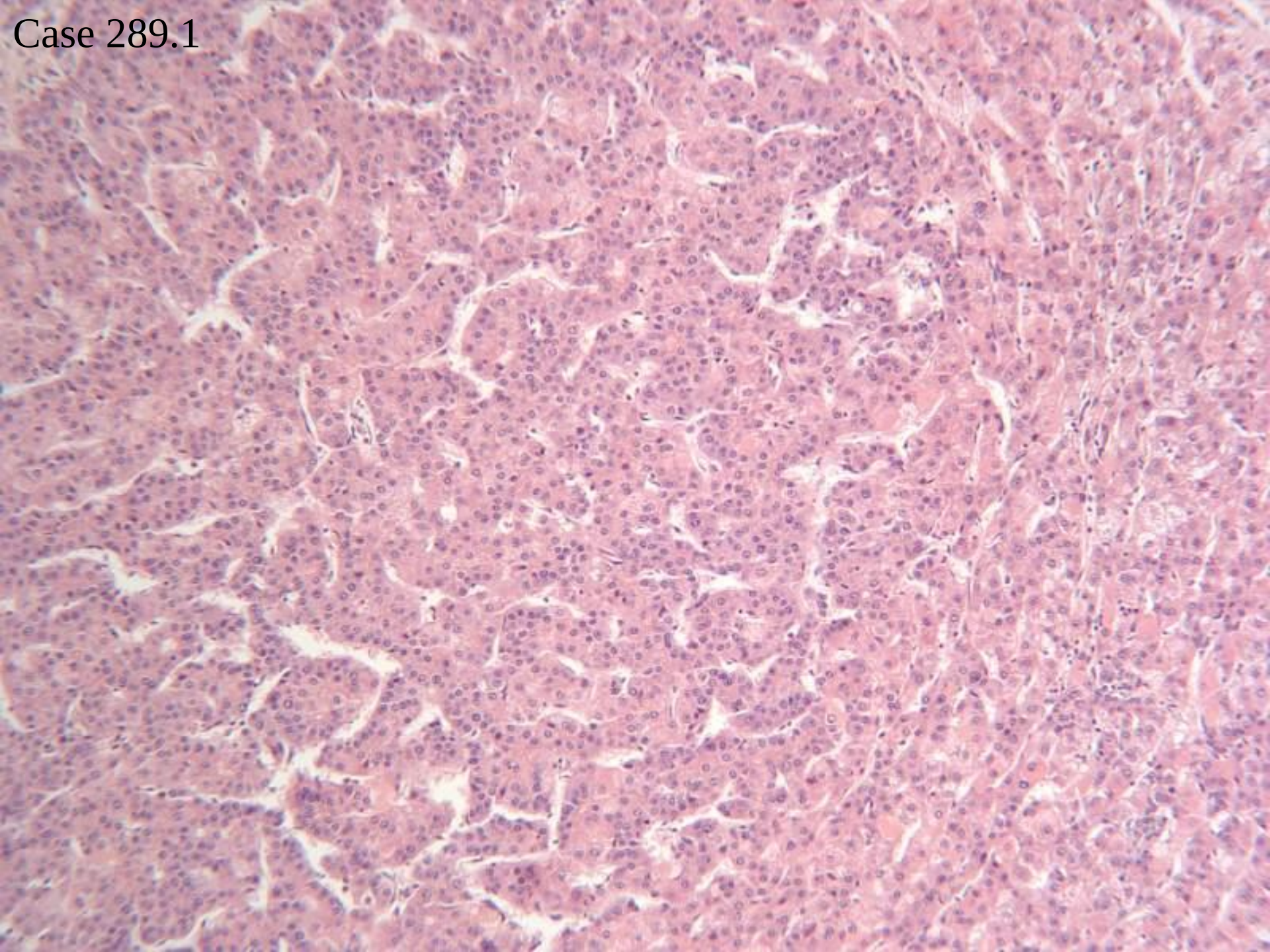
Case 289

42/male. Liver transplant for alcoholic cirrhosis. ?HCC in segment 2. Liver 1450 gm, cirrhotic appearances with 15 mm nodule in segment 2 (this block) and 3 other nodule 10 –1 5 mm.

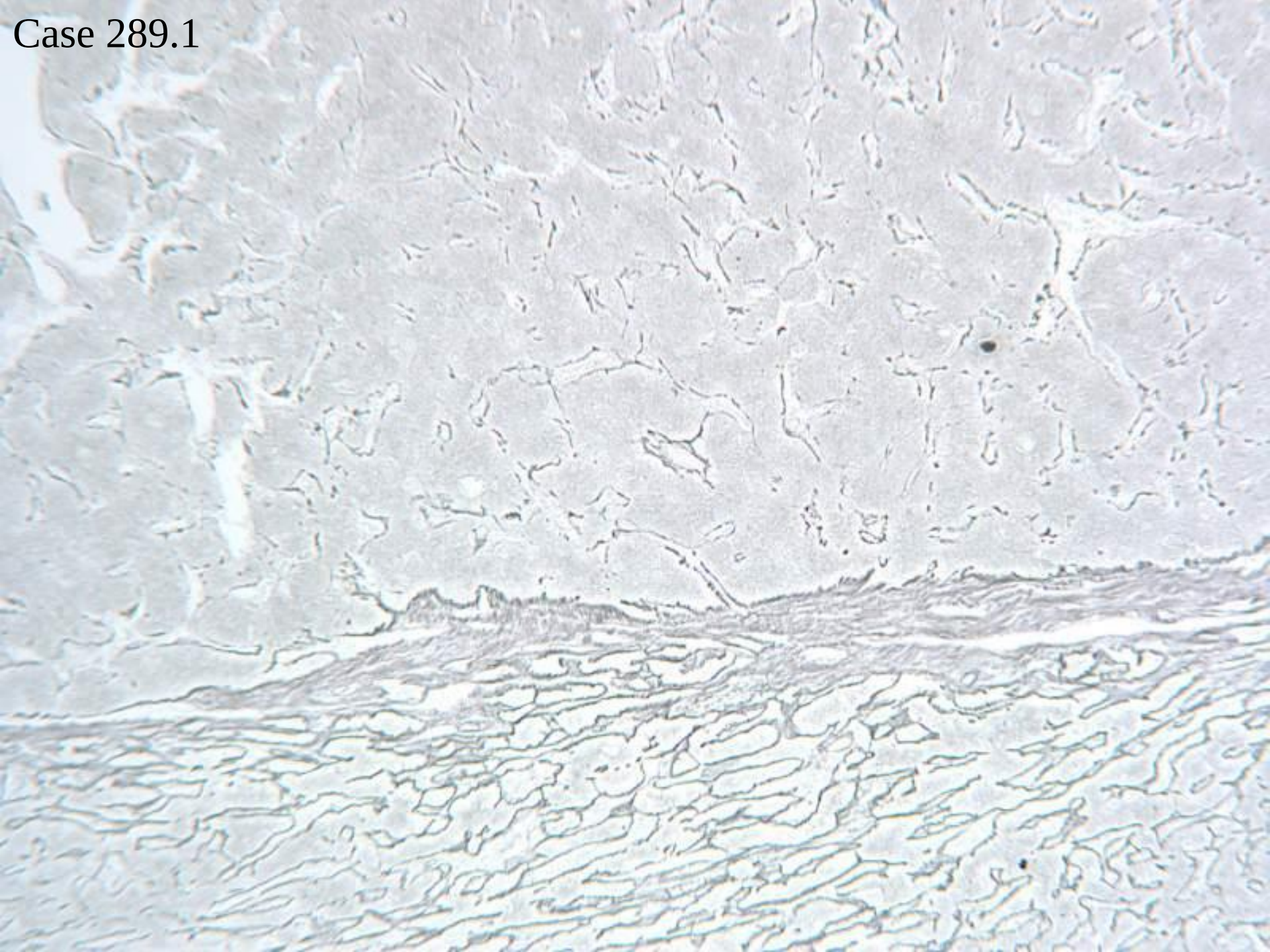
Case 289.1



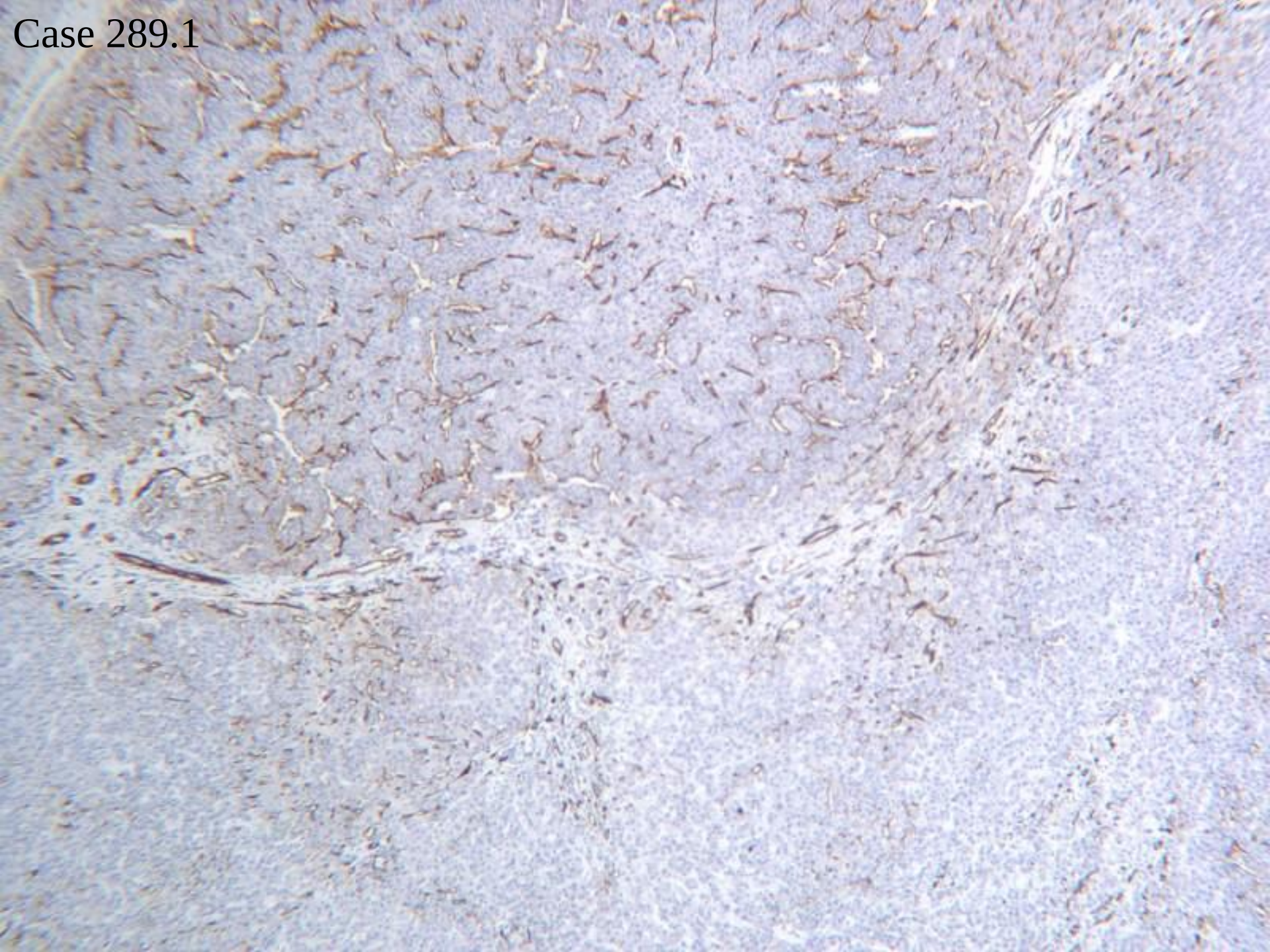
Case 289.1



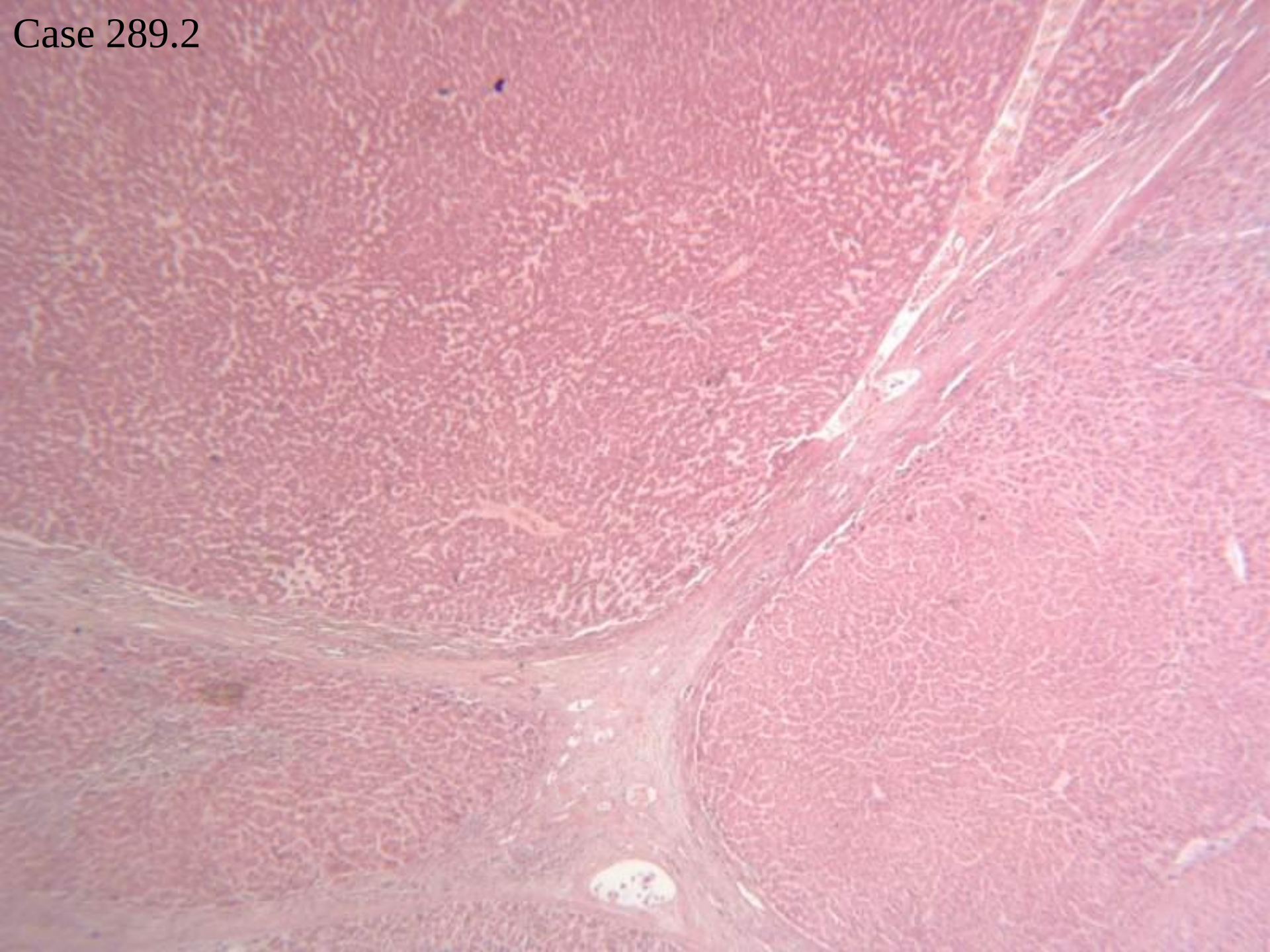
Case 289.1



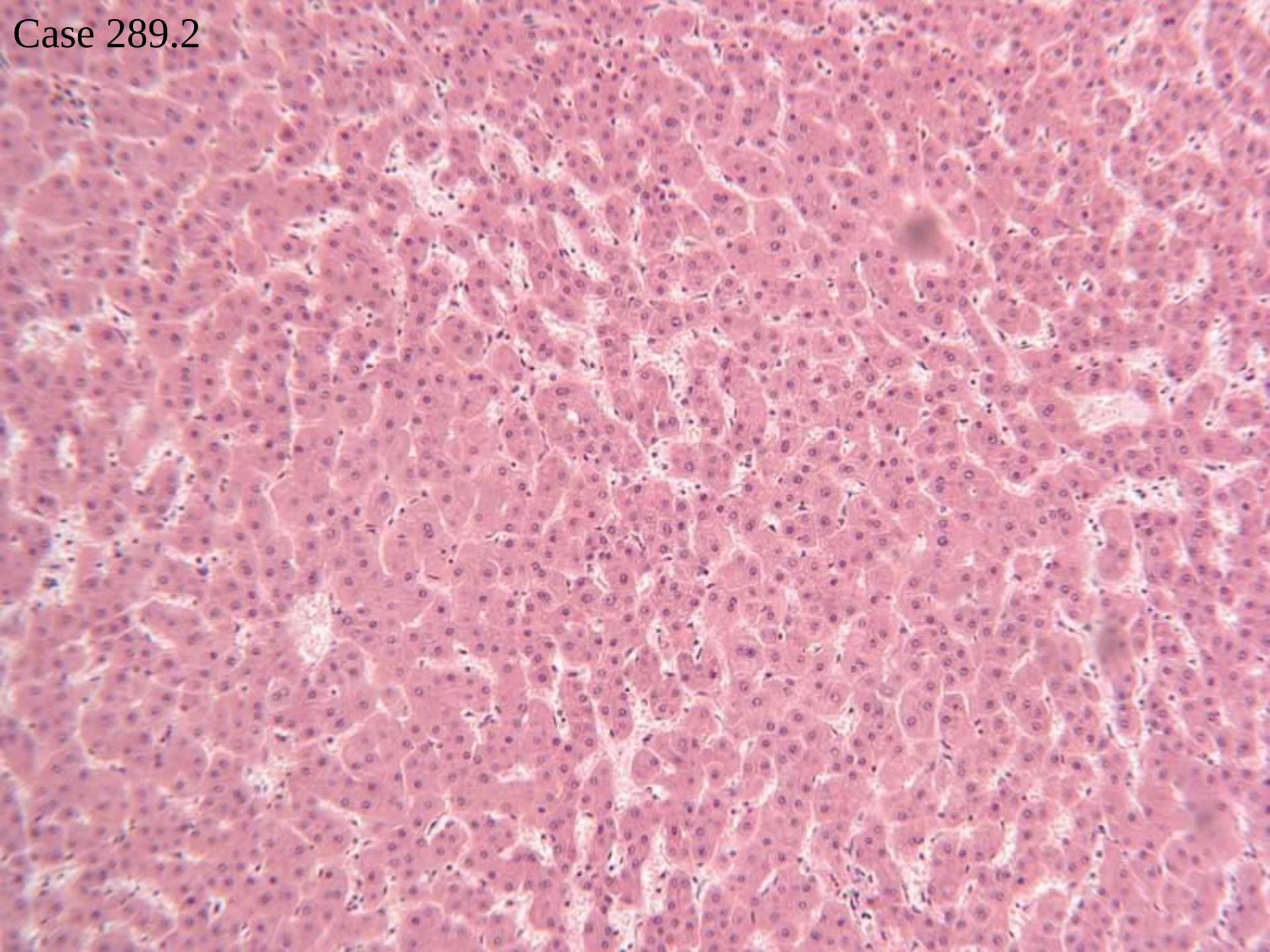
Case 289.1



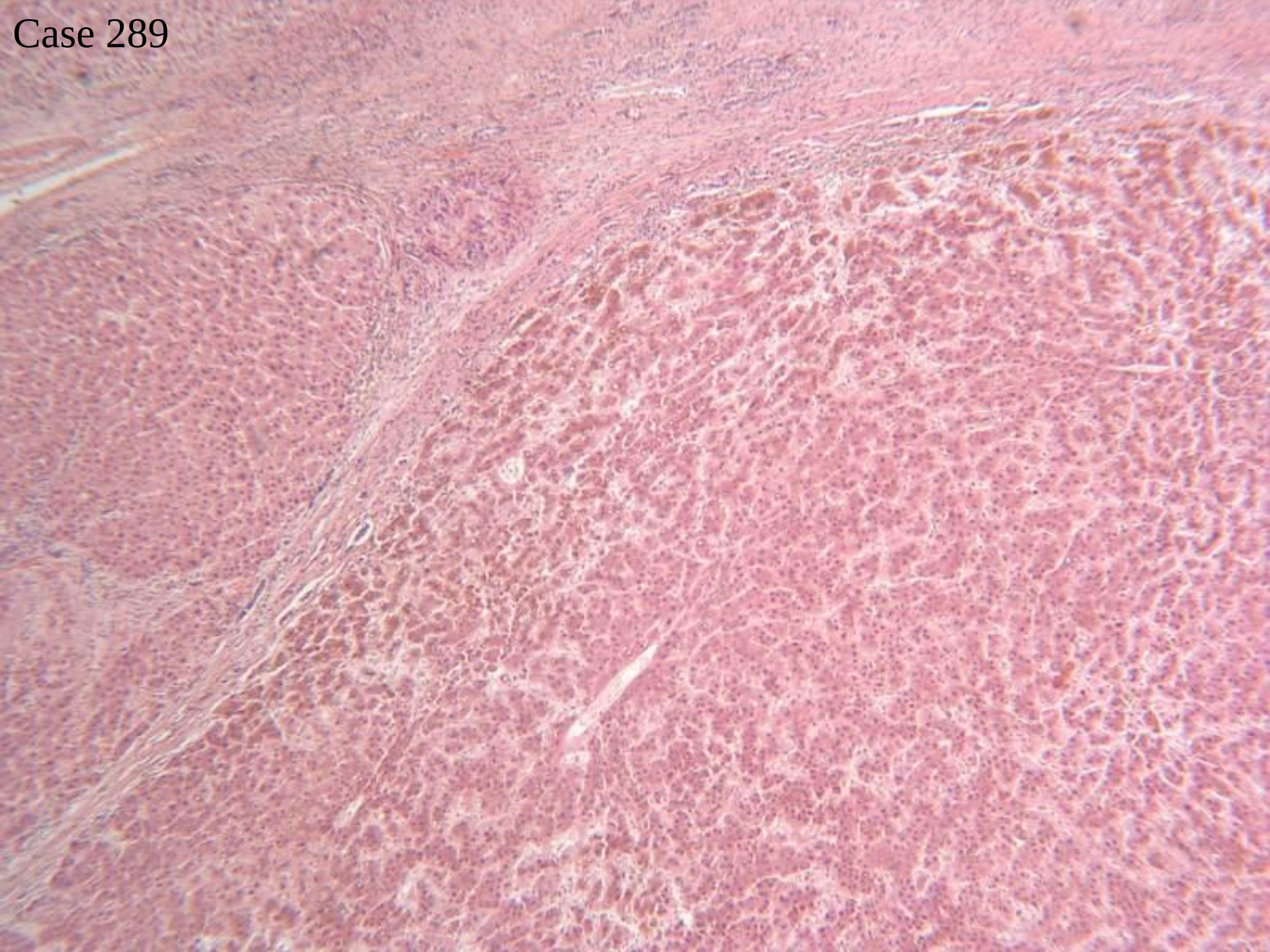
Case 289.2



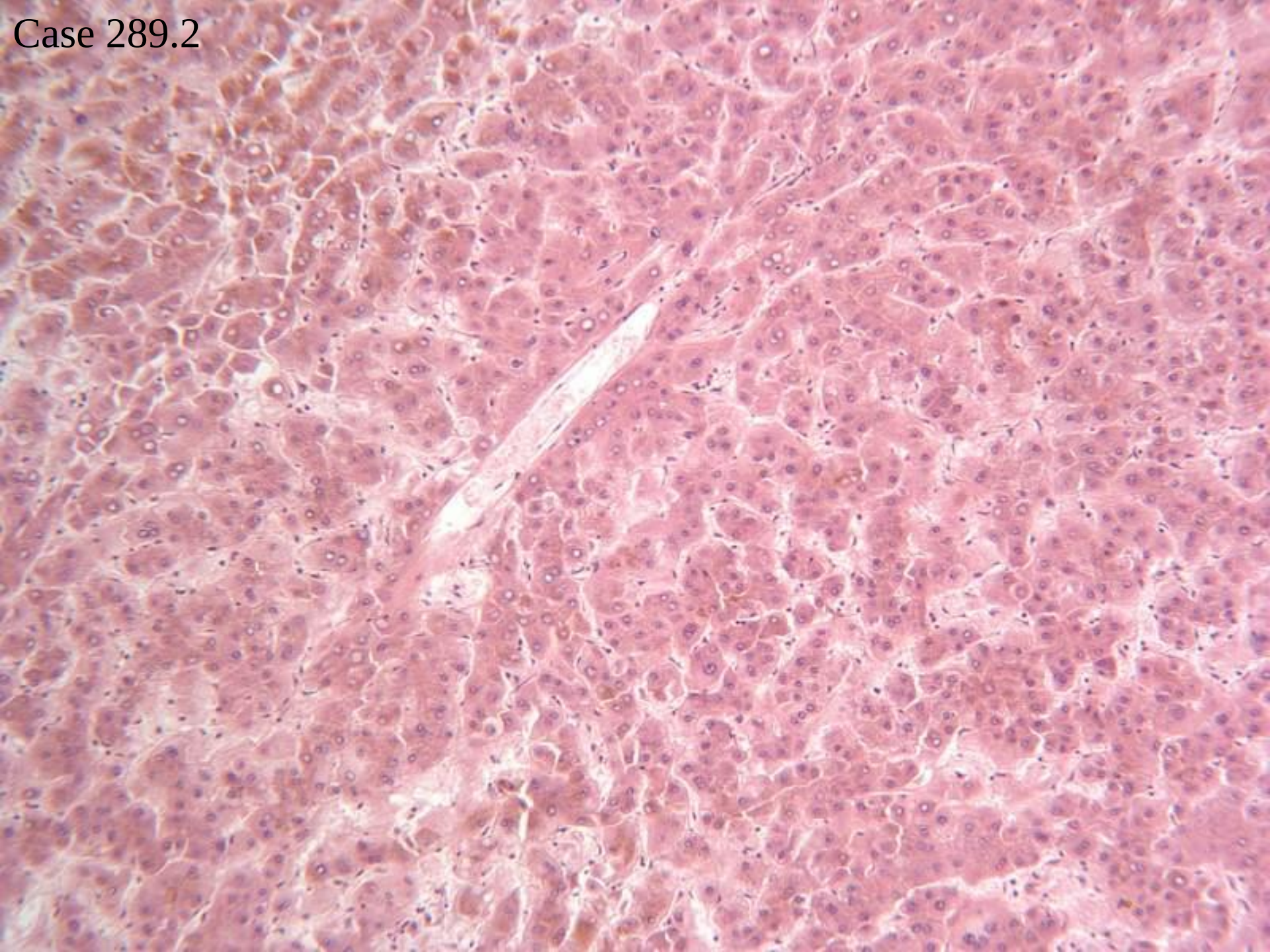
Case 289.2



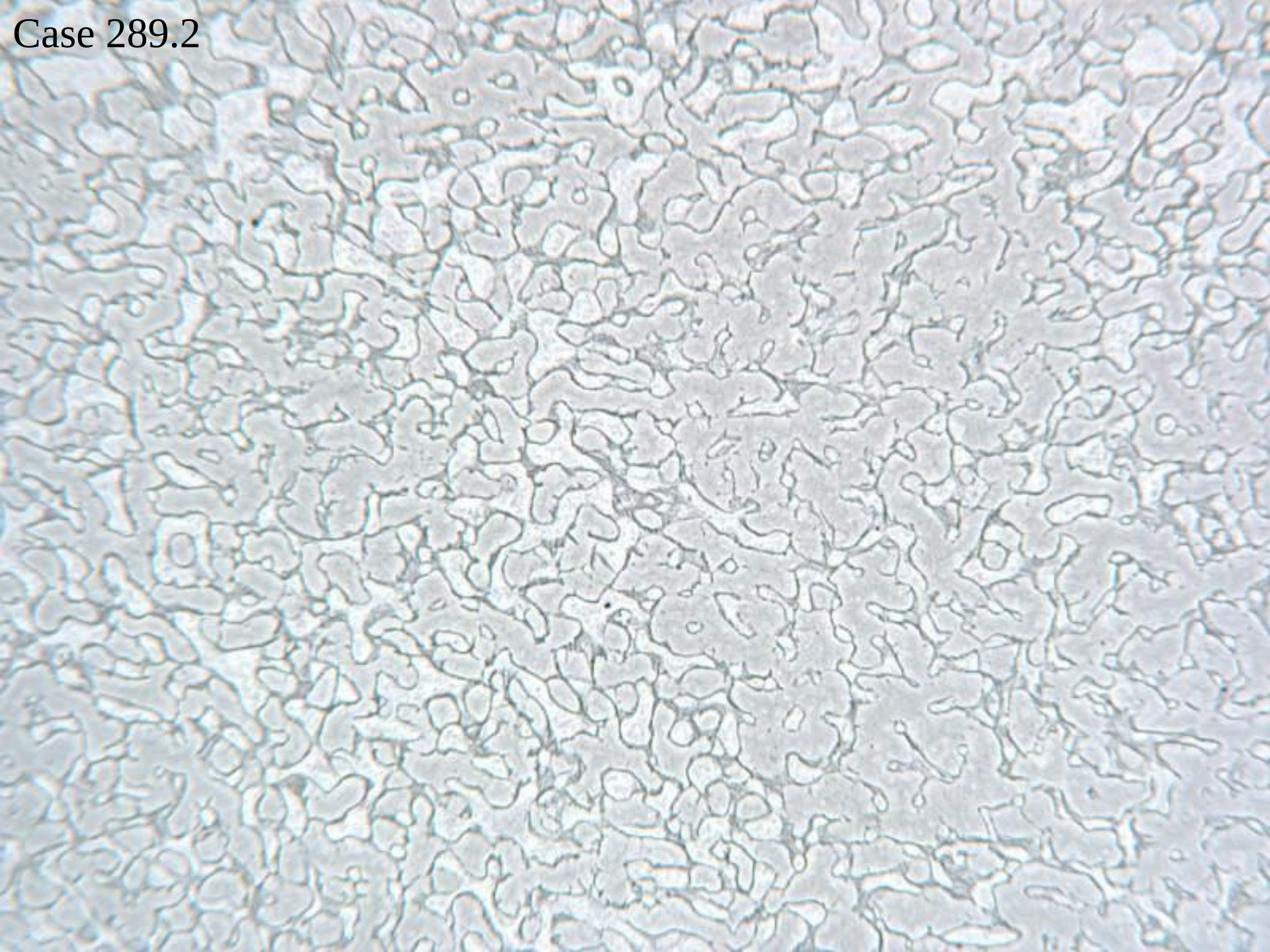
Case 289



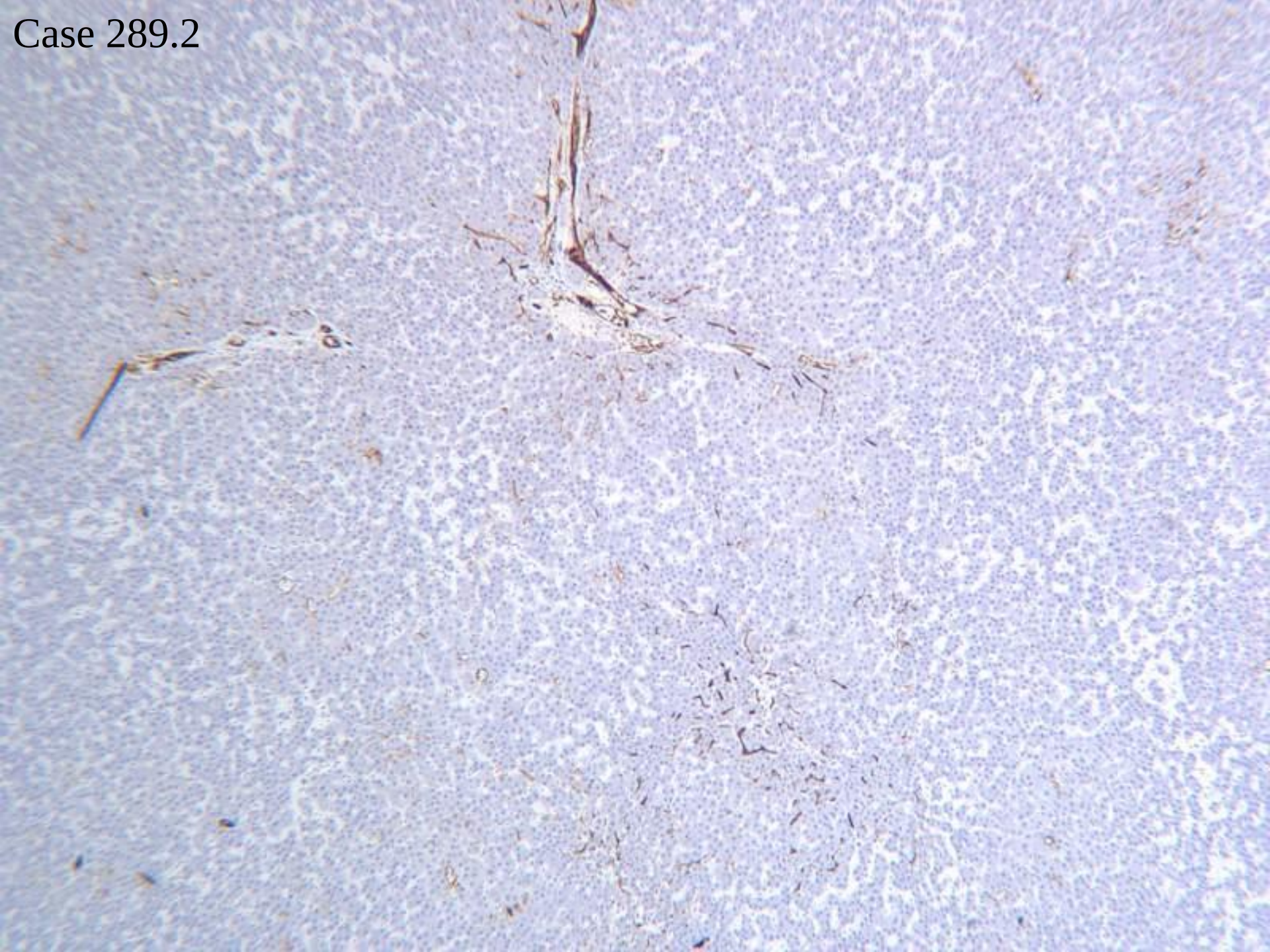
Case 289.2



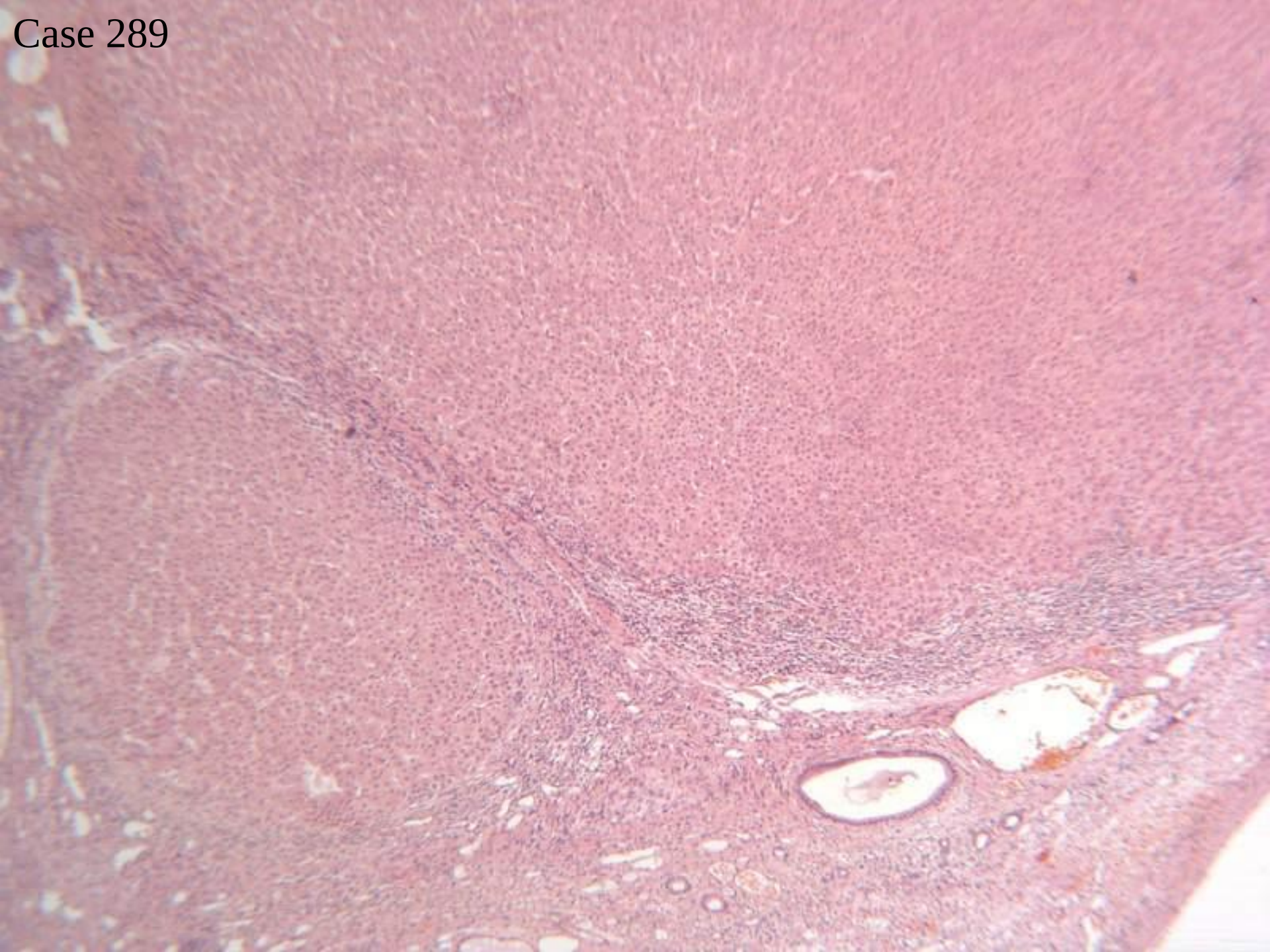
Case 289.2



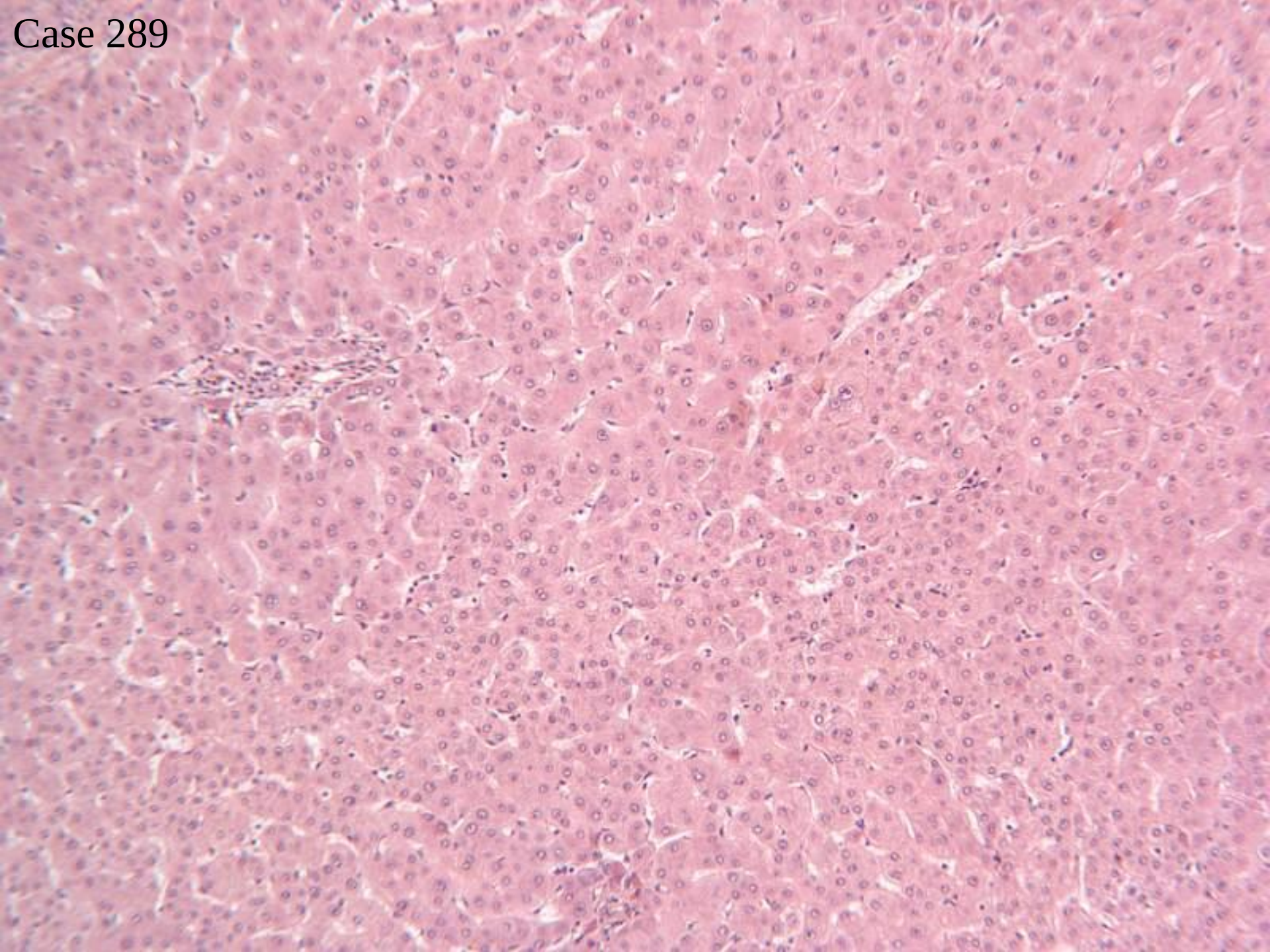
Case 289.2



Case 289



Case 289



Case 289

Responses: Slide 1

50 HCC, unequivocal diagnosis

1 hepatoma

2 highly suggestive of HCC

3 dysplastic nodule, ? HCC

5 dysplastic nodule

2 adenoma

3 FNH like lesion

1 dominant nodule

-

Responses: slide 2

26 dysplastic nodule

4 ? dysplastic nodule

24 macro-regenerative nodule

2 HCC

3 ? HCC

2 adenomatous nodule

2 focal nodular hyperplasia

1 dominant nodule

1 no diagnosis for slide 2

Background cirrhosis mentioned by 33

Case 289

Scoring: Full marks for a diagnosis including definite or possible HCC for slide 1. Slide 2 not contributing to scoring.

Discussion: 'Hepatoma' is obsolete terminology and is rejected. 'Adenoma' is inappropriate in a cirrhotic liver. 'FNH like lesion' is a recognised entity in cirrhosis, giving arterialised nodule suspicious of HCC on imaging, but the characteristics (including central stellate scar with prominent arteries) are not seen here. The deficiency of reticulin seen in this case is characteristic of HCC, although may be patchy, so not always helpful in biopsies.

Differential diagnosis of nodules falling short of HCC is difficult. Slide 2 was submitted as an example of dysplastic nodule. Diagnostic criteria for macro-regenerative nodule v. Dysplastic nodule, and for distinguishing low and high grade dysplasia have been proposed *(e.g. Roncalli M. Liver Transplantation 2004;10 S9-15))*

The end

Thank you to Anne, and to participants