National Liver EQA Scheme

Open meeting, Glasgow

March 24th 2004

Participants meeting – SOP8

- Case discussion
  - Are we quorate
  - All please sign attendance sheet

  There were 20 EQA participants and 7 non-members present.

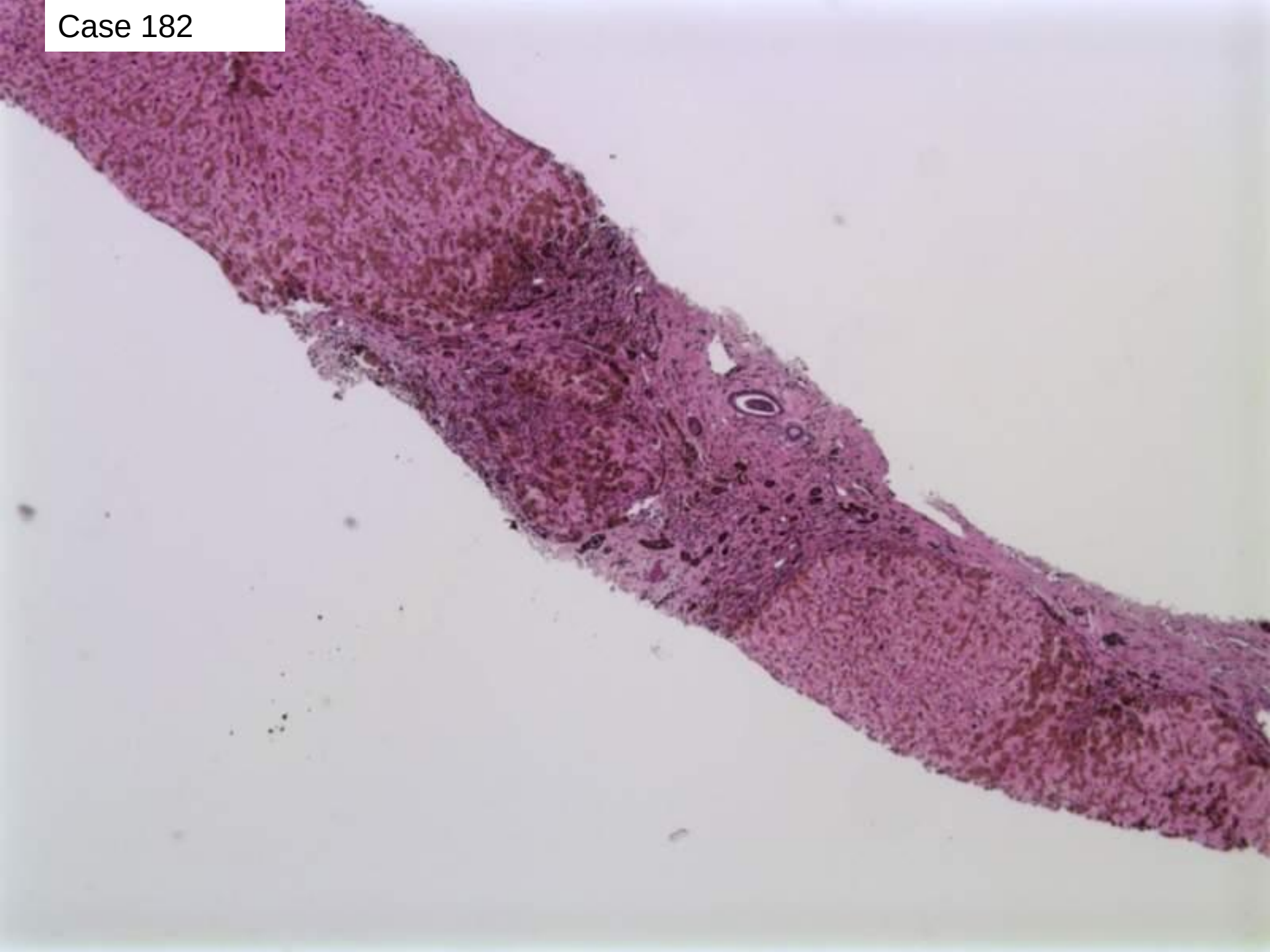
  Main diagnoses are listed below: diagnoses accepted by the group are indicated in the right hand columns.

  In scoring the results sheets, diagnoses considered not acceptable by the group were nevertheless allowed if qualified elsewhere on the score sheet to indicate general agreement with the consensus diagnosis.

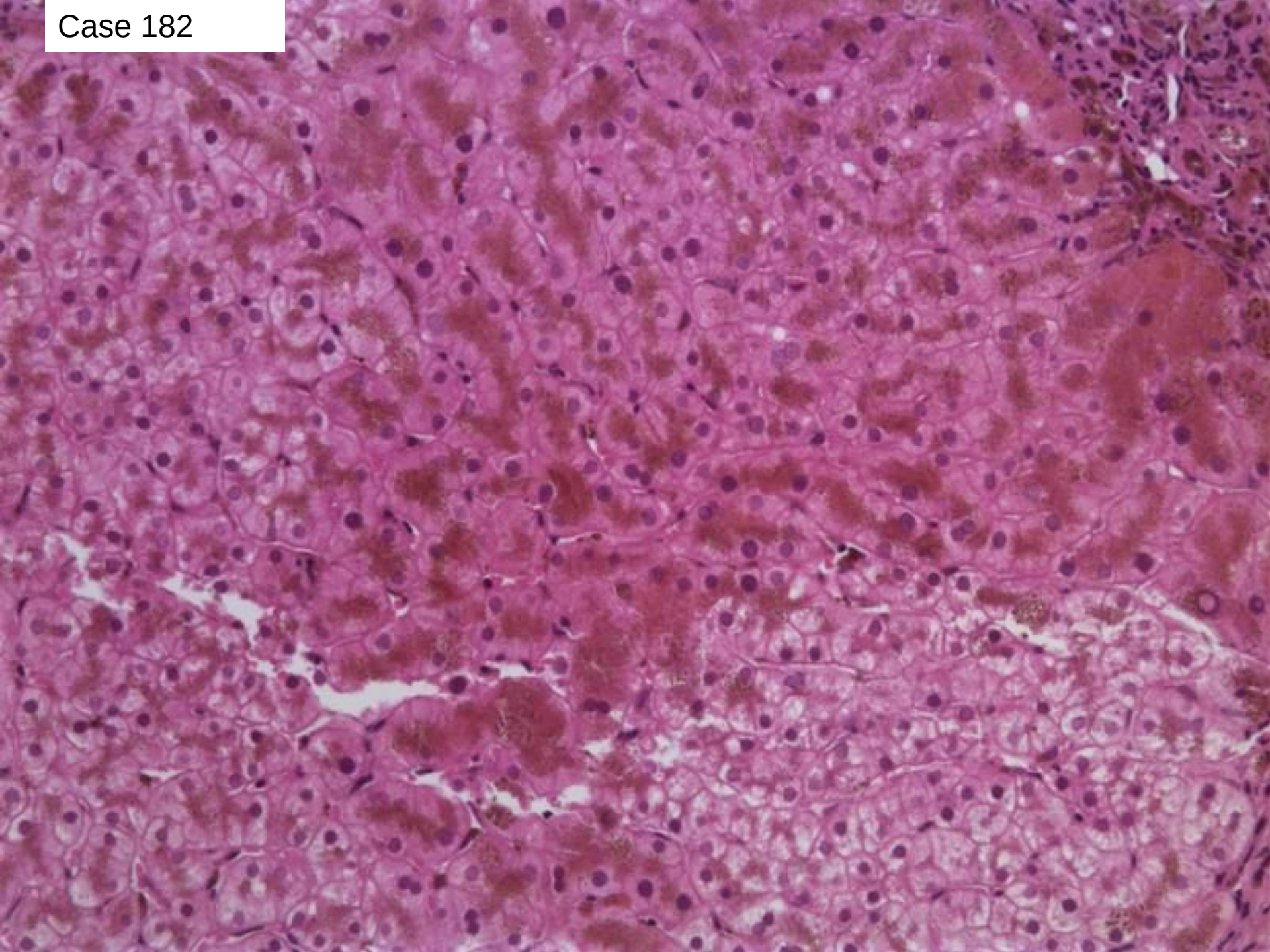
Case 182

- *Information provided*: 54 year old woman: Perl's grade 4 for siderosis. Cirrhosis confirmed on Masson's Trichrome and Reticulin. No other details available

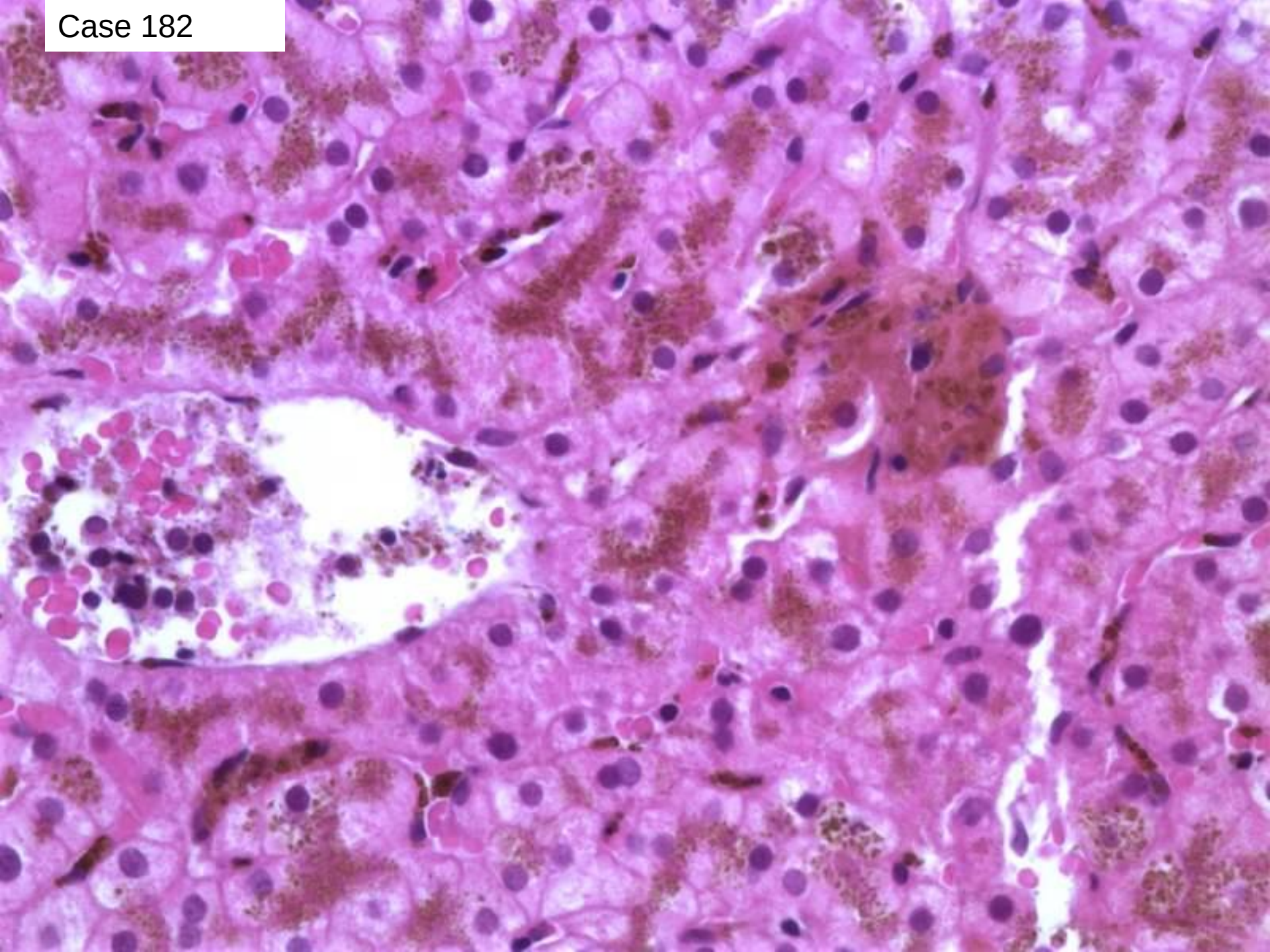
Case 182

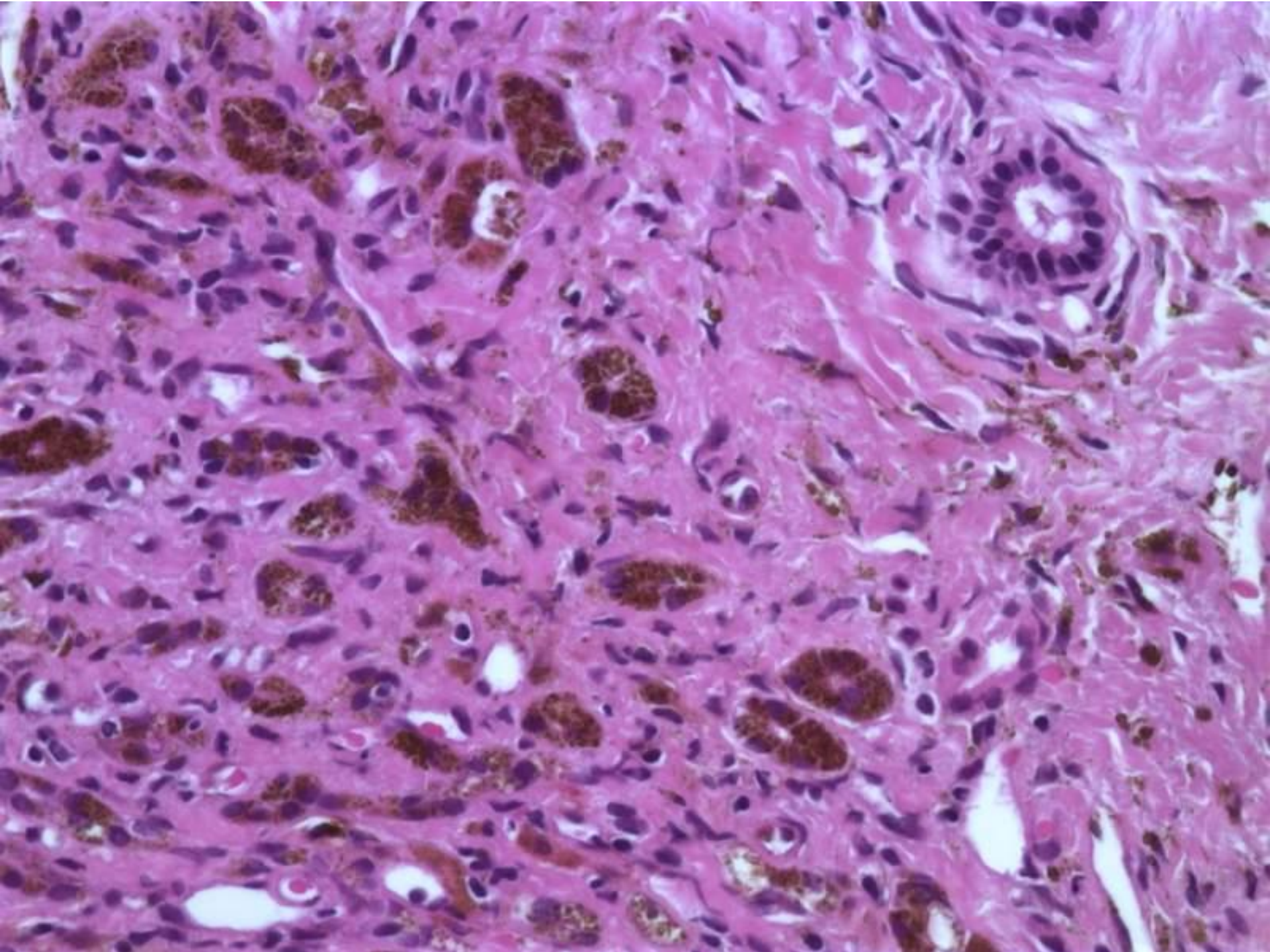


Case 182



Case 182





Case 182

Summary of responses:

- haemochromatosis and cirrhosis (probable, possible or unqualified) – 410.
- haemochromatosis/iron overload: cirrhosis/fibrosis not mentioned – 40
- transfusional type haemosiderosis, septal + bridging fibrosis –10

Comments: genetic studies for haemochromatosis - 17

Accepted diagnoses:

Yes

Yes

No

Additional comments in discussion:

Very unusual to see this in a relatively young woman would expect other reason for increase iron stores but none is known.

Case 182

Additional information: Dr Dube

Heterozygous for C282Y.

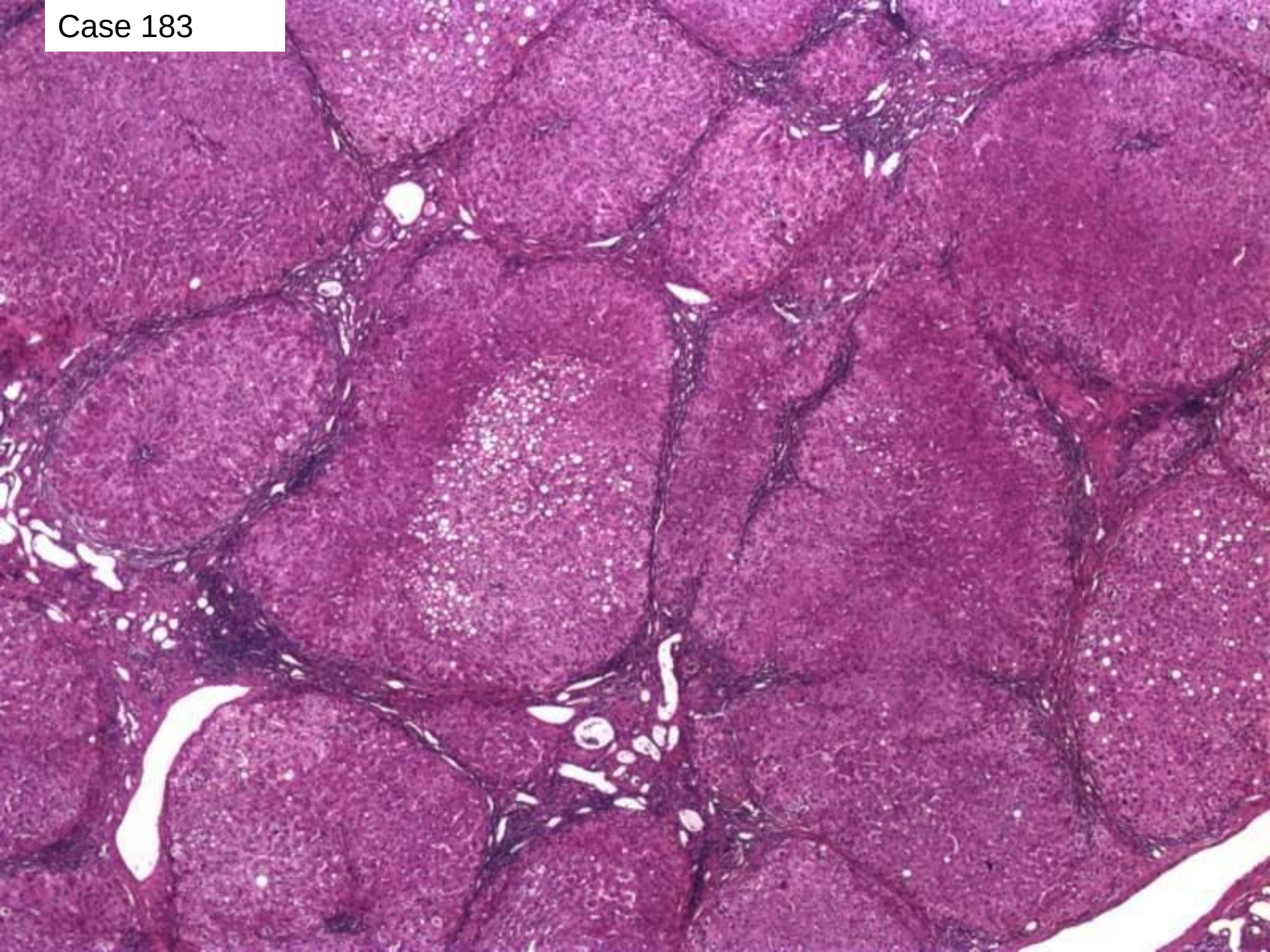
No other risk factors for liver disease.

Improved with venesection.

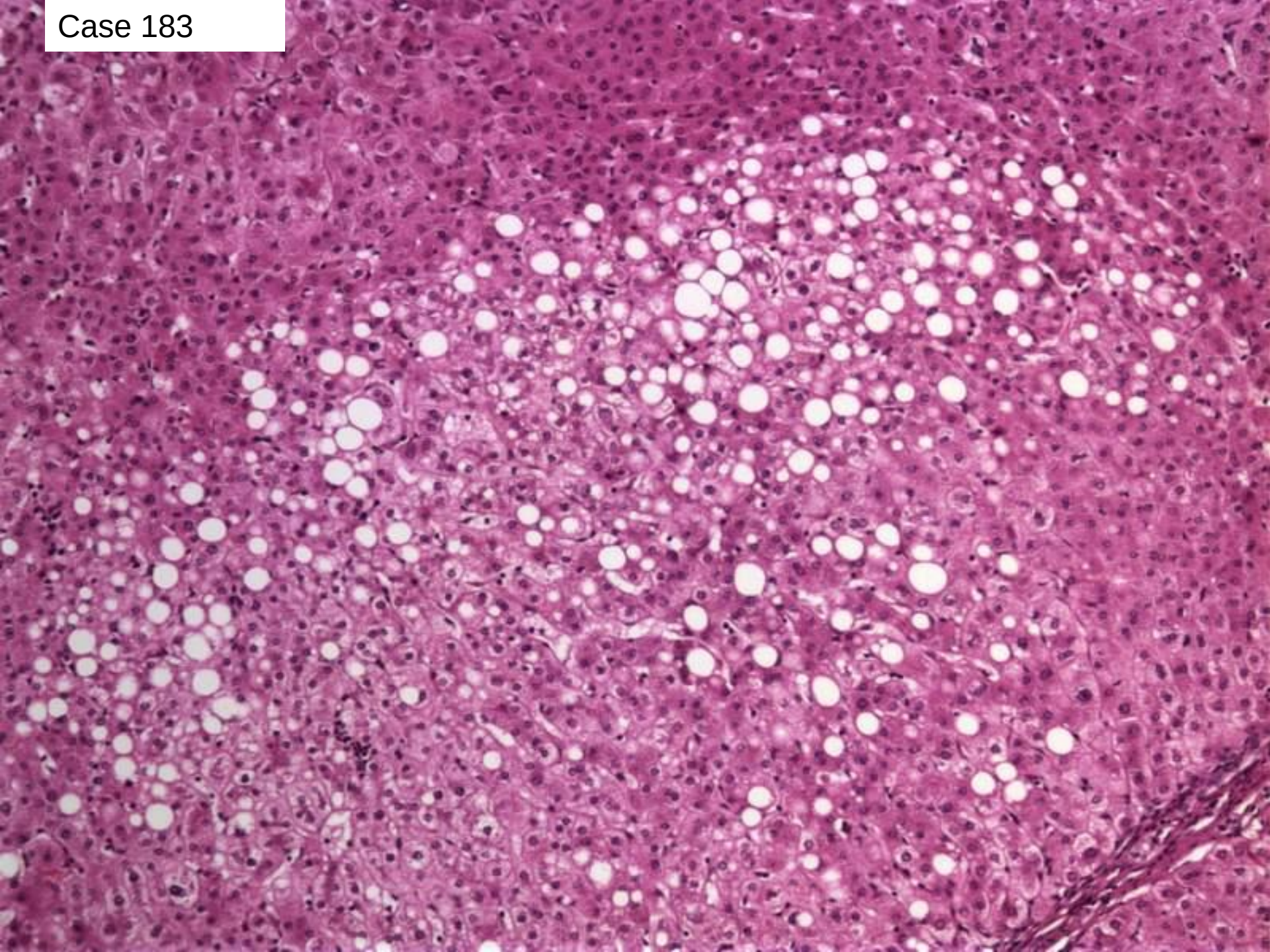
Case 183

- *Information provided*: 64 year old woman. Cirrhotic. No significant alcohol consumption history. Obese. ?drug induced liver disease (on Methotrexate for psoriasis). ?NASH.

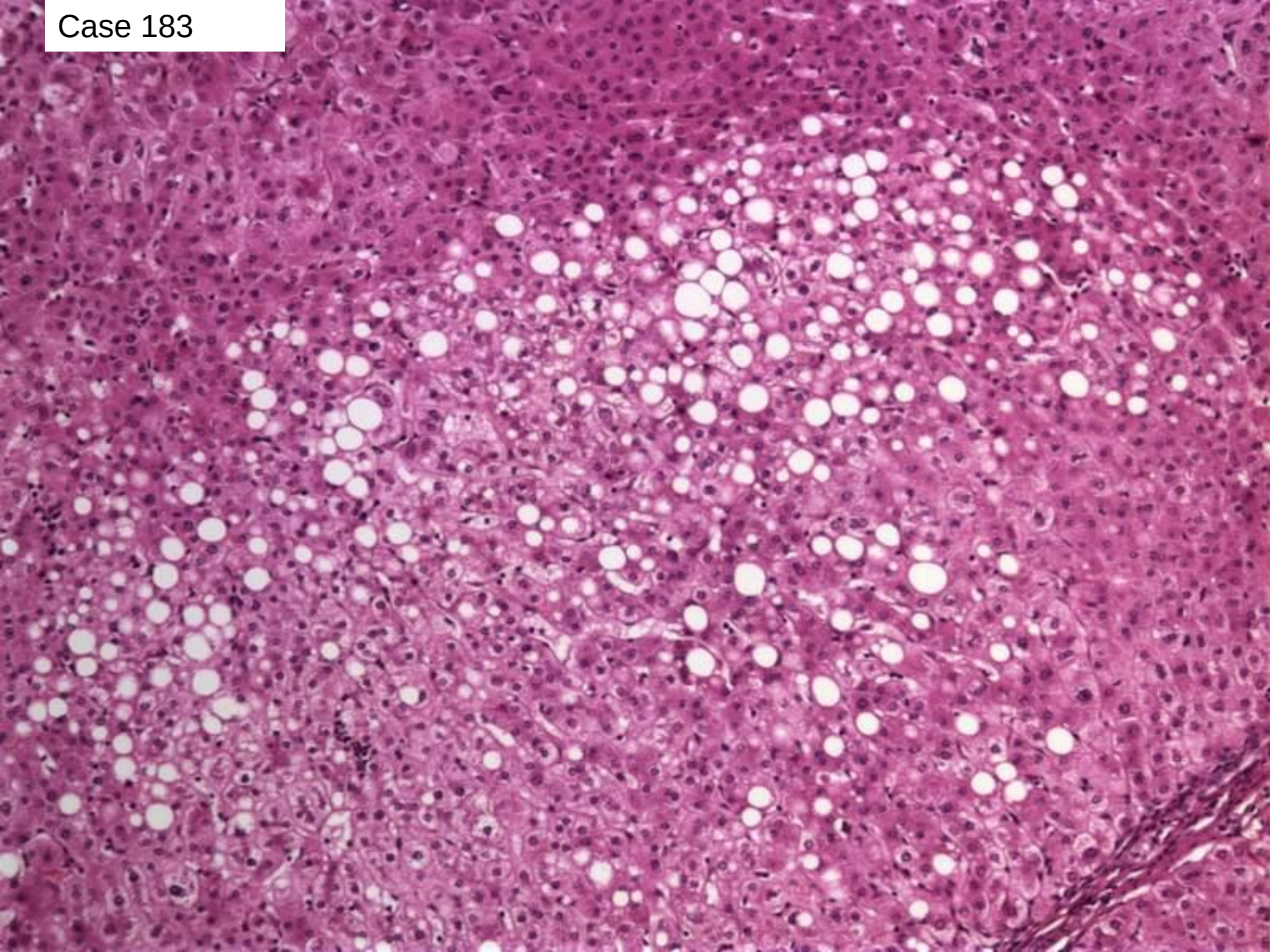
Case 183



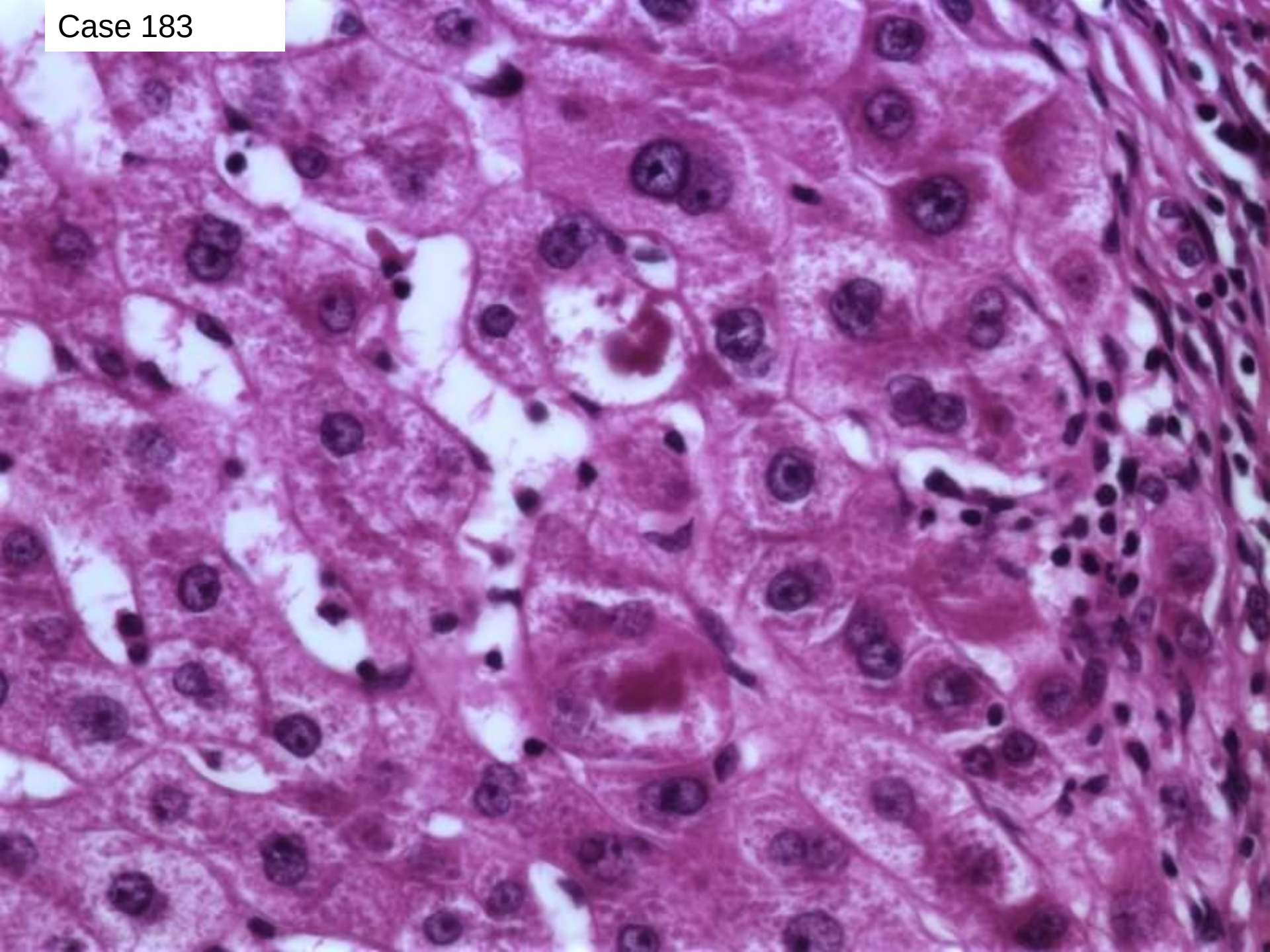
Case 183



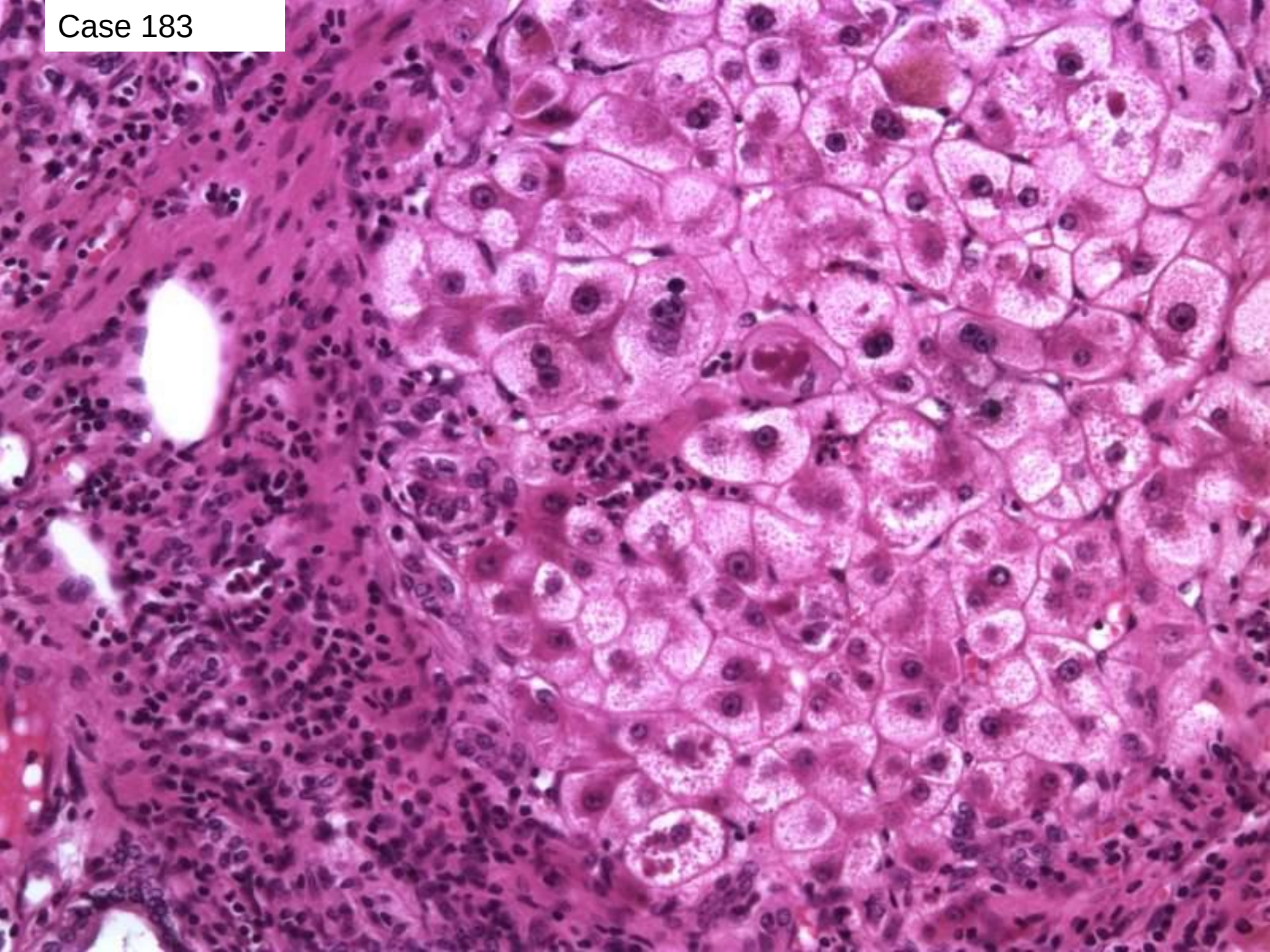
Case 183



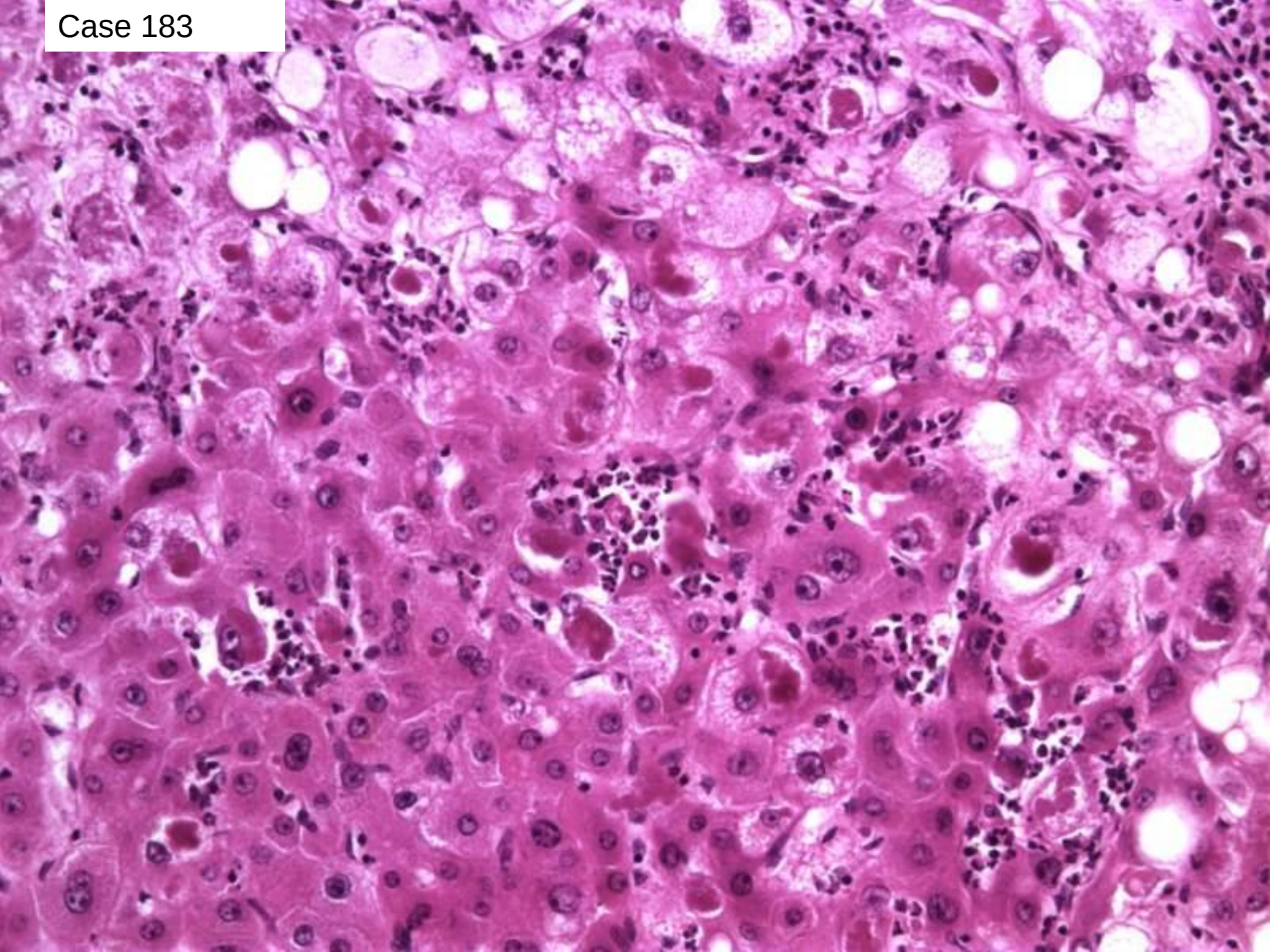
Case 183

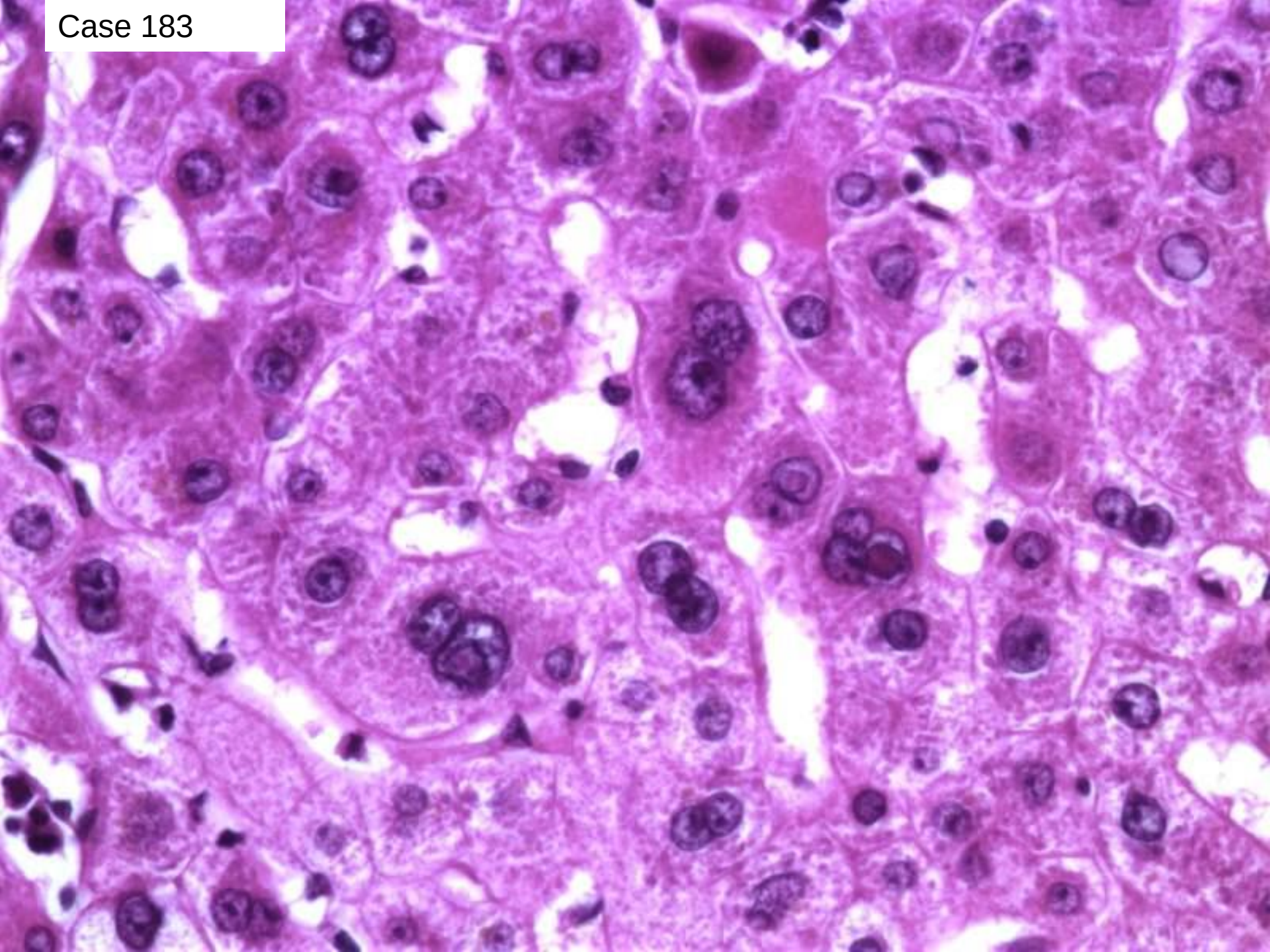


Case 183



Case 183




Case 183

Case 183

Summary of Responses:	*Accepted diagnoses*:
cirrhosis, NASH - 158	Yes
cirrhosis, steatohepatitis – 133	Yes
cirrhosis with Mallory's – 10	Yes, if qualified elsewhere
cirrhosis, more like alcoholic – 22	No
cirrhosis, drugs/Methotrexate – 50	Yes
cirrhosis unqualified – 20	No
other cirrhosis (biliary, metabolic, storage, chronic hepatitis, Wilson's) – 57	No

Case 183: points raised in discussion

There is no evidence that methotrexate can cause steatohepatitis – the lesion is steatosis with portal fibrosis. The strength of the evidence that MTX interacts with other causes of steatohepatitis was questioned.

Other causes of steatohepatitis must be excluded in patients on MTX.

The decision whether to continue treatment is a clinicopathological one, not just for pathologists

It is not possible to distinguish alcoholic from other causes of steatohepatitis – suggestions that large amounts of Mallory's were commoner in alcoholic disease were from older literature.

Case 183

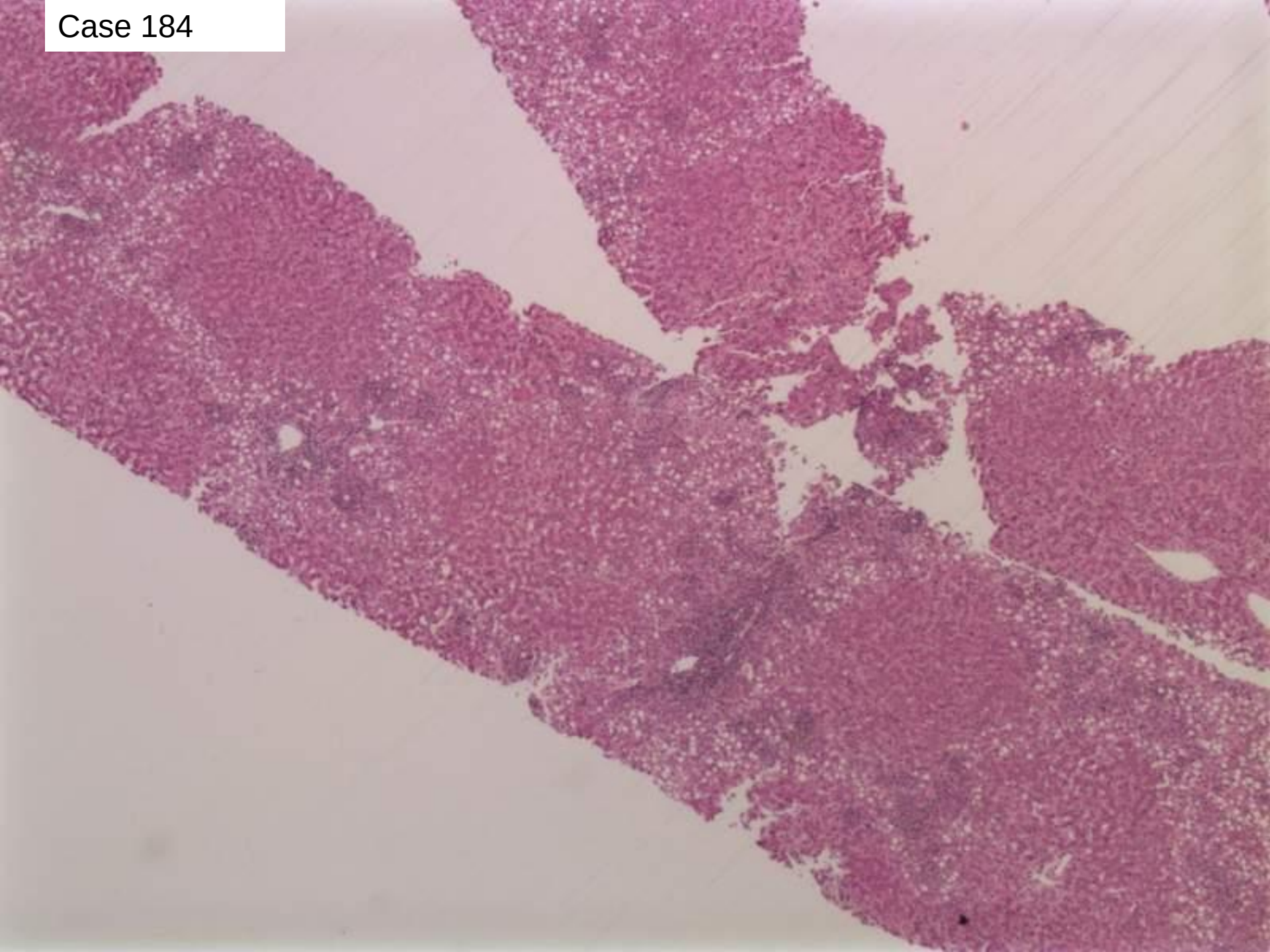
comments:

- exclude alpha-1 antitrypsin deficiency – 7
- exclude HCV – 2
- unlikely to be Methotrexate – 4
- the amount of Mallory's suggests alcoholic rather than non-alcoholic disease.
- Methotrexate has an 'additive' effect in steatohepatitis

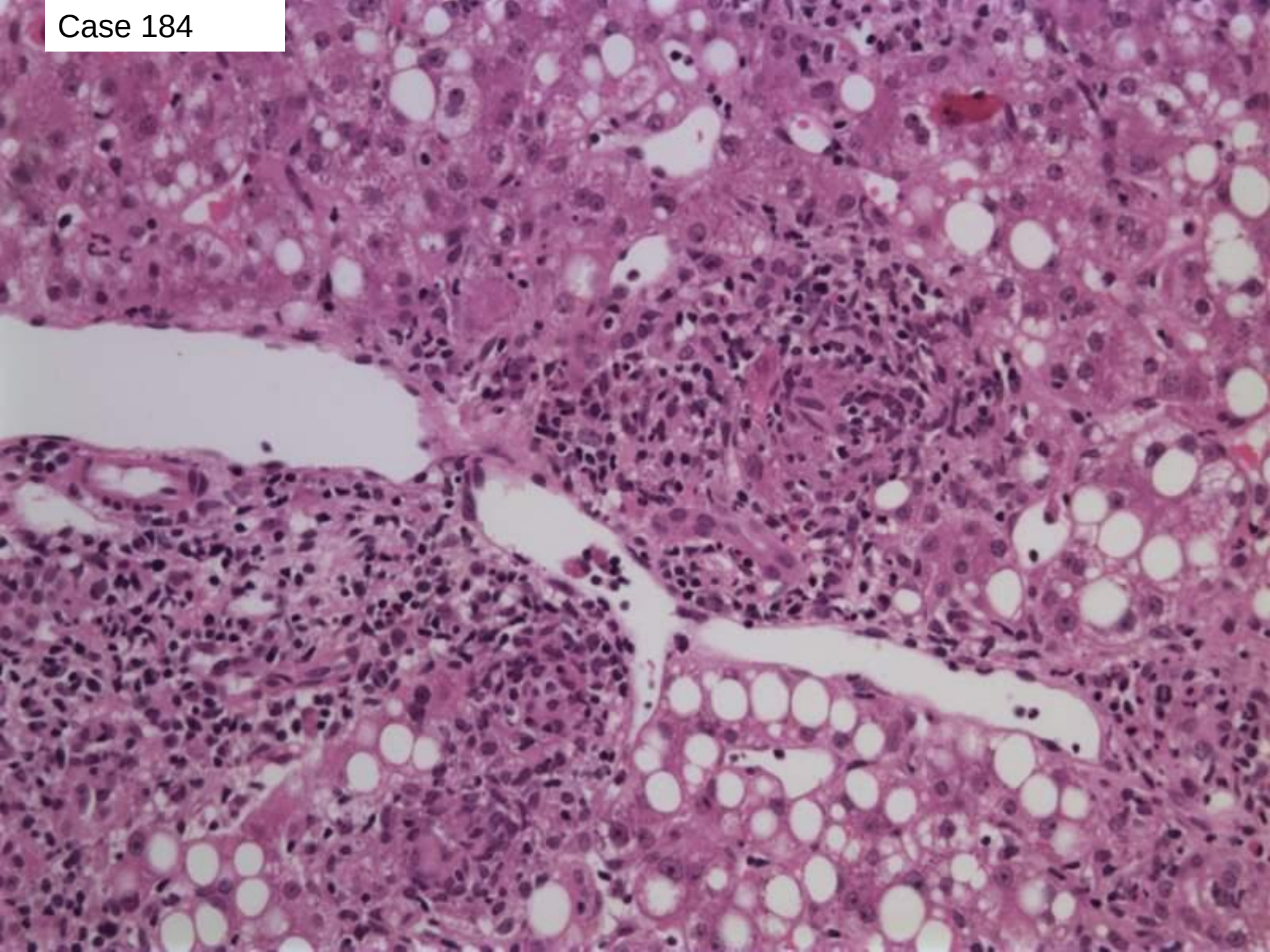
Case 184

Information provided: 21 year old female, acutely unwell, cholestatic jaundice coagulopathy.

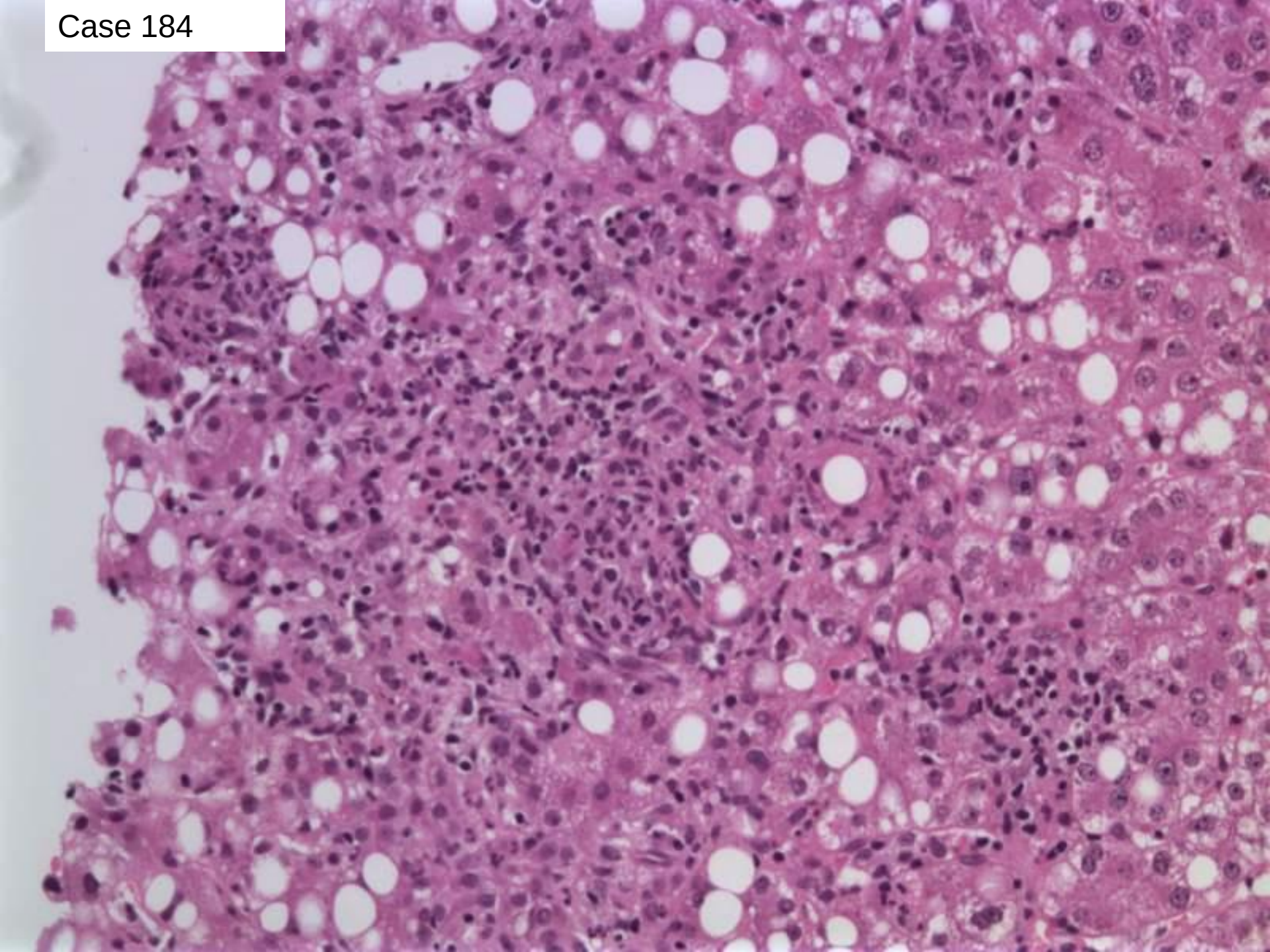
Case 184



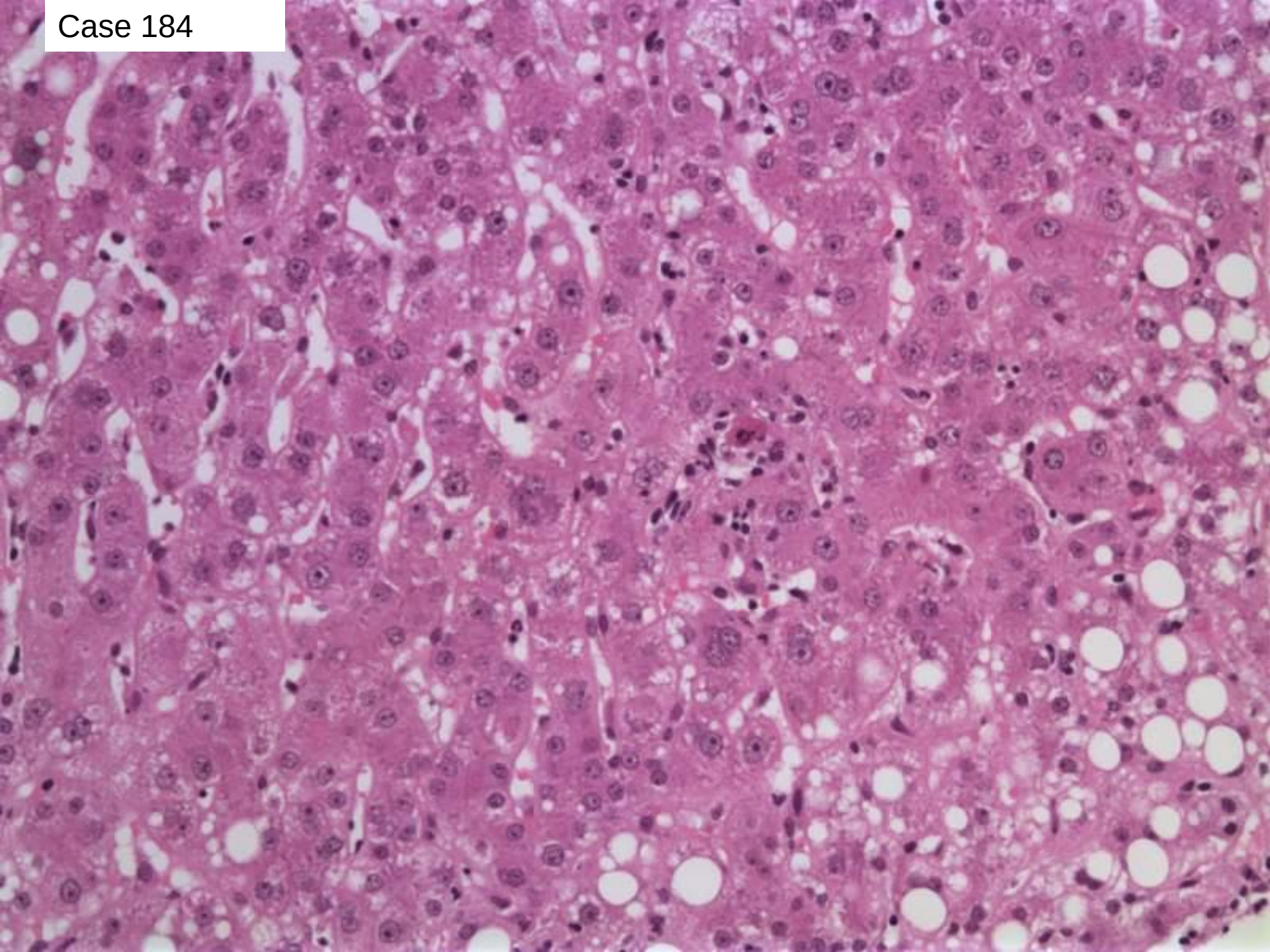
Case 184



Case 184



Case 184



Case 184

Summary of Responses:
No slide received - 10

morphological diagnosis only
granulomatous hepatitis ± steatosis mentioned – 170
steatohepatitis with granulomas – 20
granulomatous hepatitis + ductopenia – 10
+ cholangitis – 10
+ microabscesses – 10
+ cholestasis – 10
+ fibrin-ring granuloma – 20
acute steatohepatitis – 10

diagnosis with morphology and suggested aetiology
granulomatous hepatitis, ? Q fever- 95
?drug/other infection – 82

aetiology diagnosis with no morphology given
Q fever - 10,
PBC – 3

Accepted diagnoses:

Yes
Yes
Yes
Yes
Yes
Yes
No

Yes
Yes

No
no

Case 184

Comment: all made comments.

- Q-fever mentioned somewhere in response by 21. EMH mentioned by 6.
- ? fibrin ring granulomas/ needs MSB – 16
- others ?lipid ring granulomas/
  lipogranulomas

Follow up information: the patient was EBV IgM positive and made a Complete recovery. The final diagnosis in this case was therefore an Unusual pattern of EBV hepatitis.

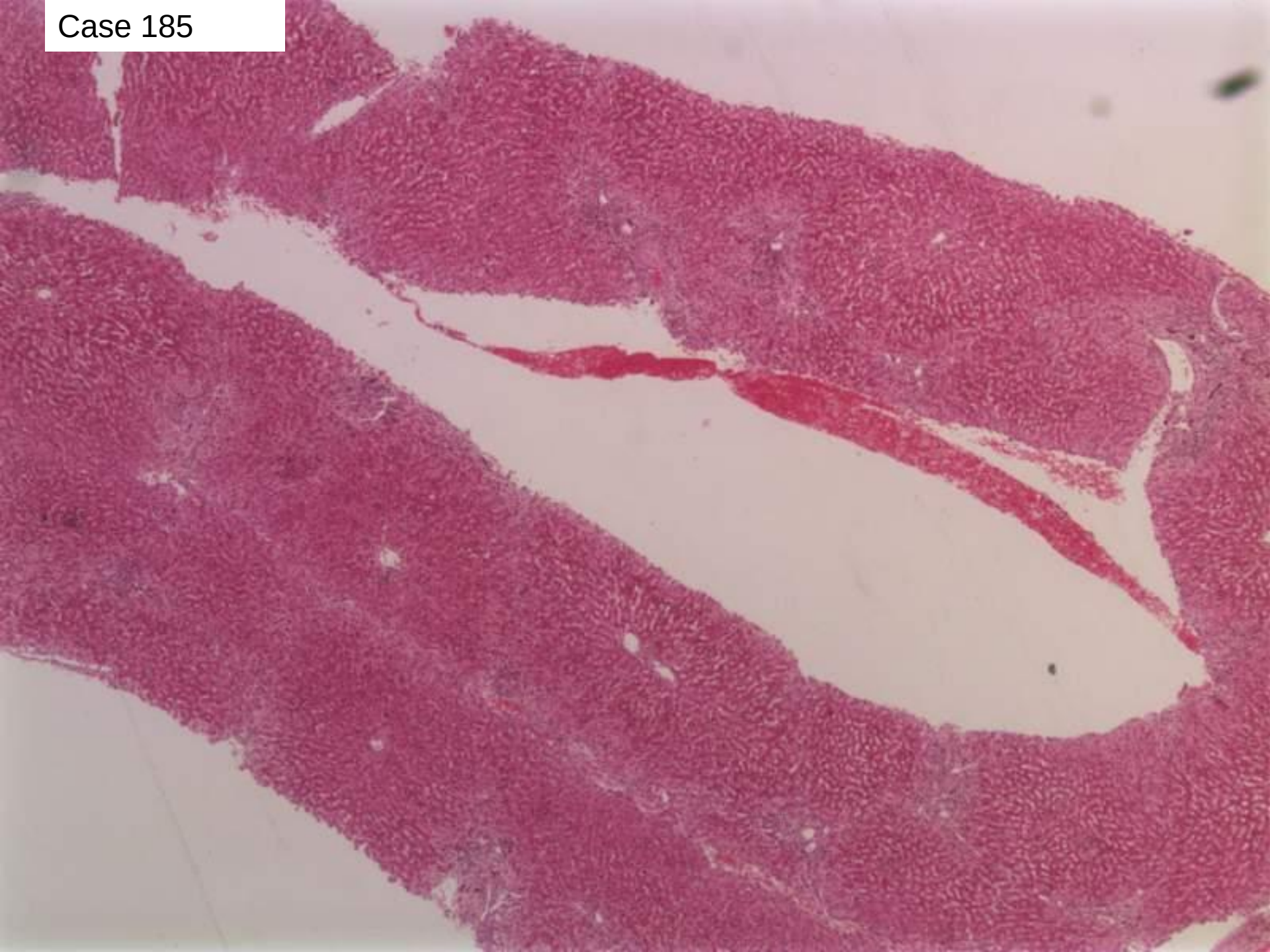
No EBV could be demonstrated by IHC; there was no fibrin in the ring Granulomas by MSB.

Case 185

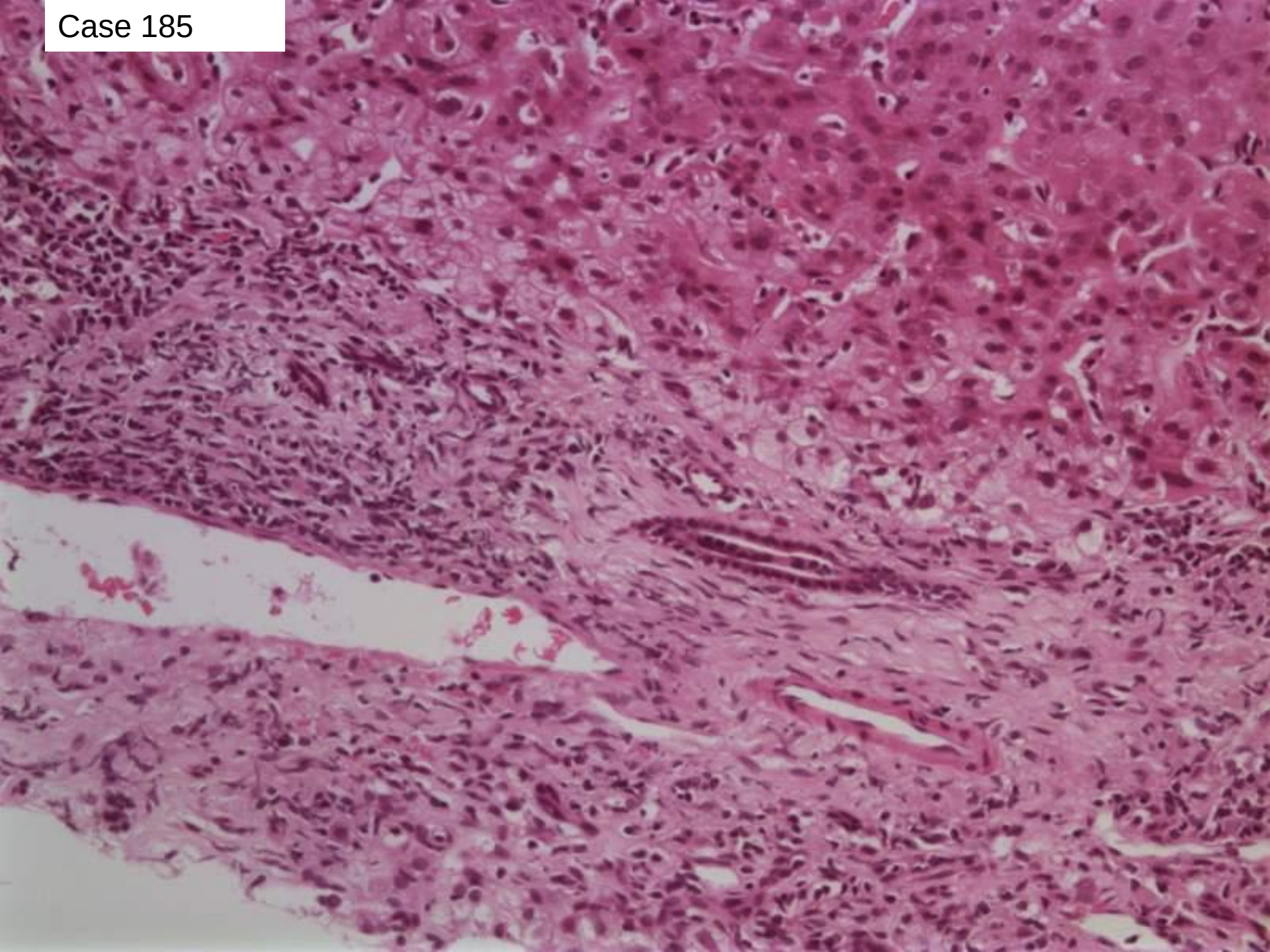
Information provided: Unwell approximately 4 weeks following return from Corfu. Took herbal remedies. Also has been on Minocyclin,

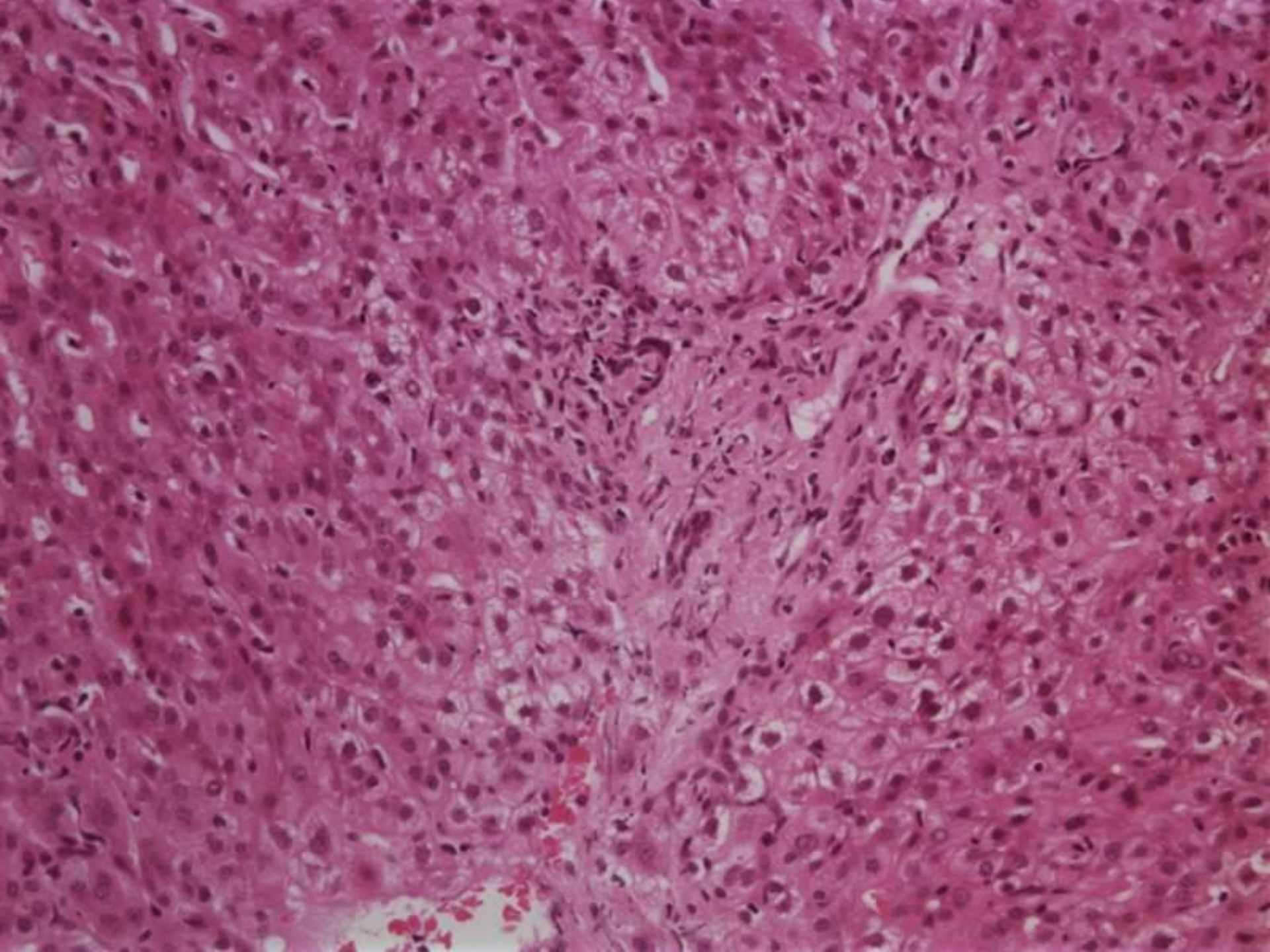
Bilirubin 436, ALP 259, AST 338, GGT 19, INR 0.89, immunoglobulins normal, autoantibodies – ANA 1: 60, ASM 1: 160, ?autoimmune, ?secondary to Minocyclin

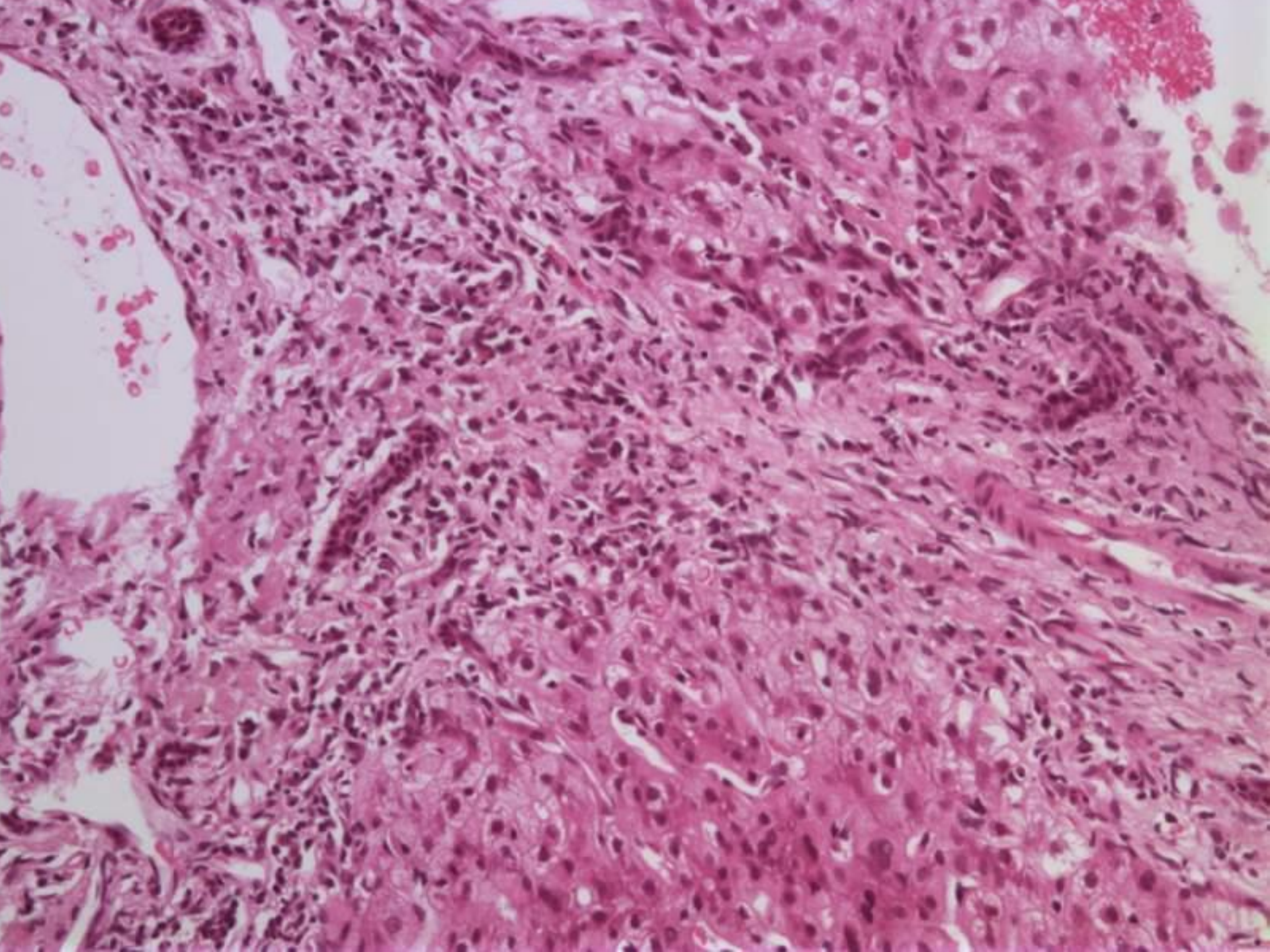
Case 185



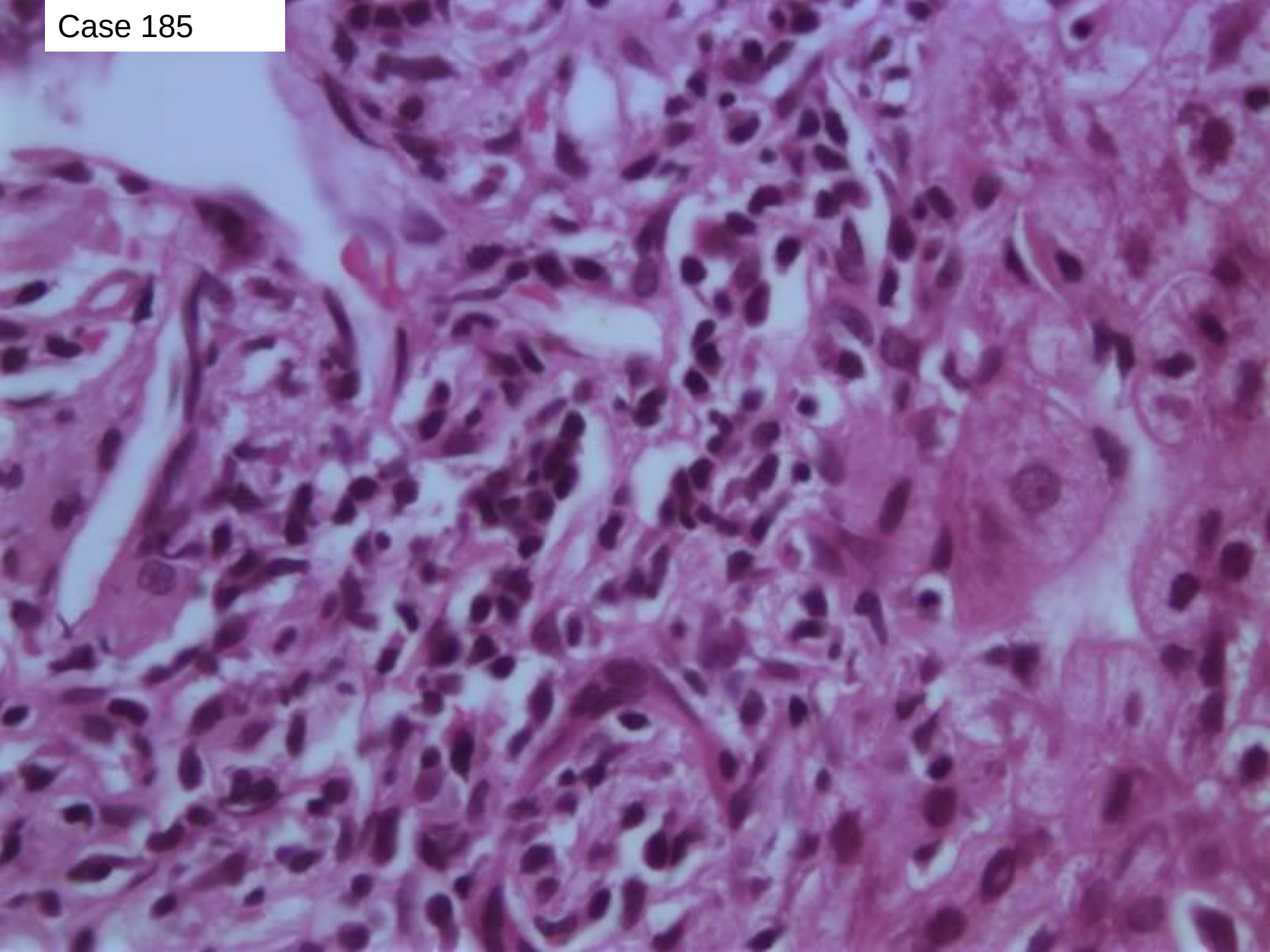
Case 185



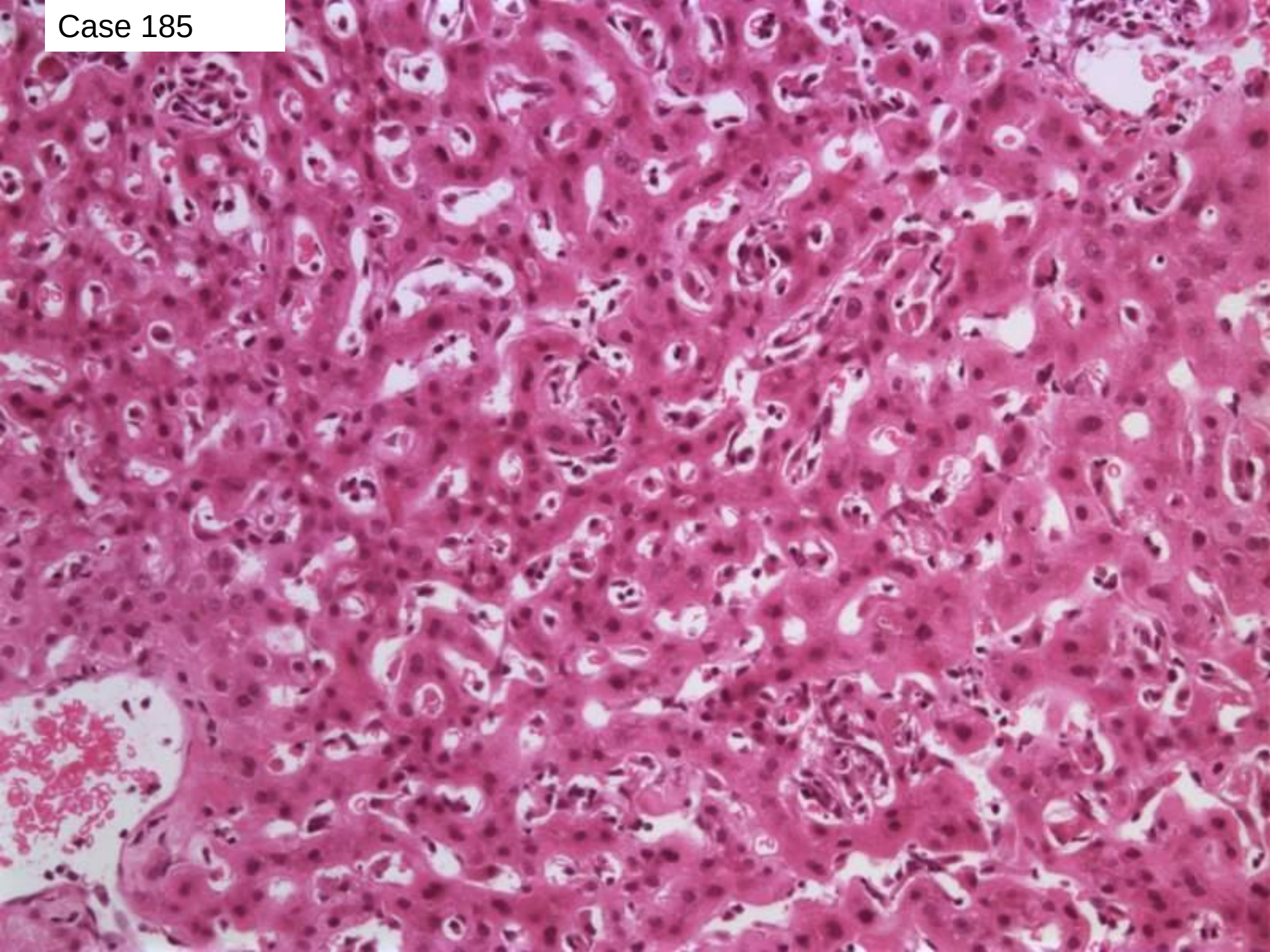




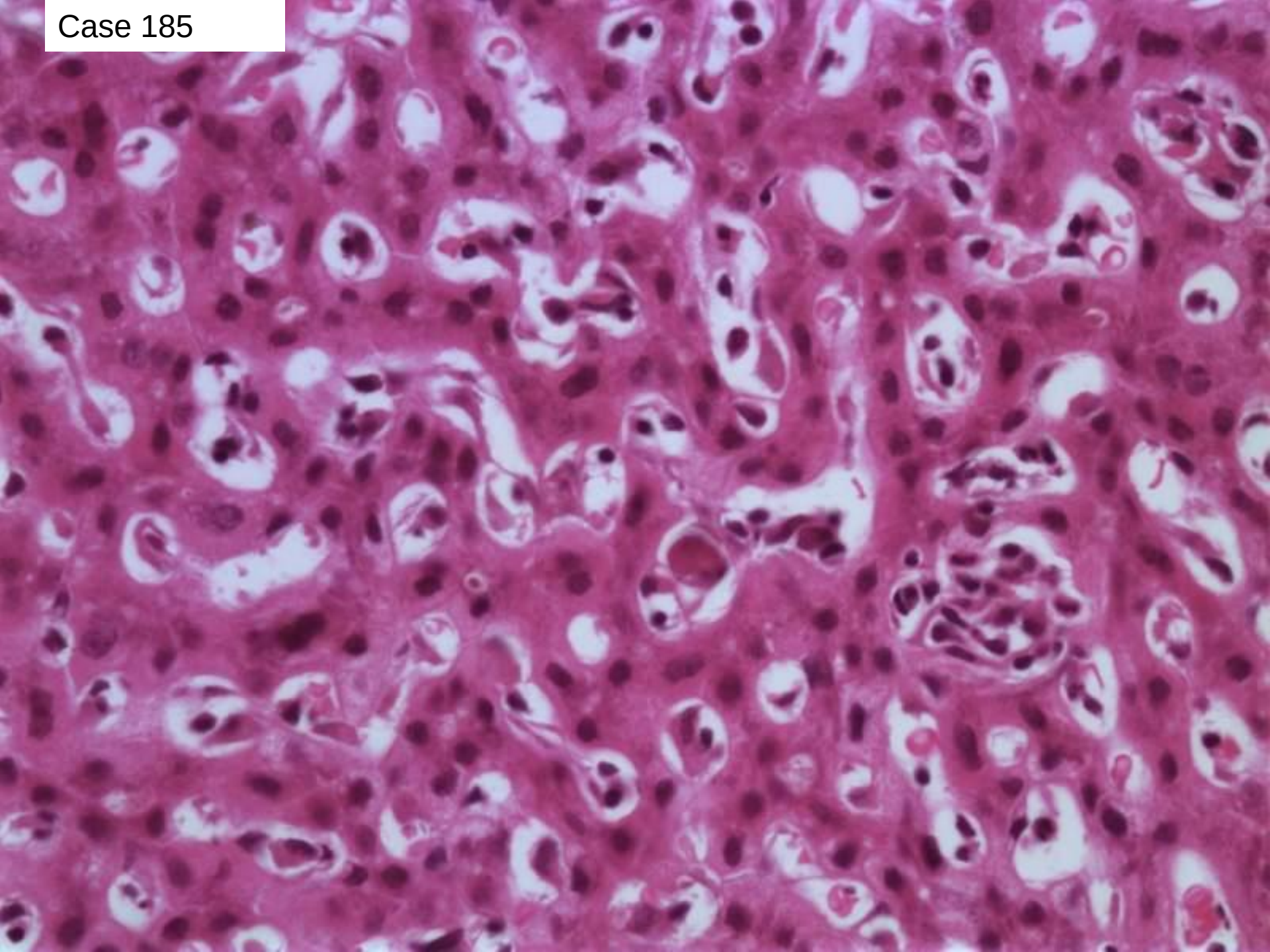
Case 185



Case 185



Case 185



Case 185

Summary of Responses:

Morphological diagnosis only

acute hepatitis or cholestatic hepatitis – 40

Morphology +aetiology

possible, probable, or unqualified drug induced hepatitis – 226

hepatitis – drug or autoimmune – 70

chronic hepatitis probably drug – 10

Aetiology only

autoimmune hepatitis – 5

PBC – 6

Comments on unusual mononuclear infiltrate:

?HBV haematological disorder, lymphoproliferative, Kupffer cell hyperplasia – 58

Other diagnoses

chronic biliary disease, ?obstruction +drug reaction – 10

florid reactive hepatitis and duct obstruction – 20

no diagnosis – suggestions for further investigations – 10

Absence of consensus
therefore case excluded from scoring

Case 185

Comments:

- doesn't look like autoimmune hepatitis despite autoantibodies – 6
- exclude EBVs, CMV etc – 3
- Leishmaniasis, listeria.
- Haemophagocystosis – 2

Follow up information from Bernard Portmann:

Cliniclpathological diagnosis: Hepatitis with autoimmune features associated with minocyclin. There was no known haematological condition.There was no known biliary disease.

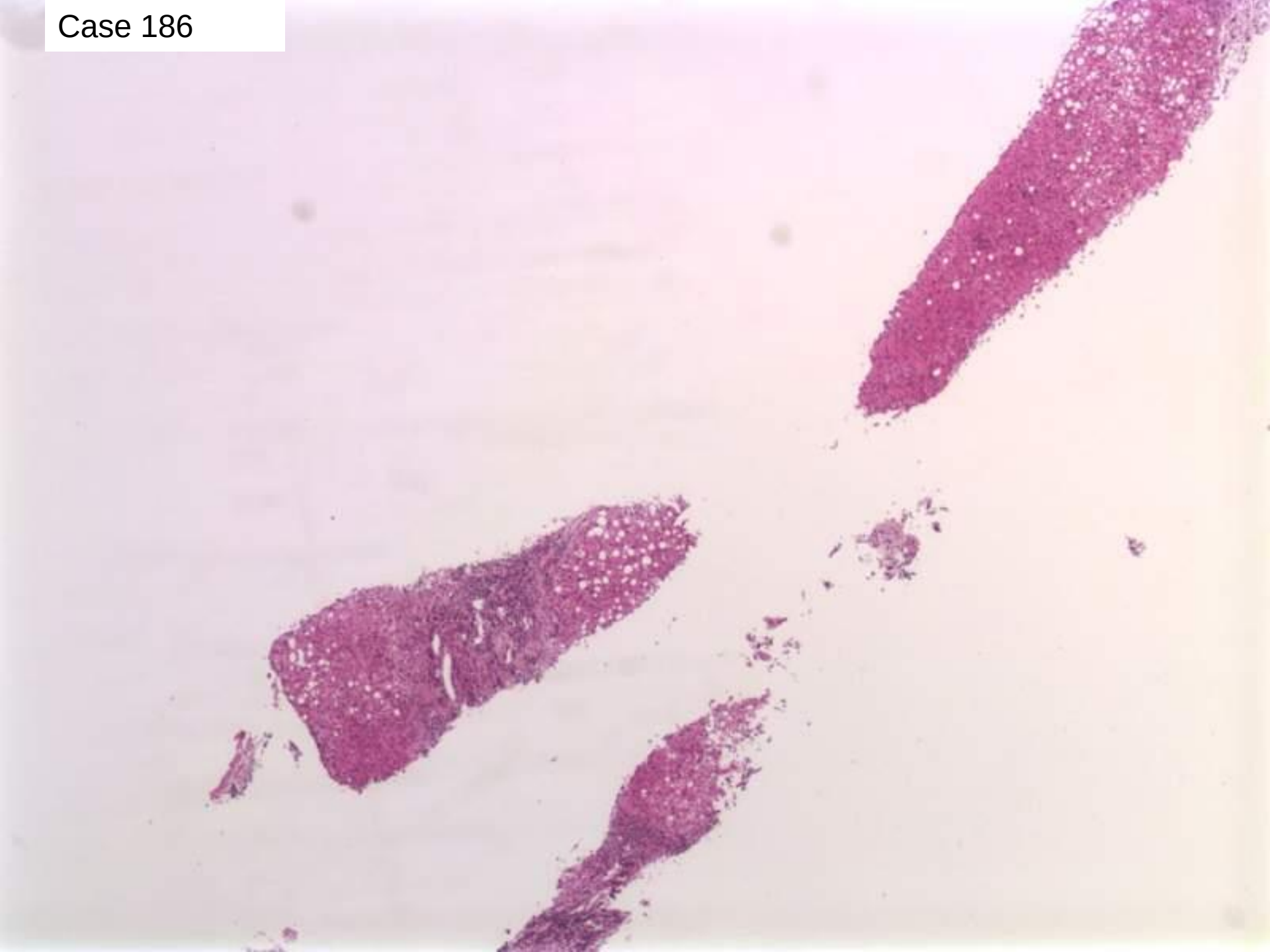
She made a slow but complete recovery over 2 months, no steroids were given.

There is a recognised association between minocycline and autoimmune hepatitis – with female preponderance, hypergammaglobulinaemia and anti-nuclear and smooth muscle antibodies.

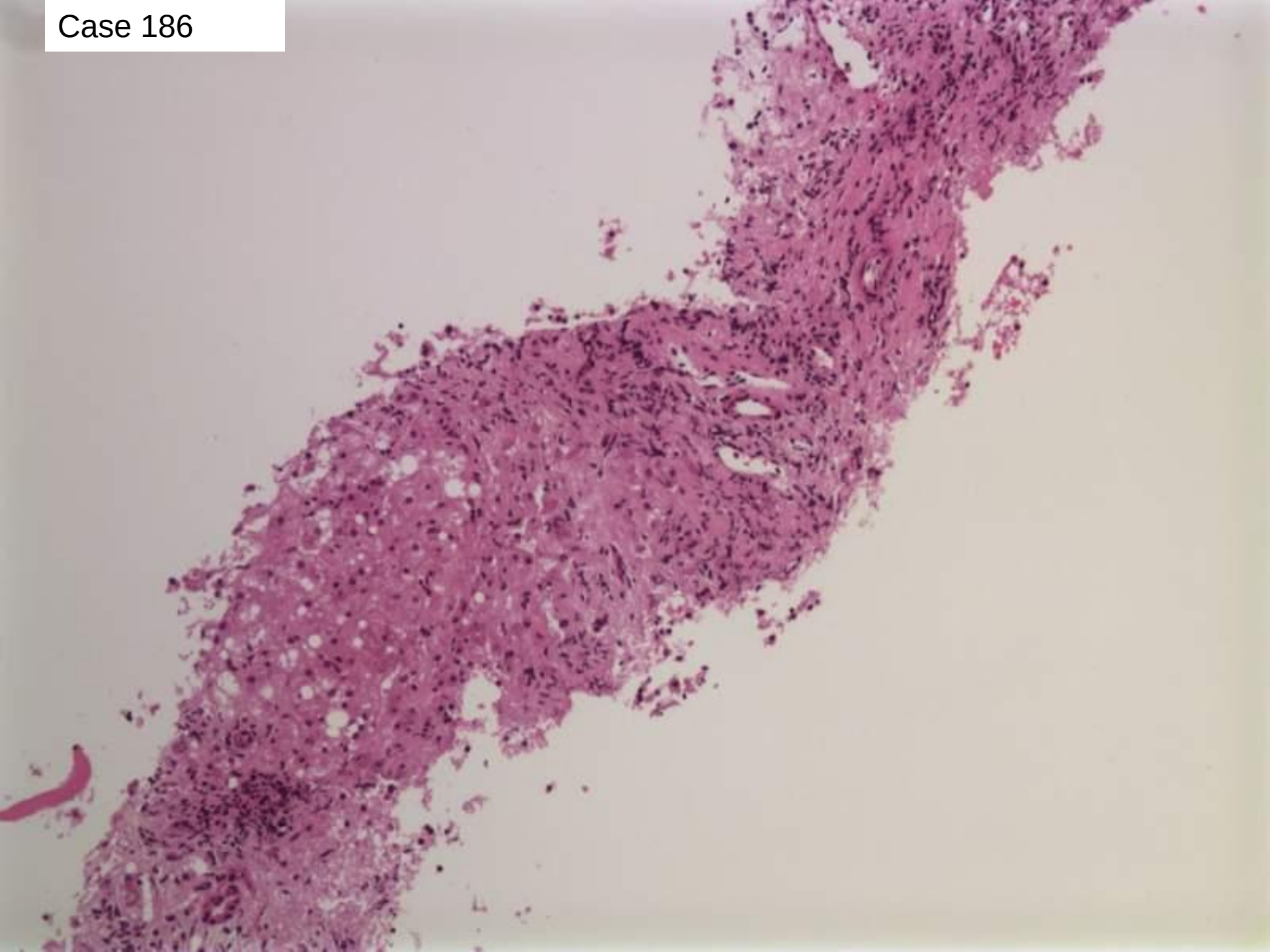
Case 186

Information provided: Female 62. Diffusely abnormal liver on ultrasound sound scan. History of diabetes.

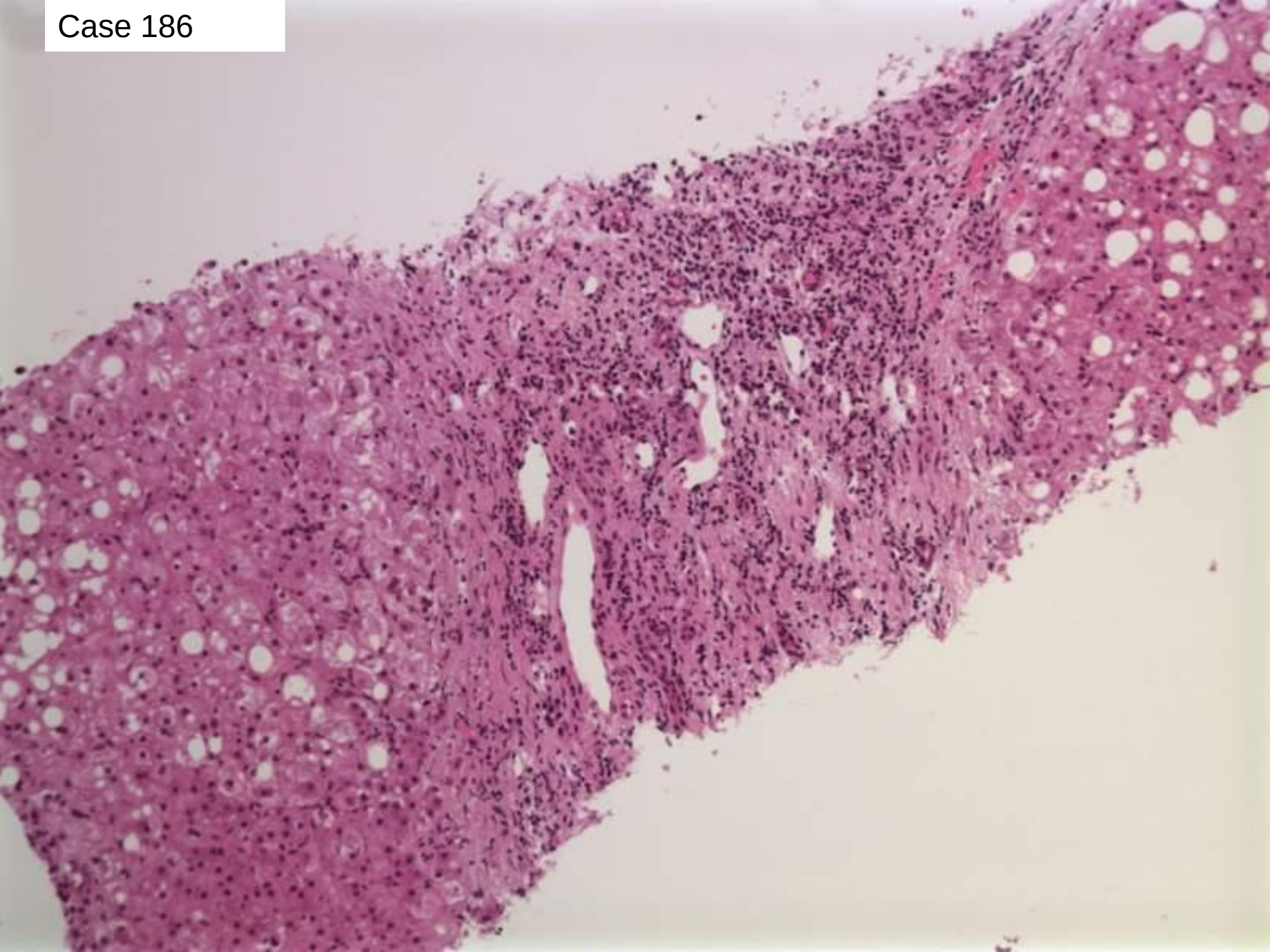
Case 186



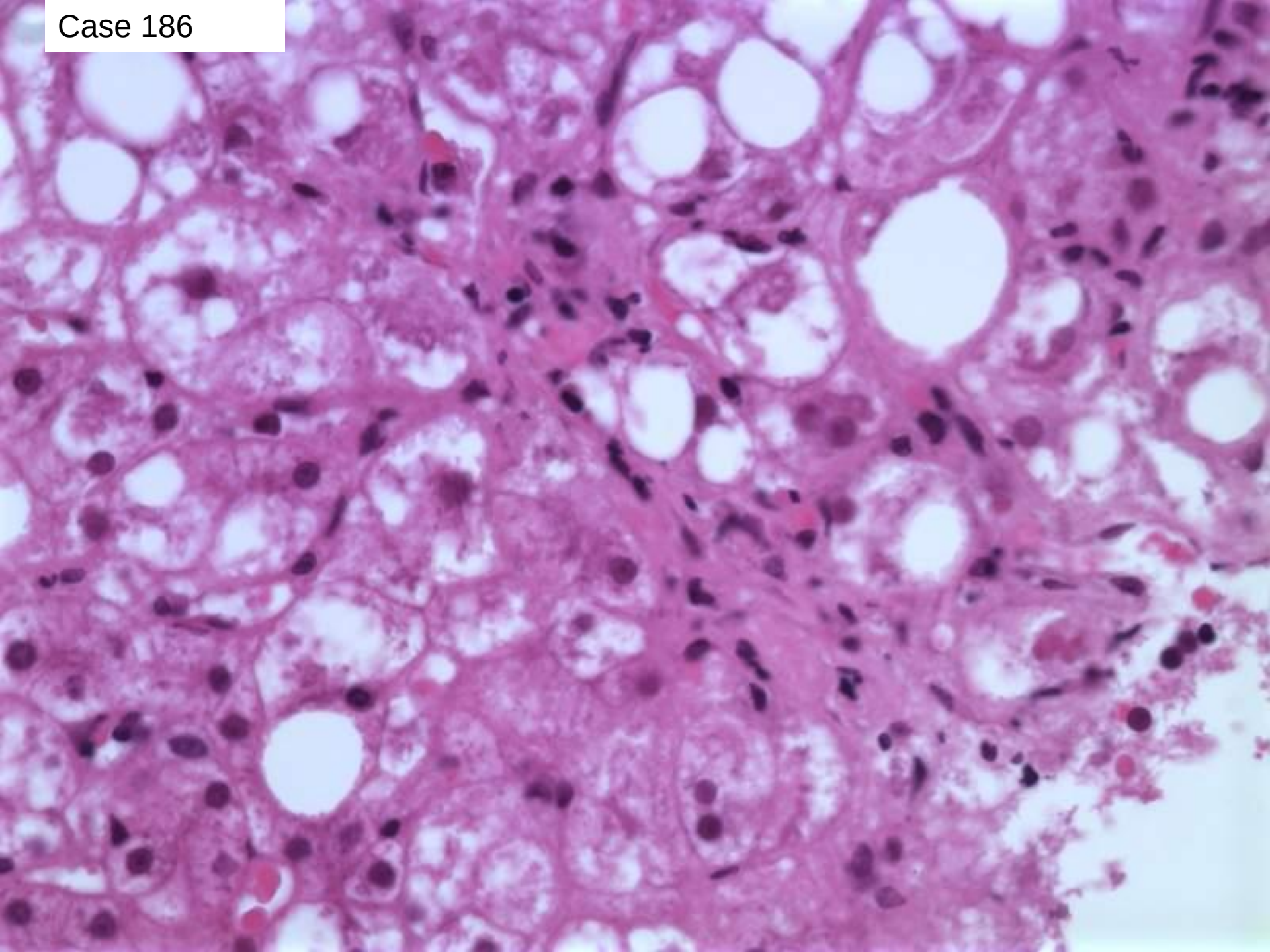
Case 186



Case 186



Case 186



Case 186

Summary of Responses:	*Accepted diagnoses:*
Morphology and aetiology	
cirrhosis + steatohepatitis consistent with ASH or NASH – 220	Yes
alcoholic cirrhosis and hepatitis – 10	No
cirrhosis – probable alcohol - 20	Yes
NASH +cirrhosis – 50	Yes
NASH +?cirrhosis – 20	Yes
Diagnoses with stage not mentioned	
NASH exclude alcohol – 10	No
steatohepatitis consistent with NASH – 20	No
fatty liver hepatitis – 10	No
Diagnoses with no aetiology	
steatohepatitis +probable cirrhosis – 70	Yes
early cirrhosis – 10	No
Others	
diabetic NASH/chronic hepatitis C – 10	No
PBC in cirrhotic stage – 10	No

Case 186

Comments

- Excess inflammation, ?HCV – 3
- Special stains – 14
- Careful alcohol history - several.

Comments during discussion:

Answers needed to include some mention of cirrhosis or probable cirrhosis to be accepted.

While fibrosis can only be accurately assessed with special stains, a comment on whether it is absent, present, or cirrhotic can be made on H&E.

Case 186

Additional information: Dr Kitching

Presented 1997 hepatomegaly to umbilicus.

Diabetic 88kg, psychiatric history, on thioridazine

Biopsy showed fatty change and ballooning.

Drug stopped, leading to dramatic shrinkage of liver.

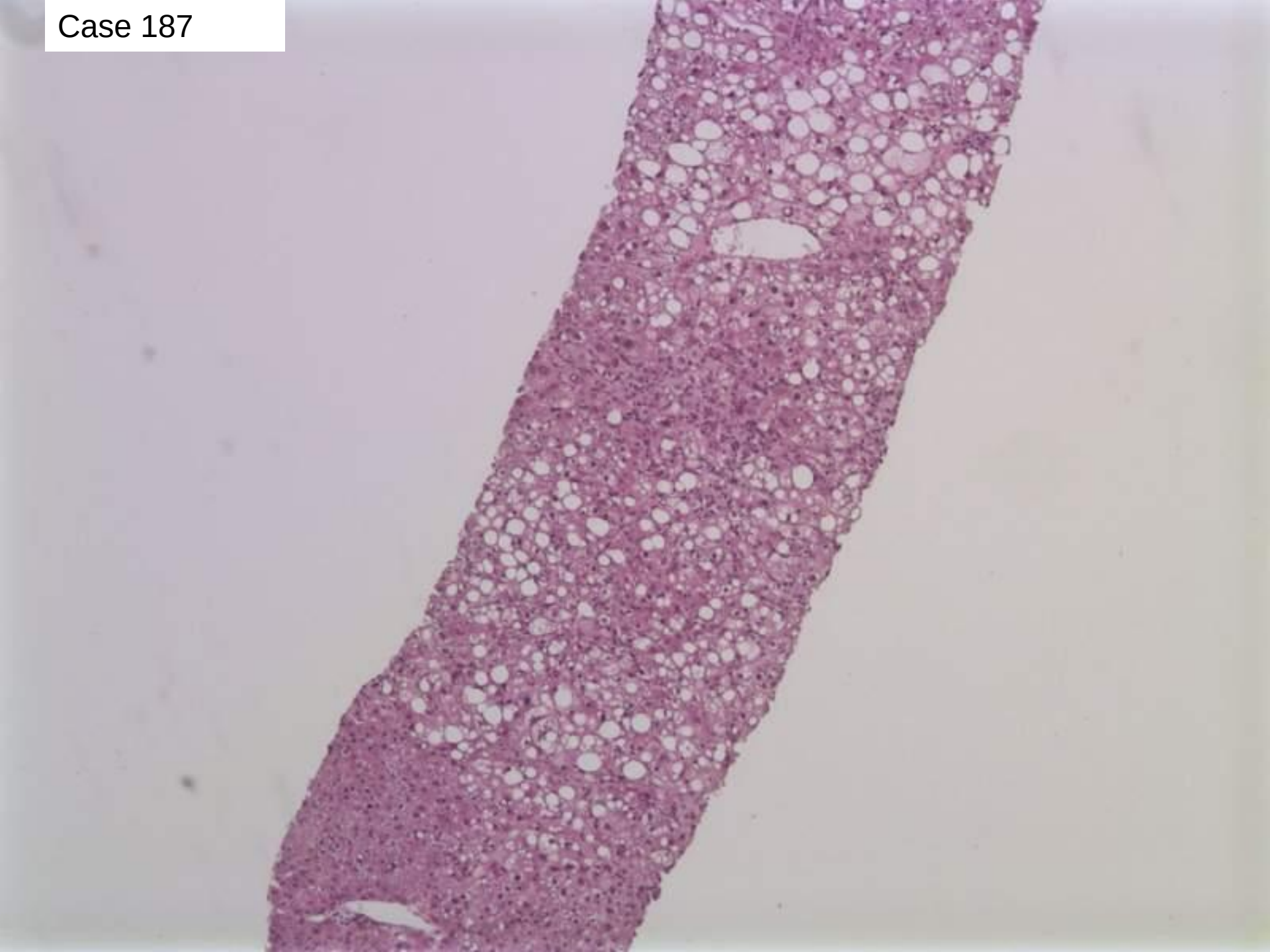
May 2003: ascites, biopsy showed cirrhosis and steatohepatitis.

Died Sept 2003: GI bleed, ascites, hepatorenal failure

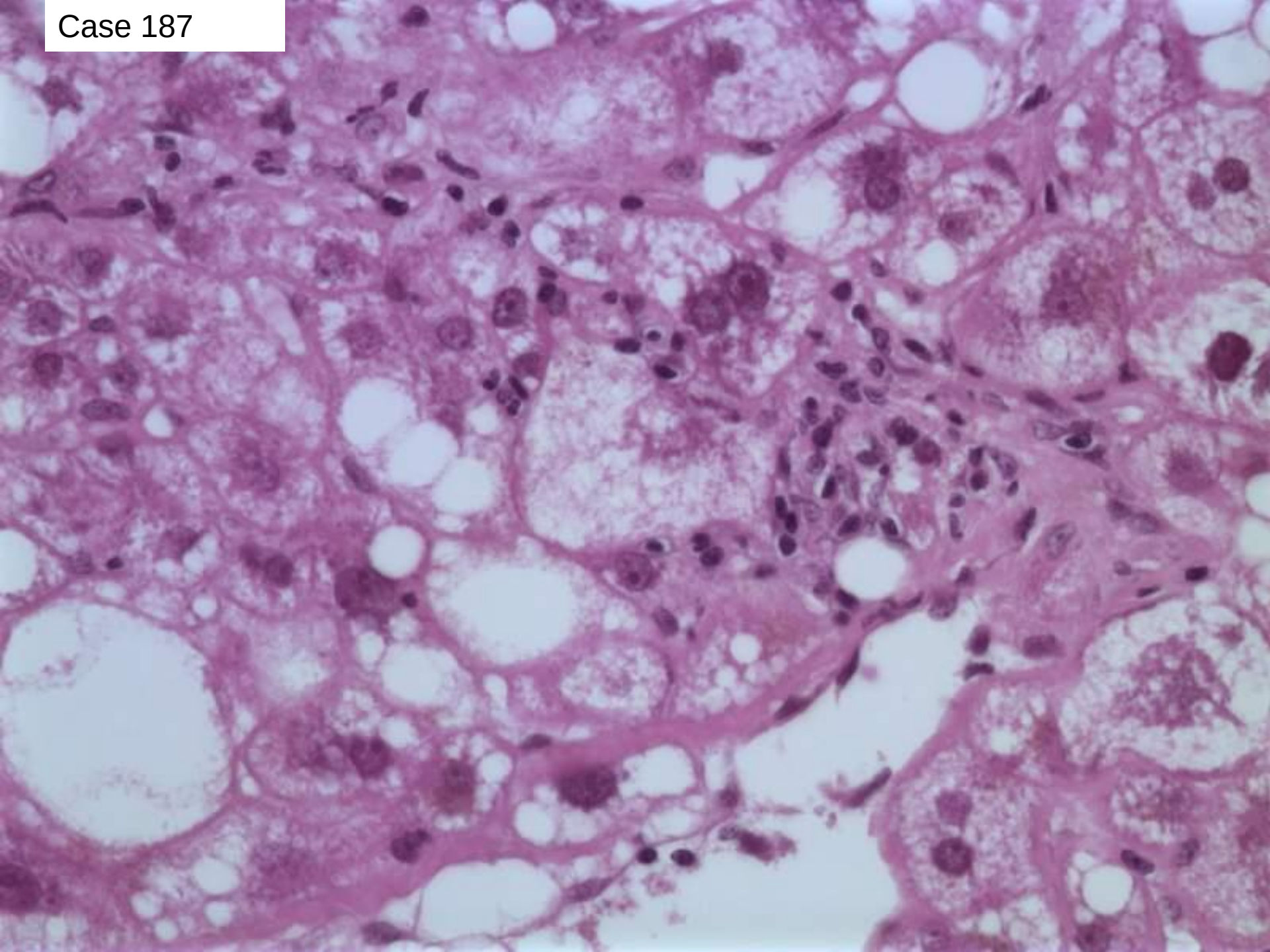
Case 187

Information provided: On Methotrexate for psoriasis. Has received 2.13 gms in total. Increased procollagen III. Also on Amlodipine and Bisoprolol. Raised alkaline phosphatase. GT upper limit of normal. ?safe to continue medication.

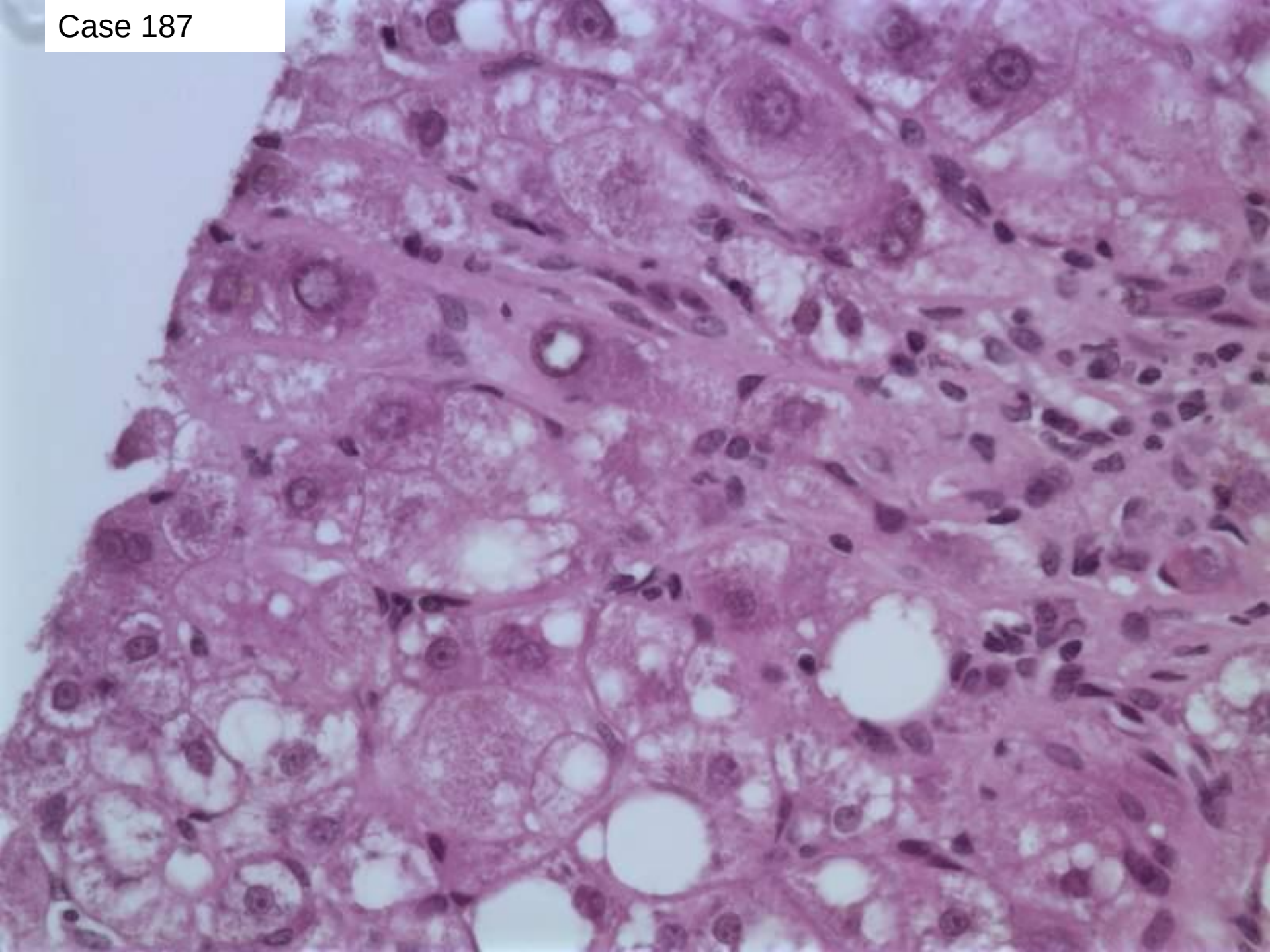
Case 187



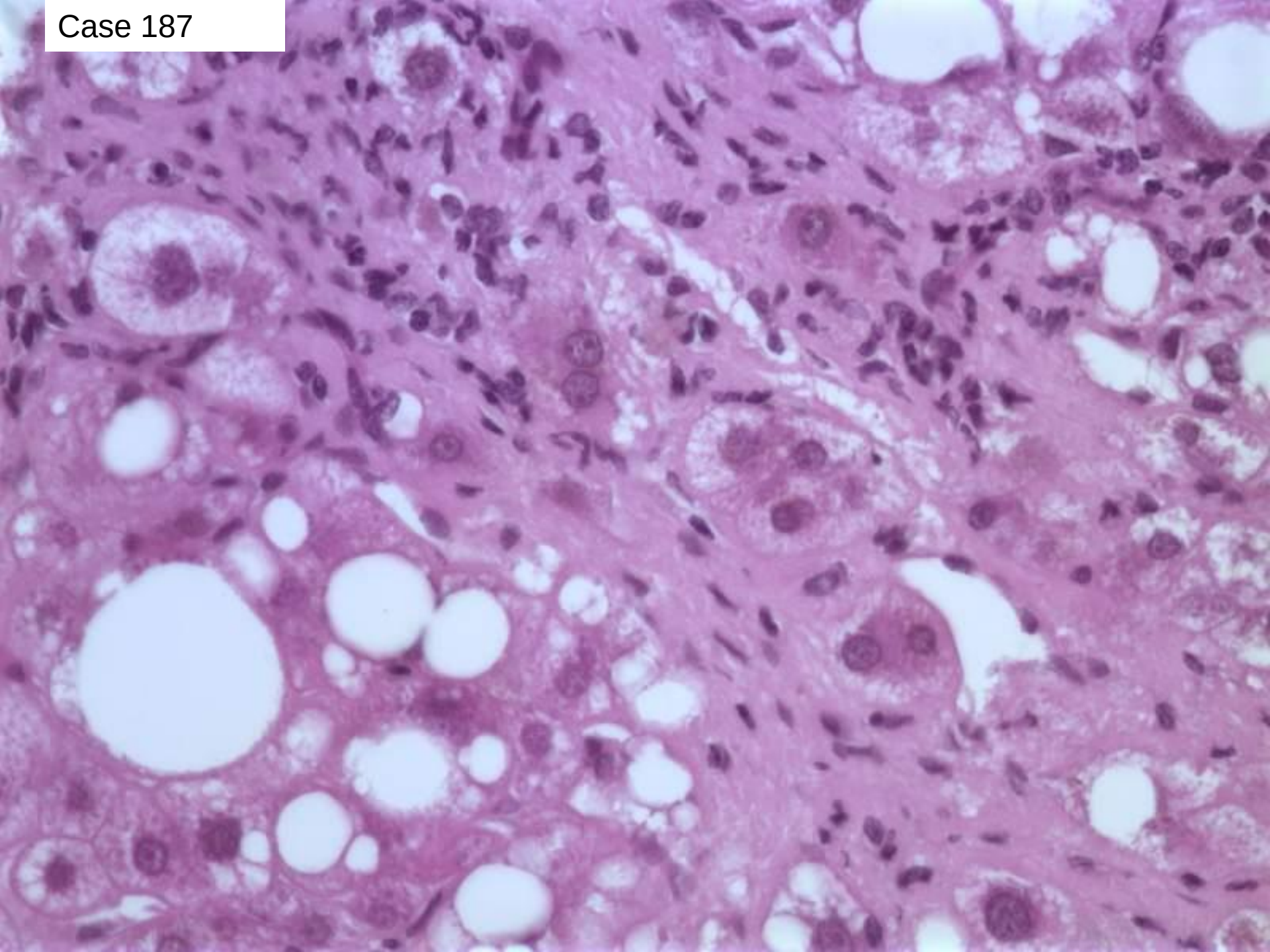
Case 187



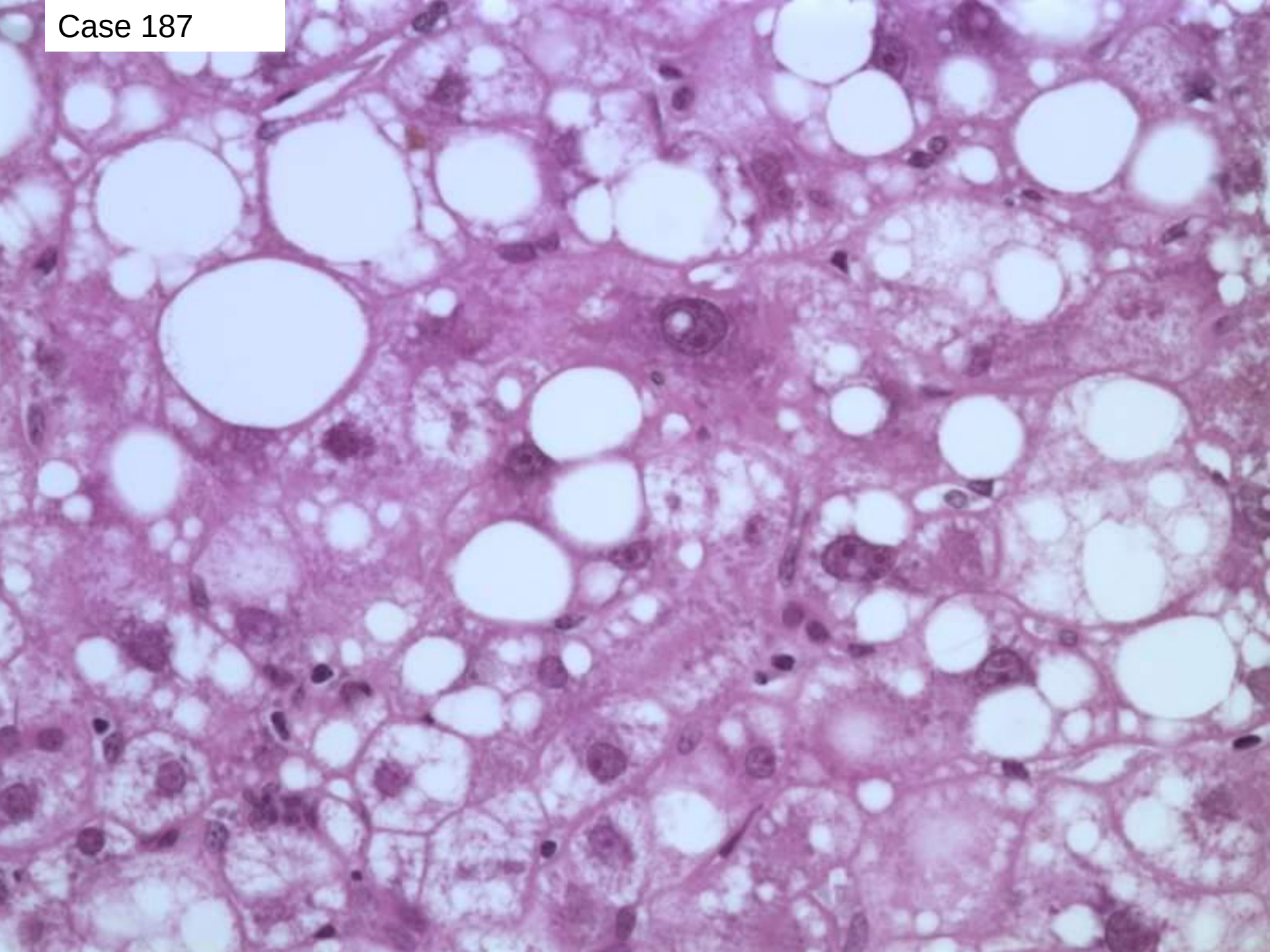
Case 187



Case 187



Case 187



Case 187

Summary of Responses:	*Accepted diagnoses:*
Morphological diagnosis:	
steatohepatitis or fatty liver hepatitis – 90	Yes
steatosis with fibrosis – 50	Yes
steatohepatitis with fibrosis – 10	Yes
steatohepatitis with cirrhosis – 10	Yes
fatty change nuclear changes ± fibrosis – 20	Yes
Responses that mention Methotrexate:	
steatohepatitis with fibrosis. Stop treatment – 120	Yes
steatosis consistent with Methotrexate, fibrosis not mentioned – 50	Yes*
steatosis with fibrosis consistent with Methotrexate – 50	Yes
Methotrexate toxicity (not otherwise specified) – 50	Yes
“no” – 10	no

*Some assessment of fibrosis should be made; however, this can only really be done with connective tissue stains. Since this has not been previously stated, this answer is accepted on this occasion.

There is usually insufficient material in biopsies to circulate additional stained slides, but photomicrographs showing the connective tissue stain should be sent with cases in the future, and by adding an interpretive element would be preferable to a description of what this stain showed.

Case 187

Comments:

- needs connective tissue stains – 24
- should stop Methotrexate indicated anywhere in the result – 28
- continue with caution – 2
- exclude alcohol - 4

Examples “due to Methotrexate but has no cirrhosis would be safe to continue”

“determine cause of profibrogenesis – if can reverse then restart Methotrexate”

Additional comments during discussion:

The information with this case posed a specific question, should answers be accepted if they don’t indicate whether it is safe to continue medication?

Participants felt that this was a clinical decision, based on balancing the risks and benefits of treatment, and that the biopsy was required to inform that assessment, but not as the only basis for determining continued treatment.

Again, steatohepatitis is not characteristic of methotrexate alone, and other causes should be explored.

Case 187

Follow up information:

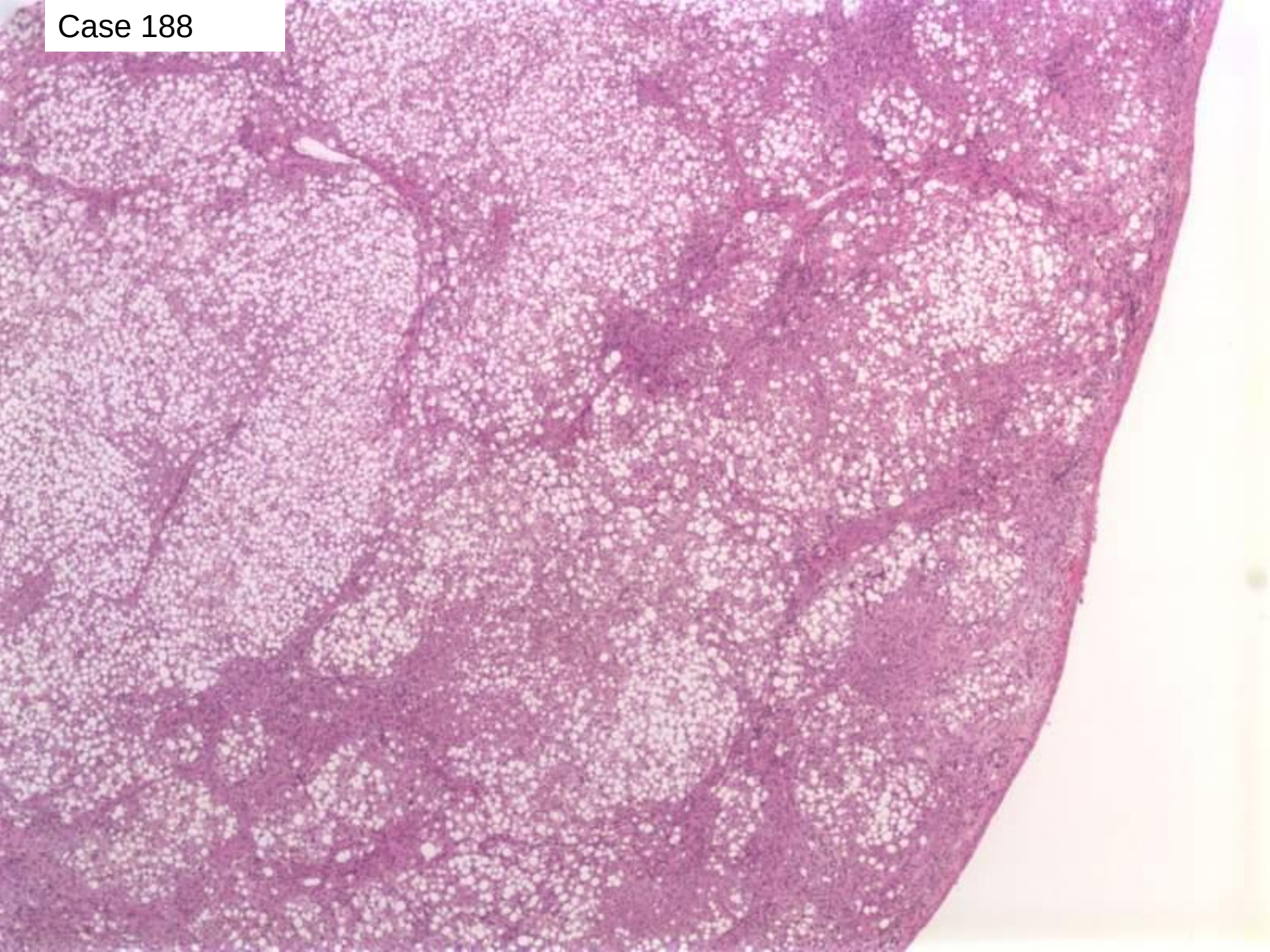
Patient with severe psoriasis with arthropathy; clinicians continued with MTX with careful monitoring.

Case 188

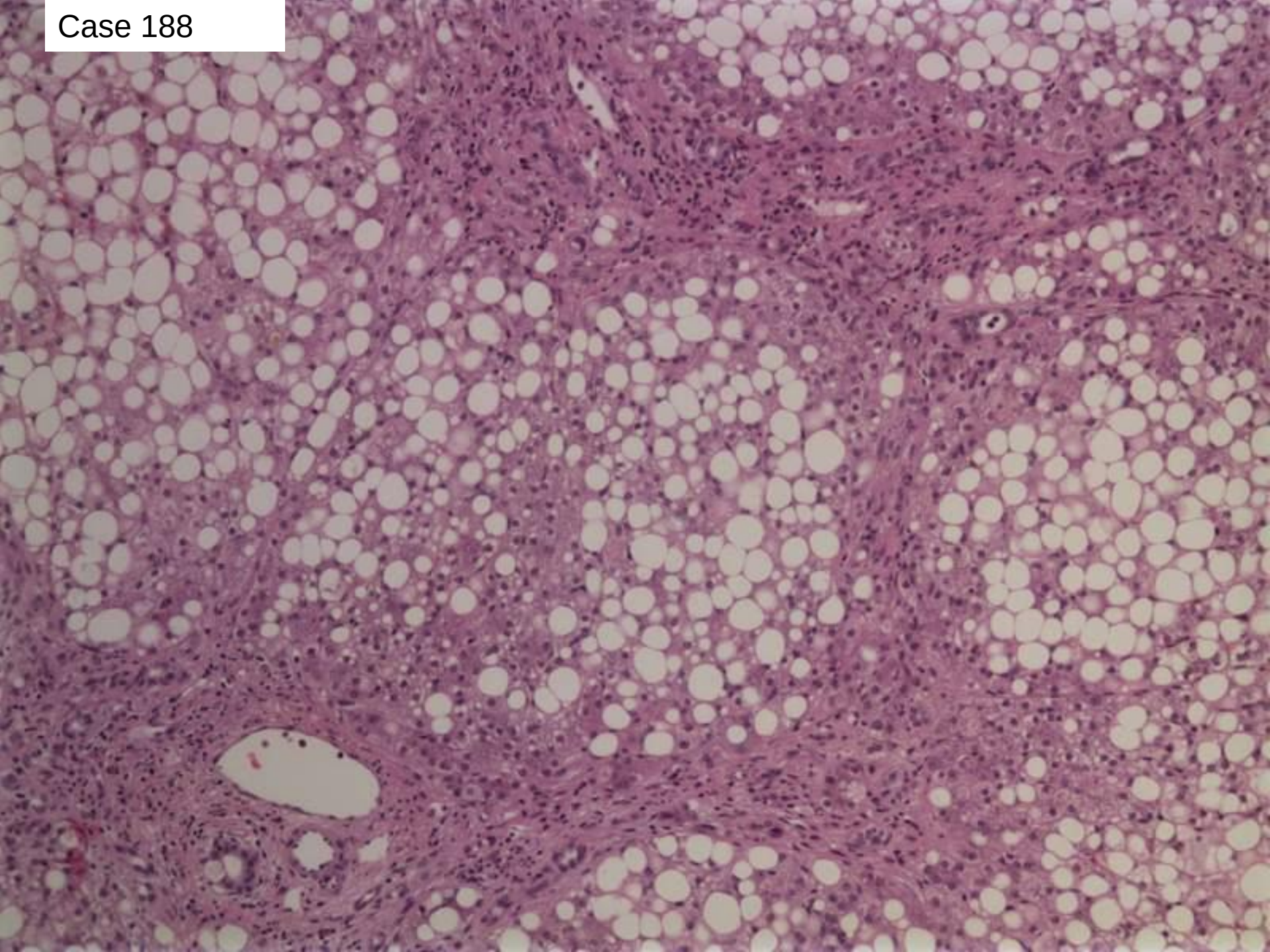
I*nformation provided:* Female 41, acute admission with perforated DU. One week of jaundice. History of depression and alcohol excess.

WVG – bridging fibrous septa with nodules and pericellular fibrosis.

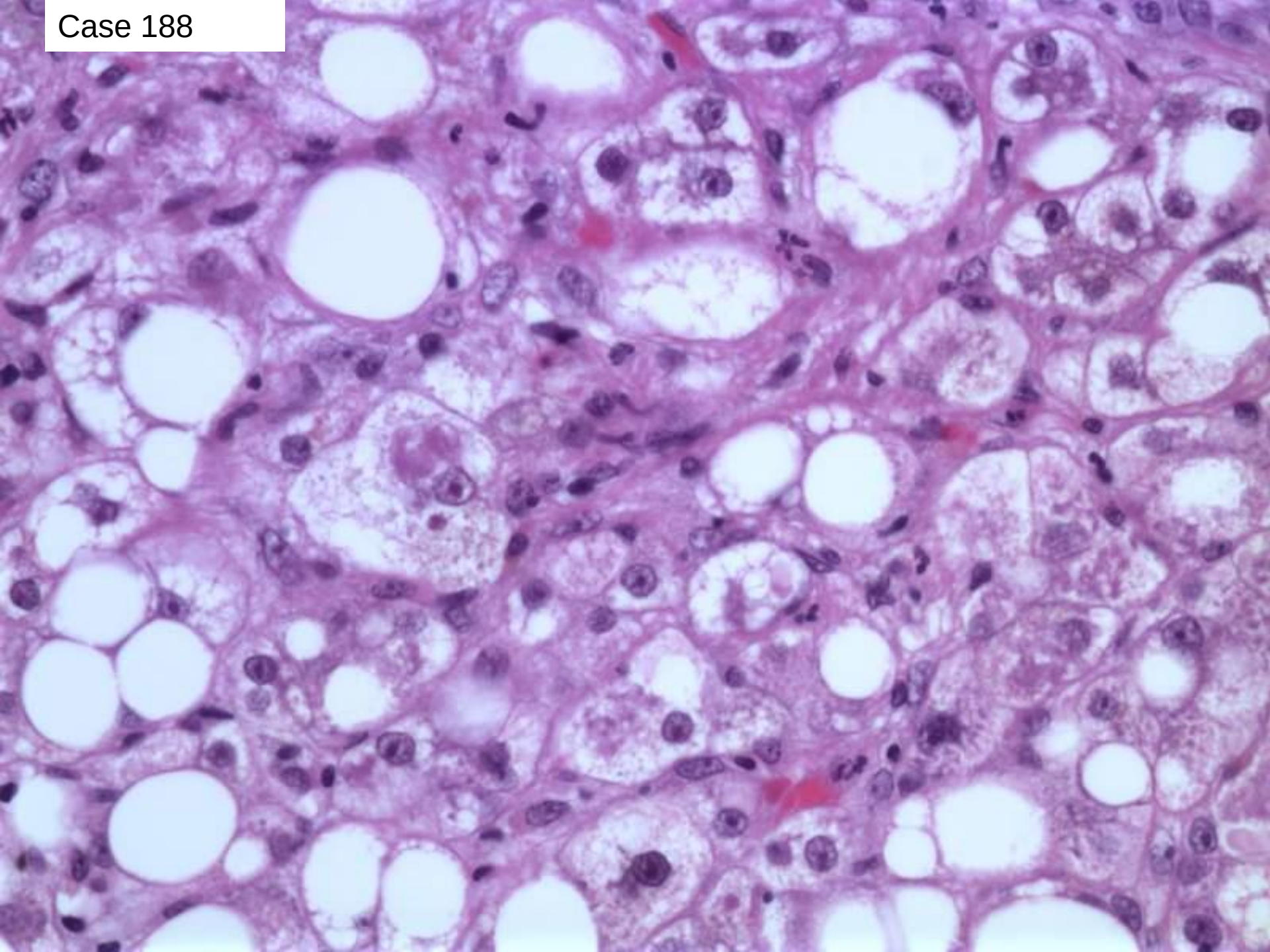
Case 188



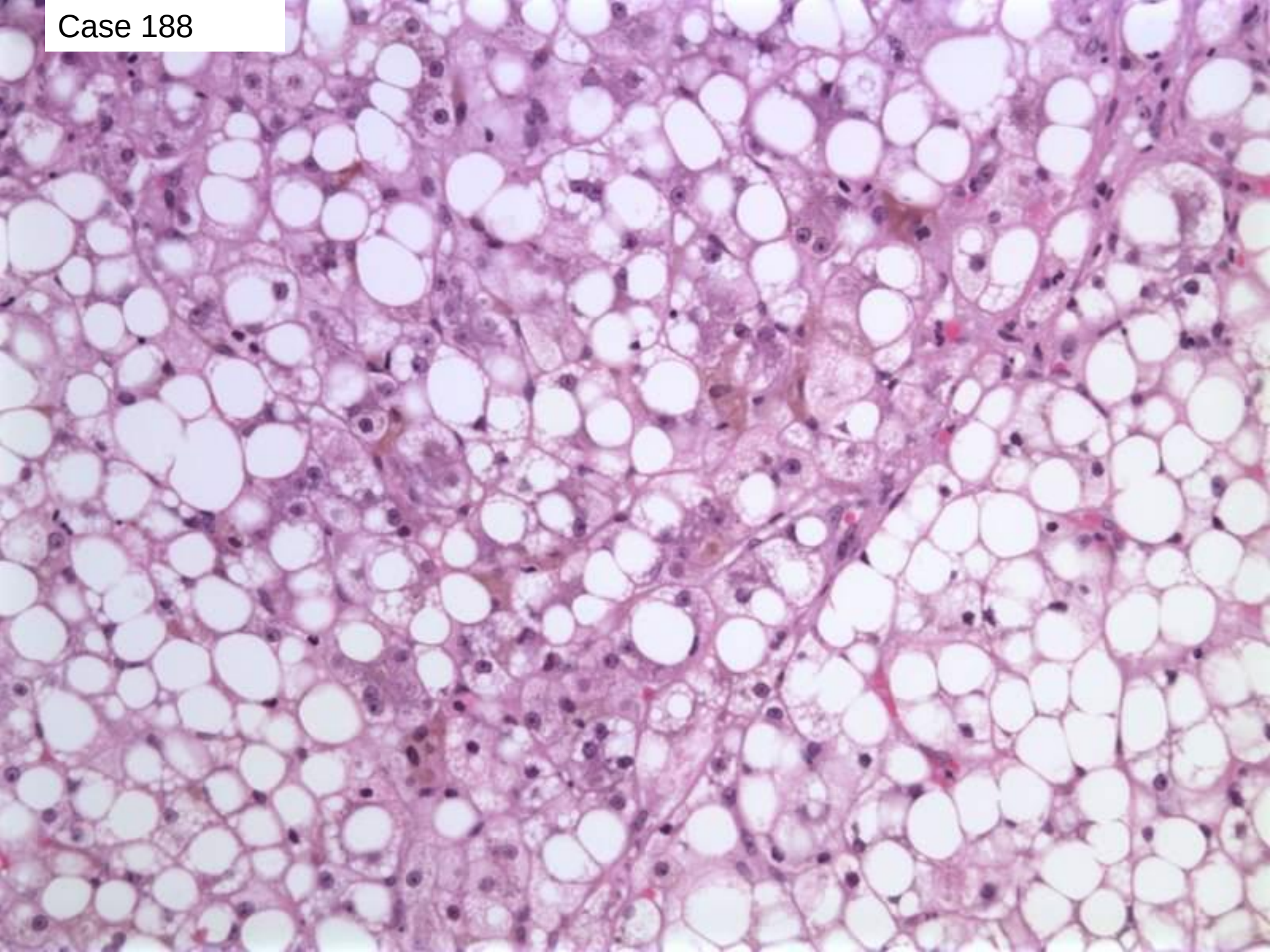
Case 188



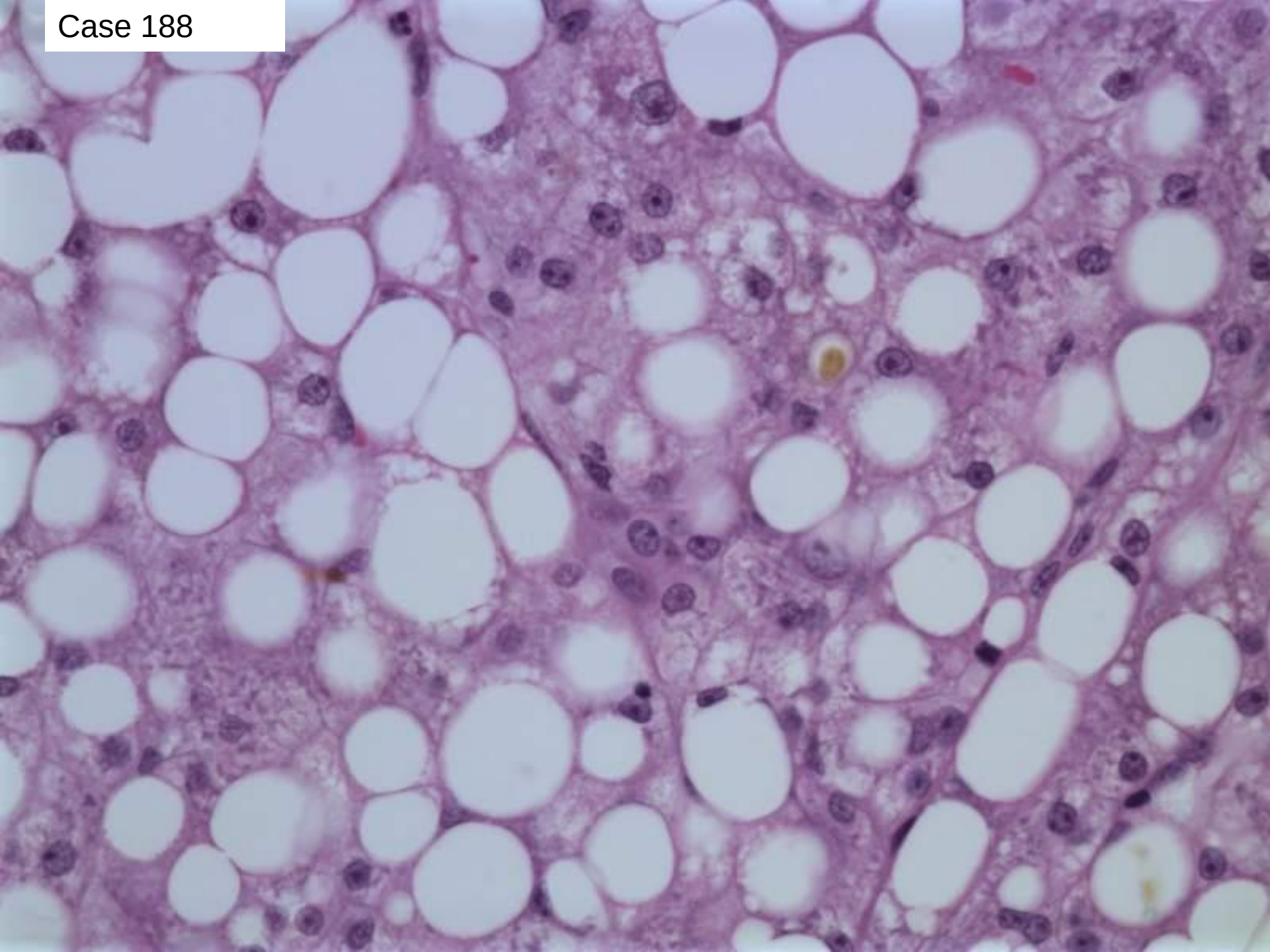
Case 188



Case 188



Case 188



Case 188

Summary of Responses:	*Accepted diagnoses:*
Alcoholic liver disease	
cirrhosis, alcoholic or probably alcoholic – 190	*Yes*
alcoholic liver disease probably cirrhosis – 50	*Yes*
alcoholic liver disease, not yet fully cirrhotic – 30	*Yes*
alcoholic fatty liver disease – 10	*No*
Consistent with alcoholic liver disease	
steatohepatitis, probable cirrhosis, consistent with alcohol – 20	*Yes*
steatohepatitis + fibrosis consistent with alcohol – 30	*Yes*
steatohepatitis with early fibrosis consistent with alcohol – 10	*Yes*
steatohepatitis consistent with alcohol – 10	*Yes*
steatosis, fibrosis and cholestasis consistent with alcohol - 7	*Yes*
Morphological diagnosis without aetiology or not alcohol	
steatohepatitis +cirrhosis – 30	*Yes*
steatohepatitis with marked pericellular/perivenular fibrosis – 40	*Yes*
steatohepatitis (unqualified) – 20	*Yes*
steatosis, fibrosis and cholestasis – NASH – 10	*No*
- drug related – 3	*no*

Case 188

Comments:

- Cholestasis ?drug/obstruction/sepsis – 4

Additional comments during discussion:

More information about alcohol consumption (how recent, how much?) is needed to make a definite diagnosis of alcoholic liver disease.

Was there an additional identified cause for the steatosis?

Steatohepatitis implies some fibrosis and so the responses that just state steatohepatitis without a comment on fibrosis are still accepted.

Follow up information from Dr Cope:

Clinical diagnosis = alcoholic cirrhosis, died within a couple of months of this biopsy.

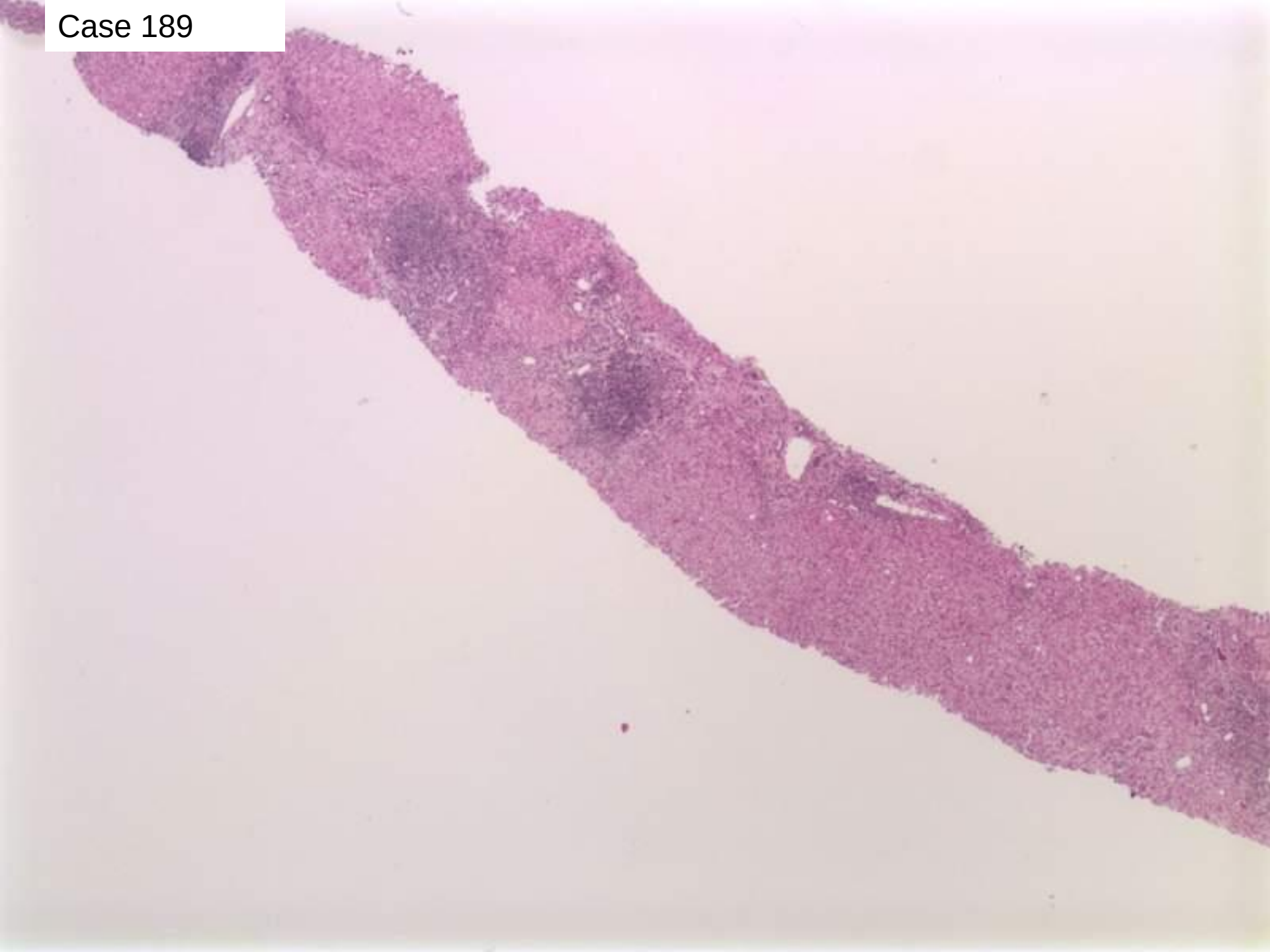
Case 189

Information provided: Male 48. Previous alcohol++.

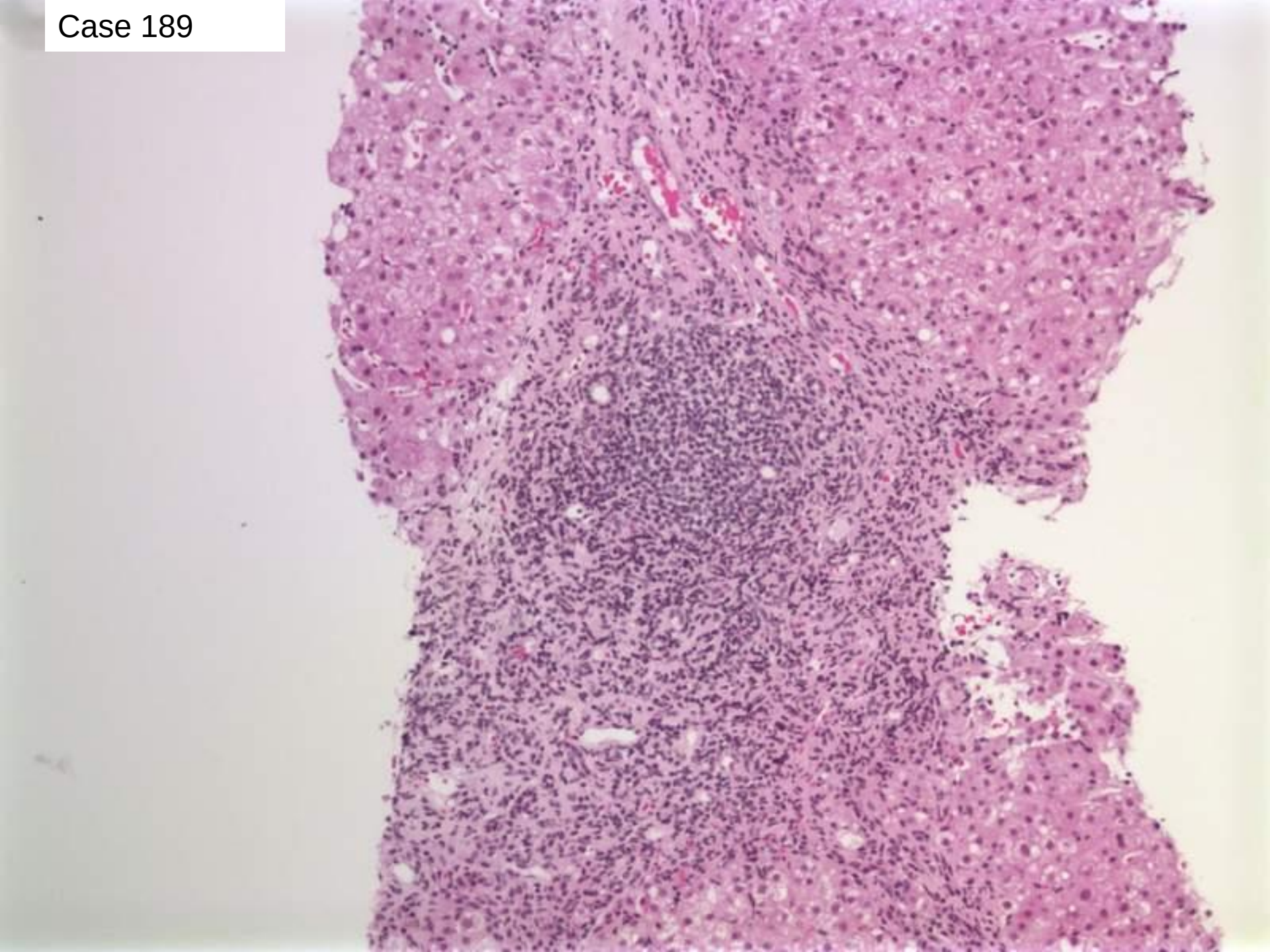
HCV positive.

AST 93.

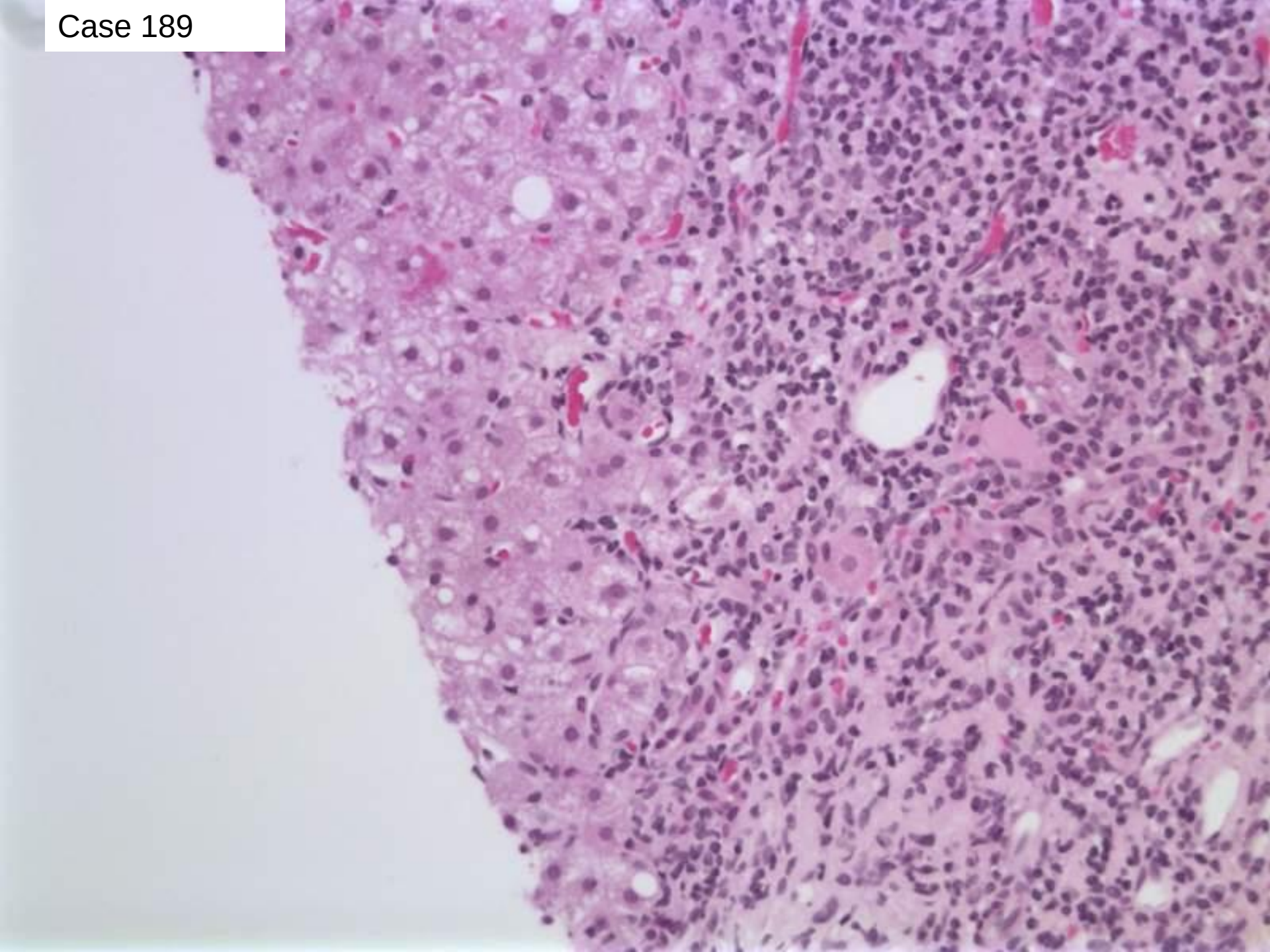
Case 189



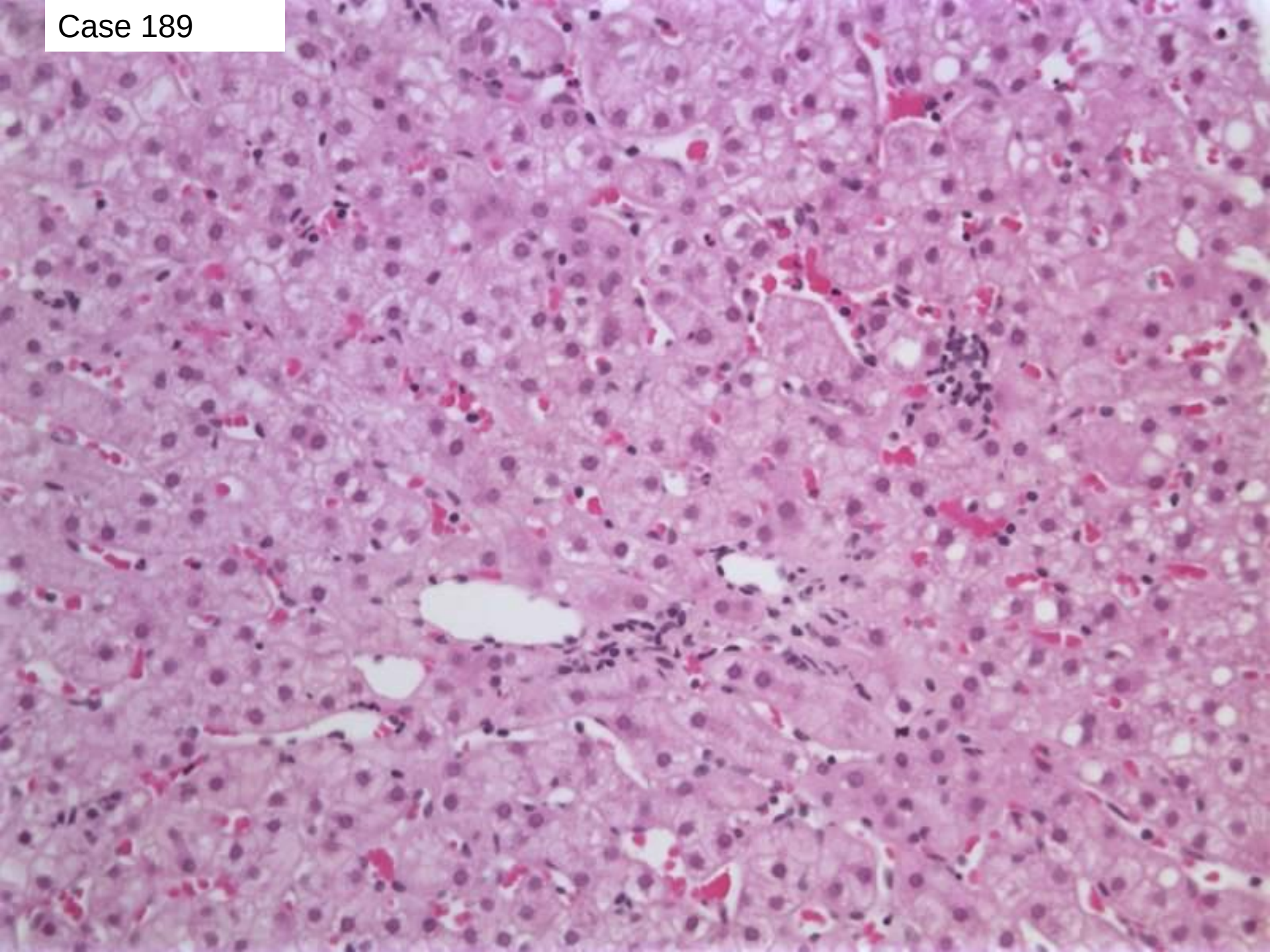
Case 189



Case 189



Case 189



Case 189

Summary of Responses:

chronic hepatitis consistent with HCV, HCV liver disease – (no mention of stage or grade) – 90

Hepatitis C, cirrhosis or probable cirrhosis – 120

HCV, developing cirrhosis or advanced fibrosis – 90

HCV, fibrosis – 60

HCV, mild fibrosis – 20

HCV, stage not mentioned – 40

Cirrhosis or chronic hepatitis - hepatitis C not mentioned – 40

Accepted diagnoses:

All answers accepted.

As 'hepatitis C positive' was stated in information provided, not all participants included it in their diagnosis.

This was discussed, and it was agreed that in future, such given information should be included in the answer when it is an essential part of the histological diagnosis.

Case 189

Comments

- No alcohol related features – 13
- Need special stains for grade and stage – 15
- Evidence of IVDA -1
- ? minimal steatohepatitis, needs ubiquitin – 3

Case 189

Additional information from Dr Dube:

Reported as chronic HCV and alcohol.

History - alcohol dependant and IVDU; off alcohol for 5 months prior to biopsy. Previously 15-20 units/day.

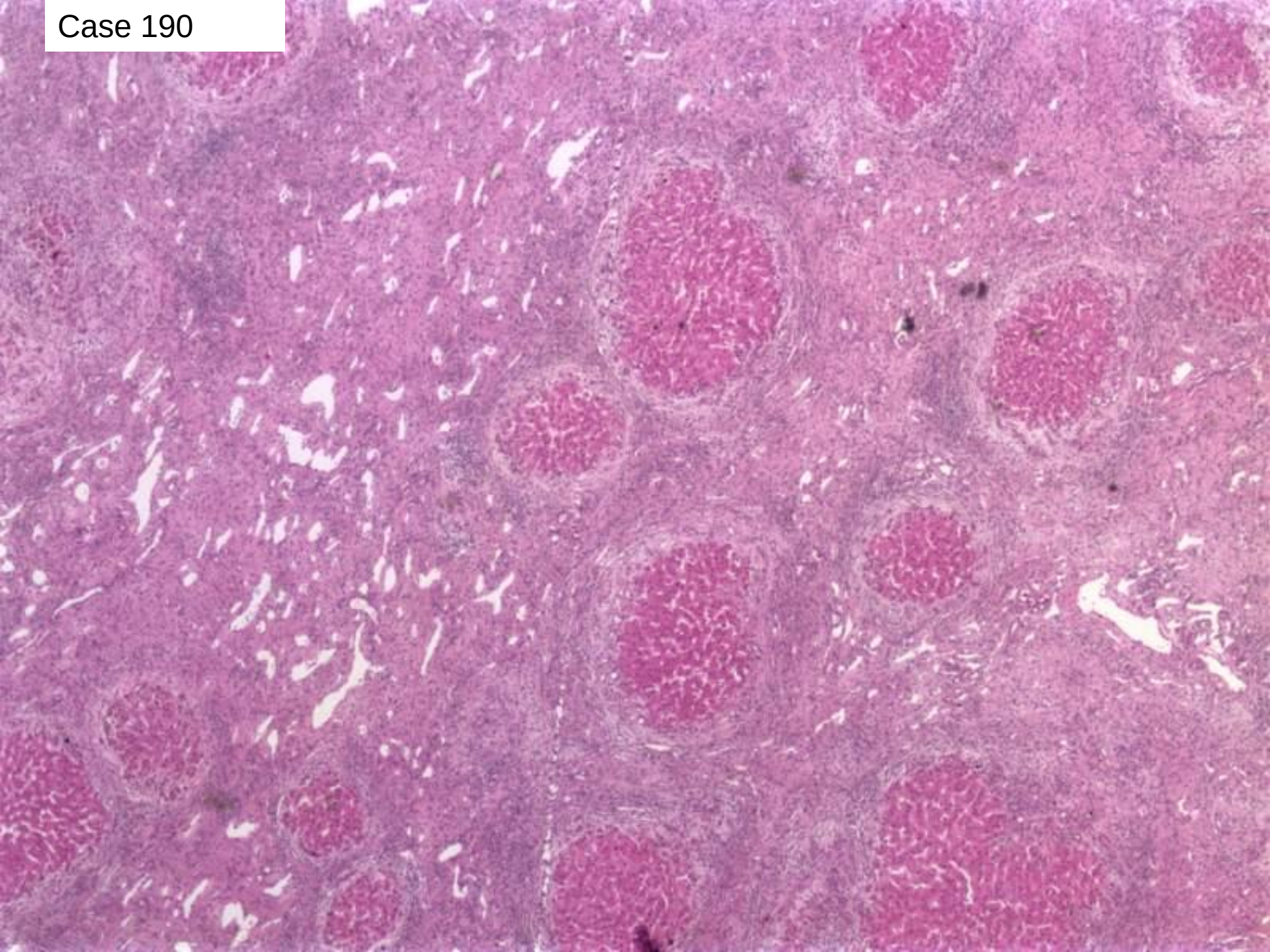
HCV genotype 1a

Considered to have chronic HCV (?exacerbated by alcohol in the past)

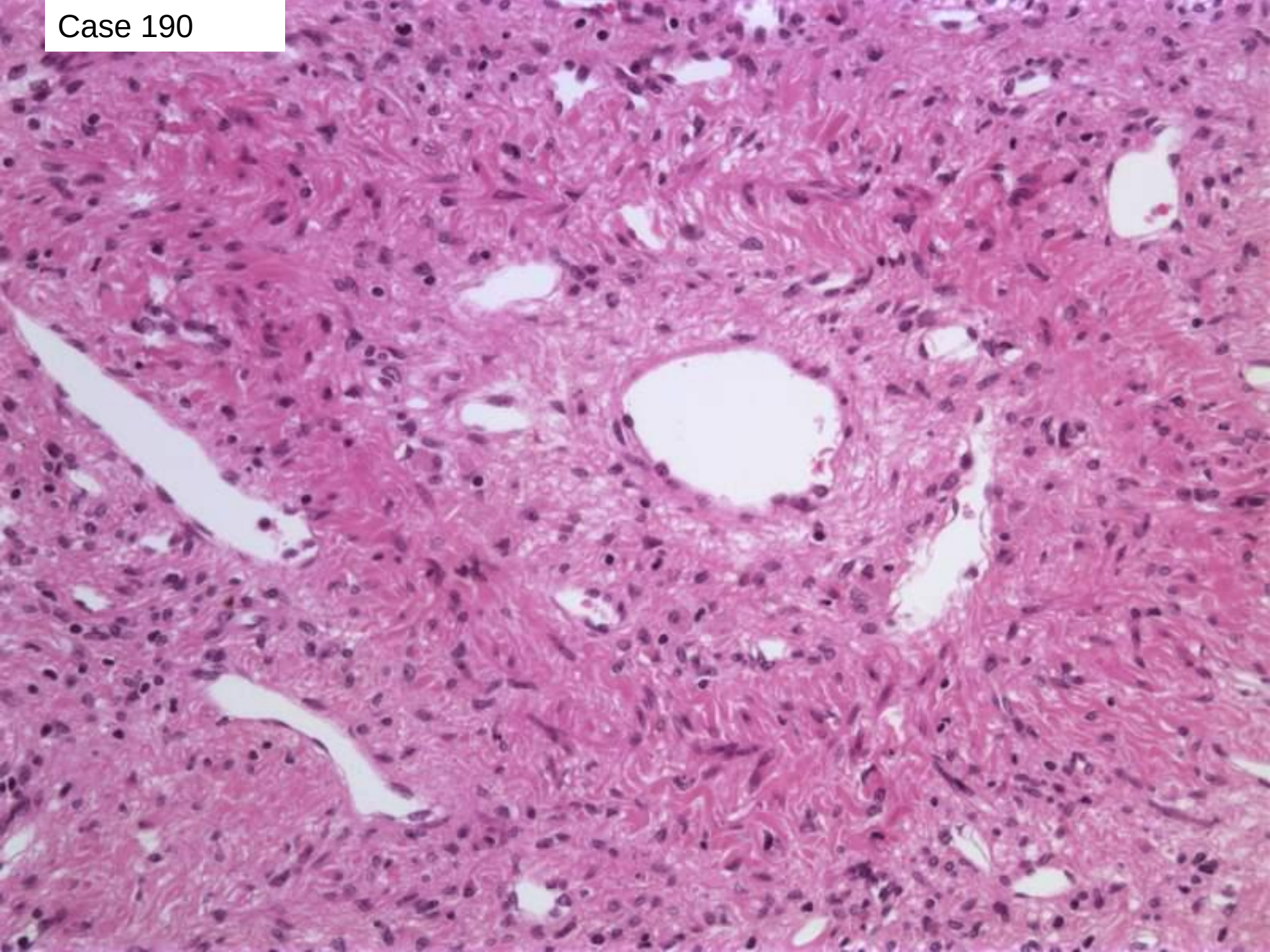
Case 190

Information provided: 25 year old man, transplanted for PSC.

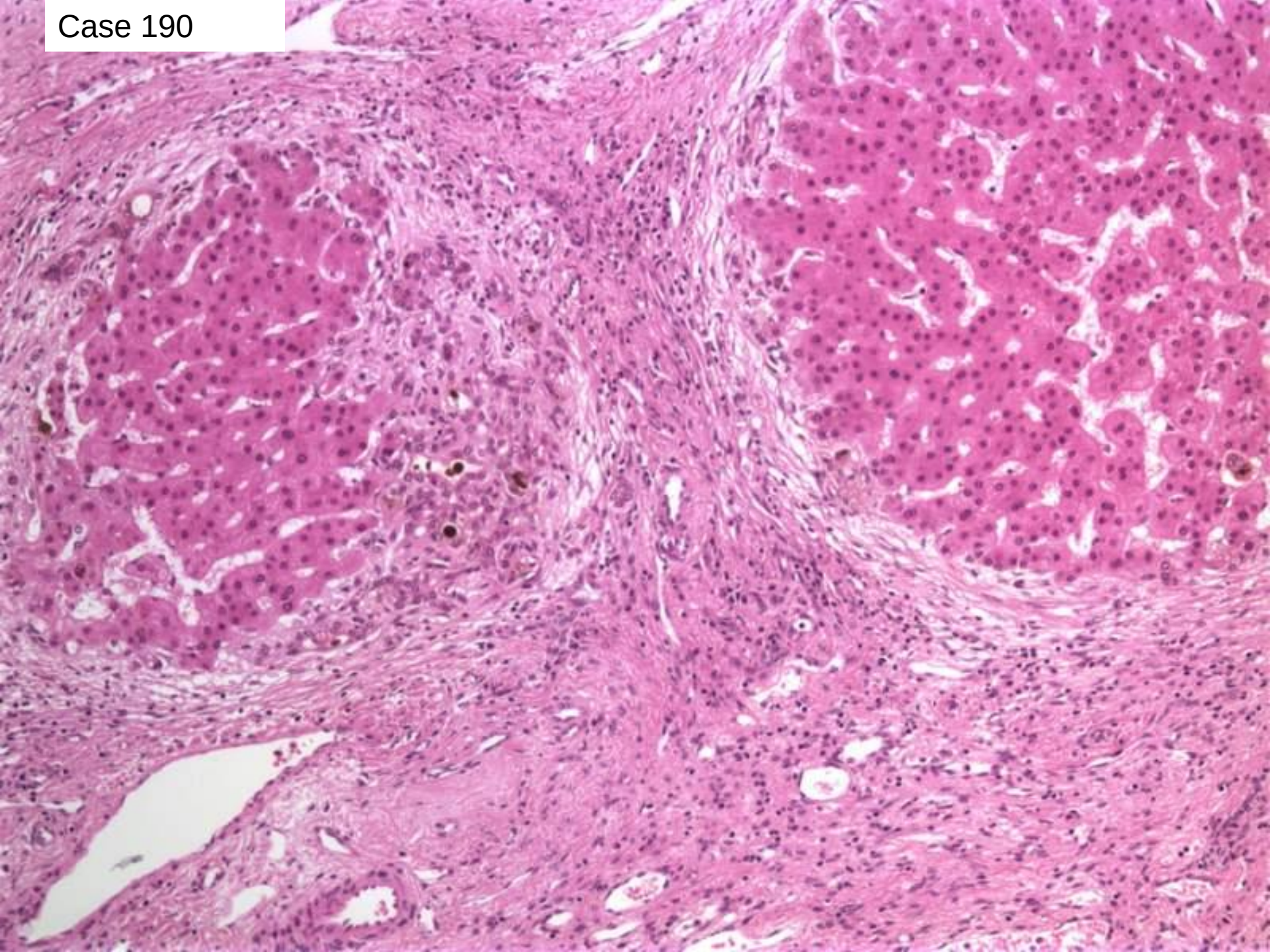
Case 190



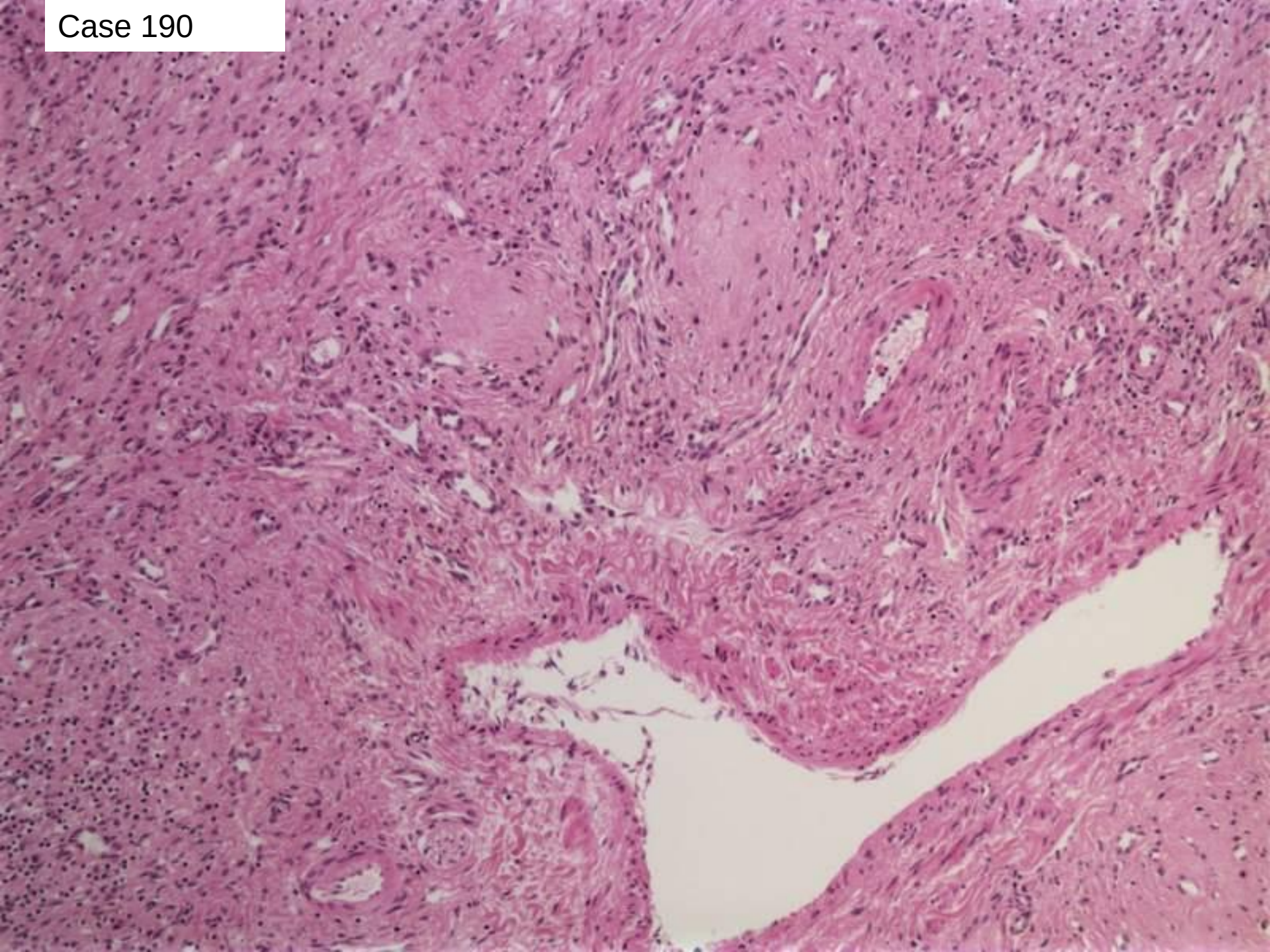
Case 190



Case 190



Case 190



Case 190

Summary of Responses:	*Accepted diagnoses:*
biliary cirrhosis, PSC – 440	Yes
PSC – 20	Yes

Case 190

Comment:

- Big liver but this block atrophic therefore dominant stricture on this side.
- Obliterative venopathy.
- Recent parenchymal collapse/extinction, ?sepsis.

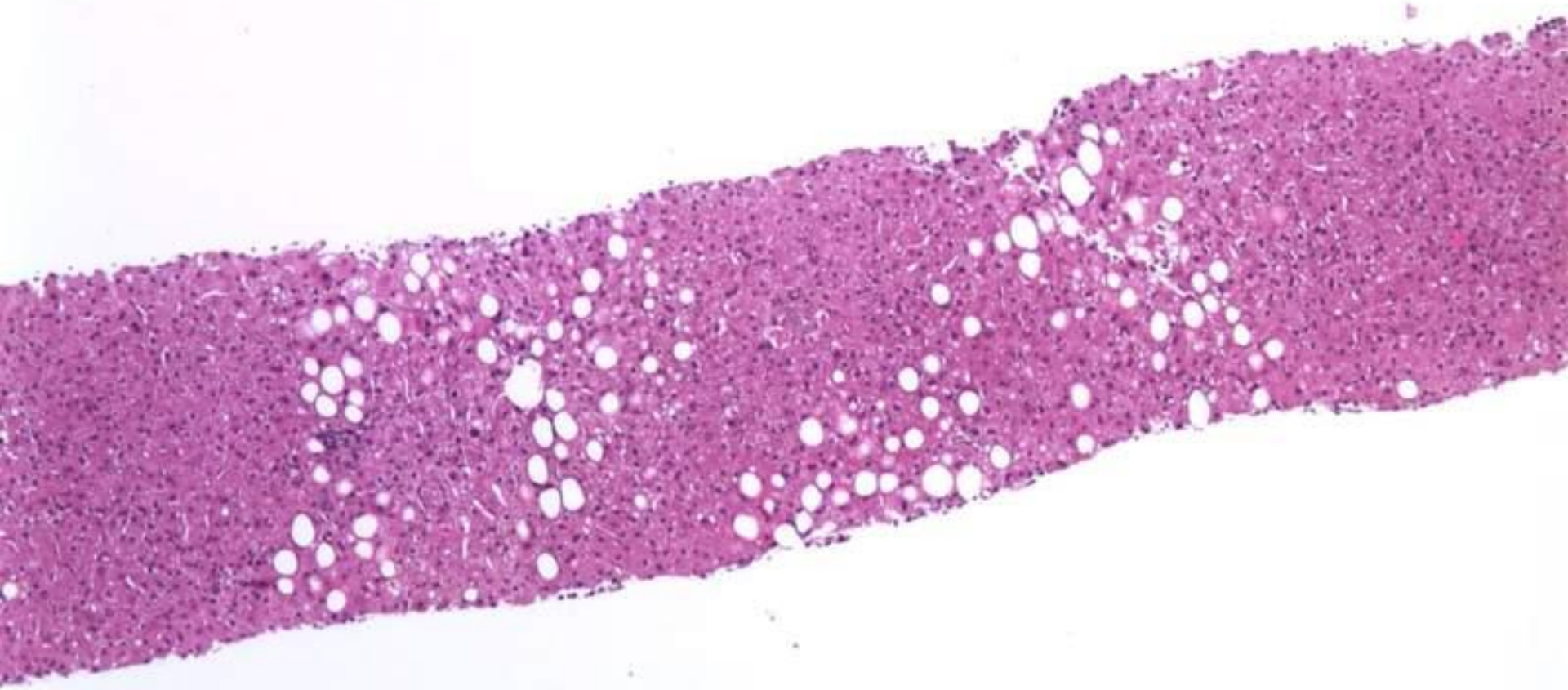
Follow up information from Dr Nolan:

Liver transplant for PSC, there had been episodes of ascending cholangitis; also has UC. Early re-transplant for hepatic artery thrombosis, now doing well post transplant

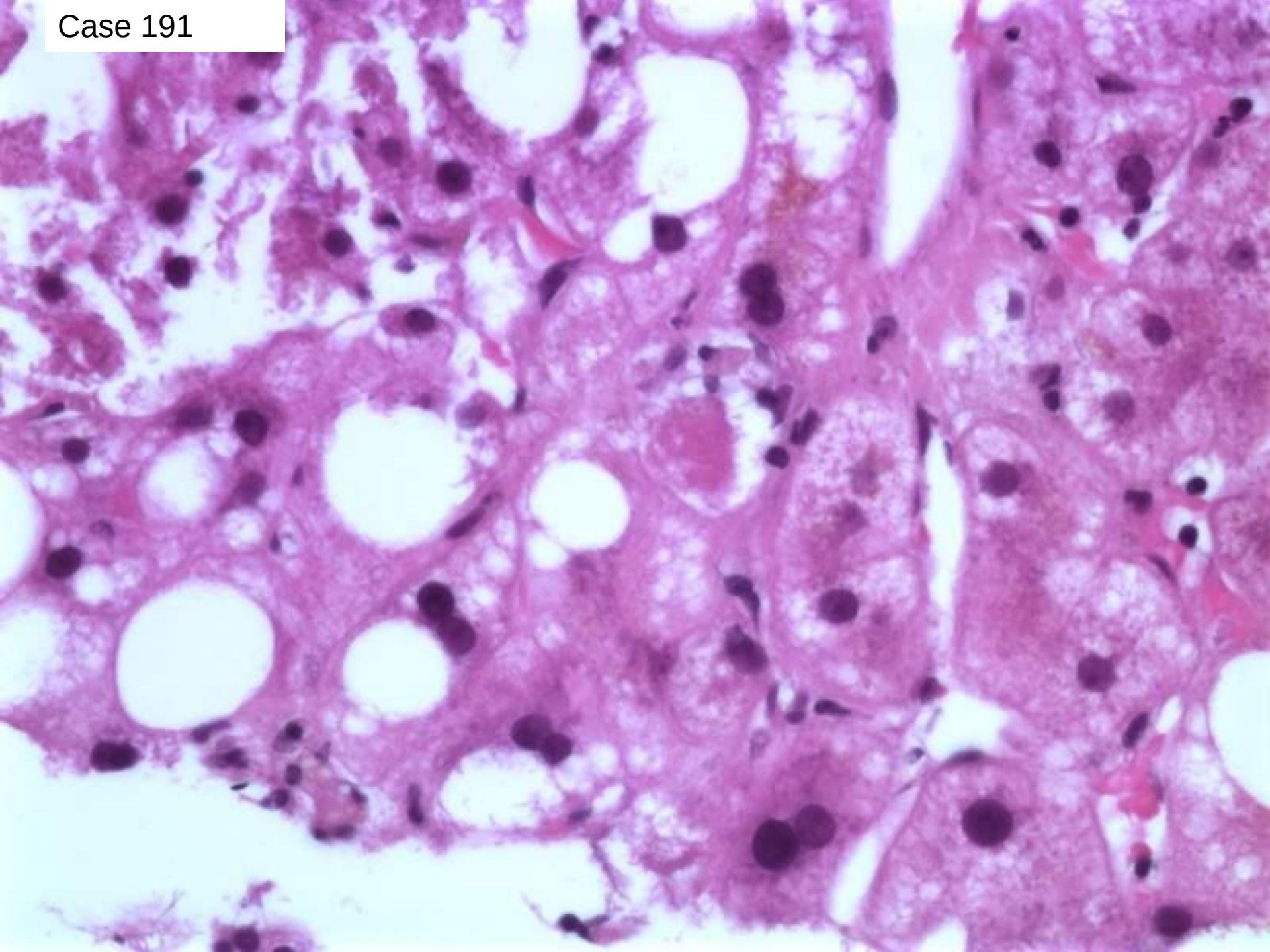
Case 191

Information provided: male 69, psoriasis and arthritis. On Methotrexate, raised ALT.

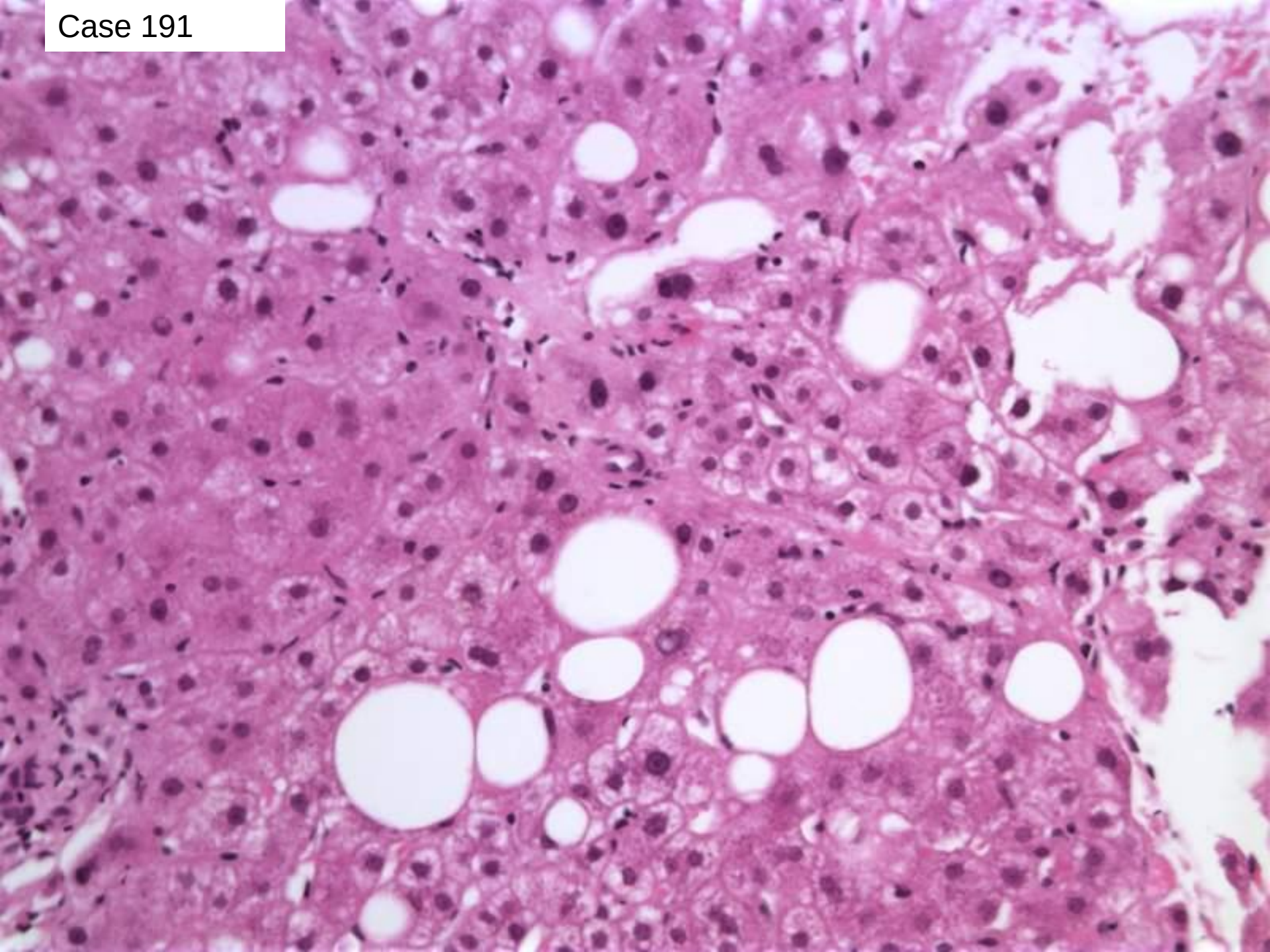
Case 191



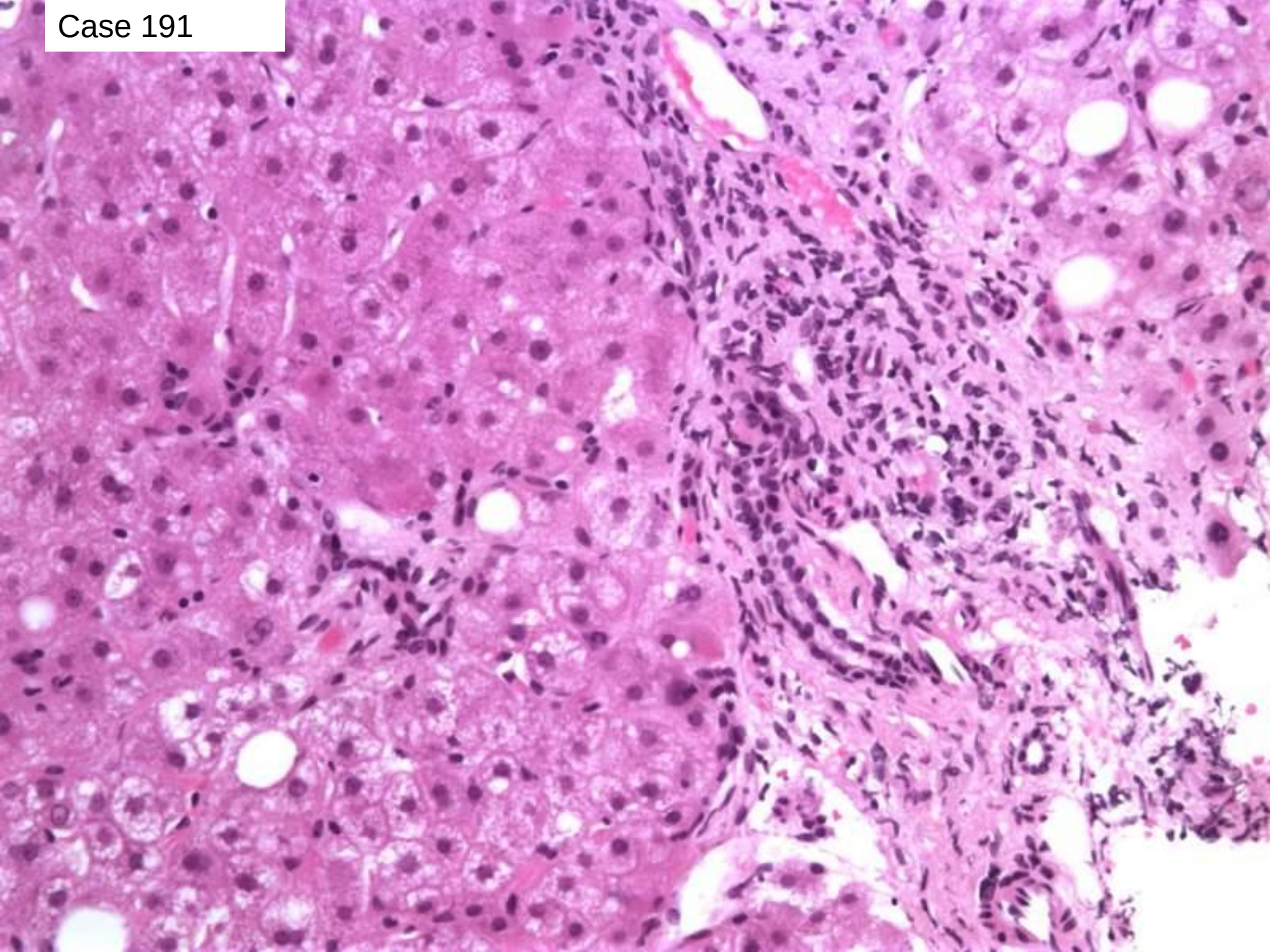
Case 191



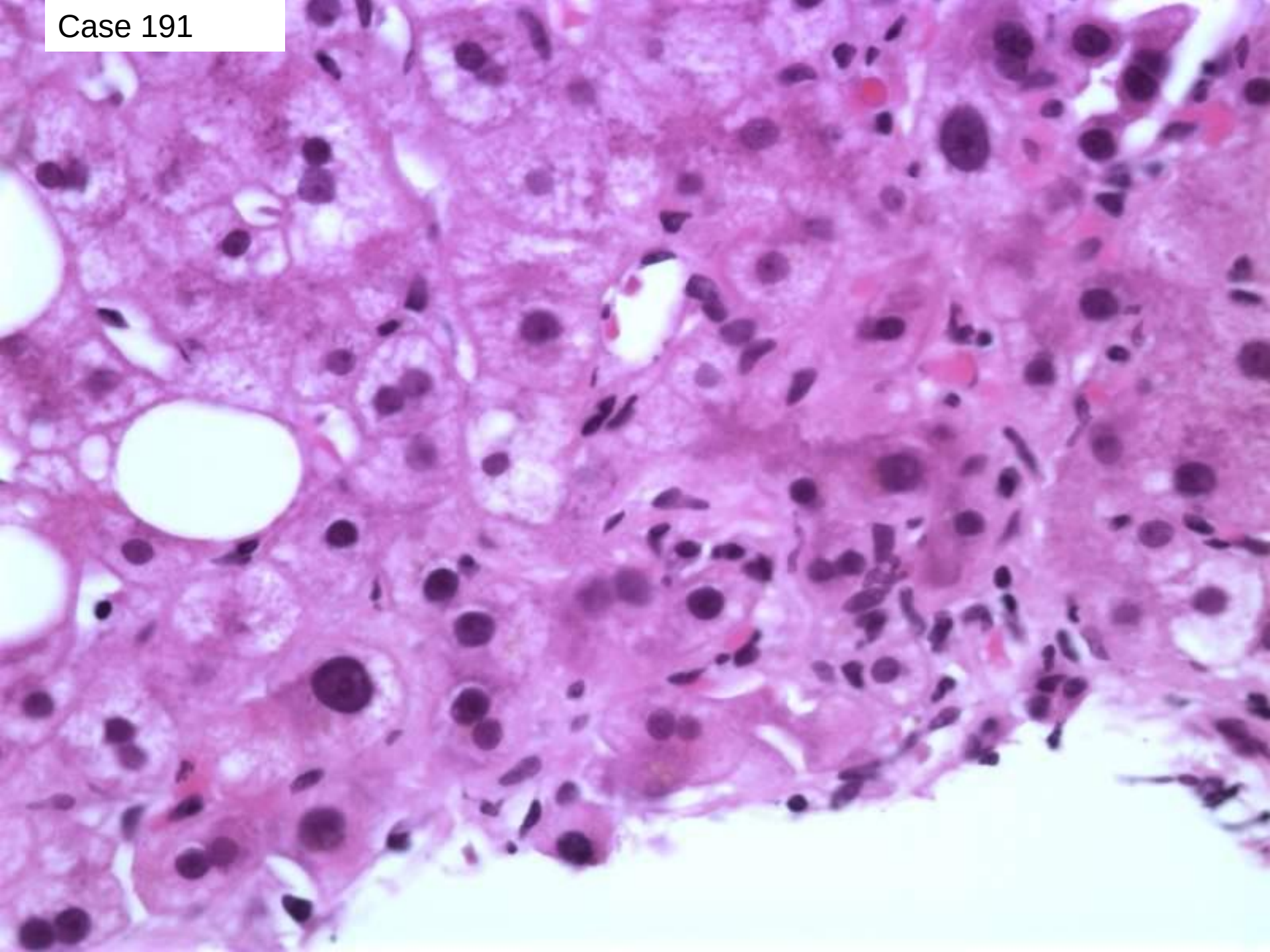
Case 191



Case 191



Case 191



Case 191

Summary of Responses:

morphology only

steatosis – 90

steatohepatitis – 10

steatosis/mild steatohepatitis – 10

Changes consistent with Methotrexate

steatohepatitis consistent with Methotrexate – 90

steatosis consistent with Methotrexate – 50

steatosis consistent with Methotrexate, mild or minimal fibrosis/inflammation – 130

steatosis with hepatocyte necrosis consistent with Methotrexate – 10

steatosis with nuclear changes consistent with Methotrexate – 10

grade 2/3 Methotrexate – needs 6-12 months follow-up biopsies – 10

features consistent with Methotrexate damage – 30

Methotrexate change +steatosis, fibrosis, ?cirrhosis. Advise stop Methotrexate – 10

Accepted diagnoses:

All answers accepted.

Case 191

Comment:

- should check other causes of steatosis - several
- do connective tissue stain to evaluate fibrosis – several

This was the third case of fatty liver in a patient taking methotrexate;

Prof. Burt presented slides summarising a recently published Newcastle study in which the main message was that the risk of fibrosis has been overestimated in the past.

Ref: Aithal BP et al. Monitoring methotrexate-induced hepatic fibrosis in patients with psoriasis: are serial liver biopsies justified? *Aliment Pharmacol Ther 2004:19;391-9*

Case 191

Additional information: Dr Kitching

Psoriasis with arthropathy, on methotrexate since 1992.

ALT rose to 116 with increased procollagen 3 peptide in 2001.

Methotrexate stopped, symptoms flared, ALT normalised.

Methotrexate restarted in 2002; biopsy performed as ALT rose to 73.

Continues on methotrexate with dose monitoring.

Case 192

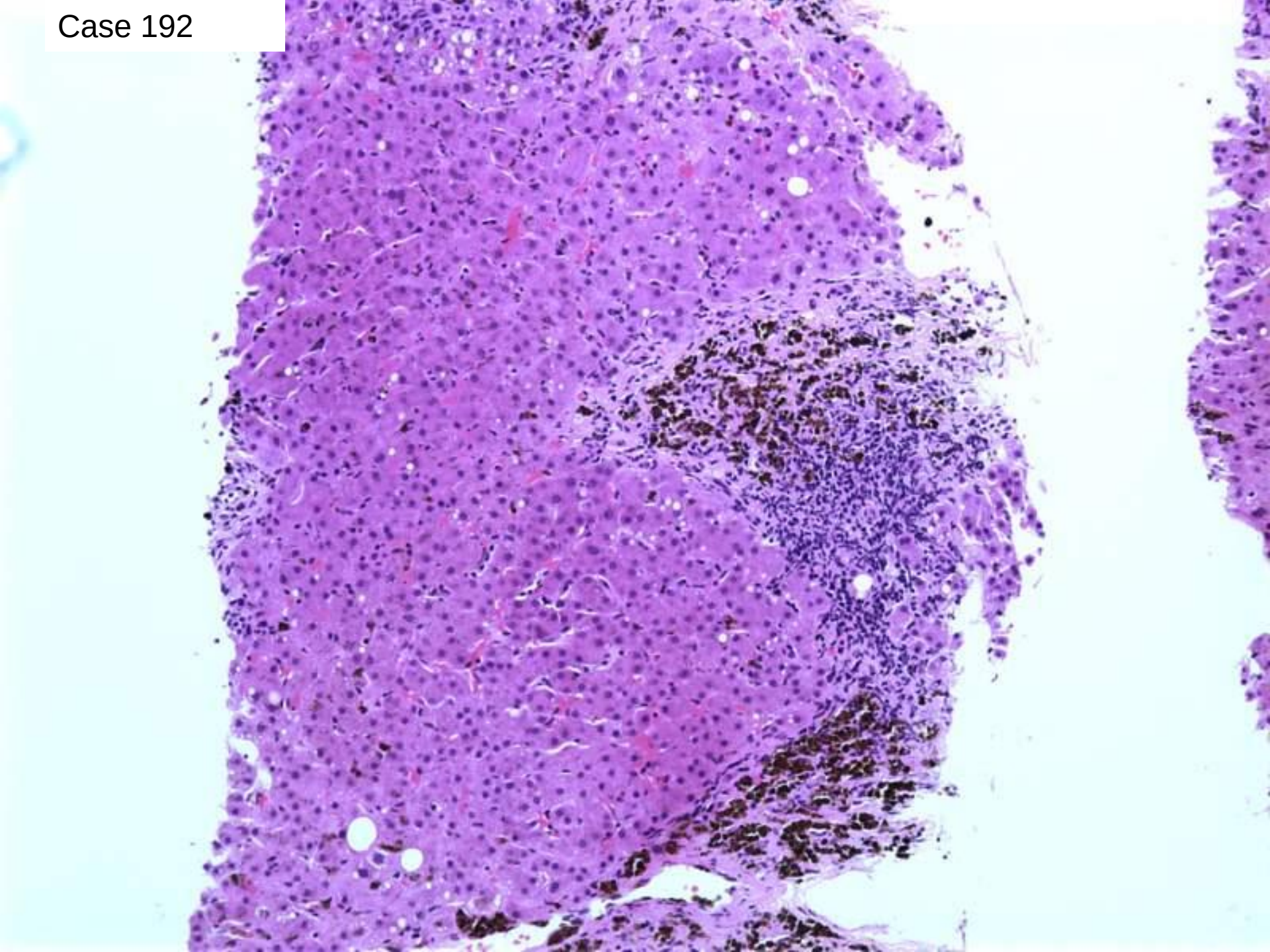
Information provided: renal patient, HCV positive on transplant list.

WVG, portal bridging fibrosis.

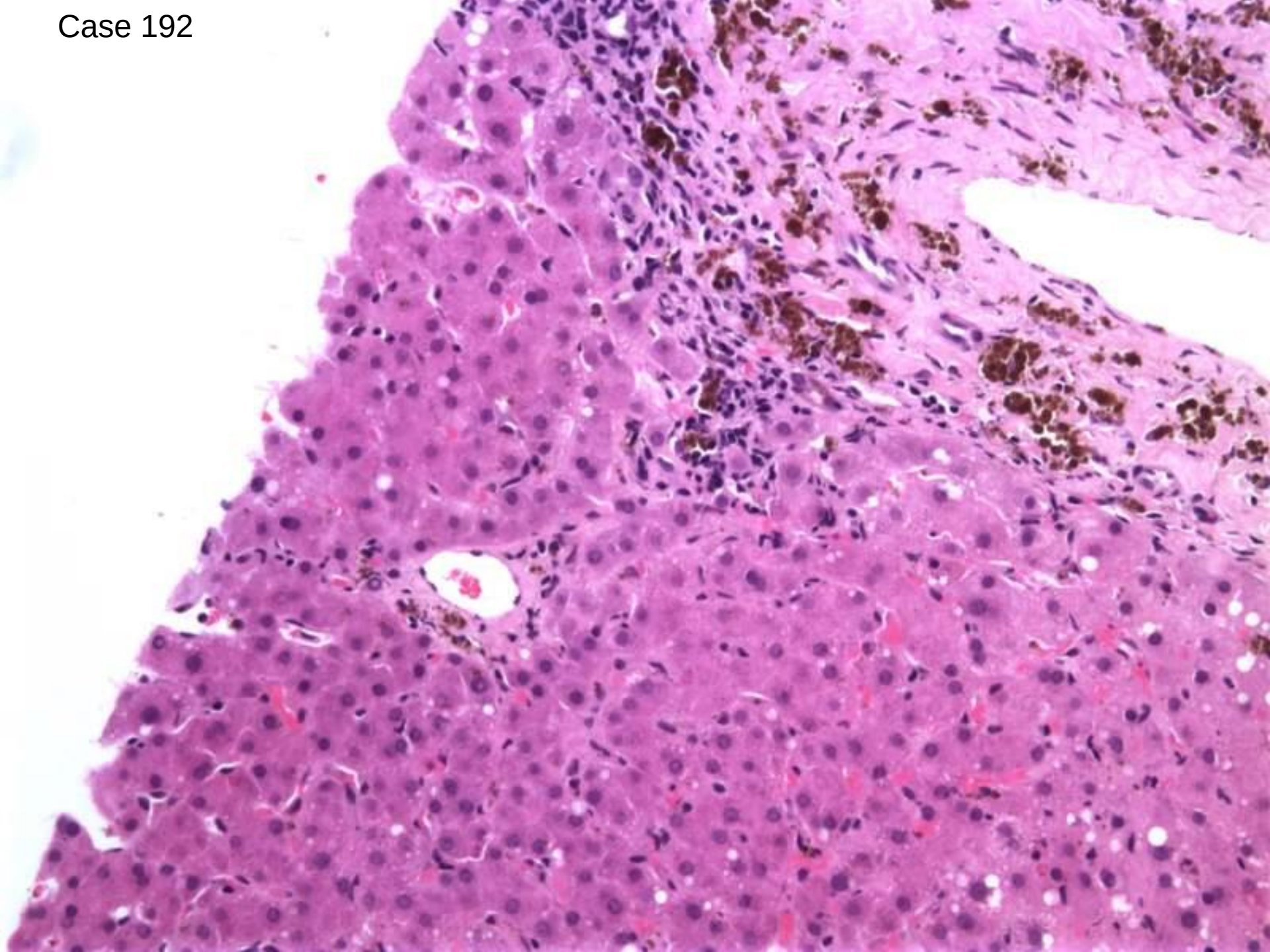
Perls positive in portal tracts and Kupffer cells.

Case 192

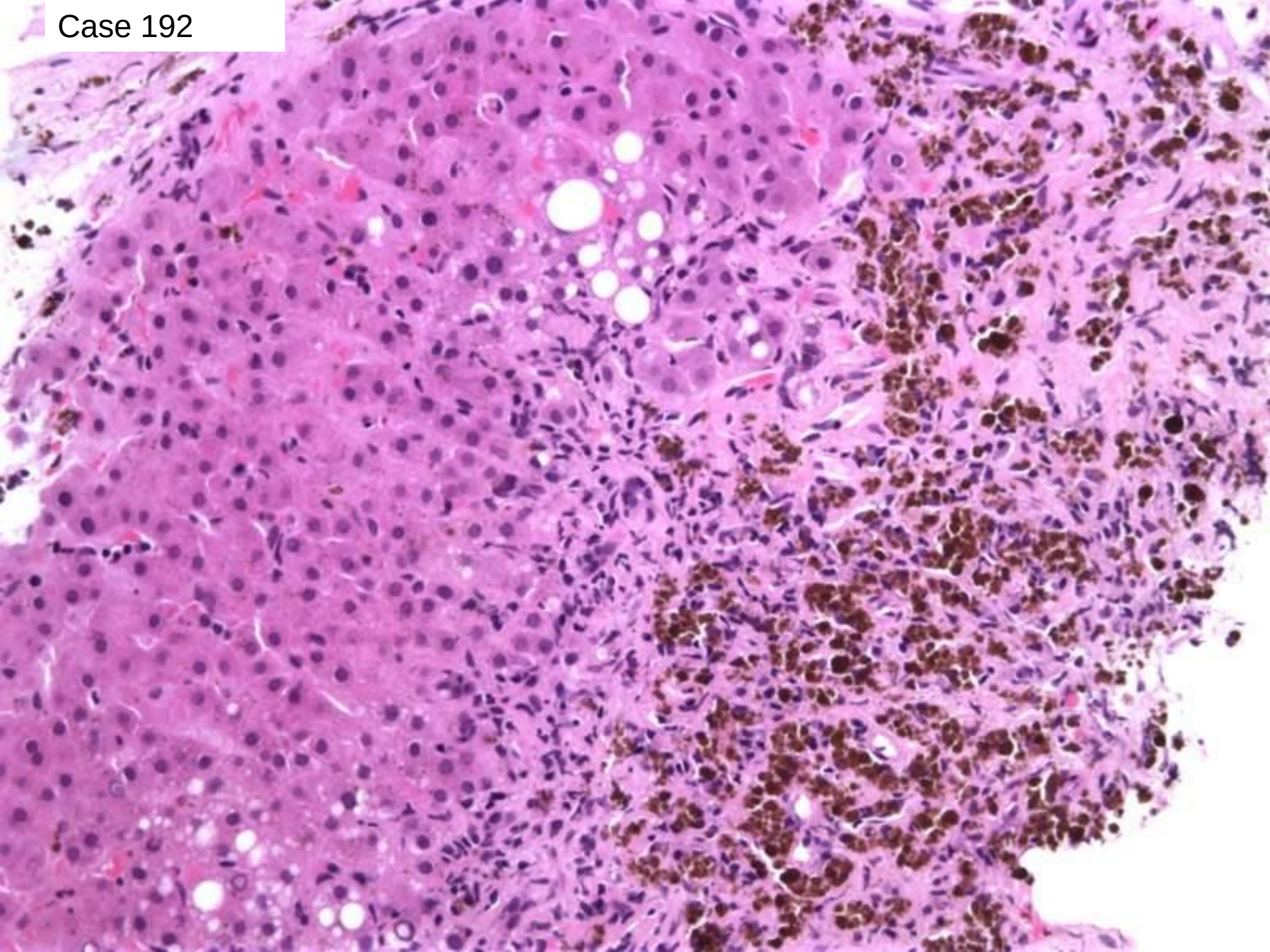
Case 192



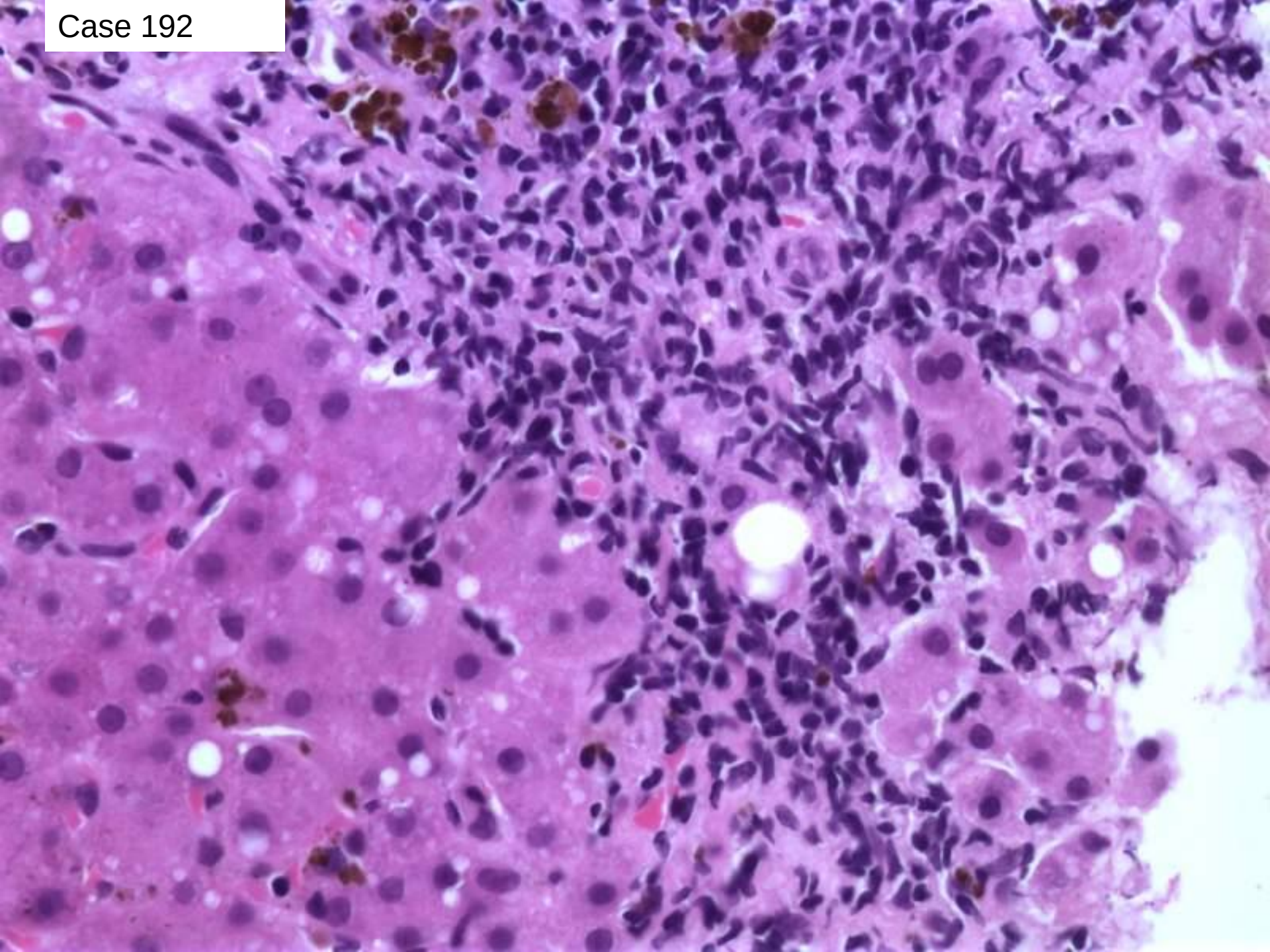
Case 192



Case 192



Case 192



Case 192

Summary of Responses:	*Accepted diagnoses:*
hepatitis C, moderate inflammation or fibrosis +iron – 210	*Yes*
hepatitis C, mild +iron – 90	*Yes*
hepatitis C, + iron overload – 60	*Yes*
haemosiderosis/iron overload (no mention of hepatitis C) – 50	*Yes*
haemosiderosis with bridging fibrosis – 30	*Yes*
secondary haemochromatosis – 10	*No*
transfusion haemosiderosis with fibrosing cholestatic hepatitis – 10	

Case 192

comments:

- needs haemochromatosis genetic studies – 5 people.
- ?needs blood transfusions to get increased iron in chronic renal failure

Comments during discussion:

Features attributable to hepatitis C are mild here.

There is co-location of heavy iron deposition and inflammation/fibrosis suggesting a role for iron in promoting liver injury in hepatitis C. This would be in keeping with the component of free radical mediated injury in hepatitis C.

(In pure haemochromatosis there is also often a component of inflammation, which may be a result of Kupffer cell activation).

Iron deposition in the liver is frequent in chronic renal failure, even without blood transfusions, although the degree in this case suggests multiple transfusions.

Case 192

Follow up information from Dr Cope:

Patient with medullary cystic kidney. Two renal transplants – last one failed 10 years prior to this biopsy, currently on haemodialysis, but keen to have further kidney transplant.

Biopsy shows fibrosis and siderosis secondary to multiple blood transfusions

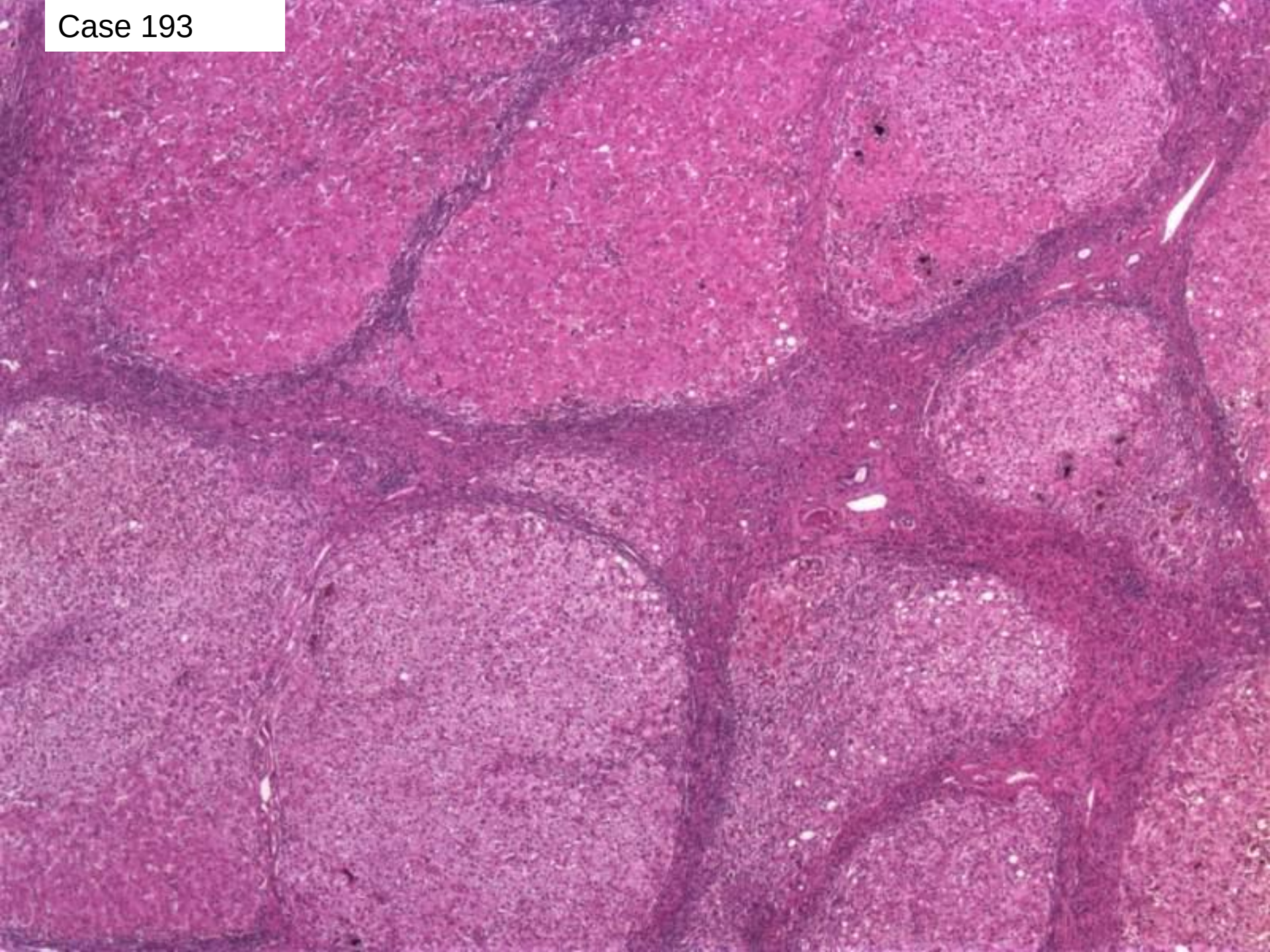
Has genotype 1 HCV, thought to be from blood transfusion in early 1980's.

Plan to treat HCV prior to transplant, although use of ribavirin is difficult in patients with renal failure.

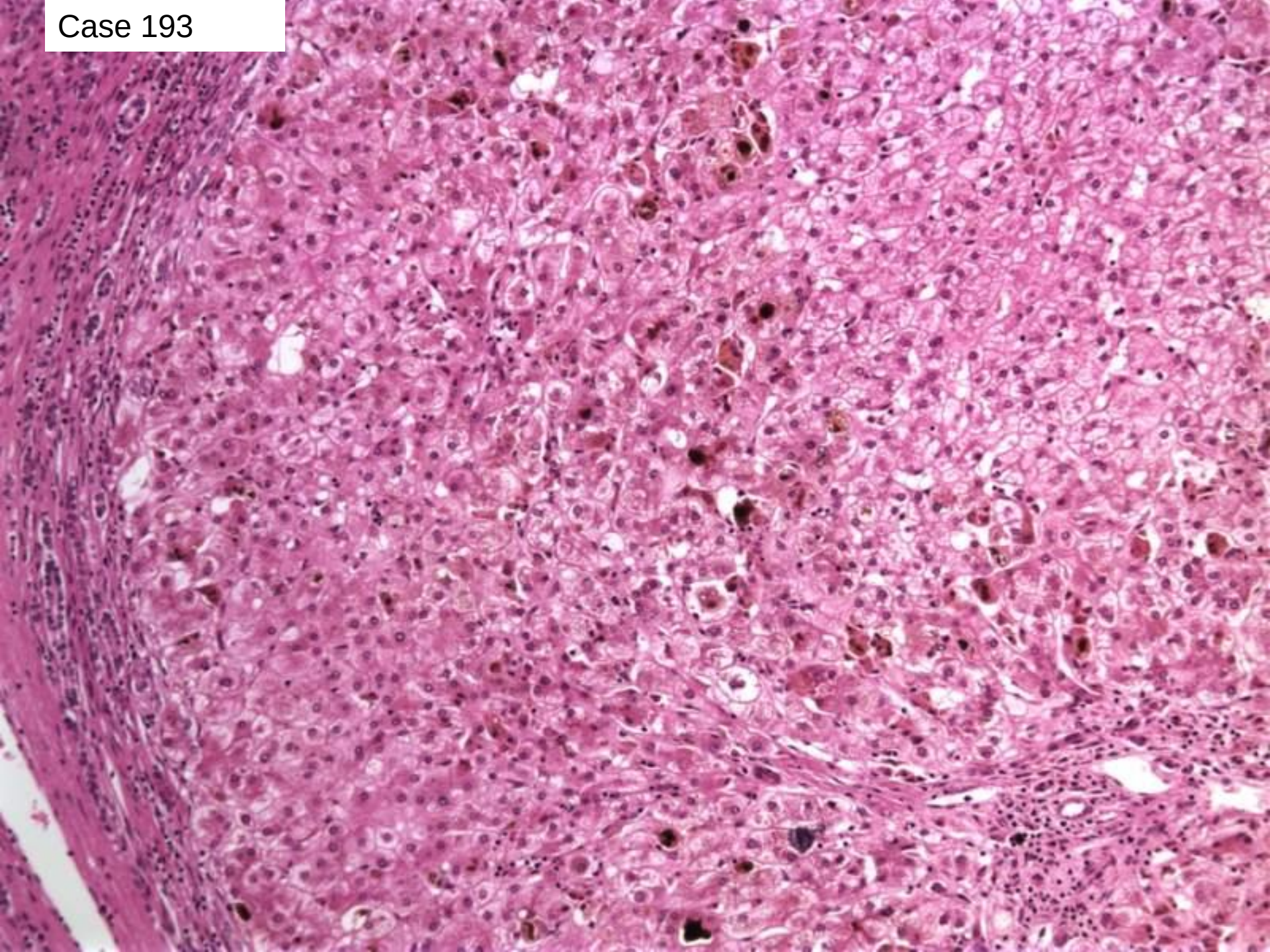
Case 193

Information provided: male 58, non-alcoholic steatohepatitis. Orthotopic liver transplant performed. No history of metabolic disease or other relevant history

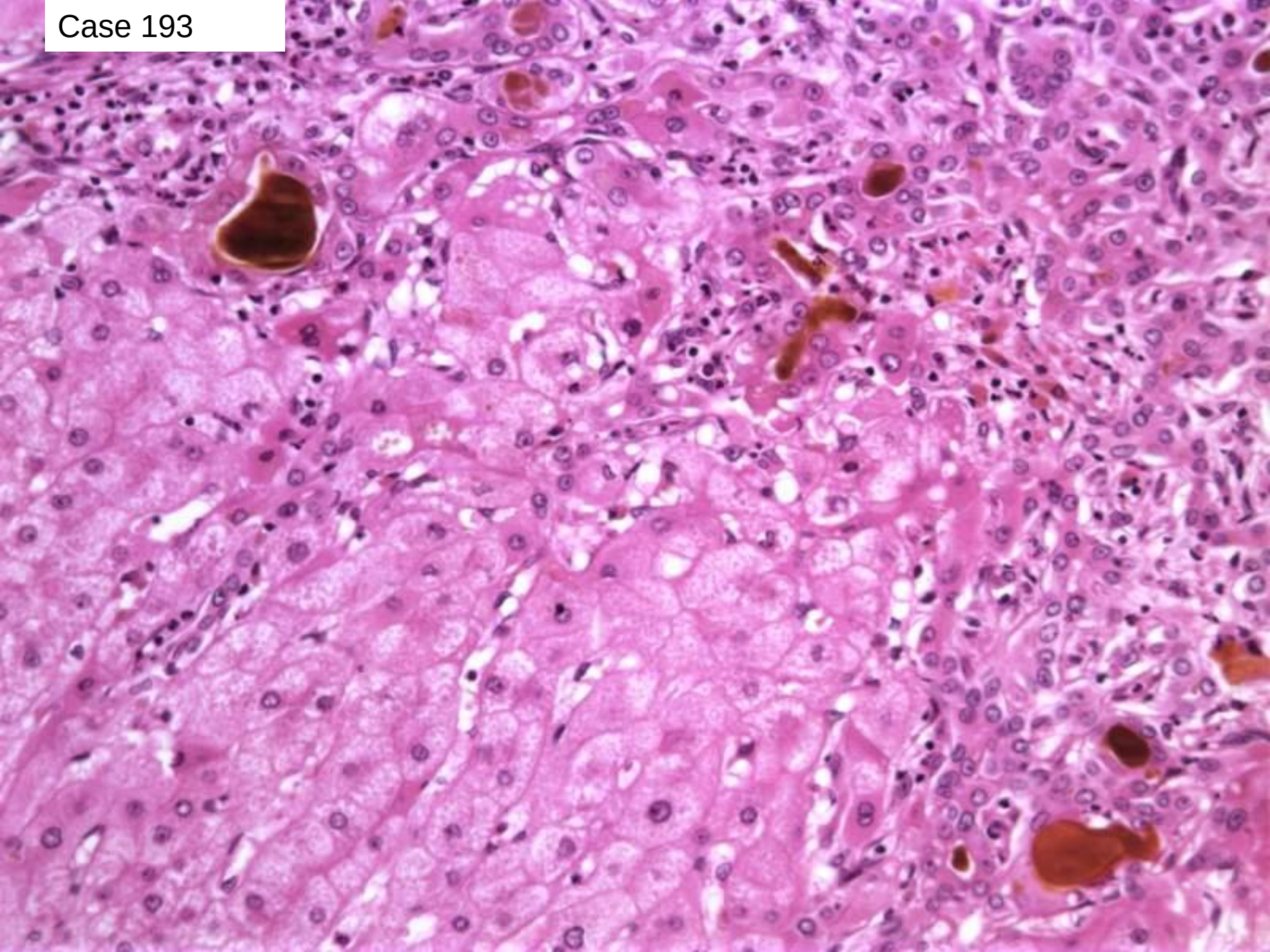
Case 193

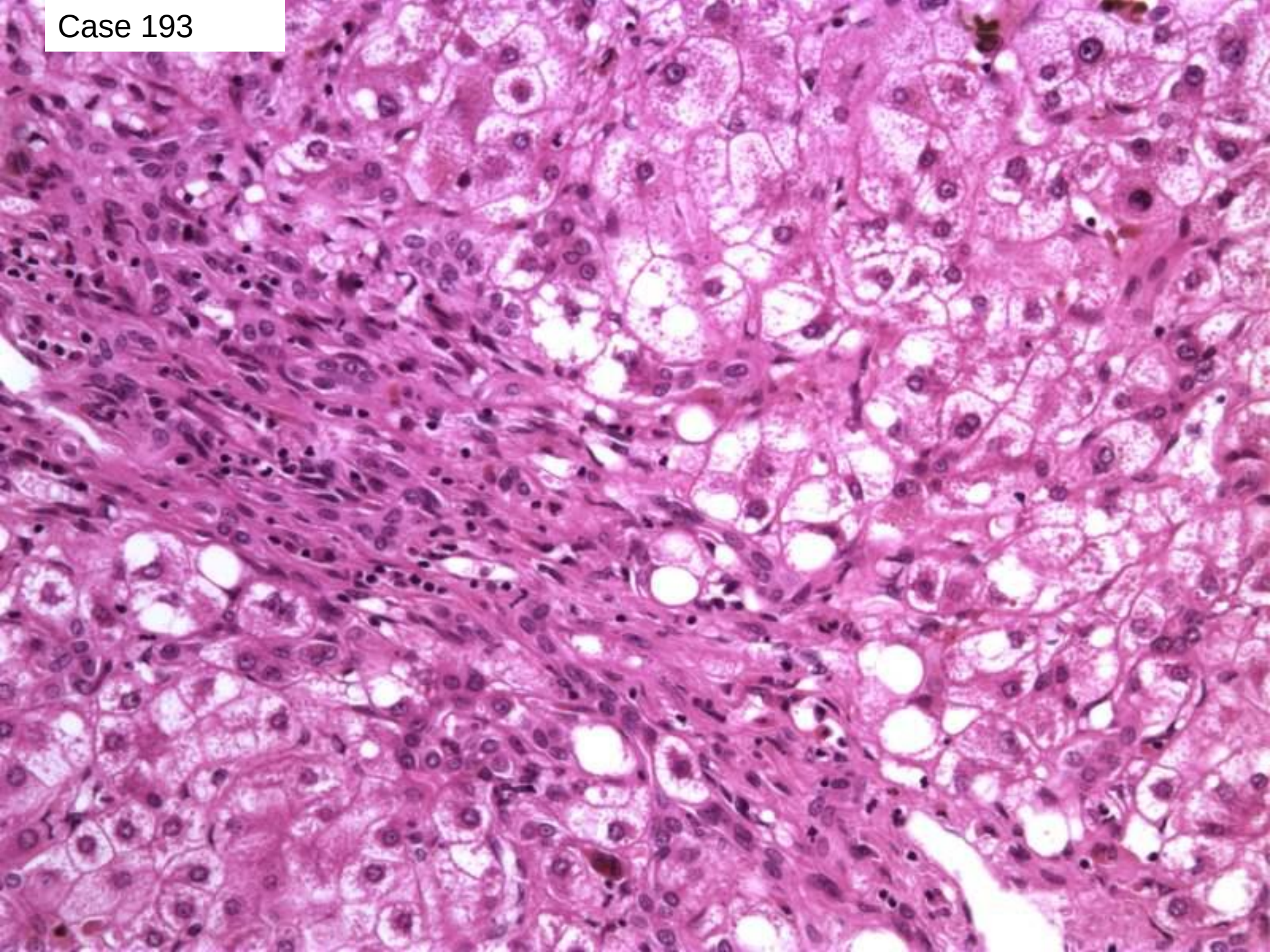


Case 193

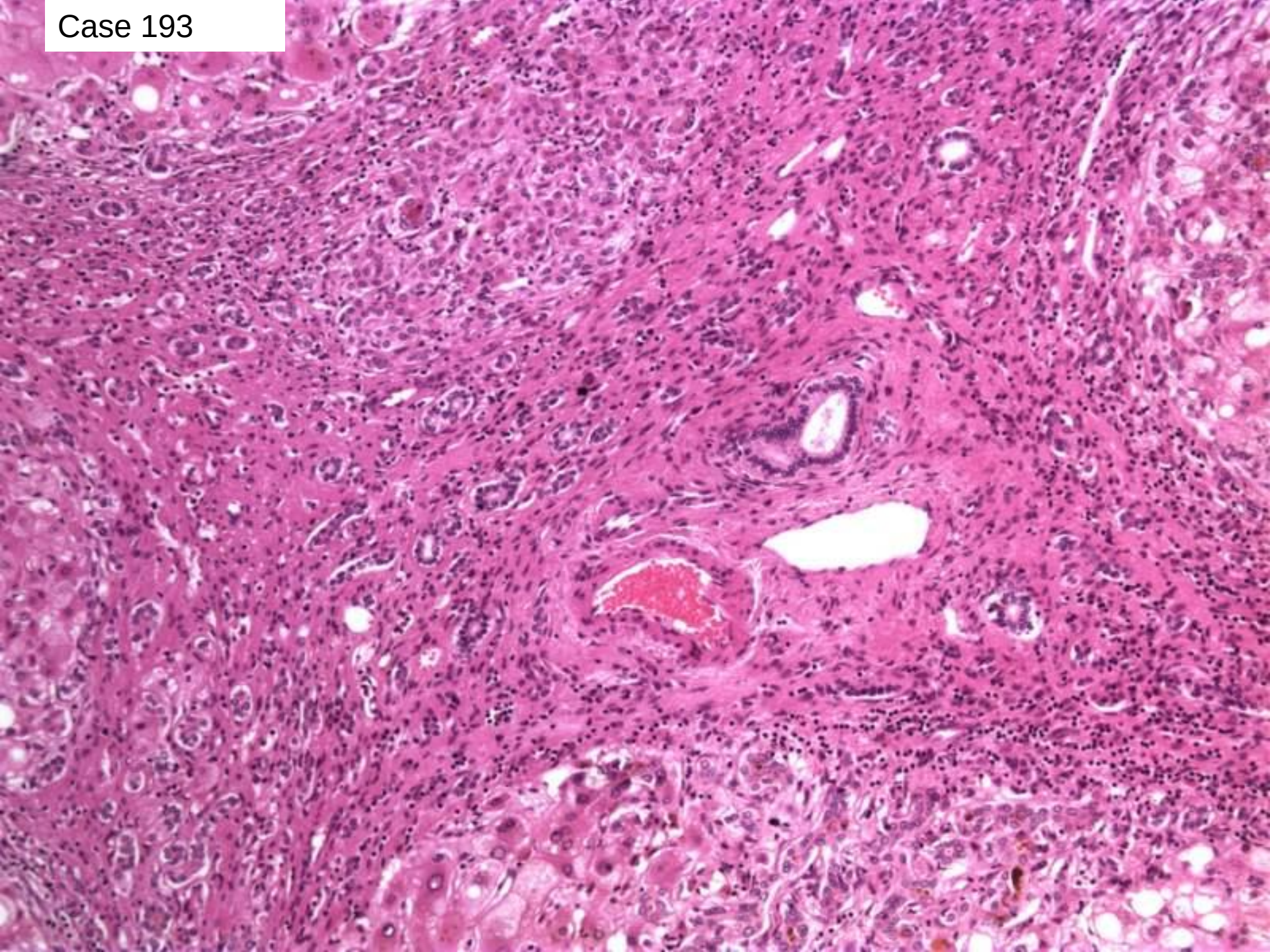


Case 193

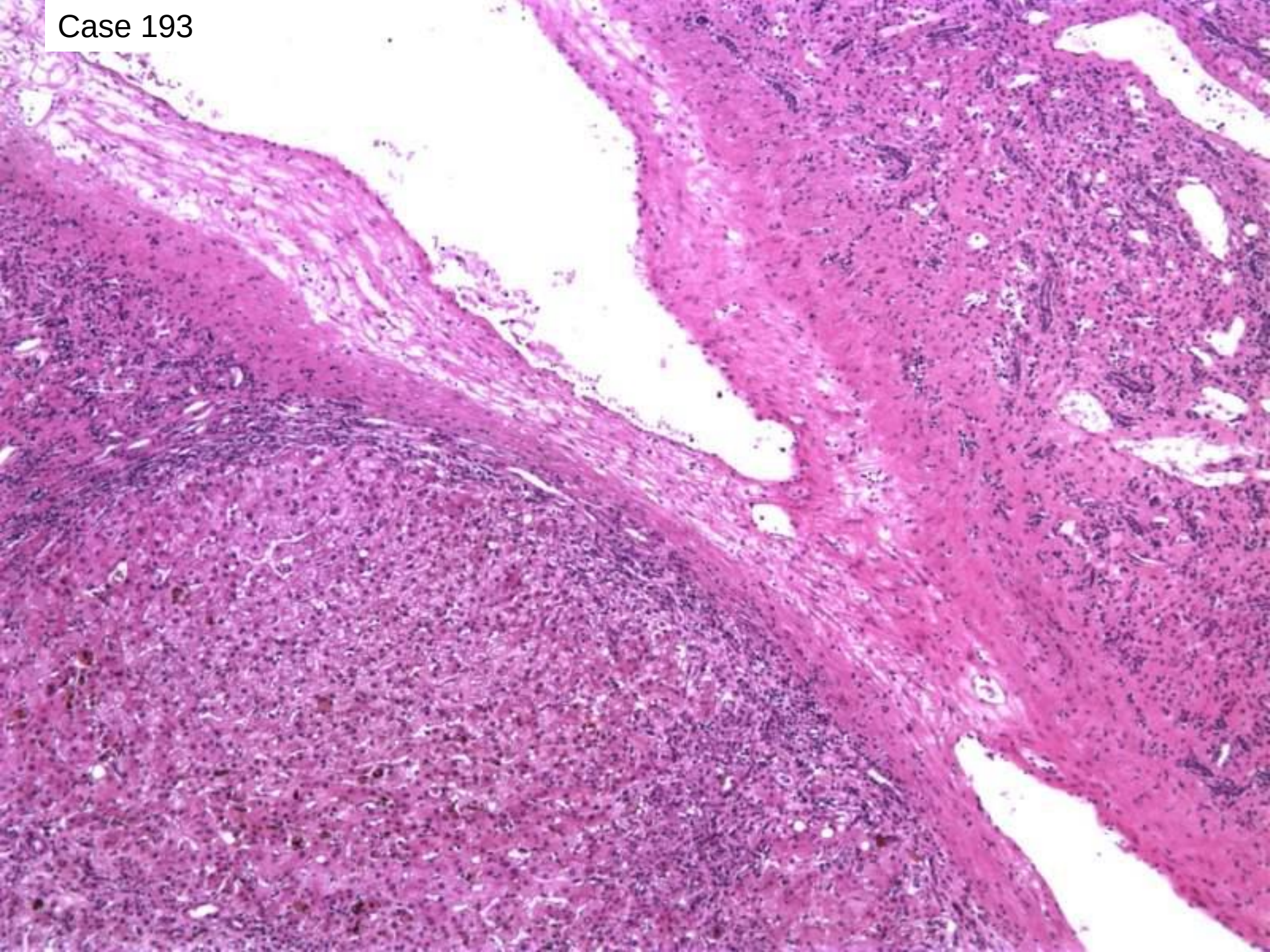



Case 193

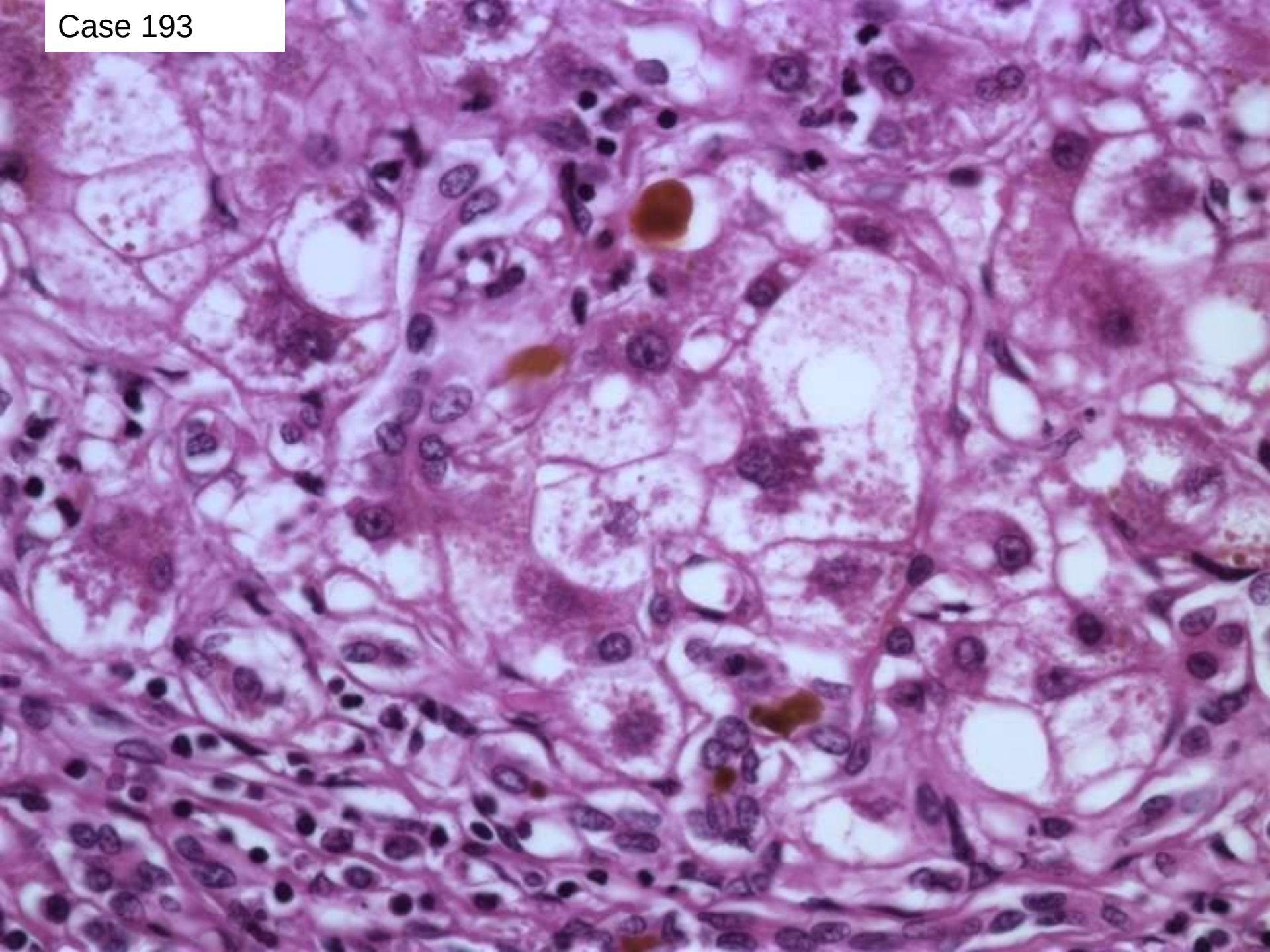
Case 193



Case 193



Case 193



Case 193

Summary of Responses:	*Accepted diagnoses:*
cirrhosis consistent with steatohepatitis	Yes
+cholestasis or sepsis – 140	Yes
cirrhosis with cholestasis – 130	Yes
cirrhosis consistent with late stage NASH – 40	Yes
cirrhosis with steatohepatitis – 10	Yes
cirrhosis (not otherwise specified) – 70	Yes
cirrhosis, ?aetiology, ?biliary – 30	Yes
cirrhosis with biliary features and cholestasis – 10	Yes
active micronodular cirrhosis, ?PBC – 10	No
moderately active cirrhosis, exclude Wilson's – 10	Yes

Case 193

comments:

- ? cause of excess cholestasis - 13
- ?malformation very large portal tracts
- Perl's, ?haemochromatosis
- Unusual appearance of hepatocytes – ground glass – 3
  Induced hepatocytes – 2
  Atypia / dysplasia – 2
  Oncocytes - 1

Follow up information from Dr Kennedy:

Patient grossly overweight, Pre-transplant diagnosis cirrhosis due to NASH – no history of high alcohol consumption. No abnormalities of biliary tree and no history of sepsis.