# National Liver Histopathology EQA Scheme

Circulation K1

Autumn 2014

# Circulation K1 – Autumn 2014

- Some problems with this circulation – apologies to those who did not receive slides
- Collation of initial 69 responses presented to the meeting.
- 80% consensus = 56 responses agree
- additional 10 responses were received between 7-12th November.
- Comments on suggested scoring from 17 members

  – shown in blue next to suggested scoring

  – 16/17 took under 30 mins.
- Master class presentations x3

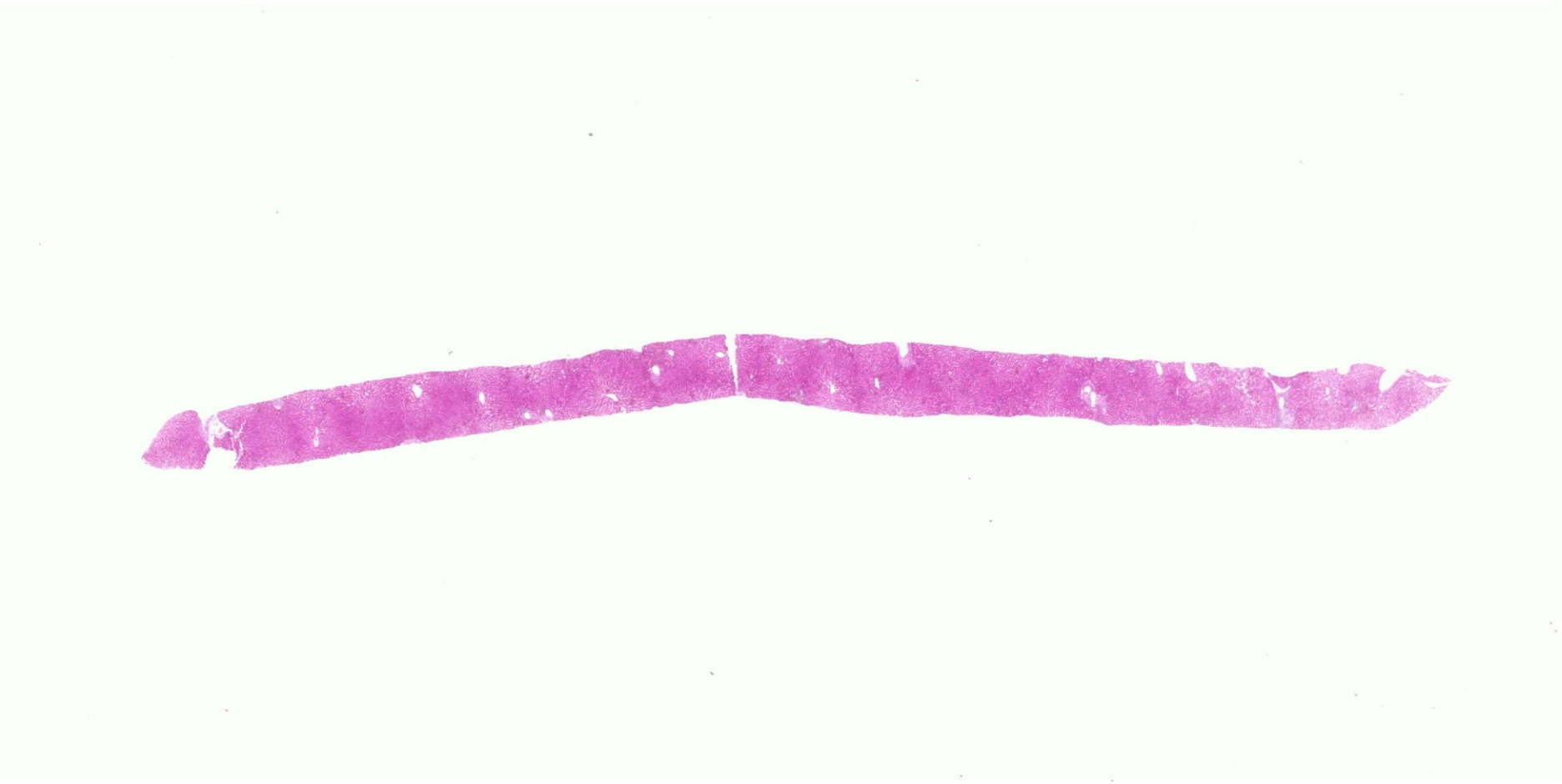
  Steatohepatitic HCC – Stefan Hubscher,

  cholestasis v cholestatic hepatitis – Chris Bellamy,

  Vascular disease in the liver – Sue Davies

**Case K1/446** Age 50, Male

Haemochromatosis, raised ferritin. Assess fibrosis ? Cirrhosis



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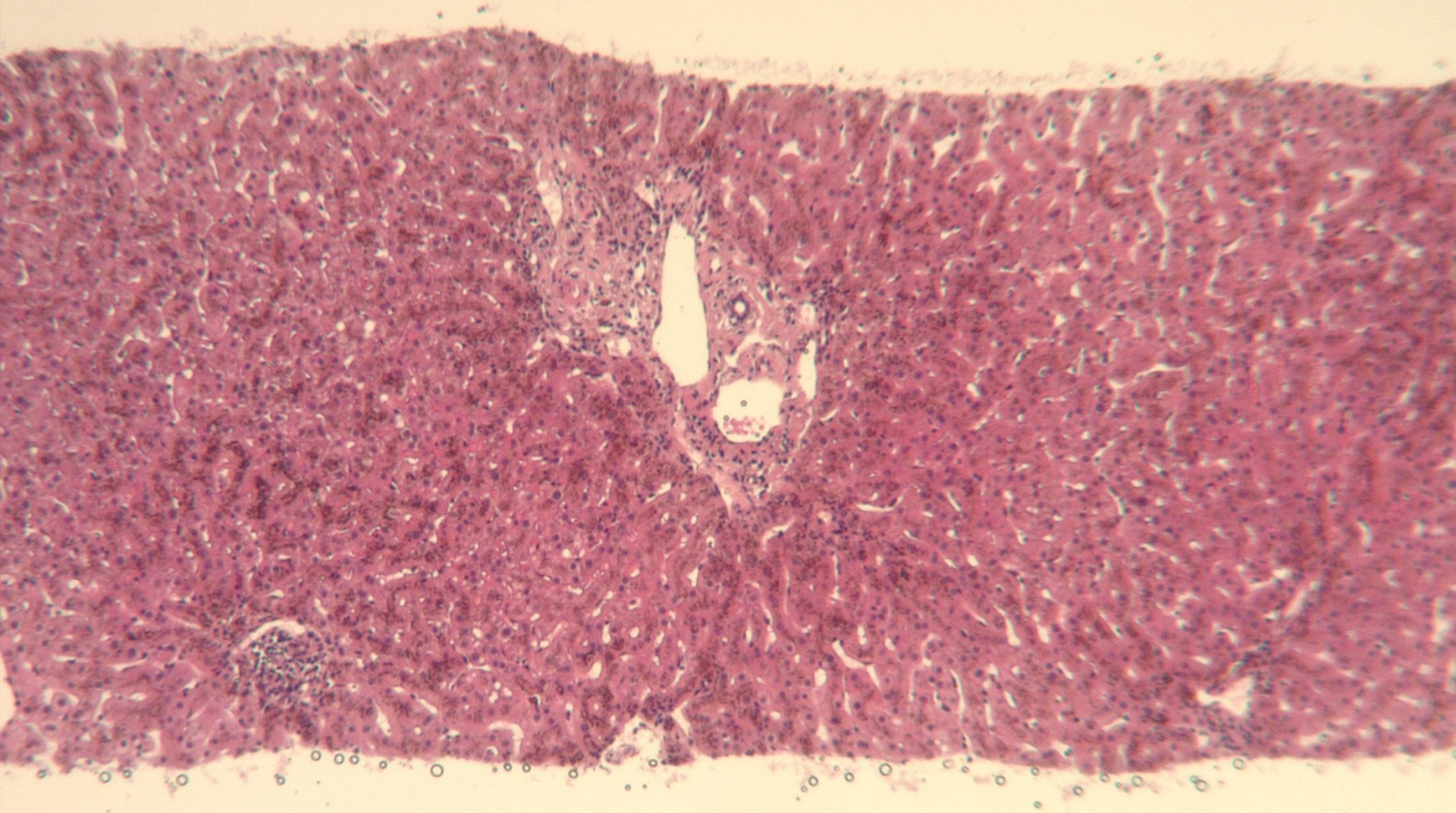

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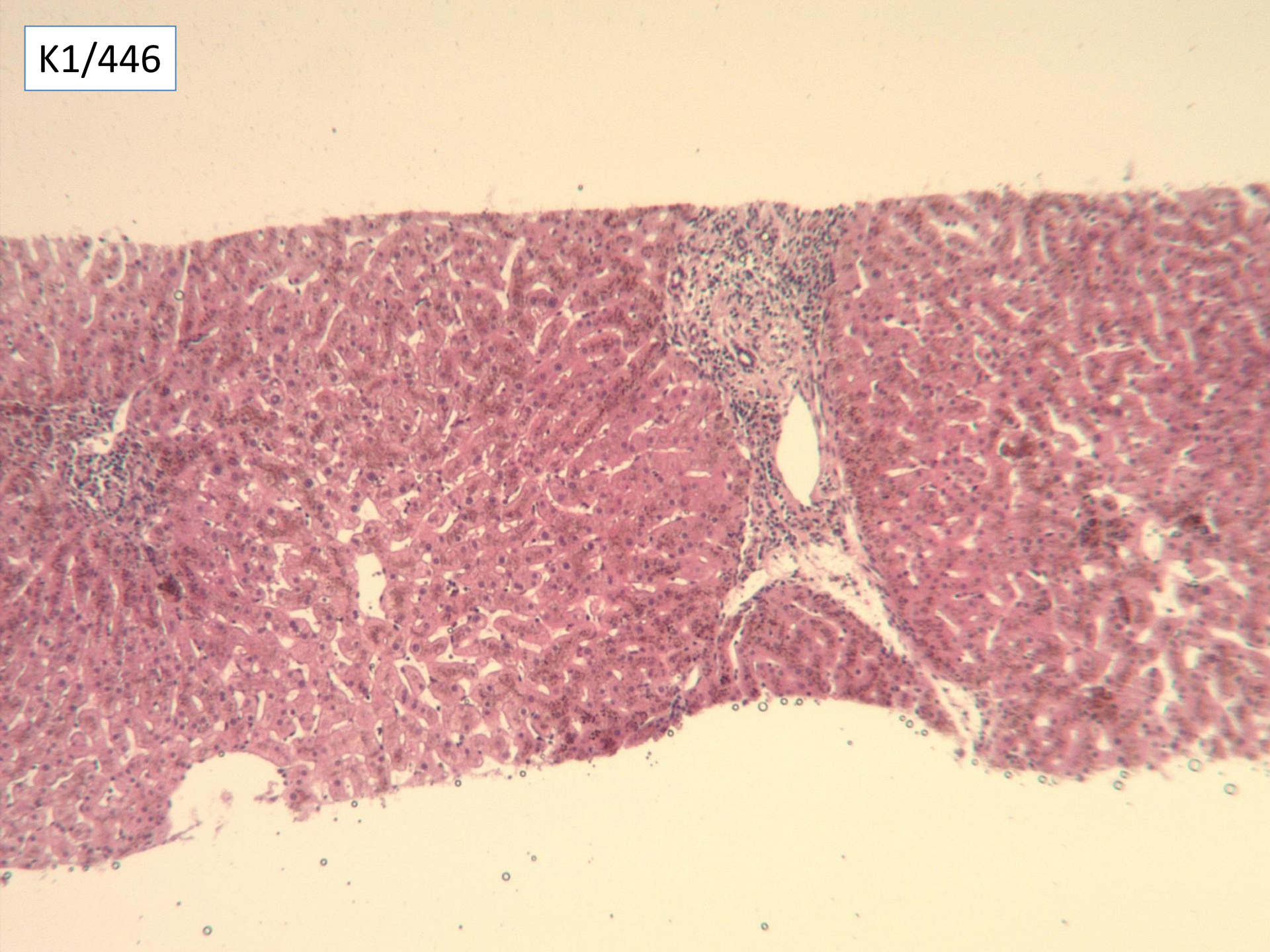
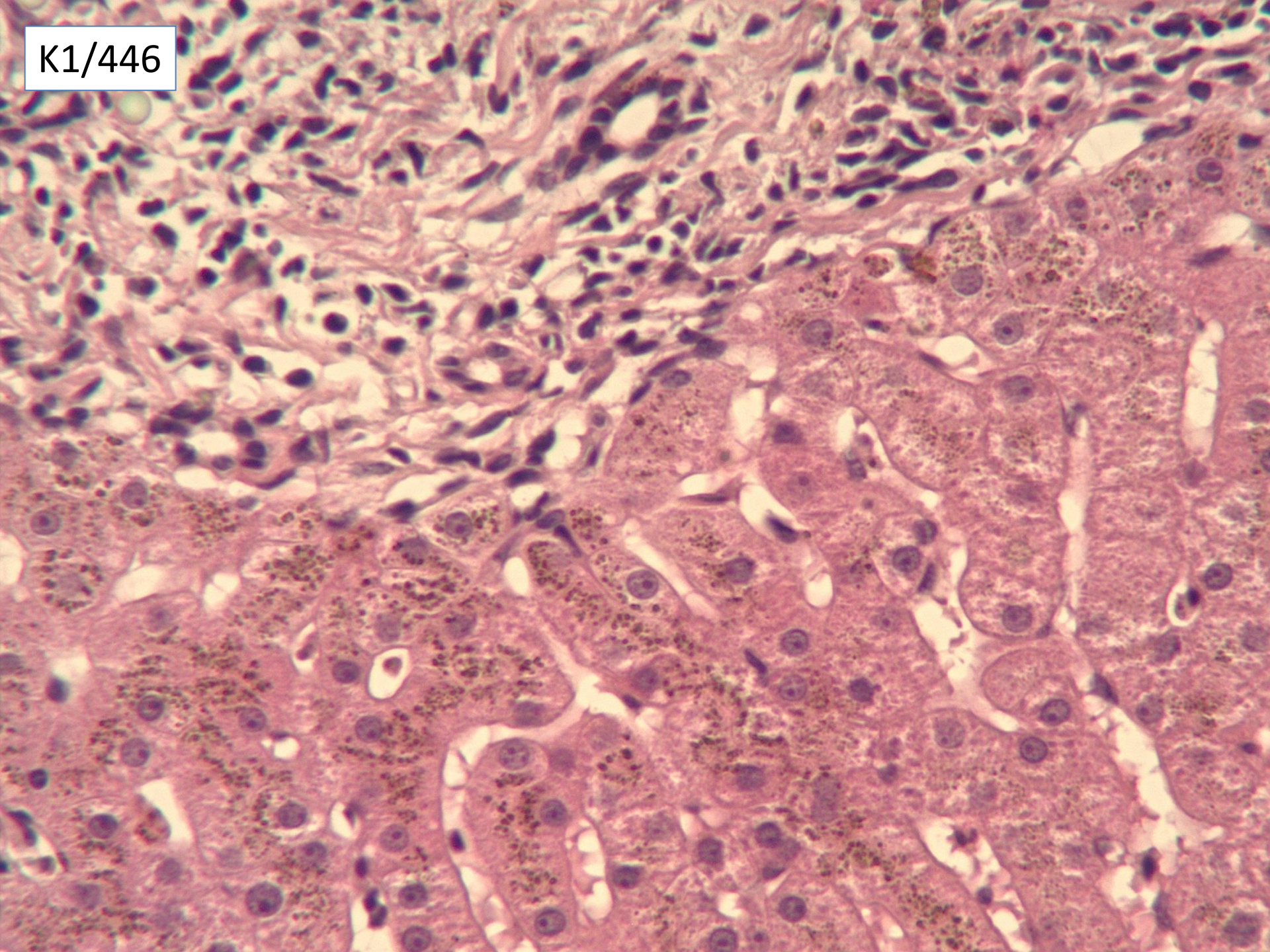
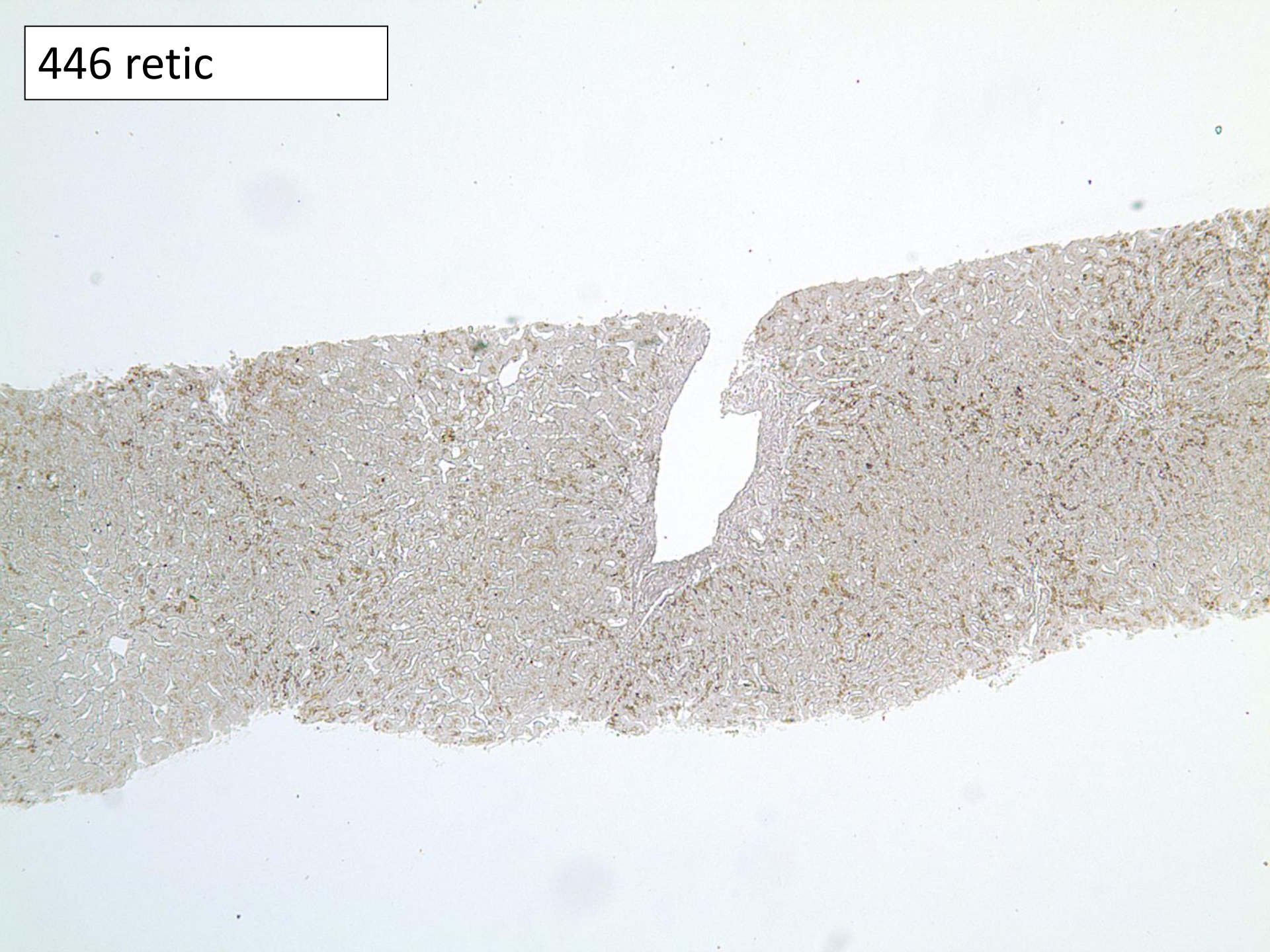
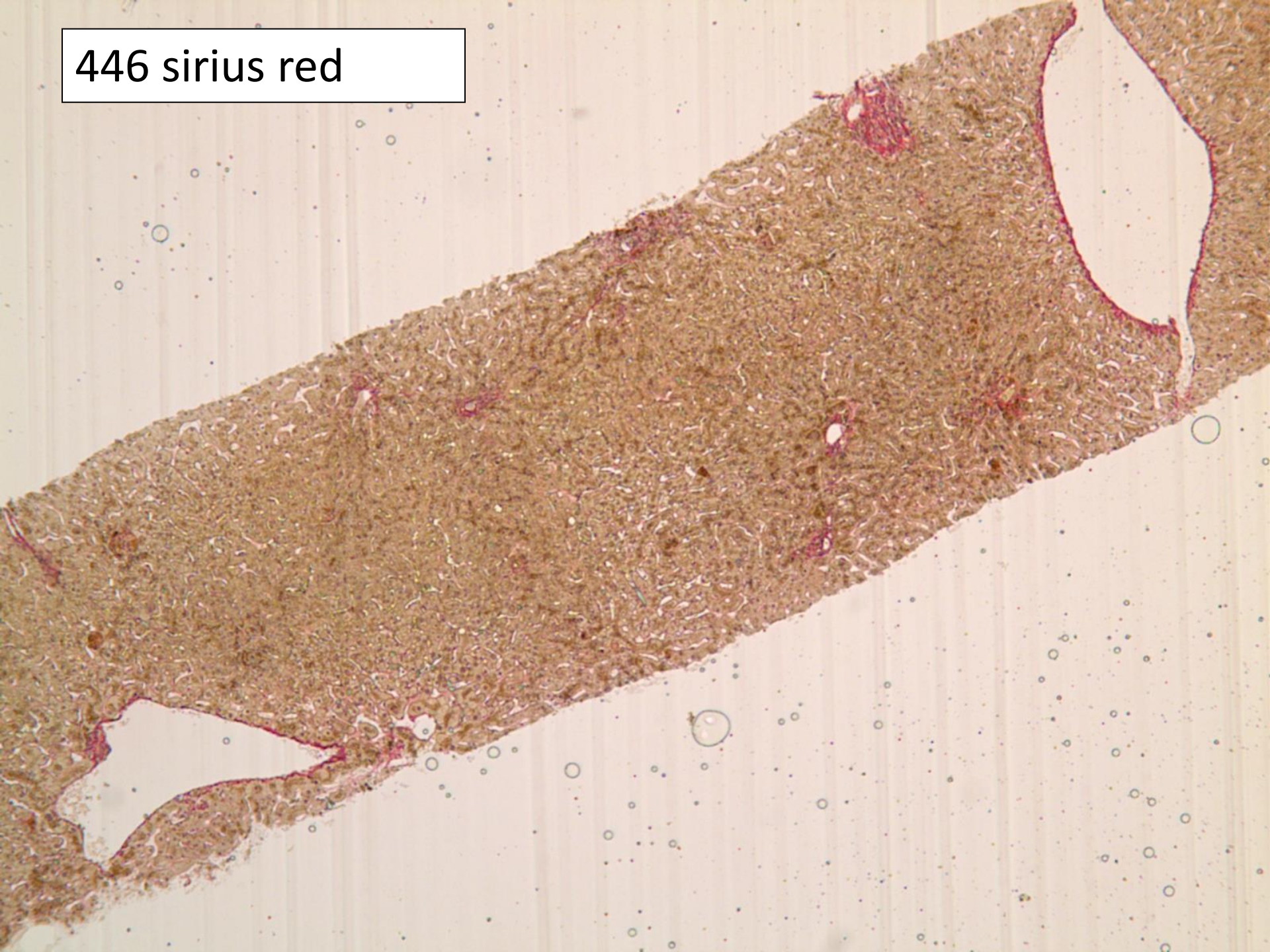
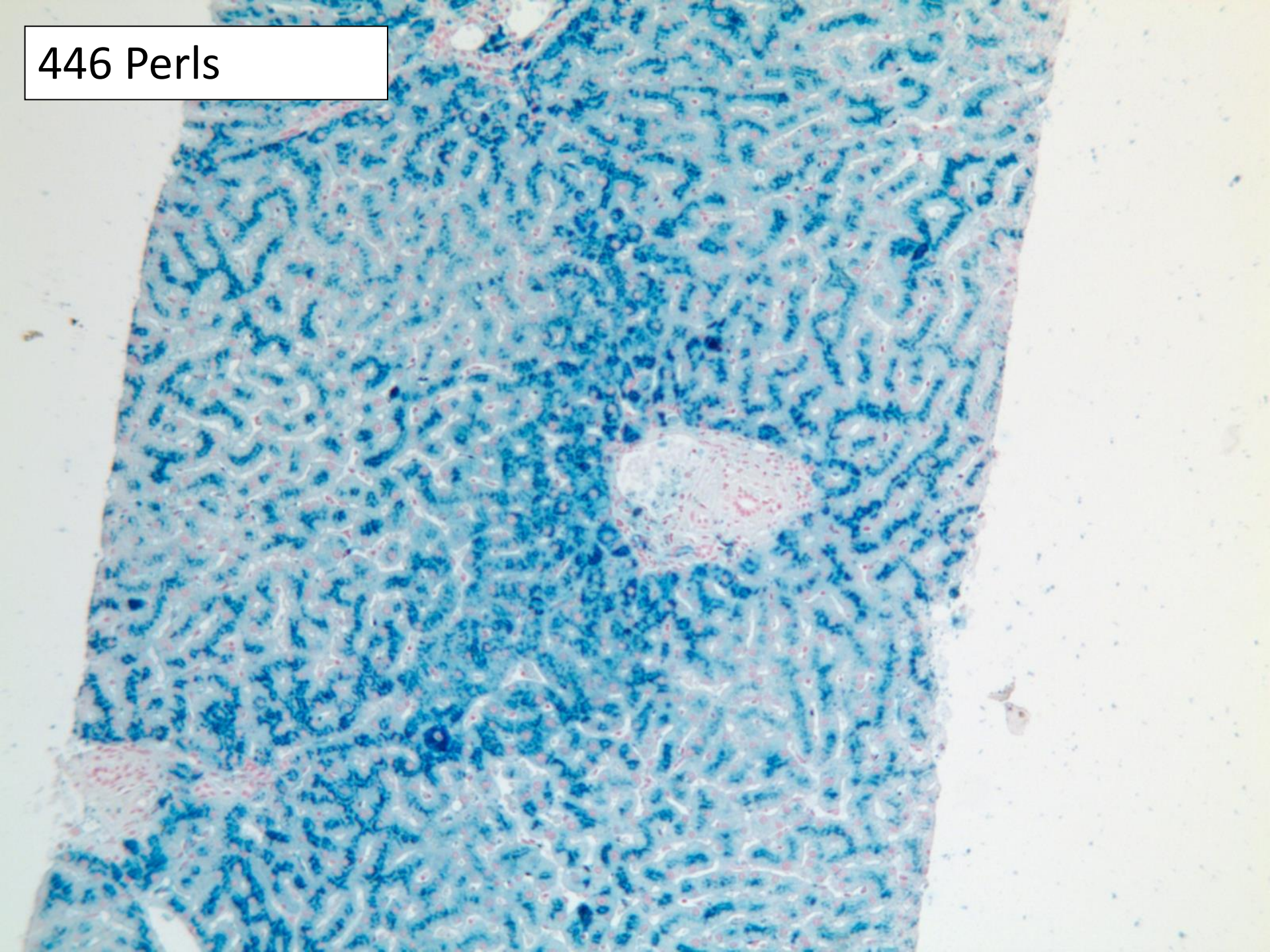



K1/446

446 retic




446 sirius red


446 Perls

**Case K1/446 Age 50, Male**

Haemochromatosis, raised ferritin. Assess fibrosis ? Cirrhosis

70 consistent with haemochromatosis

Iron:
8 grade 3
10 grade 3-4
44 grade 4

Fibrosis: - all made comment:
22 none / no significant
16 minimal
20 mild
3 early / slight
2 early fine bridging

Ishak stage: - 11 responses
– stage 0,1,2,3, number of responses = 1,5,4,1 respectively

Suggested scoring – score 10 points for iron overload consistent with haemochromatosis (all score 10).
Information on grade of iron and stage of fibrosis included for information.

15/17 agree, 0 unsuitable

**Case K1/446 Age 50, Male**

Haemochromatosis, raised ferritin. Assess fibrosis ? Cirrhosis

- Original diagnosis: severe iron deposition (grade 4) consistent with genetic haemochromatosis, no fibrosis.

- Grading iron – most use 0-4 for iron in hepatocytes

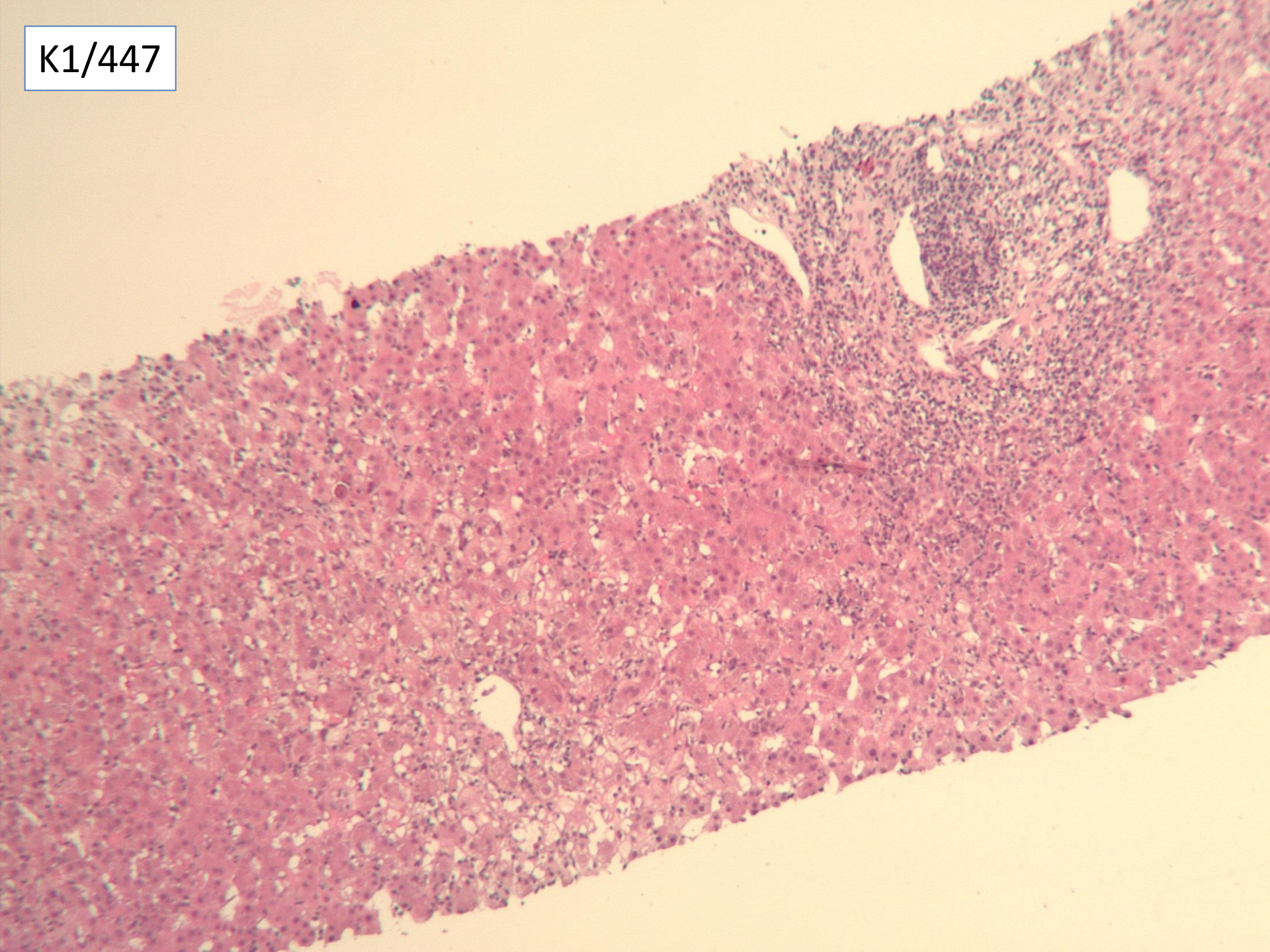
– all hepatocytes contain iron so grade 4. Little iron in Kuppfer cells, so pattern consistent with genetic haemochromatosis.

- This patient presented to rheumatologists who found high ferritin and high iron saturation. Get fibroscan?
- Managed by haematologists, not hepatology follow up.

**Case K1/447 Age 53, Male**

Acute jaundice. Deranged LFT's

? Autoimmune hepatitis (AIH)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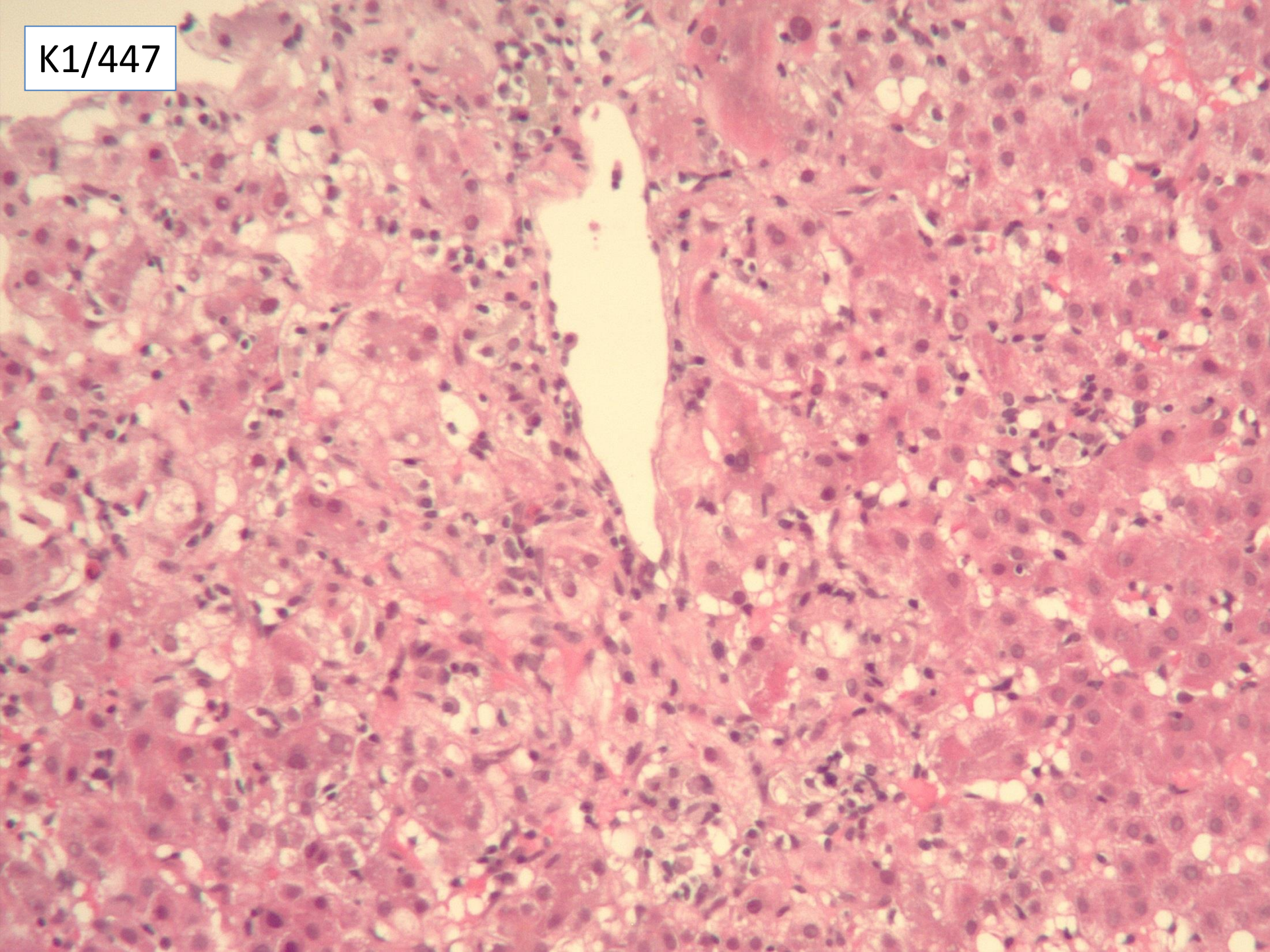
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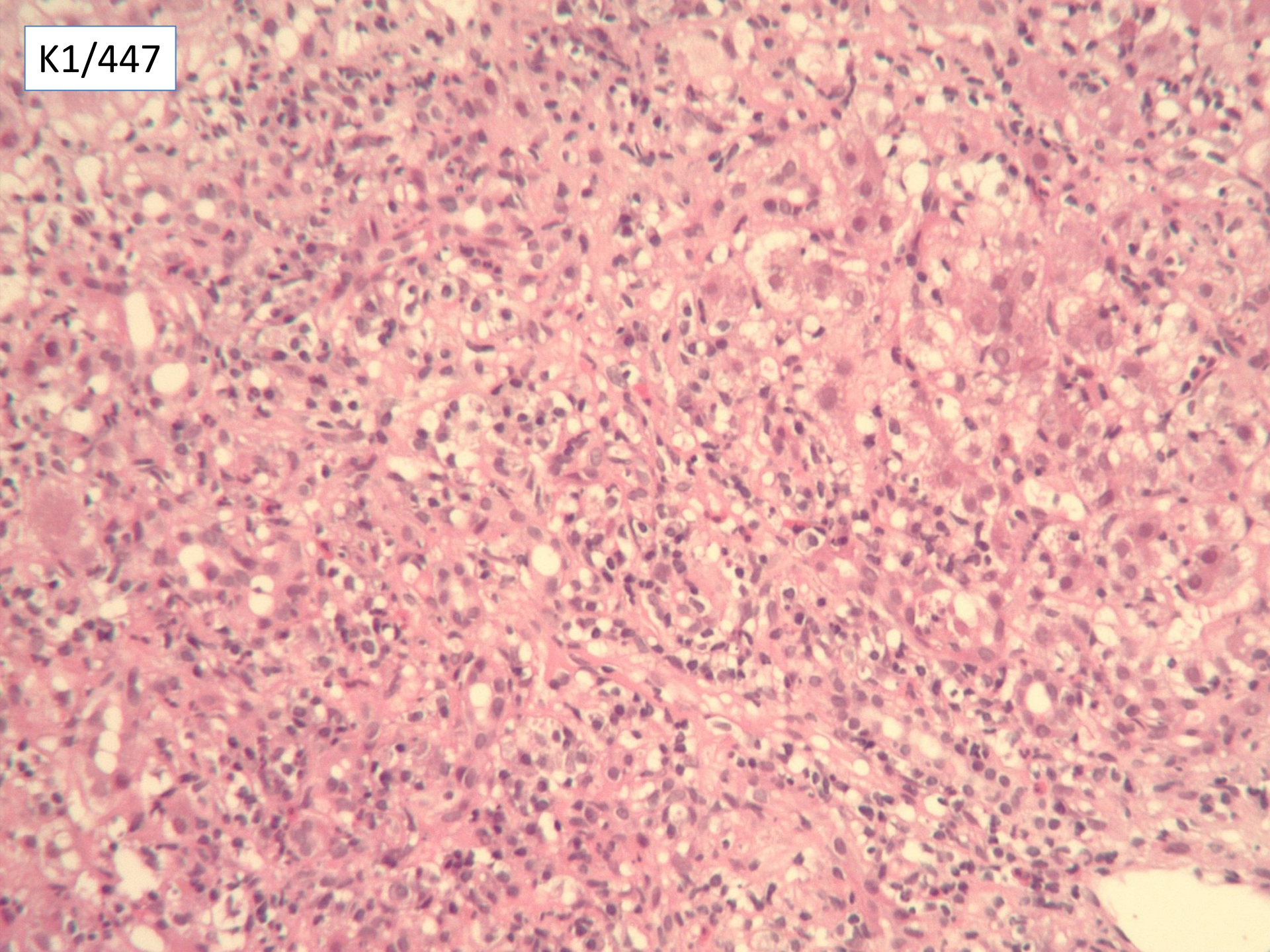
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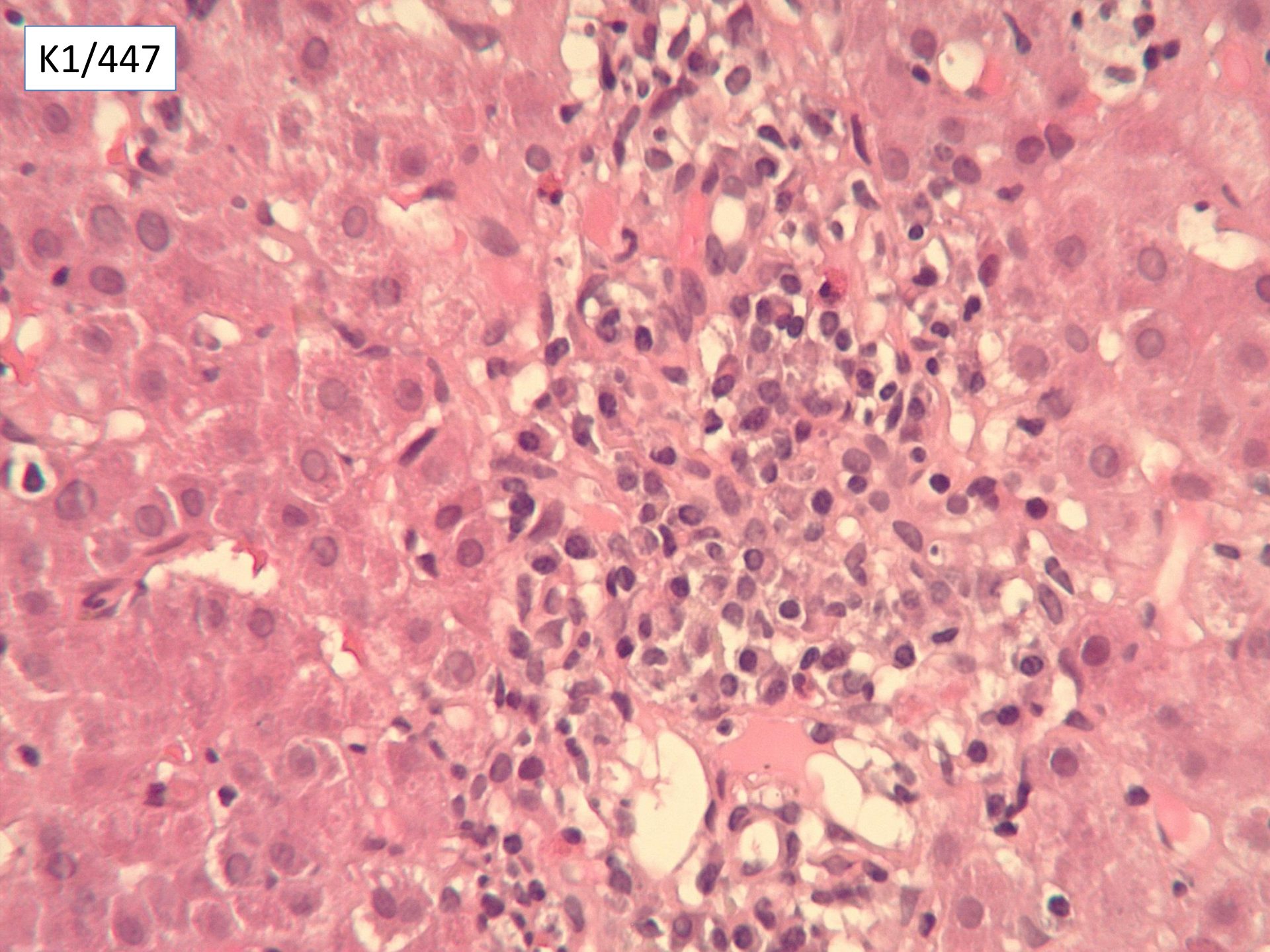

K1/447

**Case K1/447 Age 53, Male**

Acute jaundice. Deranged LFT's ? Autoimmune hepatitis

40 acute hepatitis

17 acute hepatitis with confluent/ bridging necrosis

16 hepatitis – not indicated whether acute or chronic

6 chronic hepatitis

1 acute hepatitis with ballooning and Mallory's

25 differential of AIH, drugs, viral

12 consistent with AIH only

33 consistent with AIH + differential

6 AIH or drugs

3 AIH not mentioned at all

1 "acute hepatitis with ballooning, Mallory's probably drug induced, exclude alcohol"

1 "Acute hepatitis probably alcohol"

1 ? hepatitis C infection, drugs

35 needs clinical information

8 gave Ishak grade = 6,10, 13x3, 14x2, 15.

3 gave Ishak stage = 0.1.0

Suggested scoring; no consensus, unsuitable for scoring 11/17 agree, 1 unsuitable

OR for 10 points – need acute or unspecified hepatitis

– lose 5 points for chronic hepatitis, Lose 5 points if no mention of AIH or consistent with AIH. Lose another 5 points if suggest cause may be alcoholic liver disease.

**Case K1/447 Age 53, Male**

Acute jaundice. Deranged LFT's ? Autoimmune hepatitis

Original diagnosis: pan-lobular hepatitis, autoimmune hepatitis, no fibrosis.

Additional information – alk phos and IgM normal. ALT 1500, IgG 25.9, ANA 1:80.

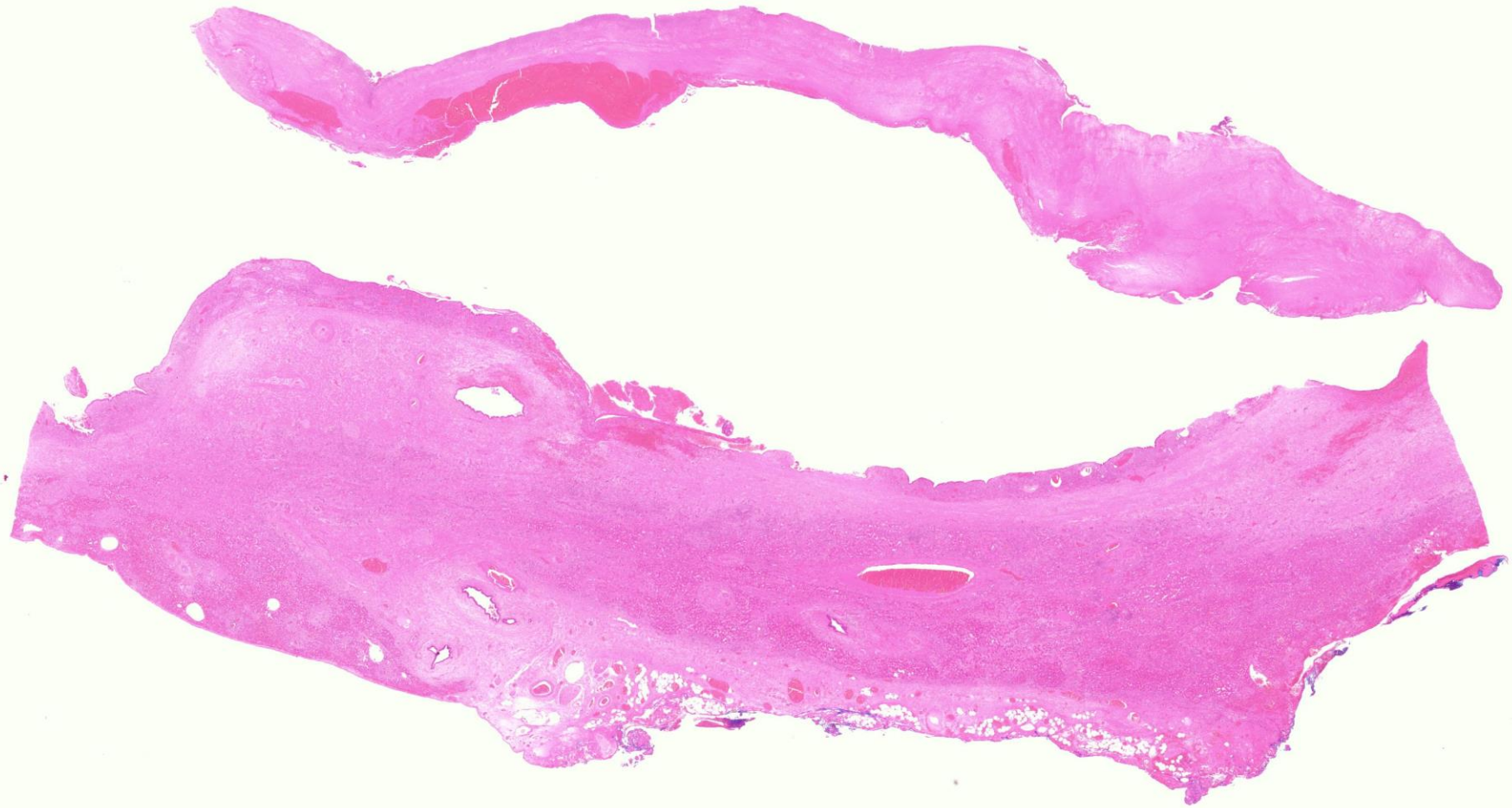
Treated as AIH with steroids, with reduction in ALT.

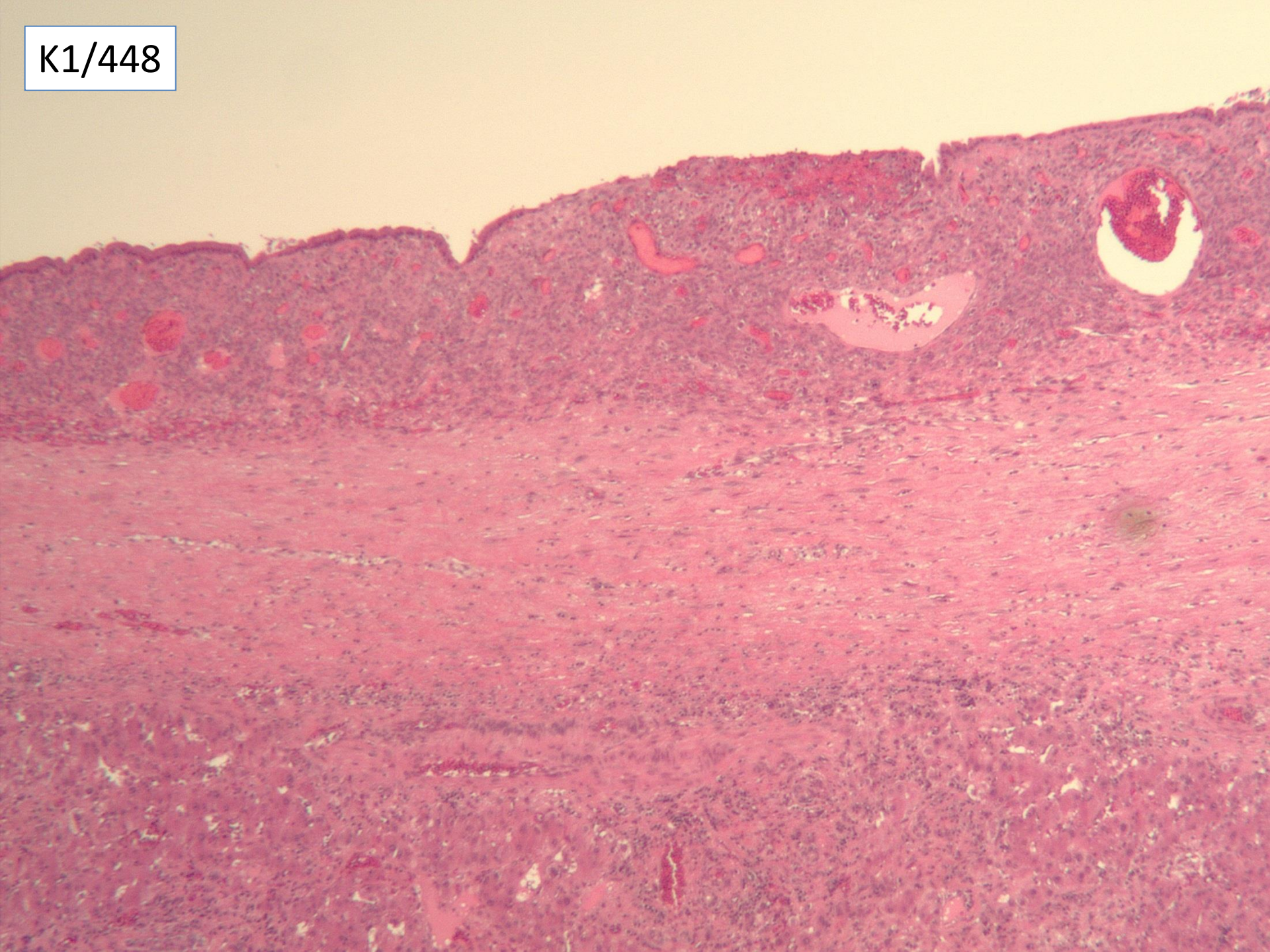
Comments from discussion: confluent necrosis present in this case, and is an important indication of severity which should be included in the report.

Severe lobular component as present here may be seen in recent onset AIH but also during flares of AIH – histology is not a clear indicator of acute v. chronic, and autoimmune hepatitis can be best reported without specifying either acute or chronic

**Case K1/448 Age 44, Female**

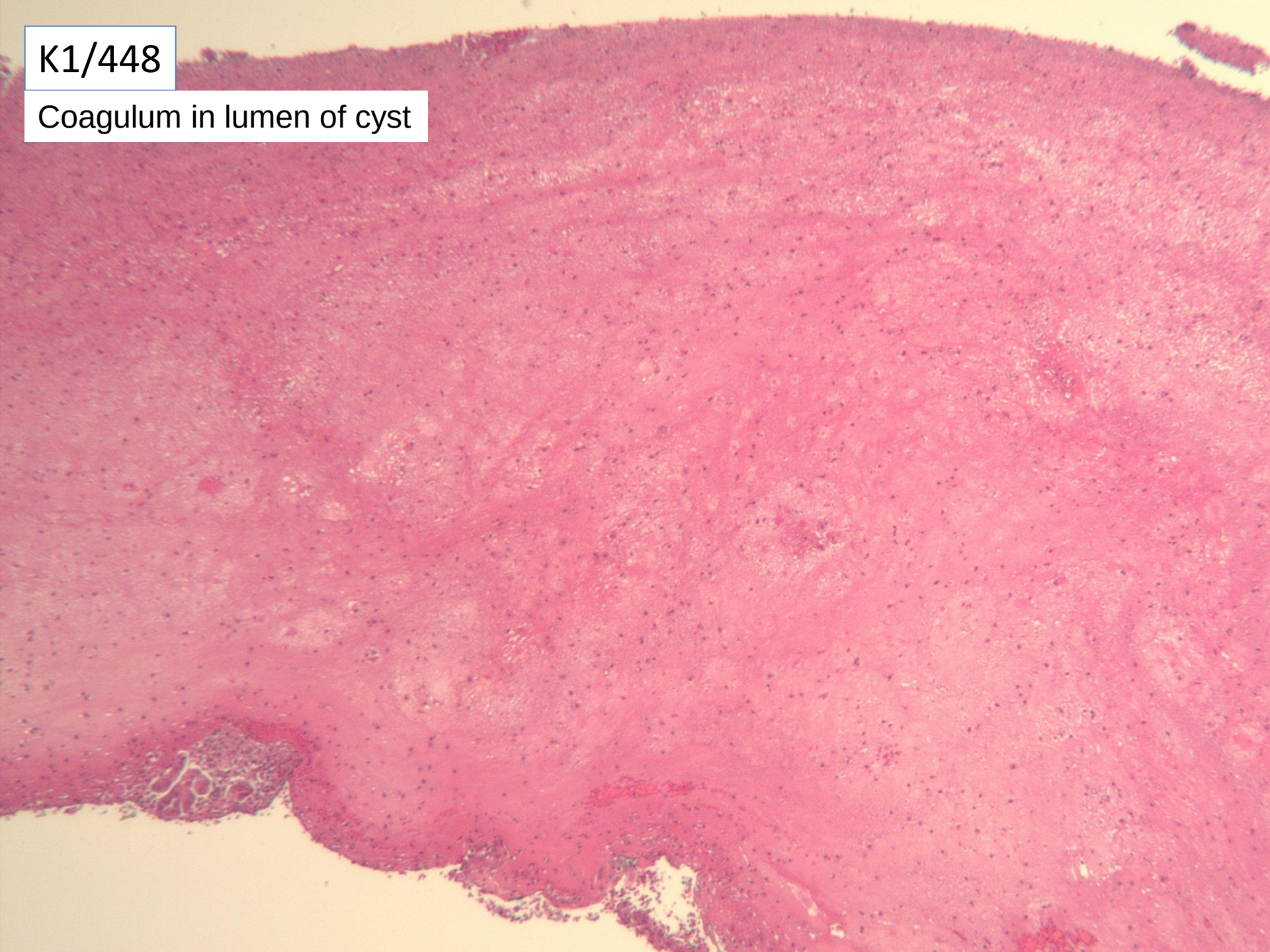
Hepatic cyst and gallbladder; obstructive jaundice.

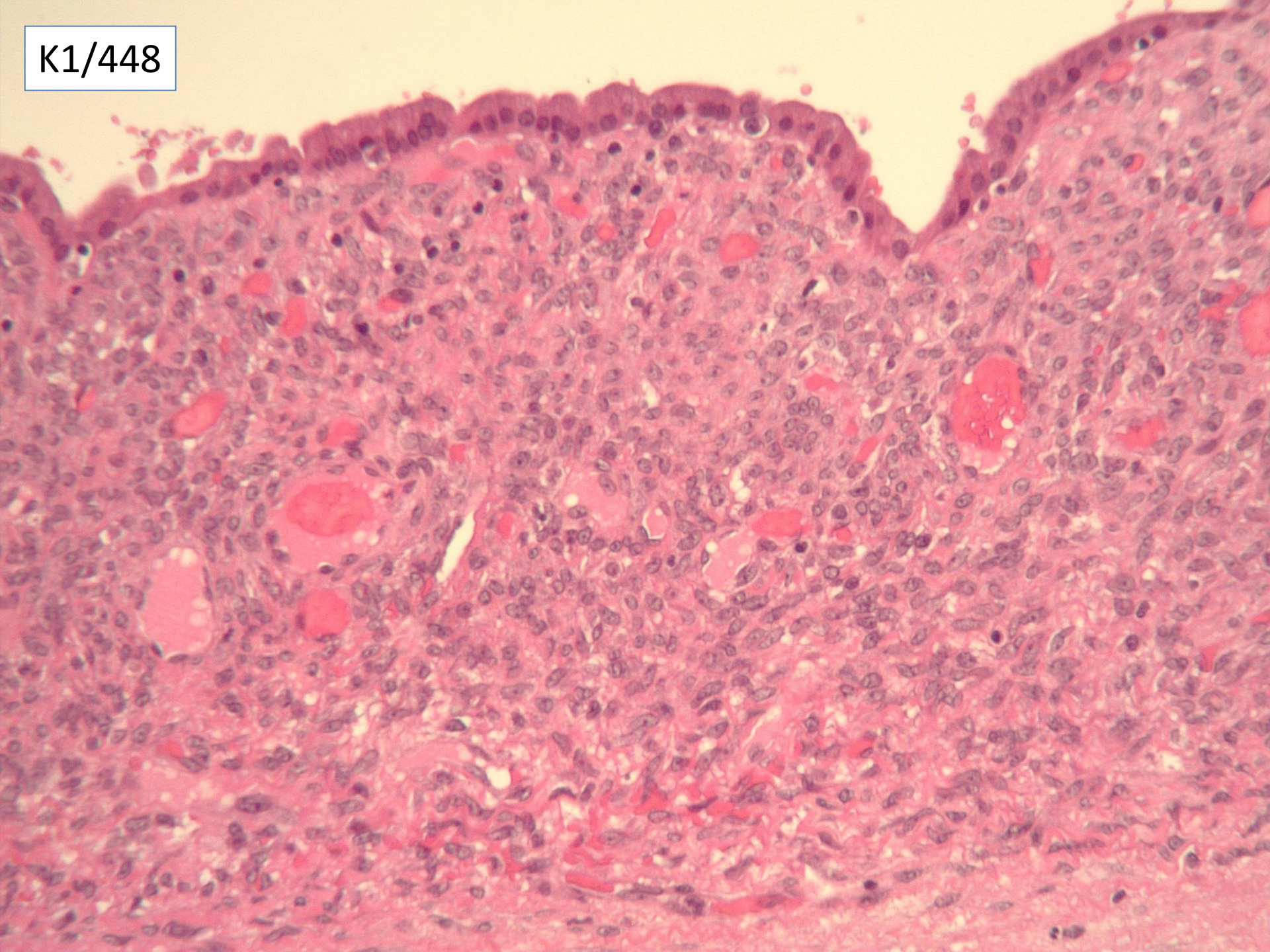



K1/448

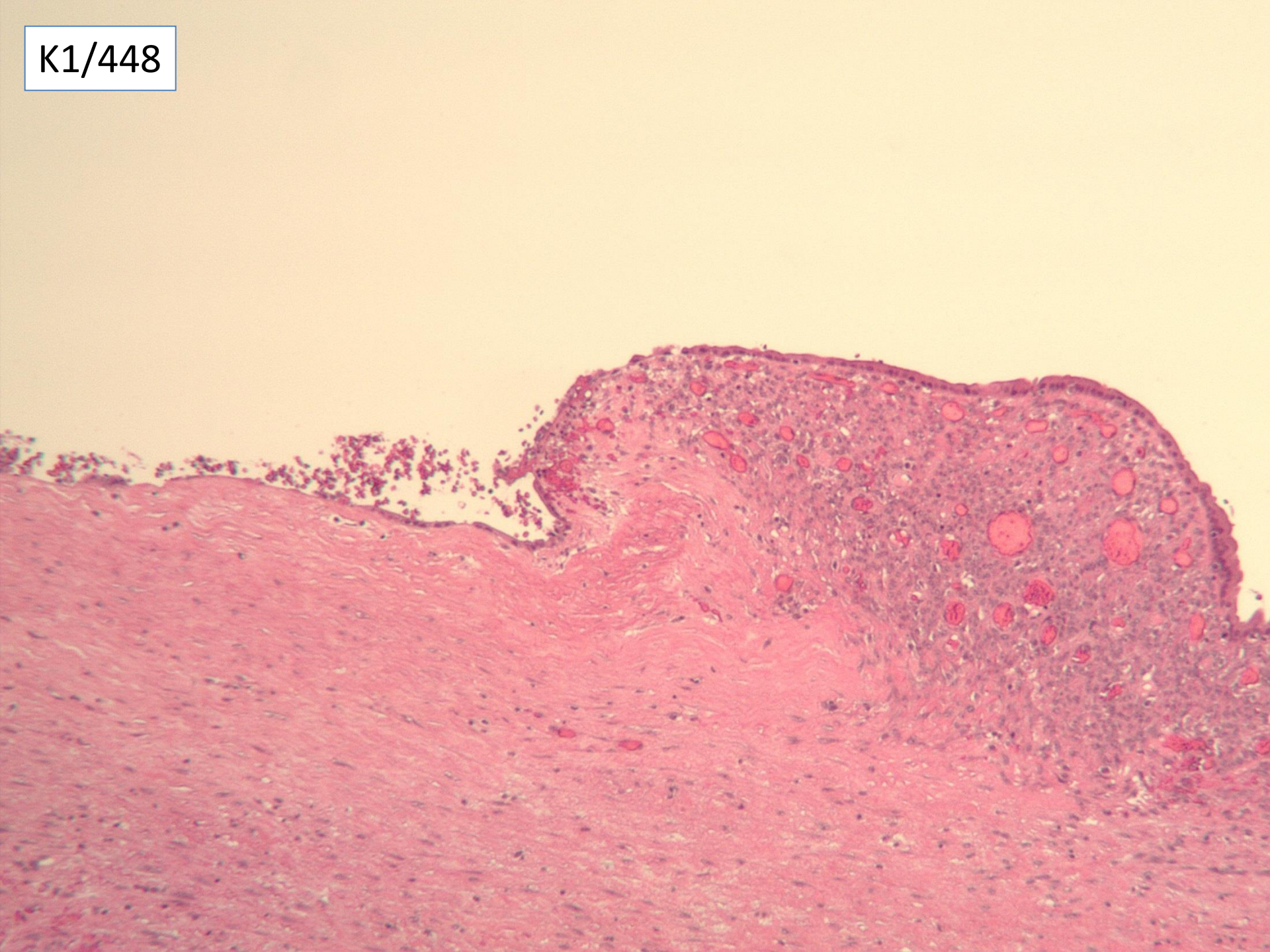
K1/448

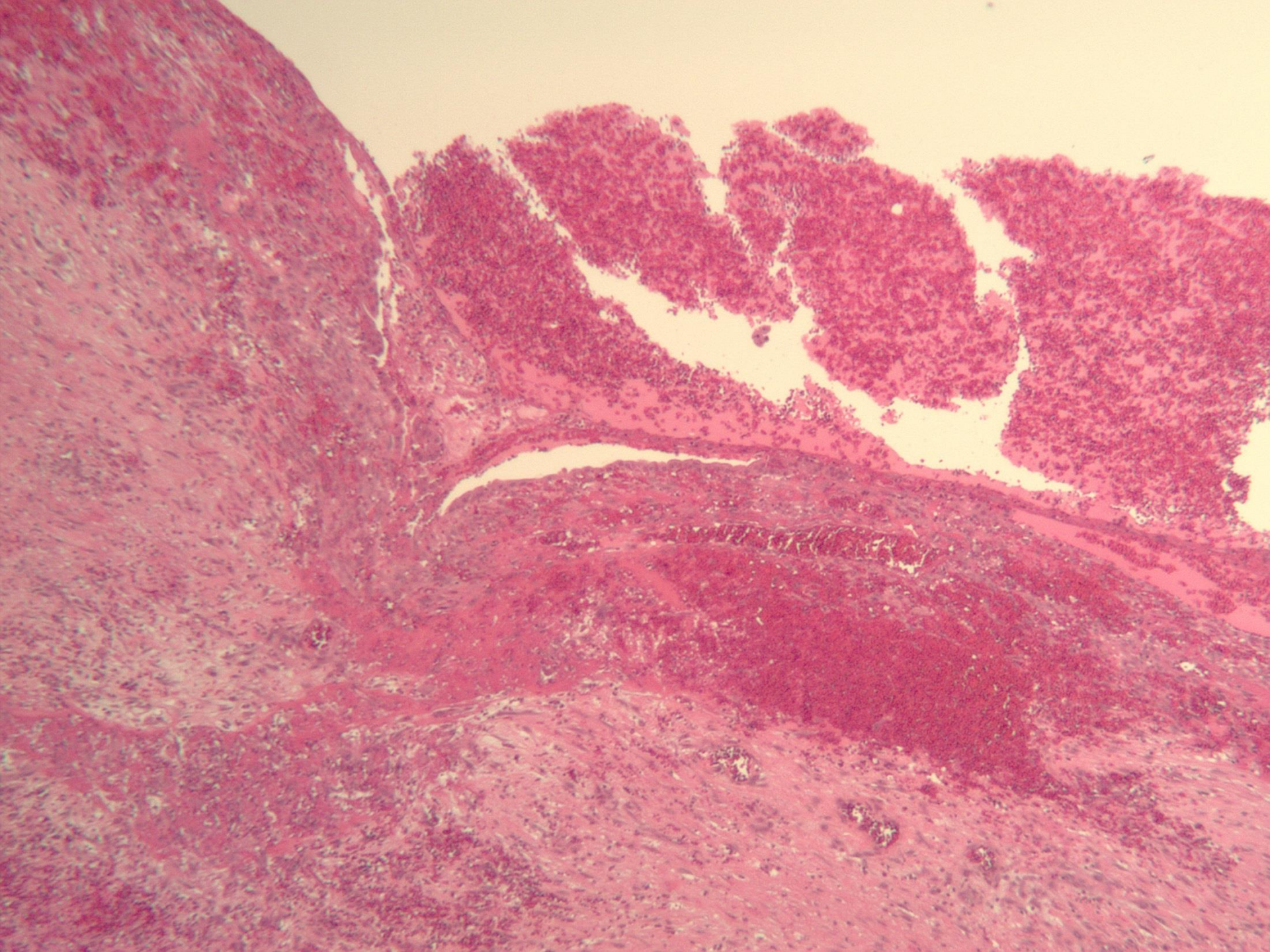
Coagulum in lumen of cyst

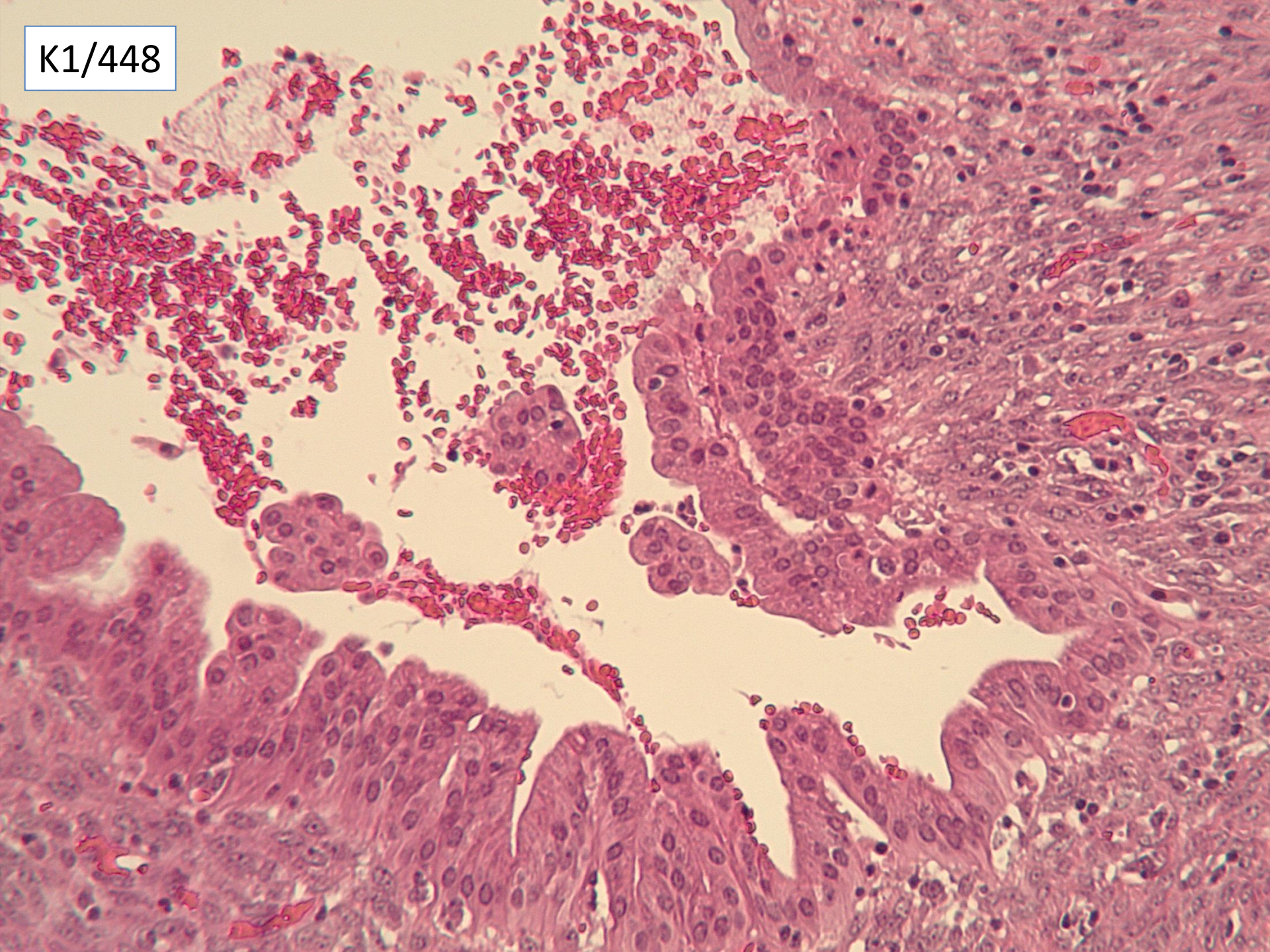



K1/448

K1/448






K1/448

**Case K1/448 Age 44, Female**

Hepatic cyst and gallbladder; obstructive jaundice.

24 mucinous cystic neoplasm / MCN

12 MCN (cystadenoma)

1 cystadenoma (MCN)

34 cystadenoma with ovarian like/mesenchymal stroma

2 choledochal cyst

4 endometriosis as only diagnosis

3 endometriosis as a differential for MCN

1 “cyst with cuboidal epithelium, cellular stroma beneath”

1 Hamartomatous cyst

Suggested scoring: for 10 points – either terminology MCN or cystadenoma with ovarian-like/mesenchymal stroma.

Score 0 points for choledochal cyst or endometriosis as definite diagnosis.

17/17 agree, 0 unsuitable

**Case K1/448 Age 44, Female**

Hepatic cyst and gallbladder; obstructive jaundice.

Original diagnosis: benign biliary cystadenoma

Comments: changing terminology to mucinous cystic neoplasm, WHO blue book – in line with pancreatic classification.

Ovarian-like stroma is implicit in the diagnosis of hepatobiliary cystadenoma, so doesn't need to be specifically mentioned for the diagnosis.

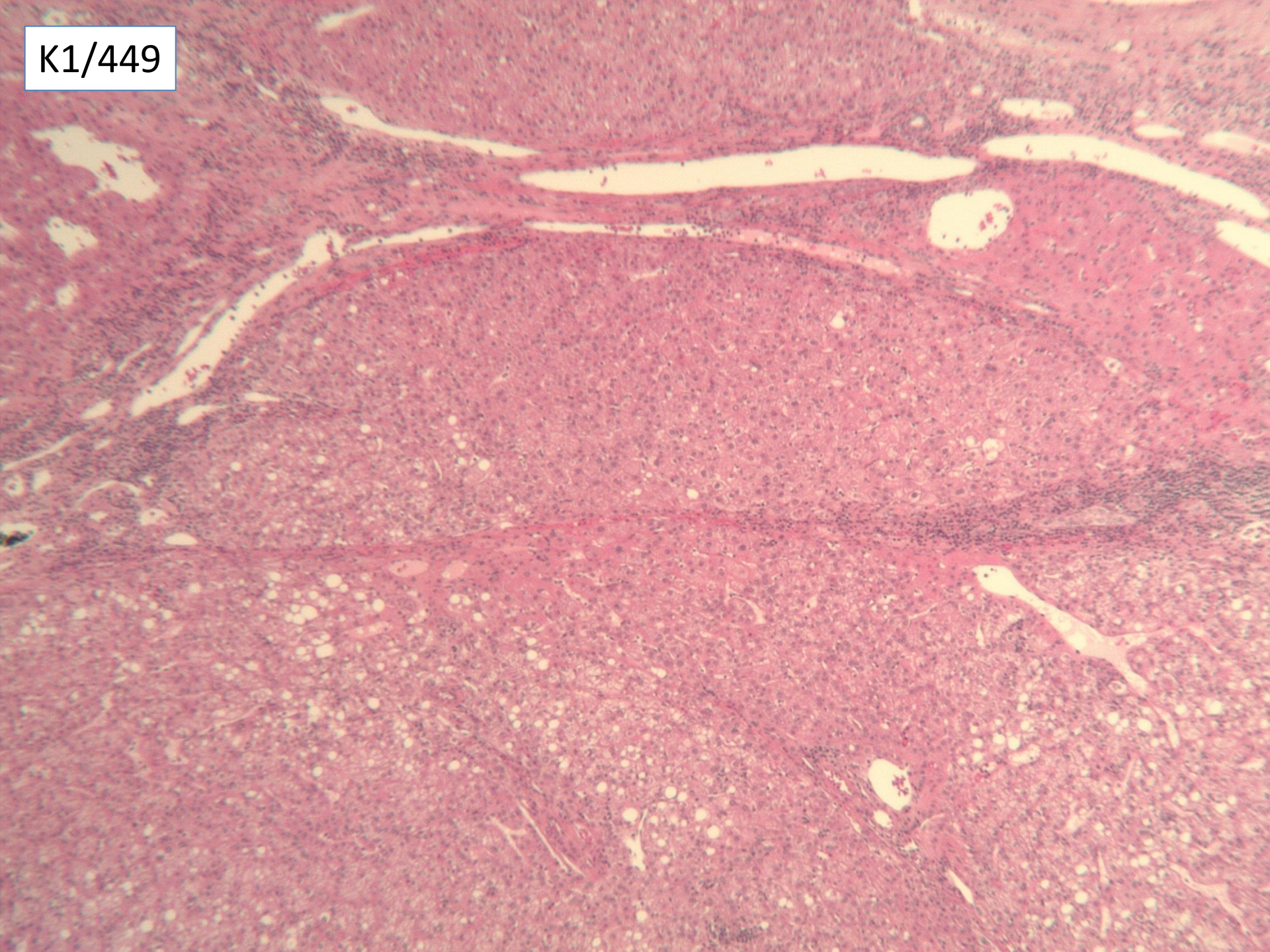
Cysts without the stroma are non-specific, biliary cysts. In practice, stroma is present in nearly all blocks of these cysts, although as here areas of ulceration may lose the stroma.

Endometriotic cysts are very rare in the liver, in patients with history of endometriosis elsewhere, and with evidence of previous haemorrhage.

The reason for the clinical presentation with obstructive jaundice in this case is not known.

**Case K1/449** **Age 73, Male**

Cirrhotic liver ? Hepatoma segment 8. segment 8 lesion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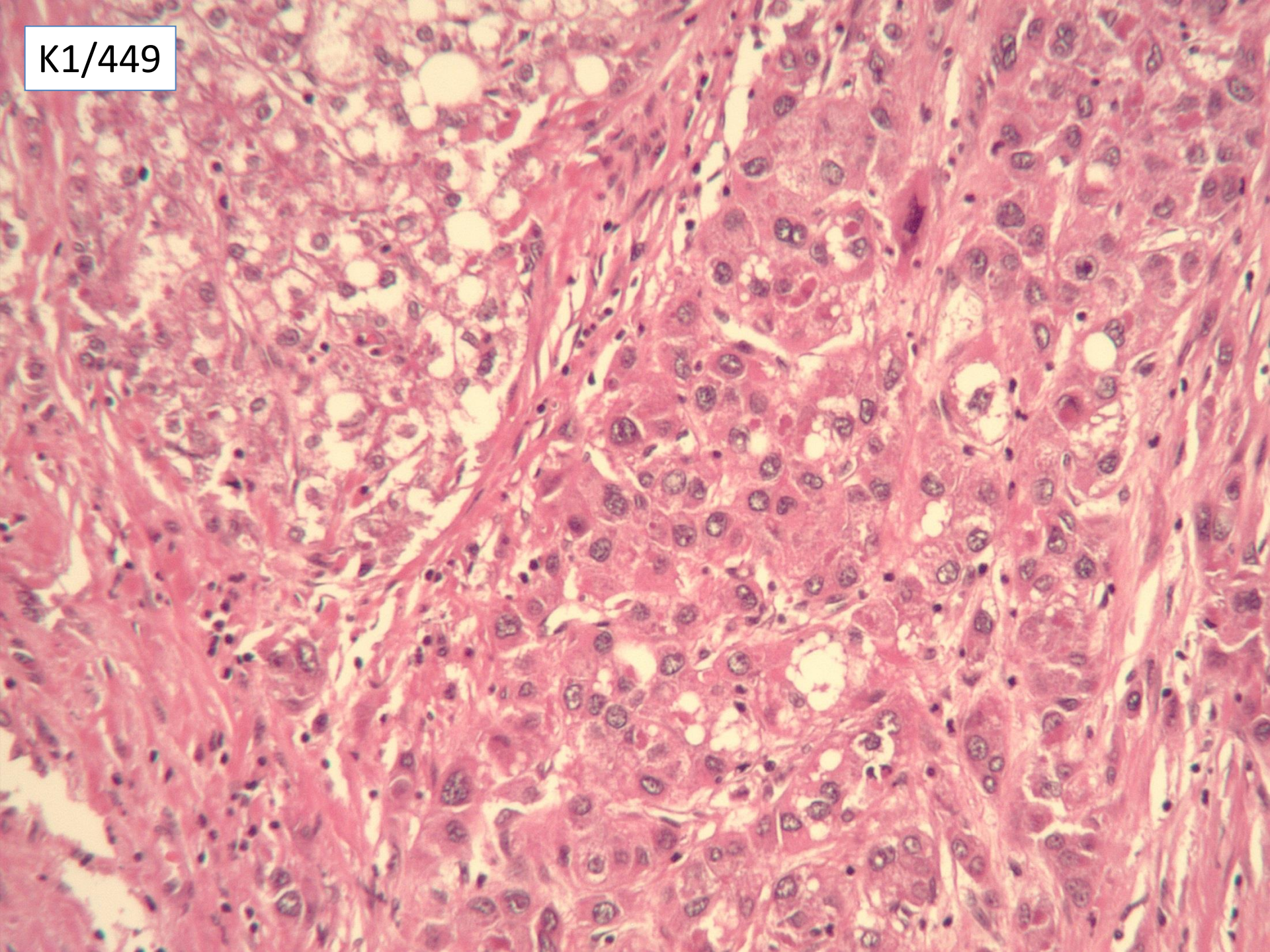
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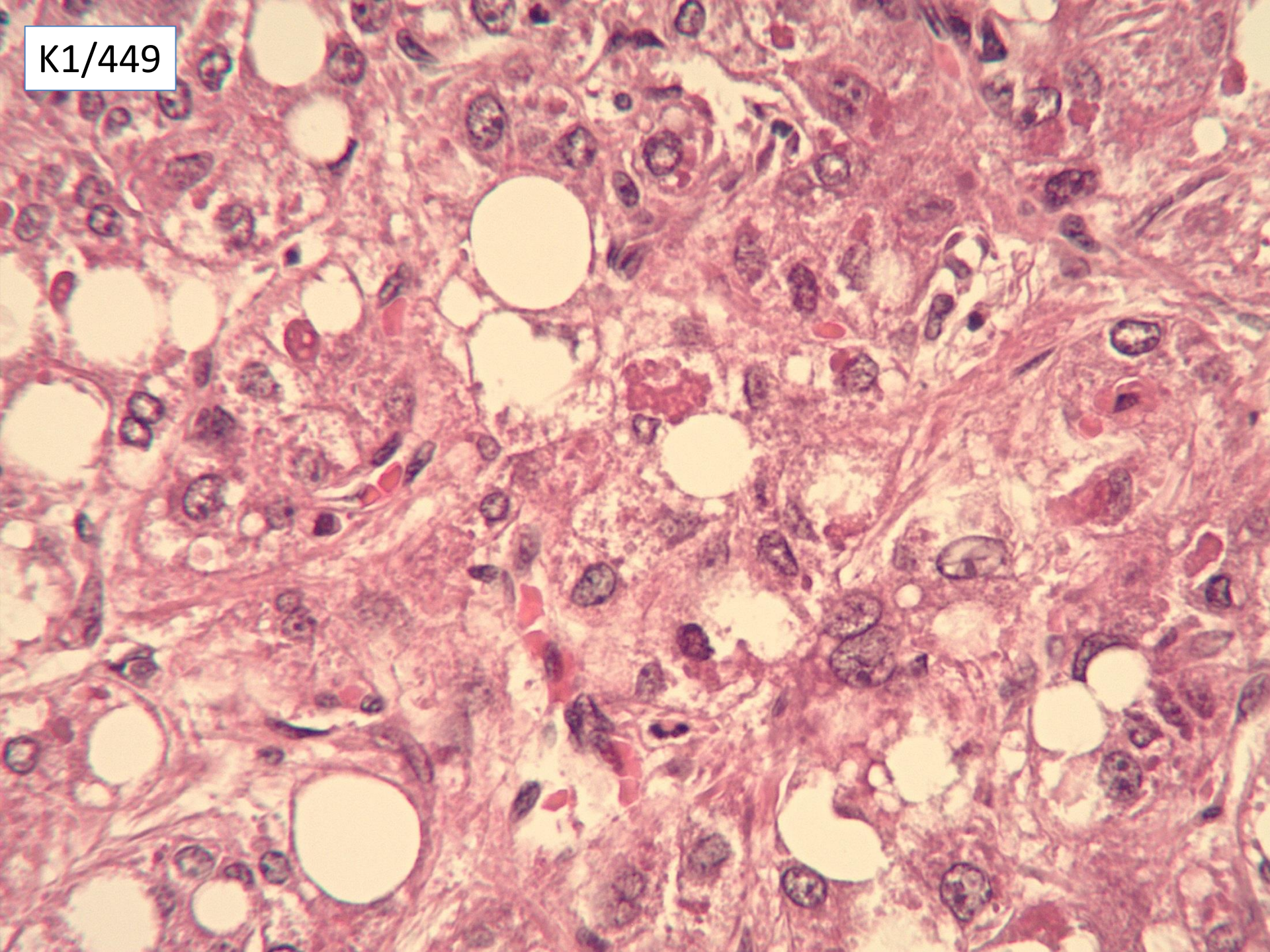
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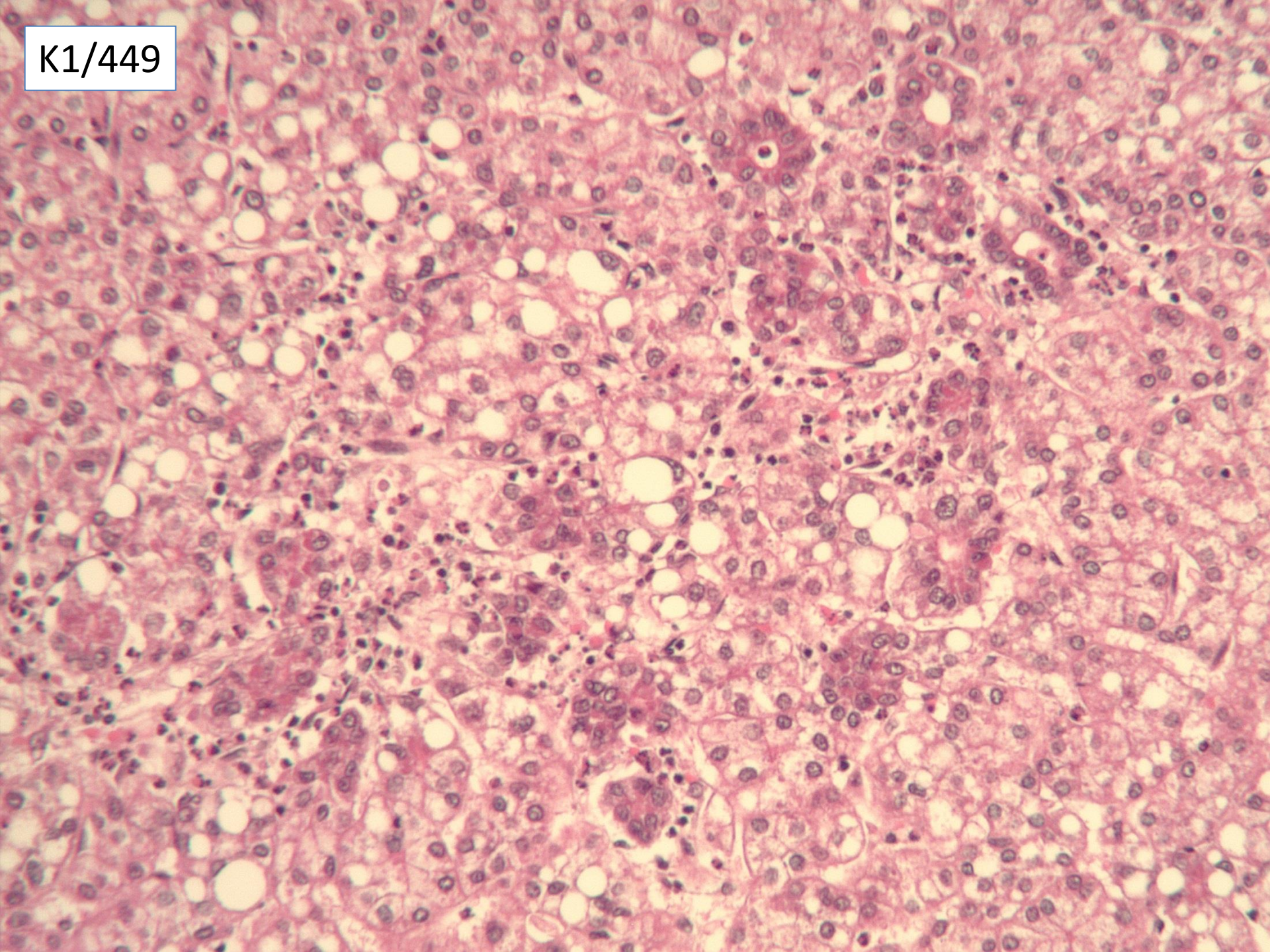
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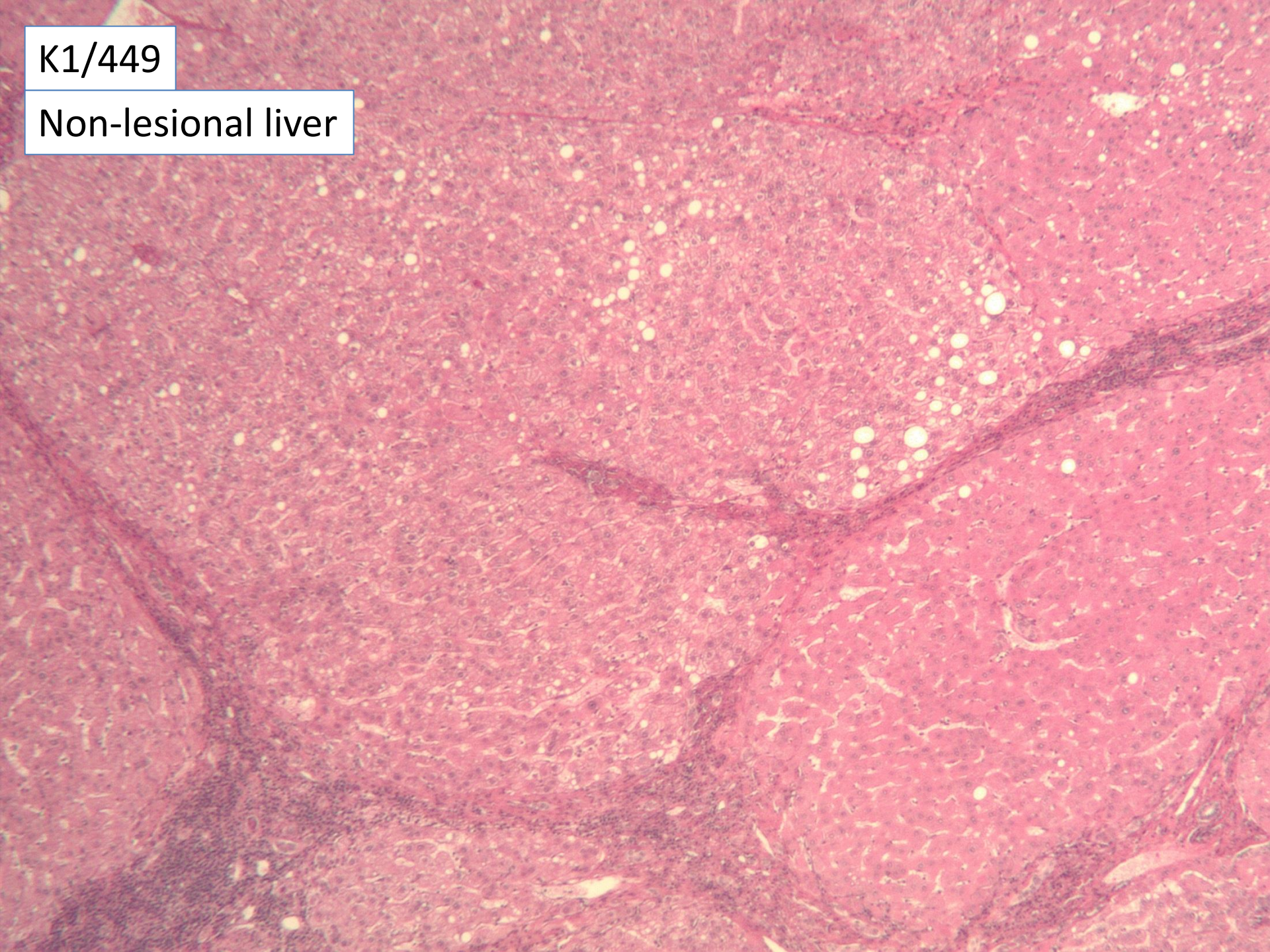
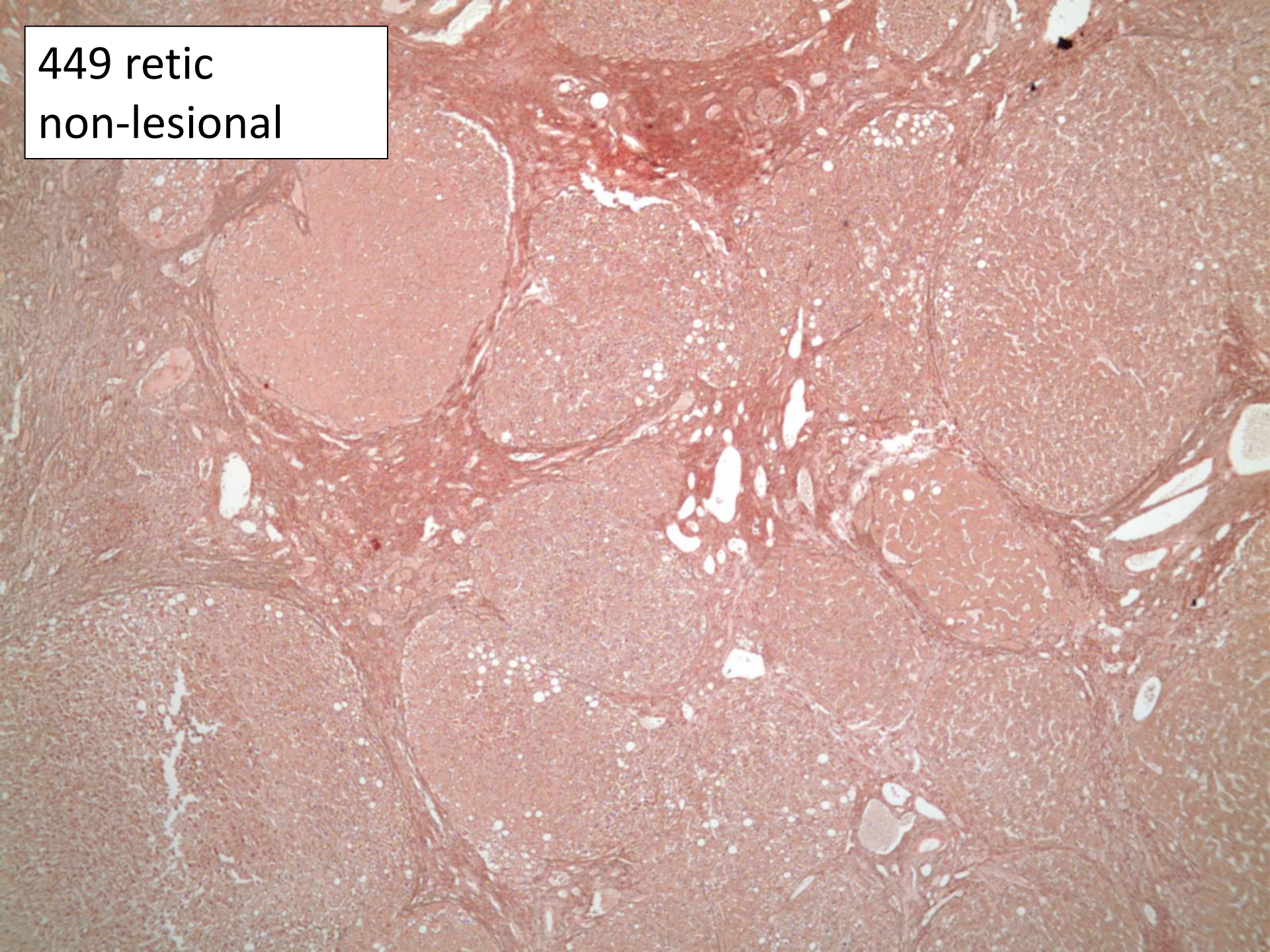

K1/449
Non-lesional liver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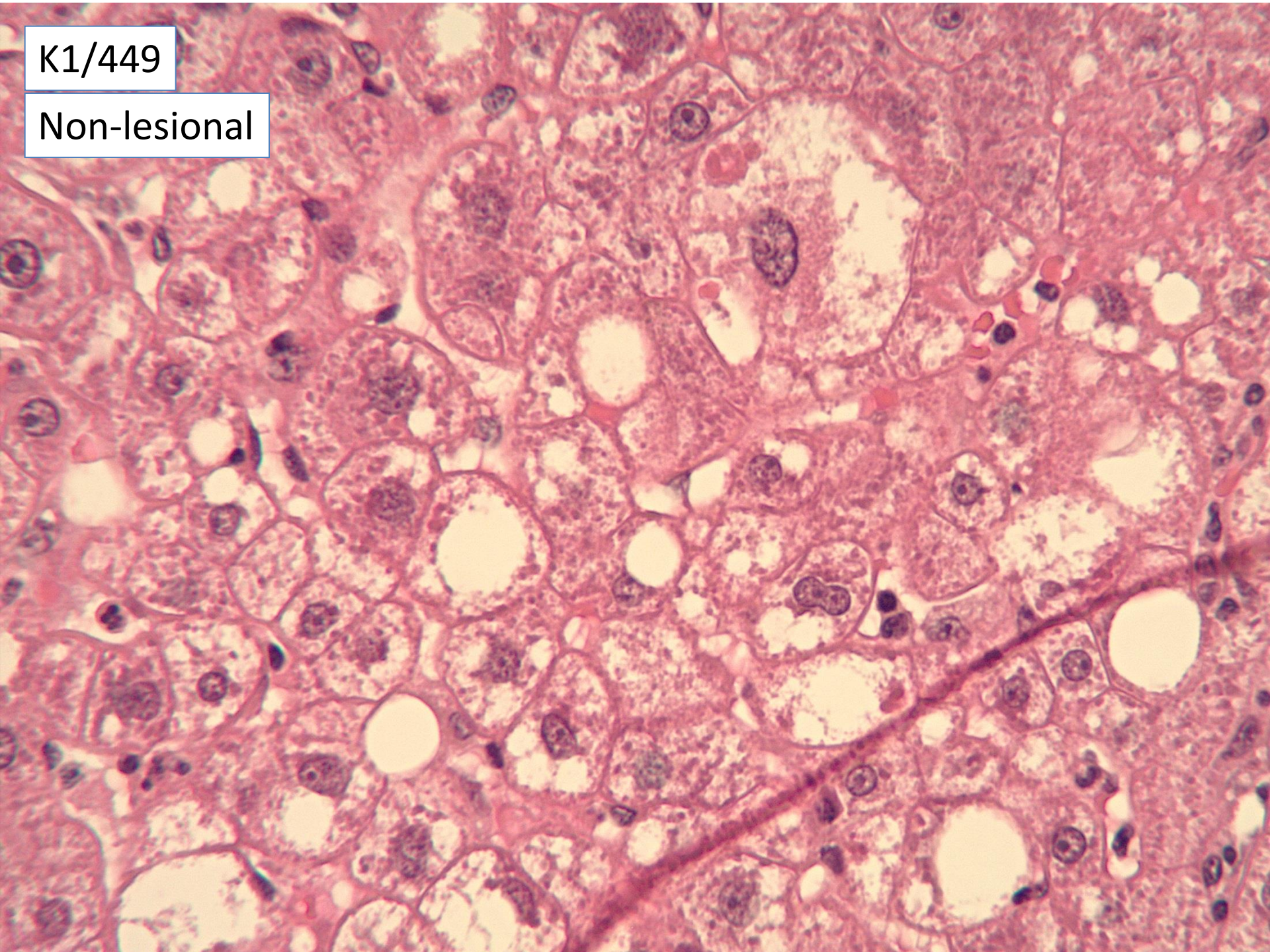
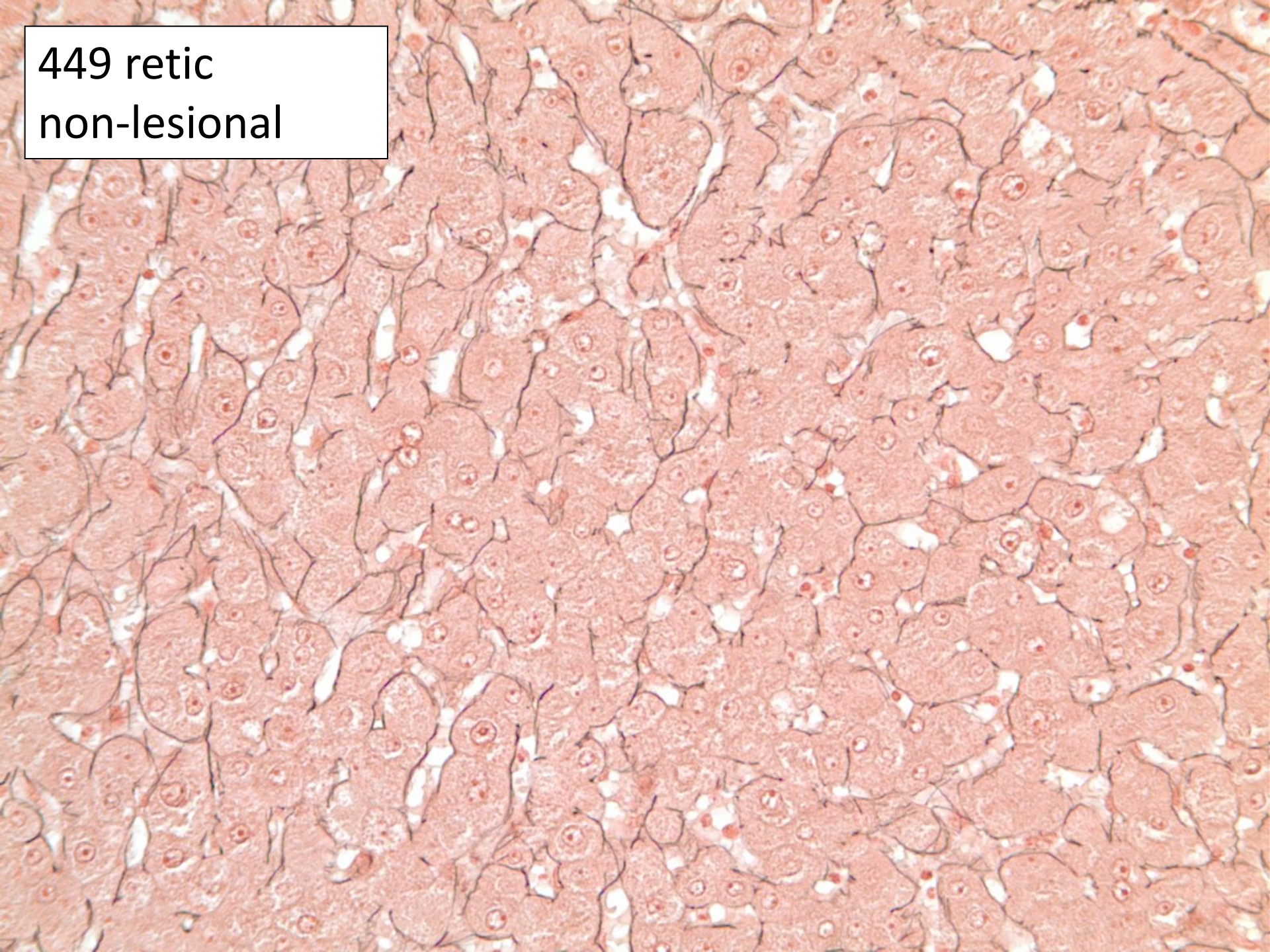
non-lesional


K1/449
Non-lesional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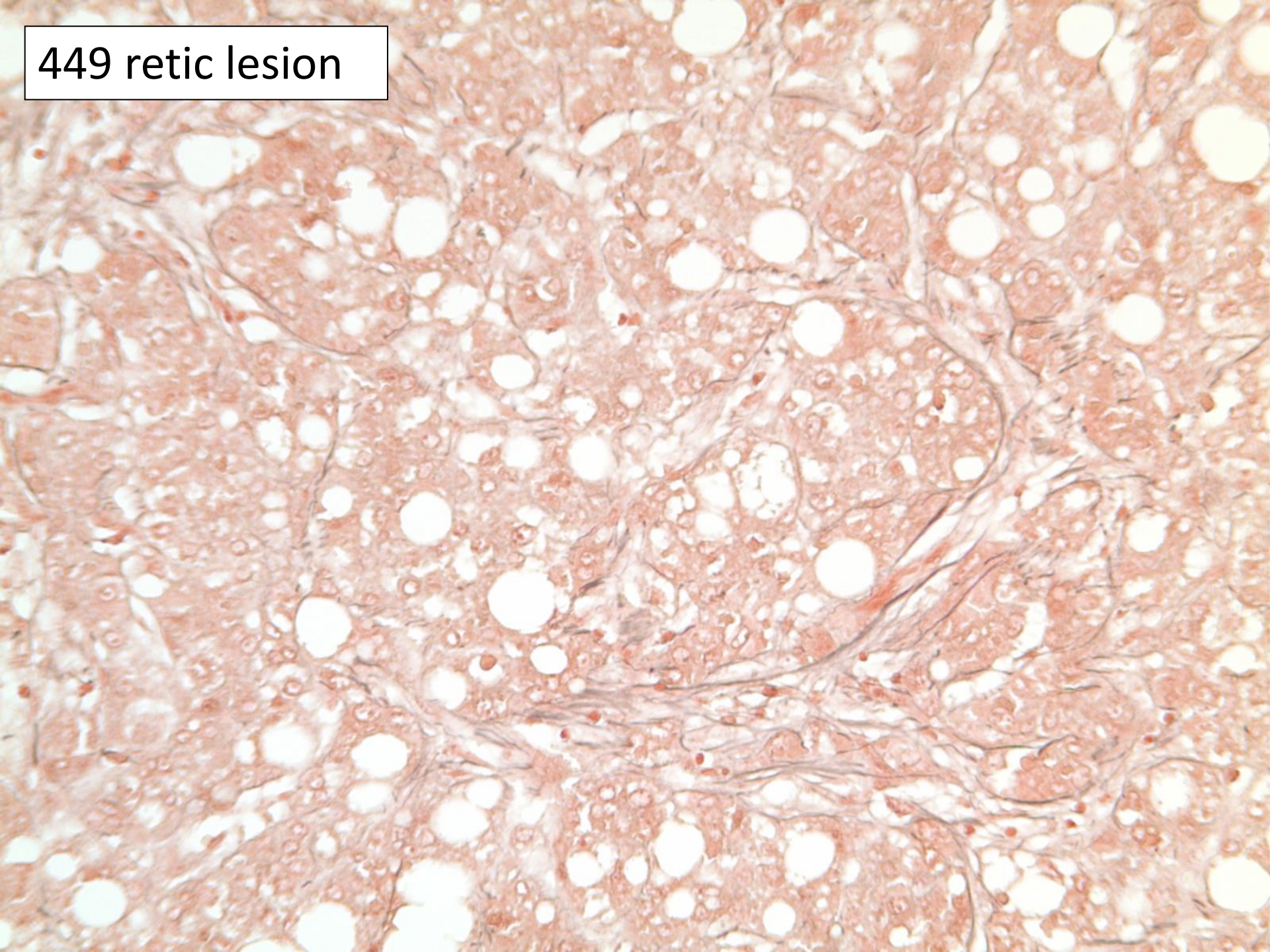

449 retic lesion

**Case K1/449 Age 73, Male**

Cirrhotic liver ? Hepatoma segment 8. segment 8 lesion.

68 HCC

Of which – 19 NOS

24 well differentiated, 32 moderately differentiated

34 mentioned steatohepatitis or Mallory bodies in description,

7 of whom used 'steataohepatitic HCC'

2 dysplastic nodule or HCC – both seek second opinion

1 steatotic hepatocellular adenoma

3 no comment on background liver

67 cirrhosis

Of which – 13 ? ALD / NAFLD, 3 ?viral or NAFLD, 2 ?viral hepatitis

Suggested scoring: for 10 points – HCC or dysplastic nodule/HCC seek second opinion.
Lose 5 points if not included cirrhosis in non-lesional liver.
Lose 10 points for nepatocellular adenoma

16/16 agree, 0 unsuitable

**Case K1/449 Age 73, Male**

Cirrhotic liver ? Hepatoma segment 8. segment 8 lesion.

Original diagnosis: well differentiated hepatocellular carcinoma

Further information: This resection and also RFA in 2011. Subsequently underwent TACE in early 2013.

Remains disease free.

Comment from meeting – features of steatohepatitis with Mallory –Denk bodies both in lesion and non-lesional cirrhotic liver.

Masterclass presentation: Stefan Hubscher:

Liver EQA Scheme
Circulation K1 – Case 449

# Discussion Points
# Steatohepatitic HCC

# Steatohepatitic HCC - Definition

**Features of "fatty liver disease" commonly present in HCC**
(Ishak - AFIP Fascicle 2001, Goodman – MacSween's Pathology of the Liver, 6th Edition 2012)

- Fatty change in 68%, severe in 10%
- Mallory-Denk bodies in 20%
- Varying degrees of inflammation

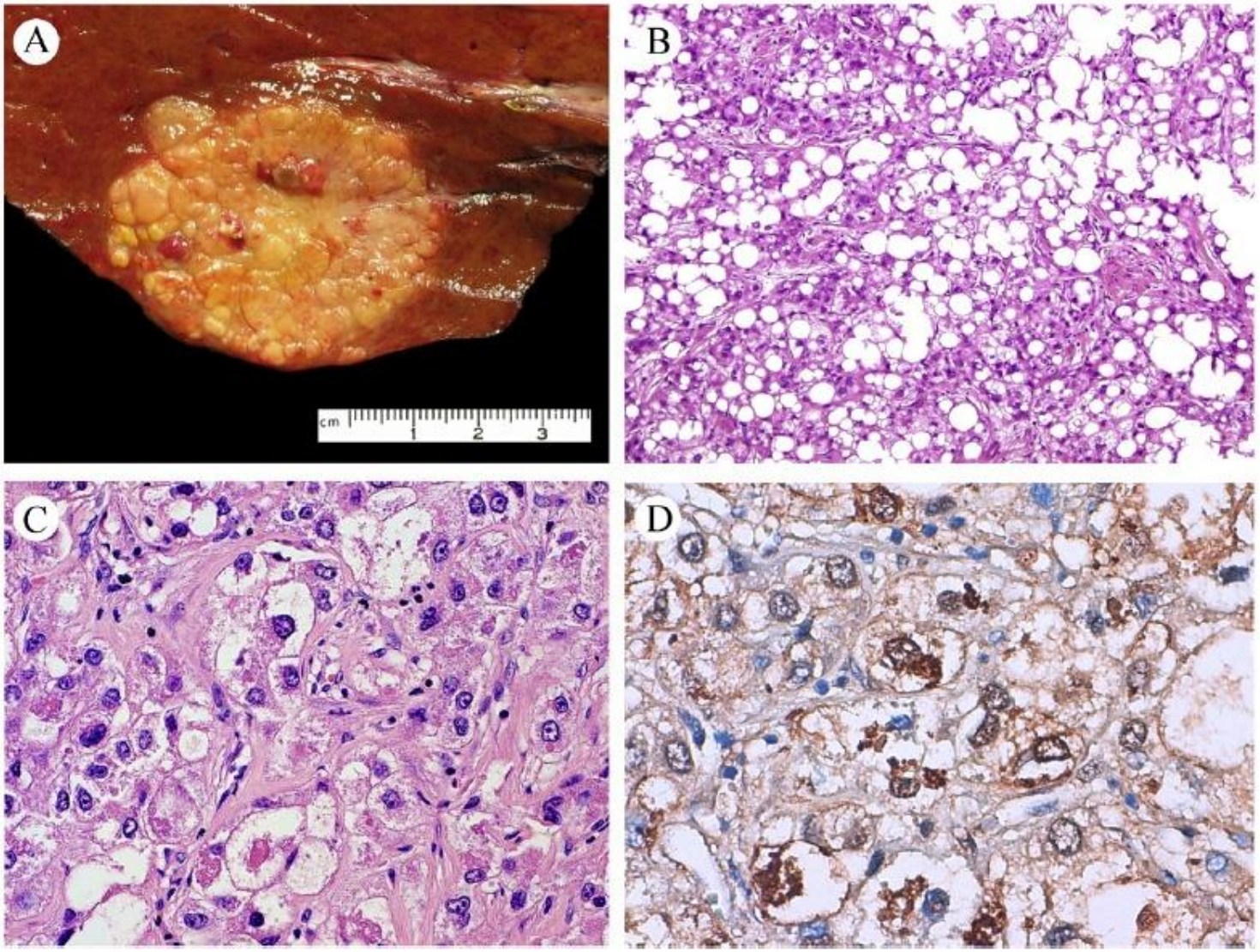
**"Steatohepatitic HCC" (** Salamao Am J Surg Pathol 2010; 34:1630 – 1636)

- Present in 22/66 patients undergoing liver transplantation for HCV cirrhosis + HCC
- Diagnosis based on combination of features seen in steatohepatitis
  i. Large droplet steatosis (100%)
  ii. Hepatocyte ballooning (100%)
  iii. Mallory-Denk bodies (91%)
  iv. Fibrosis – usually pericellular, sometimes lamellar (73%)
  v. Inflammation - usually moderate/ marked

  – **Steatohepatitic features present in ≥ 5% of tumour area**

# Steatohepatitic HCC - Histological Features

(Salomao, Human Pathology 2012: 43: 737-746)



# Steatohepatitic HCC

( Salamao 2010, Jain 2012, Salomao 2012, Jain 2013, Shibihara 2014)

## Diagnostic criteria

- All studies require combination of features (at least 3/5 features listed in previous slide)
- Extent variable
  - ≥ 5% (Salamao 2010, Jain 2013) or ≥ 50% (Salamao 2012)
  - Focal SH (≥ 5%) = SH-HCC, predominant SH (≥ 50%) = "typical" SH-HCC (Shibihara 2014)

## Prevalence – varies according to diagnostic criteria:

- ≥ 5% = 19-31% (Jain 2013, Shibihara 2014)
- ≥ 50% = 13.5% - 17.5% (Salamao 2012, Shibihara 2014)

# Steatohepatitic HCC

( Salamao 2010, Jain 2012, Salomao 2012, Jain 2013, Shibihara 2014)

## Disease Associations

1. More commonly seen in patients with fatty liver disease (especially NAFLD)
    - Prevalence 48% in NASH, 24% in ALD and 1.3% in other diseases (Salamao 2012)

2. Associated with risk factors for metabolic syndrome

3. Features of steatohepatitis commonly present in non-neoplastic liver
    - 79% SH-HCC had background steatohepatitis vs 4% other HCC (Jain 2013)

# Steatohepatitic HCC – Clinical Relevance

( Salamao 2010, Jain 2012, Salomao 2012, Jain 2013, Shibihara 2014)

**May behave less aggressively than conventional HCC:**

- Most studies show no overall difference in overall/disease free survival

- Trend for lower grade (p = 0.06) and less vascular invasion (p = 0.08) (Salamao 2012)
- Less frequent deaths from recurrent HCC following transplantation (1/19 vs 6/76) (Jain 2013)

- Strictly defined "typical" SH- HCC (5/5 features present in ≥ 50% of tumour) associated with improved disease free survival compared with conventional HCC and "other SH-HCC" (Shibihara 2014)
  - "Typical SH-HCC" smaller and better differentiated than "other SH-HCC"
  - Steatohepatitis may be a feature of early neoplasms, which diminishes as they progress

# Steatohepatitic HCC – Clinical Relevance
# Distinction Between Inflammatory and Neoplastic Steatohepatitis

→ May cause problems with liver biopsy diagnosis

**Features helpful to confirm diagnosis of malignancy** (Salamao 2010)

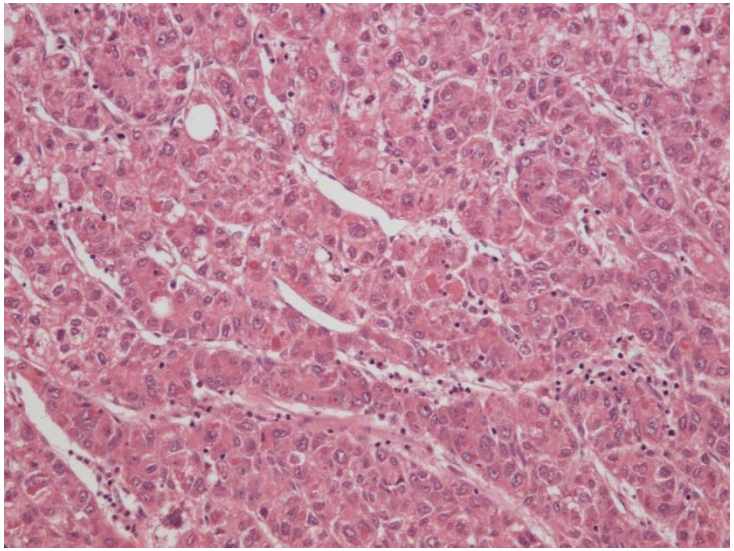
1. **Loss of reticulin**

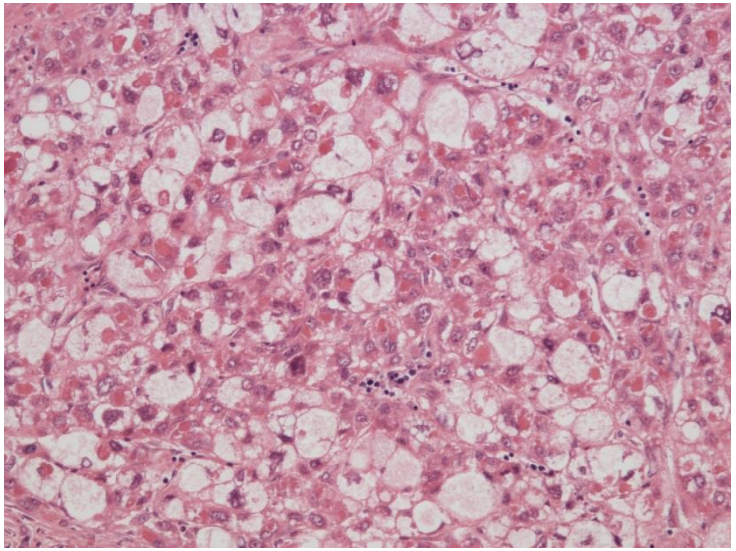
- BUT - reticulin fibres may be lost in benign fatty liver disease (Singhi 2012)

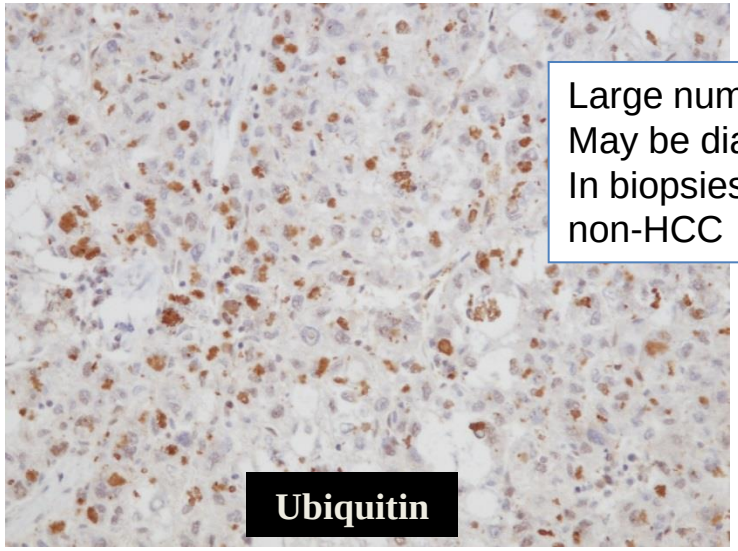
2. **Immunohistochemistry**
    - Glypican 3, glutamine synthetase, HSP 70
    - All 7 cases tested positive for at least 2 of 3 markers

# Steatohepatitic HCC – Immunostaining for Ubiquitin and CK 8/18

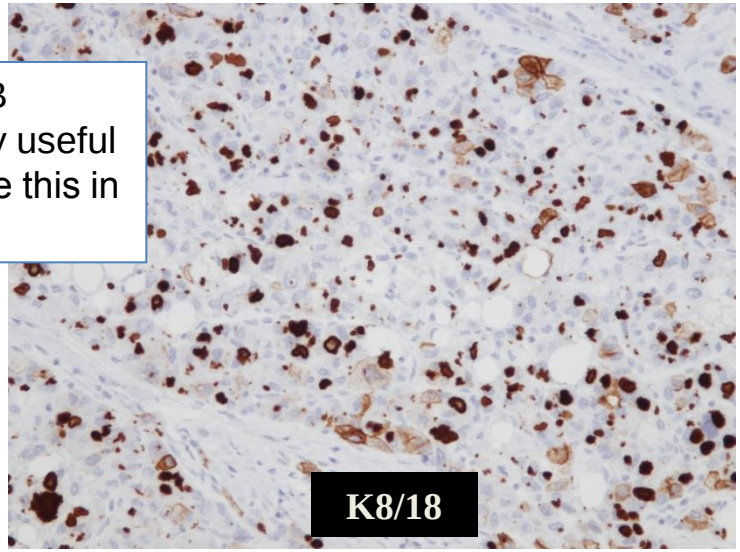
77 M, 3.4 cm lesion resected from left lobe. Type 2 DM, hyperlipidaemia, BMI 29
Background liver shows steatohepatitis with bridging fibrosis (Kleiner stage 3)





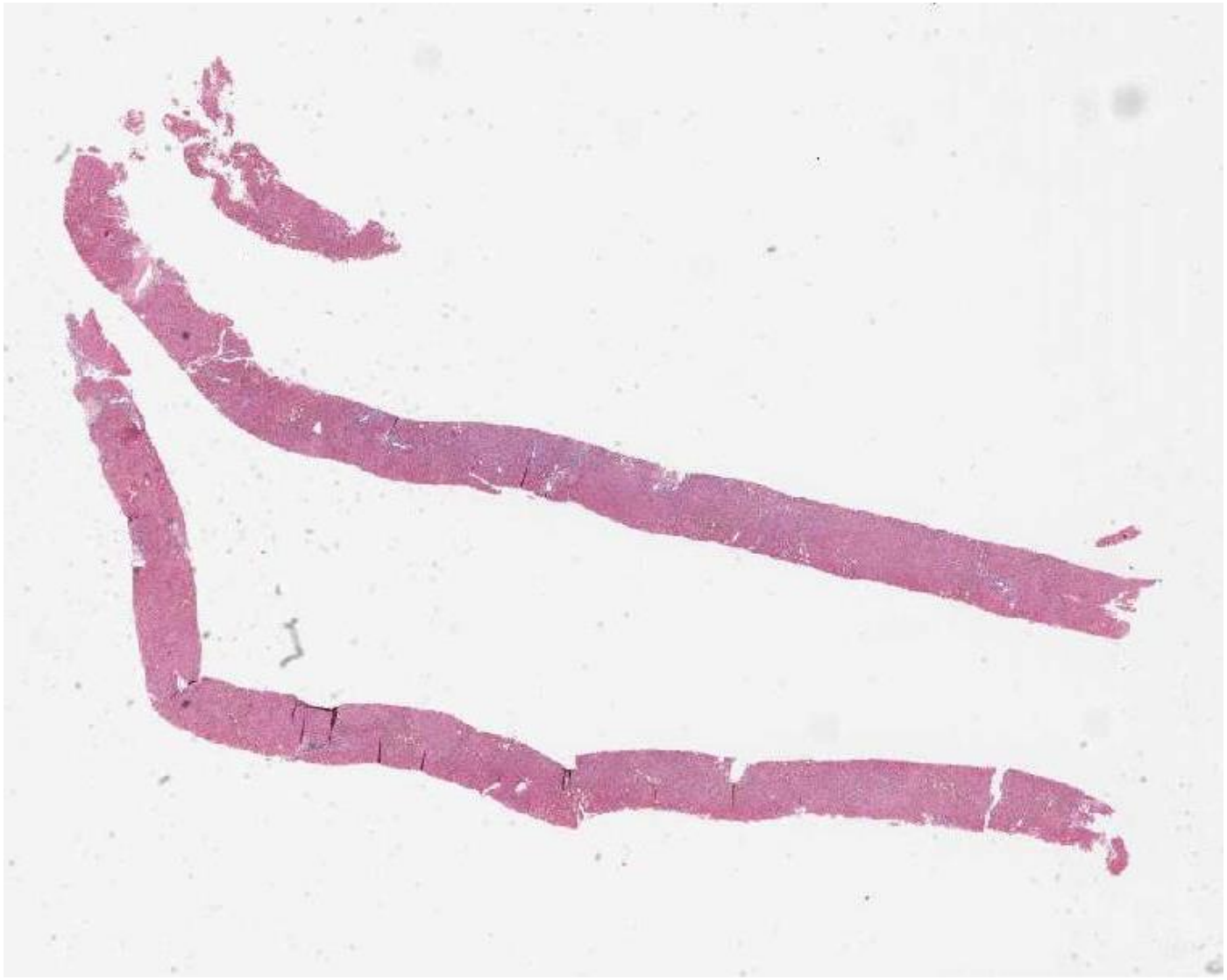



Large numbers of MB
May be diagnostically useful
In biopsies - don't see this in non-HCC

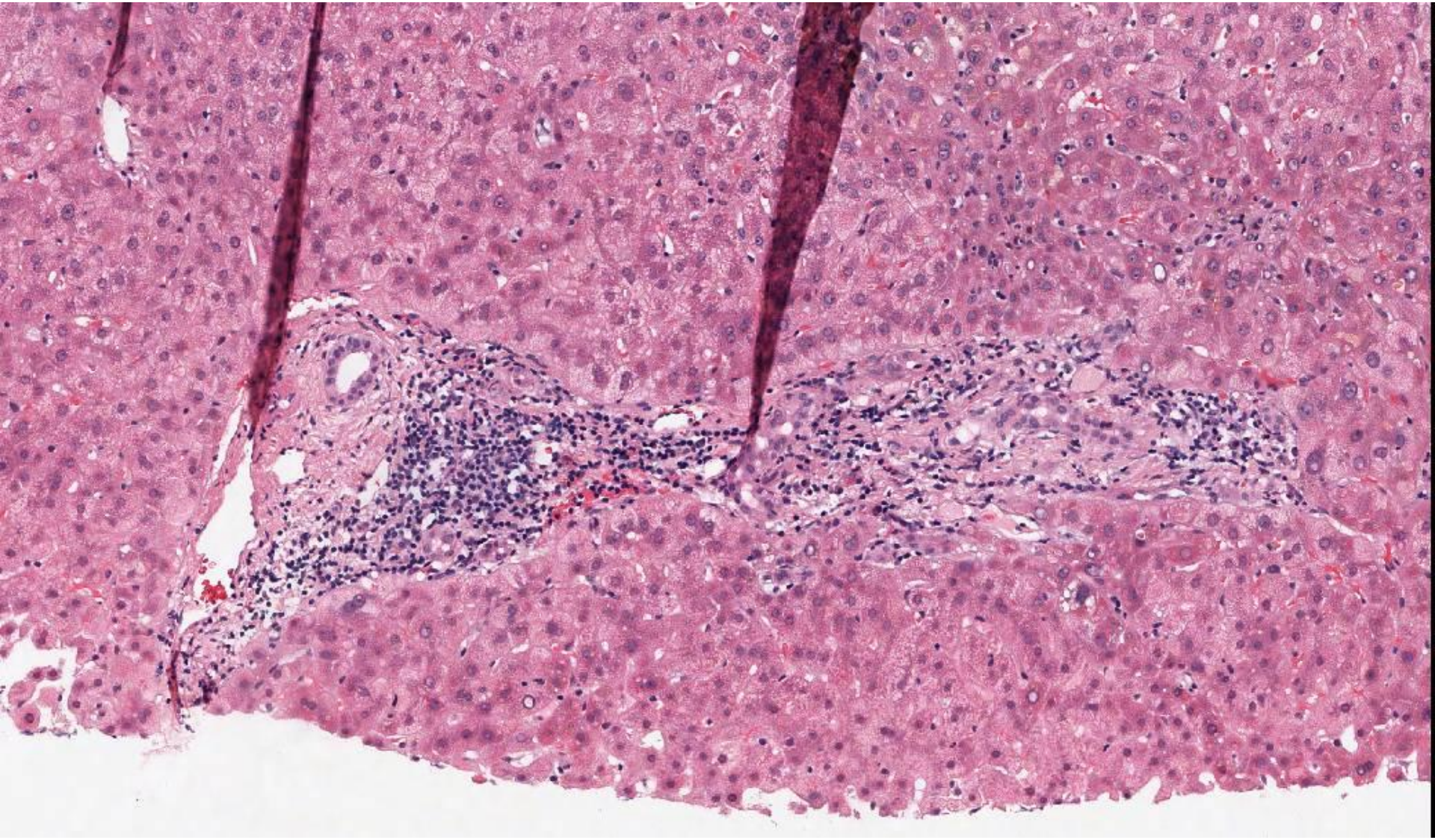


**Case K1/450 Age 72, Male**

Acute severe jaundice mixed picture ?AIH



K1/450



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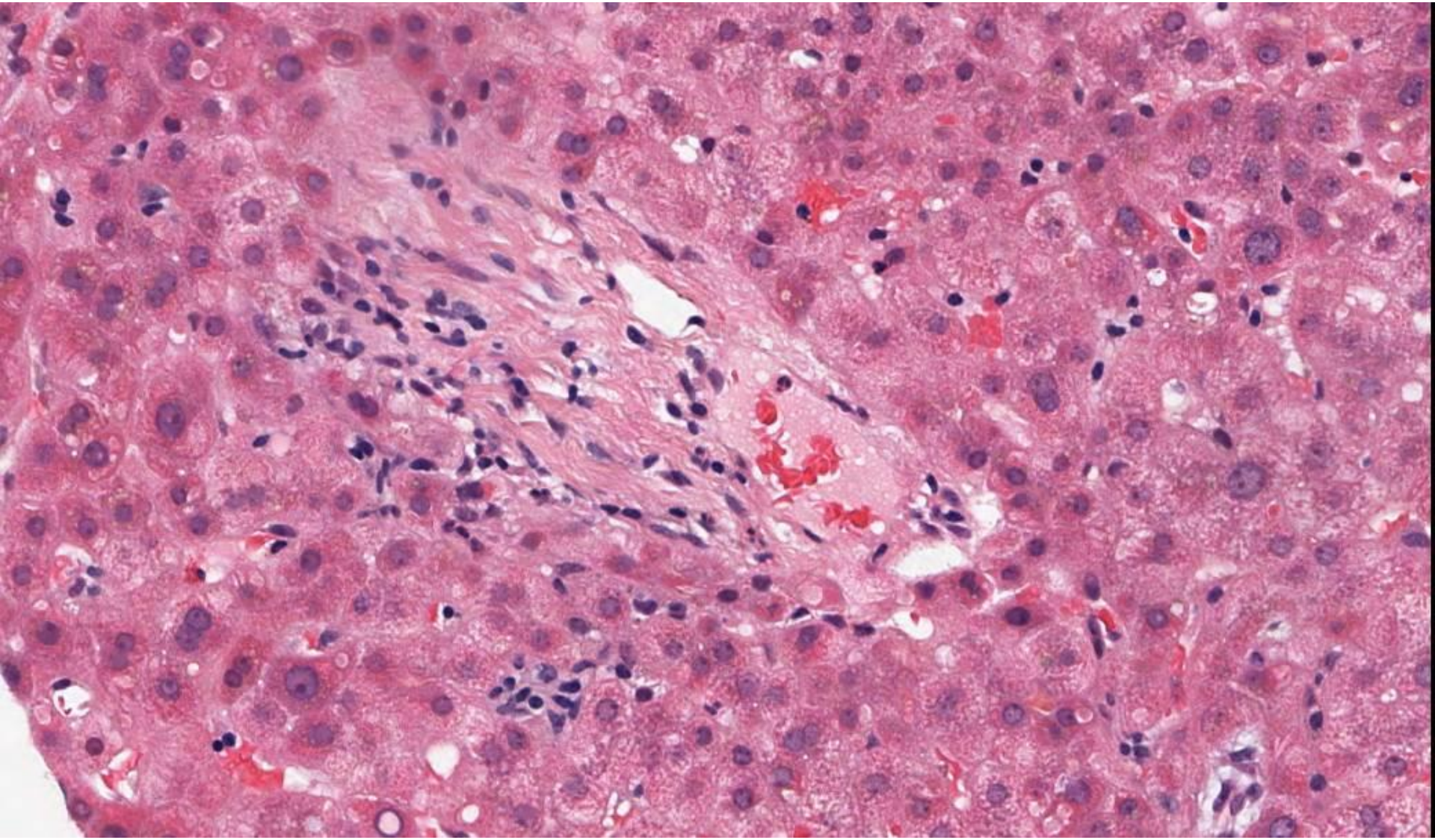

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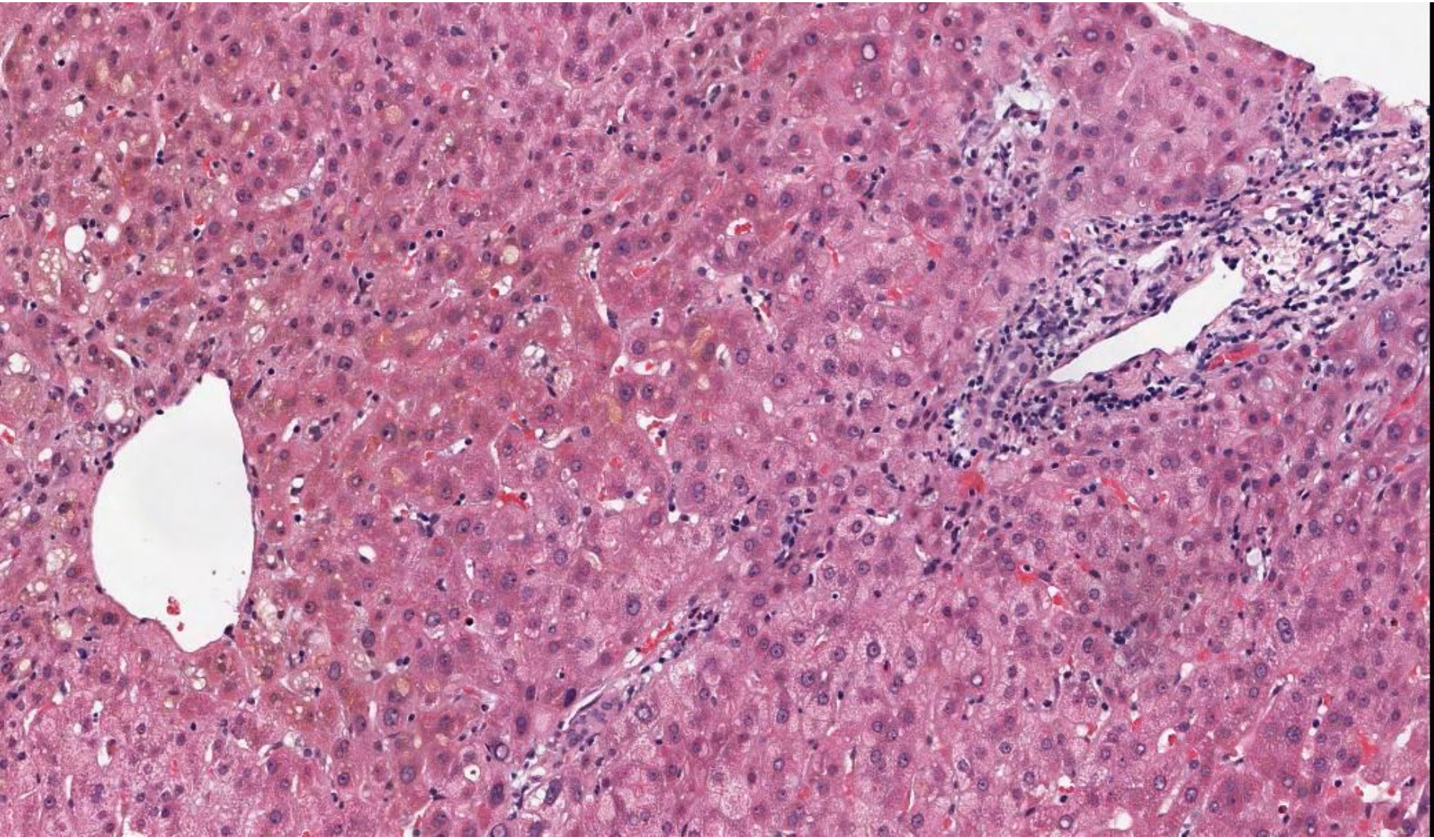
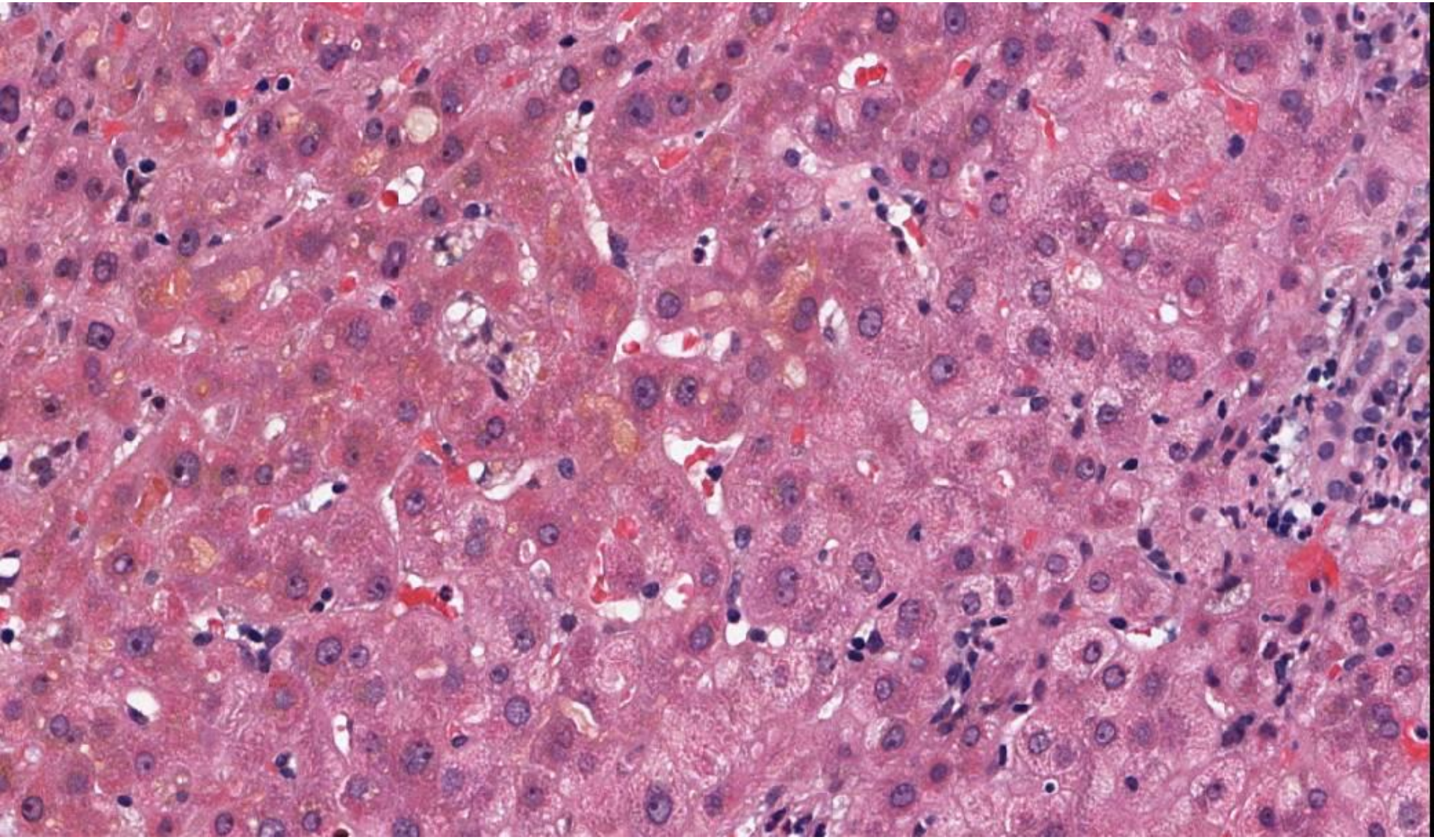
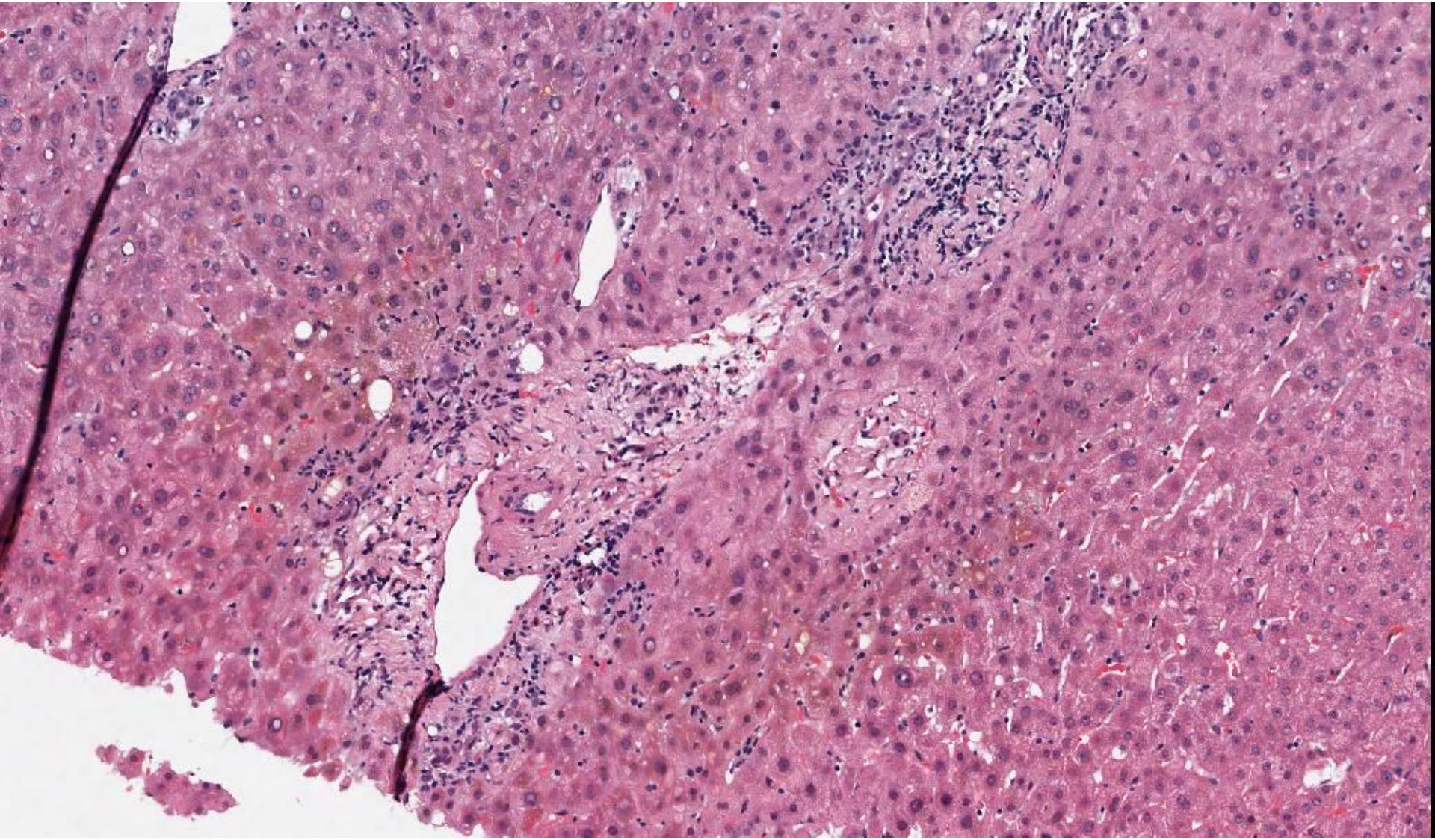


K1/450



K1/450



## Case K1/450 Age 72, Male

Acute severe jaundice mixed picture ?AIH

29 cholestasis

33 cholestatic hepatitis

3 cholestasis and chronic hepatitis

2 acute hepatitis

2 ductular reaction ? large duct obstruction

1 chronic active hepatitis

2 cholestasis not mentioned

1 steatohepatitis

4 description only, no clear diagnosis

15 drugs only

39 drugs likely, with differential

15 differential includes drugs, not favoured

3 drugs not mentioned

3 support/consistent with AIH

36 AIH unlikely / not AIH

26 AIH not mentioned

2 Not AIH

25 ? large bile duct obstruction / exclude LBDO first

Others within the differential diagnosis:

3 ? hepatitis E, 1 ? alcohol,

1 ? PBC, 1 ? Wilson's, 2 ? sepsis

Suggested scoring: ? unsuitable for scoring – or for 10 points – cholestatic liver injury, not chronic hepatitis, and aetiology that includes the possibility of drugs.

Lose 5 points if no mention of cholestasis, if morphology is steatohepatitis or chronic hepatitis, or if no mention of drugs among possible causes.

Other aetiologies insufficient consensus for scoring.

13/17 agree, 2 unsuitable

**Case K1/450 Age 72, Male**

Acute severe jaundice mixed picture ?AIH

Original diagnosis – large duct obstruction.

Get more info from Dr Mozayani, Bristol

Comments from discussion: Are we sure this patient didn't have antibiotics e.g. pre-procedure?

Is this suitable for scoring, since the final diagnosis of LBDO did not appear in the consensus diagnosis? – on show of hands, retained for scoring.

We seldom see duct obstruction on biopsy these days, since imaging performed before biopsy in jaundiced patients.

Bile infarcts, as here, can also be seen in DILI jaundice. Drugs remain the most likely cause.

This case was neither pure bland cholestasis, since some portal tract inflammation, nor amounting to clear cholestatic hepatitis.

Possibility of LBDO should be included, but insufficient to score on this.

# Masterclass: Chris Bellamy: terminology of cholestasis and cholestatic hepatitis.

**Cholestasis**

- bile visible in the section
  - yellow-orange, green, green-brown
  - sometimes very pale
  - iron stain (Fe vs lipofuscin dirty brown vs bile green-brown)
- canalicular cholestasis
  - zone 3
  - with time, rosettes form
- cytoplasmic cholestasis
  - subtle fine cytoplasmic brownish granularity becoming coarser with time
  - swelling with pale reticular cytoplasm (feathery degeneration), multinucleation
- ductular cholestasis

# Pure cholestasis

- Ludwig/Bates: Bile pigment (bilirubin) is present in hepatic tissue without other prominent morphologic abnormalities. The pigment is usually found in centrilobular canaliculi. A clear distinction between cholestatic hepatitis and pure cholestasis is not always possible.
  - amyloid, drugs esp sex steroids, warfarin, trimethoprim, fluconazole, gold, PFIC, TPN, 3rd trimester, congenital hepatic fibrosis, lymphoma (paraneoplastic: esp Hodgkin's)

- Lewis/Kleiner; Scheuer/Lefkowitch: *bland/steroid-type cholestasis* is perivenular canalicular
  - no lobular inflammation beyond that attributable to the cholestasis itself.
  - Isolated feathery degeneration, rosettes if prolonged
  - no/minimal portal inflammation (else consider idiosynchratic drug-induced e.g. chlorpromazine)

- Scheuer/Lefkowitch
  - Spectrum between bland cholestasis and viral hepatitis-like
  - portal and variable acinar inflammation & necrosis
  - hepatocanalicular (Zimmerman/Ishak)

- Lewis/Kleiner
  - intrahepatic cholestasis with significant lobular or portal inflammation should be classified as *mixed hepatocellular & cholestatic injury*

    - ΔΔ spectrum
      - bland
      - idiosyncratic drug (chlorpromazine, erythromycin)
      - acute viral hepatitis
      - duct obliterative (cholaniogdestructive: ductopenic)
      - large duct obstruction

# Cholestatic hepatitis

- Ludwig/Bates: a morphologic diagnosis describing lobular inflammation with profuse bile pigment (bilirubin) present, with or without fatty change.
  Bile is most commonly found in canaliculi and hepatocytes, or in extrusions (sometimes forming small “bile infarcts”)
- Scheuer/Lefkowitch: best kept as a clinical description of patients with a prolonged clinical course.
  Prefer *hepatocanalicular*

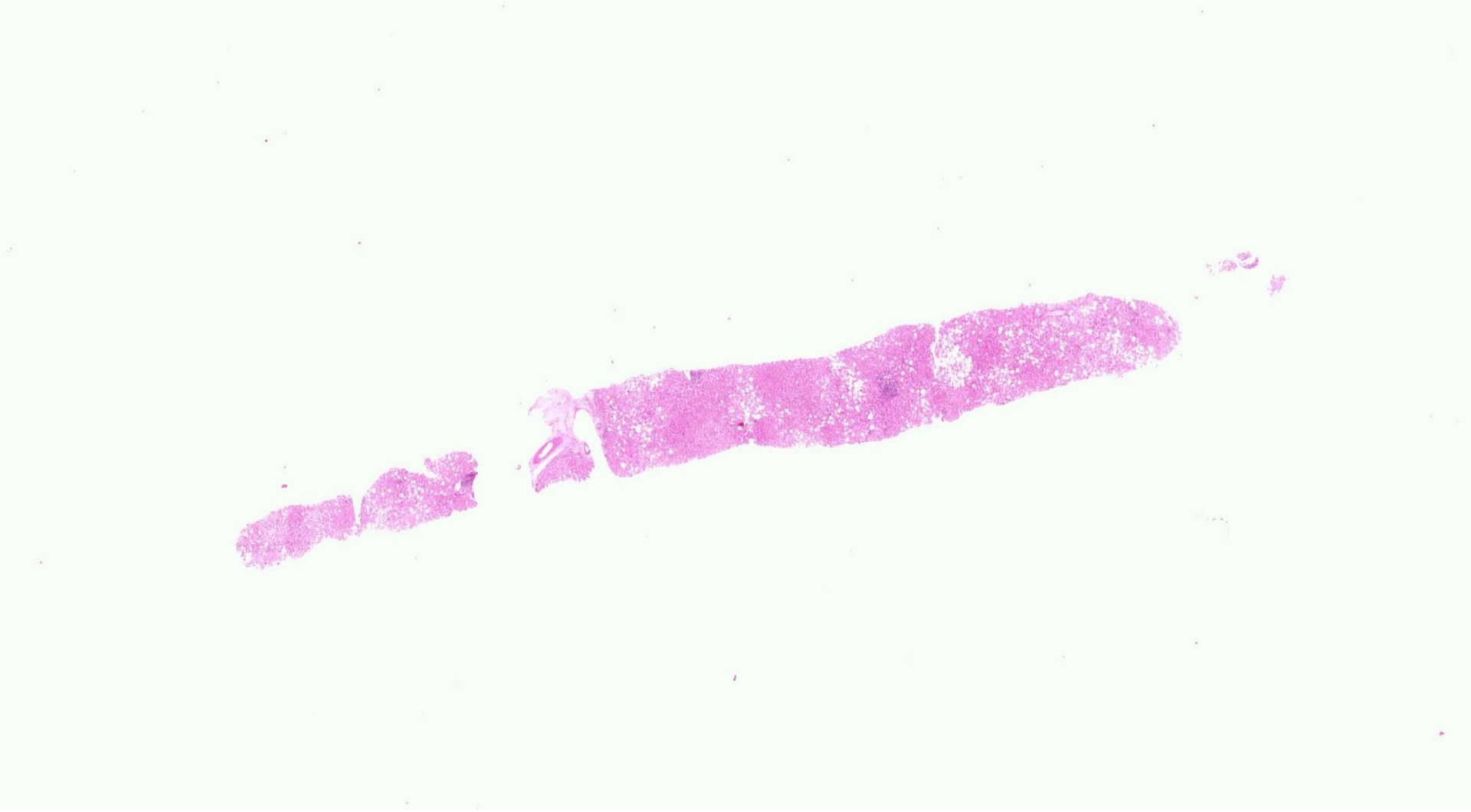
# The spectrum of intrahepatic cholestasis in liver injuries

- canalicular
  - bland/pure (steroids), z3
    - ± feathery degeneration, rosettes, but uninflamed
- minor portal inflammation
    - ± eosinophils, induction changes, duct epithelial irregularity
- cholestatic hepatitis

  (hepatocanalicular injury); (mixed hepatocellular & cholestatic injury)
  - significant hepatitic necroinflammation (± mild duct inflammation)
    - acute hepatitic (think viral hepatitis)
    - chronic hepatitis (think drug injury)
- cholangiodestructive injury/cholangiopathy

**Case K1/451  Age 42, Male**

Hep  B +ve, viral load x1.7 $x10^8$ weakly +ve ANA, ALT increasing ?Fibrosis. Fatty liver on US



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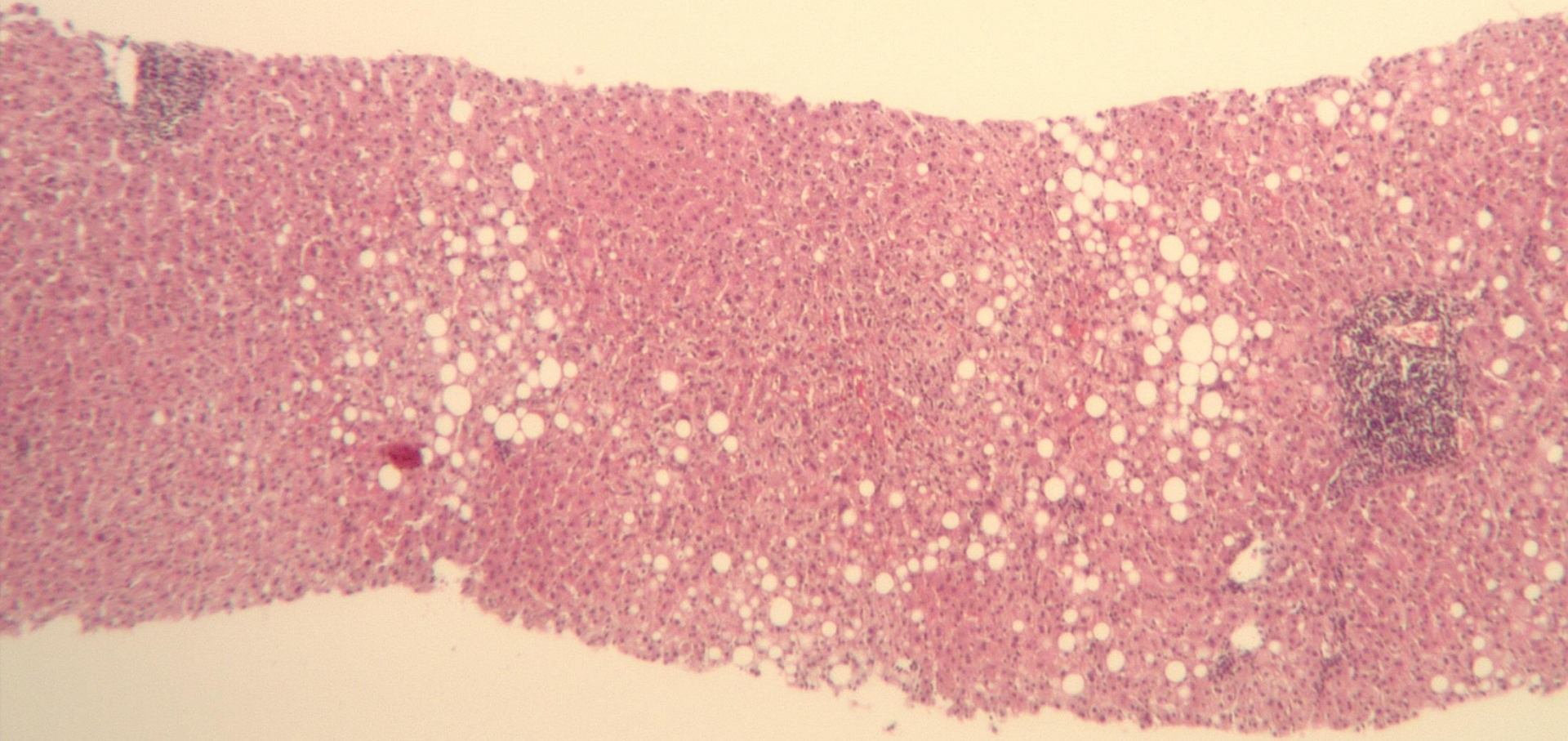

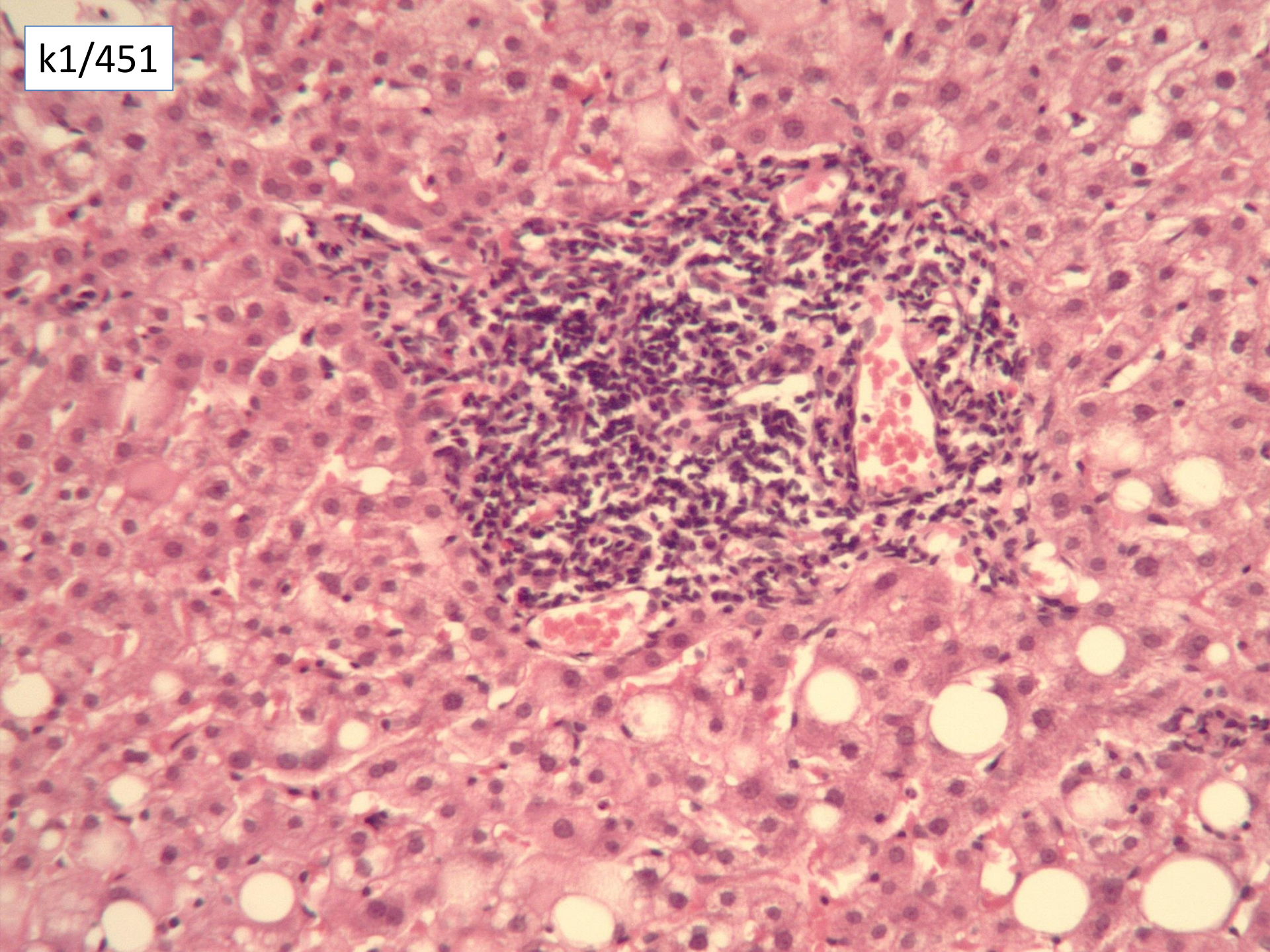
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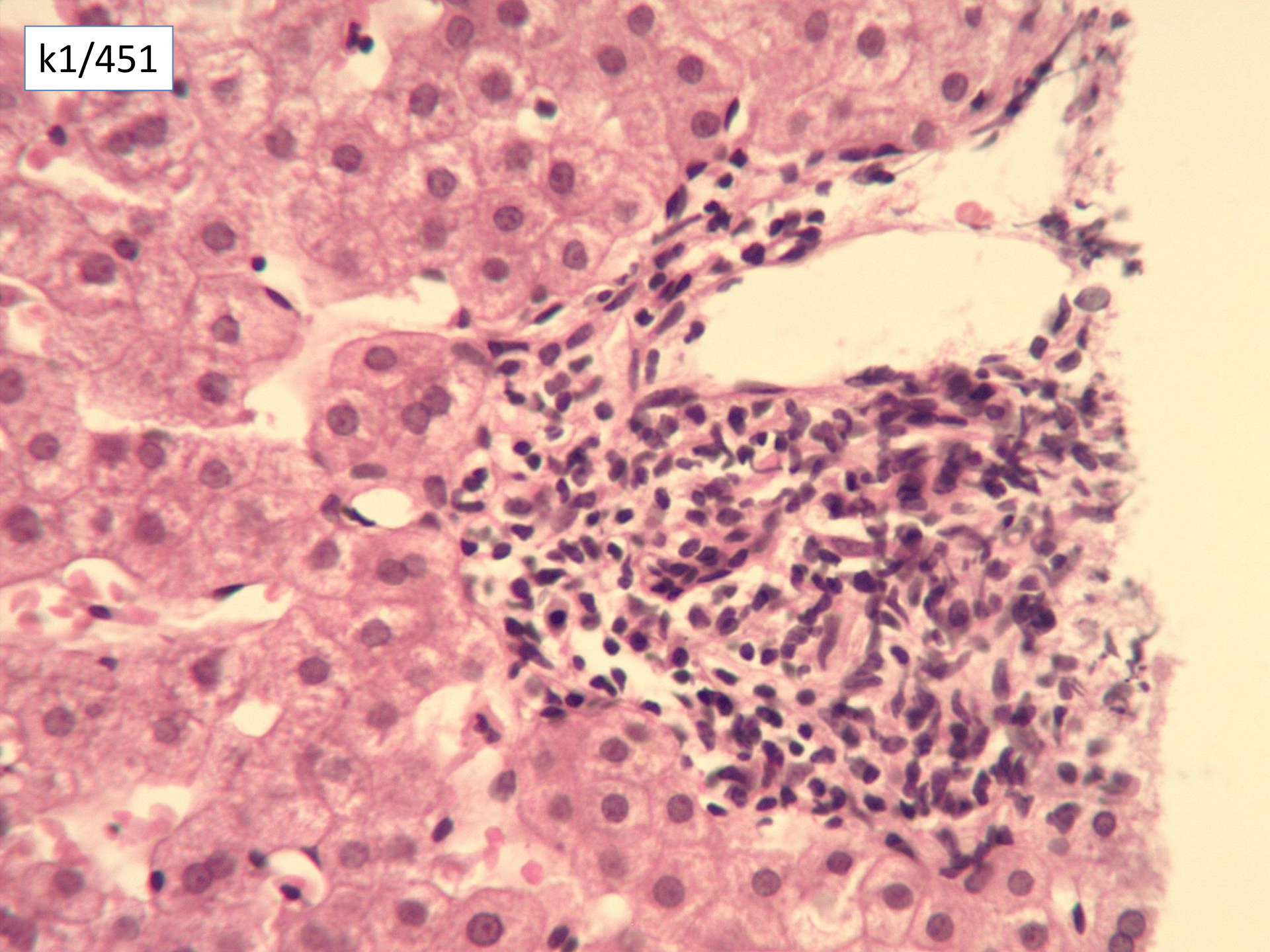
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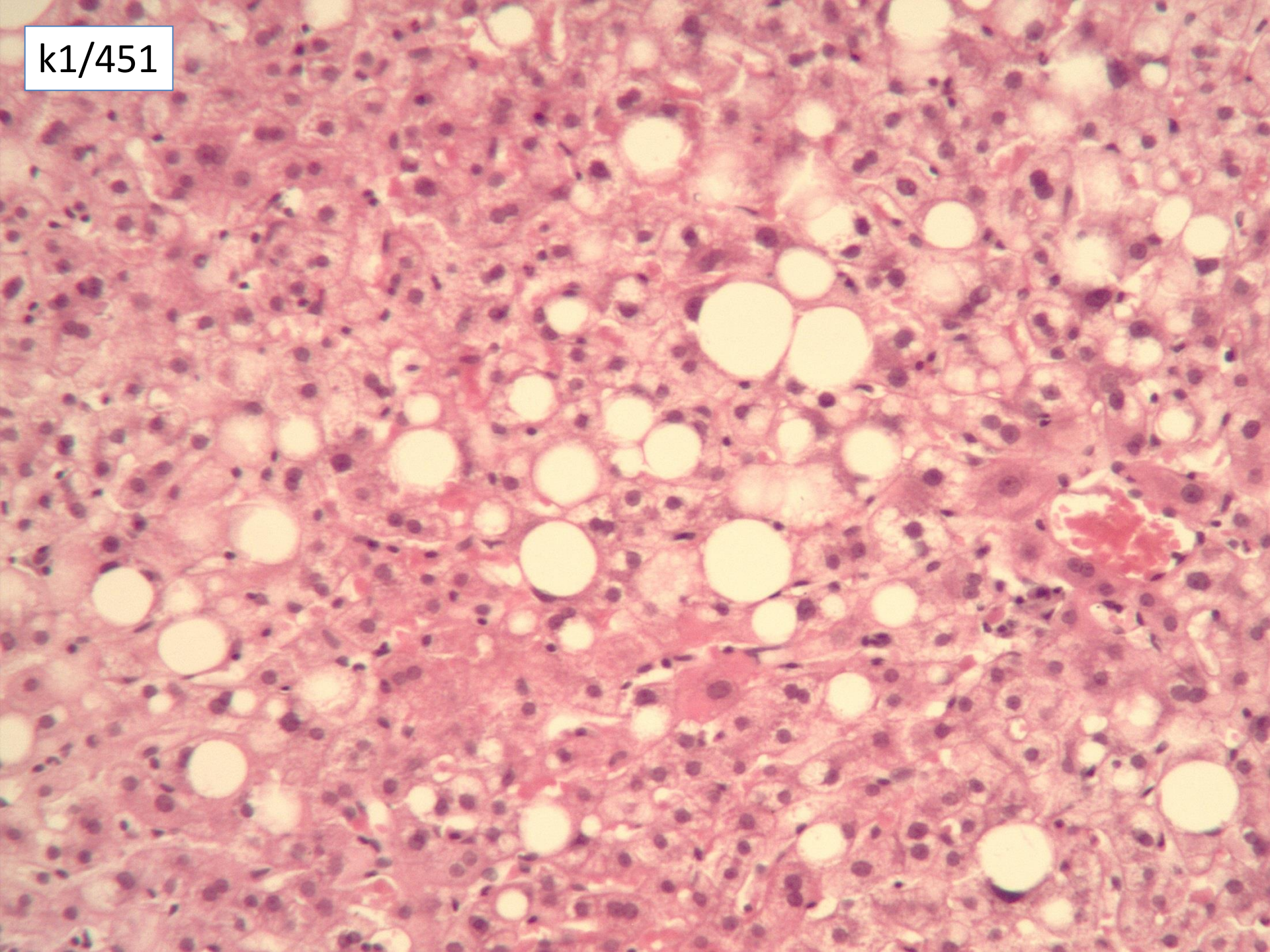
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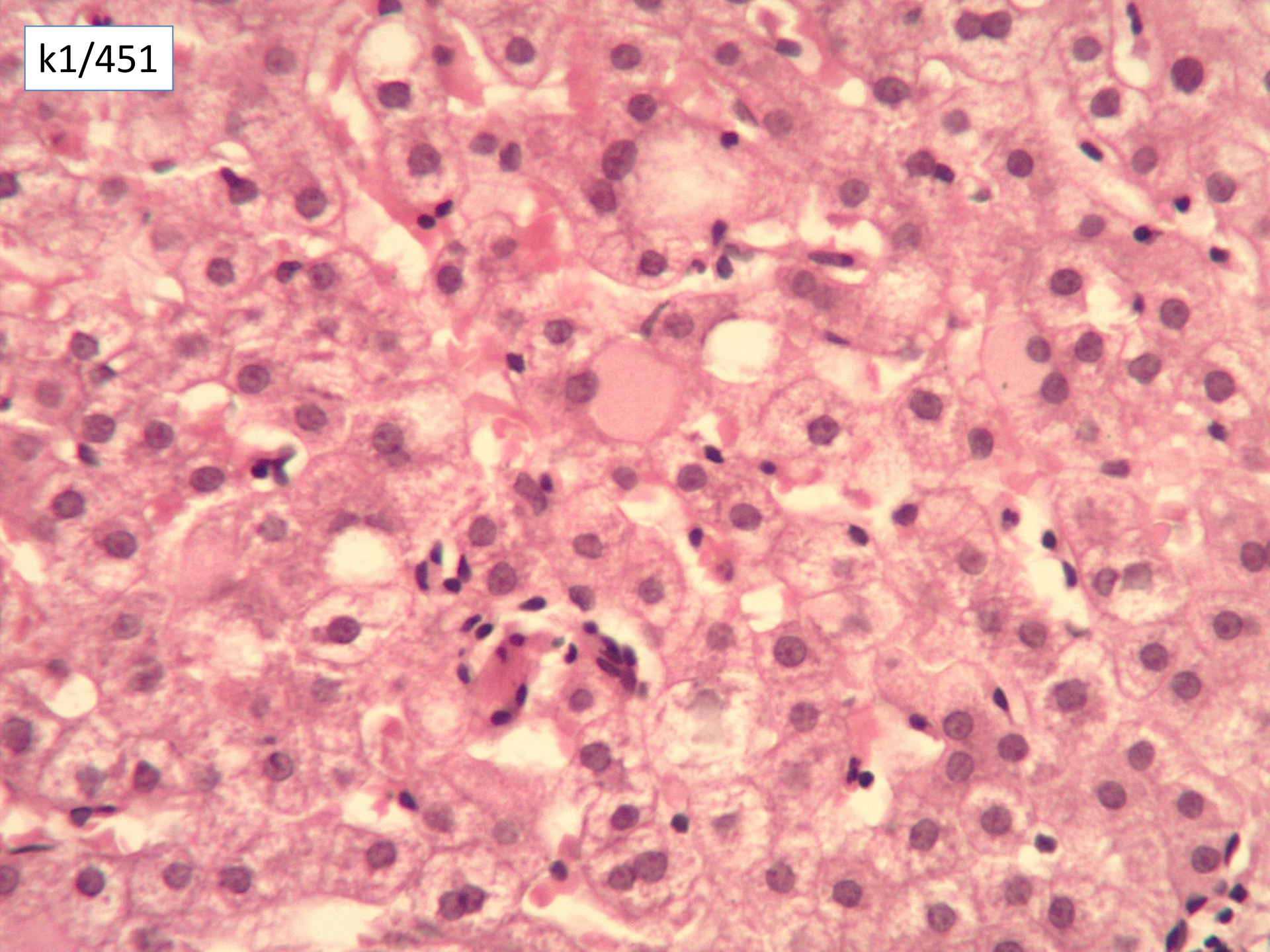
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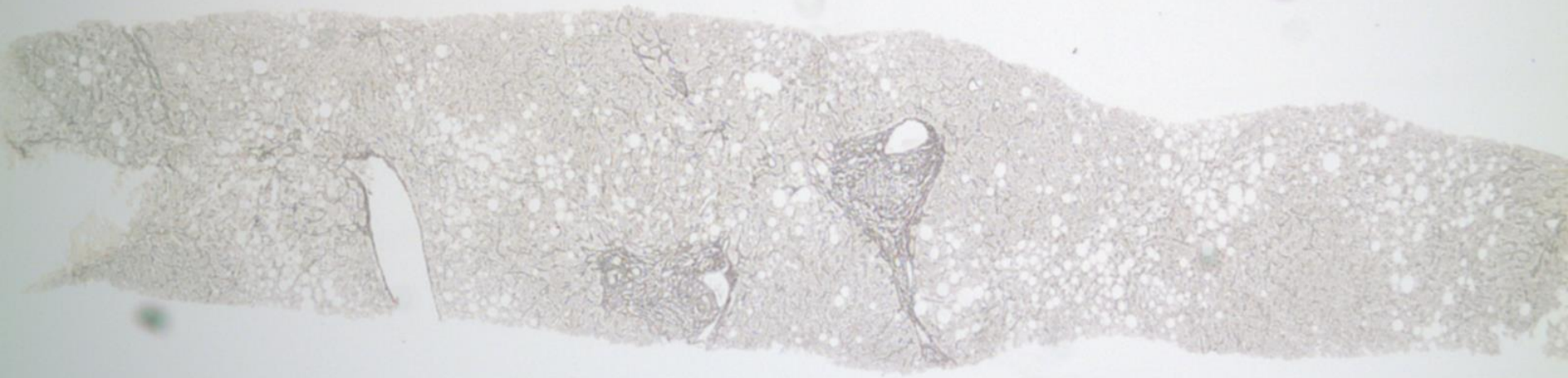
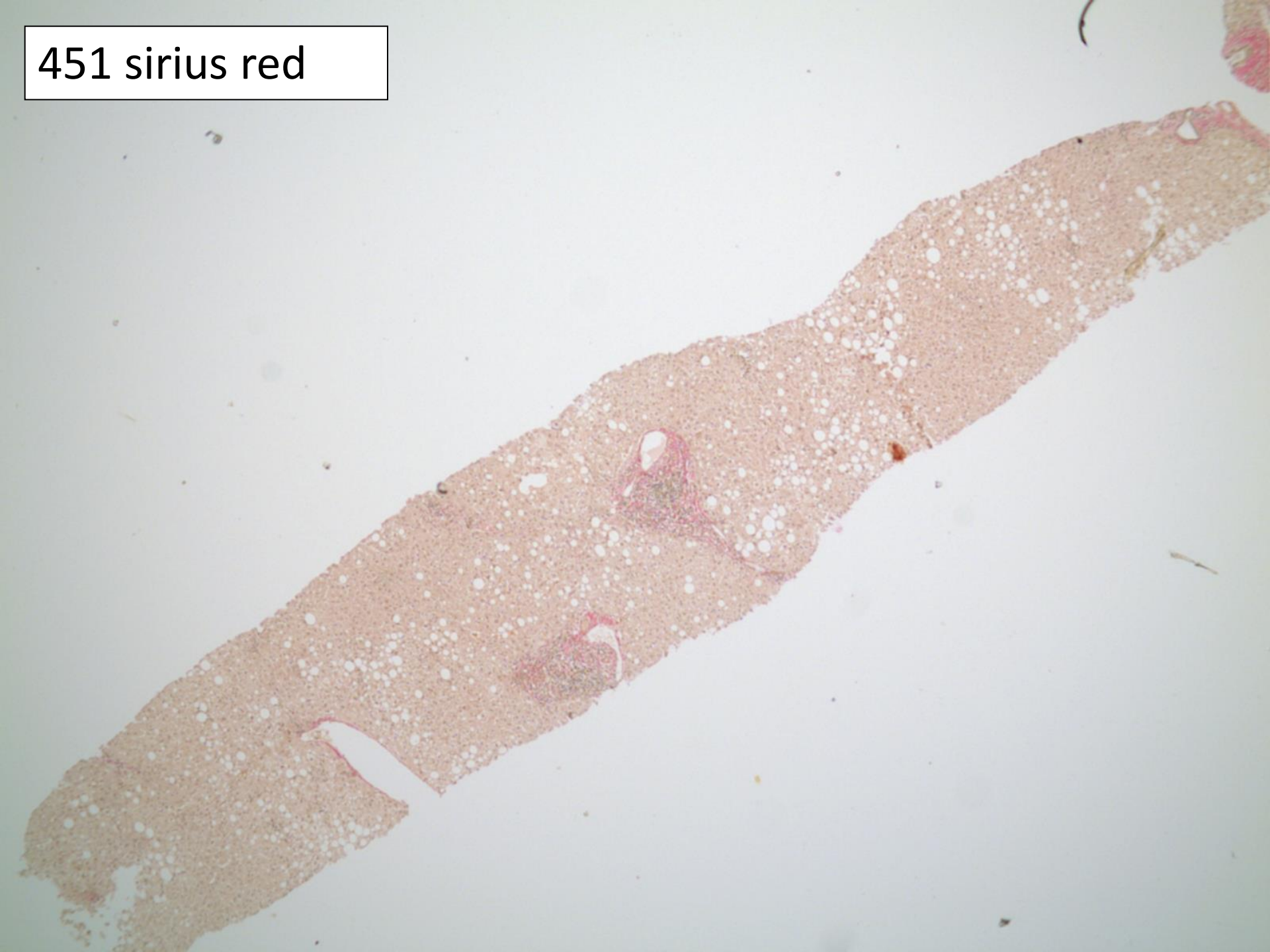
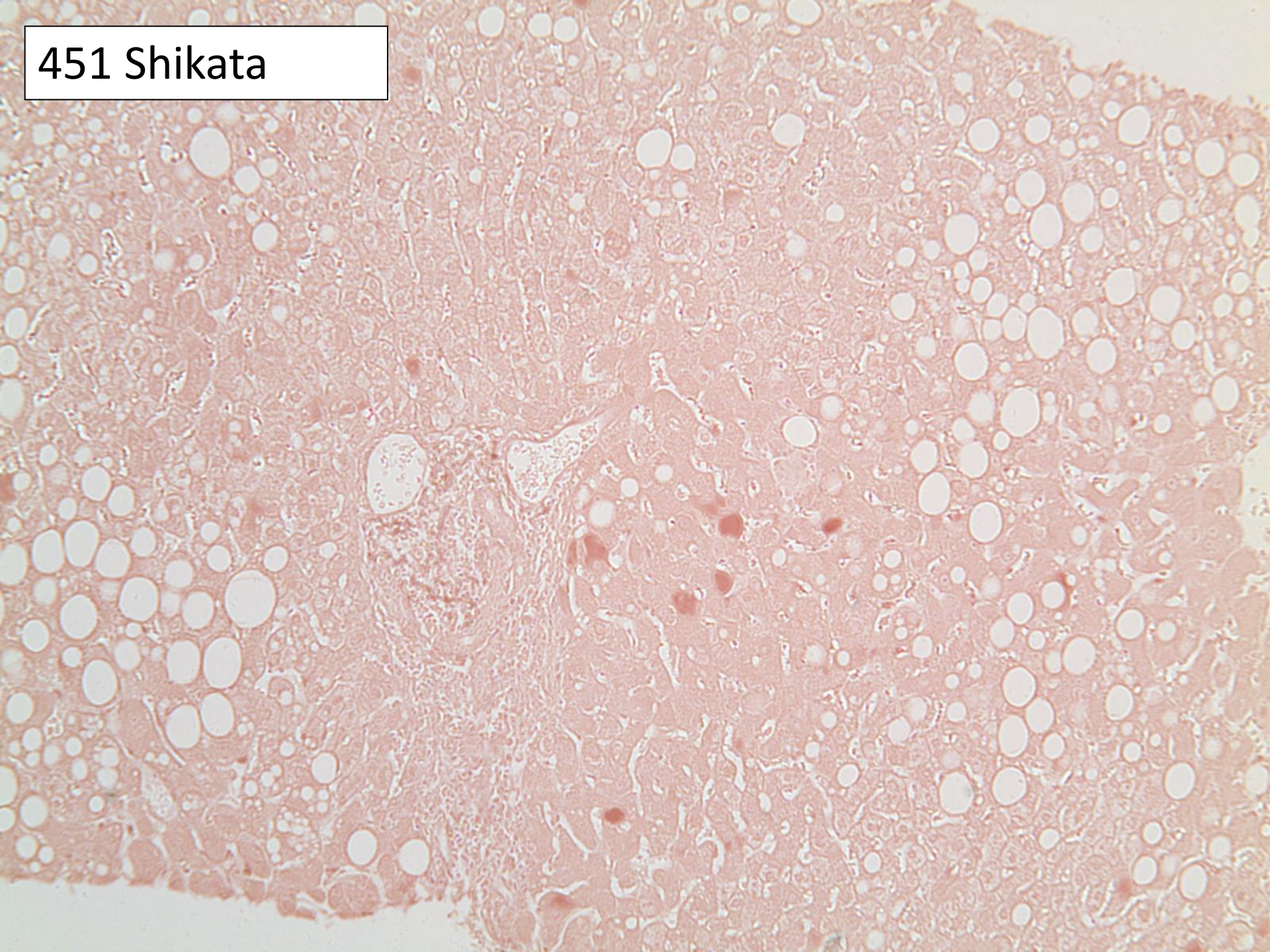



451 sirius red


451 Shikata

# Case K1/451 Age 42, Male

Hep B +ve, viral load x1.7 x$10^8$ weakly +ve ANA, ALT increasing ?Fibrosis. Fatty liver on US

76 hepatitis B

2 ground glass hepatocytes, but hepatitis B not specifically included

2 steatohepatitis, hepatitis B not mentioned

Stage

33 Ishak – see below

3 Metavir, 1 each for F0, F1, F2.

29 Descriptive: 6 = none, 12 = min/mild/early, 3 = moderate, 3 = bridging

Others descriptive e.g. portal, not bridging, etc, or can't stage because dual pathology

1 fatty change not mentioned

49 steatosis or suspect/borderline steatohepatitis

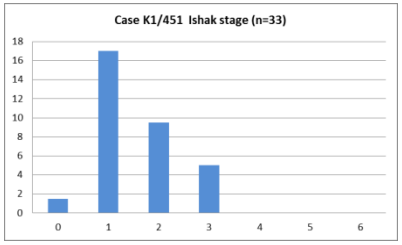
26 steatohepatitis

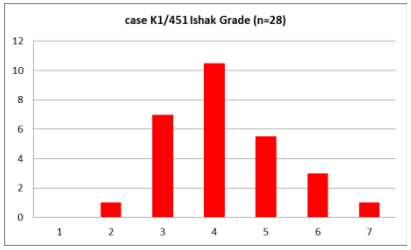
1 steatofibrosis

32 ? cause NAFLD/ALD

26 cause not mentioned

8 mentioned AIH unlikely




Suggested scoring; For 10 points – features of hepatitis B and also fatty liver disease with some comment on fibrosis. Score 0 if suggest whole pathology is ALD/NAFLD, or no mention of hep B. Lose 5 points for fatty change not mentioned.

? lose 5 points if ground glass hepatocytes but hepatitis B not mentioned – discussed, rejected.

14/16 agree, 0 unsuitable

**Case K1/451 Age 42, Male**

Hep B +ve, viral load x1.7 x$10^8$ weakly +ve ANA, ALT increasing ?Fibrosis. Fatty liver on US

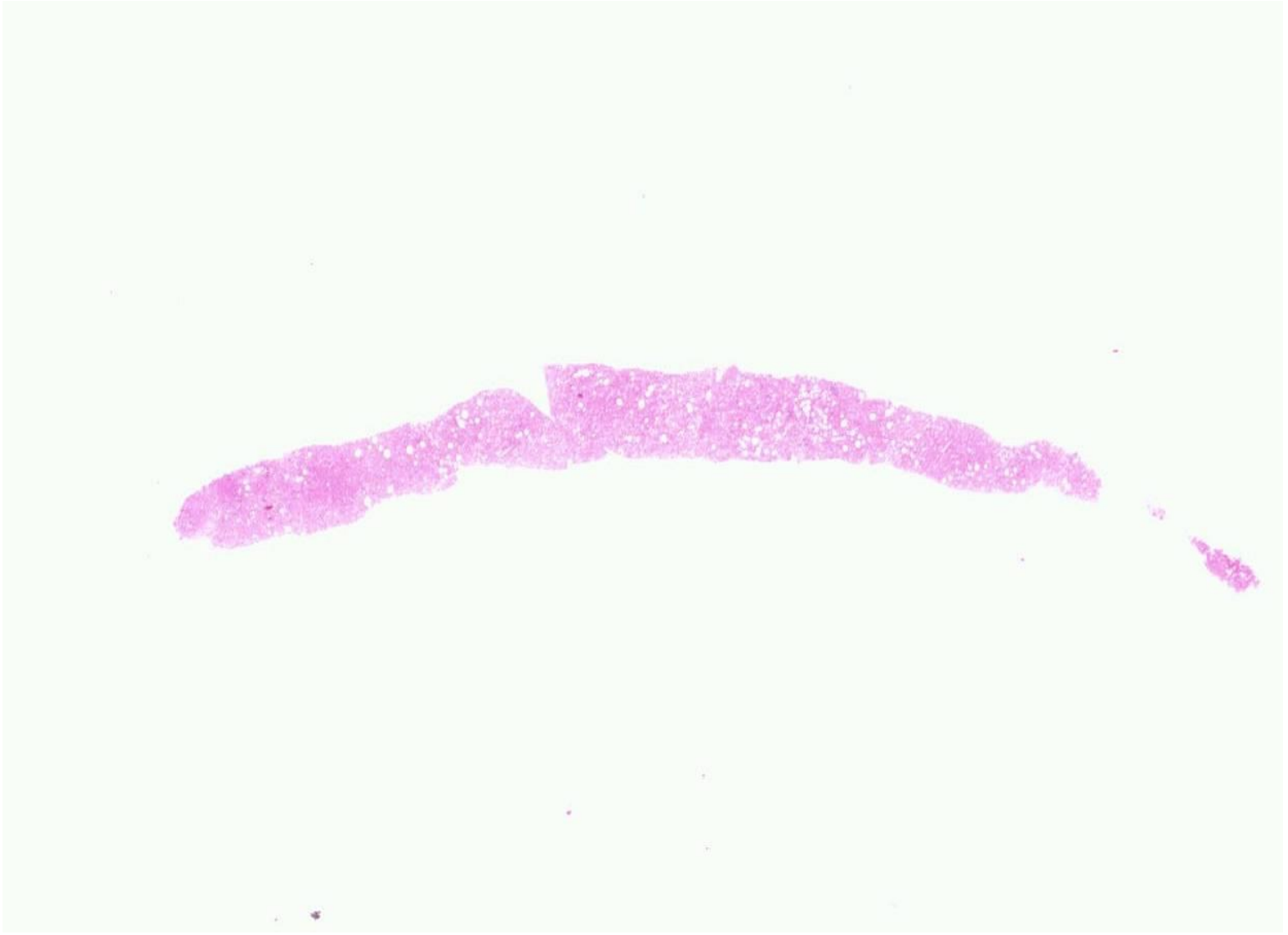
- Original diagnosis: Chronic hepatitis B, stage 2 grade 4. moderate steatosis without steatohepatitis.
- Follow up information – initially eAg +ve with high viral load and lobular activity. Immunos: HBcAg in hepatocyte nuclei and cytoplasm – treated with pegasys IFN for 24 weeks to try to achieve seroconversion, but remained eAg +ve. Converted to entecavir, viral load and LST have decreased since, now $10^{4.}$

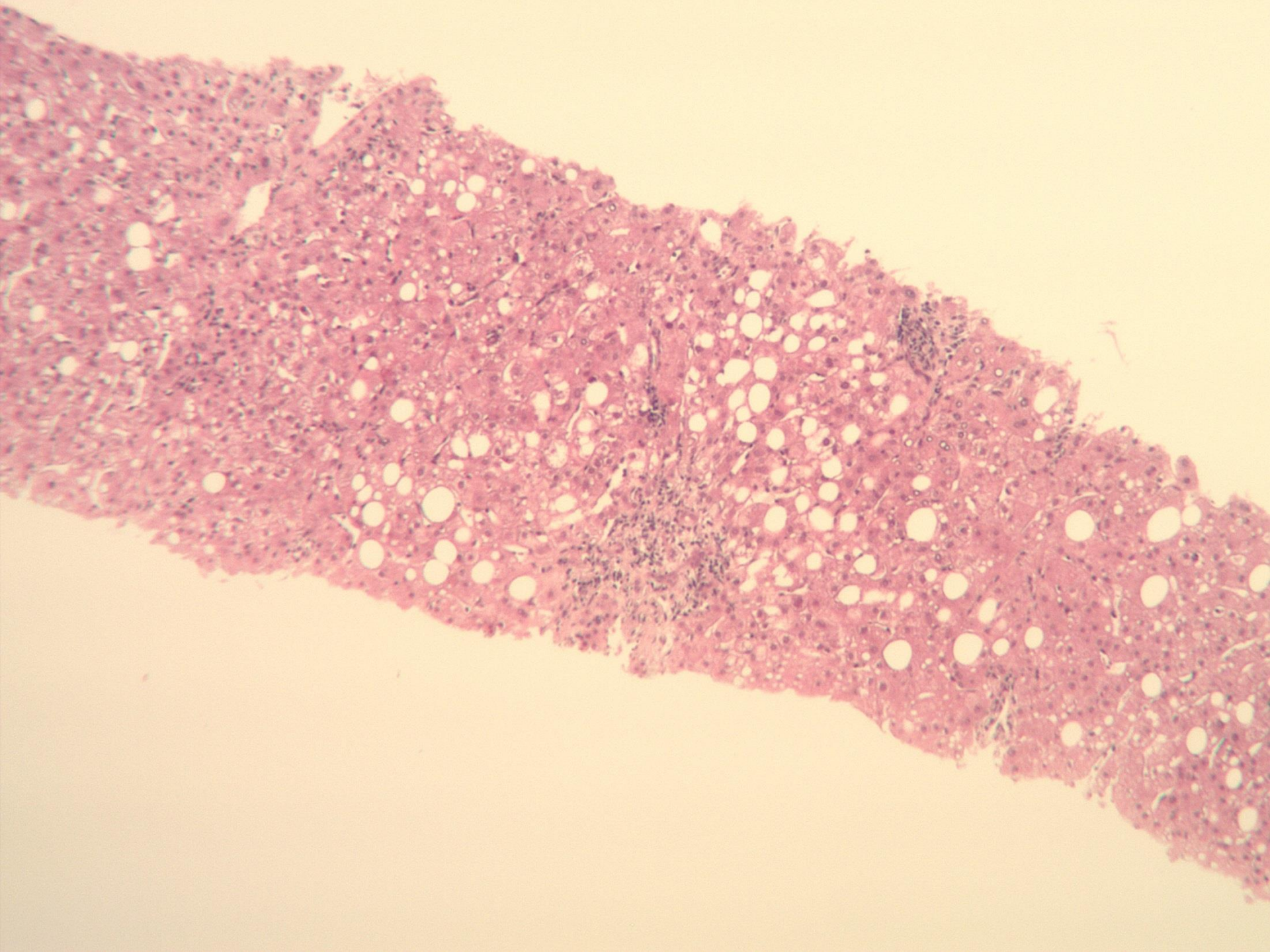
- Hepatitis B not a cause of steatosis - ? Other factors in history.

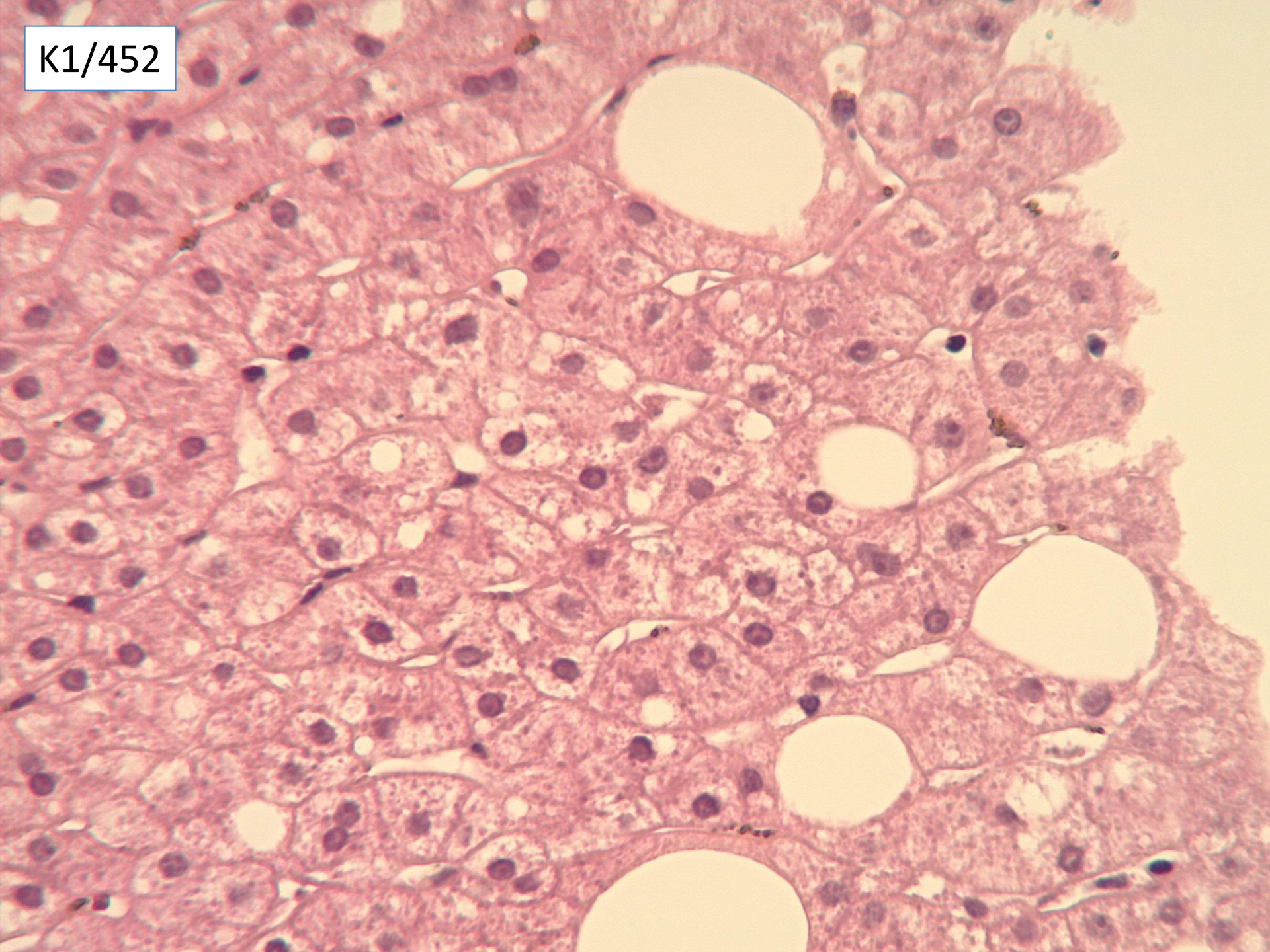
**Case K1/452 Age 71, Female**

Deranged LFT's. Nodular liver. Coeliac disease.

?Cirrhotic liver ?autoimmune hepatitis



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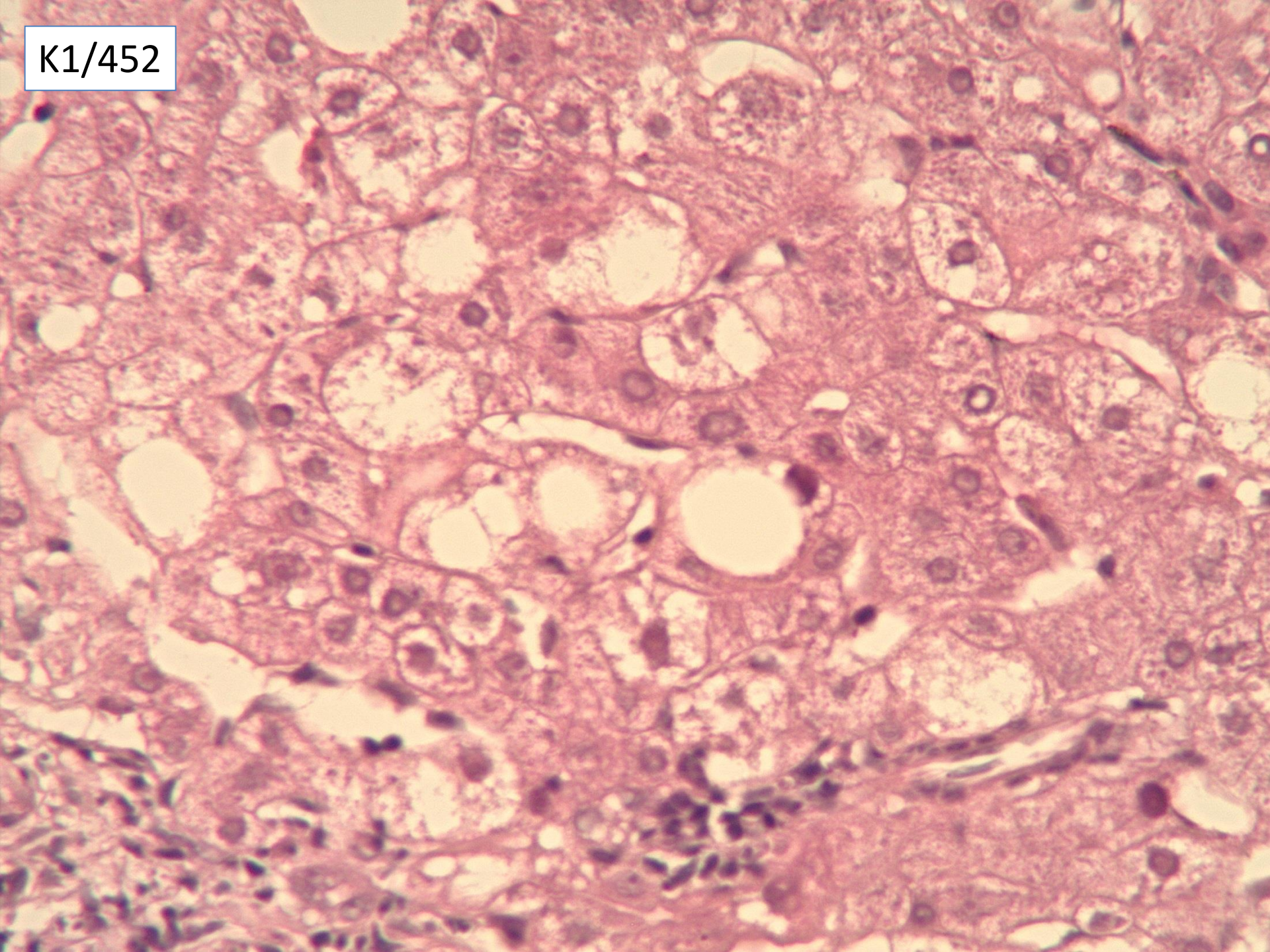
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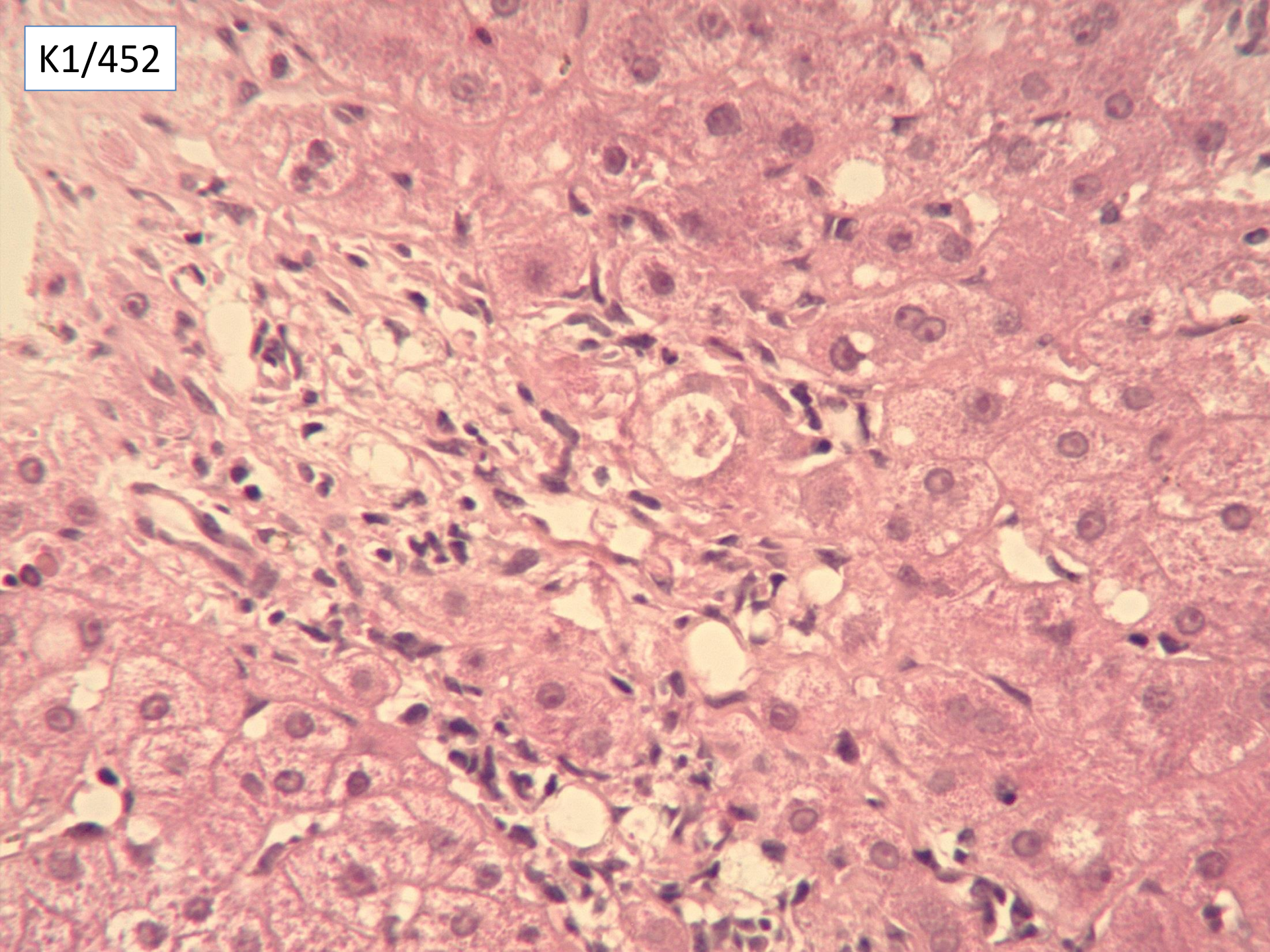
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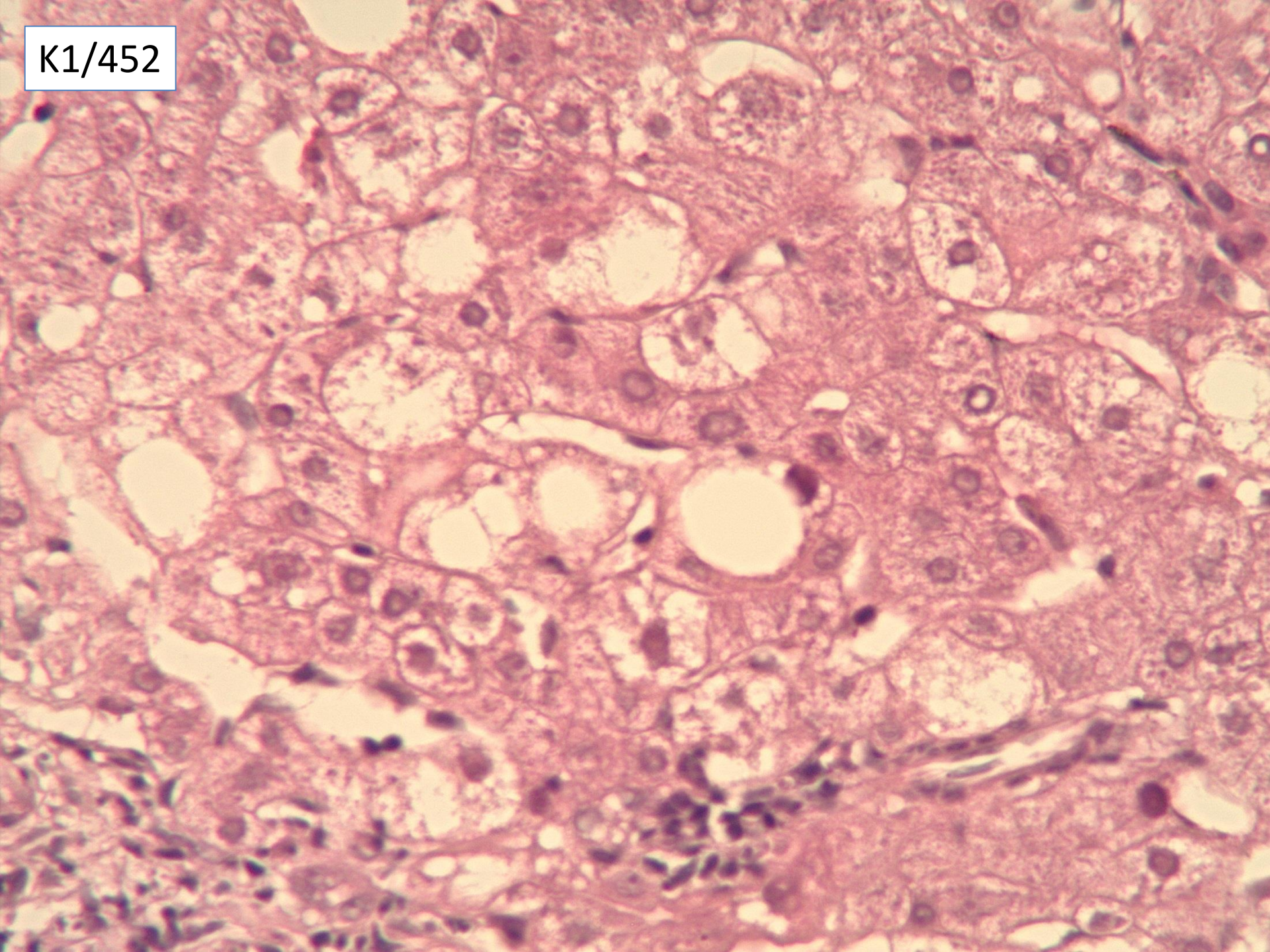
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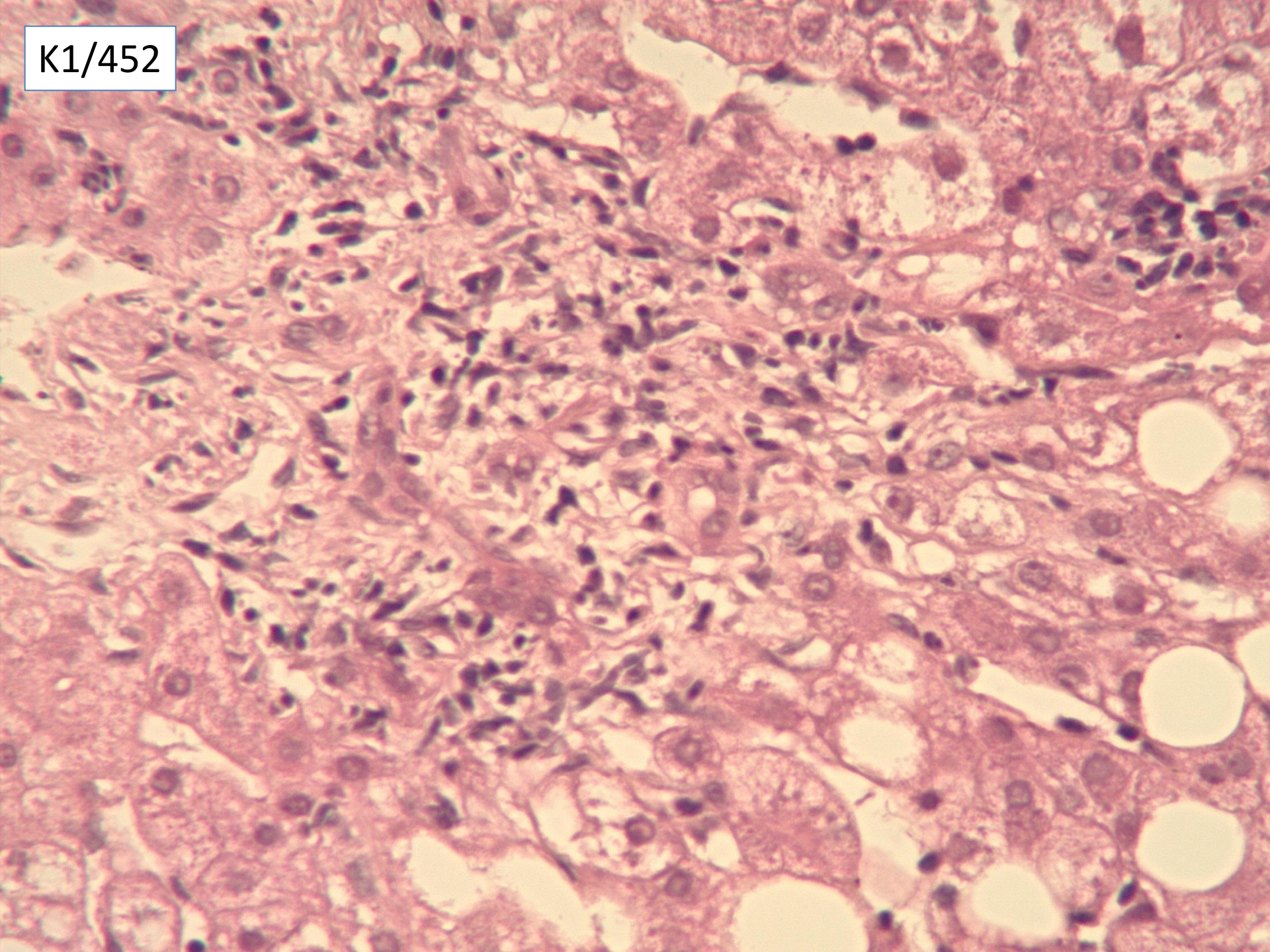
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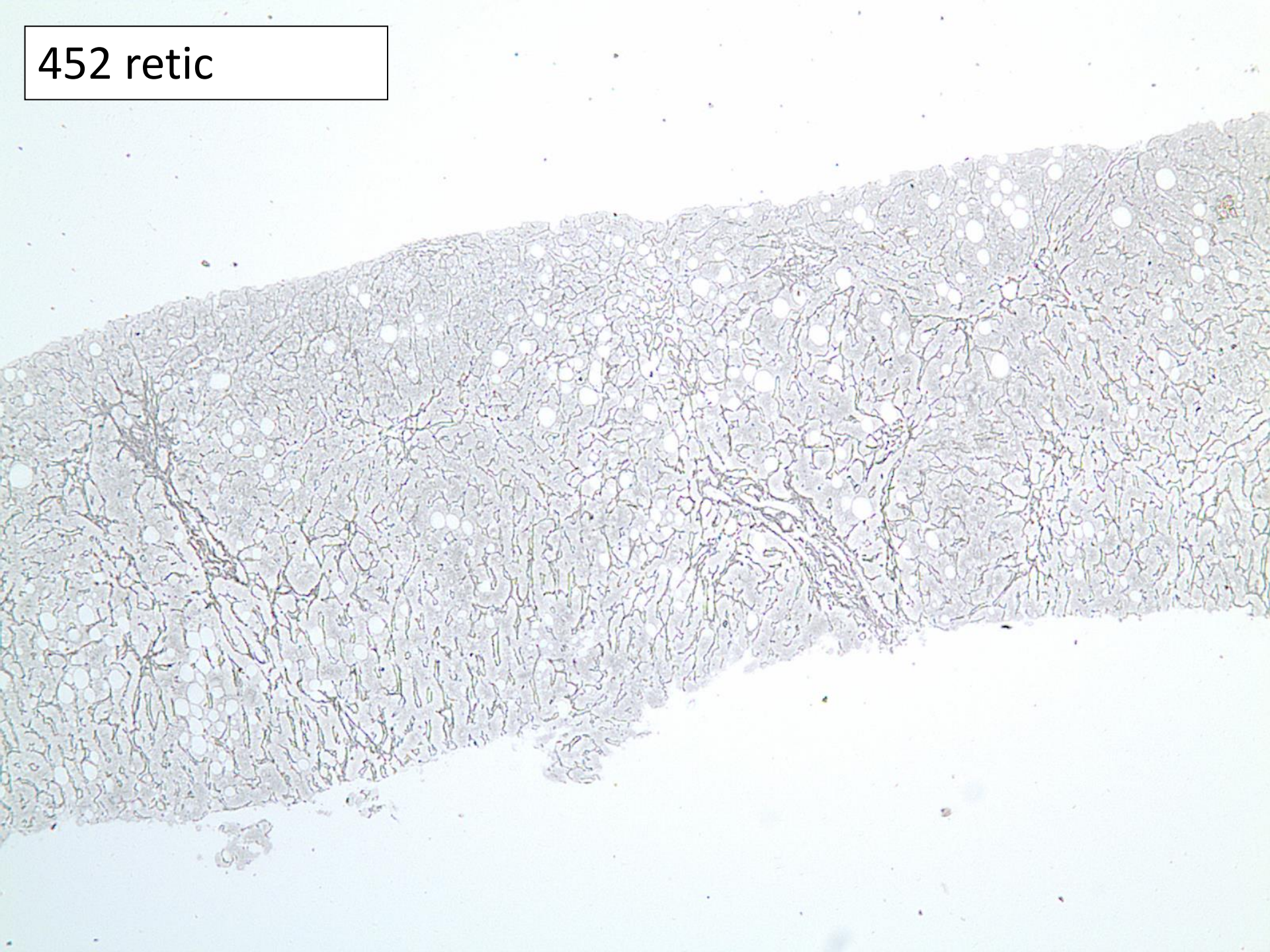

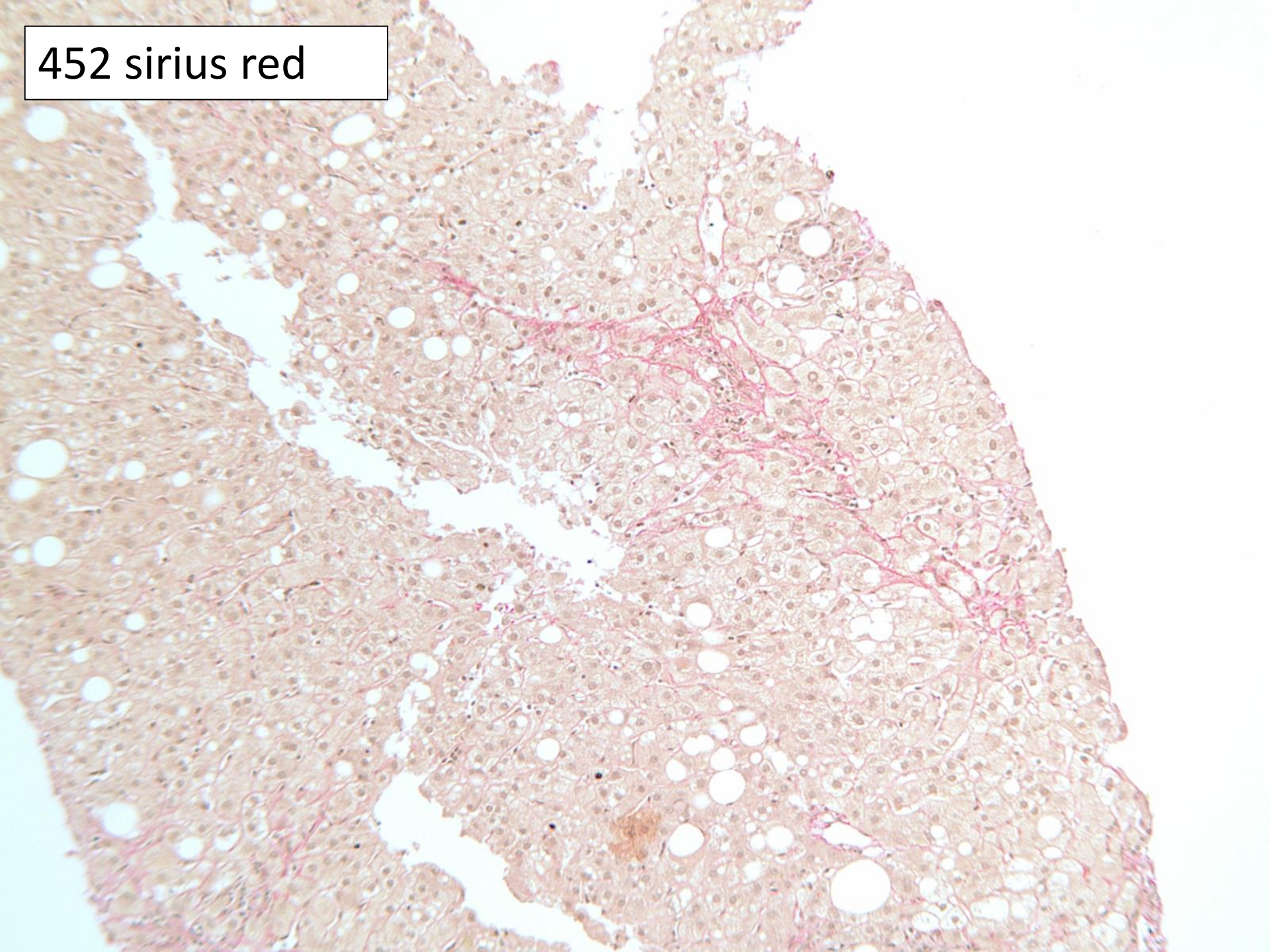
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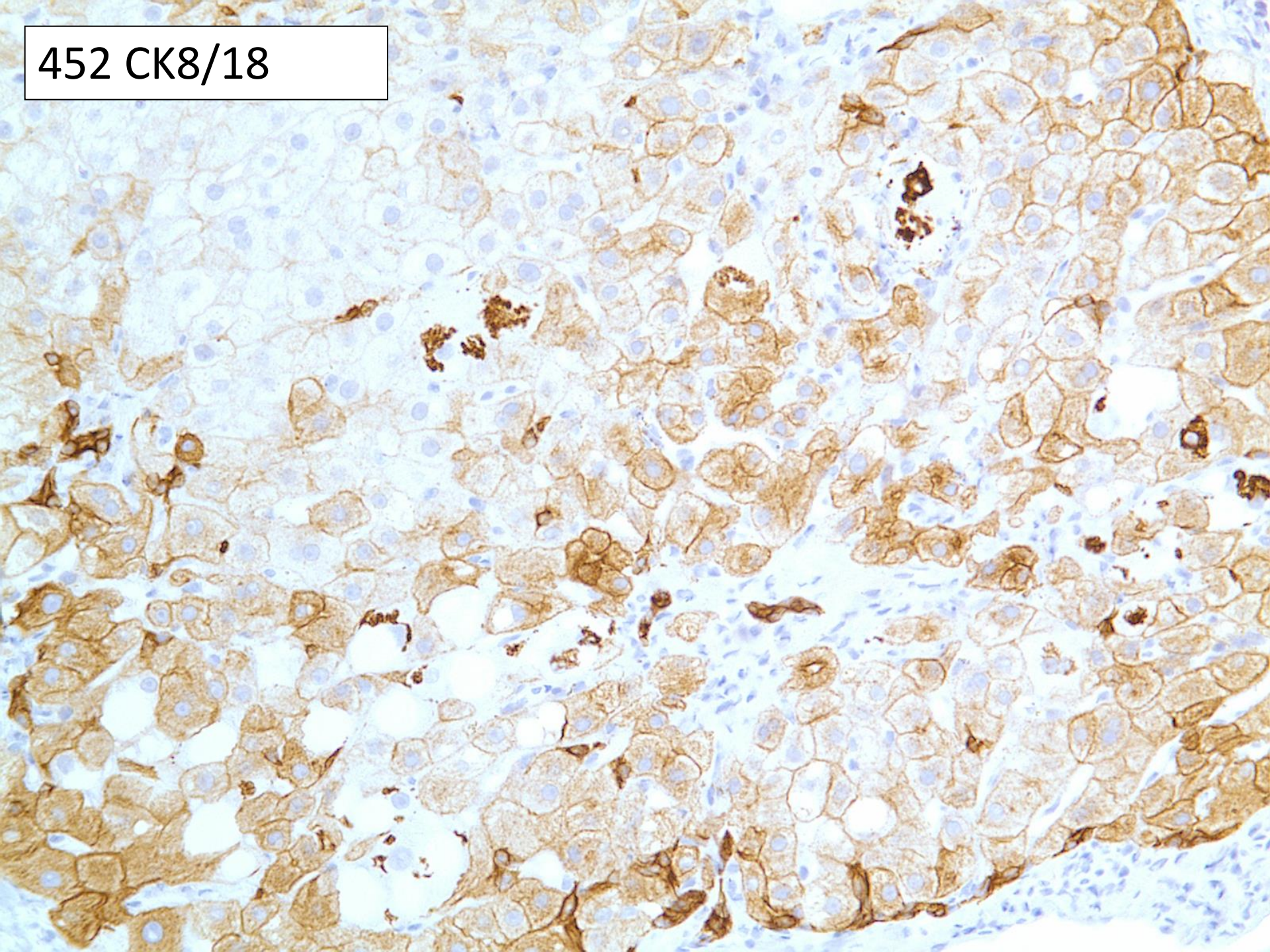

452 CK8/18

## Case K1/452 Age 71, Female

Deranged LFT's. Nodular liver. Coeliac disease. ?Cirrhotic liver ?autoimmune hepatitis.

65 steatohepatitis
4 steatosis
1 chronic hepatitis, mild fibrosis 5/6 no mention of fat
2 biliary and fatty liver disease
1 biliary and ? nodular regenerative hyperplasia, not a fatty liver disease
4 description, steatohepatitis not mentioned
1 Biliary cholestasis, Drug/LBDO
1 resolving viral hepatitis or AIH
1 Steatosis and chronic active hepaitits ? alcohol

Fibrosis 13 Kleiner: stage 1 = 4, stage 2 = 7, stage 3 = 2
40 Descriptive comment on fibrosis

31 specifically stated not cirrhosis
2 No comment on fibrosis/stage

43 aetiology of fatty liver disease – ALD / NAFLD
35 specifically commented not autoimmune hepatitis
14 evidence of bile duct damage
5 ? nodular regenerative hyperplasia
14 findings related to coeliac disease in some way – biliary(3) fatty(5) inflammation(2) NRH (1)

1 "consistent with primary biliary cirrhosis, also some steatofibrosis"
1 "don't report it without asking the hepatologists just what is going on"

Suggested scoring: For 10 points – need steatohepatitis and some comment on stage of fibrosis. Lose 5 points if a different sort of liver disease, and lose 5 points if no comment on stage

16/17 agree, 1 unsuitable

**Case K1/452 Age 71, Female**

Deranged LFT's. Nodular liver. Coeliac disease. ?Cirrhotic liver ?autoimmune hepatitis.

Original diagnosis: steatohepatitis, mild fibrosis.

Follow up information – coeliac disease is well managed.

BMI is 31, high cholesterol, not diabetic. Alcohol 20units/week. Fibroscan 10.4 (corresponds to F2-3).

Also grade 1-2+ iron, patient has high ferritin, and raised iron binding saturation – for haemochromatosis genes.

Comment: Mallory-Denk bodies much more evident on K8/18 stain than H&E. IHC can be useful for borderline cases of ? Steatohepatitis (ubiquitin, p63 are alternatives).

Coeliac disease – may have raised transaminases on presentation (around 20-30%), usually improve on treatment of coeliac disease.

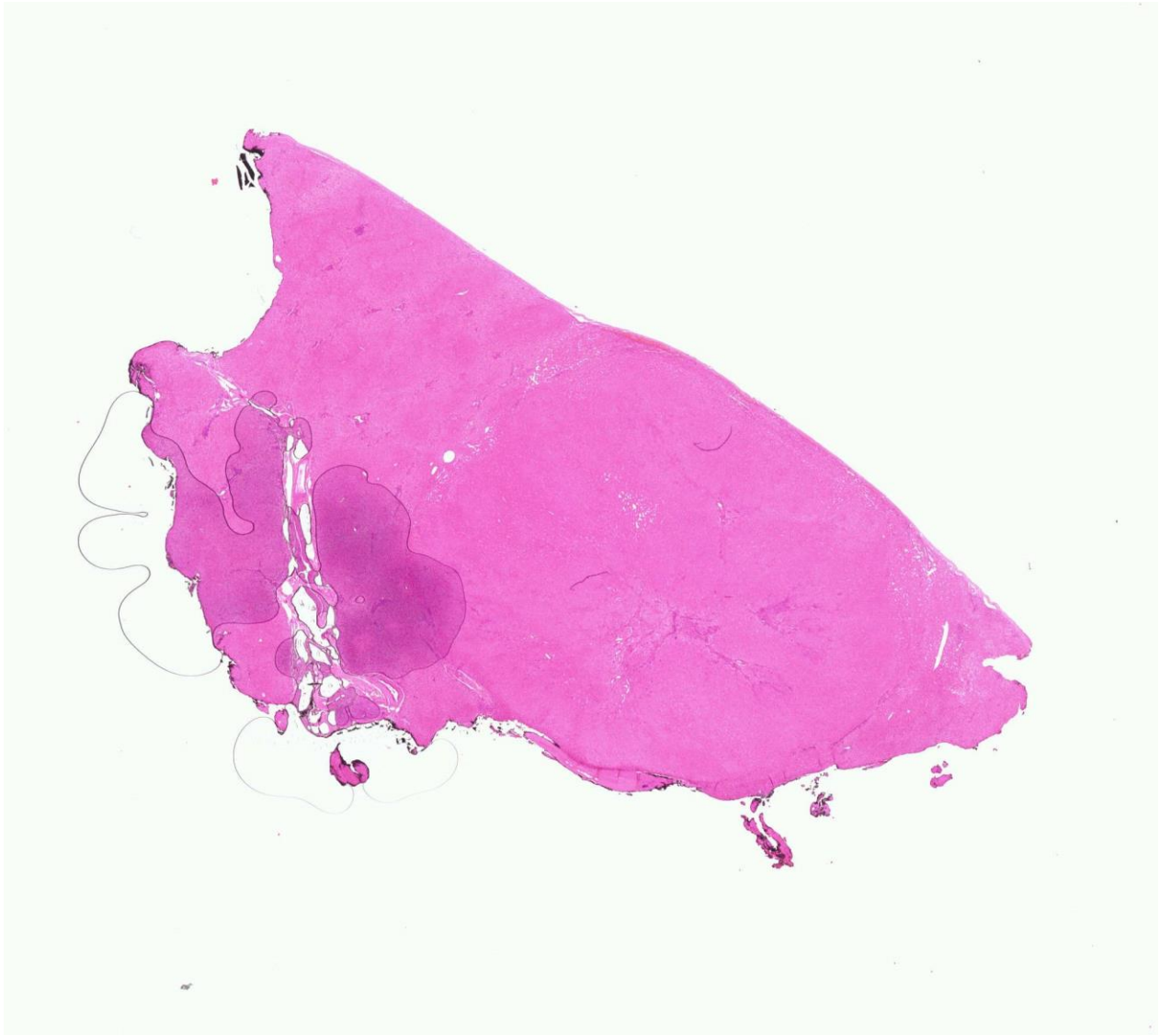
? Cause – thought to be related to increased gut permeability and antigen presentation in the liver – non-specific reactive change.

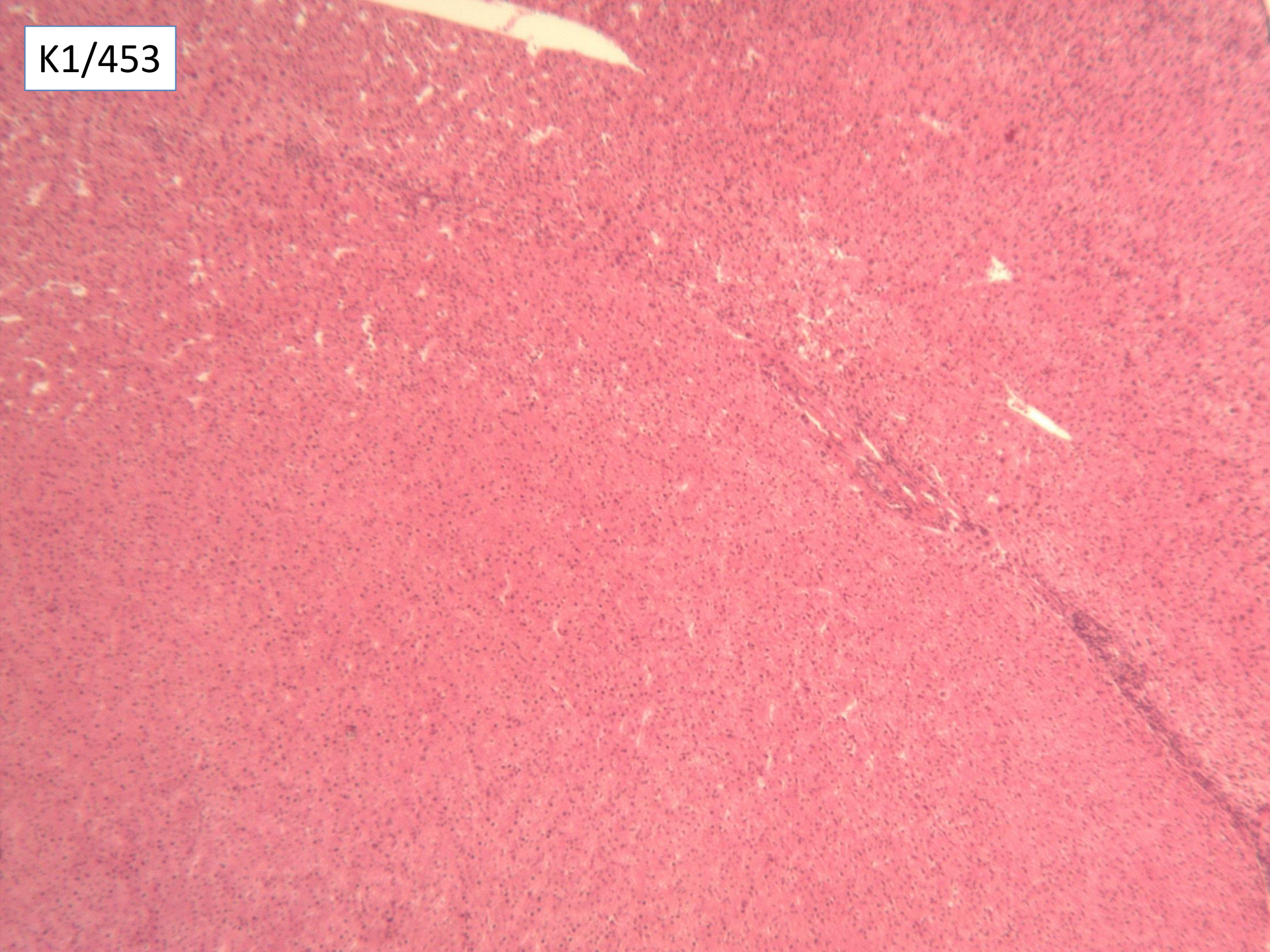
There is also an association with PBC.

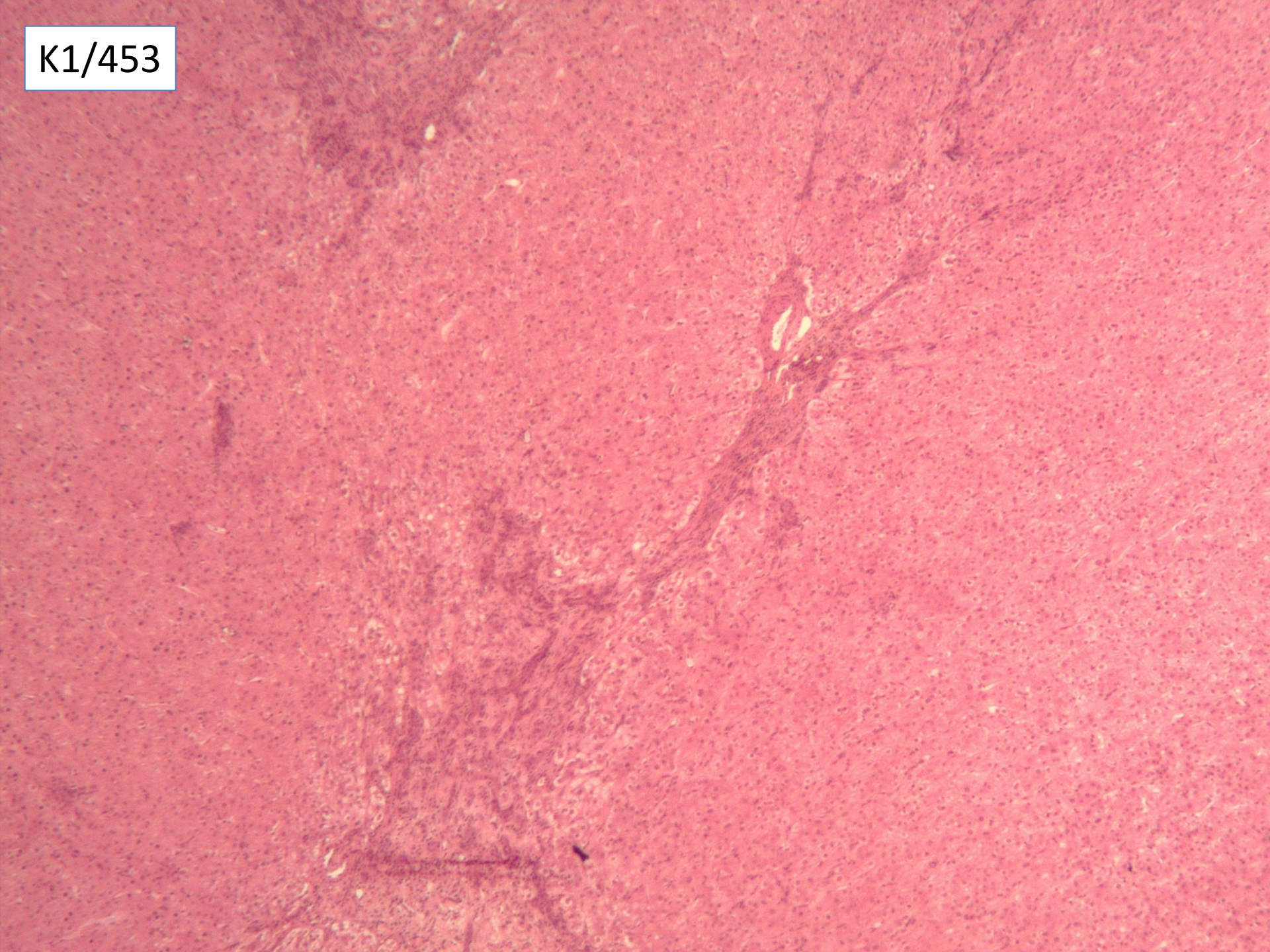
**Case K1/453 Age 27, Female**

? Biliary adenoma

Small cream colour nodule measuring 8 x 6 x 10mm




K1/453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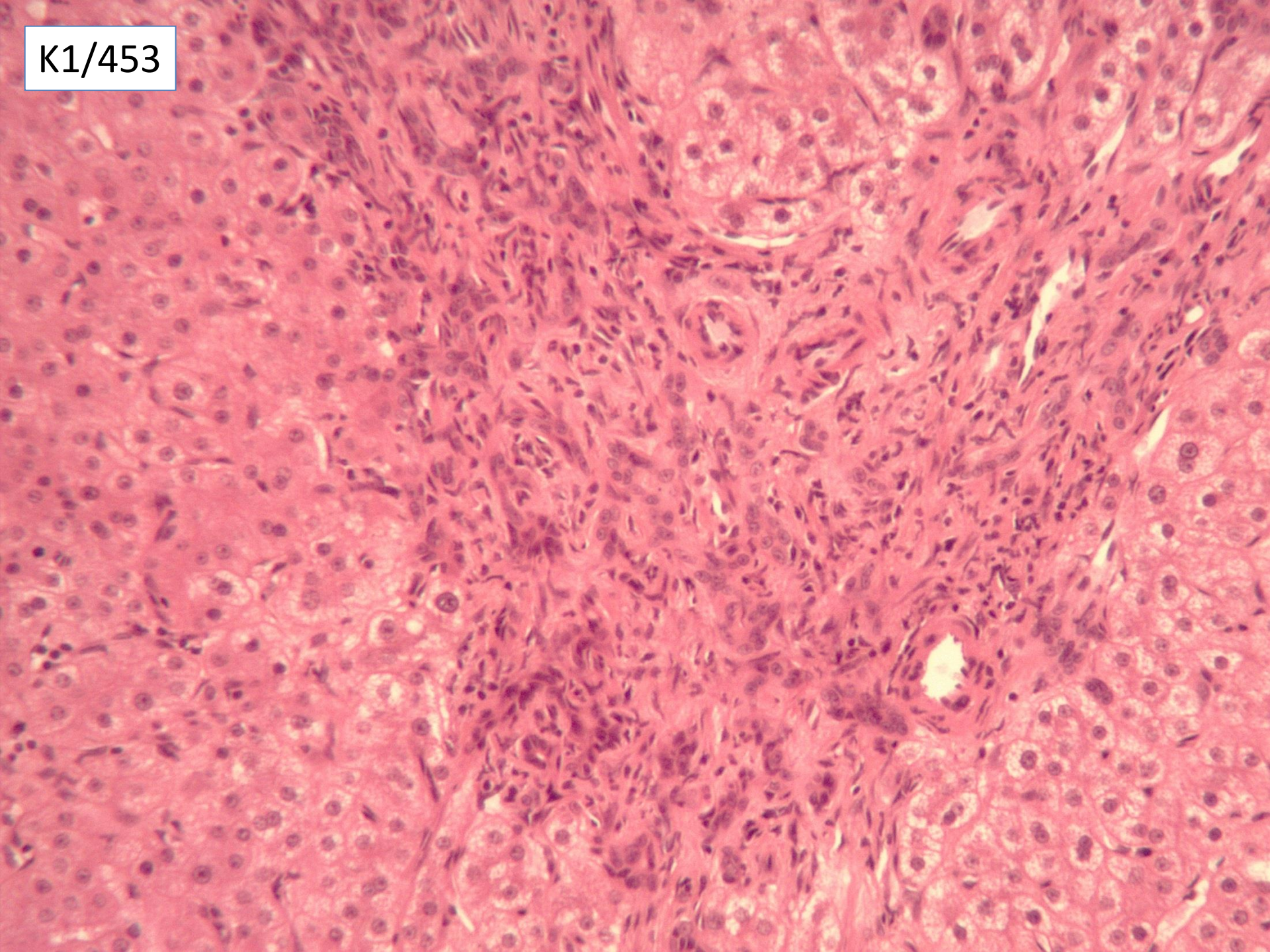
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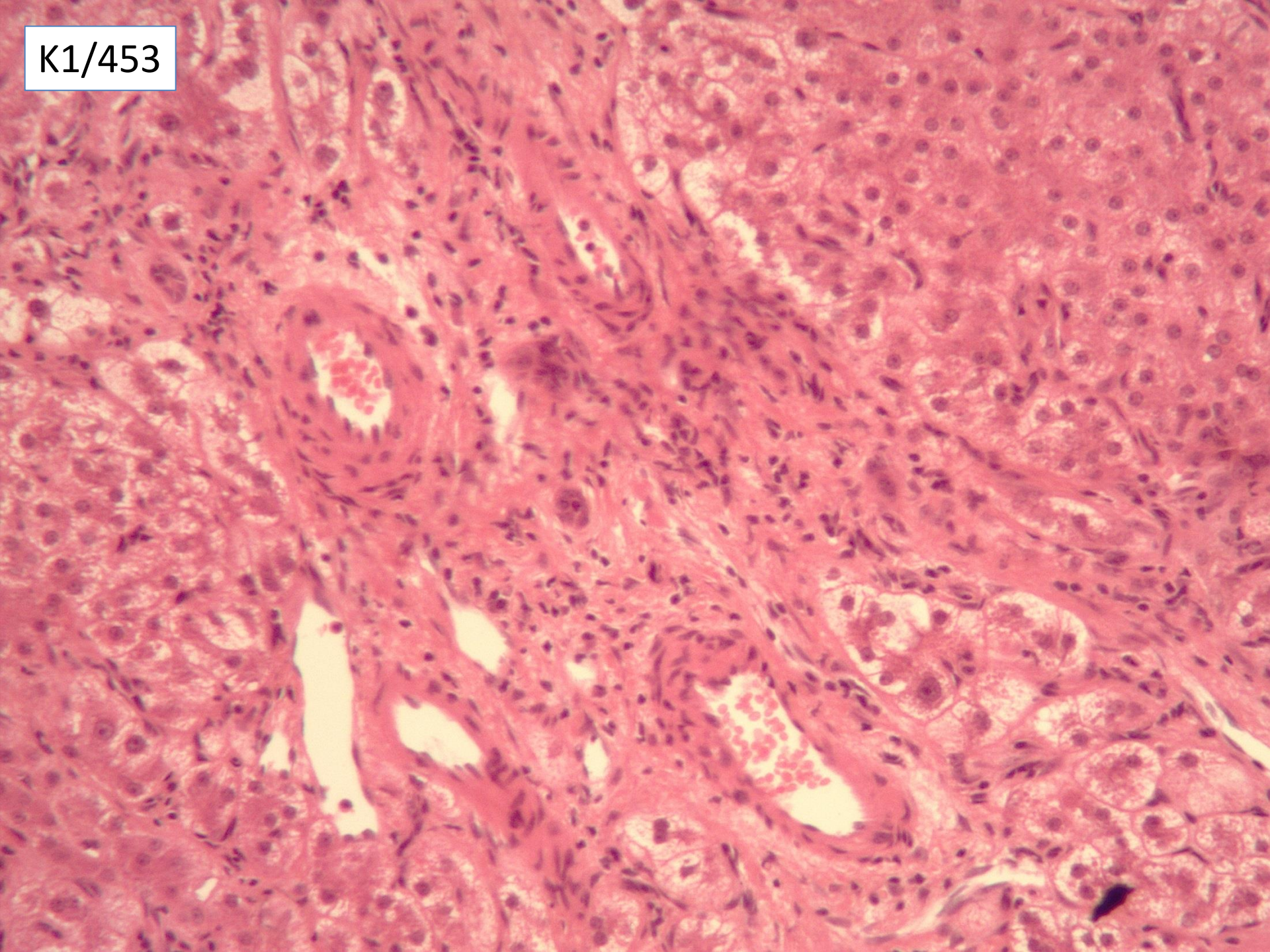
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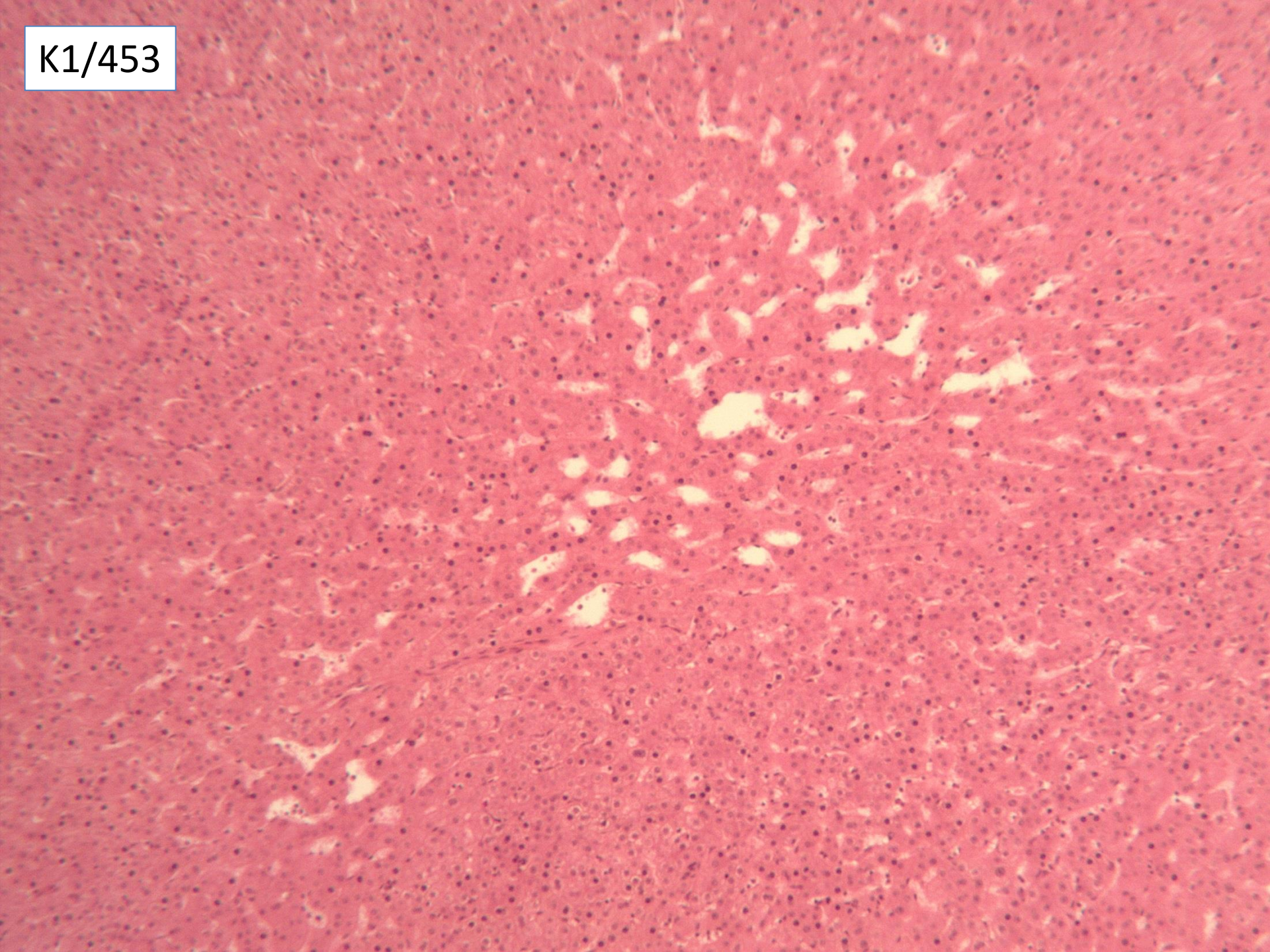

K1/453

**Case K1/453 Age 27, Female**

? Biliary adenoma. Small cream colour nodule measuring 8 x 6 x 10mm

74 focal nodular hyperplasia (FNH)

3 differential diagnosis FNH or adenoma, favours FNH

1 possible FNH, need more sections

1 differential diagnosis FNH v inflammatory hepatocellular adenoma

1 Hepatocellular adenoma rather than FNH (no mention of stains)

7 glutamine synthetase to confirm

1 needs amyloid and CRP

Suggested scoring: for 10 points, FNH as main diagnosis or within differential with confirmatory stains.

Discussion – 10 points if FNH within differential

15/16 agree, 0 unsuitable

**Case K1/453 Age 27, Female**

? Biliary adenoma. Small cream colour nodule measuring 8 x 6 x 10mm

Original diagnosis: focal nodular hyperplasia

Comment: recognition of inflammatory adenoma which can mimic FNH has muddied the waters

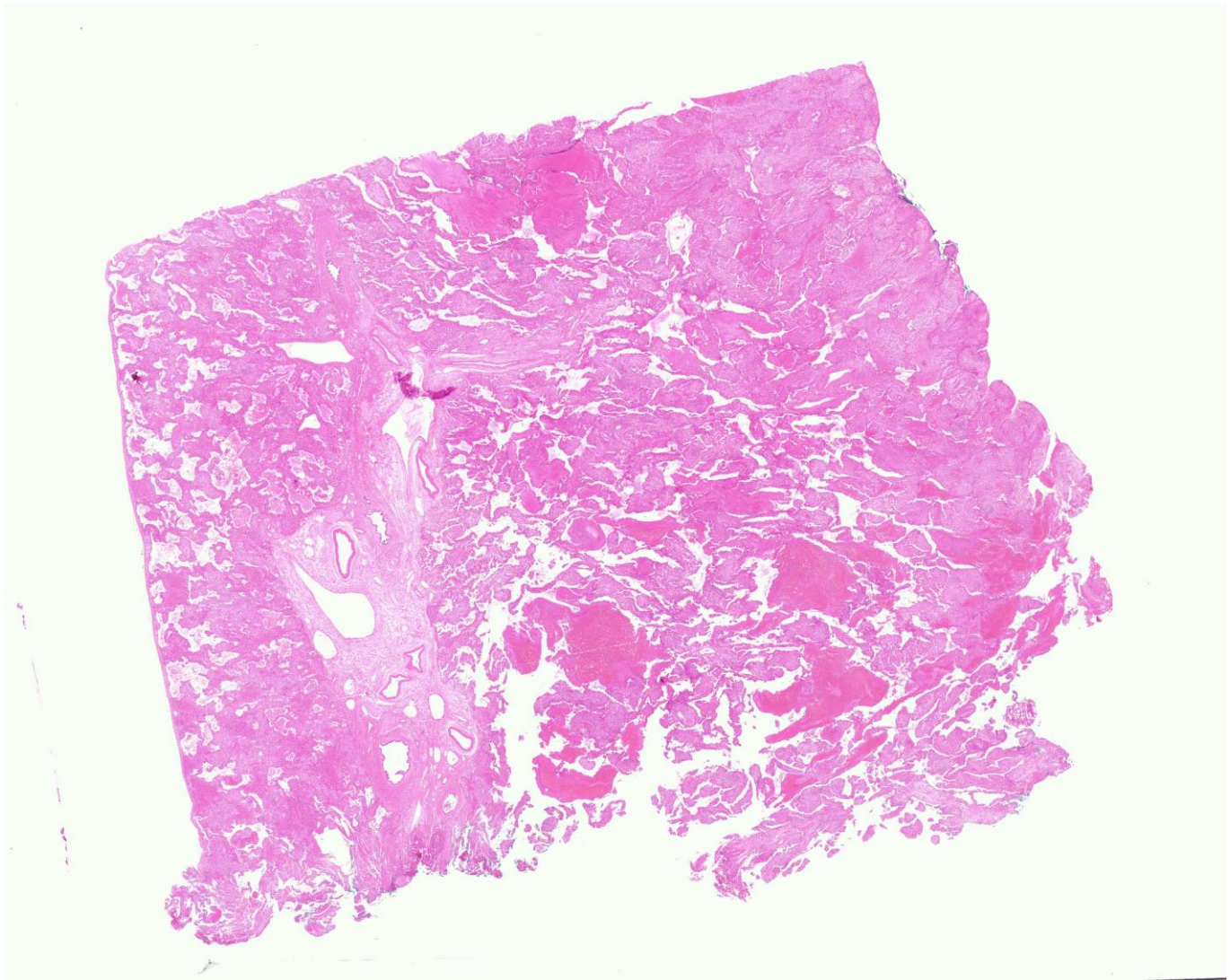
– FNH used to be more unanimously diagnosed in the EQA scheme.

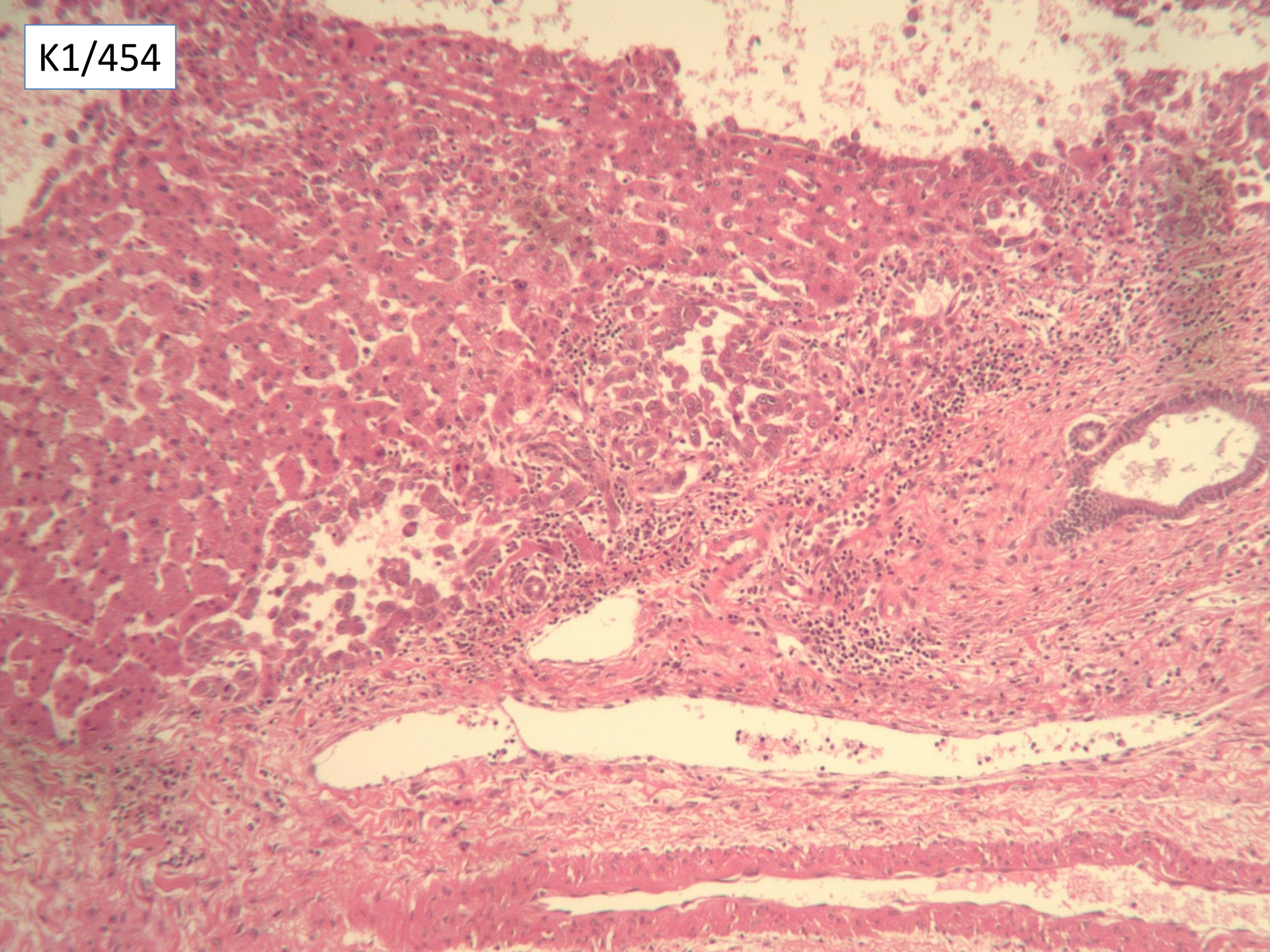
From Dina Tiniakos talk – IHC may be helpful, but can also be misleading – still use histological features as basis for diagnosis if unclear.

**Case K1/454** **Age 30, Female**

Ruptured adenoma x 2

Irregular piece of liver 9 x 5.5 x 3 cm and weighing 66g. It appears unusually soft. The cut surface appears spongy.

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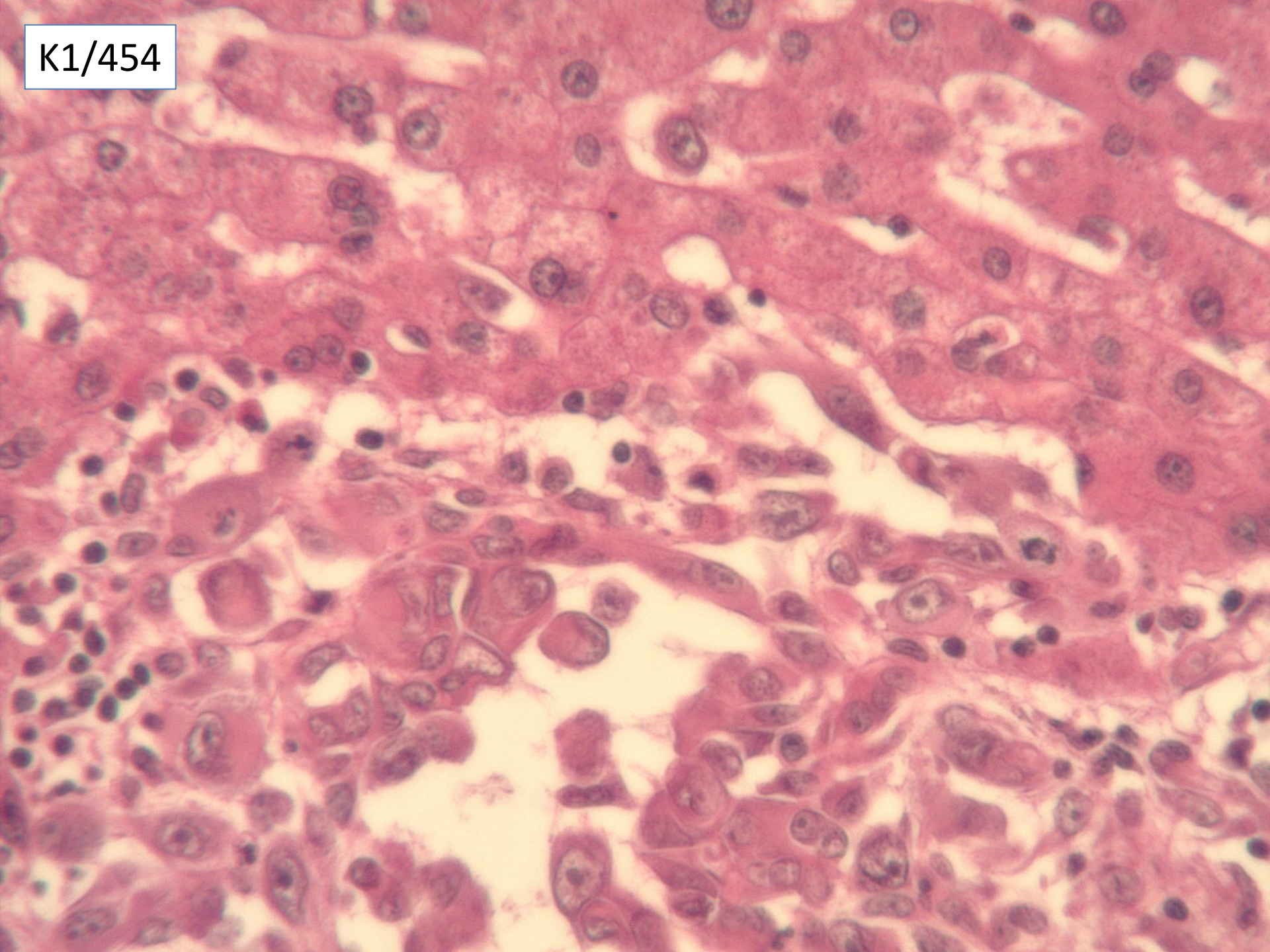
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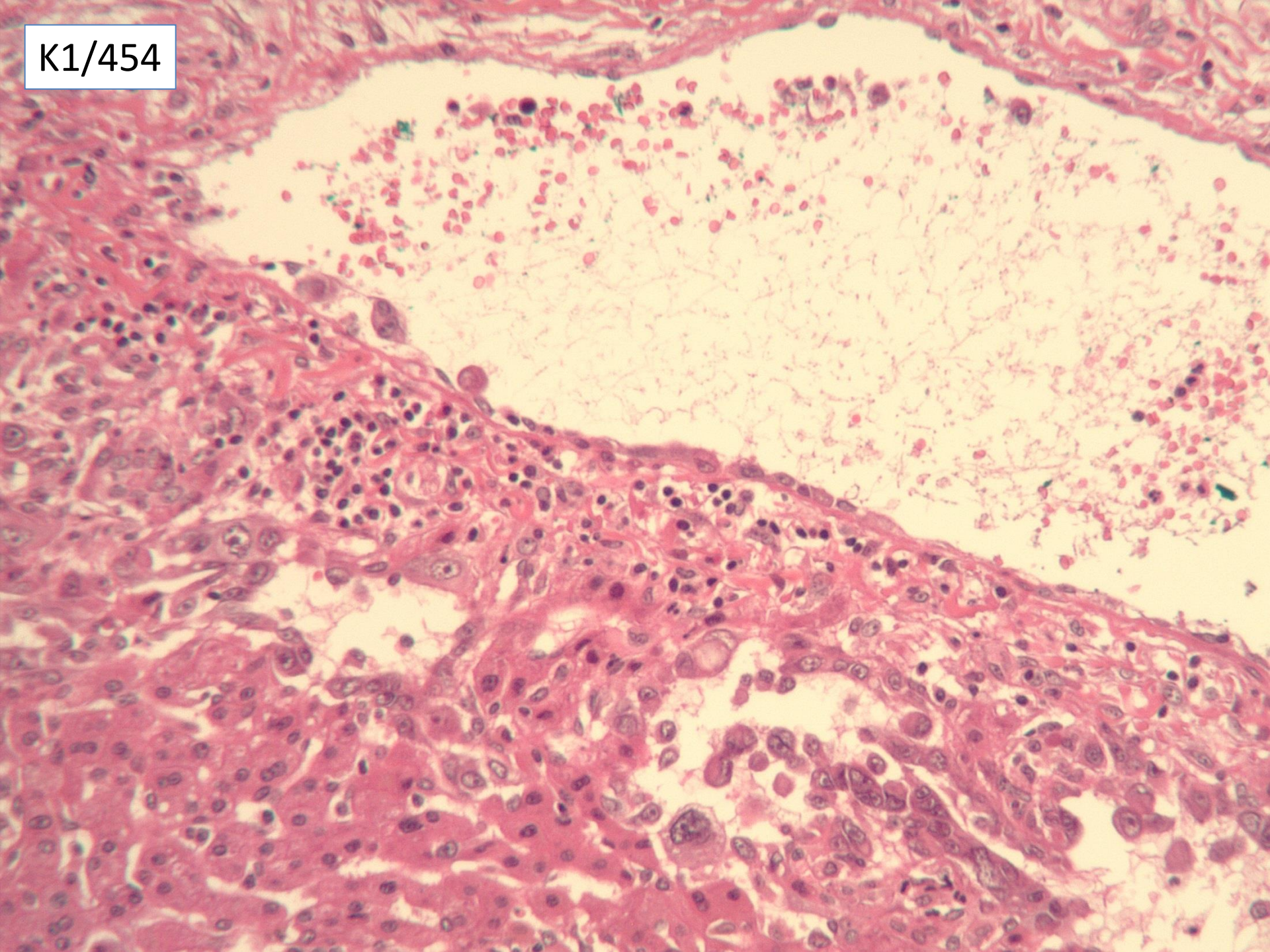
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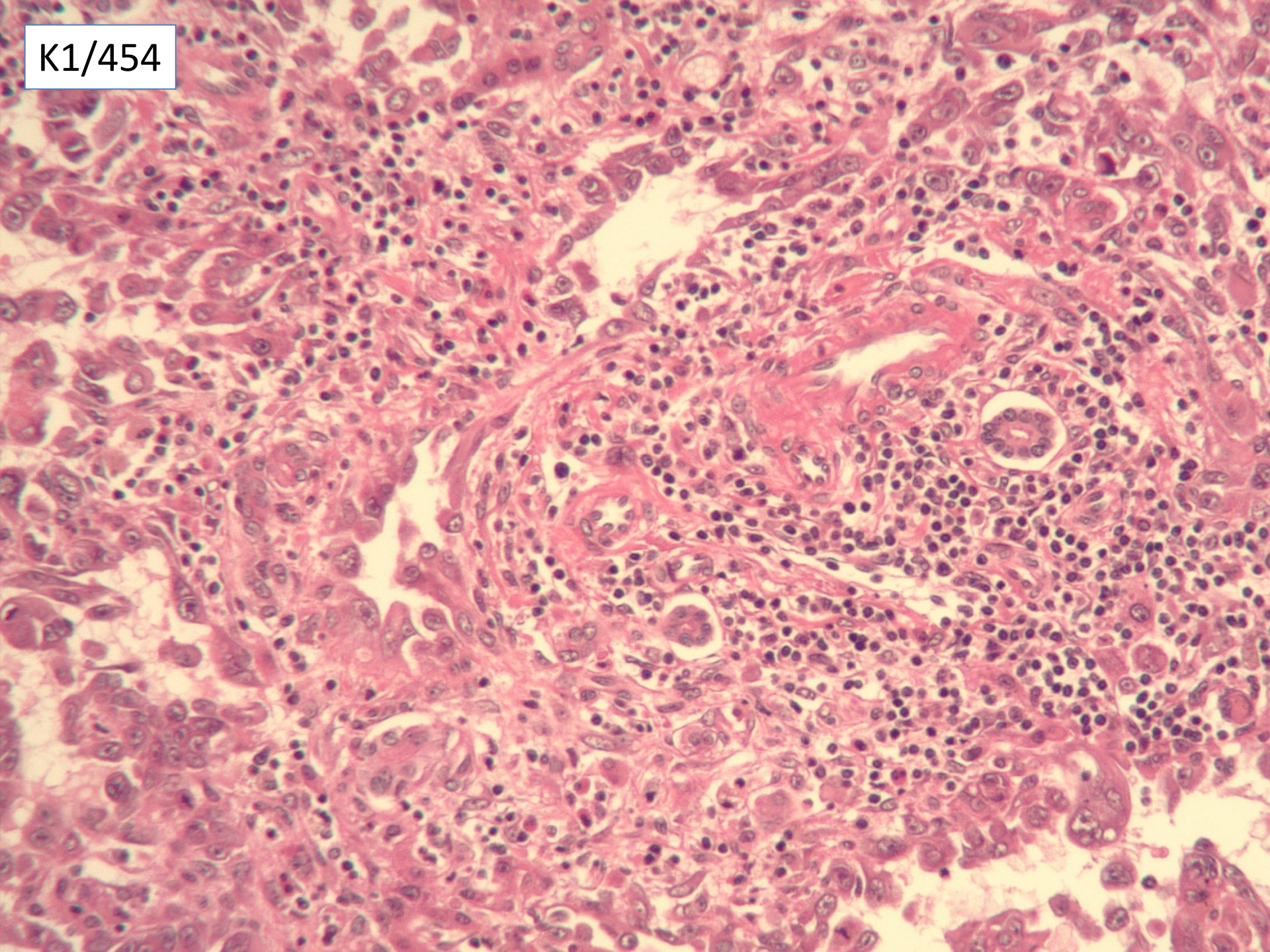
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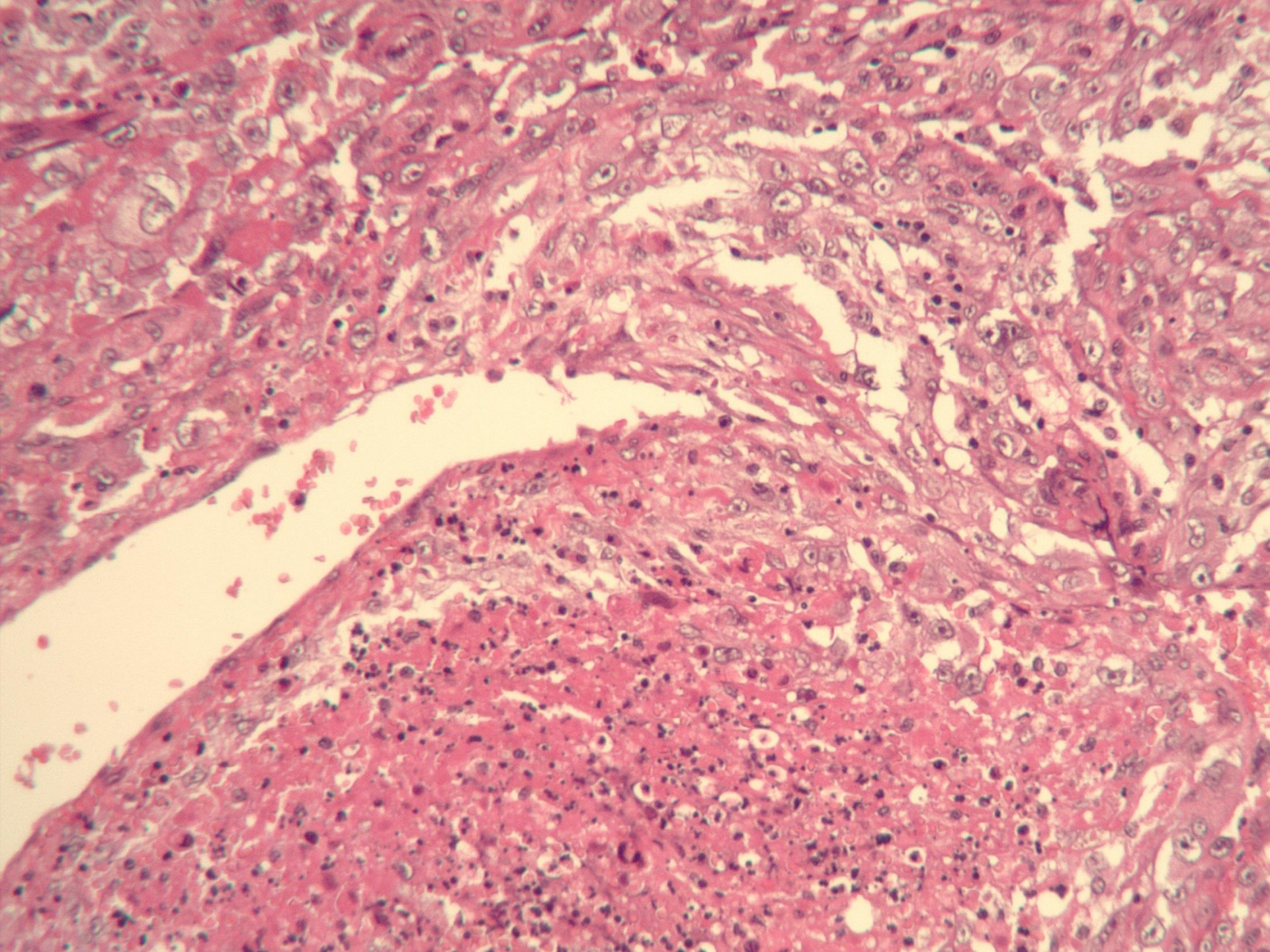
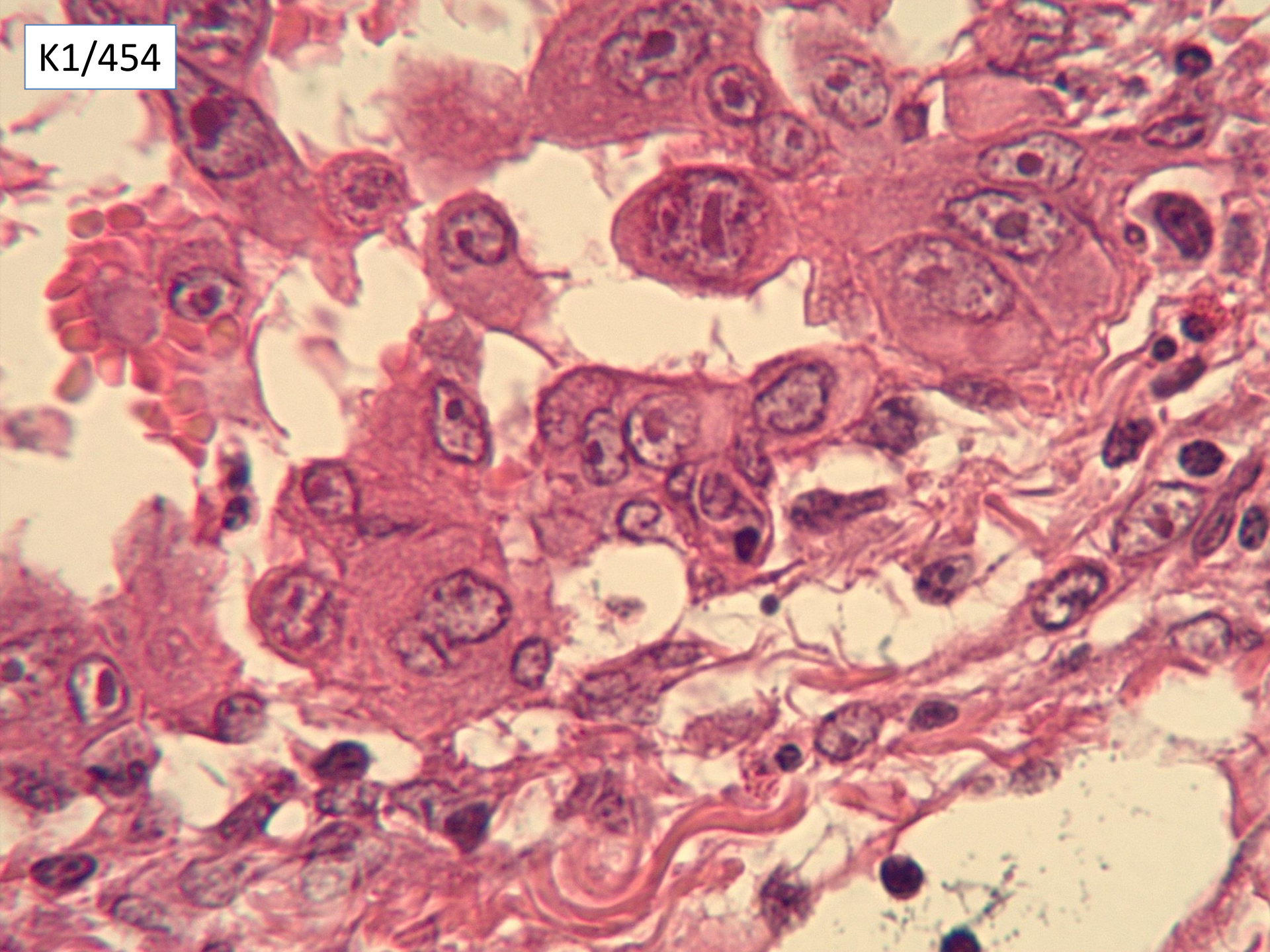



K1/454

**Case K1/454 Age 30, Female**

Ruptured adenoma x 2

48 angiosarcoma +/- epithelioid, or malignant vascular tumour as only, or favoured +/- differential

18 differential diagnosis that includes angiosarcoma,

18 differential includes hepatocellular carcinoma

2 hepatocellular carcinoma, no differential

3 peliosis in hepatocellular adenoma (of which 1? HCC)

2 epithelioid haemangioendothelioma

1 germ cell tumour most likely

1 Poorly differentiated carcinoma, needs immunos

Other malignancies mentioned: melanoma, lymphoma, embryonal carcinoma, choriocarcinoma, Kaposi's

Overall:

10 malignant, differential diagnosis not including angiosarcoma

2 hepatic peliosis, no mention of malignancy

56 needs immunos

20 immunos not mentioned

"I hope this will be an educational case"

Suggested scoring: no consensus, not scored. Or – 10 points for any response that includes angiosarcoma/ malignant vascular tumour.

Lose 5 points for malignant differential not including malignant vascular neoplasm.

Lose 10 points for no mention of malignancy.

12/17 agree, 2 unsuitable

**Case K1/454 Age 30, Female**

Ruptured adenoma x 2

Original diagnosis: epithelioid angiosarcoma

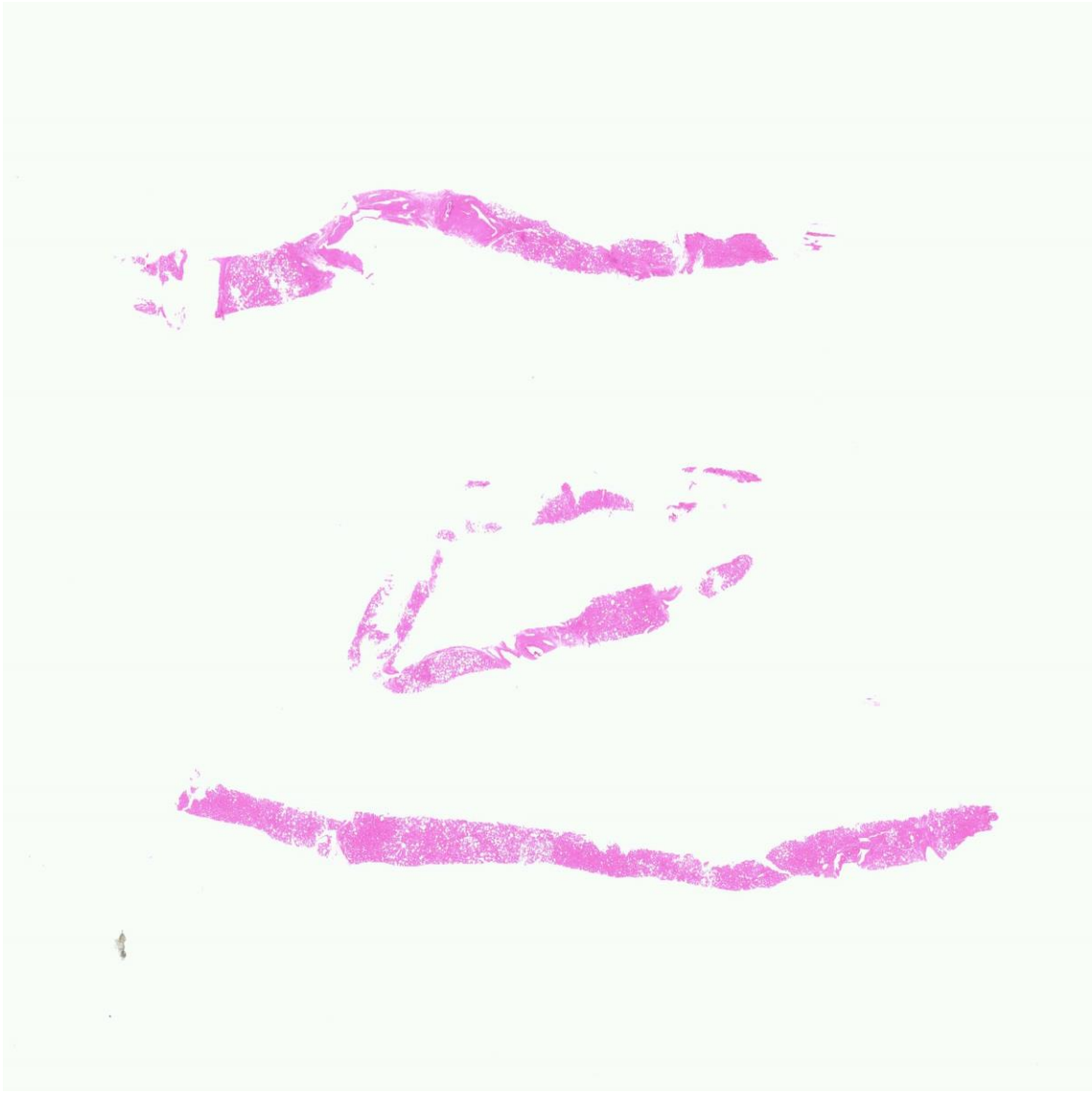
Follow up: The patient developed metastases in chest and mediastinum, and has since died. There were no risk factors for angiosarcoma.

Comment: sufficient features of epithelioid malignancy infiltrating vascular channels and replacing endothelium and sufficient consensus of responses including angiosarcoma within the differential diagnosis to enable scoring.

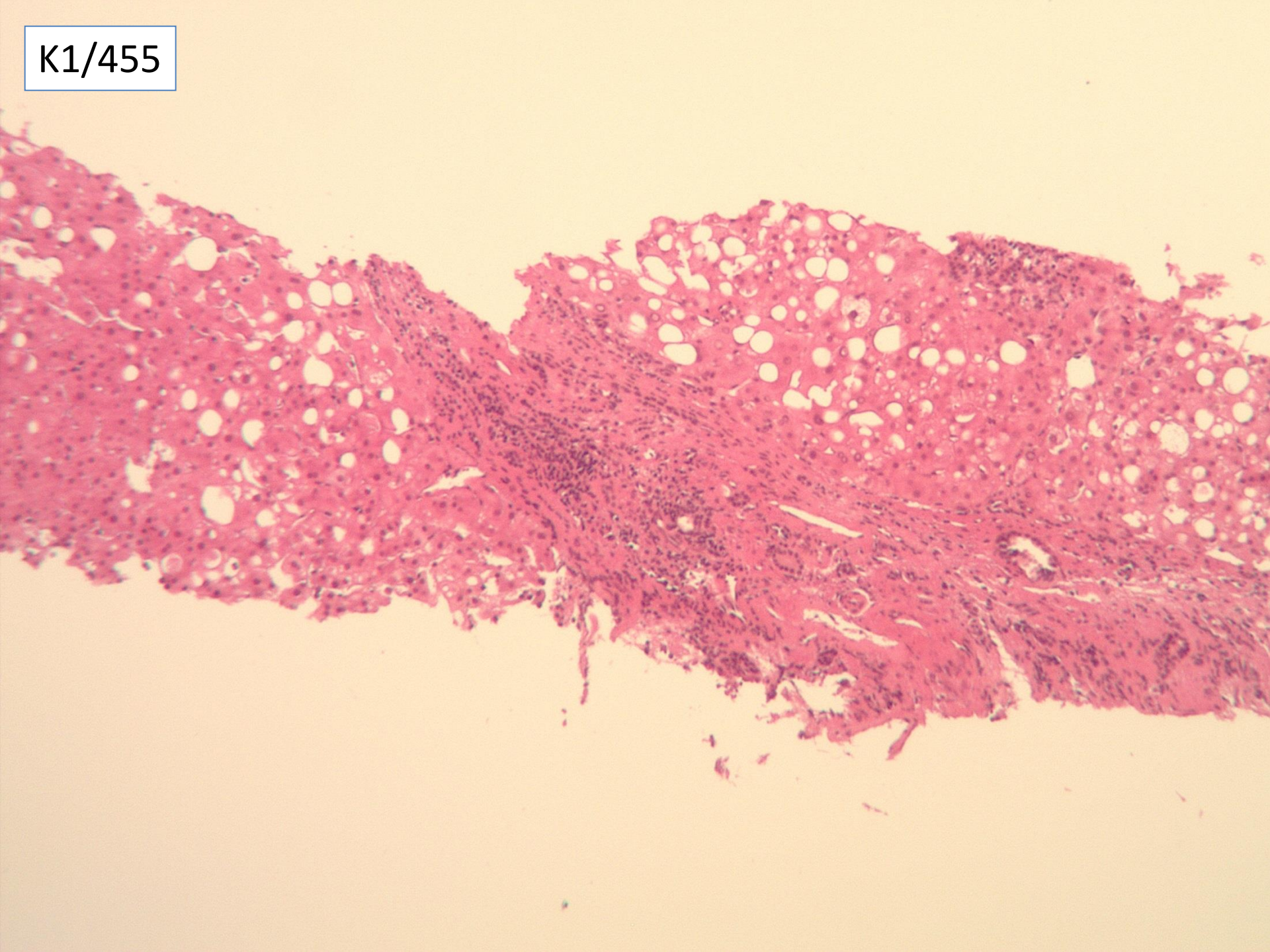
Angiosarcoma may affect any age, and these days it is rare to have an environmental risk factor.

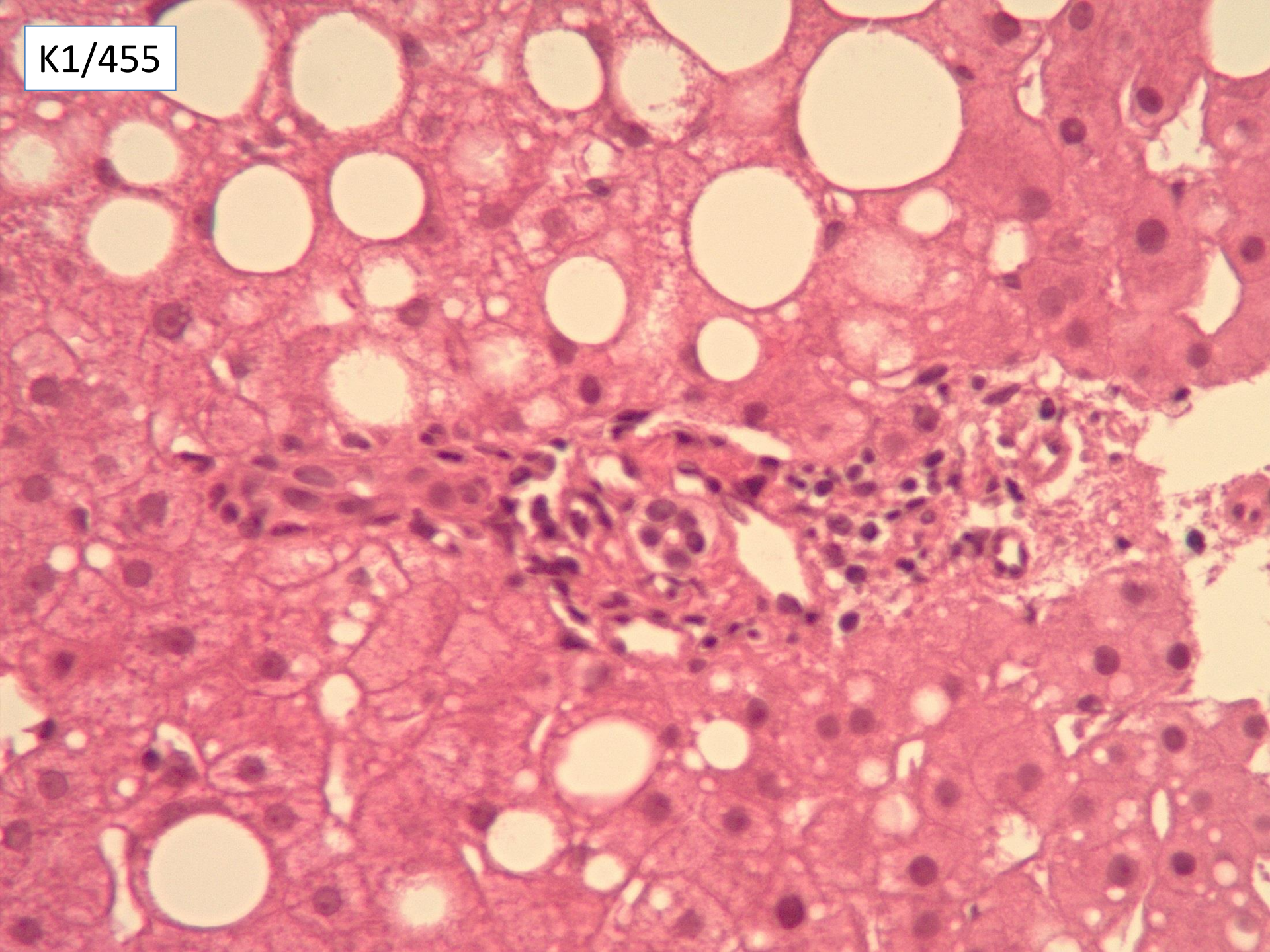
**Case K1/455** **Age 49, Male**

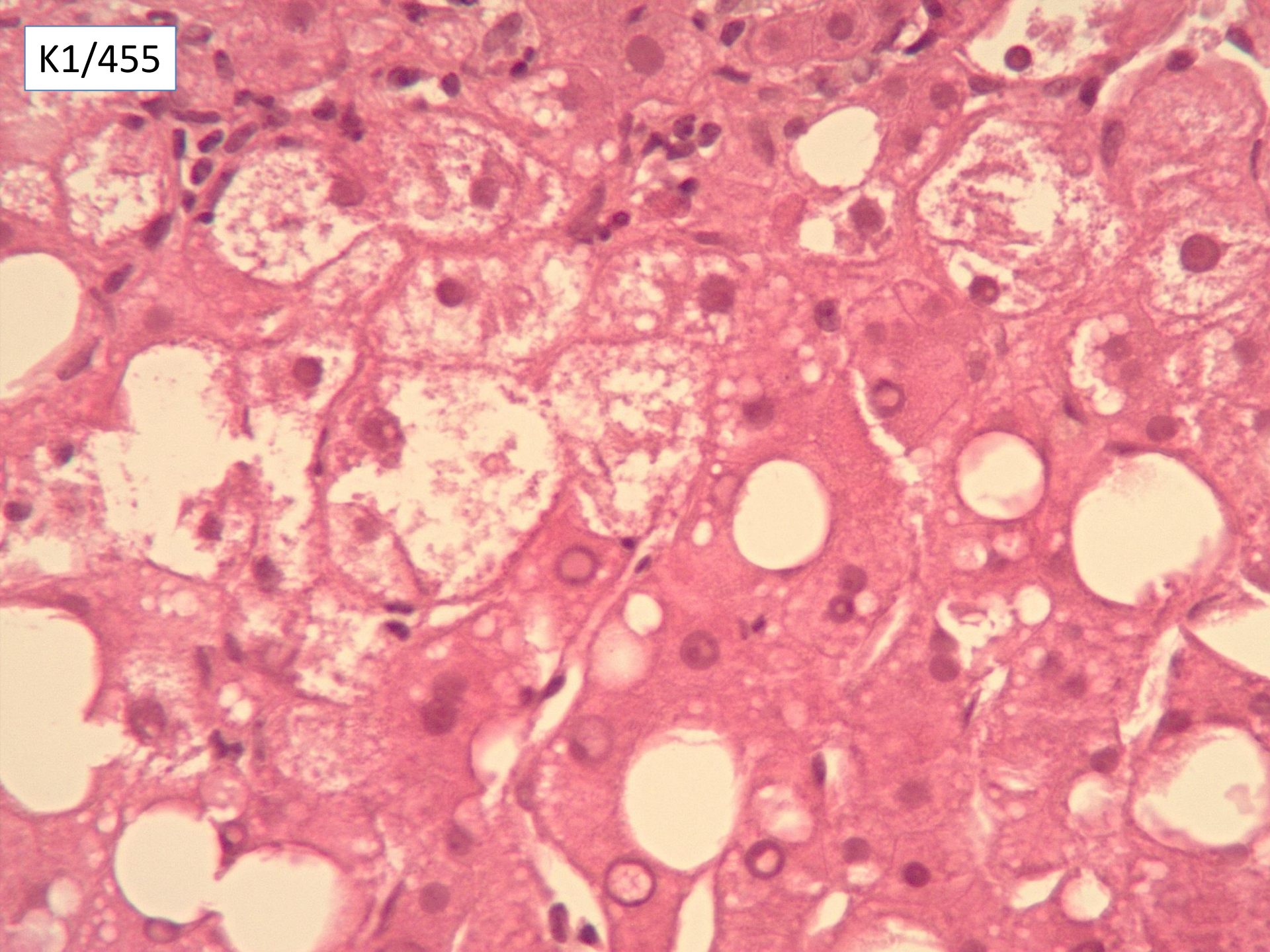
Abnormal liver function tests



K1/455




K1/455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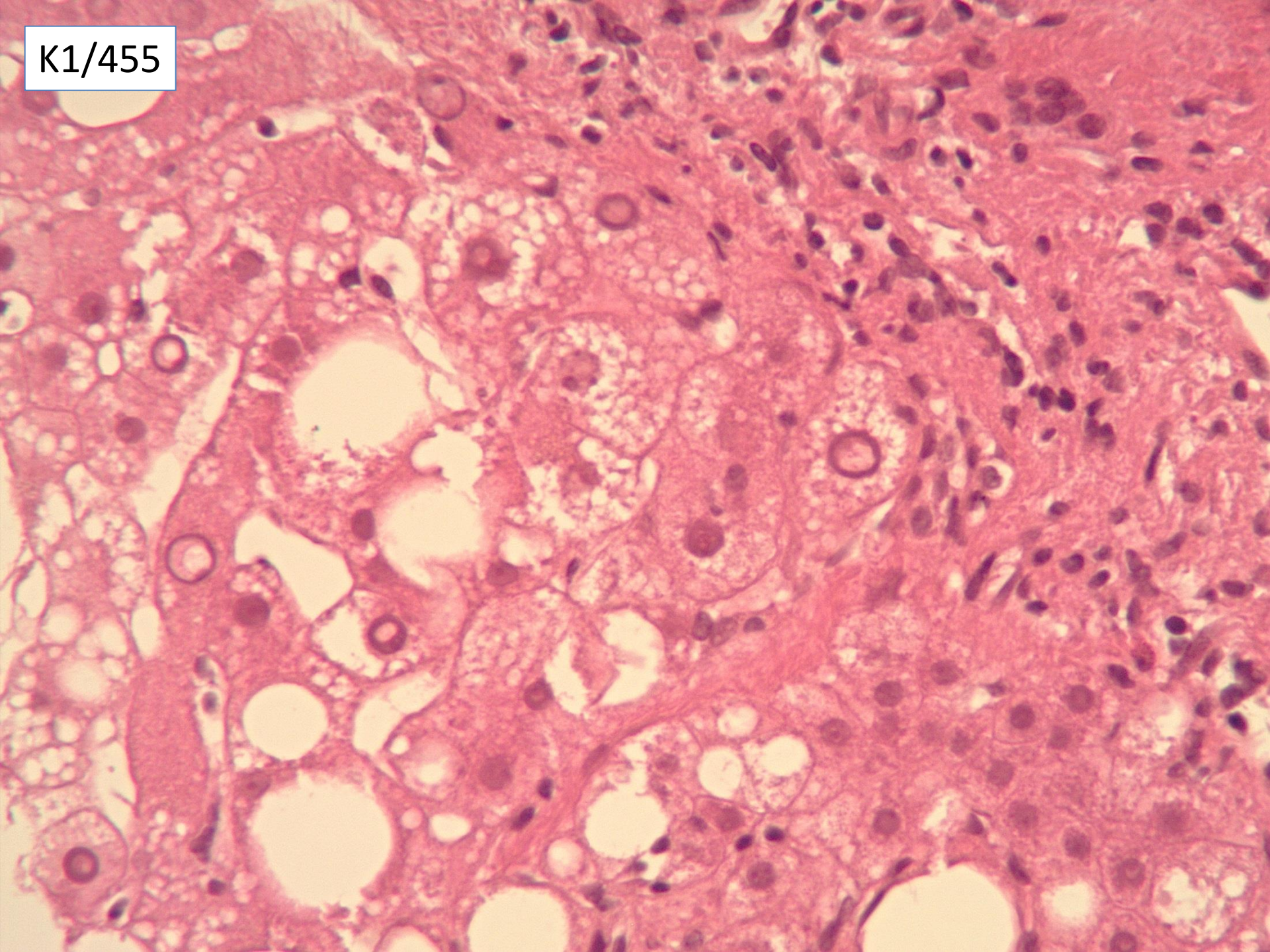
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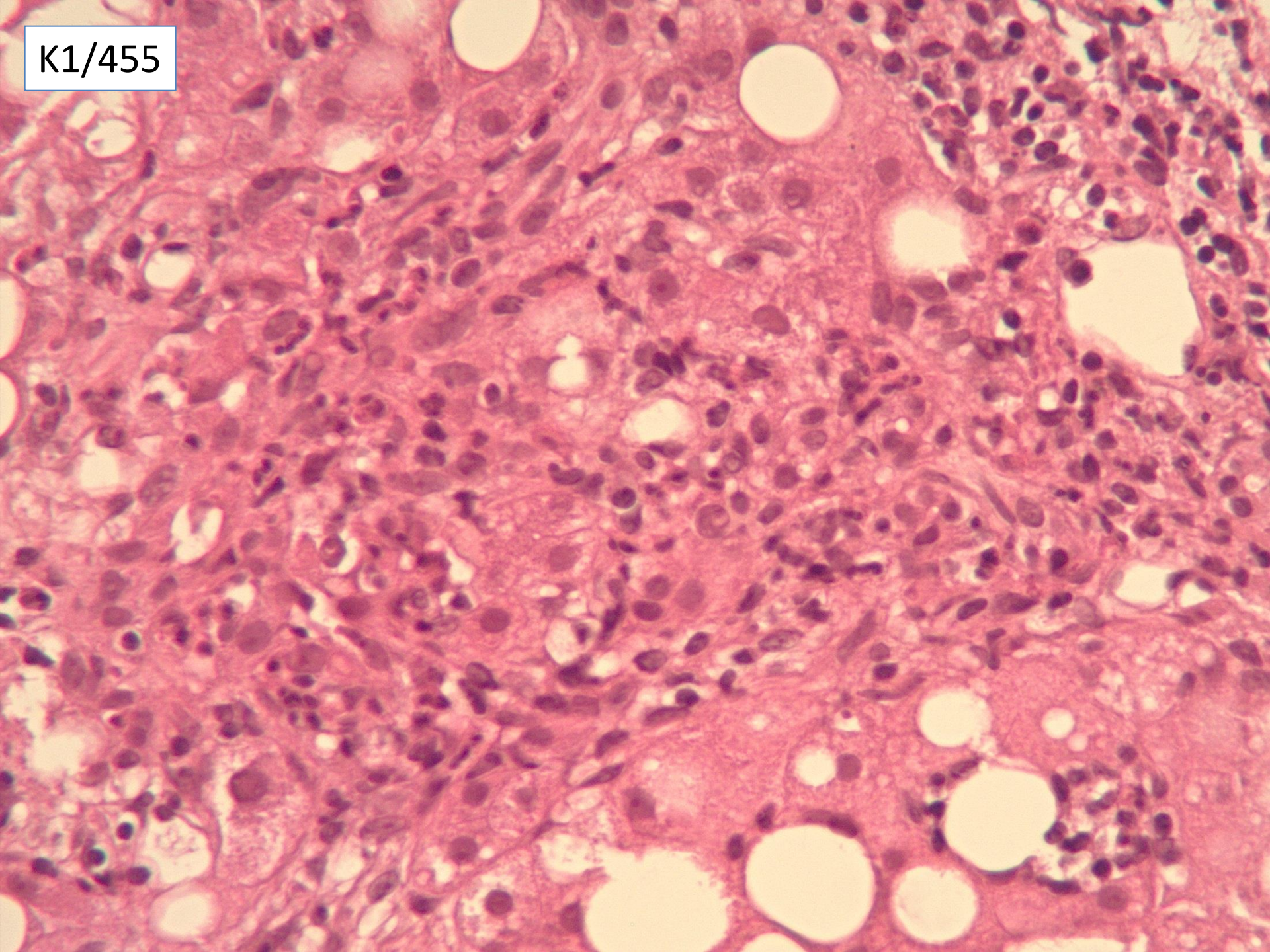
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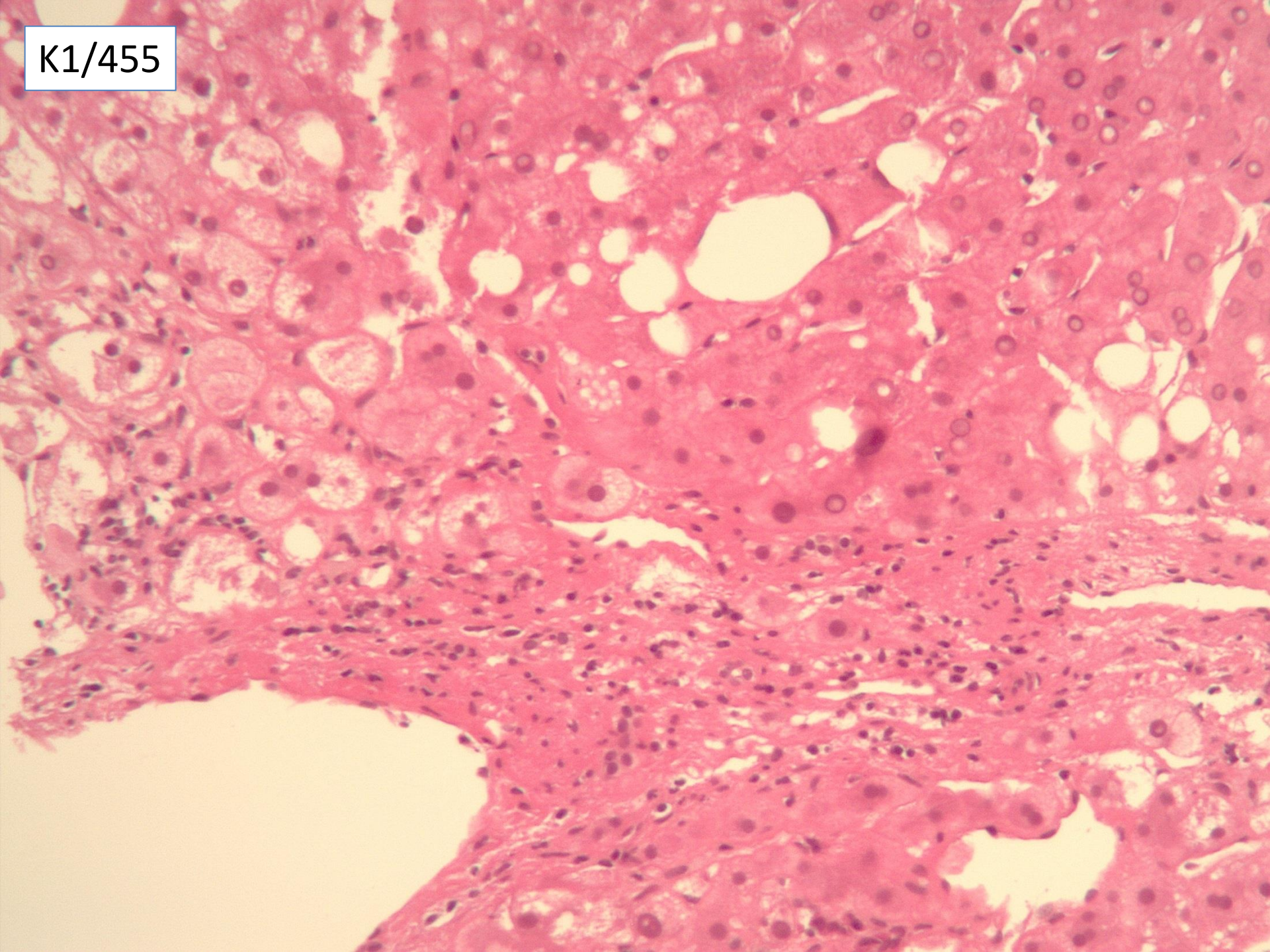
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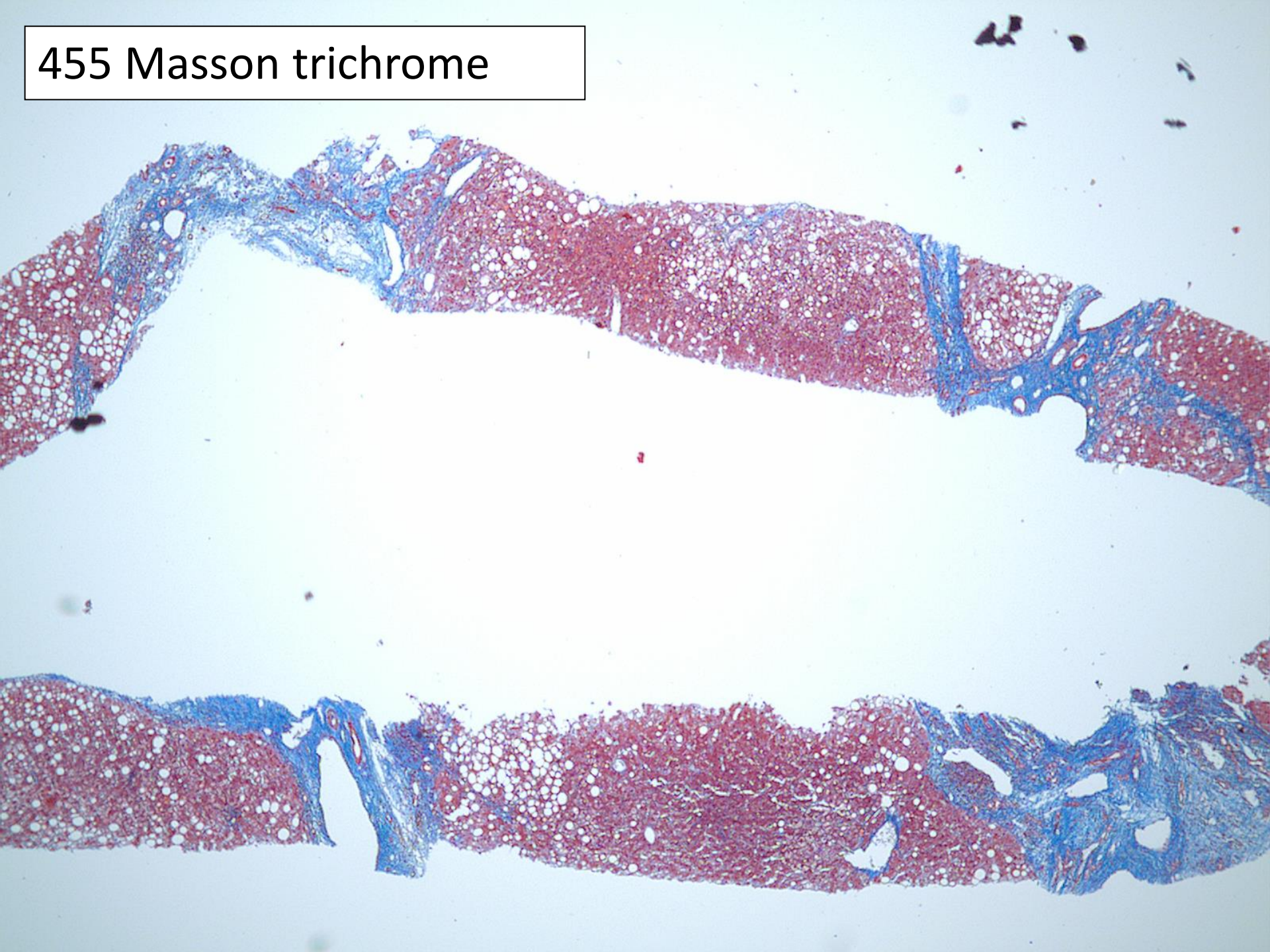
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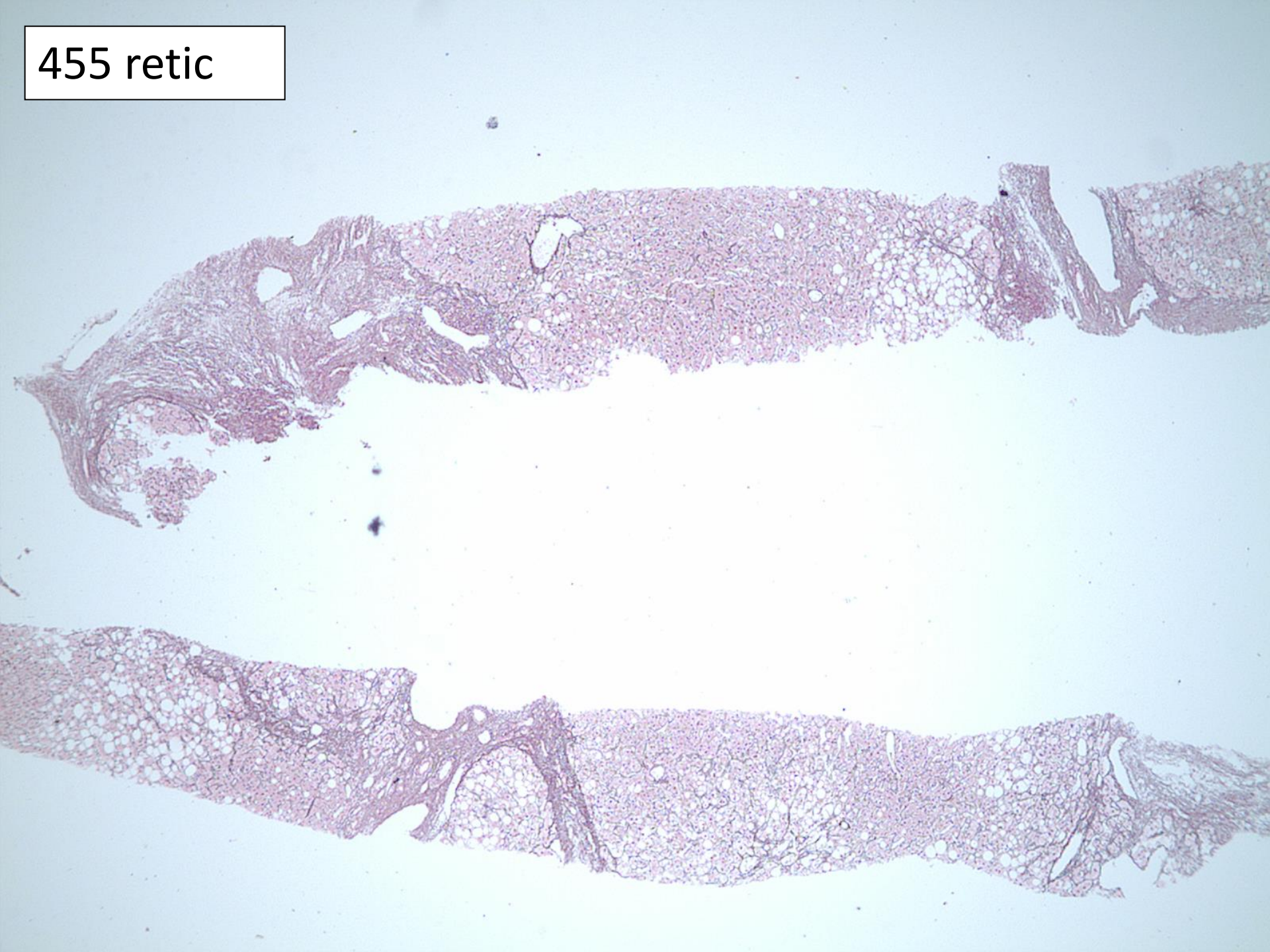

455 retic

**Case K1/455** **Age 49, Male**

Abnormal liver function tests

66 steatohepatitis

10 steatosis

1 fatty liver disease and cirrhosis

2 description only – evolving cirrhosis, needs autoantibodies, virology , drugs etc. – implies not a fatty liver disease

24 of which 4 lipogranuloma,
4 sarcoid granuloma,
16 NOS +/- suggestions for cause

52 ALD / NAFLD

Stage:

10 used Kleiner,

of which 1 = stage 1,
1 = stage 2,
5 = stage 3,
1 = stage 3-4,
2 = stage 4.

66 descriptive, of which
2 =minor, no cirrhosis;
16 = bridging;
1 = extensive
28 = early/possible cirrhosis;
28 = probable or definite cirrhosis

Suggested scoring: for 10 points, state steatohepatitis and comment on stage that is at least bridging fibrosis.

deduct 5 points if steatosis and cirrhosis but not steatohepatitis

deduct 5 points for stage less than bridging fibrosis.

16/16 agree, 1 unsuitable

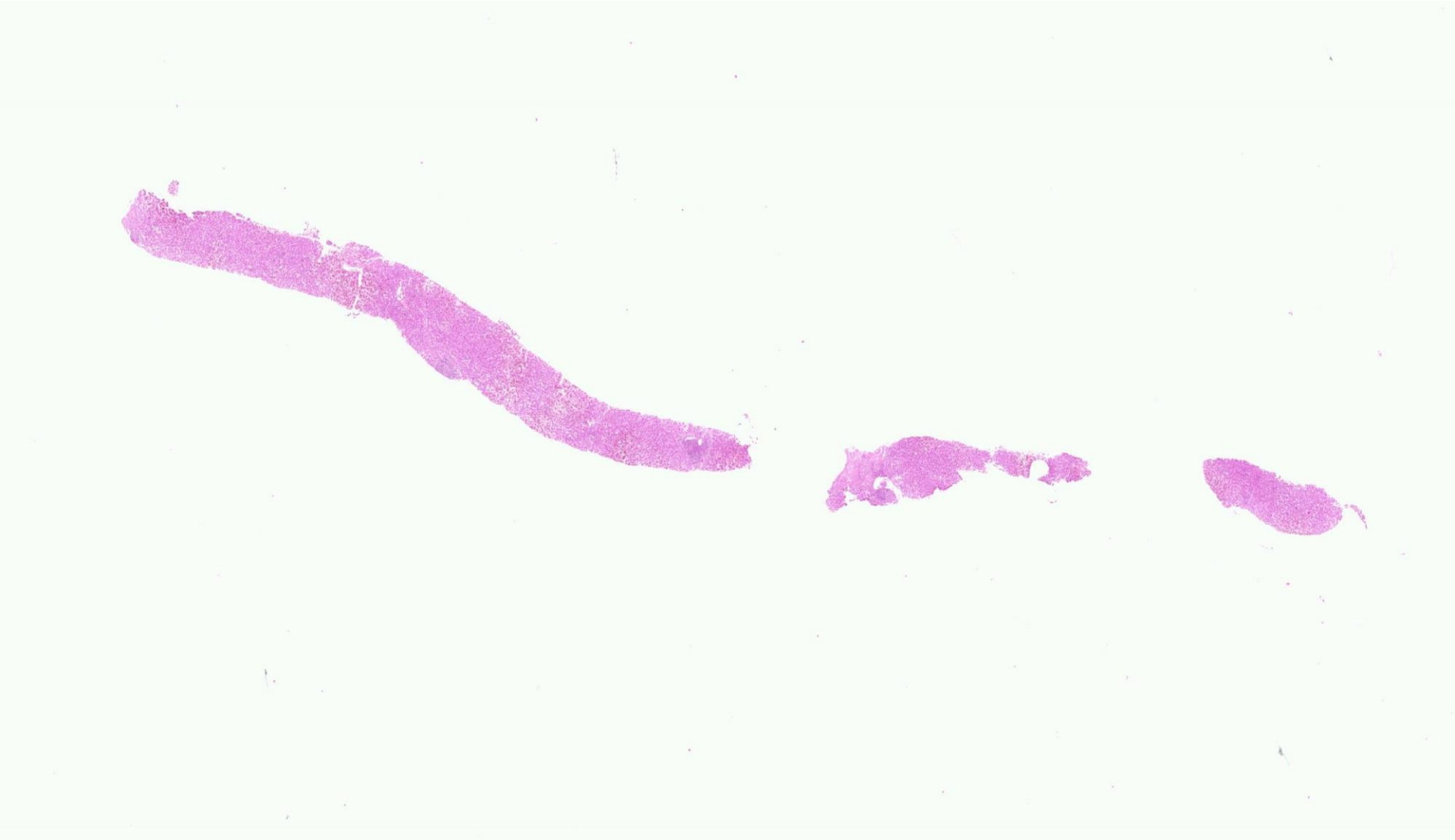
**Case K1/455 Age 49, Male**

Abnormal liver function tests

- Original diagnosis: Non-alcoholic steatohepatitis. At least bridging fibrosis, possible cirrhosis.
- Follow up information: raised blood glucose and HbA1c – diabetic. Granulomas not reported – no relevant follow up.

**Case K1/456** **Age 47, Female**

Unwell jaundice 1 week. High LFT's ?acute hepatic failure.



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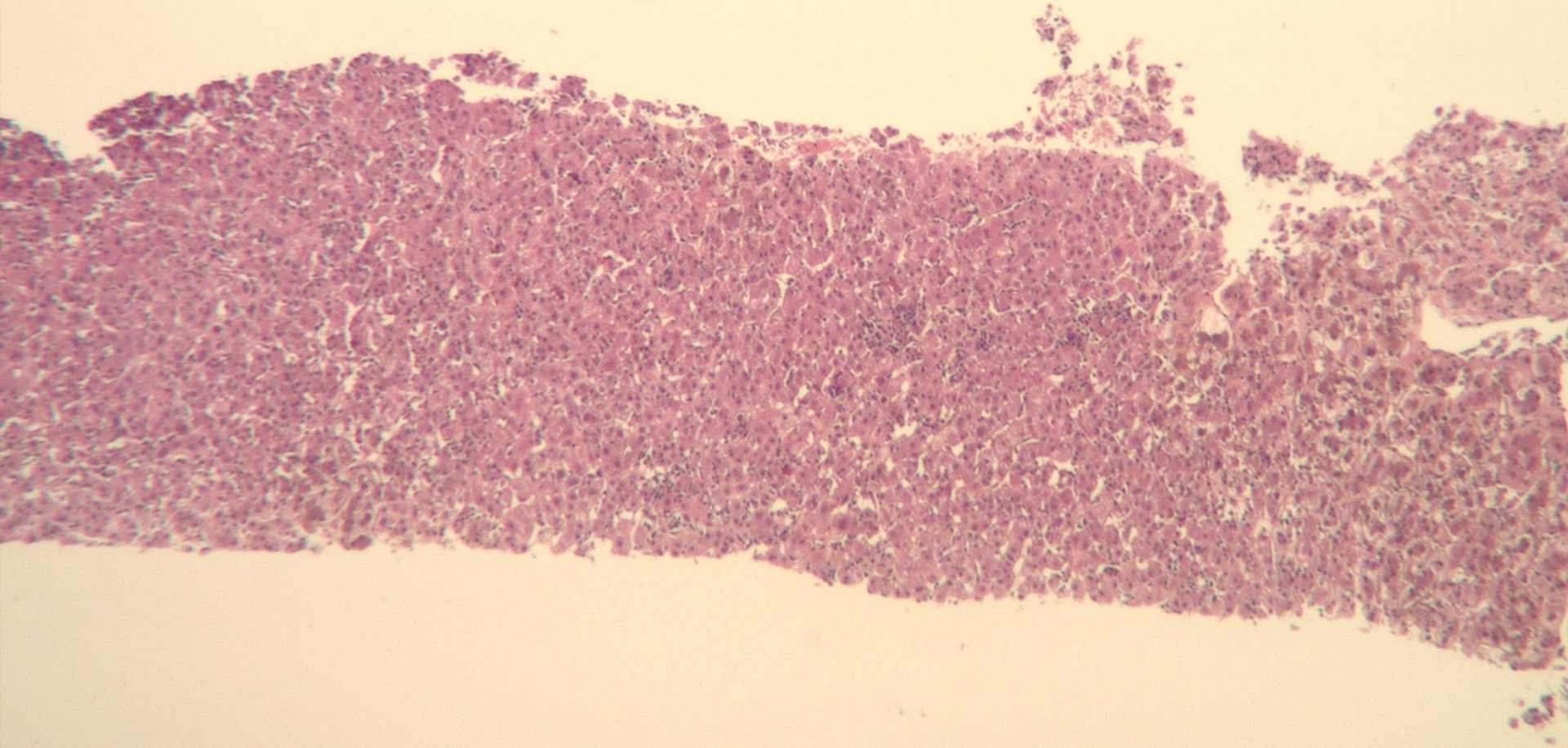

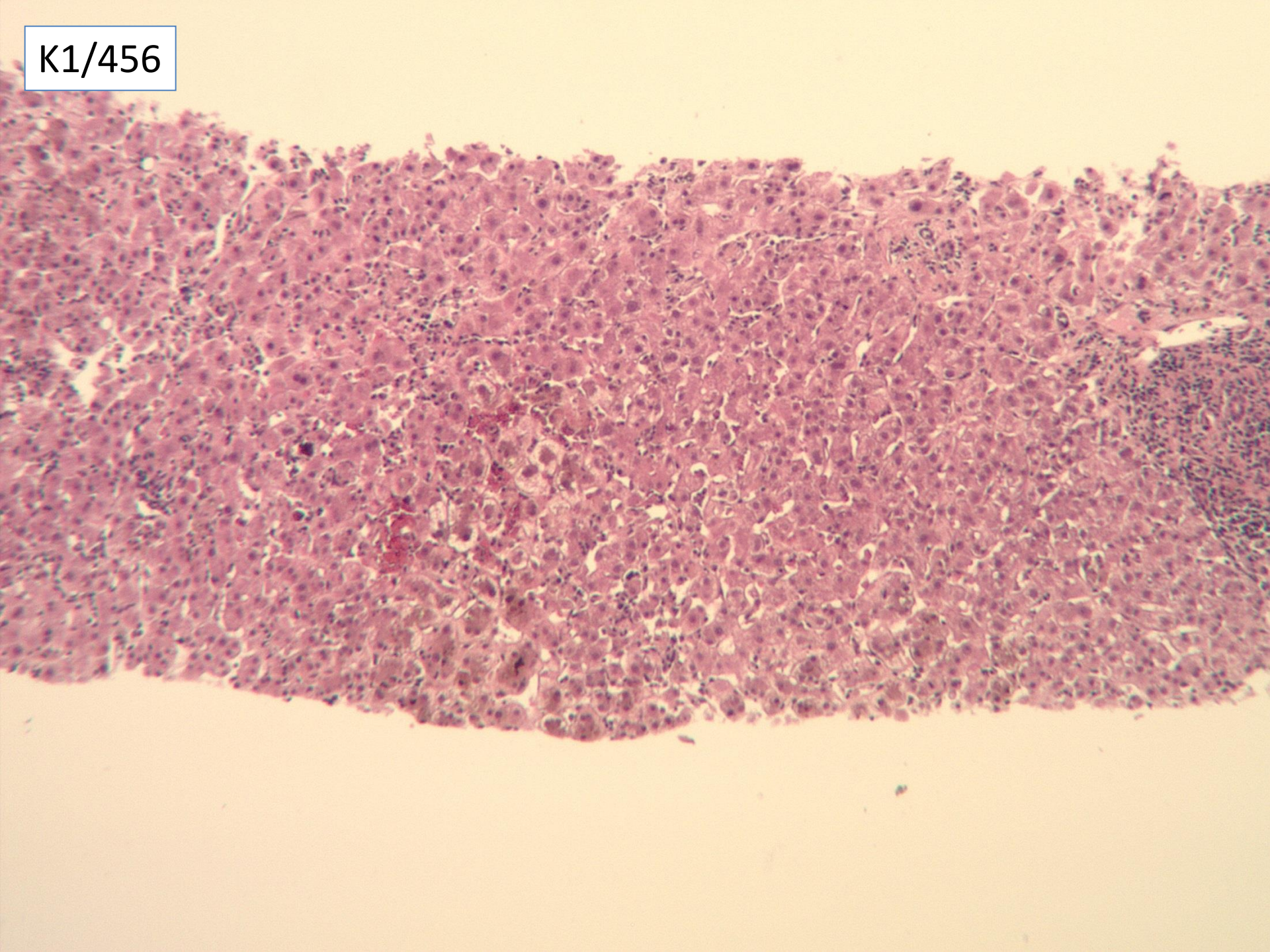
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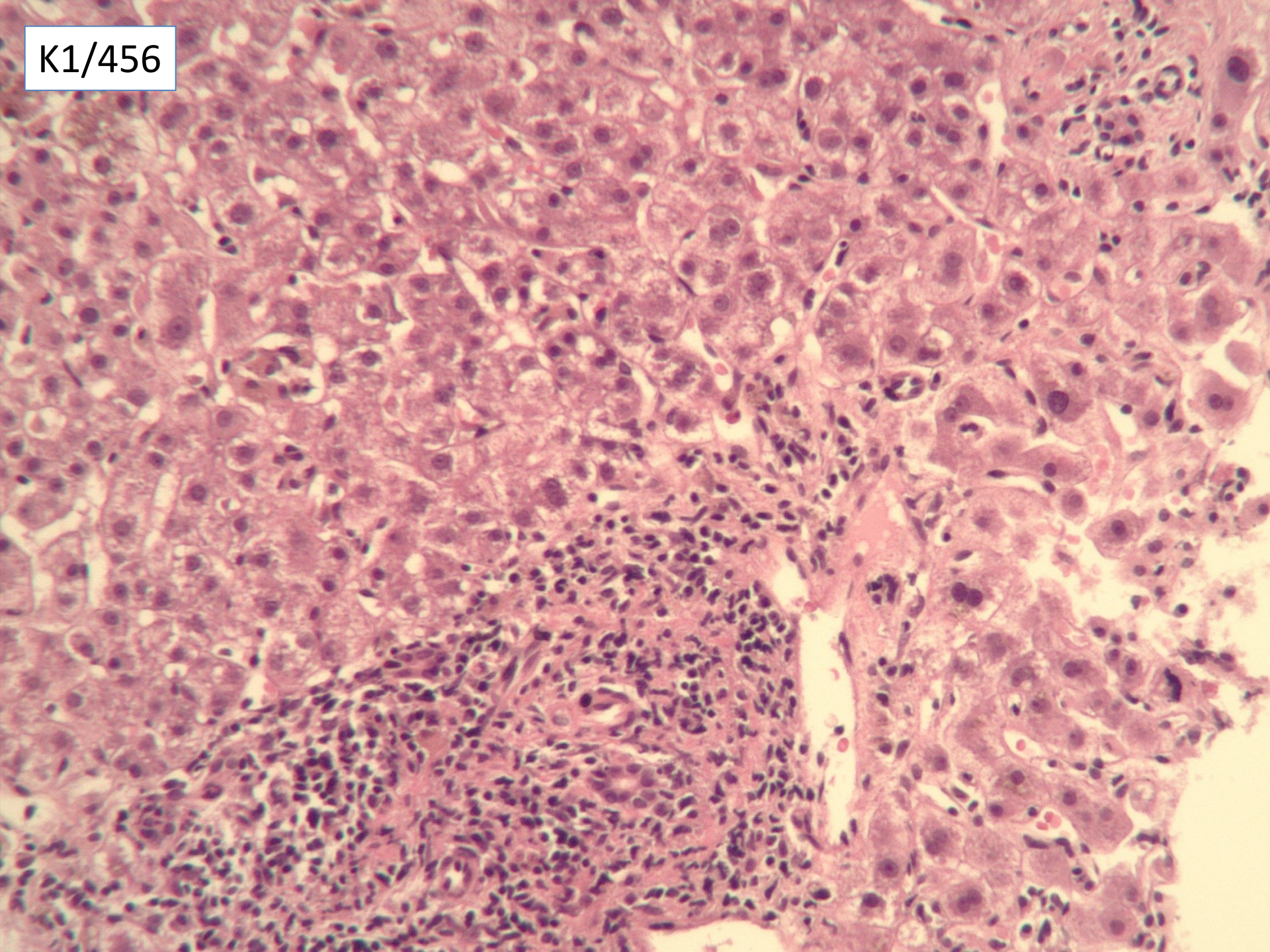
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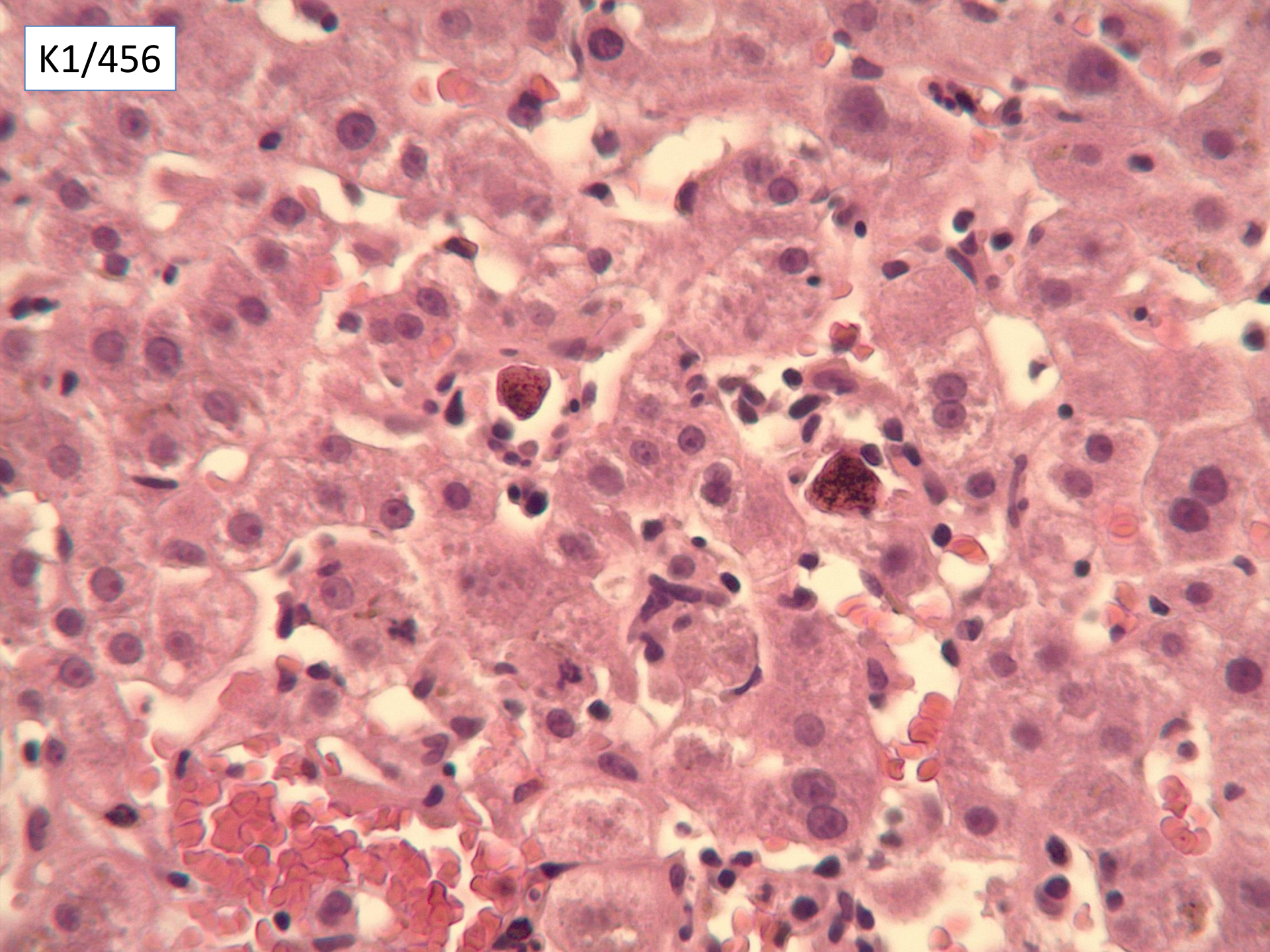
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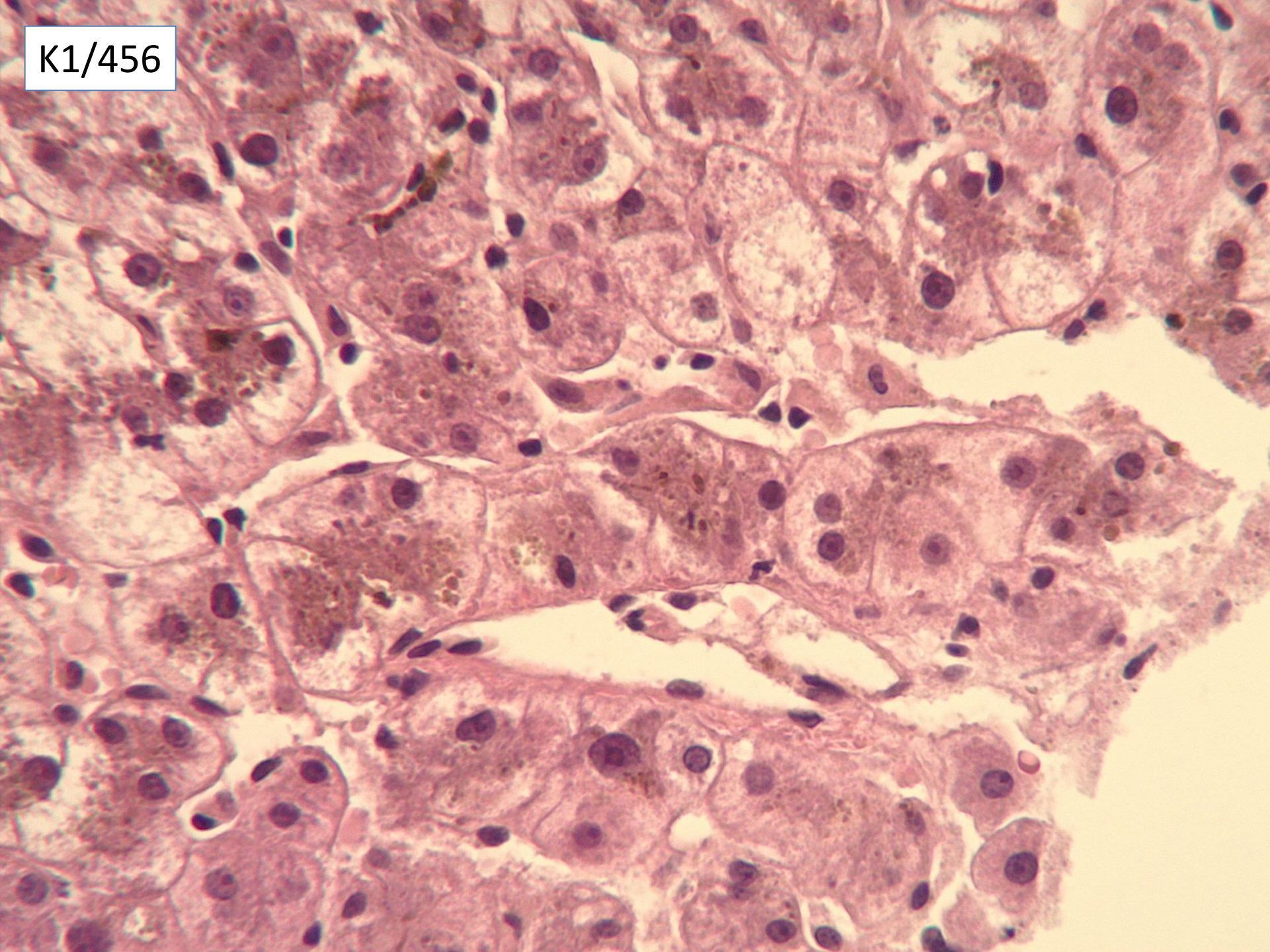

K1/456

## Case K1/456 Age 47, Female

Unwell jaundice 1 week. High LFT's ?acute hepatic failure.

45 acute cholestatic hepatitis

16 acute hepatitis

2 acute liver injury, or description 'hepatitis' not stated

1 "acute intrahepatic cholestasis ? ductopenia, - drugs or underlying ductopenic disease"

2 descriptive, no conclusion

1 lymphoma with cholestatic liver injury

1 large bile duct obstruction – no mention of hepatitis

41 drugs/viral/autoimmune, none favoured

13 virus/drugs, AIH less likely/not AIH

8 differential, favours drug

4 drugs as only cause

4 favours AIH

2 drugs or AIH (not virus)

1 favours viral

Specific ones suggested:

4 hepatitis E, 3 hepatitis A, 2 EBV

2 ? haemochromatosis

3 ? Wilson's

1 exclude lymphoma,

1 suspect lymphoproliferative disorder or large bile duct obstruction

2 ? alcohol

6 drugs not mentioned

5 no aetiology suggested

Suggested scoring:.
for 10 points need acute hepatitis. Lose 5 points for report not mentioning hepatitis. Lose 10 points for misleading diagnosis.

12/17 agree, 3 unsuitable

**Case K1/456 Age 47, Female**

Unwell jaundice 1 week. High LFT's ?acute hepatic failure.

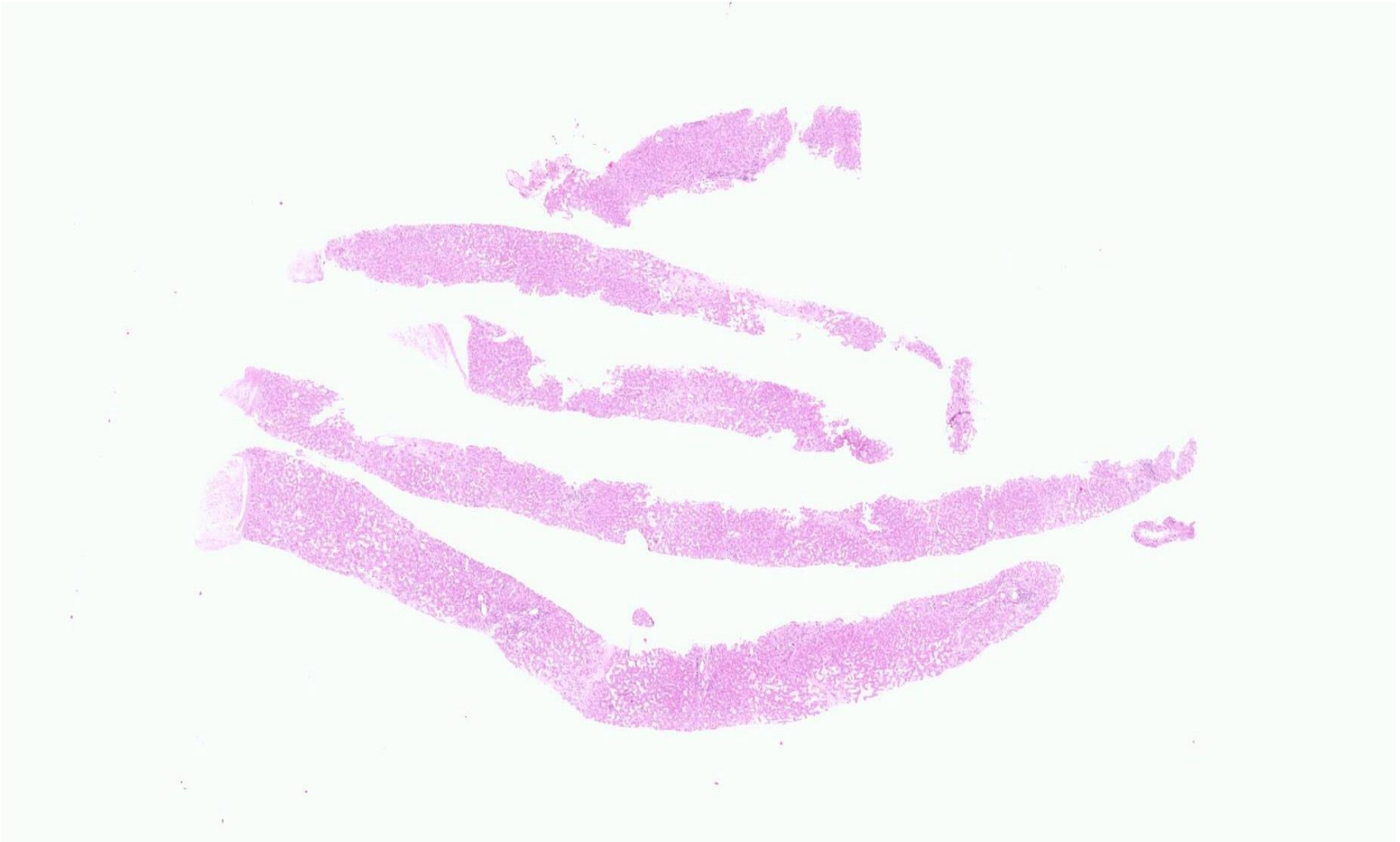
- Additional clinical information - initial ALT >2500, coagulopathy (peak INR 2), now normalised. Bilirubin 255. Hepatitis A/B/C –ve. Alcohol >42u/week, not dependant.
- Original diagnosis: Acute cholestatic hepatitis. Subsequently acute hepatitis E. IgM +ve, PCR $2x10^5$.
- Treated with steroids before the IgE results was known. ALT steady fall, normalised in 4 weeks. Follow up in local hospital.

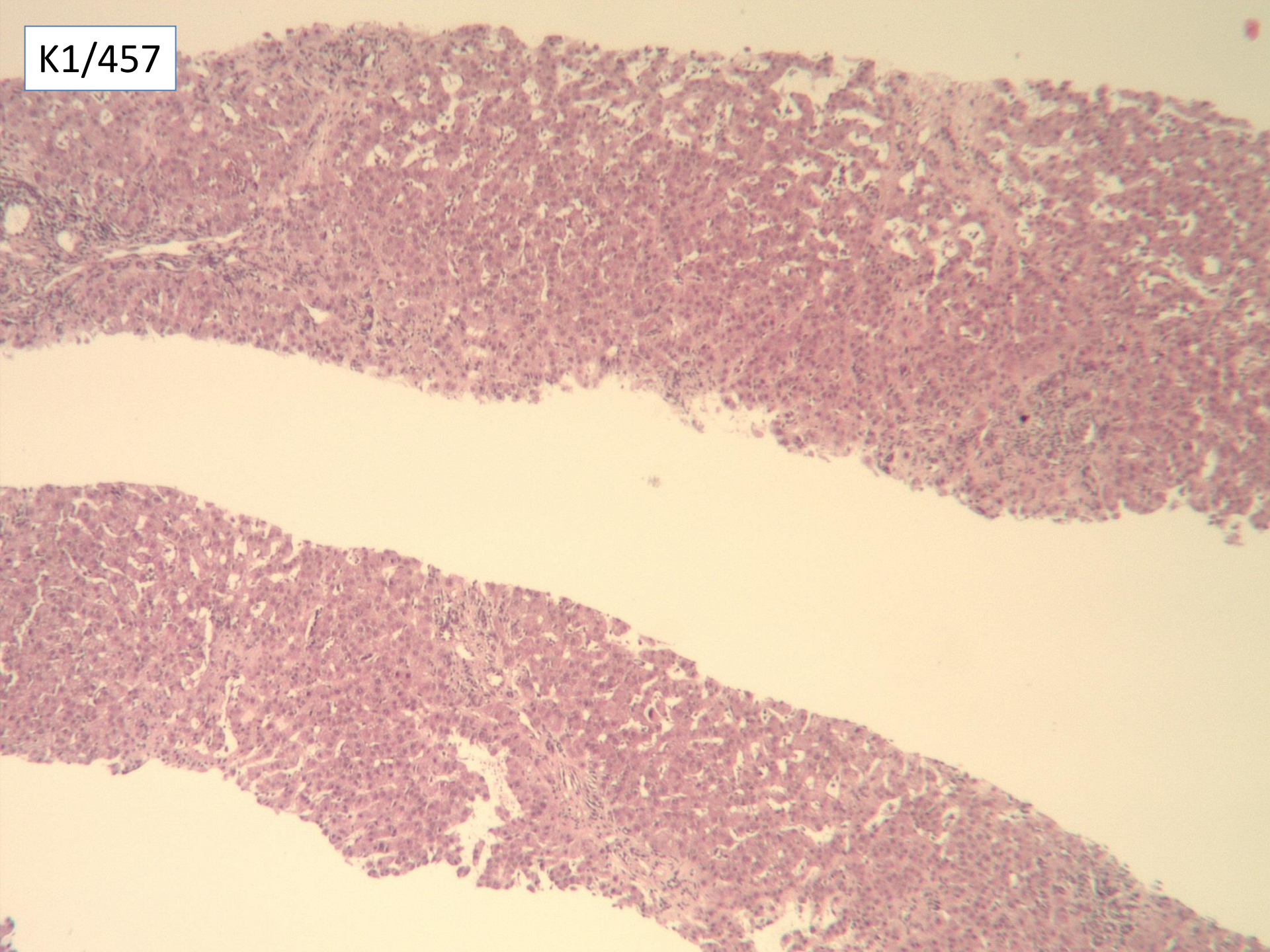
- See presentation by Chris Bellamy for discussion of histology of hepatitis E.

**Case K1/457 Age 36, Male**

Budd-Chiari syndrome. Factor V Leiden deficiency (heterozygous positive on results server).

Had hepatic vein stent insertion today. Trans-jugular biopsy taken at same time.

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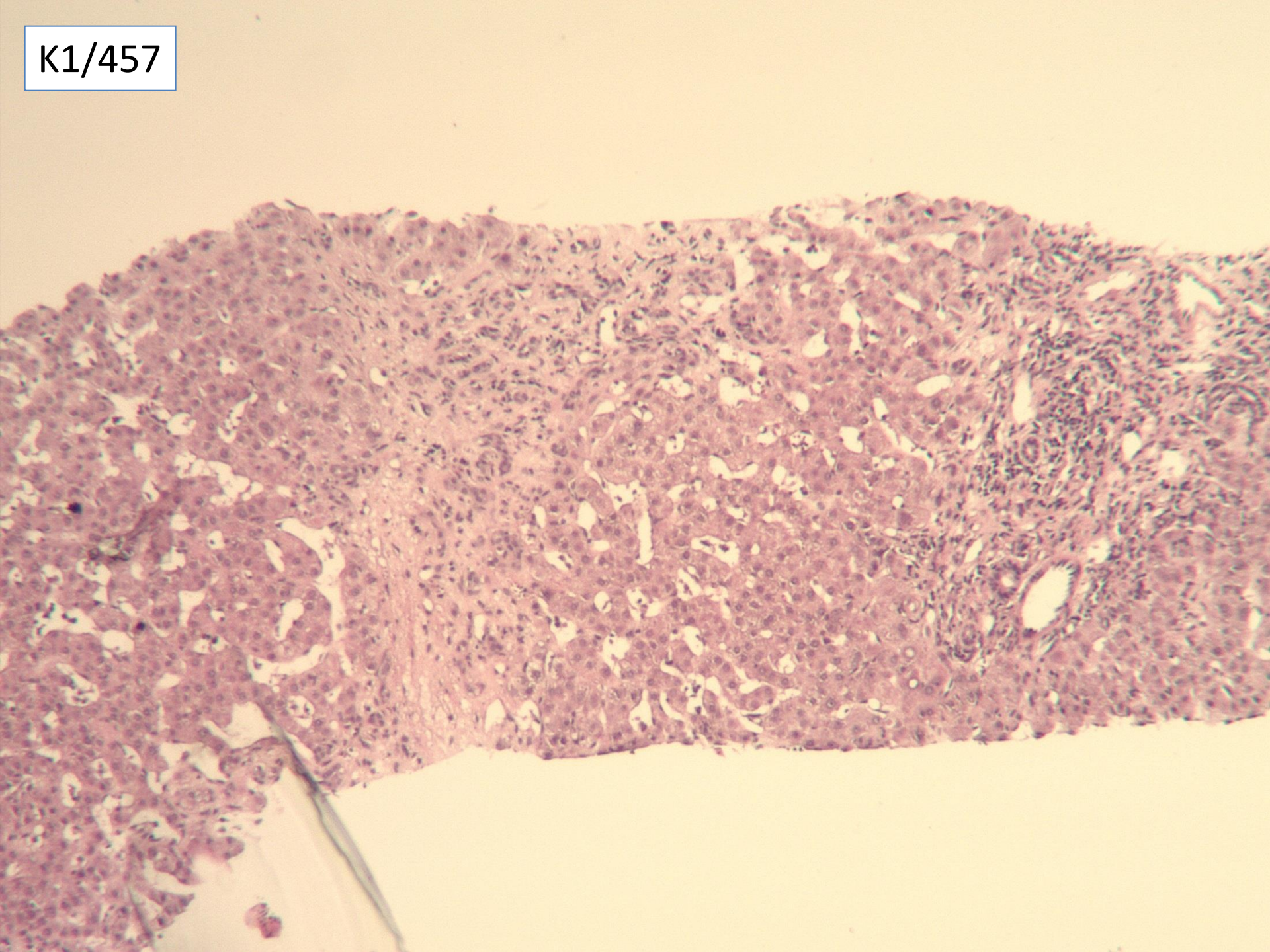
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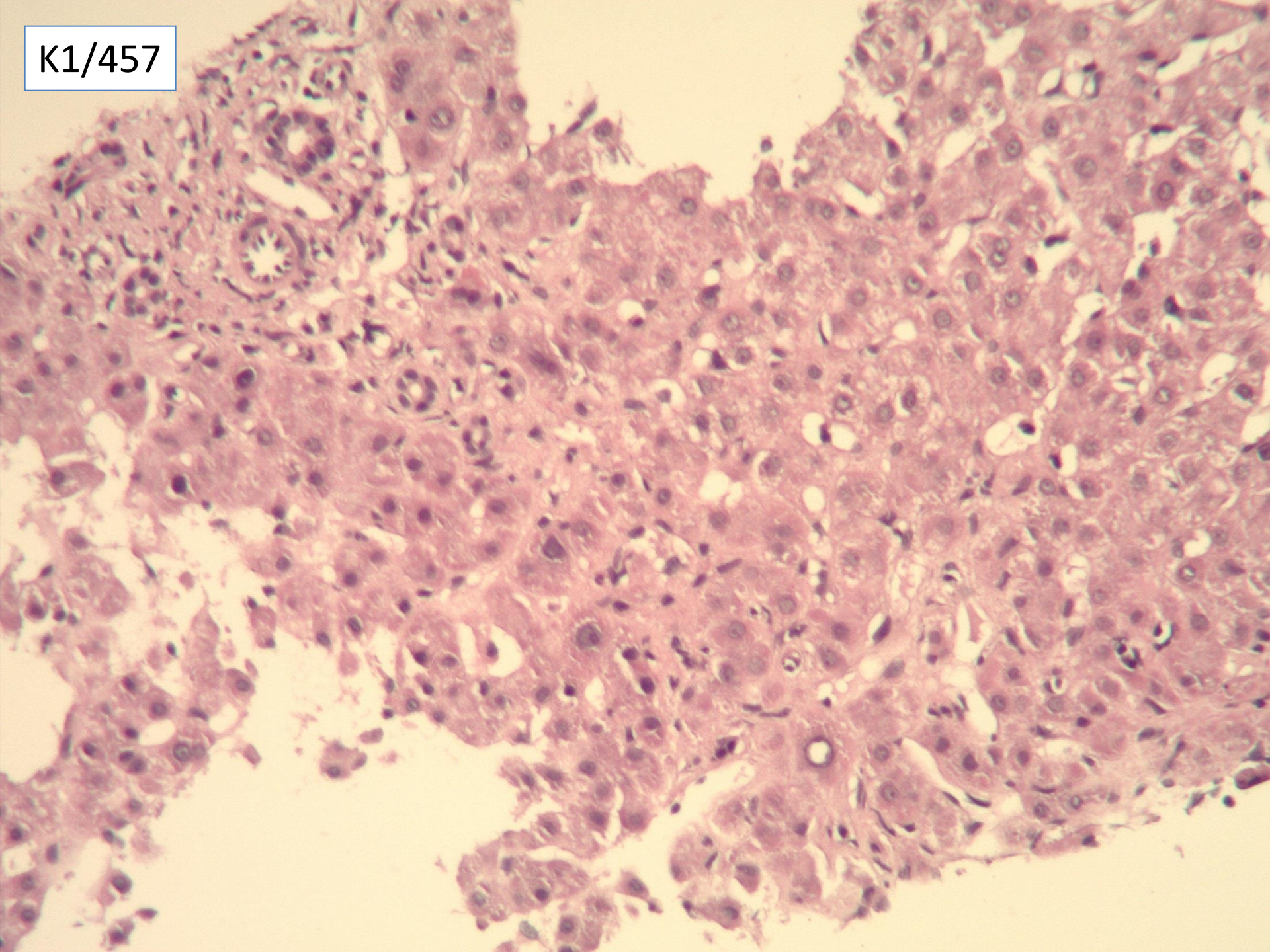
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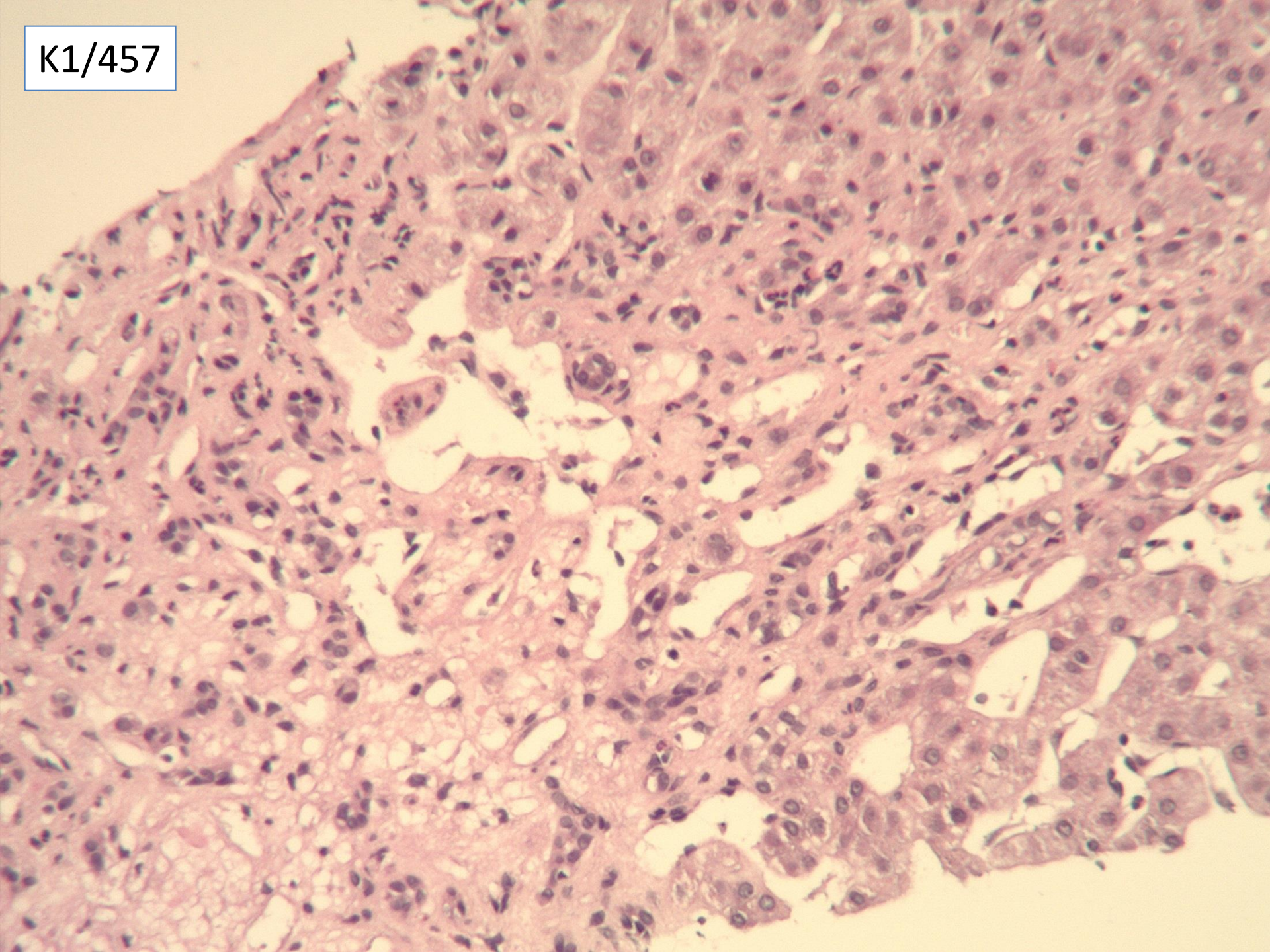
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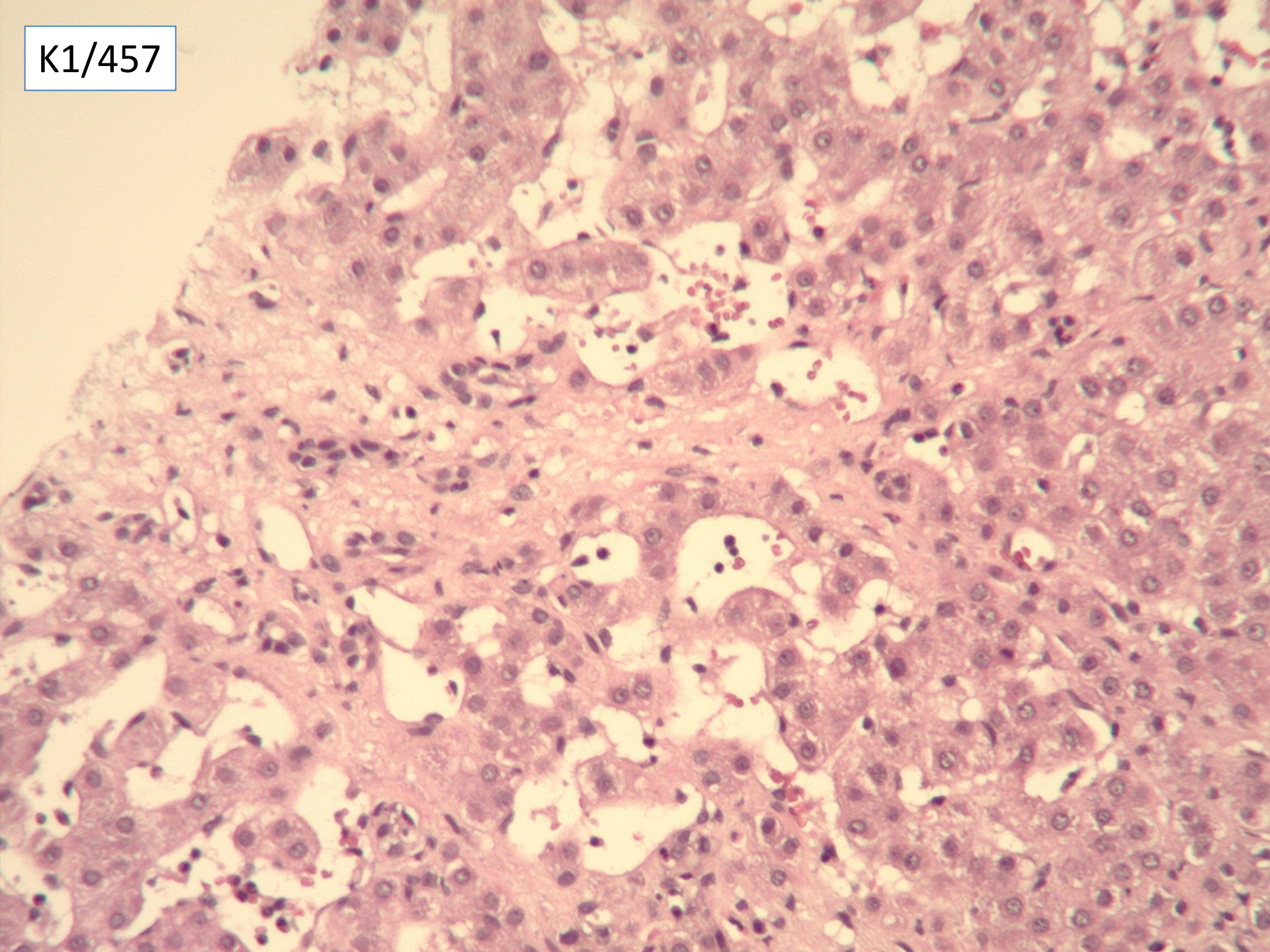
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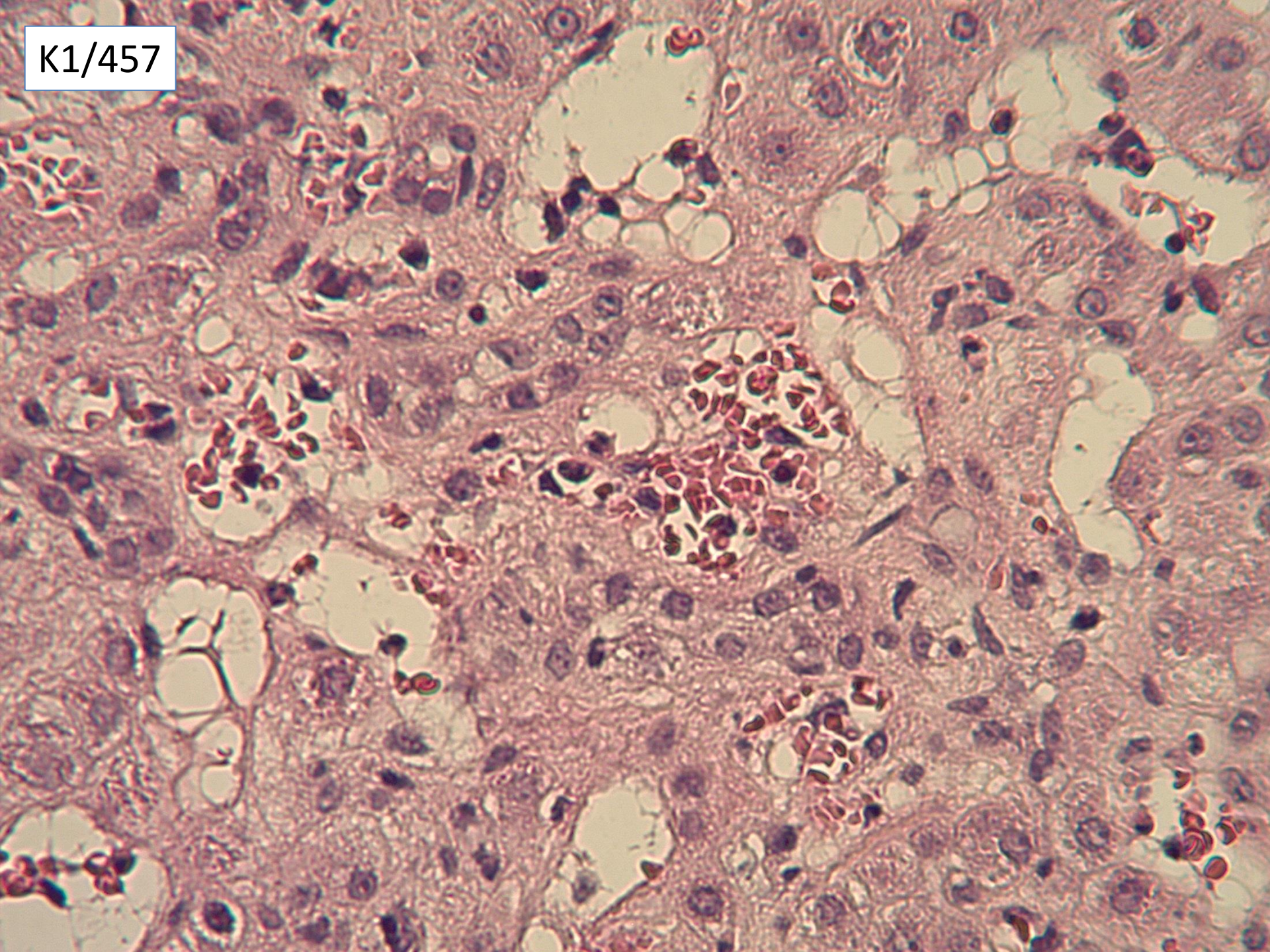
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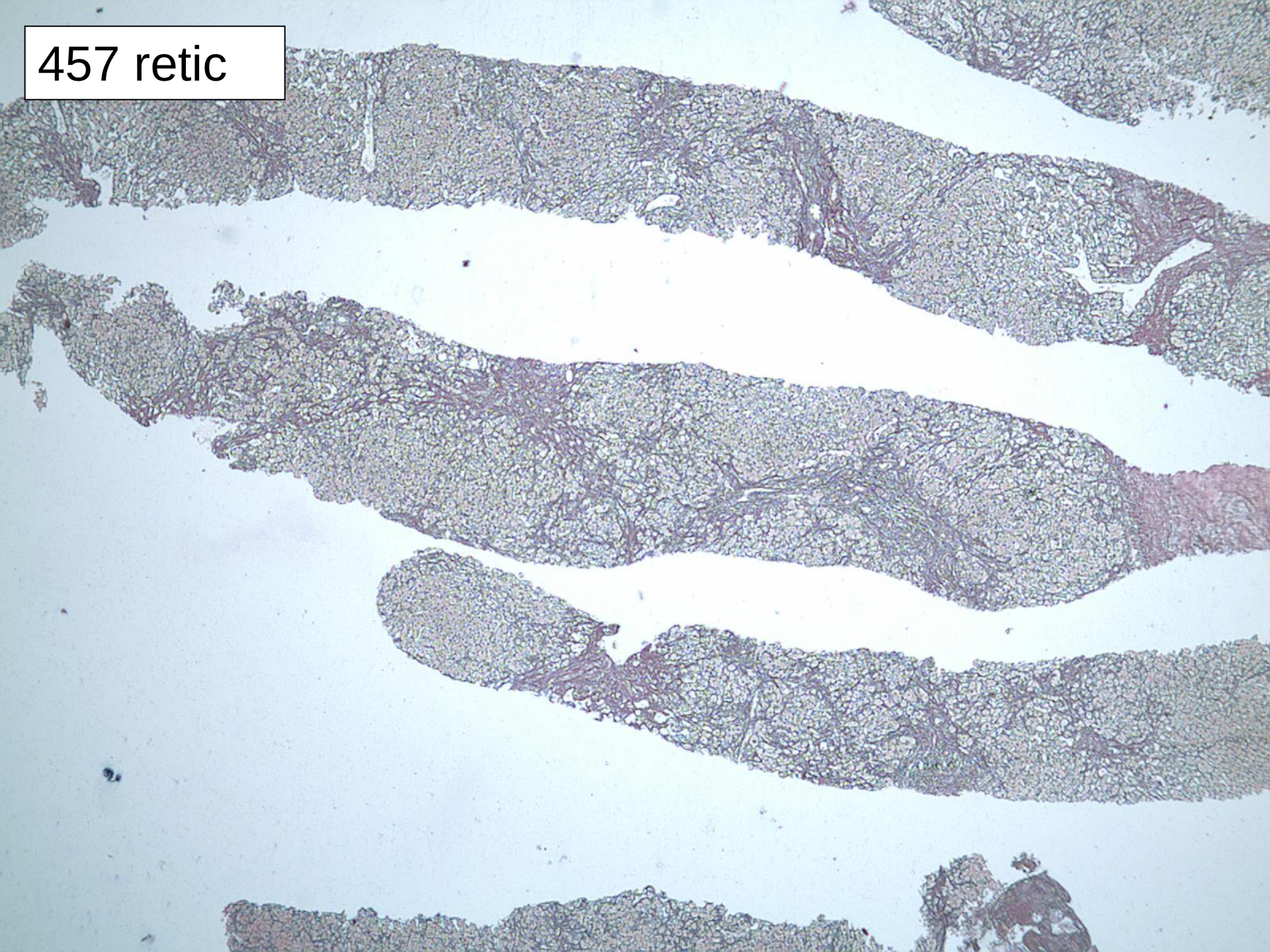
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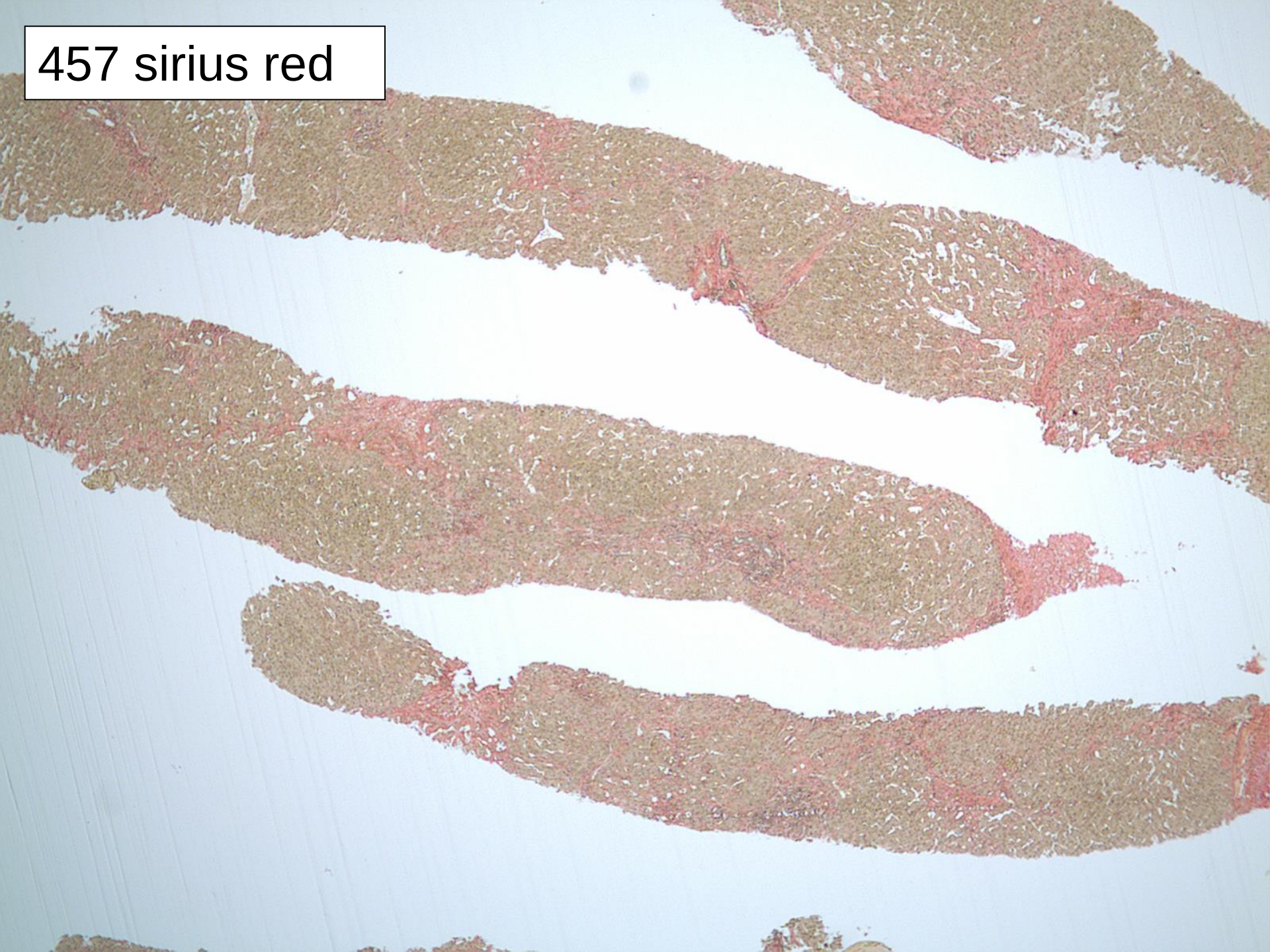
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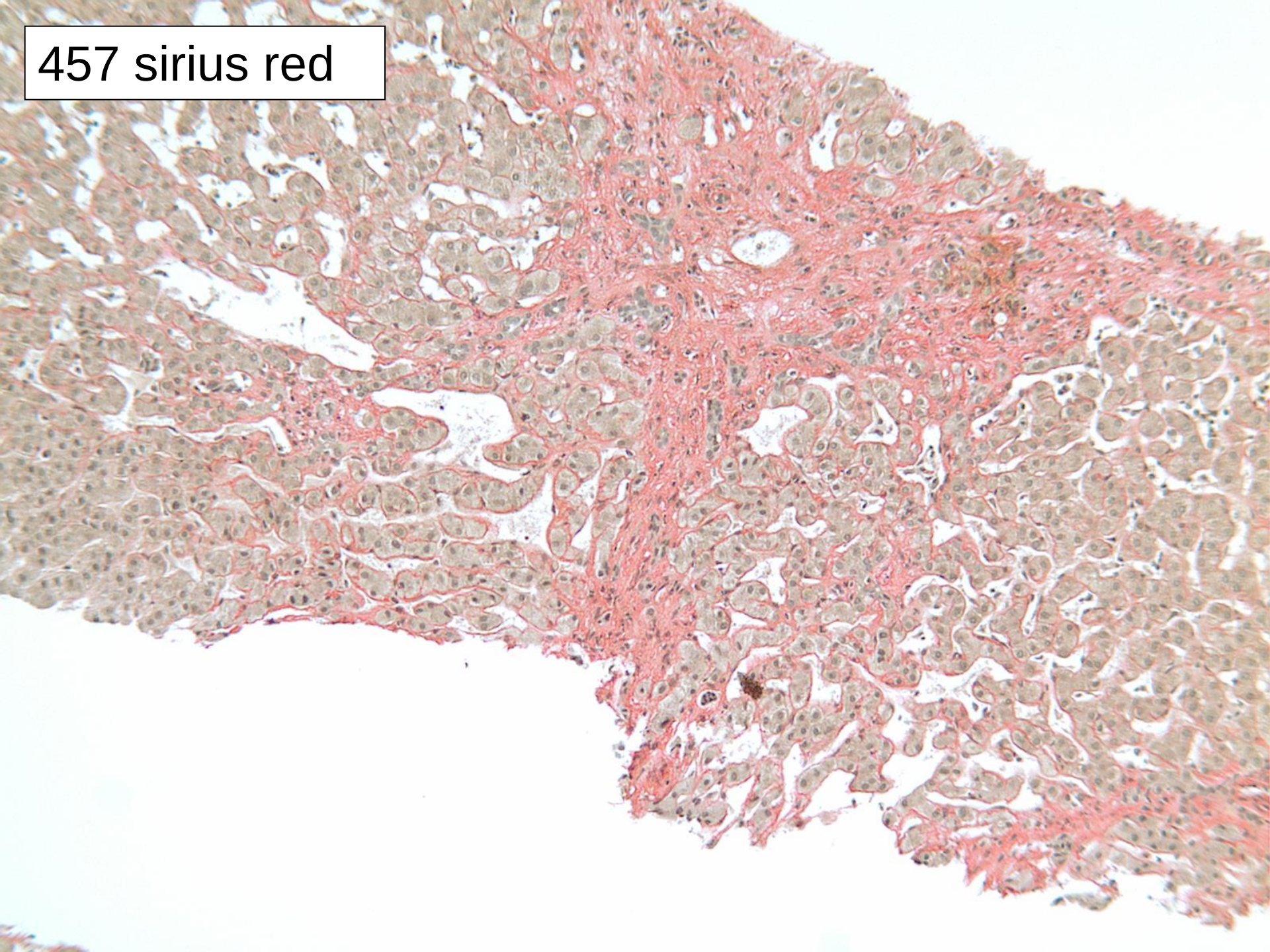
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# Case K1/457 Age 36, Male

## Budd-Chiari syndrome. Factor V Leiden deficiency

63 chronic venous outflow obstruction

5 venous outflow obstruction (not indicating chronic)

1 "portal inflammation, fibrosis, could be BCS but exclude virus, drug"

66 consistent with Budd Chiari Syndrome (BCS)

9 c/w hepatic vein thrombosis

1 "portal fibrosis with bridging and nodules, features c/w chronic venous obstruction"

1 "cirrhosis on a background of veno-occlusive disease"

1 "fibrosis and narrowing of portal veins and hepatoportal sclerosis"

1 "obliterative portal venopathy – evidence of sinusoidal obstruction c/w clotting defect and BCS

1 "obstructive portal venopathy, c/w procoagulant state

1 "consistent with SOS/VOD of efferent veins

1 "chronic portal vein thrombosis/BCS"

1 c/w BCS/NCPHT/NRH spectrum

Suggested scoring - ? suitable for scoring? Score 10 points if features attributable to chronic vascular pathology, rather than some other cause. Lose 5 points if suggest alternative diagnosis, or if not clear that this is a chronic process.
Various terminologies in use, some responses unclear if the changes were due to hepatic or to portal vein occlusion or to both.

10/16 agree, 4 unsuitable

**Case K1/457 Age 36, Male**

Budd-Chiari syndrome. Factor V Leiden deficiency

- Original diagnosis: chronic venous outflow obstruction (Budd-Chiari Syndrome) with significant fibrosis
- Follow up:

Masterclass: Sue Davies:

# Liver biopsy and vascular disease

EQA, autumn 2014

Case K1/ 457

# Vascular Diseases of the Liver

- Portal vein thrombosis
- Hepatic artery (aneurysm, thrombosis)
- Sinusoidal obstruction syndrome (= hepatic veno-occlusive disease)
- Budd-Chiari syndrome
- Radiation-induced liver disease
- Peliosis hepatis and sinusoidal dilatation
- Congenital vascular malformations

- Commonest is acute and chronic PVT complicating cirrhosis – high morbidity
- Several are very rare

- Liver bx can show a mild biliary abnormality – portal cholangiopathy – cavernous transformation around the occluded vein.

# Sinusoidal Outflow Syndrome = Veno Occlusive Disease

- Predominantly seen with high dose chemotherapy +/- radiotherapy in conditioning for bone marrow transplant
- Long term lower dose azothioprine, 6-thioguanine, other agents including oxaliplatin
- Herbal teas / food contamination (pyrrolizidine alkaloids)
- Disturbance of the sinusoids with hepatic vein involved in more severe cases.

# Budd-Chiari Syndrome

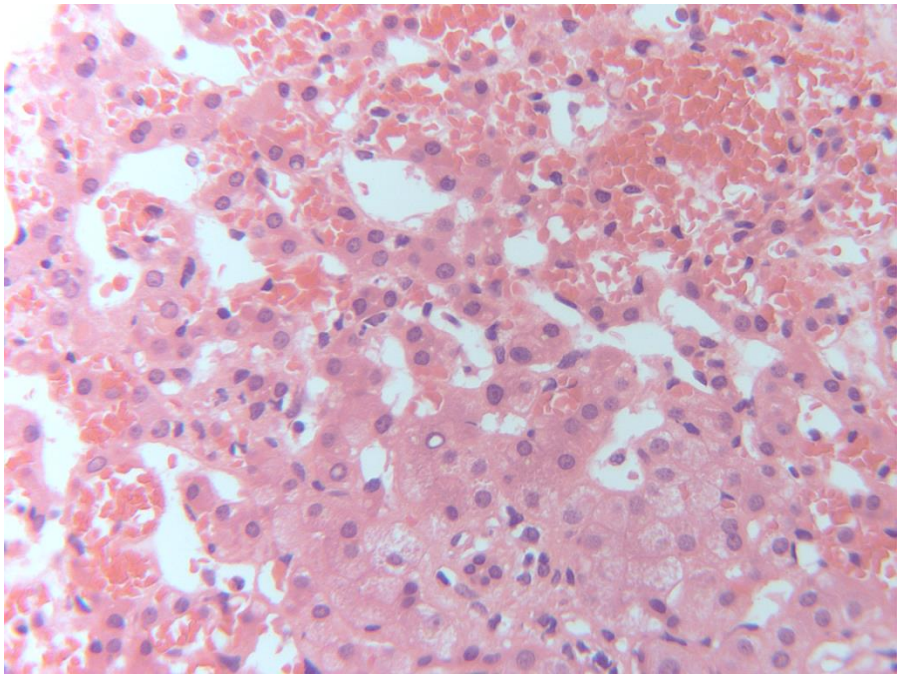
- Hepatic venous outflow tract obstruction
  - can be at any level; small, large HV or IVC
- Excludes SOS or cardiac causes
- Secondary BCS – compression or invasion from outside veins
  - neoplasia, infection, cysts, trauma
- Primary – venous (thrombosis, phlebitis)

# Primary B-CS

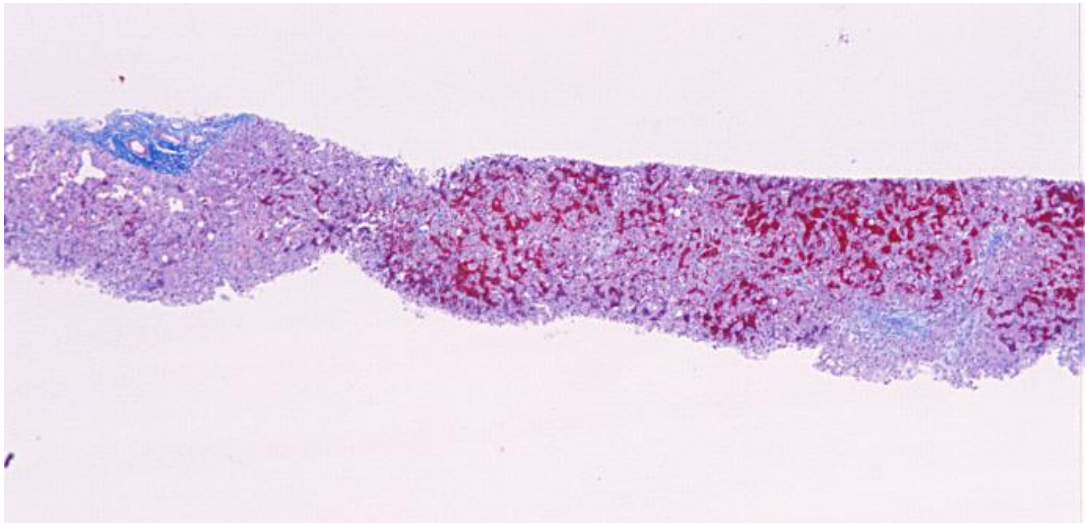
- ~90% have identifiable thrombotic disorder
- Can be difficult diagnosis; low levels in peripheral blood due to poor hepatic synthetic function
- ~25% have combination of factors

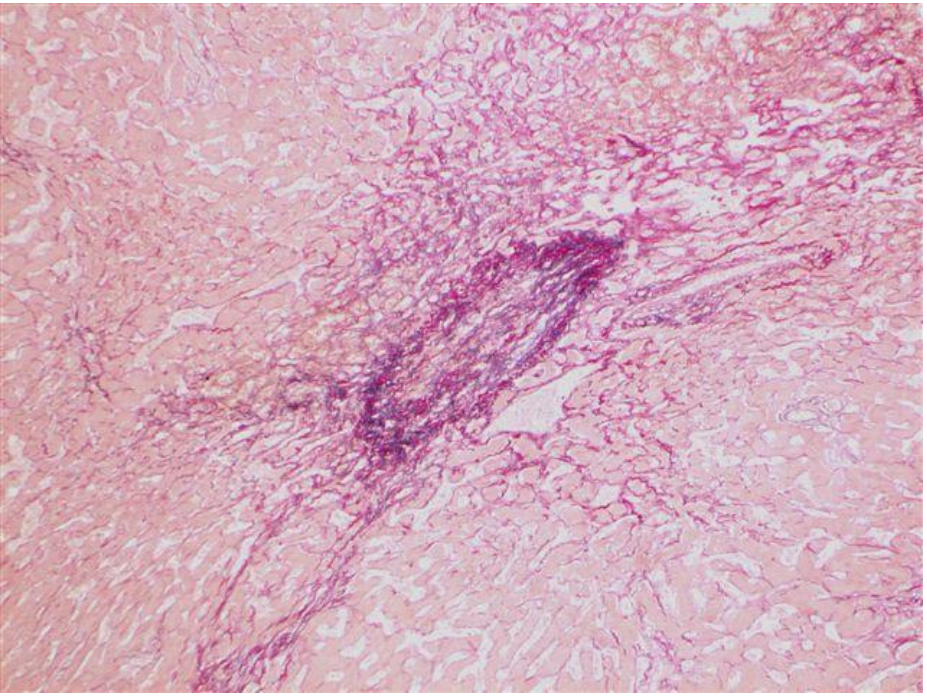
  factor V Leiden, pregnancy, OC pill
- Unknown local factors – why hep veins

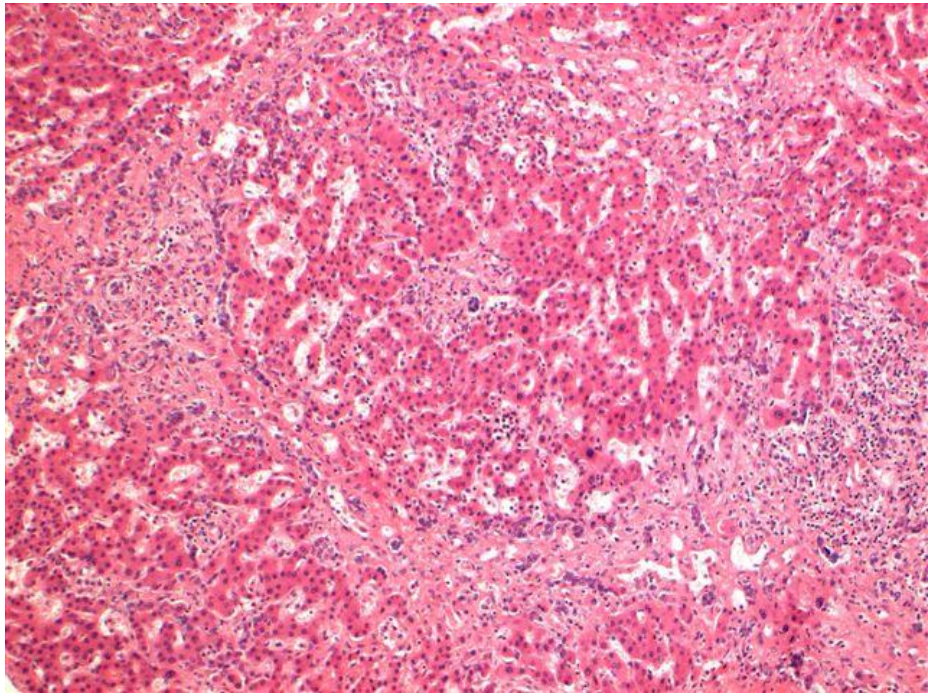
- Hepatomegaly, ascites, abdominal pain +/- some dysfunction



- Acute dilatation of sinusoids, necrosis , haemorrhage into plates, with thrombus (rarely seen)

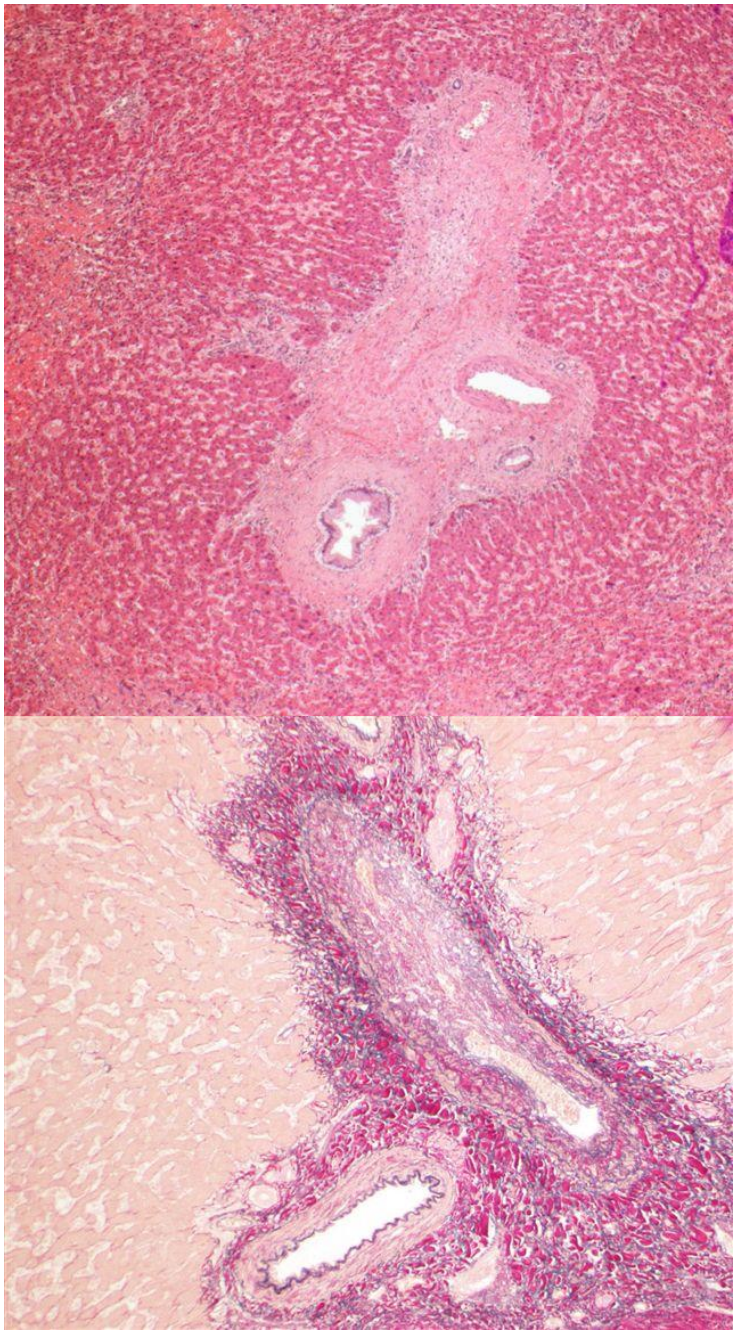






- Fibrosis - perisinusoidal and atrophy of hepatocytes, obliteration of hepatic venules, septum formation and reverse lobulation of cirrhosis

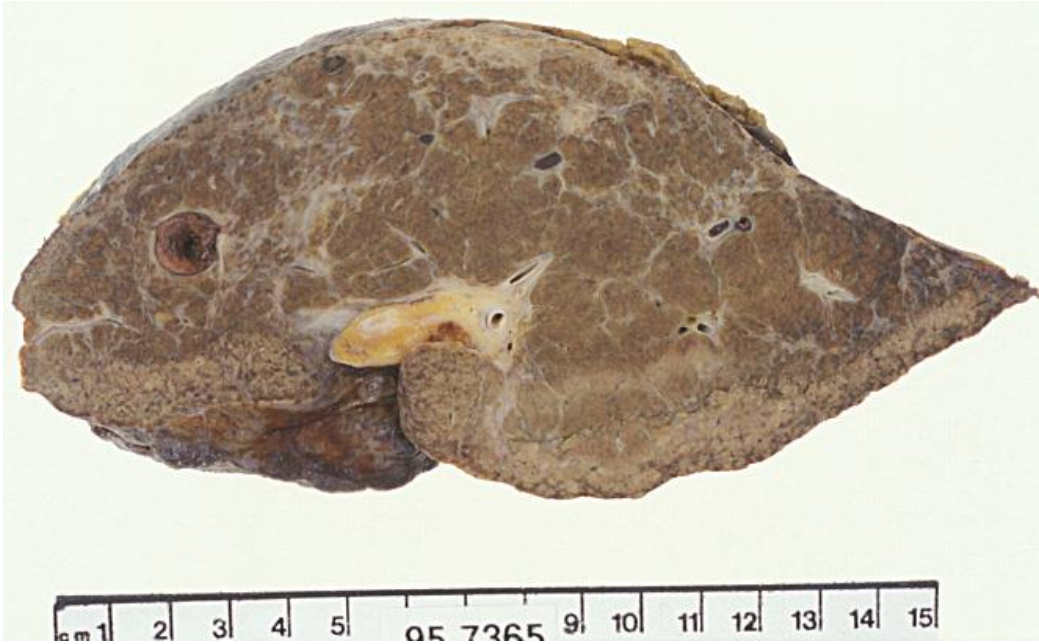
- Secondary portal vein thrombosis is frequent, may lead to hepatic extinction and regenerative nodules
  - Tanaka & Wanless Hepatology 1998

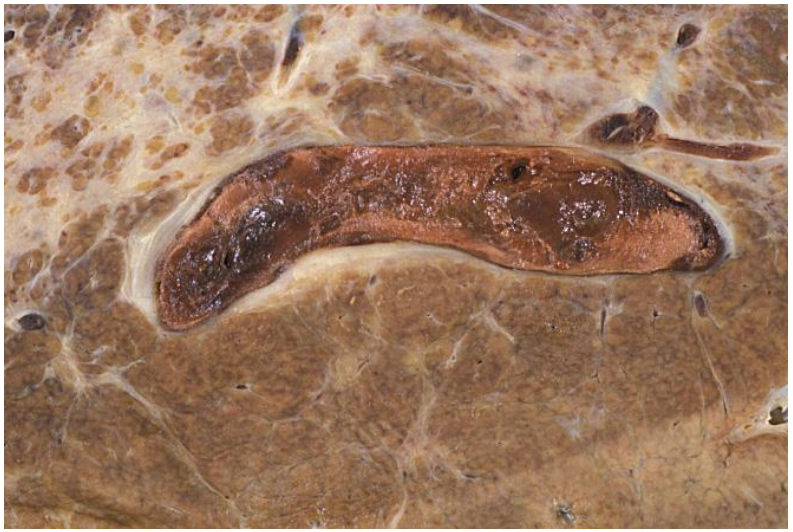


# End-stage

- Irregular fibrosis
- Hypertrophy of uninvolved areas,

  especially caudate lobe



The end

Circulation K1
Autumn 2014