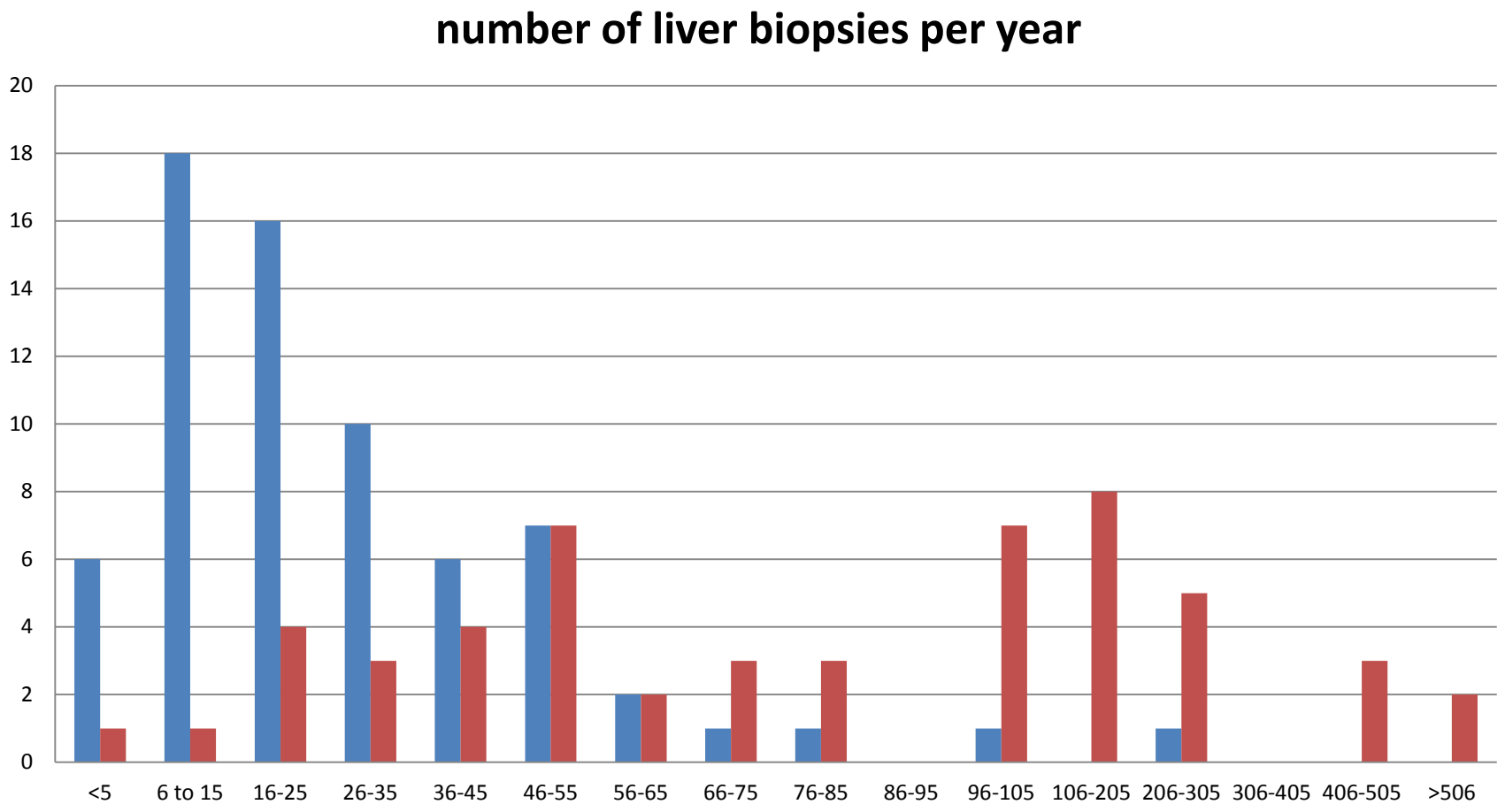
National Liver Histopathology EQA Scheme

Circulation I1

Autumn 2013

Histories, photomicrographs, scoring and comments

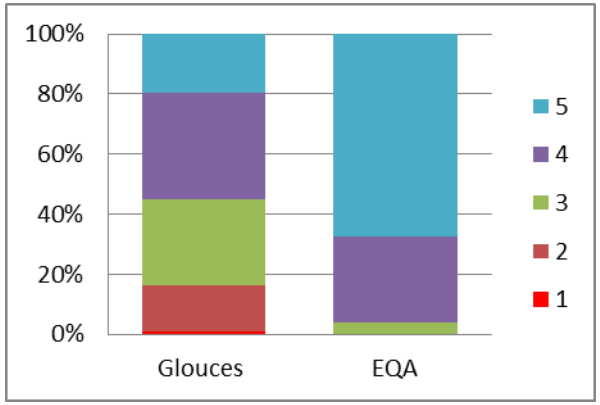


Replies from 69 from Gloucester GI course in 2011 (in blue), (13 liver EQA members and overseas consultants excluded)

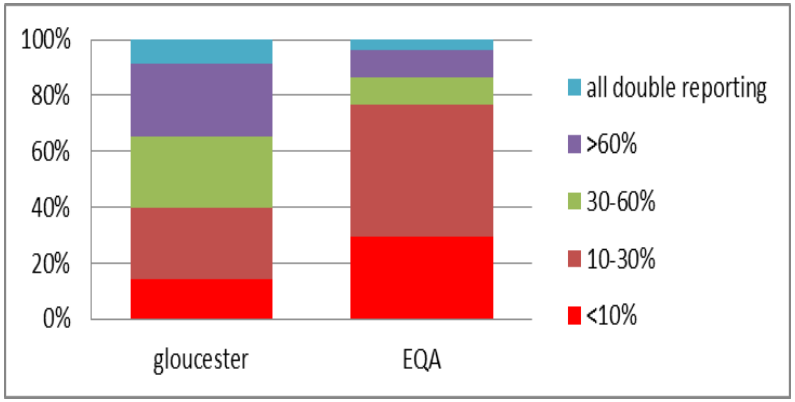
and from 53 liver EQA members, 2013 (in red).

Questionnaire scored 1-5 where 1 = strongly disagree (red) and 5 = strongly agree (blue)

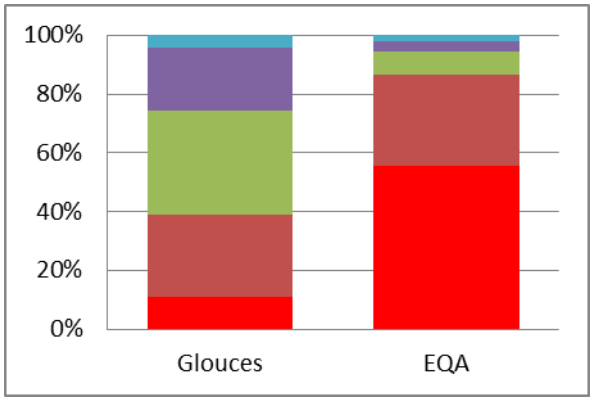
In general I enjoy reporting liver biopsies



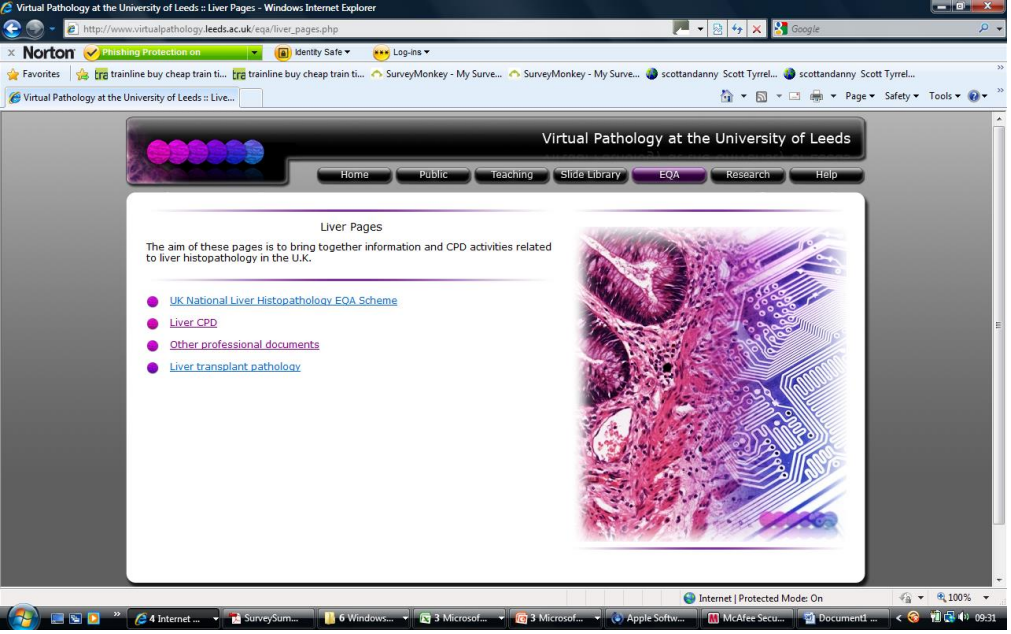
Proportion of reported cases that has been discussed with a colleague:



I feel 'rusty' in liver pathology and wonder if my report covers what the clinician needs



Summary:
Pathologists who are not liver EQA members feel less confident about reporting liver biopsies and are more often discuss cases with colleagues



Liver subcommittee of pathology section of BSG

EQA scheme
Programme of annual meetings
Website
RCPath documents
admin

In 2014: UK and Eire Liver Pathology Group

Why now? – developments in diagnosis, treatment, tumours, networks etc.

Tissue Pathways for liver biopsies, 2nd edition – due in December 2013
lead for liver pathology,
reporting liver biopsies? do enough to maintain skills.

- EQA members
- **corresponding members – everyone else who reports liver biopsies**
- trainee members

UK and Eire Liver Pathology Group

Purpose:

Best possible liver histopathology service across all levels of specialisation

- Educational,
- professional liaison,
- research

Circulation I1

- 88 responses
- 80% agreement = at least 70 responses for sufficient consensus to use case for scoring.
- Suggested scoring shown in box –
  - Red text = score 0
  - Brown text = score half marks
  - Green text – please comment on proposed scoring
- Comments received from 4 members
- Masterclass cases:
  - Liver biopsy in HIV patients – case 424 – Rob Goldin
  - Liver biopsy in patients taking methotrexate – case 427 – Sue Davies

Case I1/422

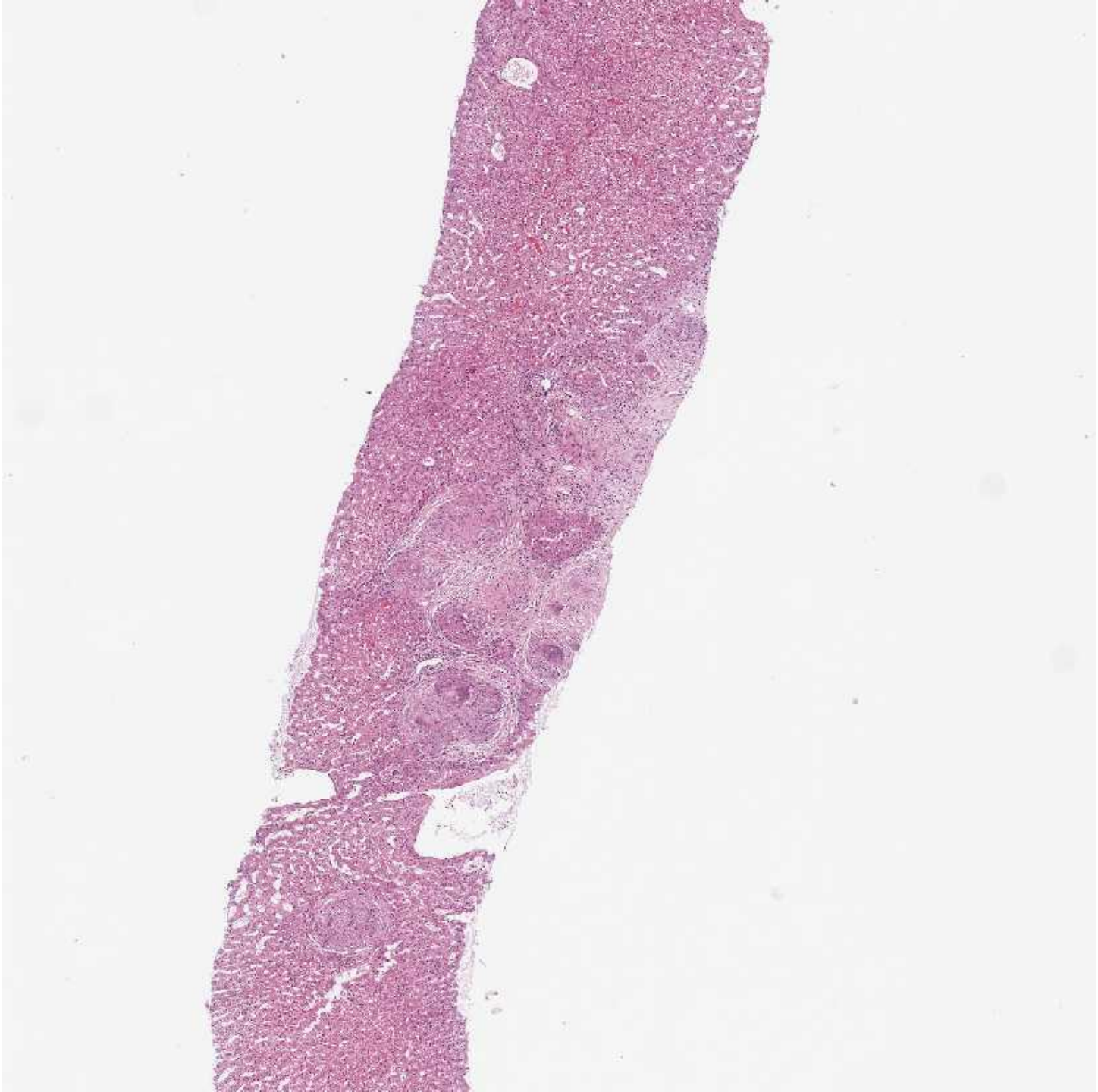
Age 53, Female

Patient with multisystemic sarcoidosis - deranged liver tests. Suspicious of liver sarcoidosis

One core 17mm long

422

422



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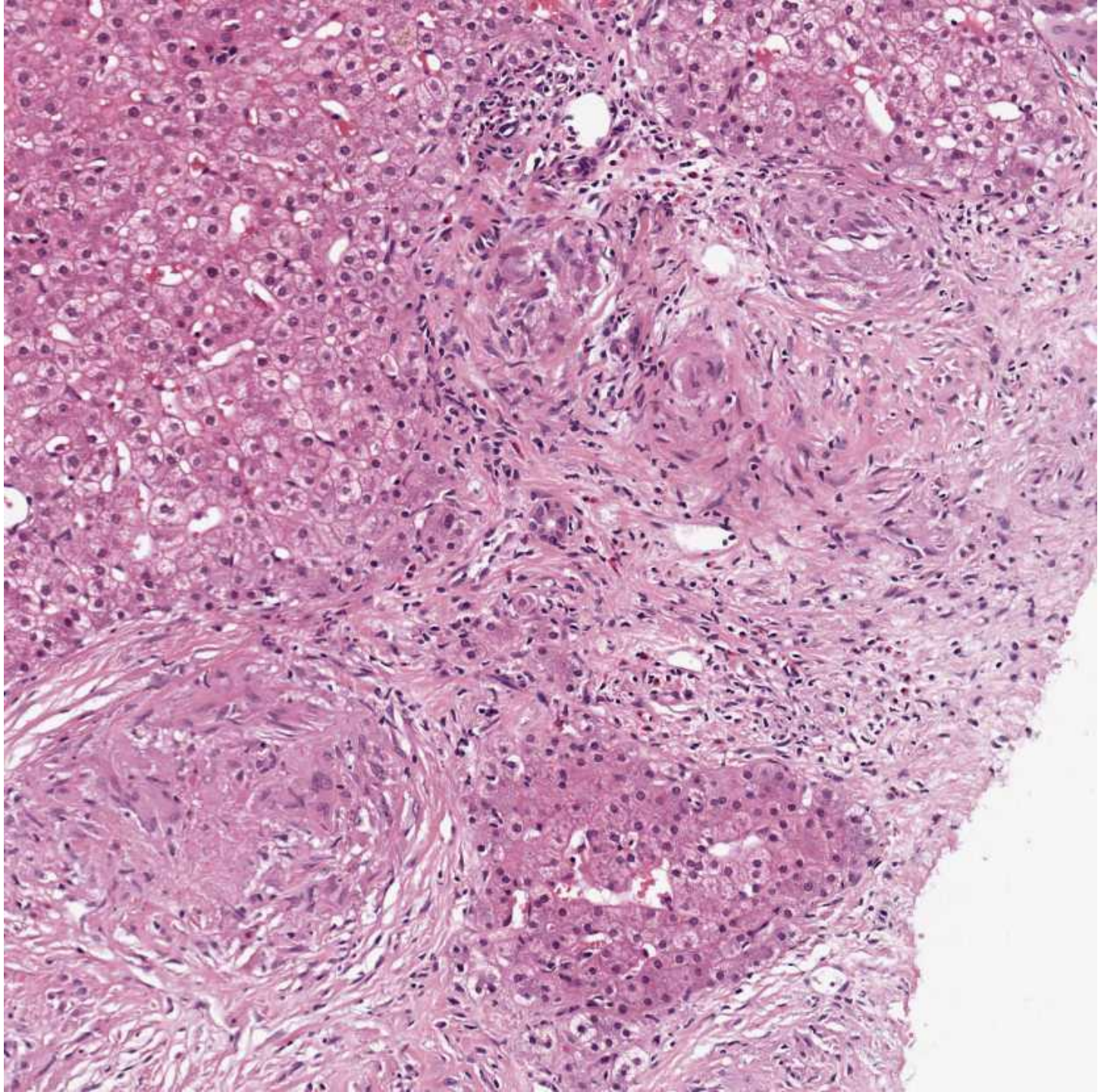
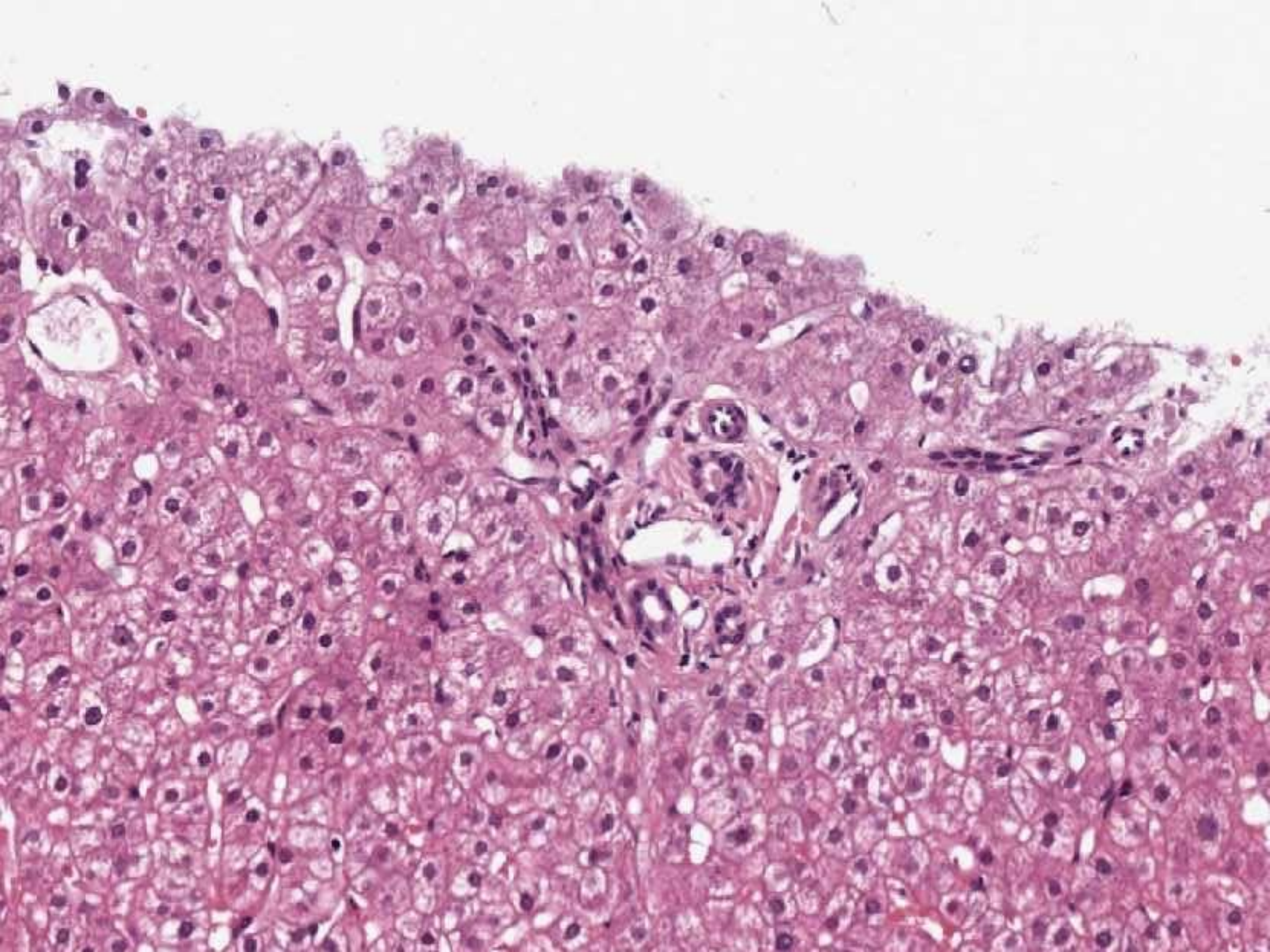




Case I1/422 Age 53, Female

88 Granulomas

21 comment on absence of biliary features

46 consistent with sarcoid as only comment

42 Consistent with sarcoid, but exclude TB etc.

Suggested scoring: accept all = agreed at meeting

Original diagnosis: Liver biopsy - sarcoidosis

Case I1/423
Age 66, Male

Persistently high ALT. AMA Positive.

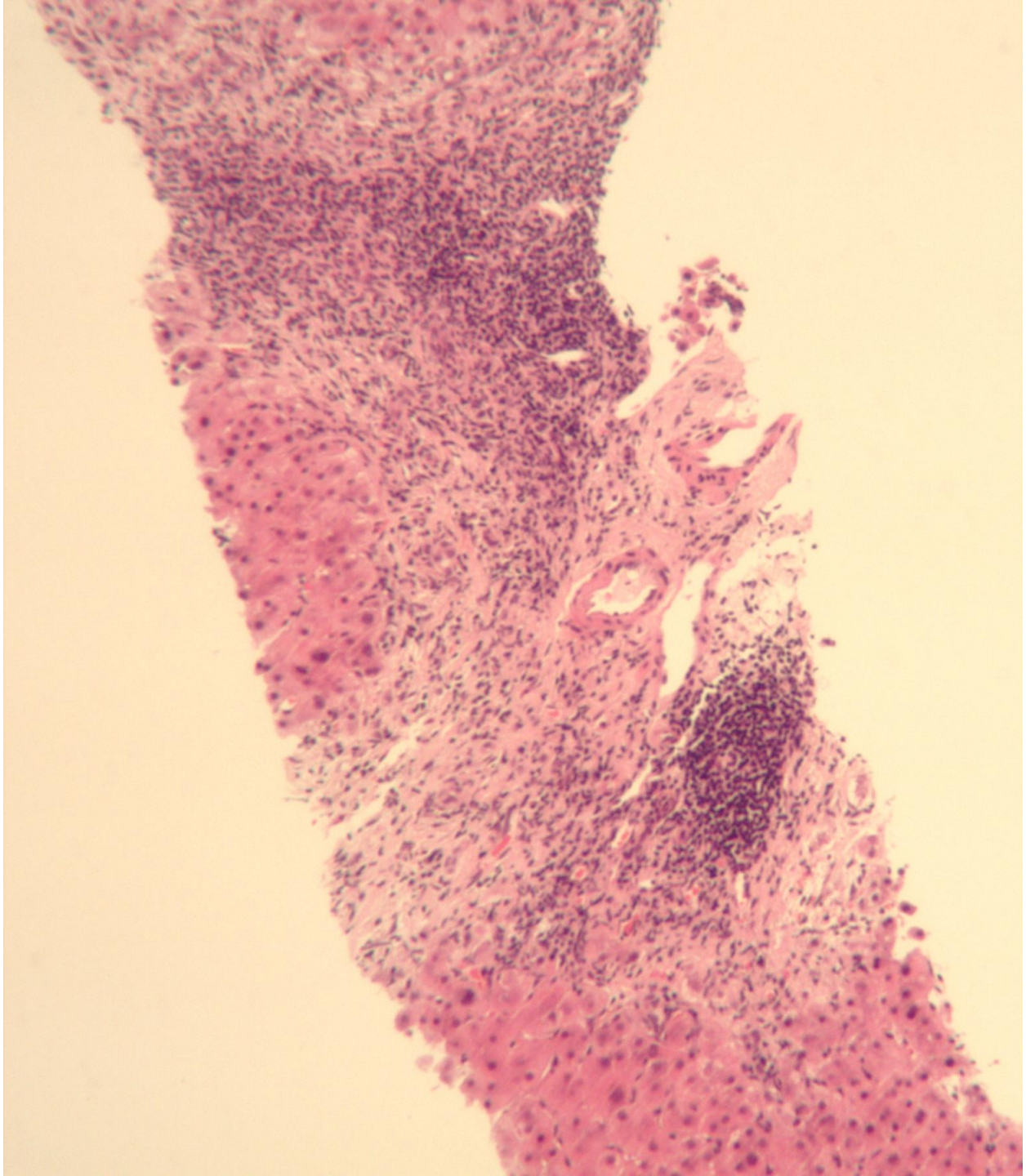
Serum electrophoresis = polyclonal hypergammaglobulinaemia

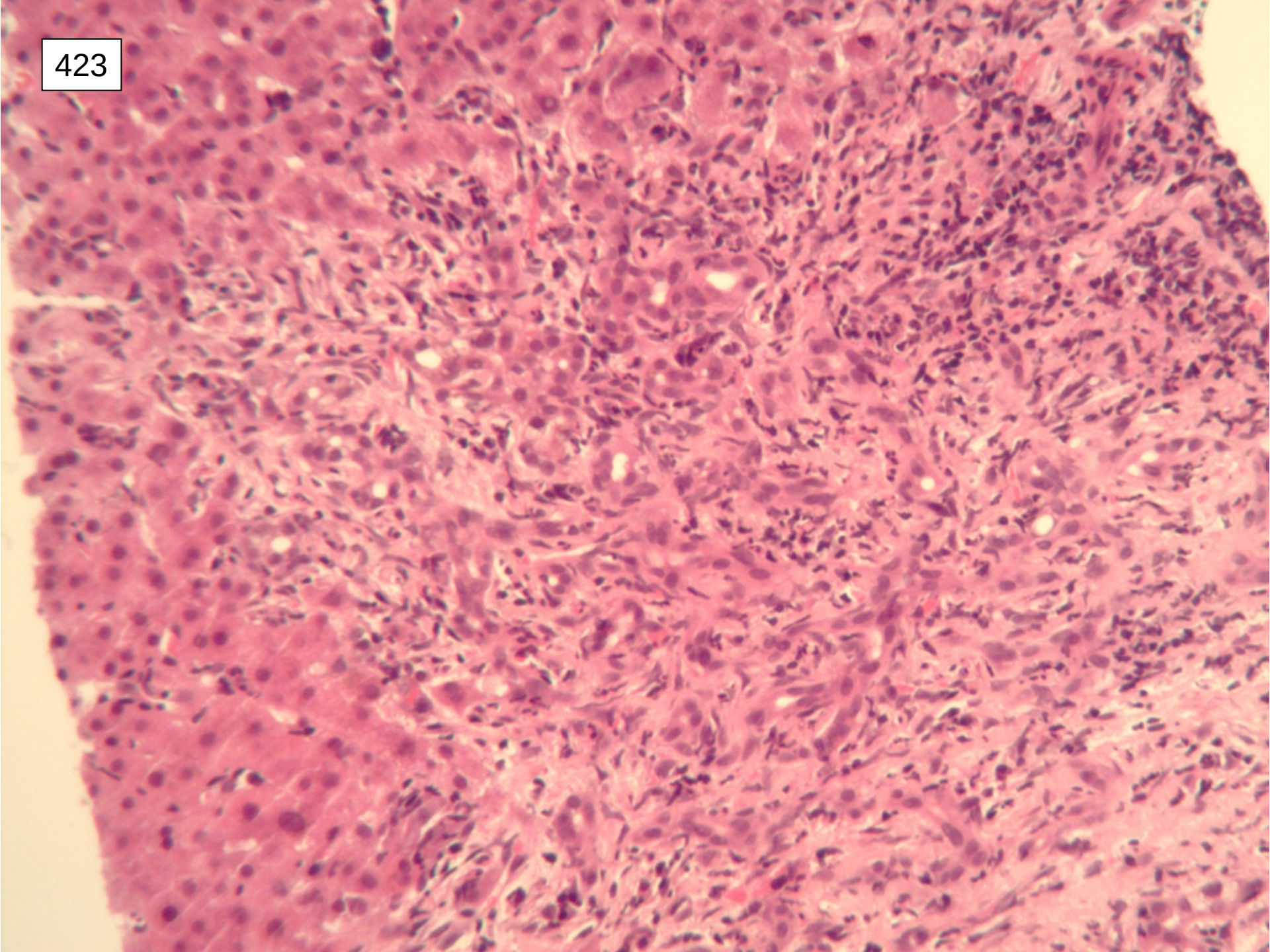
Core biopsies tan liver tissue

(please also see reticulin, sirius red and orcein on website)

423

423

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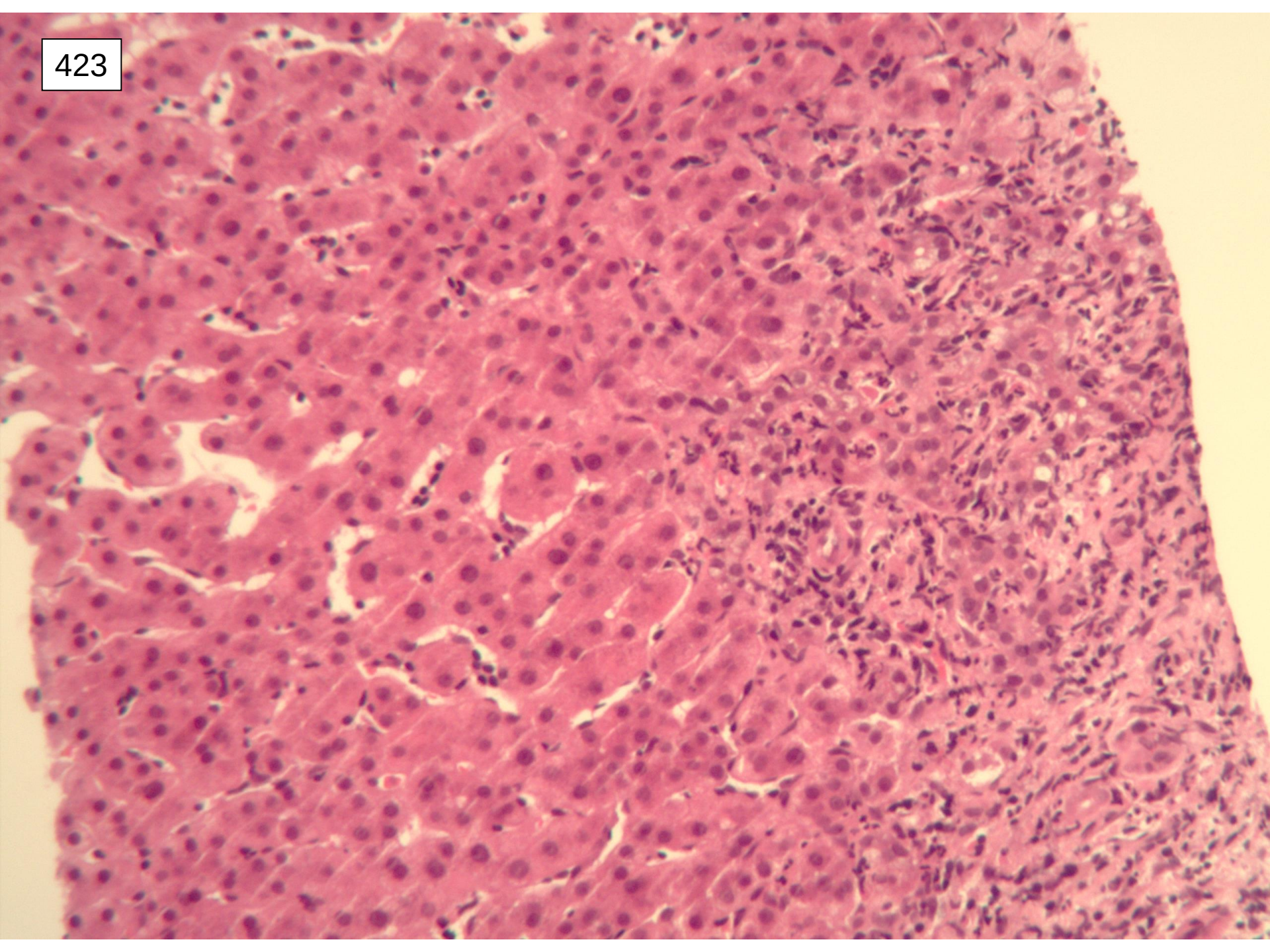
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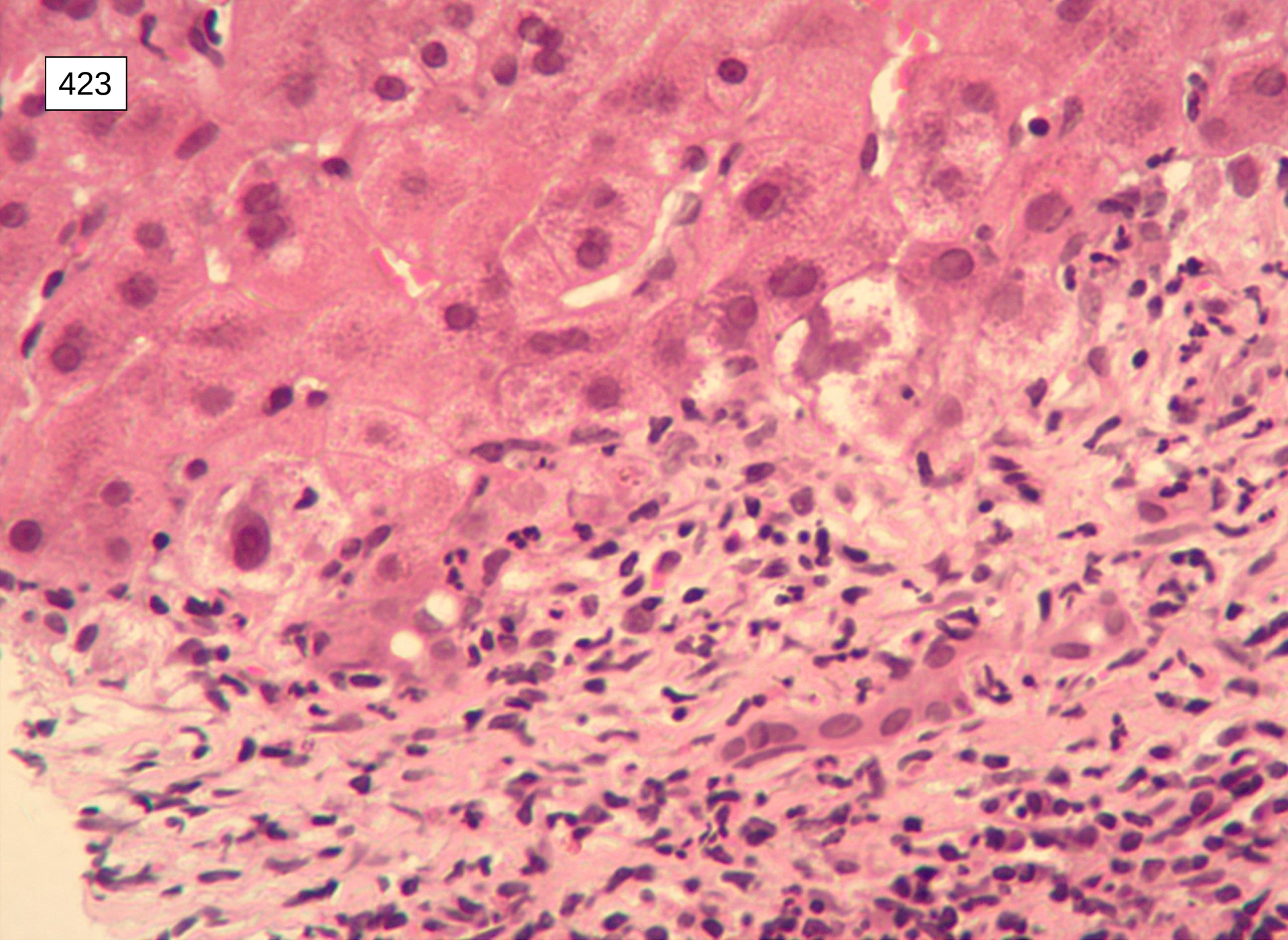
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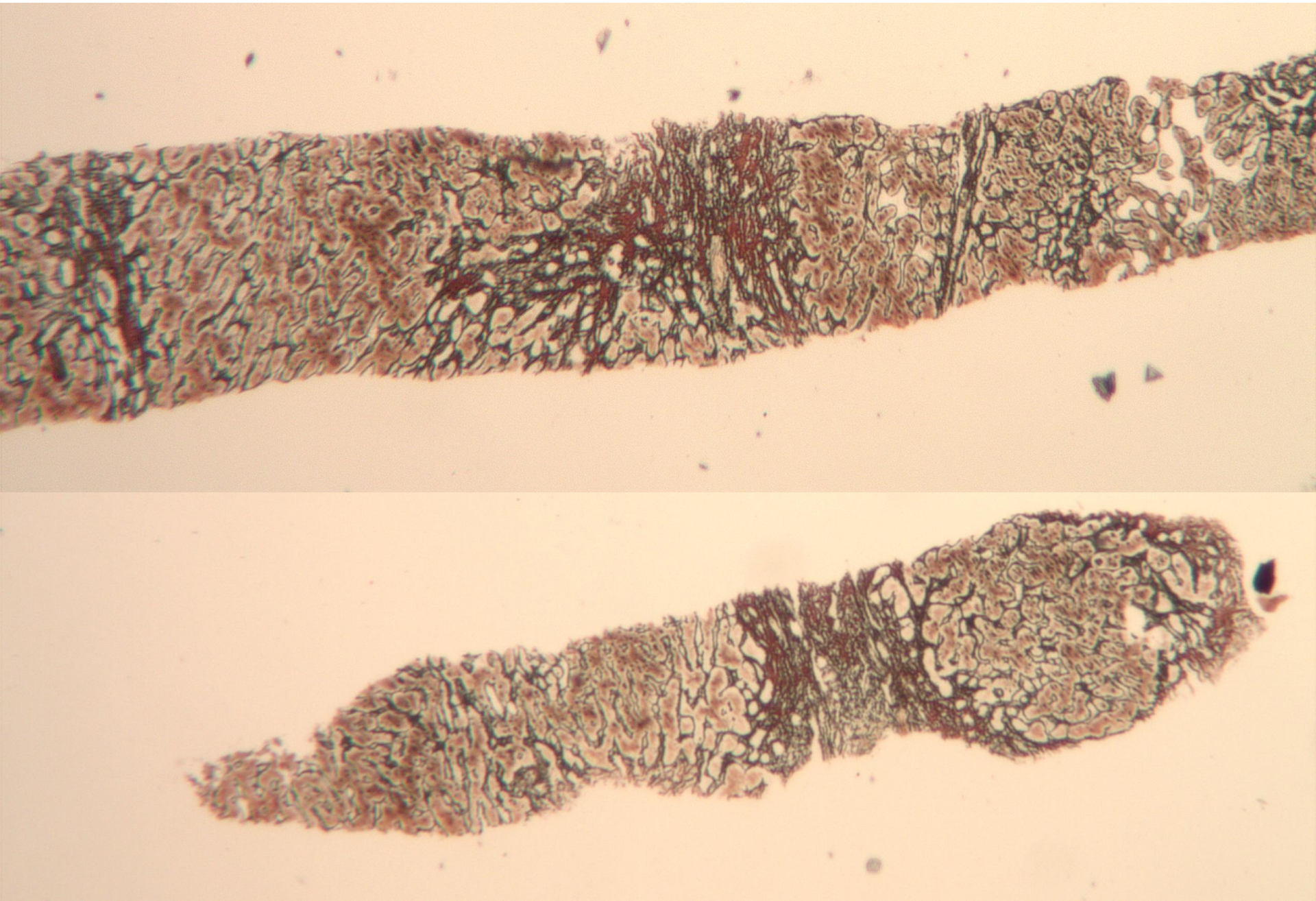
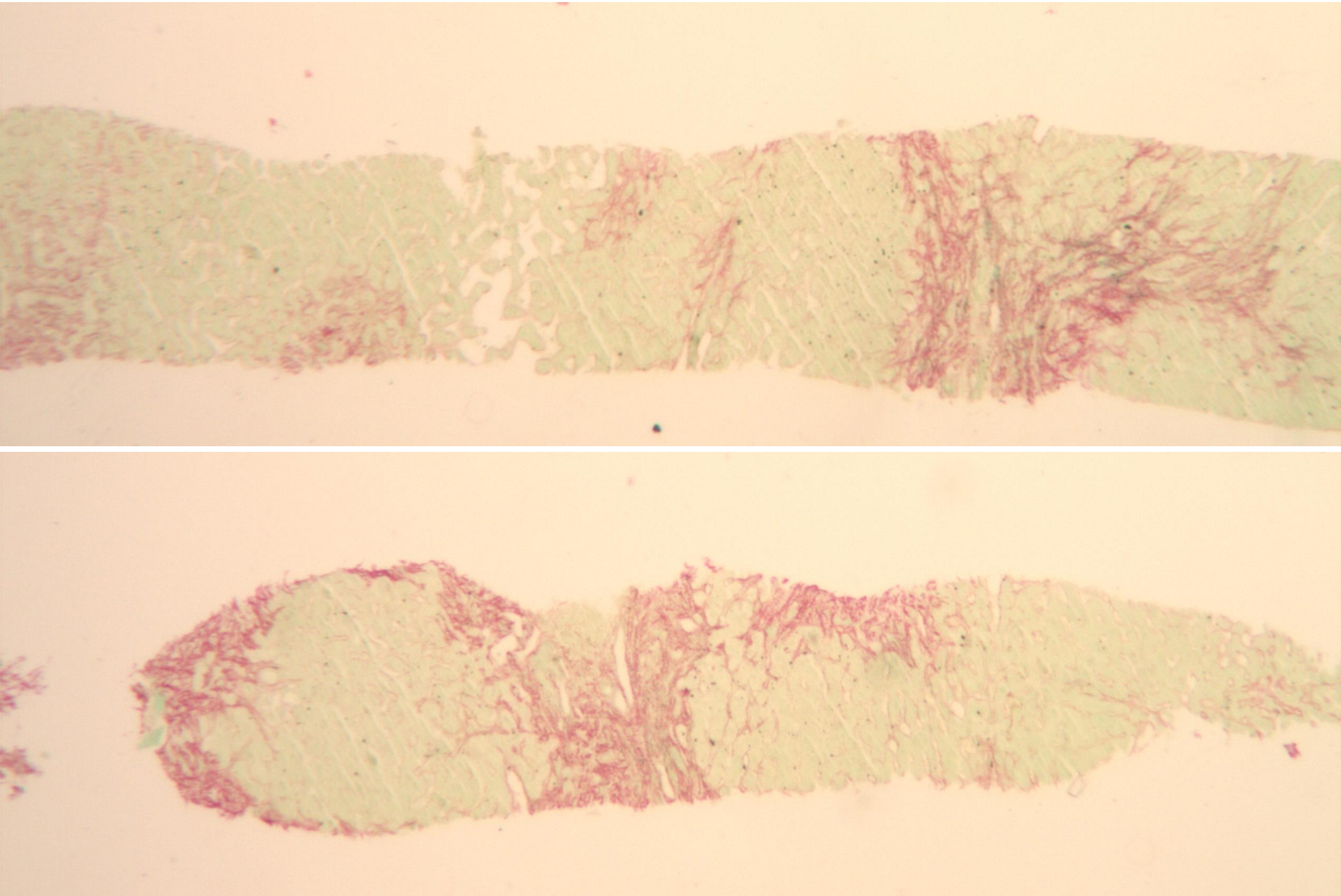
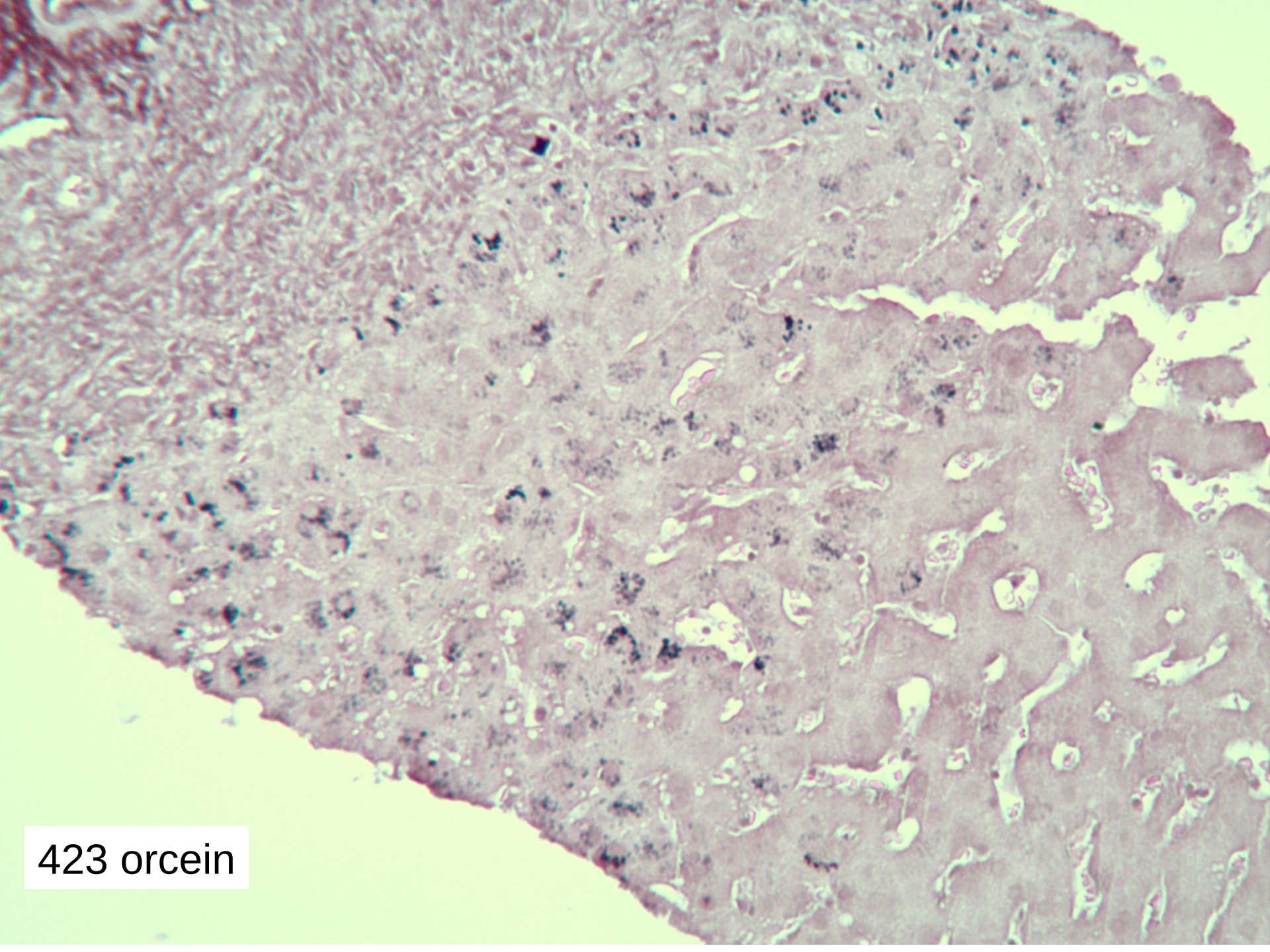
423 retic



423 sirius red




423 orcein

Case I1/423 Age 66, Male

Morphology

79 Biliary features definitely

5 Biliary features not described at all

Stage:

36 Cirrhosis

28 possible/developing/incomplete cirrhosis

11 Bridging fibrosis

1 Severe fibrosis

5 fibrosis NOS

1 Collapse

5 No comment on stage

Clinico-path:

81 Primary Biliary Cirrhosis

25 – consider overlap, PBC first

2 - consider overlap, AIH first

6 – not overlap

1 AIH only

1 'cirrhosis on a background of AIH'

1 AIH, differential PBC, Wilson

1 'high stage with cholestatic features and early amyloid'

(2 others also mentioned amyloid)

1 Wilson disease, differential AIH

1 'chronic active hepatitis due to chronic biliary tract disease, suggestive of PBC; metavir A2F3'

Suggested scoring: accept all with PBC as main diagnosis
Score 0 if no mention of PBC, 5 if PBC in differential, not main diagnosis, Insufficient consensus to score stage. 'Chronic active hepatitis' answer score 5 because confusing terminology. Suggested scoring agreed at meeting.

Case I1/423 Age 66, Male

Original diagnosis: established cirrhosis – primary biliary cirrhosis.

Comment: Biliary features of ductular reaction and copper associated protein dominate. Insufficient clinical information for full evaluation of overlap with AIH, but not suggested by the histology – little interface hepatitis, few plasma cells.

Case I1/424
Age 53, Male

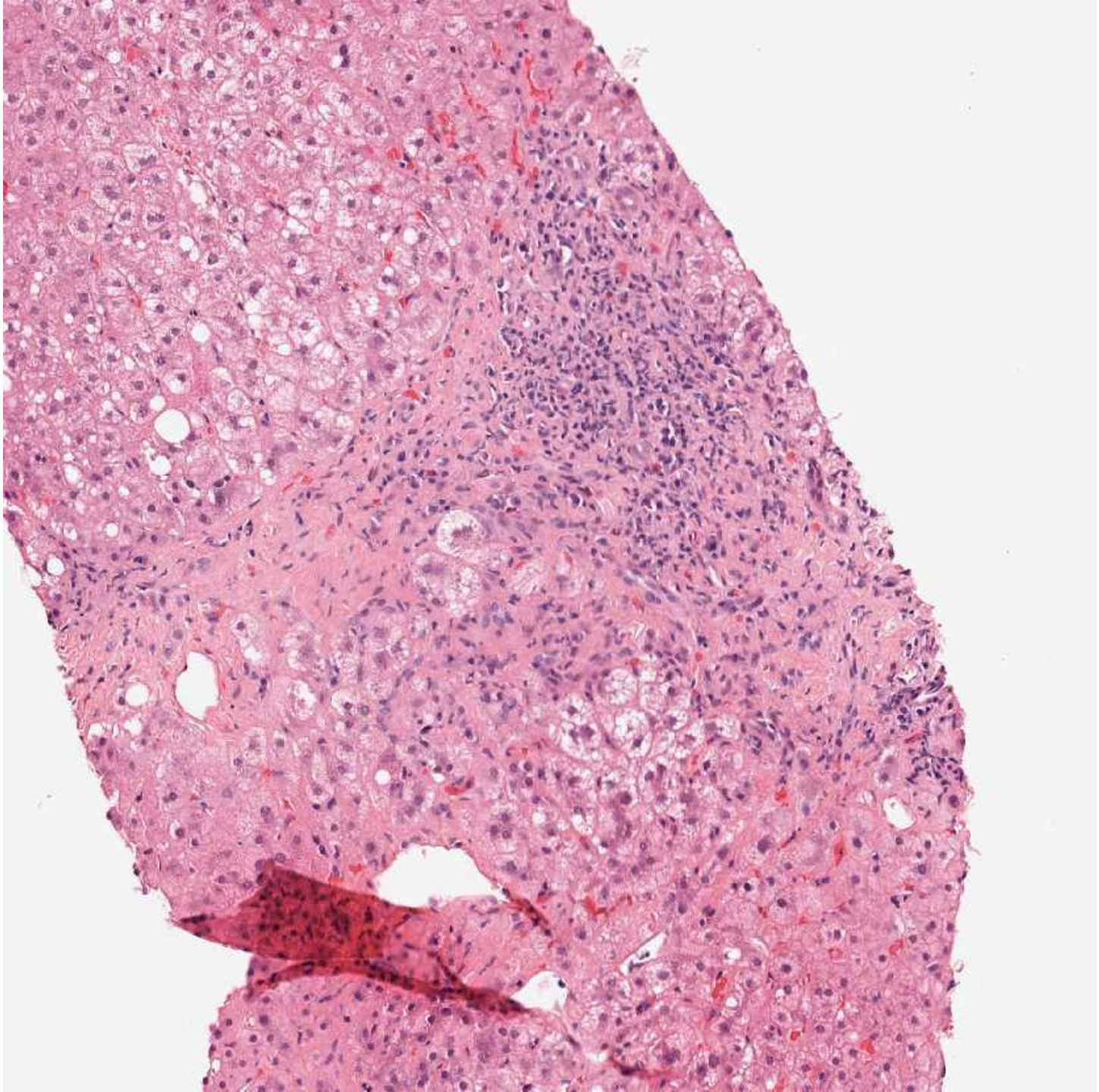
HIV (CD4 =370) on HAART,
history of diabetes mellitus, excesss alcohol.
Hepatomegaly

Single core 16mm length

(please also see van Gieson on website)

424

424



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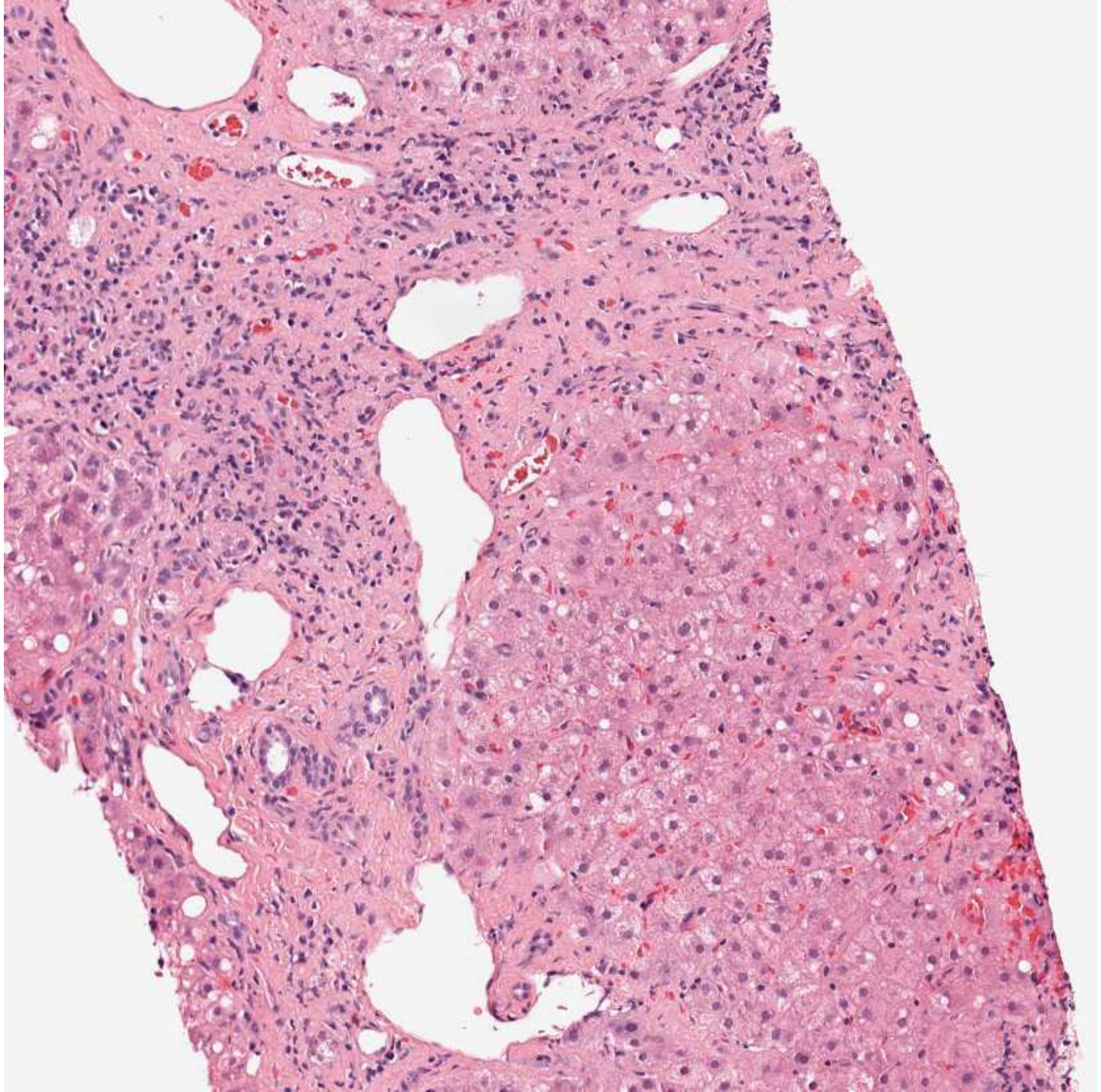

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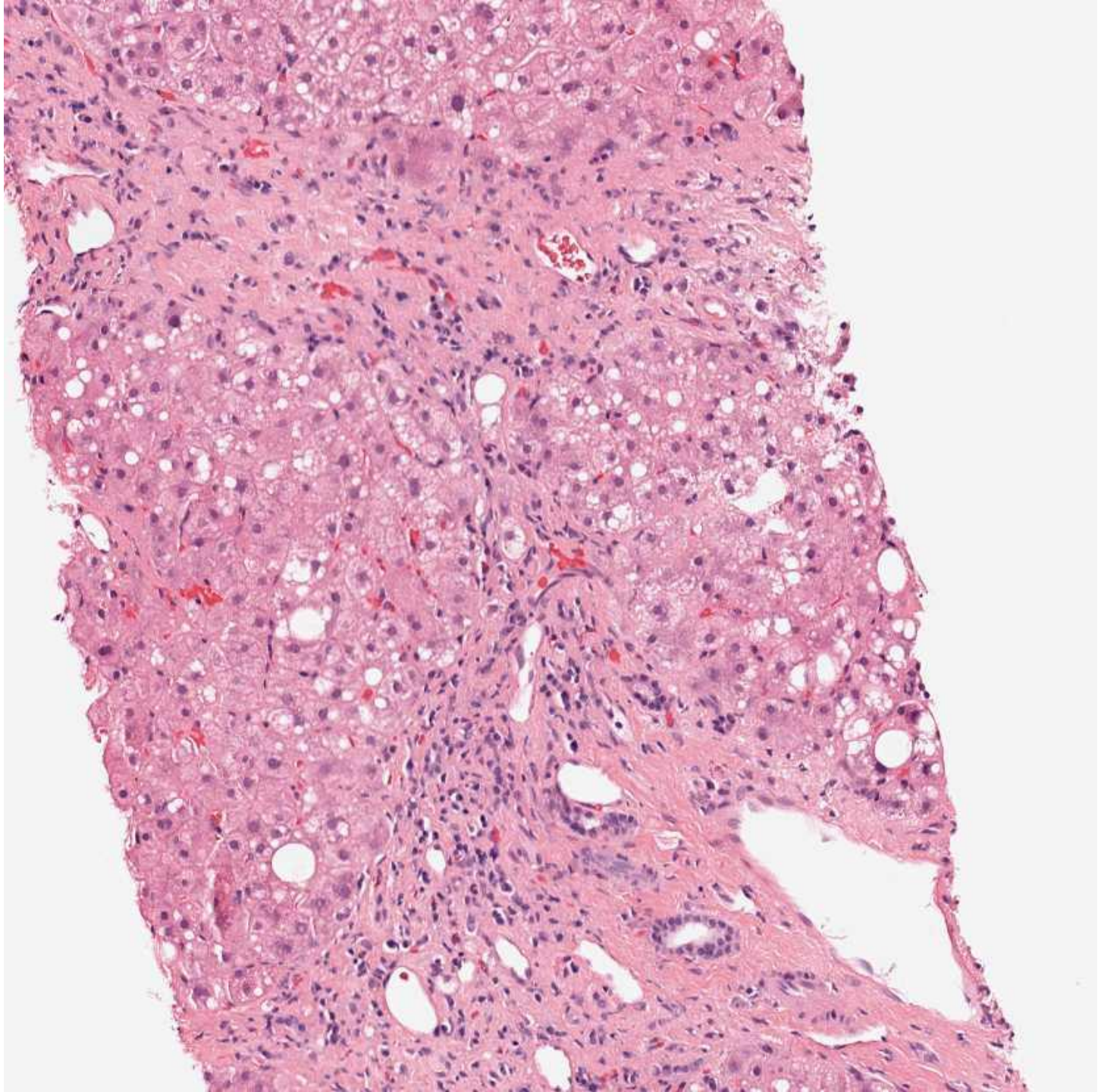

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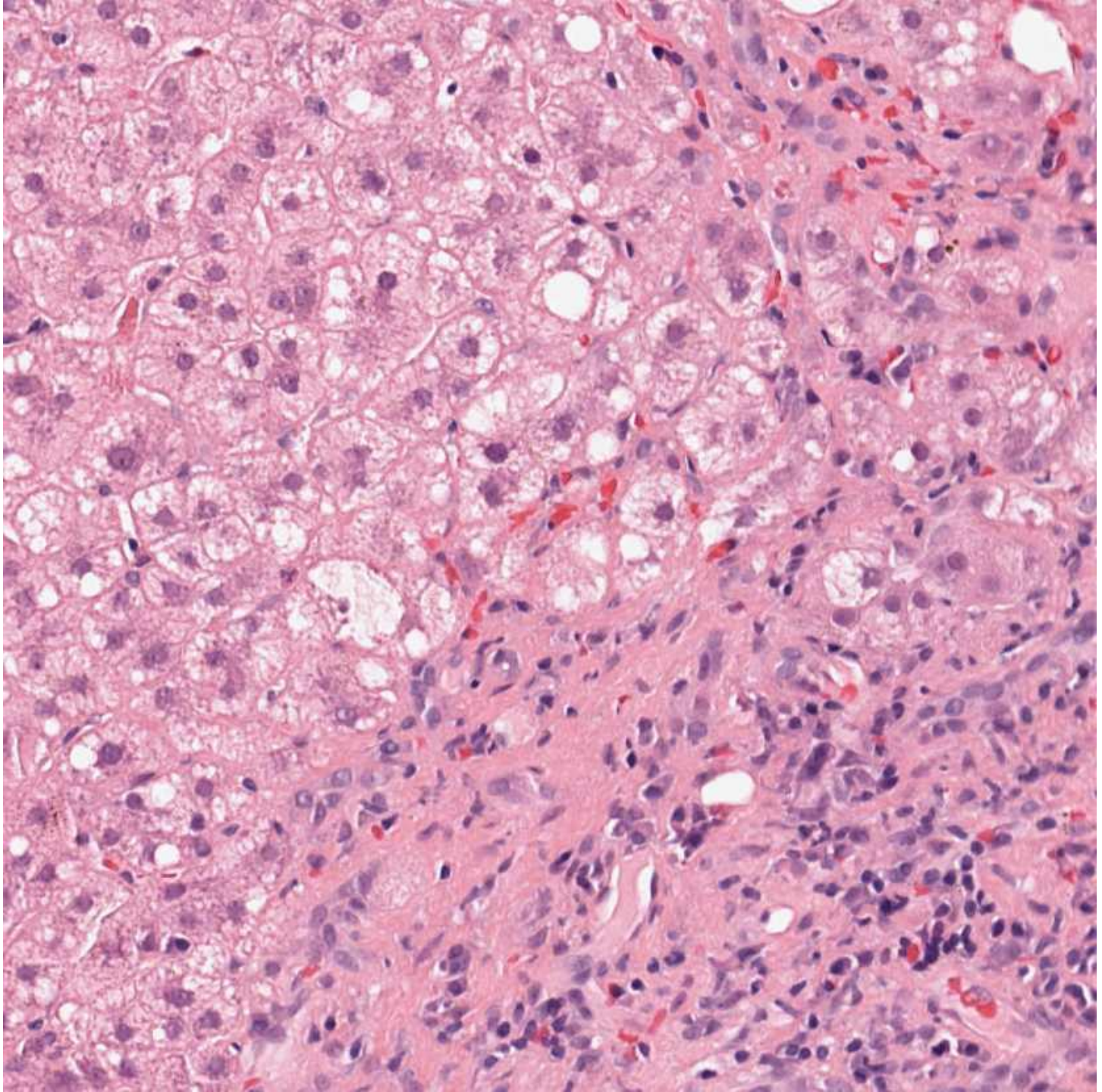

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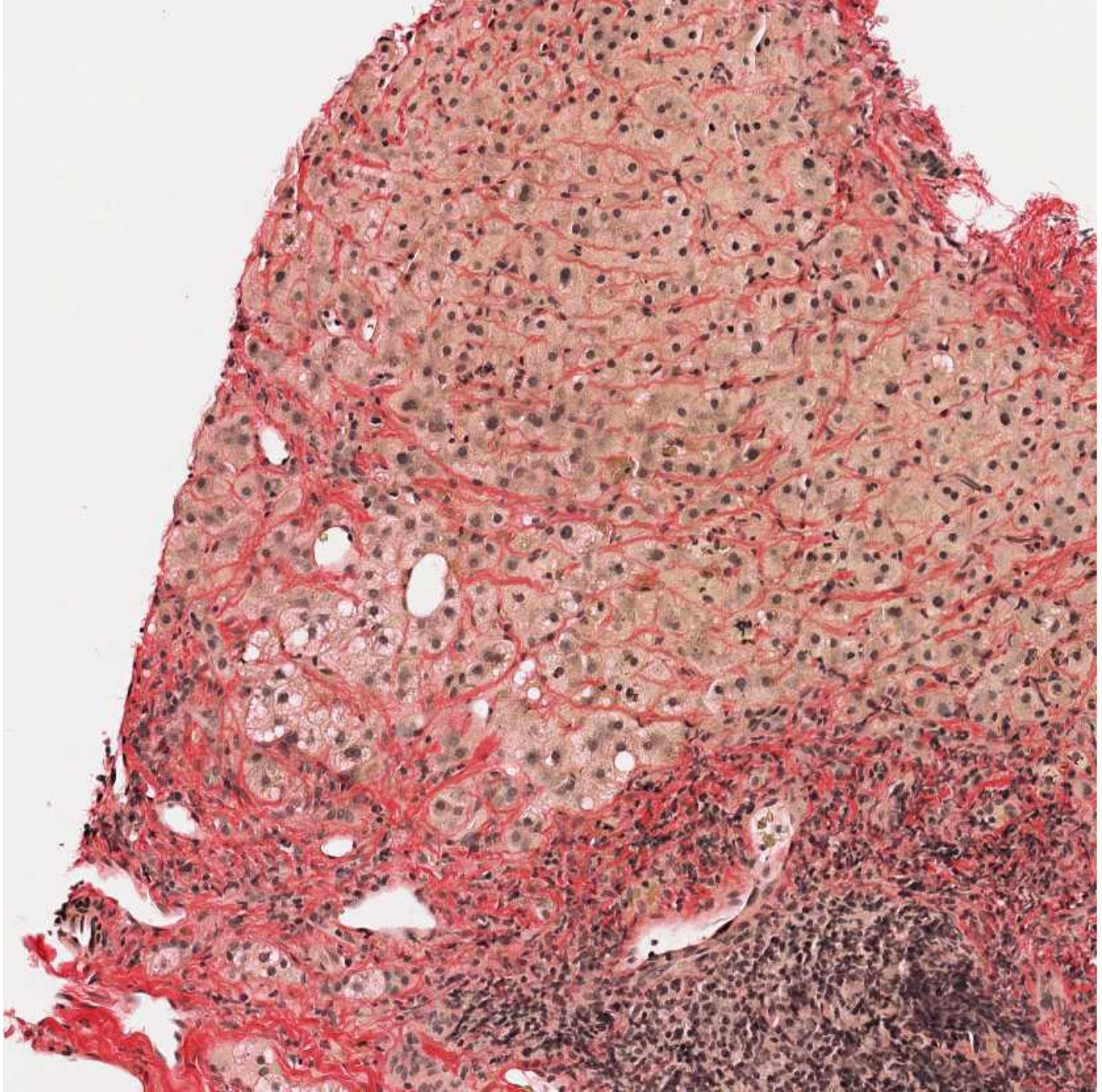
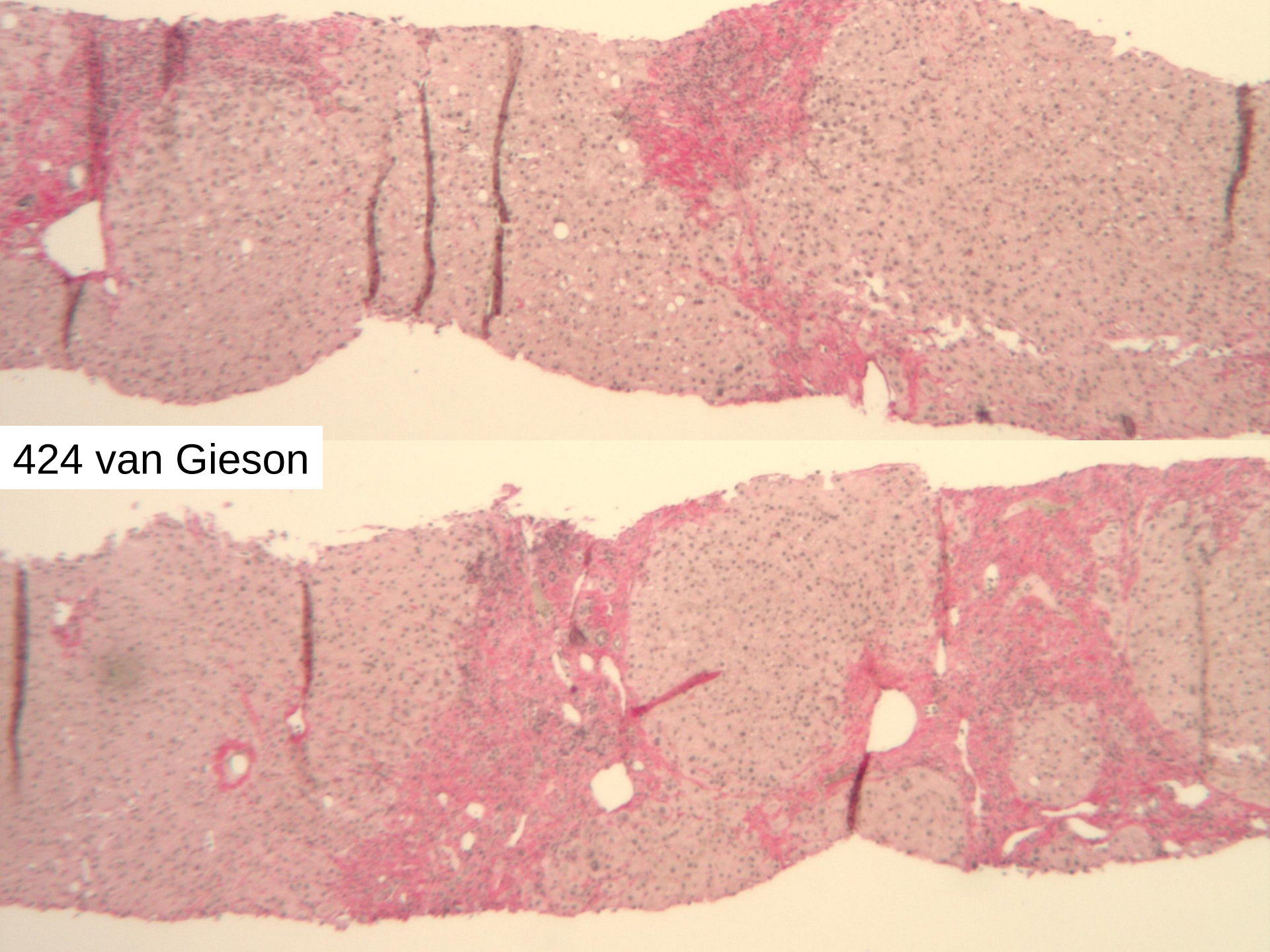



424 van Gieson

Case I1/424 Age 53, Male

Morphology

73 Cirrhosis
10 developing cirrhosis /Ishak stage 5
4 bridging fibrosis
1 developing fibrosis

39 steatohepatitis
24 steatosis
4 not fatty liver disease
5 fatty liver not mentioned
10 hepatitic process
1 cholestatic hepatitis
1 acute on chronic hepatitis

Suggested scoring:
Insufficient consensus for scoring

Clinicopath

4 No aetiological features
48 c/w ALD/NAFLD
9 ALD only
2 NAFLD only
5 Not a fatty liver disease
17 ALD/NAFLD not mentioned
27 ? Also HAART contributing to FLD
1 HAART as only cause

9 ? AIH
27 Exclude Hepatitis C
7 Features of raised venous pressure
4 drug induced hepatitis (not as part of fatty liver)
1 parasite/fungi as only cause
2 HIV as cause
1 CMV- HIV cholangiopathy

Case I1/424 Age 53, Male

Original diagnosis: cirrhosis on a background of steatohepatitis.

Masterclass presentation by Rob Goldin:

Liver biopsy in patients with HIV.

HIV and the liver

Rob Goldin

Anything can happen.

All the usual causes of liver disease are worse.

Opportunistic infections have become less common.

Drug induced liver disease is very common.

As people live longer liver disease becomes an increasing important cause of morbidity and mortality

Review of liver function in HIV patients

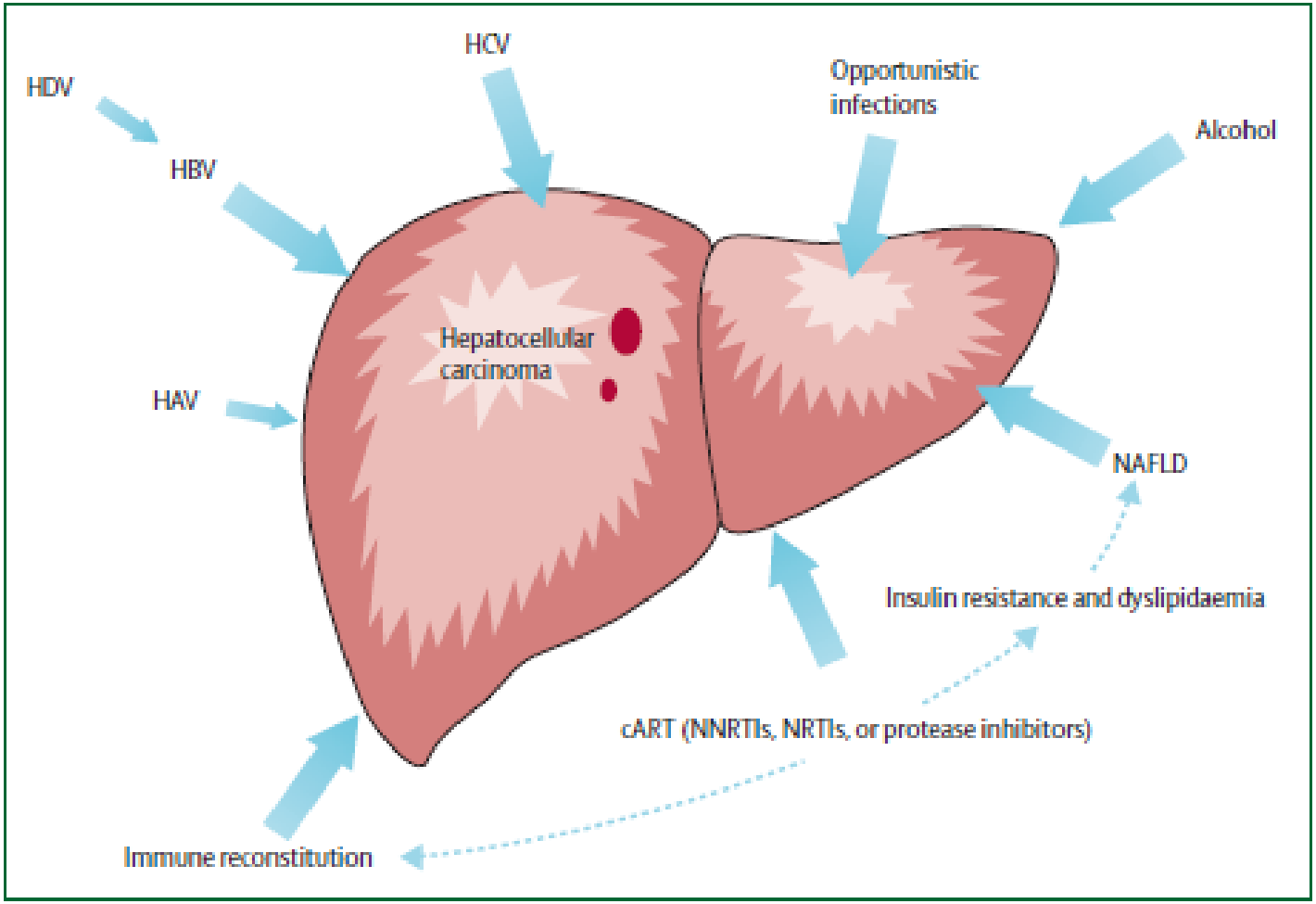
Attendance between 1st January and 31st December 2009

1,412 patients had 3,947 sets of LFTs requested

Abnormality of LFT was common , only 12% were “normal” (<40 IU/l)

Cowan et al, EASL 2012

Factors involved in aetiology of liver disease in HIV



Source : Joshi 2011

Case 424: Rob Goldin: Masterclass: HIV and the liver

Differential diagnosis of liver disease in HIV infection in the ART-era

Clin Gastroenterol Hepatol. 2010 December; 8(12): 1002–1012.

Case 424: Rob Goldin: Masterclass: HIV and the liver

HEPATIC PARENCHYMAL DISEASE

Infection

Viral Hepatitis: HCV, HBV, HDV, HAV, HEV, CMV, EBV, HSV, VZV, HHV6

Mycobacterium avium complex

Cryptococcus neoformans

Microsporidium

Pneumocystis jirovecii

Bacillary peliosis hepatis

Histoplasma capsulatum

Nonalcoholic fatty liver disease

Medication toxicity

Alcoholic liver disease

Recreational Drugs

Cocaine

MDMA (Ecstasy)

Neoplasm

Lymphoma

Kaposi's sarcoma

Hepatocellular carcinoma

Nodular regenerative hyperplasia

Autoimmune hepatitis

Hemochromatosis

Wilson's disease

Alpha-1 antitrypsin deficiency

BILIARY DISEASE

AIDS Cholangiopathy

Cryptosporidium

CMV

Microsporidium

Cyclospora cayetanensis

Mycobacterium avium intracellulare

Histoplasma capsulatum

Acalculous cholecystitis

Cryptosporidium

CMV

Isospora

Microsporidium

Neoplasm

Lymphoma

Kaposi's sarcoma

Primary sclerosing cholangitis

Primary biliary cirrhosis

Case 424: Rob Goldin: Masterclass: HIV and the liver

Most common ART agents associated with liver injury in HIV-infected patients

Case 424: Rob Goldin: Masterclass: HIV and the liver

MEDICATION	TYPICAL DOSE	DOSE ADJUSTMENT FOR HEPATIC INSUFFICIENCY	MECHANISM OF LIVER INJURY
NNRTI			
Nevirapine (NVP)	200 mg po bid	Child-Pugh Class B or C: Contraindicated	Hypersensitivity reaction, direct drug toxicity/drug metabolism
Etravirine (ETR)	200 mg po bid	Child-Pugh Class A or B: No adjustment Child-Pugh Class C: Not defined	Hypersensitivity reaction
PI			
Ritonavir (RTV) full-dose	No longer used		Direct drug toxicity/drug metabolism
Tipranavir (TPV) + RTV low-dose	(TPV 500 mg + RTV 200 mg) po bid	Child-Pugh Class A: Use with caution Child-Pugh Class B or C: Contraindicated	Direct drug toxicity/drug metabolism
Atazanavir (ATV)	400 mg po once daily	Child-Pugh Class B : 300 mg po once daily Child-Pugh Class C: Contraindicated	Indirect hyperbilirubinemia: does not cause liver injury
Indinavir (IDV)	800 mg po q8h	Mild to moderate hepatic insufficiency: 600 mg po q8h	Indirect hyperbilirubinemia: does not cause liver injury
NRTI			
Stavudine (D4T)	≥60 kg: 40 mg po bid <60 kg: 30 mg po bid	Not defined	Mitochondrial toxicity
Zidovudine (AZT, ZDV)	300 mg po bid	Not defined	Mitochondrial toxicity
Didanosine (ddI)	Enteric coated: ≥60 kg: 400 mg po once daily <60 kg: 250 mg po once daily	No adjustment	Mitochondrial toxicity, cryptogenic liver disease, noncirrhotic portal hypertension
	Oral Solution: ≥60 kg: 200 mg po bid or 400 mg po once daily <60 kg: 150 mg po bid or 250 mg po once daily		
Abacavir (ABC)	300 mg po bid	Child-Pugh Class A: 200 mg po bid (use oral solution)	Hypersensitivity reaction, especially in HLA-B*5701 positive patients
		Child-Pugh Class B or C: Contraindicated	
Lamivudine (3TC)	300 mg po once daily or 150 mg po bid	No adjustment	HBV reactivation due to medication withdrawal or resistance
Emtricitabine (FTC)	Oral capsule: 200 mg po once daily Oral solution: 240 mg po once daily	Not defined	HBV reactivation due to medication withdrawal or resistance
Tenofovir (TDF)	300 mg po once daily	No adjustment	HBV reactivation due to medication withdrawal or resistance
Other			
Enfuvirtide (T20)	90 mg subcutaneous bid	Not defined	Hypersensitivity reaction
Maraviroc (MVC)	Recommended dose depends on other drugs in regimen		

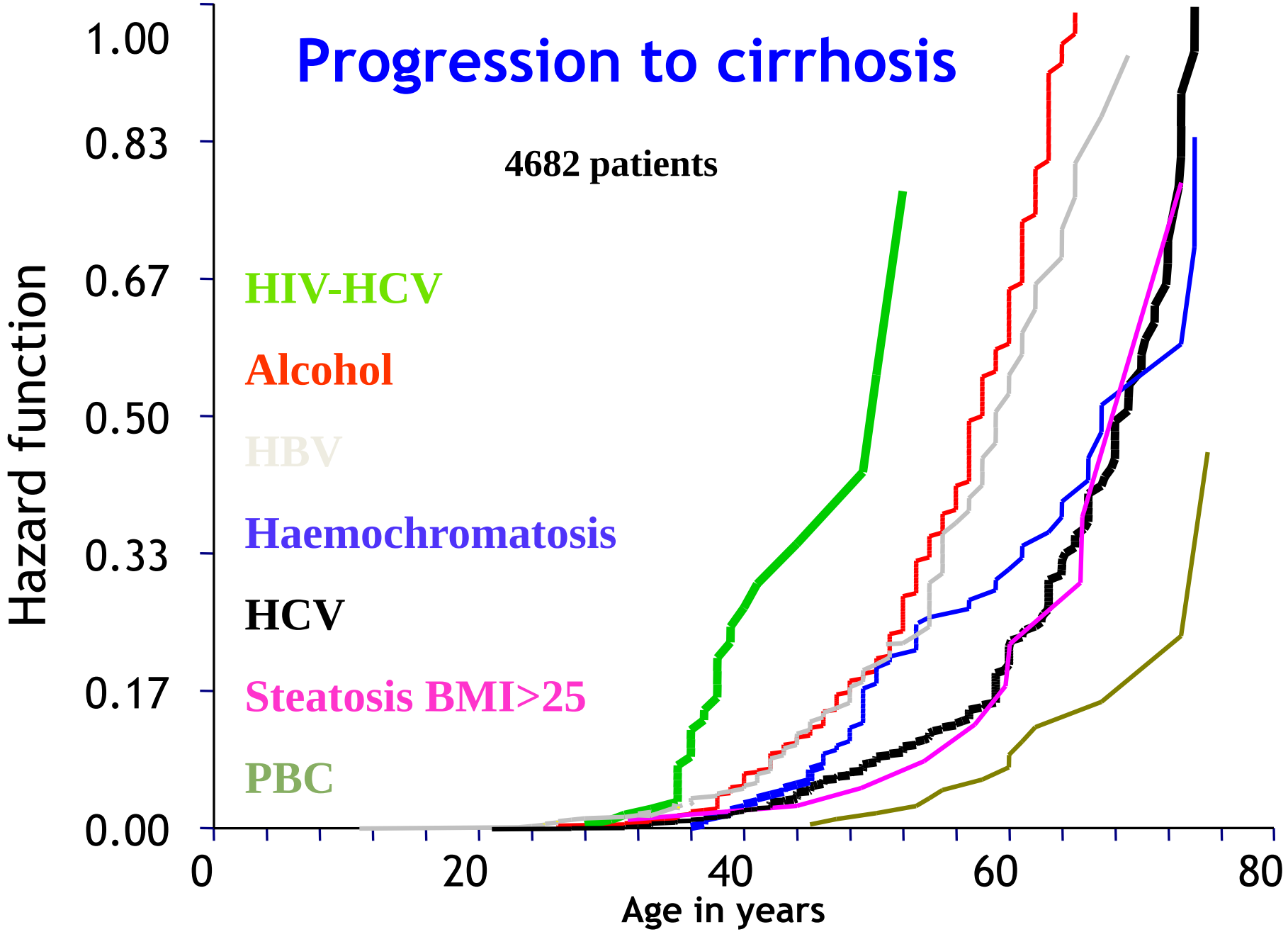
Partial list of potentially hepatotoxic non-ART medications prescribed to HIV-infected individuals

Case 424: Rob Goldin: Masterclass: HIV and the liver

MEDICATION	PATTERN OF LIVER INJURY
Antifungals	
Ketoconazole, Fluconazole, Amphotericin B	Hepatocellular injury
Antibiotics	
Ciprofloxacin	Hepatocellular injury
Azithromycin, Dapsone	Cholestatic injury
Trimethoprim-sulfamethoxazole	Mixed hepatocellular-cholestatic injury
Tuberculosis treatment	
Isoniazid, Rifampin, Pyrazinamide	Hepatocellular injury
Ethambutol	Cholestatic injury
Anti-virals	
Ganciclovir, Acyclovir	Hepatocellular injury
Anabolic/Androgenic steroids	
Testosterone, Nandrolone, Oxandrolone	Cholestatic injury, liver tumors, peliosis hepatis

Viral hepatitis and HIV

Case 424: Rob Goldin: Masterclass: HIV and the liver



Poynard, T. et al., (2003) A comparison of fibrosis progression in chronic liver disease. *Journal of Hepatology* 38:257-265

Fibrosis progression influenced by:

1. CD4 cell count (< 200 cells/microlitre)
2. Age at infection (> 25 years)
3. Male sex
4. Alcohol consumption (> 50g/d)

HIV and NALFD

NAFLD more common in HIV positive v HIV negative controls

Present in up to 1/3 patients

Factors

- direct: drug toxicity
- indirect: insulin resistance, high BMI, lipid abnormalities (↓LDL, ↑TG), DM

Sources : Angulo 2007, Moyle 2002, Guaraldi 2008

Non-cirrhotic portal hypertension

First described in 2006

Patients with no known risk factors for liver disease presenting with features of late stage disease (variceal bleeds)

Liver biopsies failed to show fibrosis/cirrhosis

Range of pathological findings

- Nodular regenerative hyperplasia (NRH)
- Evidence of venous dilatation/thrombosis
- Normal

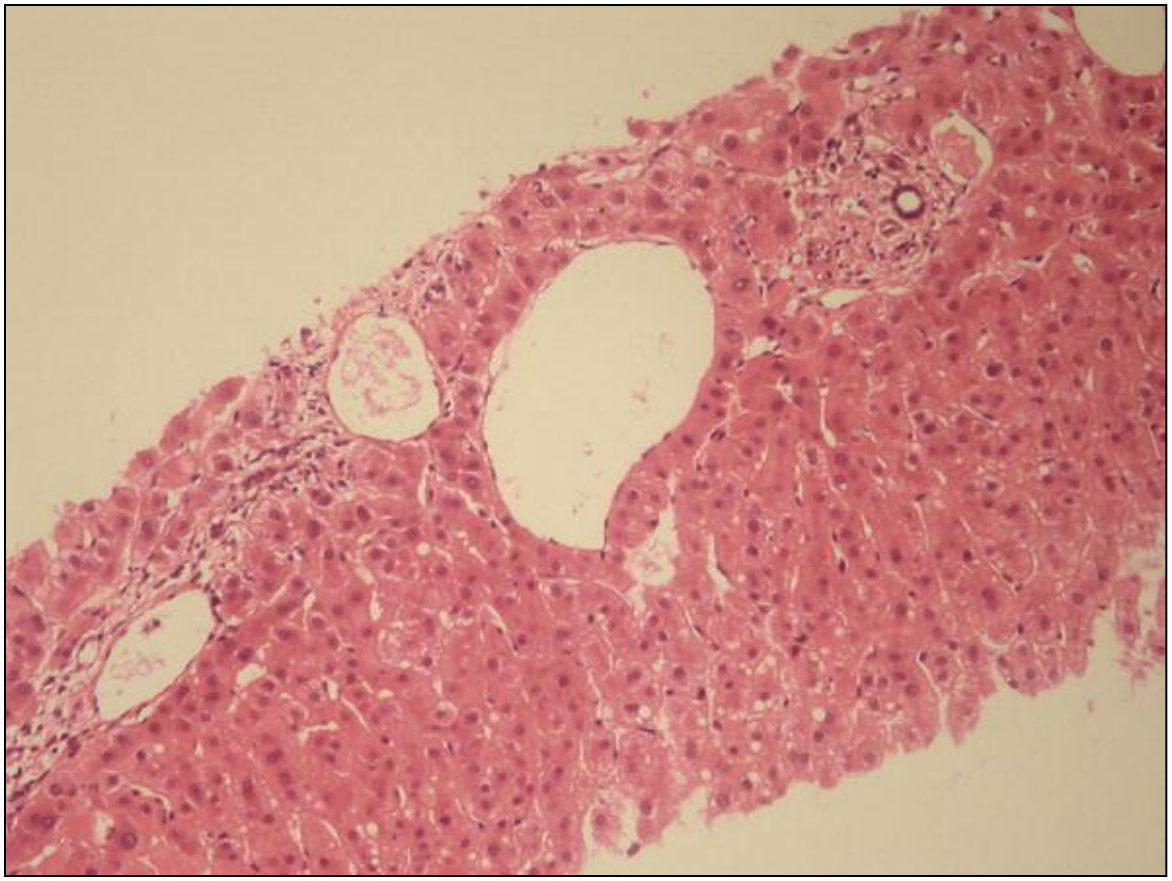
Range of pathological findings

About 1/3 Nodular Regenerative hyperplasia

About 1/4 Venous outflow obstruction

About 1/3 mild inflammation/ mild steatosis

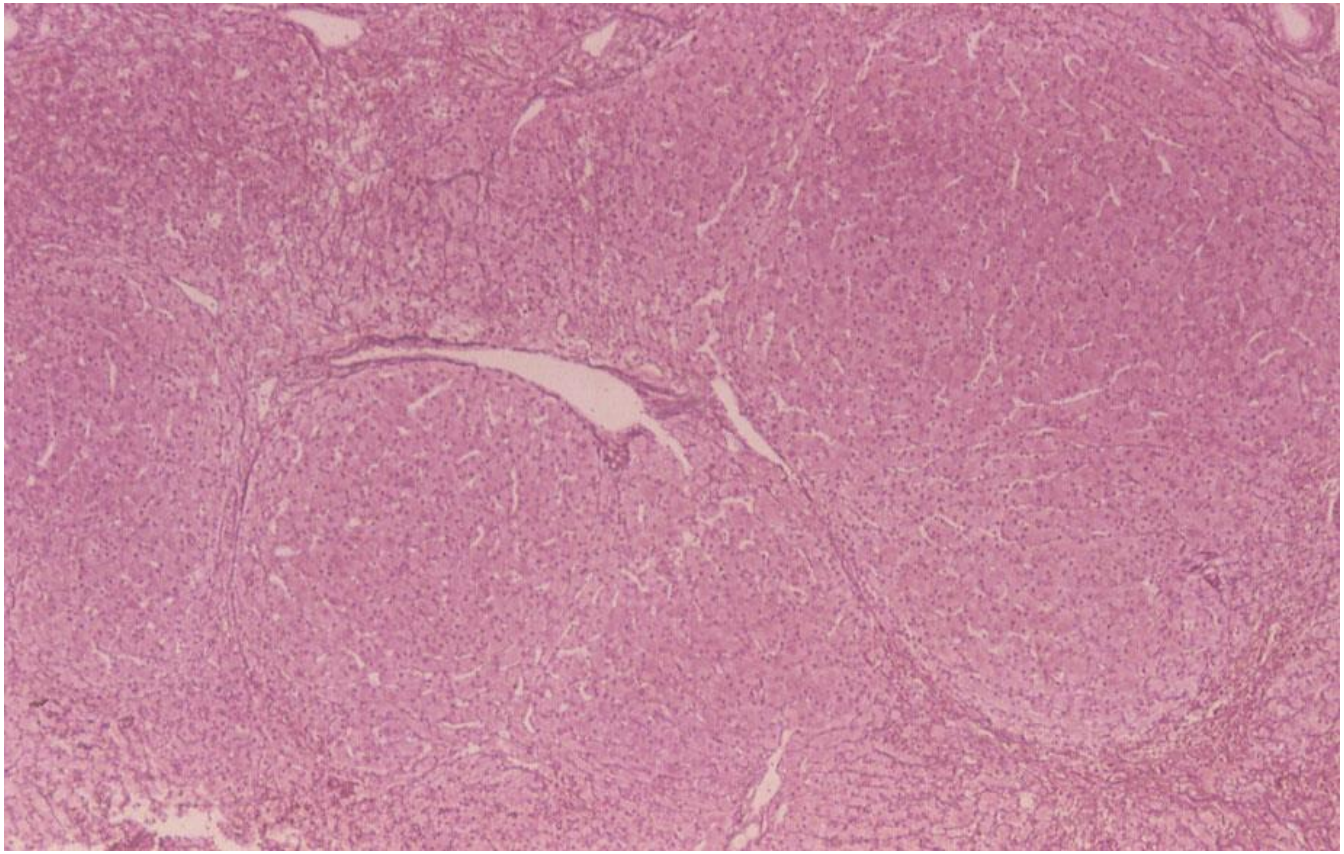
Case 424: Rob Goldin: Masterclass: HIV and the liver



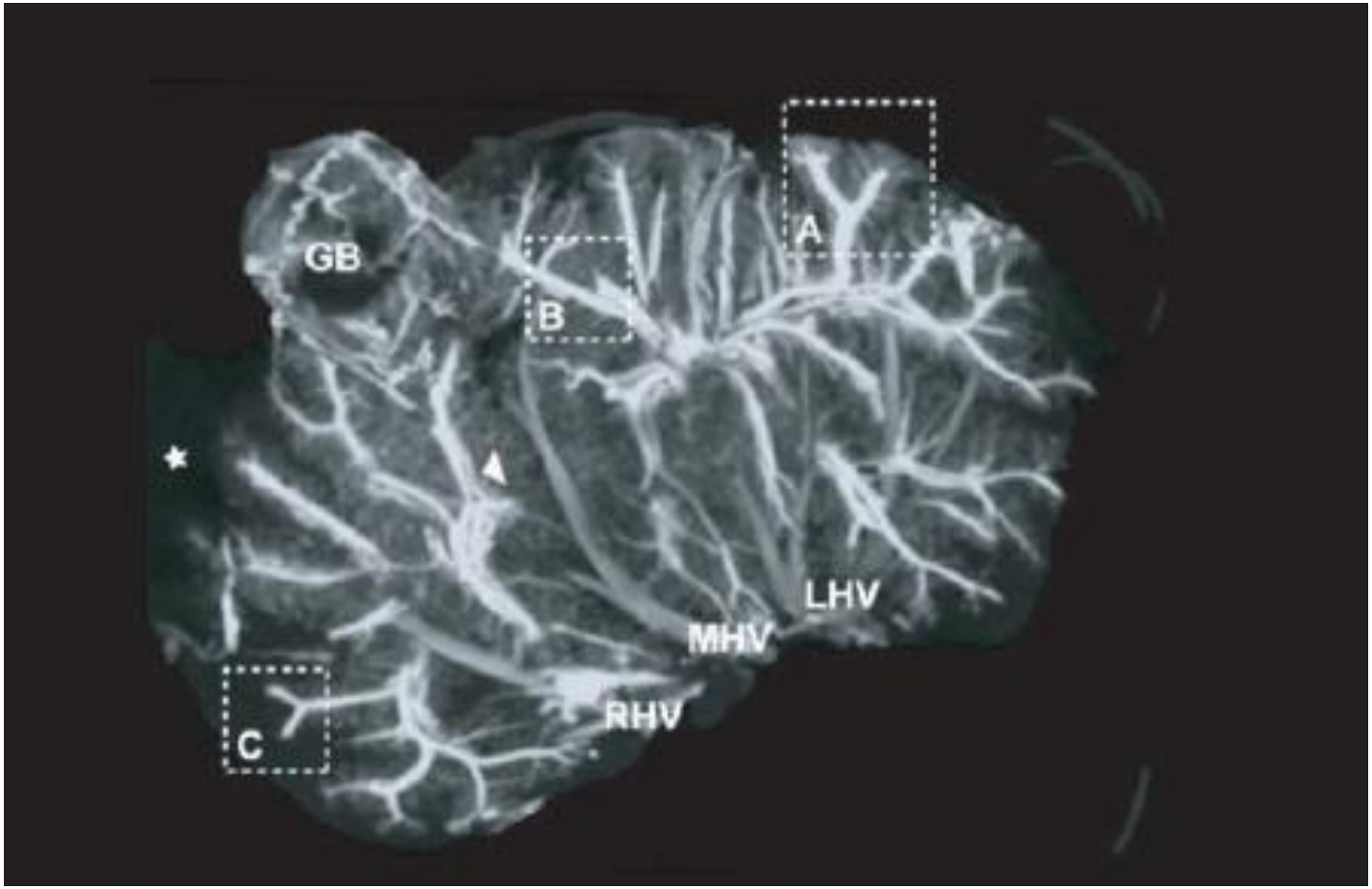
Imperial College London

Source: Rob Goldin, Garvey 07

Case 424: Rob Goldin: Masterclass: HIV and the liver



Source: Rob Goldin



Source: Mallet et al 2009

What is the prognosis/natural history?

First recognised in approximately 2006, limited follow-up

Significant mortality – at least 10%, mostly in first two years

Some evidence of normalising ALT after discontinuing drug (Maida et al 2008), possible increase in platelet counts

Pretty soft - this is debated (cotte et al 2008)

No evidence that there is significant resolution of liver disease or portal hypertension (Maida et al 2008, Cachay 2012)

Case I1/425

Age 24, Male

Abnormal LFT's. Portal hypertension ? Non-cirrhotic portal hypertension ?

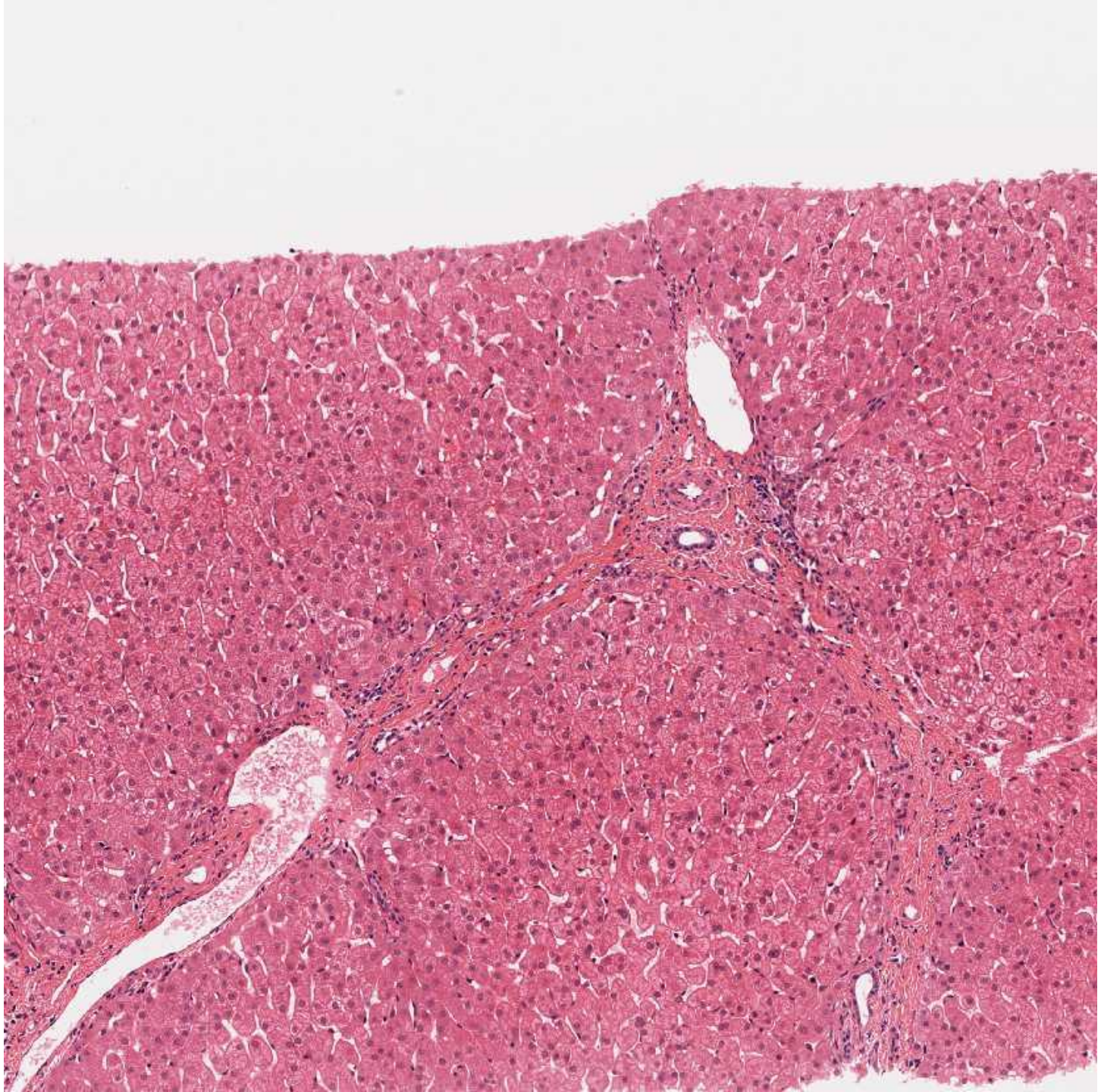
Pale core 29mm

(please also see reticulin, sirius red and orcein on website)

425

425

425



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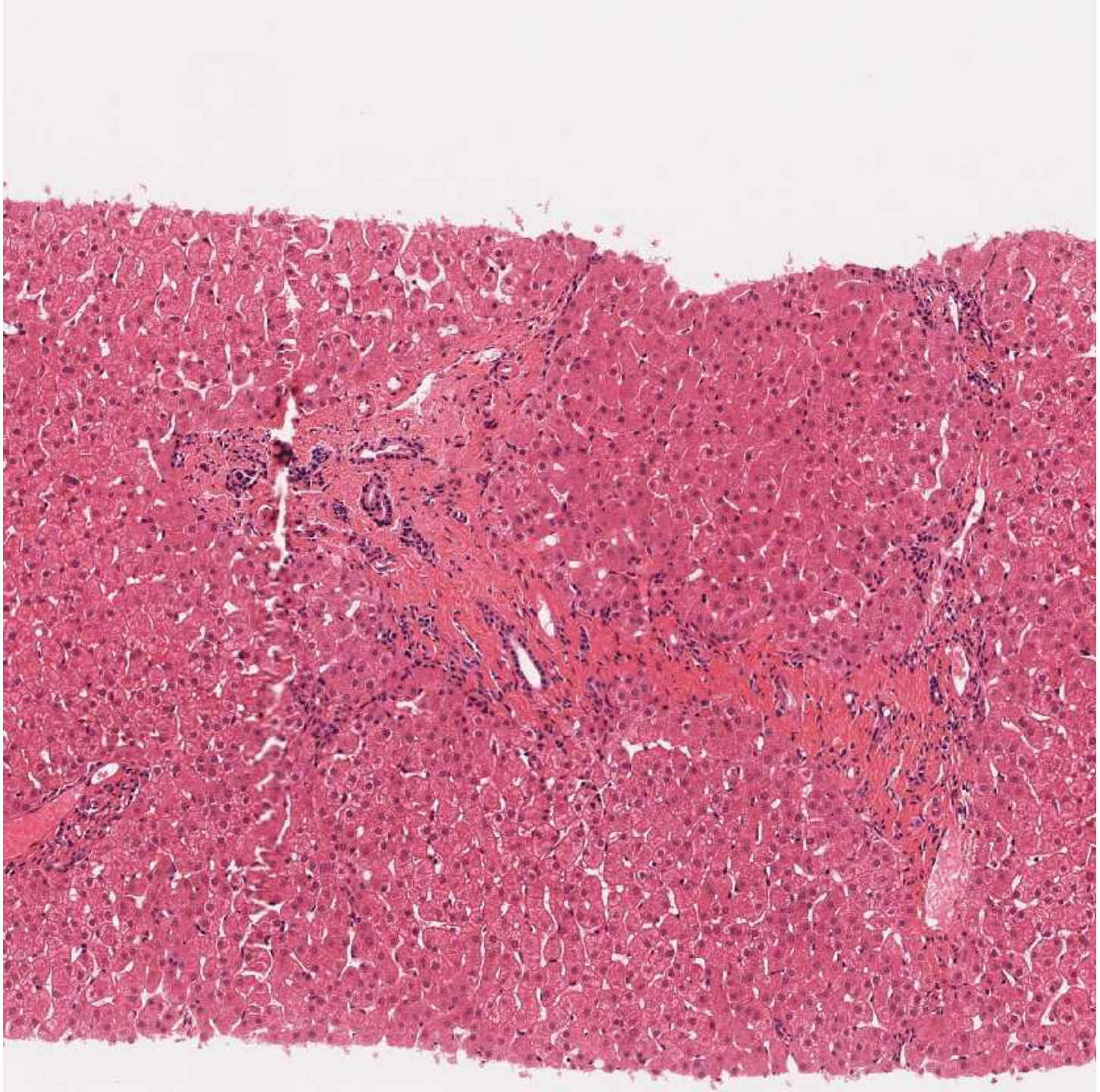

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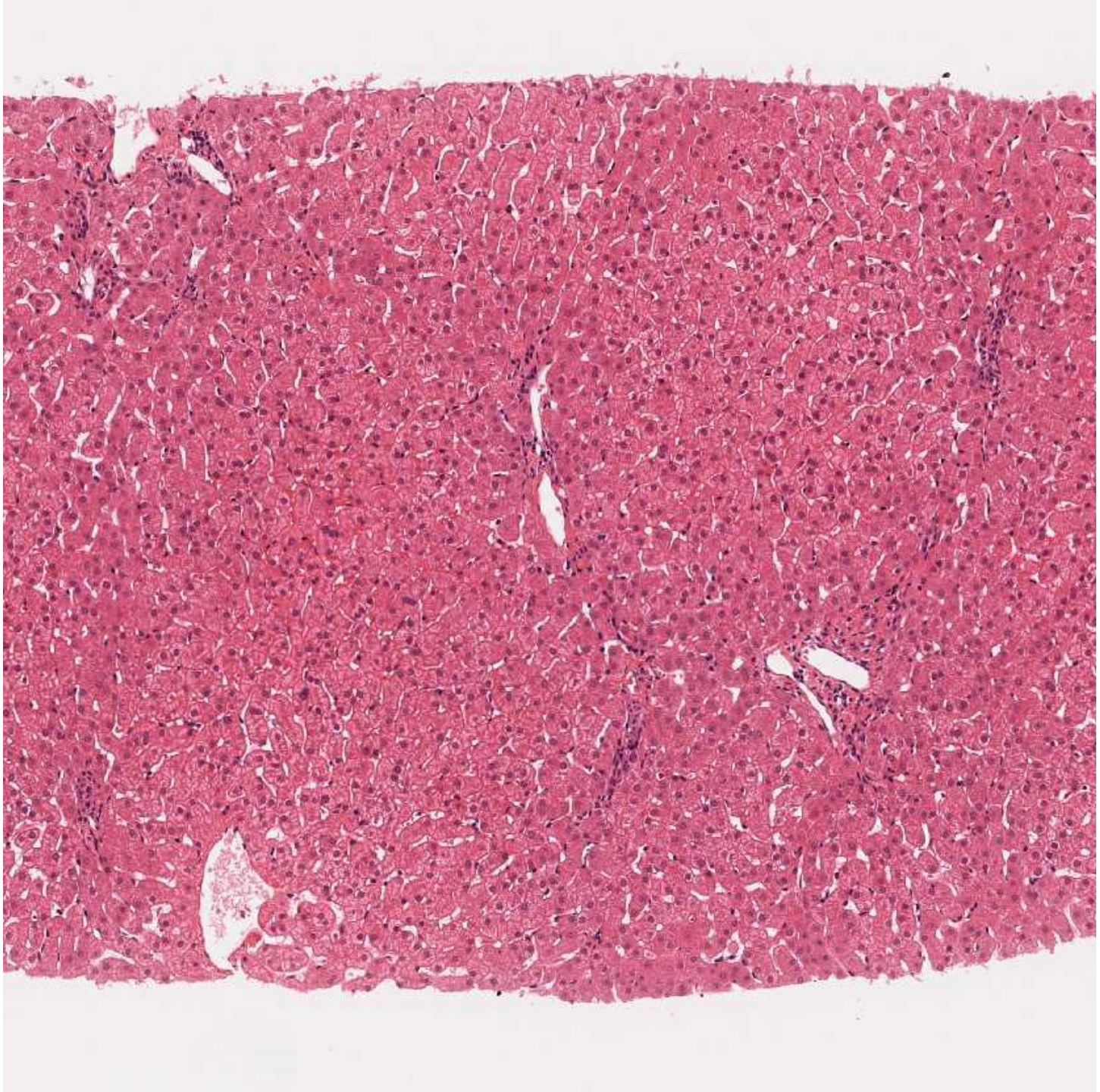

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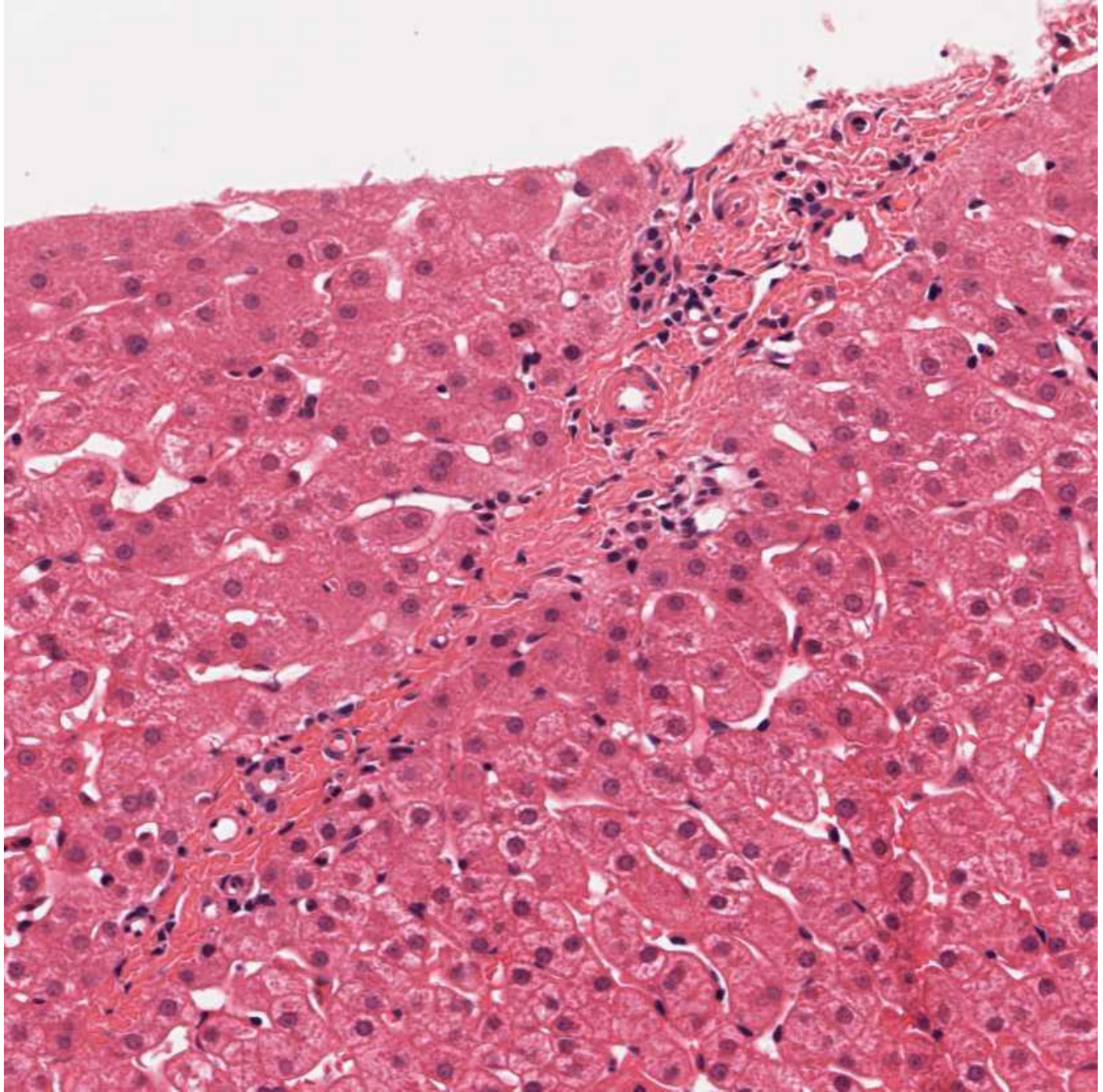
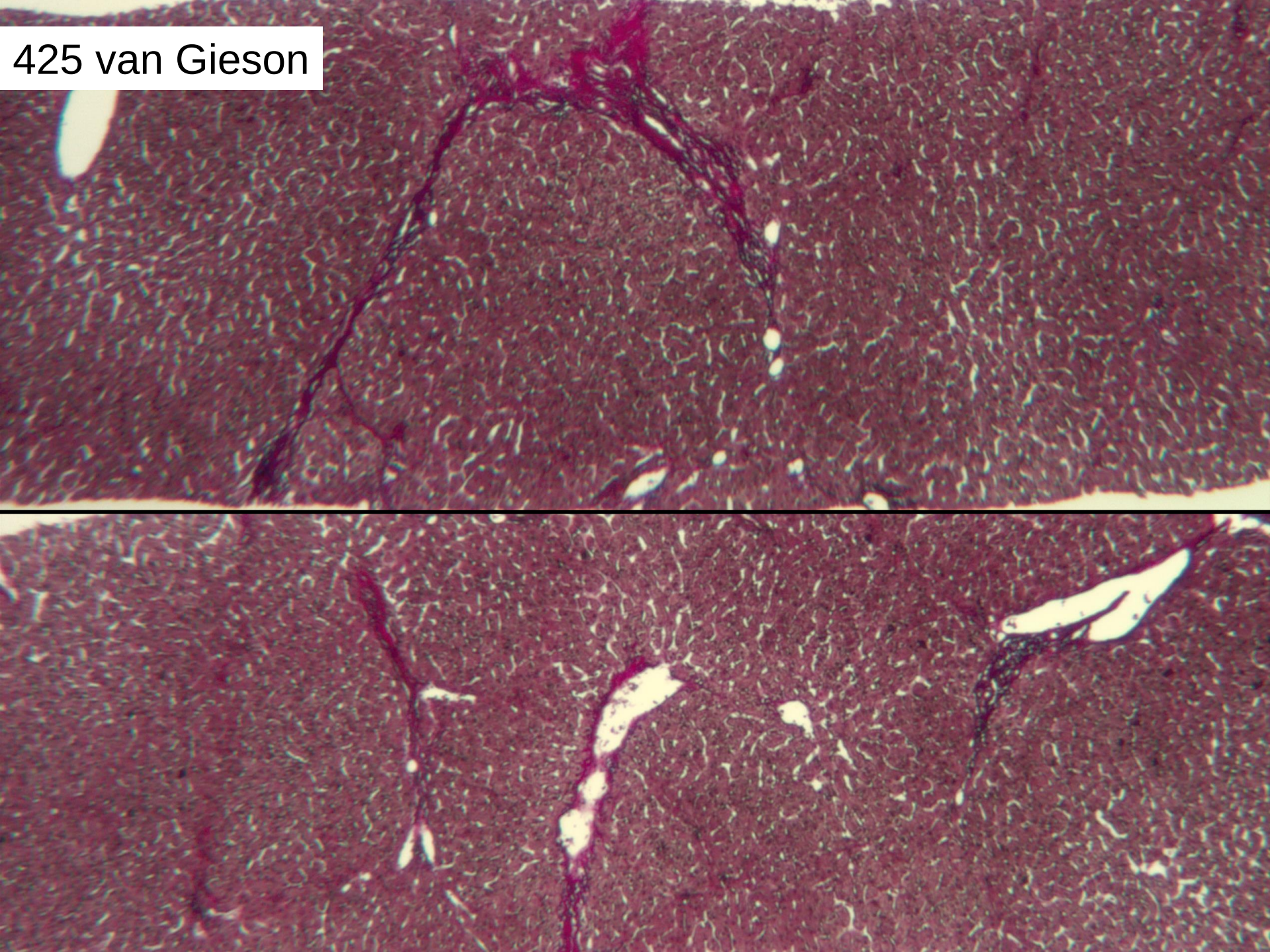



425 van Gieson

Case I1/425 Age 24, Male

76 – anything in NCPHT spectrum:

48 non-cirrhotic portal hypertension
23 Incomplete septal cirrhosis
14 nodular regenerative hyperplasia
7 Hepatoportal sclerosis
2 Partial septal fibrosis
1 Obliterative portal venopathy
1 ? Portal vein thrombosis
4 remodelling/resolving fibrosis

12 - Other:

1 Bridging fibrosis, not yet cirrhotic, not typical of NCPHT

1 Architectural and biliary changes, no definite diagnosis

1 odd pattern, suggests previous damage

1 Possible macronodular cirrhosis

1 Liver with mild portal-portal fibrosis

2 Regressed cirrhosis

1 canalicular cholestasis with bridging fibrosis,Drug induced ?Steroids

1 Bridging fibrosis/veno-occlusive disease

1 ? Outflow obstruction

1 p-p bridging and early nodule formation ? Cause

1 Post hepatic vascular obstruction

Suggested scoring:

Suitable for scoring?

10 points for 76 in NCPHT spectrum,

0 points if suggests a different diagnosis

5 points for description, but not indicating diagnosis of NCPHT

Discussion at meeting: unsuitable for scoring

Case I1/425 Age 24, Male

Original diagnosis: vascular and architectural changes in keeping with non-cirrhotic portal hypertension.

Comments: Educational case – fibrosis and nodularity more than often seen in non-cirrhotic portal hypertension, and regressing fibrosis is a possibility. Further comments from Rachel?

Case I1/426
Age 39, Male

e antigen positive hepatitis B ALT>60,
viral load 2 x 106.
Biopsy 2006 no fibrosis. To re-stage disease.

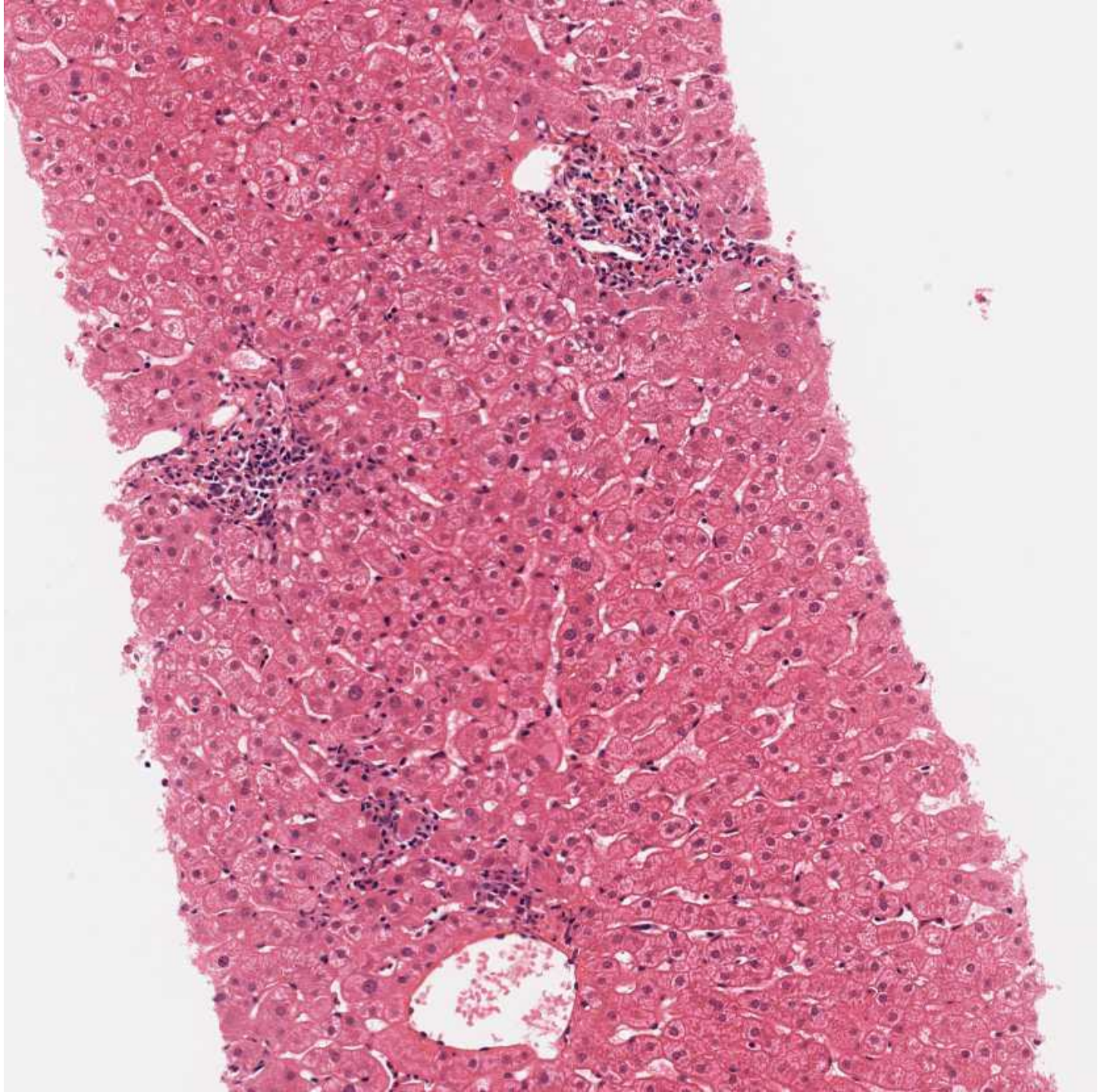
Tan core 30mm

(please also see reticulin, sirius red and orcein on website)

426

426

426



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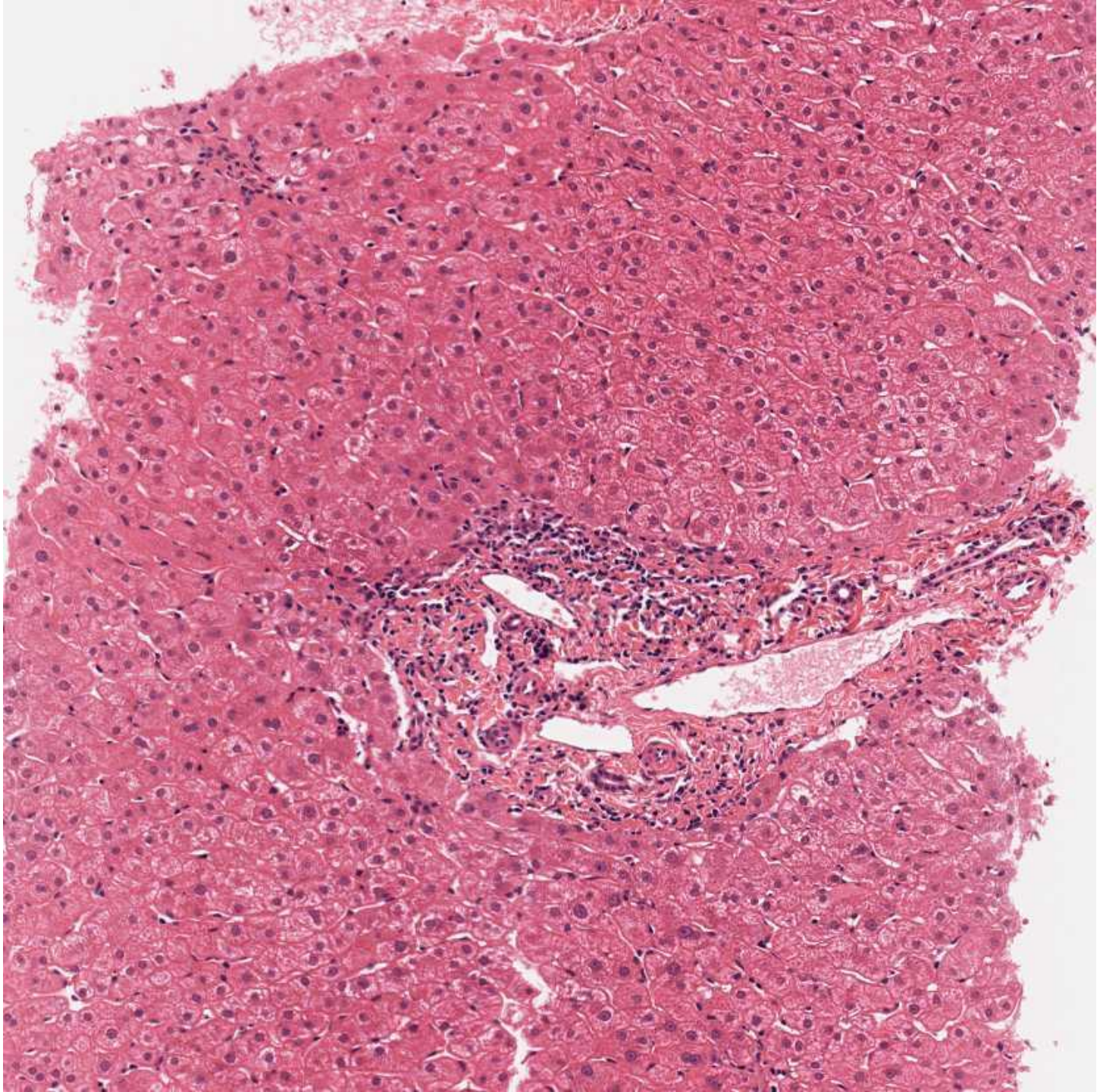

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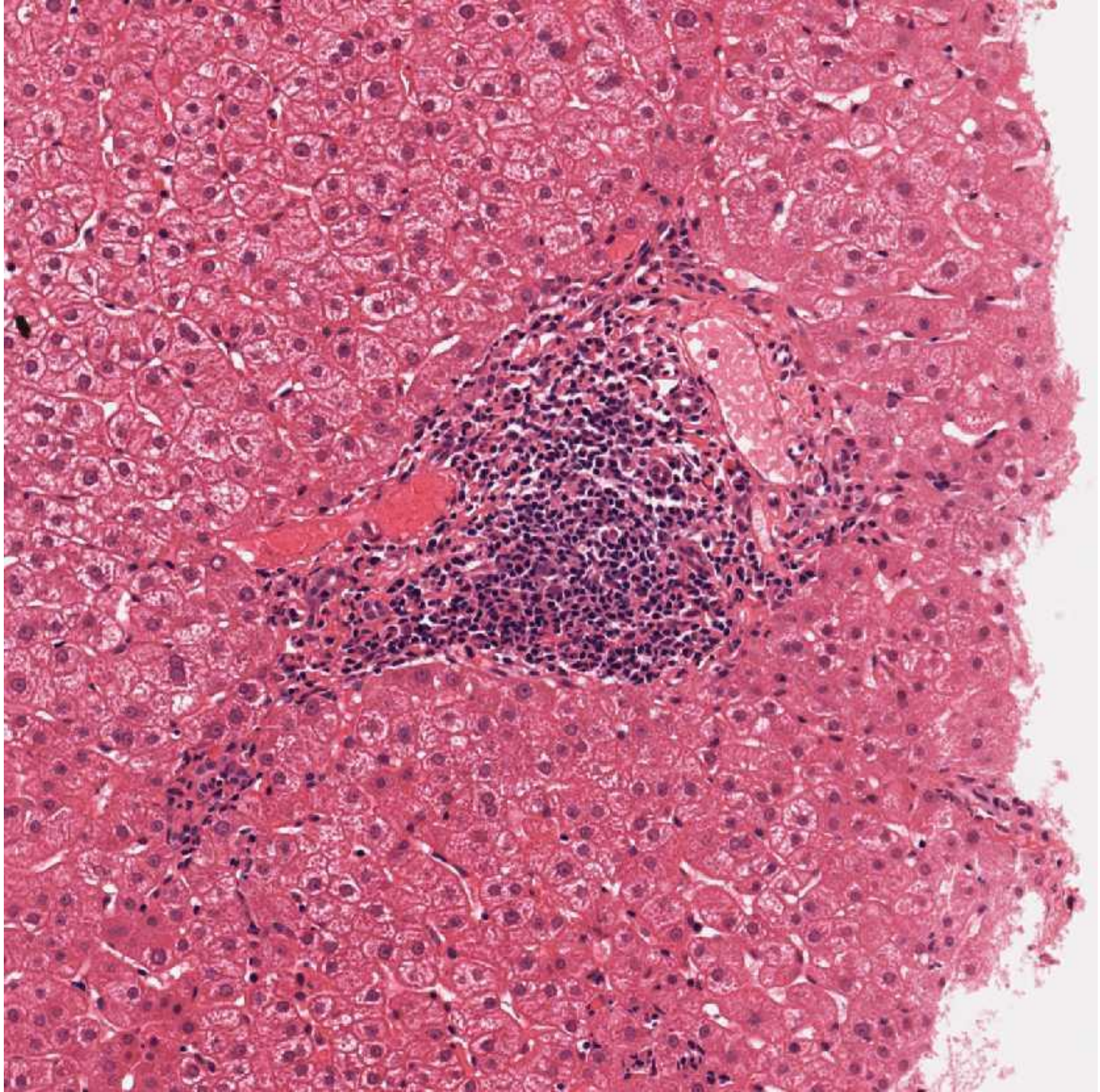

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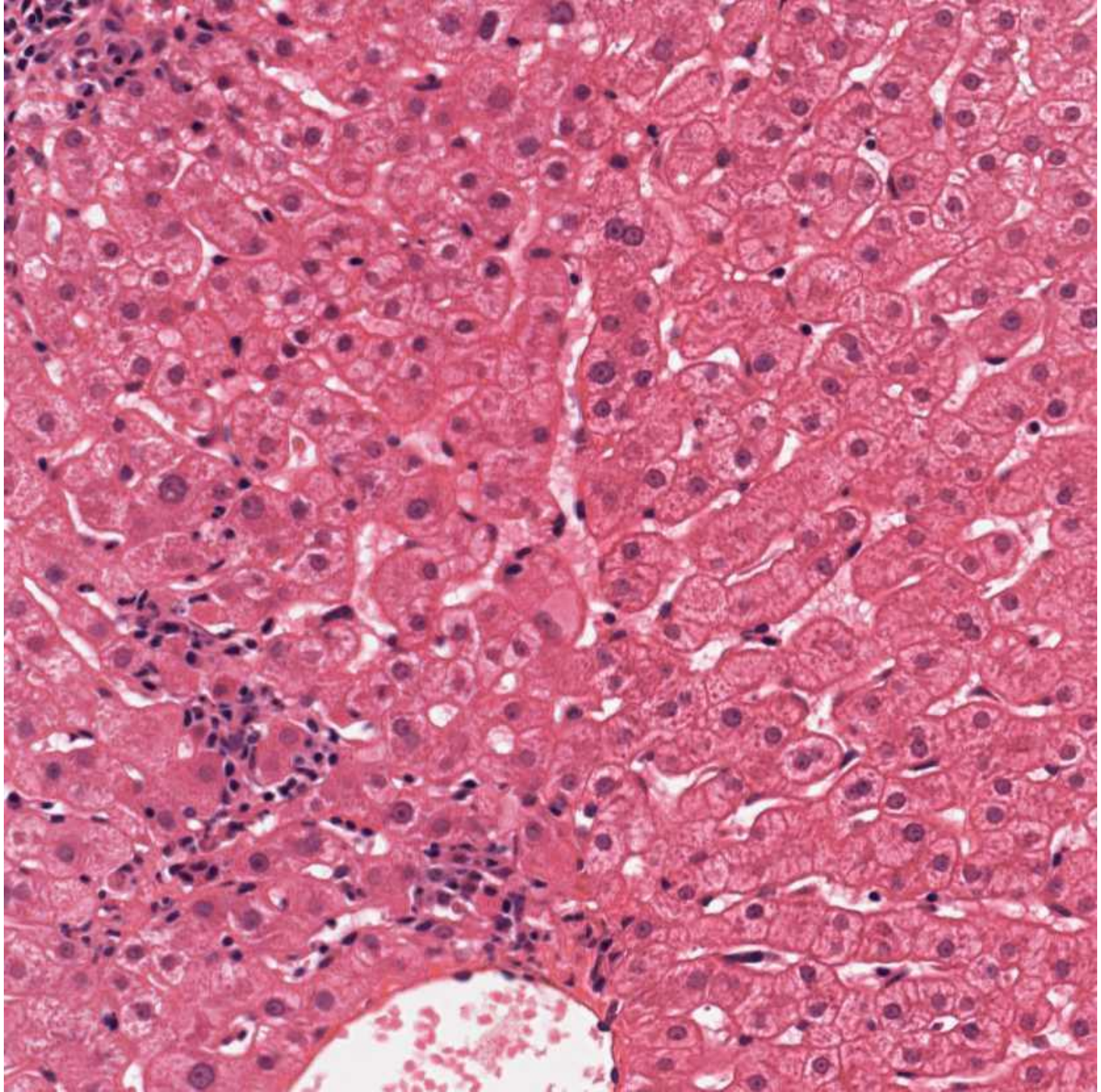
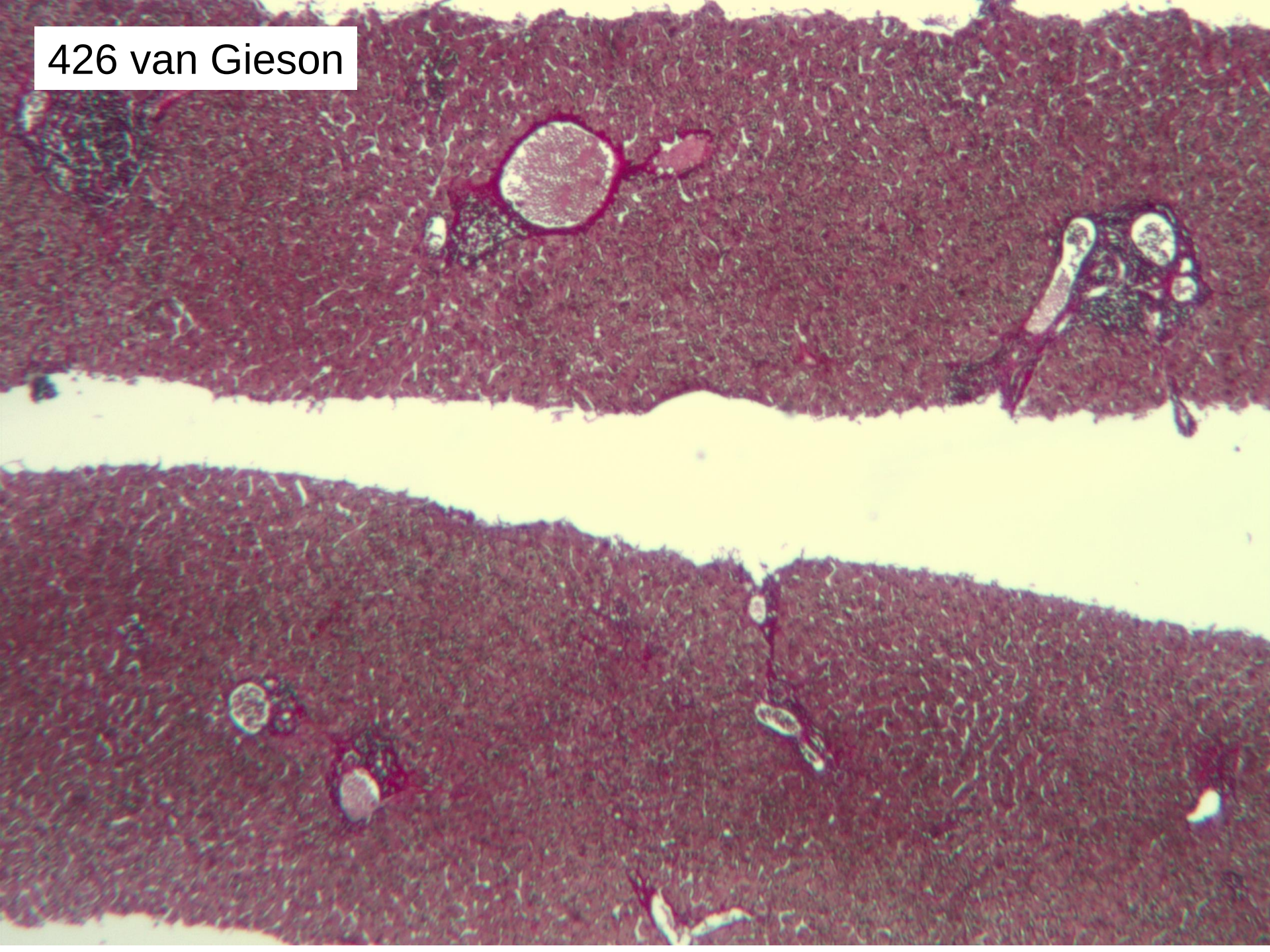



426 van Gieson

Case I1/426 Age 39, Male

80 Chronic hepatitis, c/w hepatitis B

8 Hepatitis B not mentioned:

2 c/w viral hepatitis

1 Ground glass hepatocytes

2 Hepatitis E

4 no mention of virus

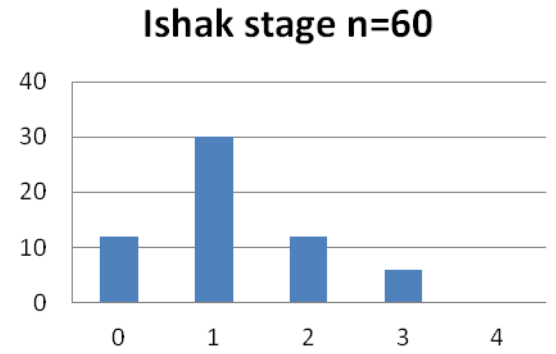
0 No comment on fibrosis

24 – text comment on fibrosis

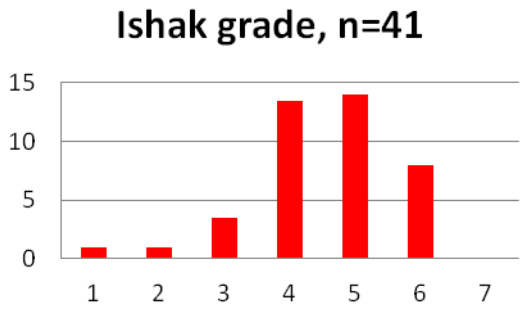
7 no comment on grade

33 text comment on activity grade:

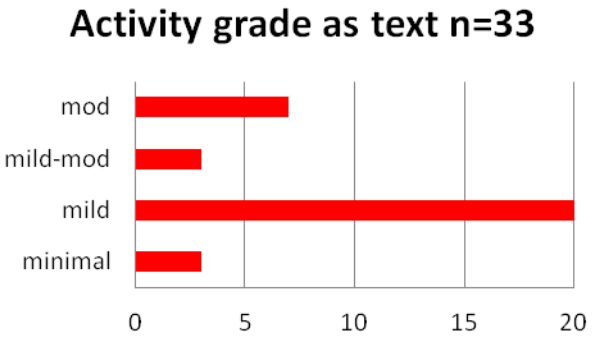
Suggested scoring: for 10 points need Hepatitis B and comment on stage/grade Agreed at meeting.



24 used descriptive text for fibrosis



Metavir: F1 = 4, A1=3



Case I1/427
Age 56, Female

MTX therapy. Increased LFTs.
Ultrasound scan indicates fatty change/fibrosis
? Cirrhosis

Two pale yellow cores measuring 17mm and 15mm.

(no special stains)

427

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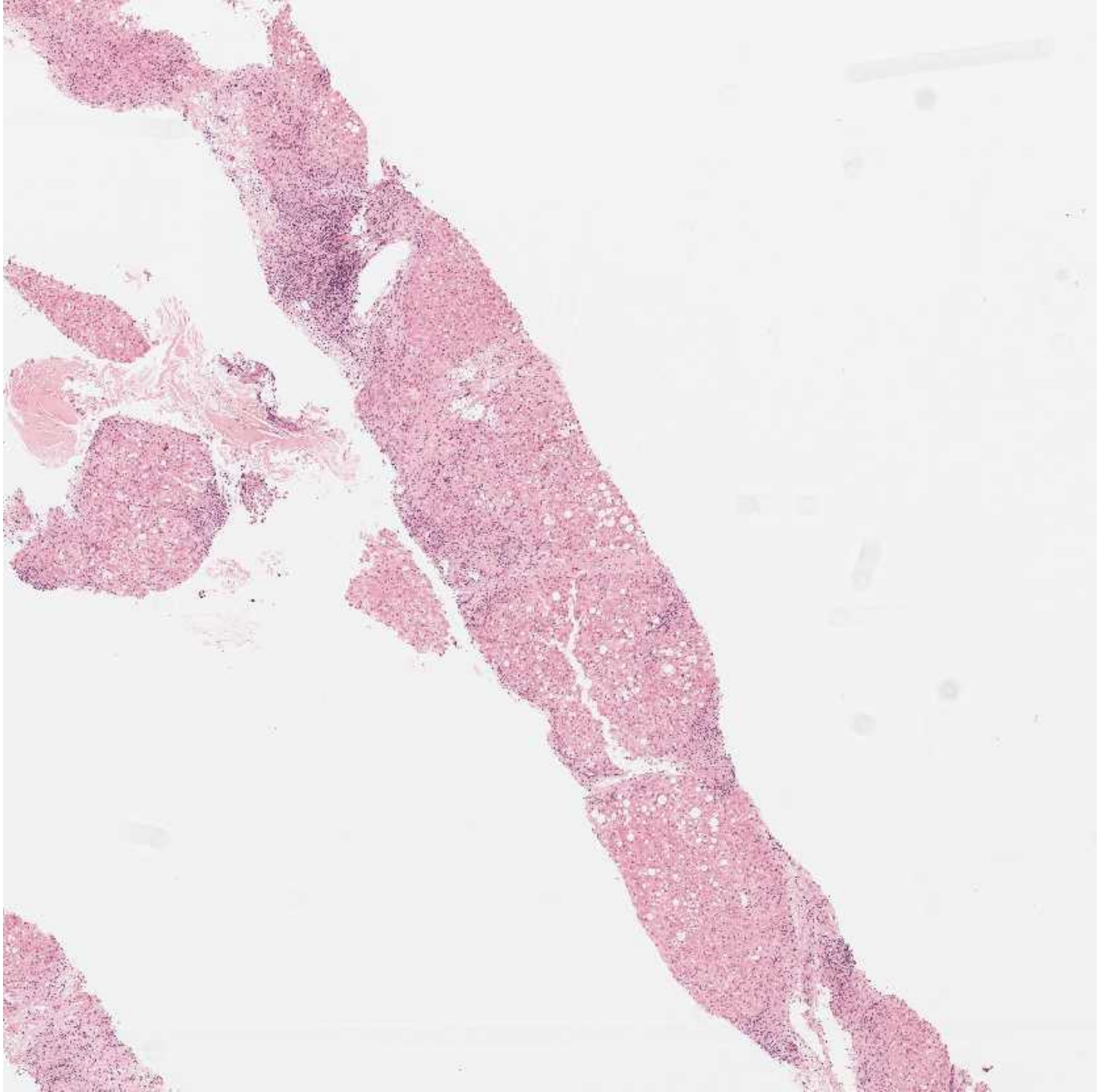

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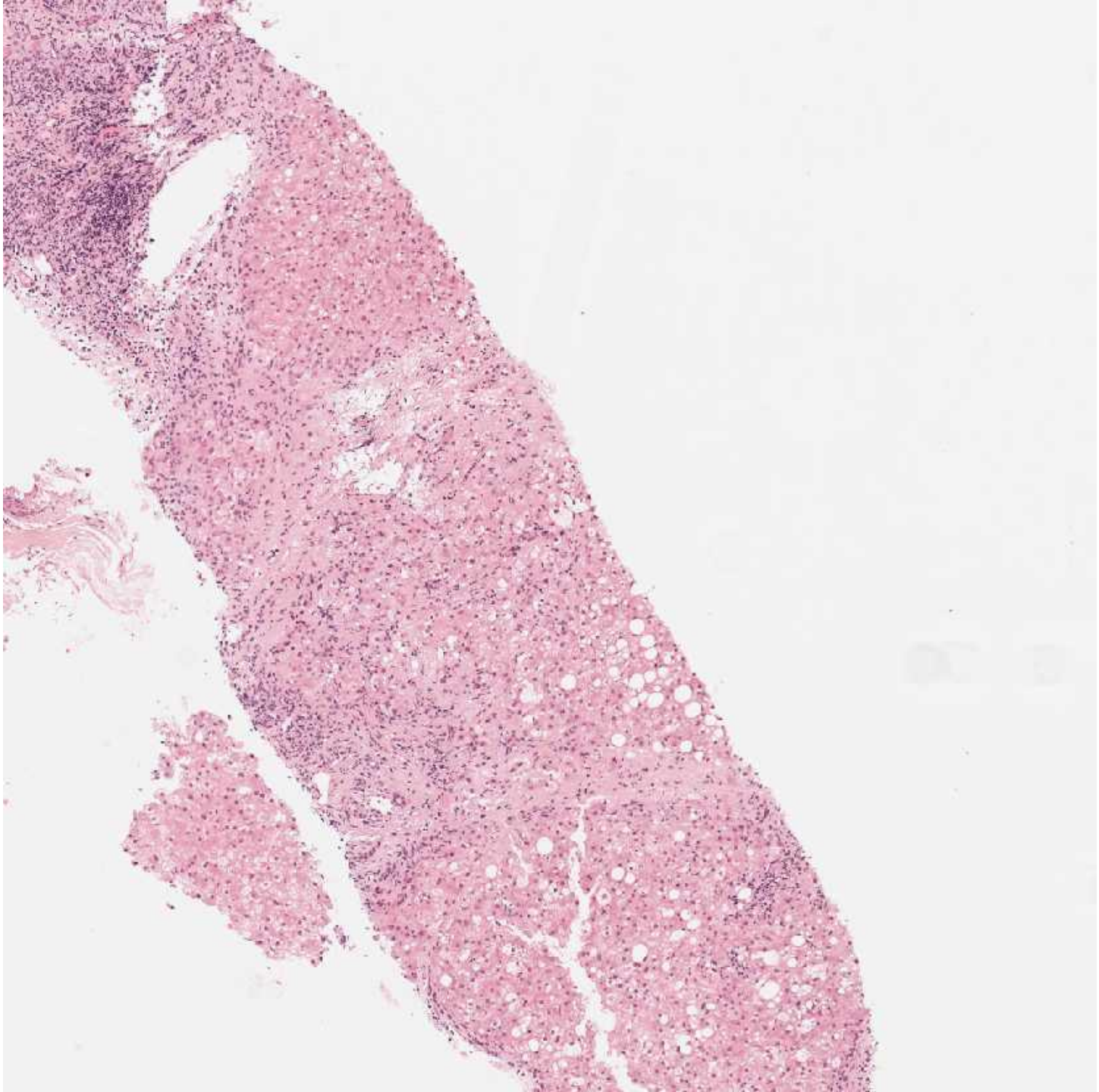

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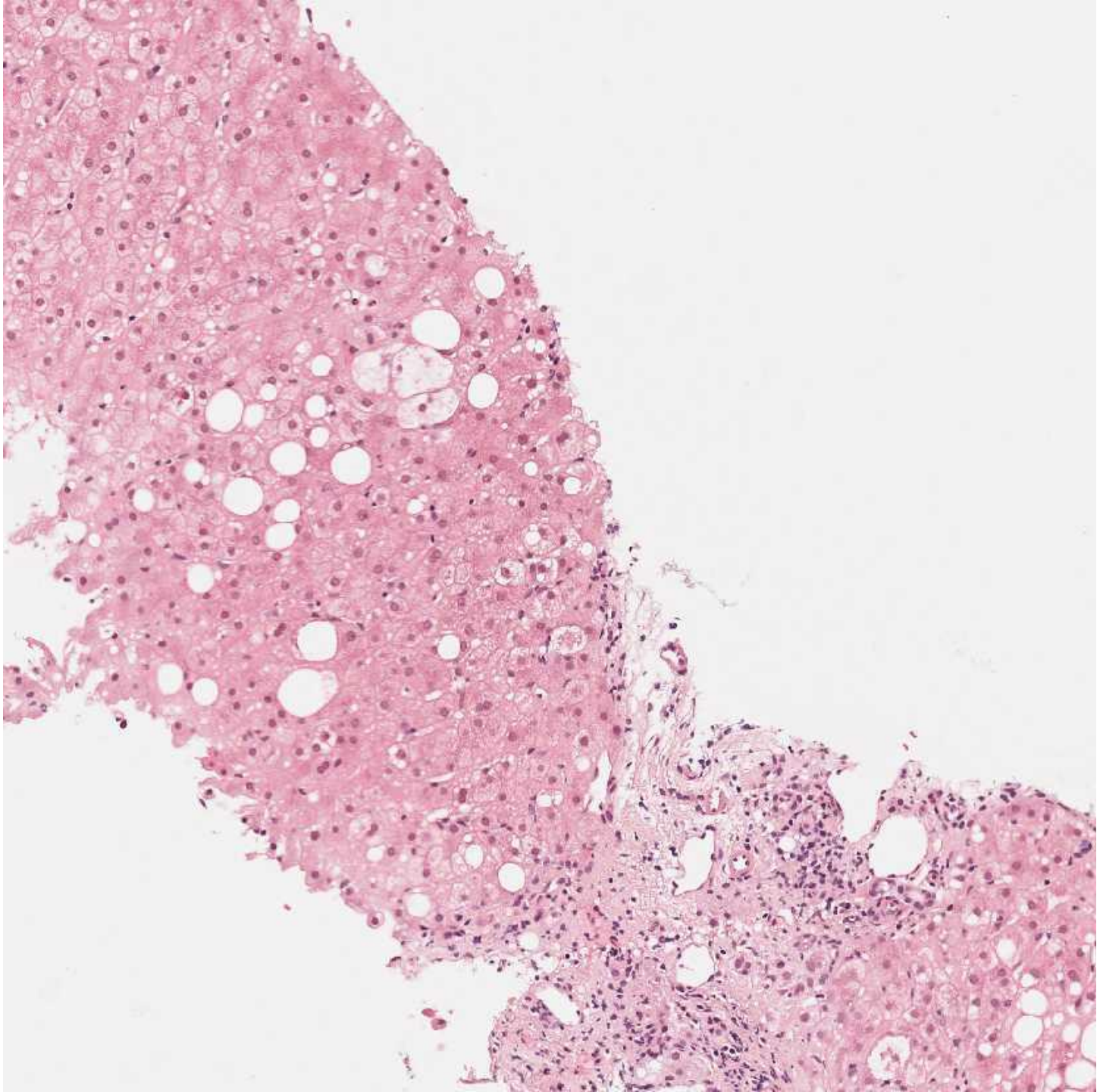

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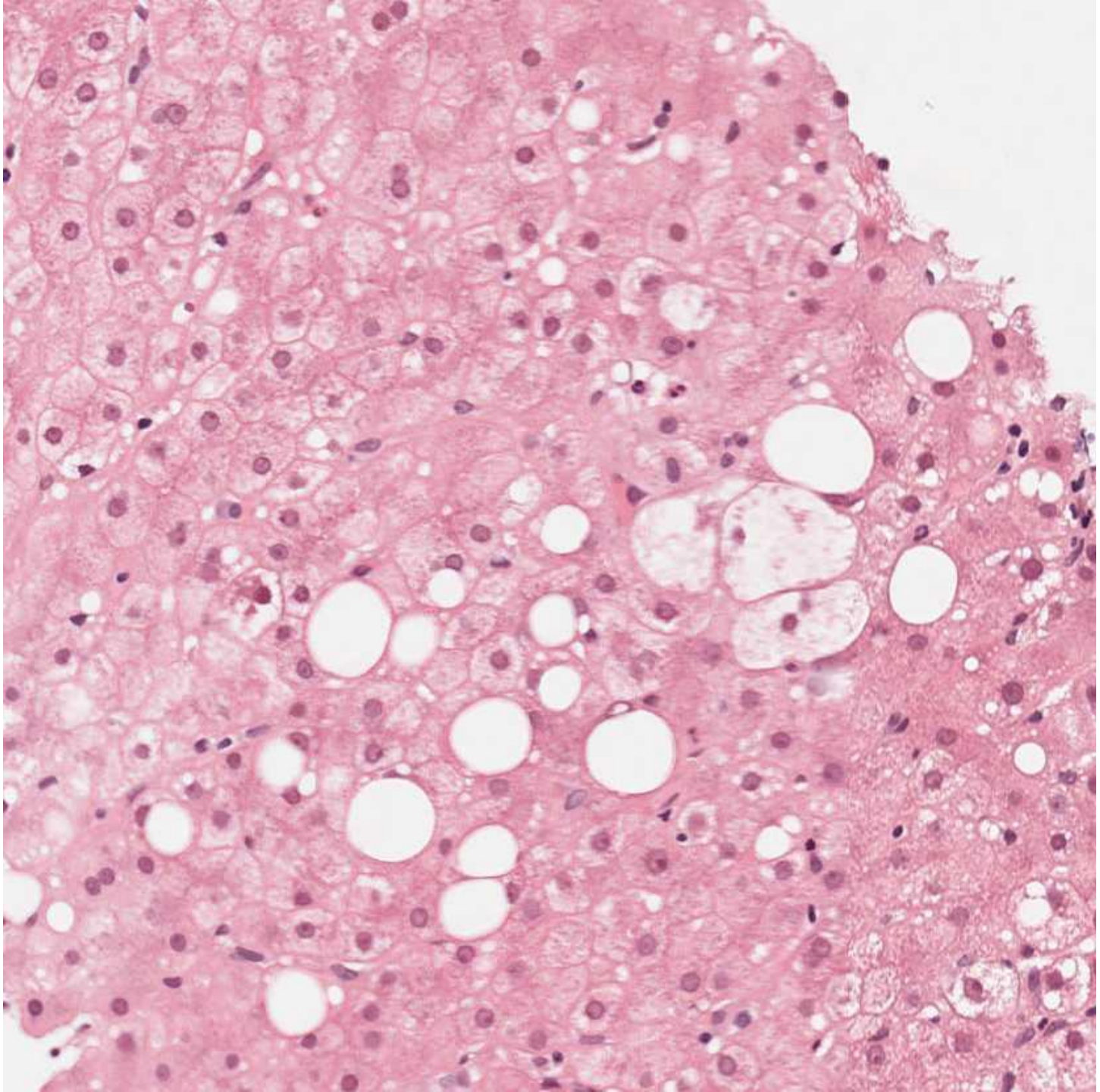

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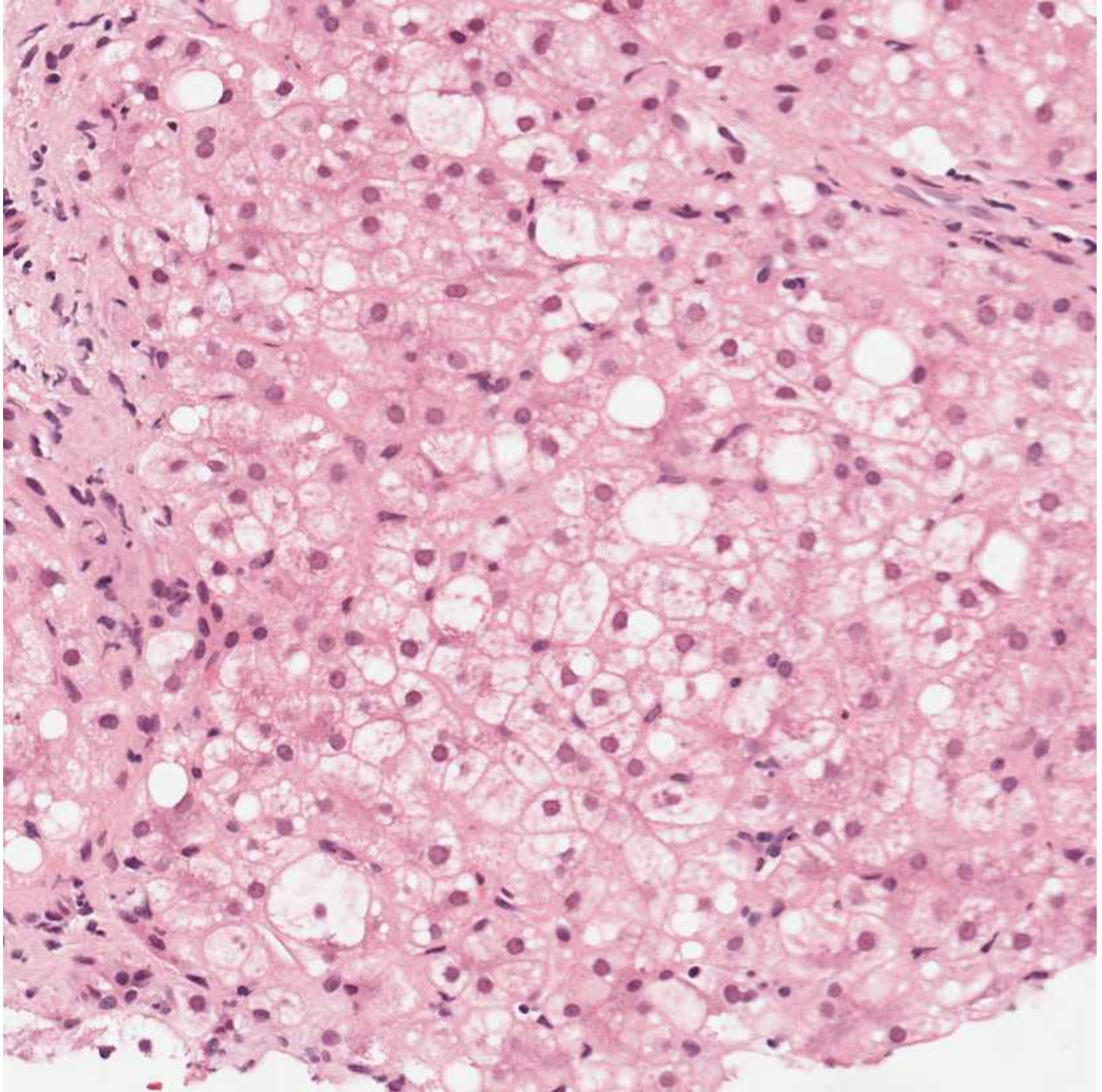


Case I1/427 Age 56, Female

Morphology

73 cirrhosis
12 developing/incipient cirrhosis
3 Needs stains for staging

67 steatohepatitis
13 steatosis
1 cirrhosis with CAH, mild fatty change

5 no mention of fatty liver disease:-
1 chronic active hepatitis
1 mildly active chronic hepatitis
1 CAH 9/18 stage 5 c/w MTX differential viral, alc, AIH
1 chronic hepatitis, fibrosis, possibly drug related, cannot exclude biliary disease
1 'cirrhosis due to methotrexate'

Clinico-path

52 alcohol/NAFLD
49 methotrexate as co-factor
21 methotrexate only
11 methotrexate not mentioned
1 multifactorial aetiology
5 no cause suggested
1 cause not mentioned but 'stop methotrexate'
1 'exclude drug (eosinophils)'
1 'cirrhosis, probably alcohol abuse or drug induced'
1 'active cirrhosis, drug induced, methotrexate'
1 no cause 'need more history'

Suggested scoring: Suitable for scoring? Score 0 if implies that the disease process is not some form of fatty liver disease. Insufficient consensus on clinico-path for scoring. Suggested scoring agreed at meeting.

Case I1/427 Age 56, Female

Original diagnosis: Cirrhosis, ? Due to methotrexate.

Masterclass presentation by Sue Davies, on liver biopsy in patients on methotrexate:

Methotrexate

- Antimetabolite, folate antagonist;
  - Anti-neoplastic - initially used in treatment of leukaemia and solid organ cancers (1950s)
  - Anti-inflammatory - 70s in psoriasis, RA in late 80s
- Common side effects; skin, GIT, bone marrow
- Dose related – acute injury (ALT x10-20) with hi IVD, occ J or hepatitis

Methotrexate – toxicity with chronic use recognised in 70s

- Fat, inflammation, anisonucleosis, fibrosis & cirrhosis
- Risk of fibrosis: cumulative dose (>2-4g)
  - Rate of administration – (daily, low dose worse than weekly)
  - Chronic alcohol ingestion
  - Factors associated with NAFLD (obesity, DM)
- Large individual variation

Abnormal LFTs

- Reported 15-50% have rapid raised ALT
- ~5% significant (> x2ULN) – resolves with stopping, lowering drug or even continuing!
- Folic acid use decreases the abnormalities
- Asymptomatic fibrosis, ALT is poor predictor of fibrosis; severe fibrosis and cirrhosis with N ALT
- No immuno-allergic features

? Guidelines

- BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the BAD. Chakravarty et al Rheumatology 2008.
- Typical dose of MTX is 7.5-25mg per wk; possible toxicity related to cumulative doses > 1.5g
- Normal scans and LFTS are possible with significant fibrosis

Further advice

- Alcohol < 4-6 units per wk (not use in abusers)
- Serum pro-collagen III amino-terminal peptide monitoring useful.
- RA – rare significant liver disease – biopsy not useful in 1st 10yrs with low dose.
- Psoriasis – bx more commonly indicated (abN PIIINP) or H/O pre-existing liver disease.

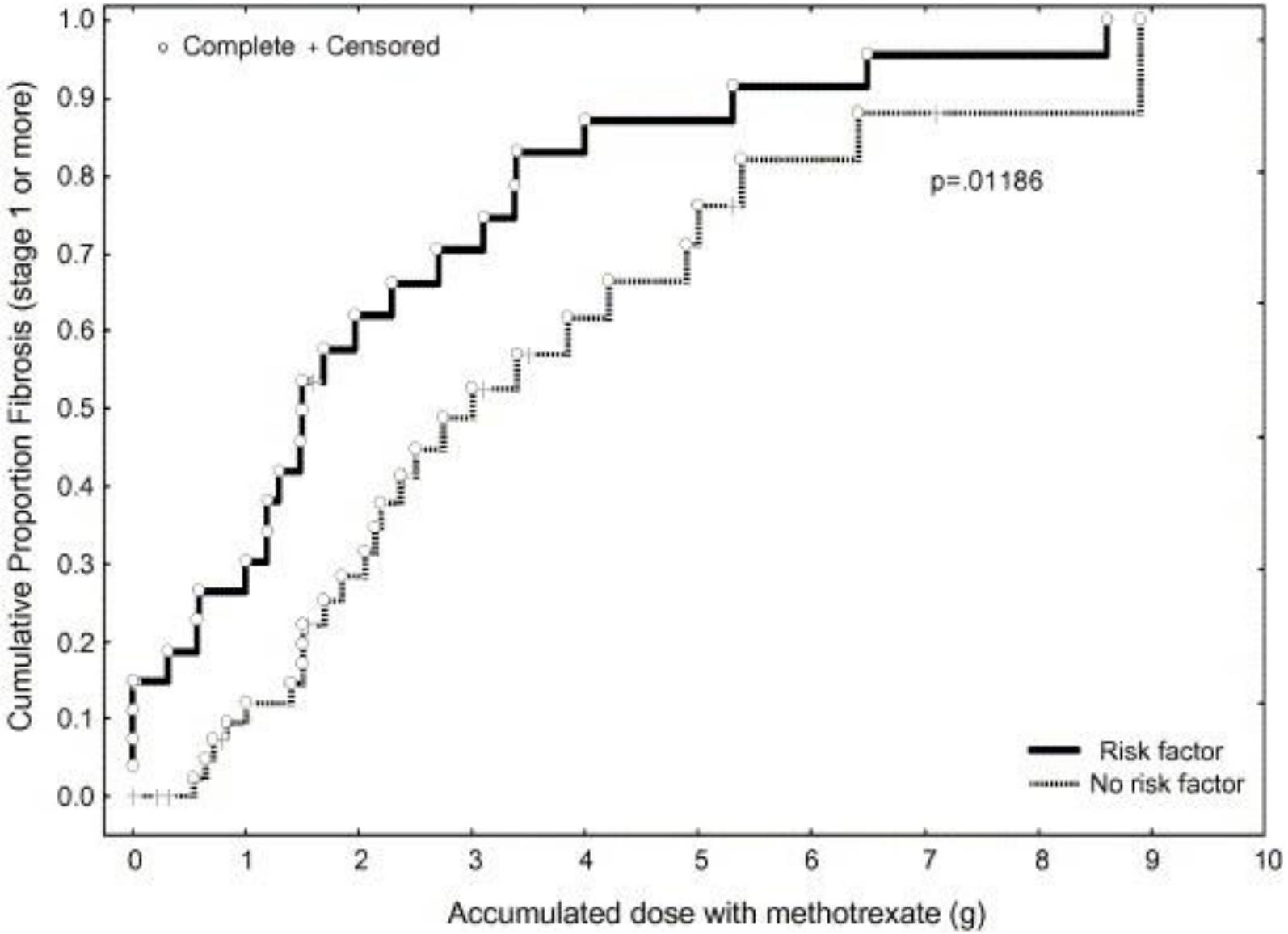
Psoriasis & NAFLD

- Both associated with cardiovascular disease and metabolic syndrome
- Prevalence of NAFLD in patients with chronic plaque psoriasis ~ 60%c.f. 20% in general Italian population.
- ~50% when compared with matched controls (inc BMI) and related to psoriatic disease activity.

Psoriasis patients with diabetes type 2 are at high risk of developing liver fibrosis during methotrexate treatment

- Rosenberg et al J Hepatol 2007
- 71 Pts (169 biopsies) on MTX monitoring
- 96% of cases with 1+ risk factors had fibrosis (mean dose 1.5g) c.f. 58% without (mean dose of 2.1g)

Case 427: Sue Davies: Masterclass: Methotrexate hepatotoxicity



? Risk of Fibrosis

- Literature Review – meta-analysis of 23 studies from 1980 - 2010 in MTX in psoriasis
  Montaudie 2011
- Unable to quantify risk of fibrosis
- Different regimens, time of assessmnet and exclusion of other factors.
- DM & obesity significantly associated , more modest with HCV, HBV & not with alcohol
- Fibrotest , fibroscans and procollagen III aminopepetide important monitors.

Conclusion

- The pattern of fibrosis associated with MTX is expanding.
- Other risk factors, commonly associated with plaque psoriasis, contribute to NAFLD and NASH.
- MTX appears to accelerate this disease process.
- Overall rate and risk of fibrosis for an individual is not clear.

Rare incidence of methotrexate-specific lesions in liver biopsy of patients with arthritis and elevated liver enzymes.

- Quintin et al Arthritis Research & Therapy 2010
- Study 1,571 arthritis long-term low-dose MTX: 41 persistent abN LFTs c.f. disease controls
- Biopsies - 17 AIH-like, 13 NASH -like lesions, 7 – NSRH (without fibrosis), 2- PBC.
- Only 2 MTX-specific lesions with anisonucleosis & PSF.

Case I1/428

Age 64, Female

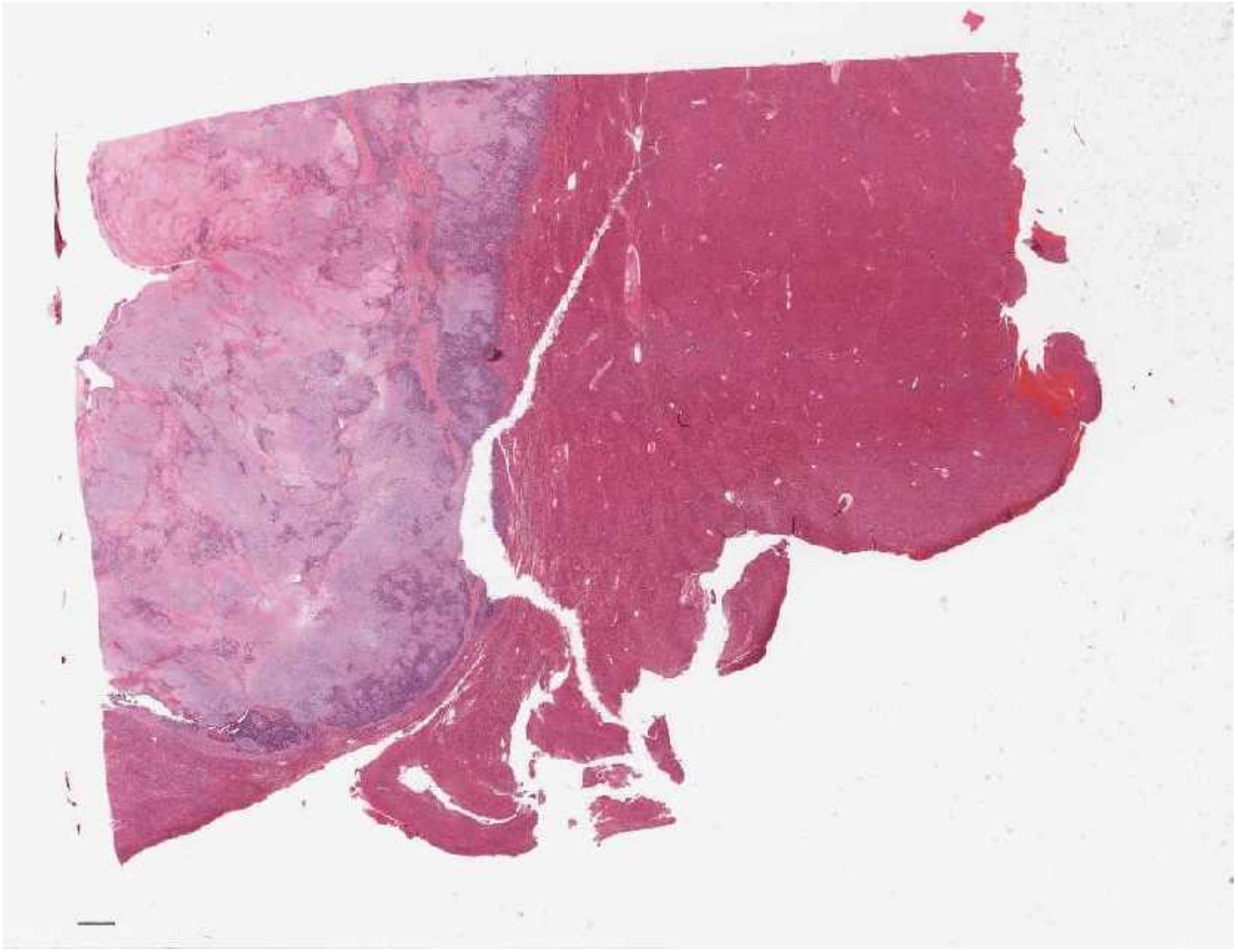
Recurrent ovarian tumour + liver;

right lobe R1 resection

Liver measuring 11 x 8 x 6cm, attached to a irregular mass of tumour 16 x 11 x 5 cm,

together weighing 553g;

428



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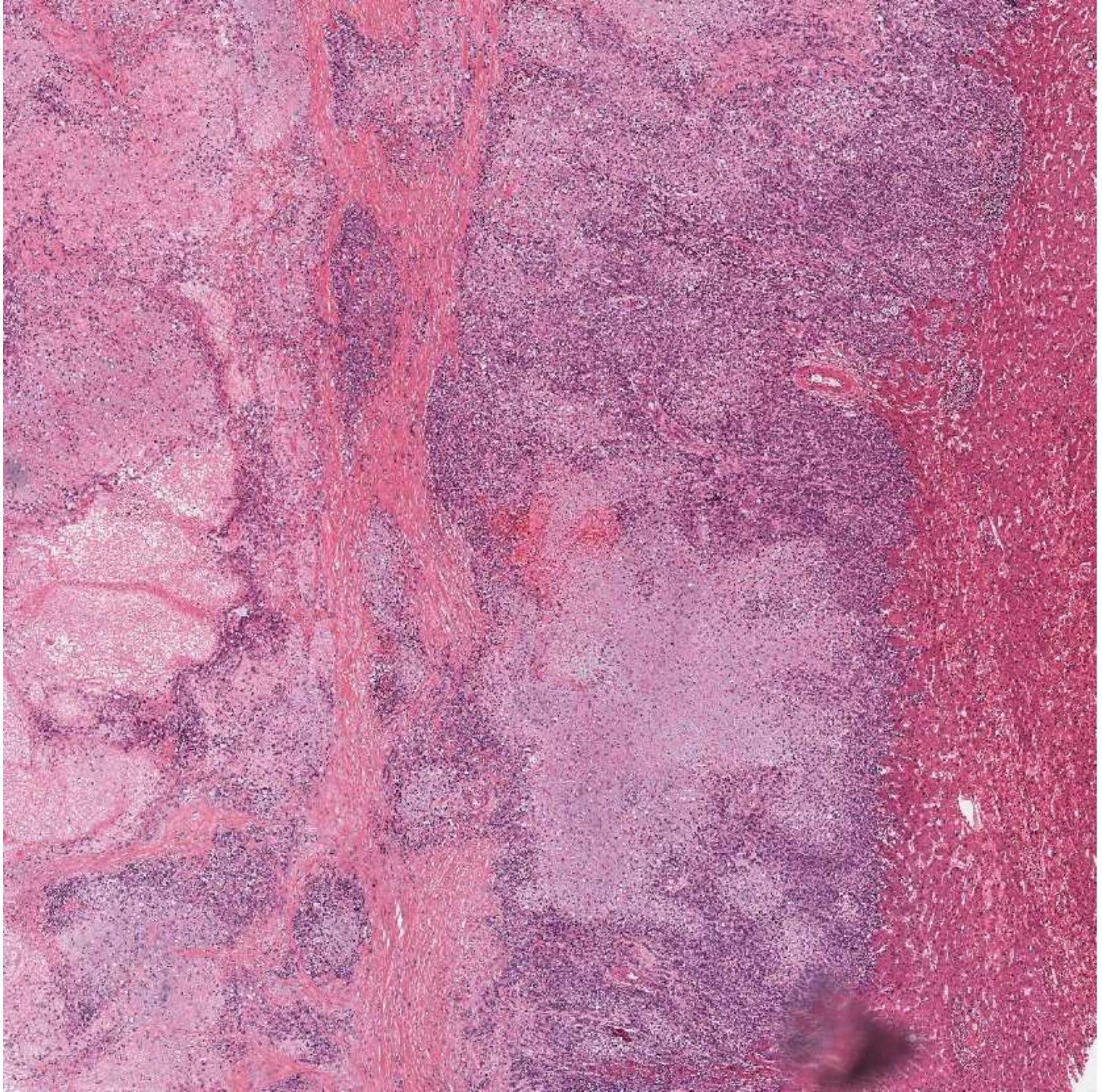

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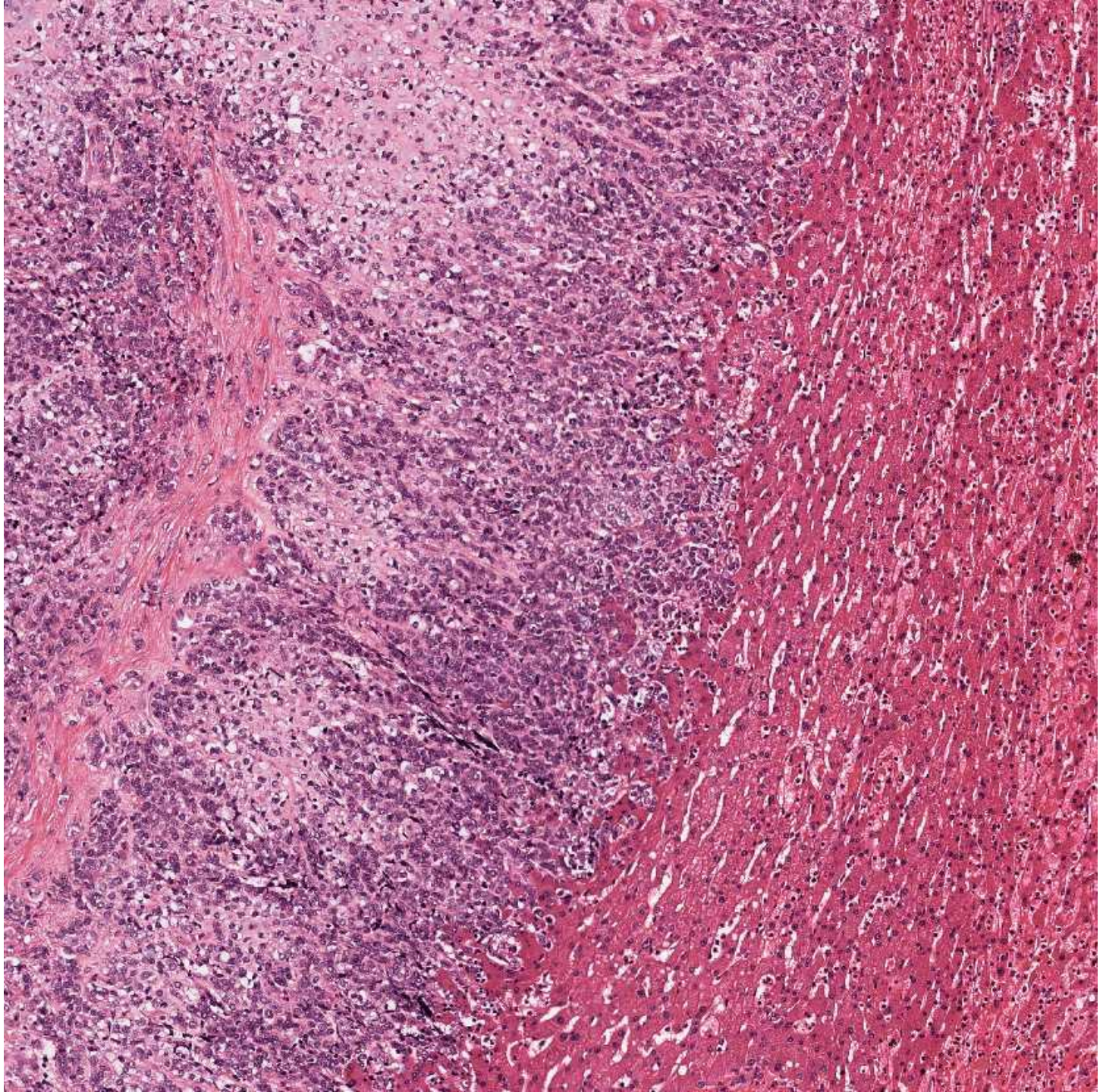

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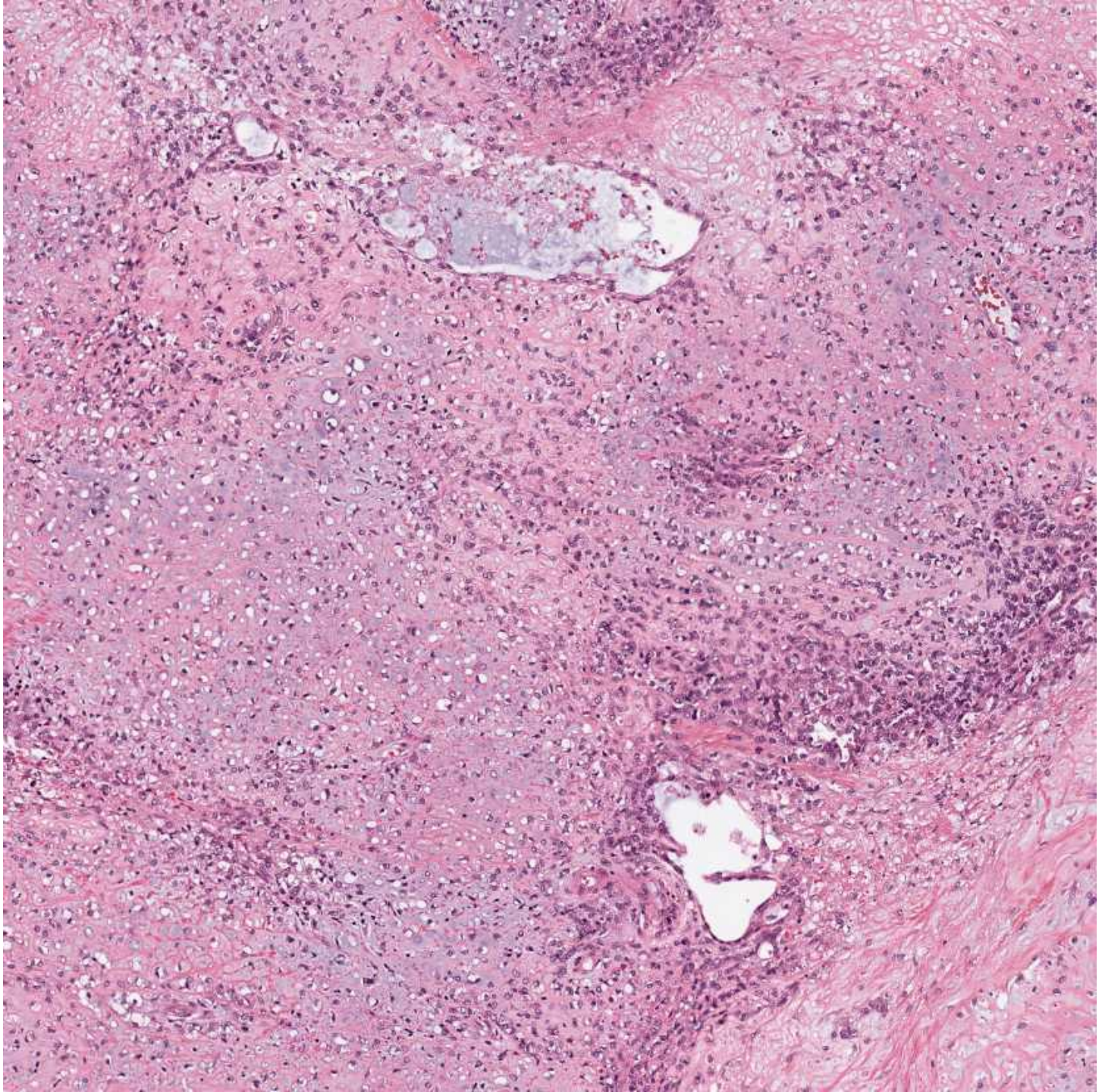

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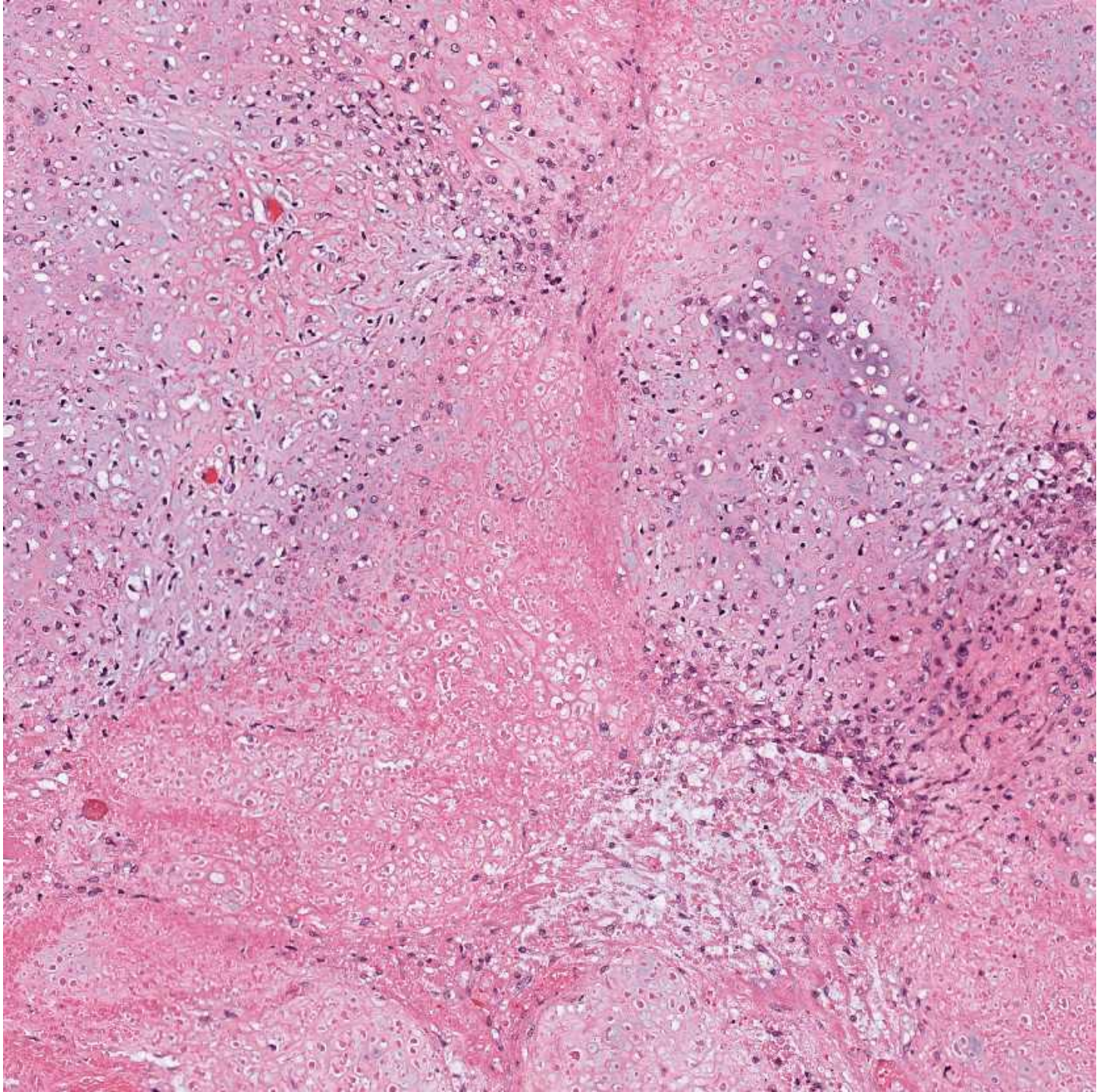

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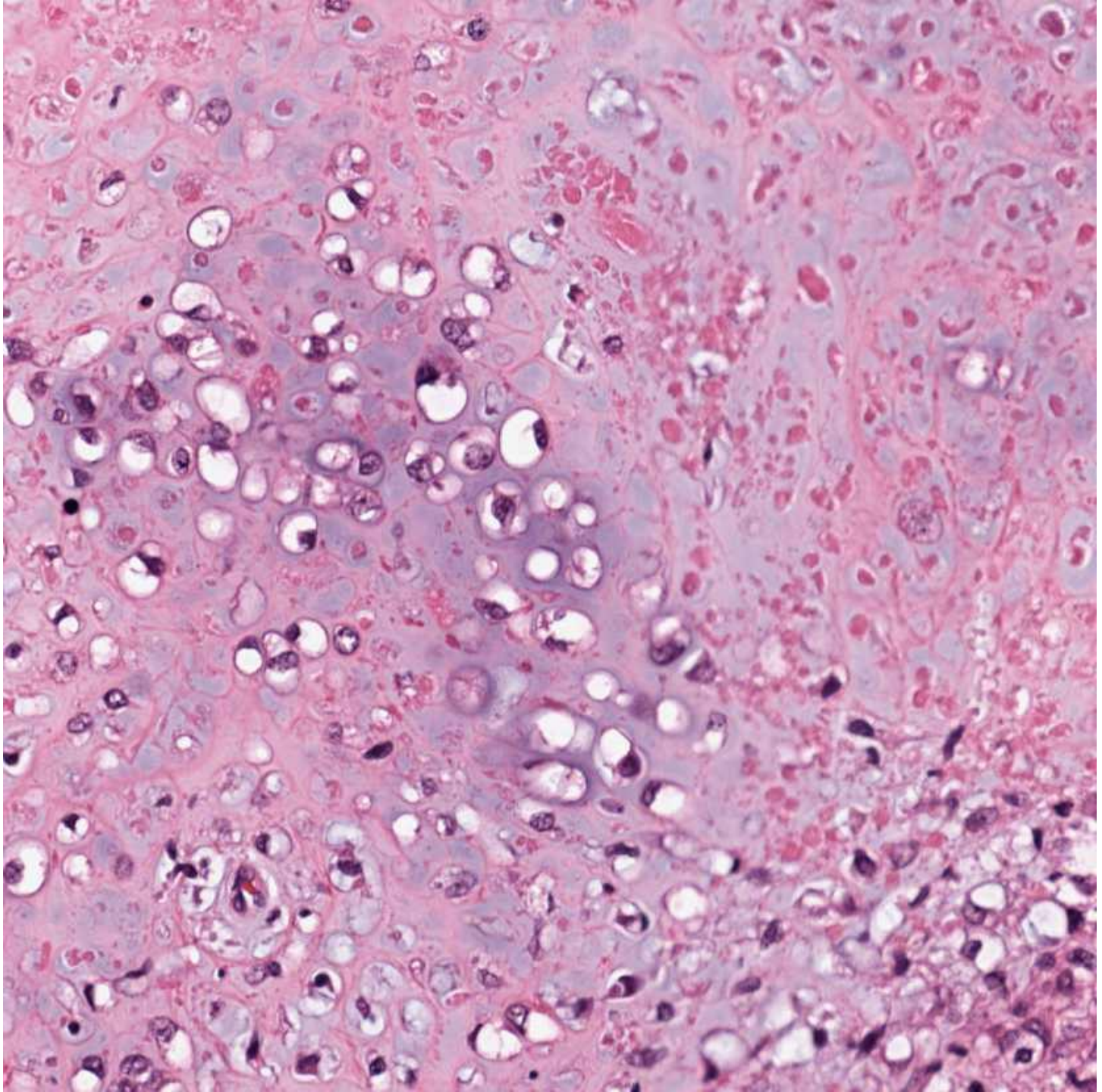


428

Case I1/428 Age 64, Female

86 Chondrosarcomatous elements

2 Chondroid differentiation not mentioned

(9 - ? Mixed up with case 431)

85 Consistent with metastasis from ovary, if the original tumour was malignant Mullerian or teratoma

2 Chondrosarcoma NOS – no mention of the ovary

1 Metastatic granulosa cell tumour with therapeutic embolisation

Suggested scoring: for 10 points – need to include chondroid tumour and consistent with ovarian metastasis as long as an appropriate primary tumour

Scoring agreed at meeting

Case I1/428 Age 64, Female

Original diagnosis: secondary carcinosarcoma

(with chondrosarcoma predominating) from ovarian primary. Original tumour confirmed at subsequent MDT meeting.

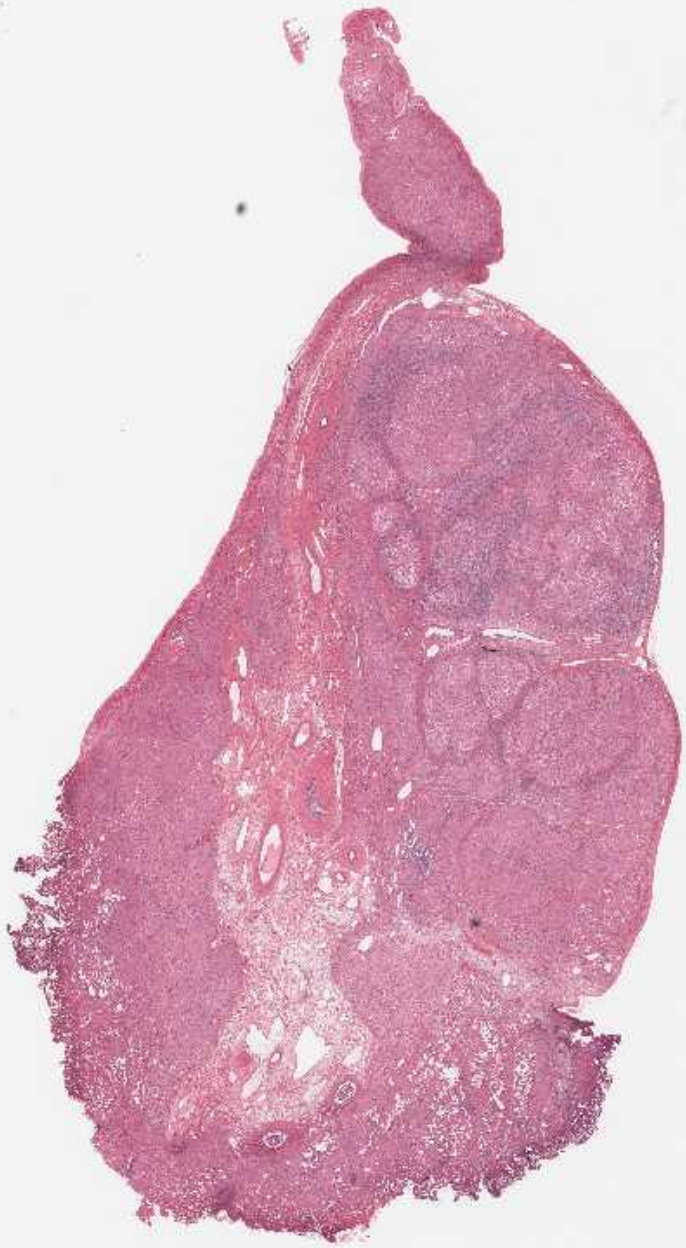
Case I1/429

Age 60, Female

GIST tumour stomach,
lesion noted in liver and resected

Wedge of liver 2.2x2x1.1cm

429



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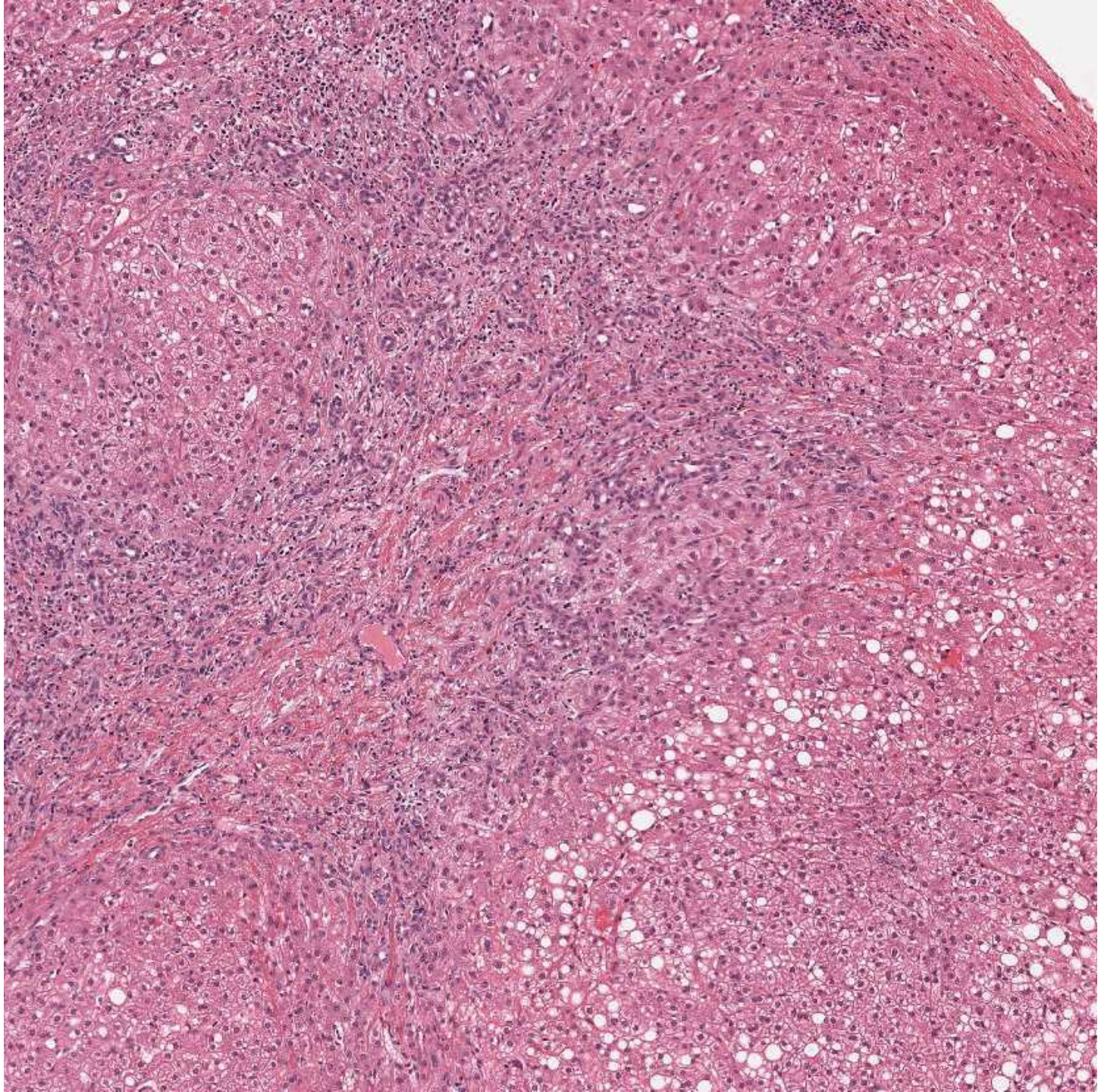

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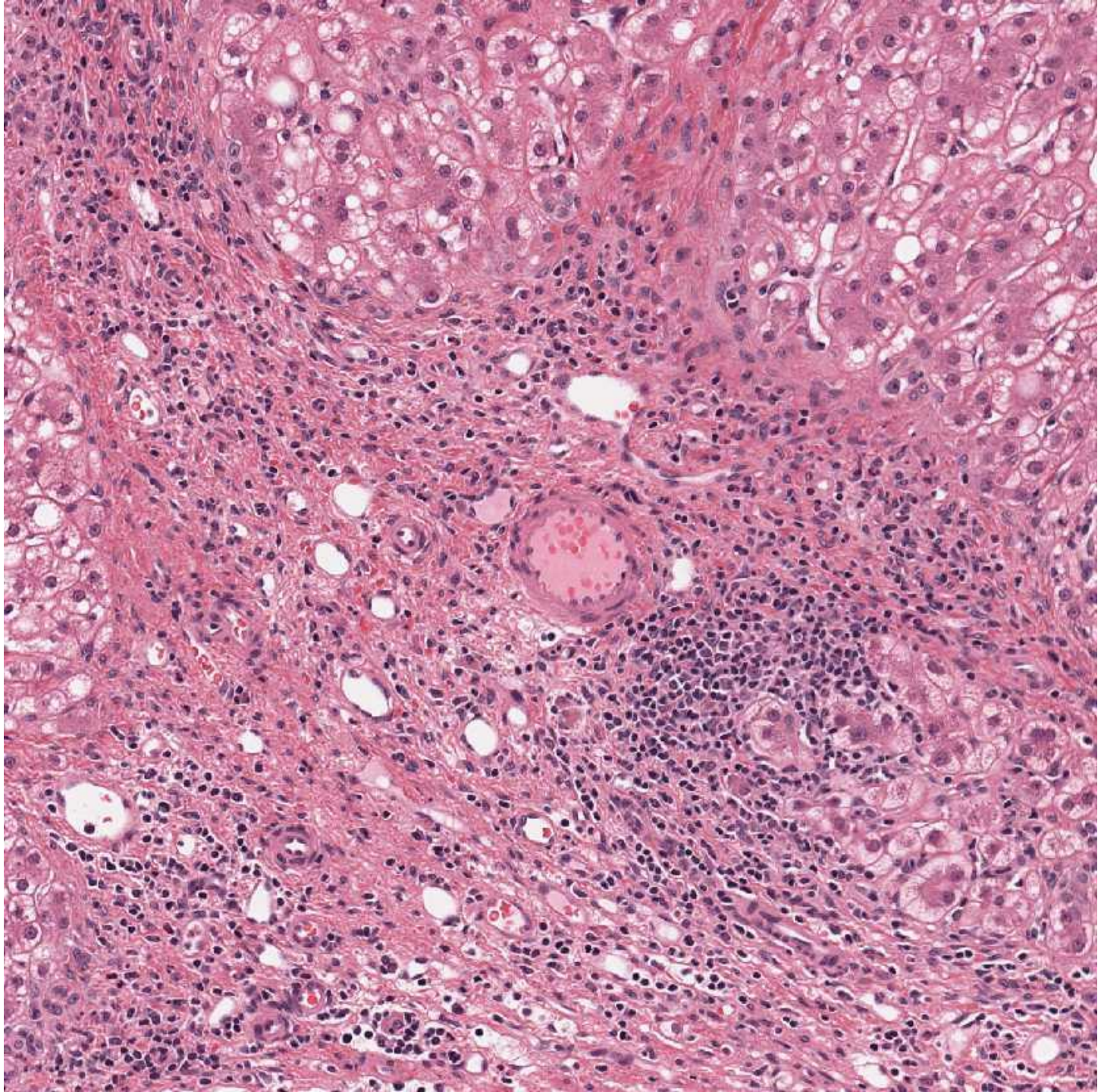

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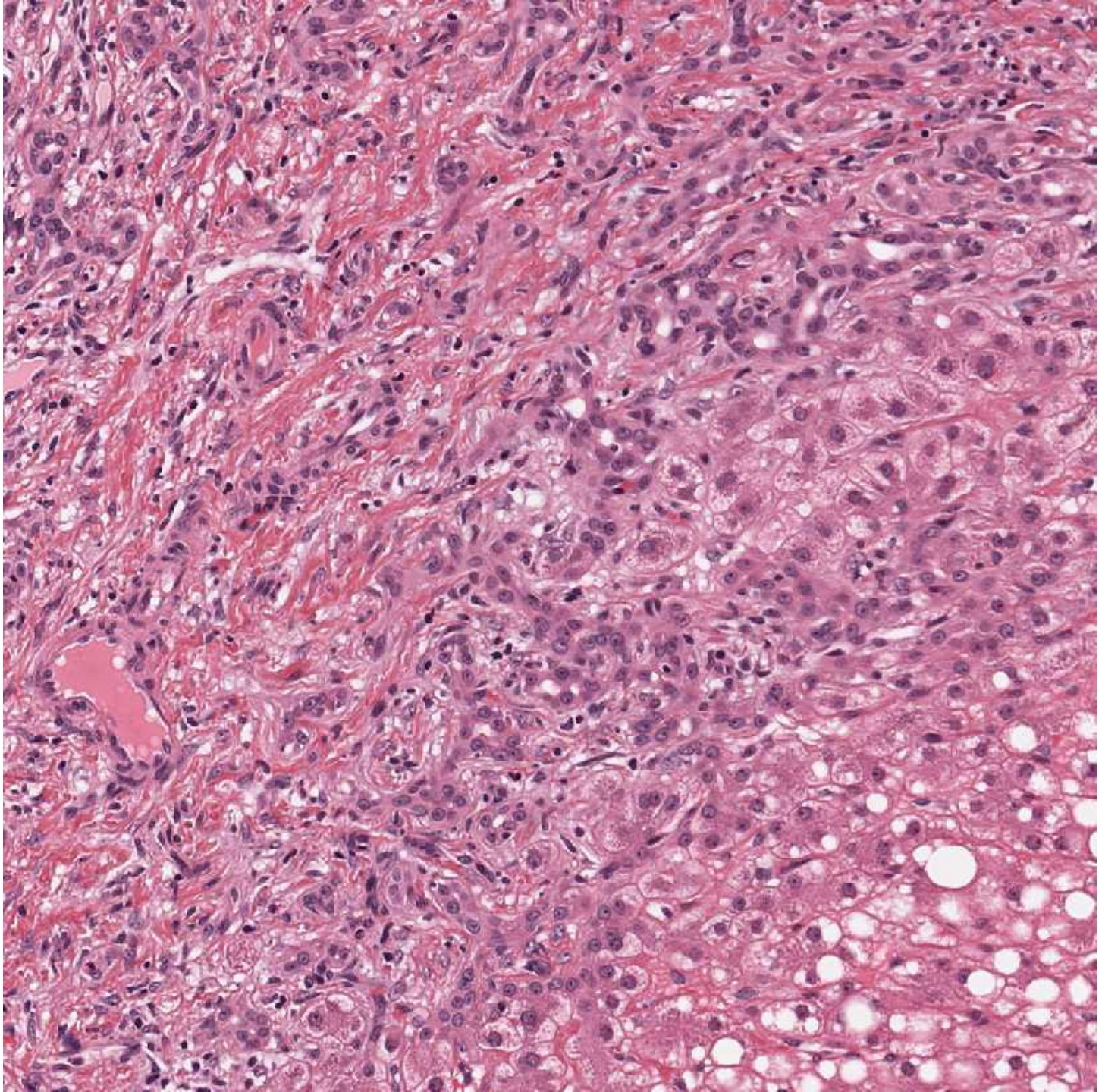

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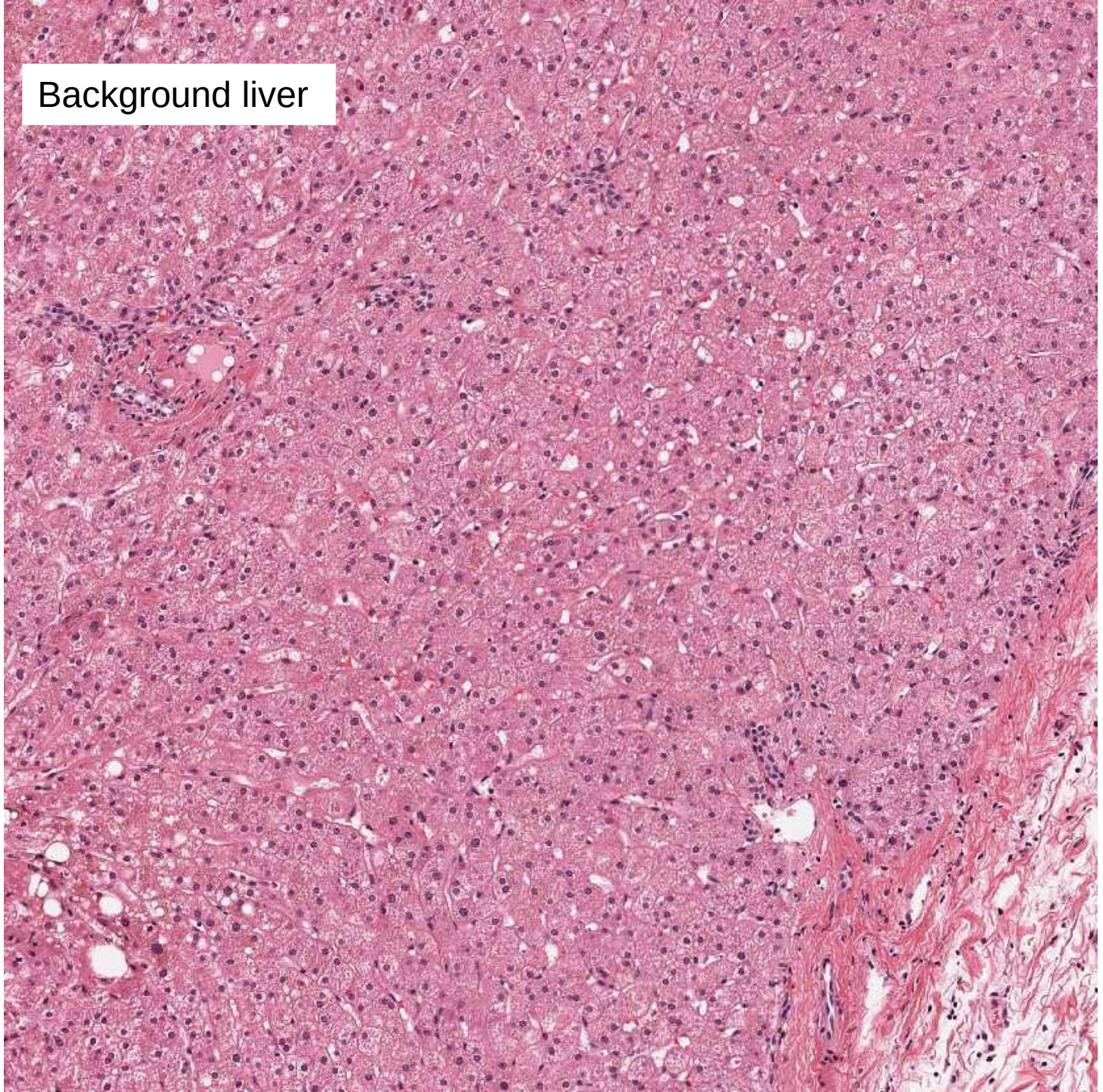


Case I1/429 Age 60, Female

84 Focal nodular hyperplasia

1 FNH – exclude adenoma (GS, CRP, SAA, LFABP)

1 Haemangioma ?? FNH, possibly treated GIST with regression

1 'Focal cirrhosis – focal nodular regenerative hyperplasia'

1 Cirrhosis, steatohepatitis, no tumour

59 Commented that there is no evidence of GIST/malignancy

29 No comment on no evidence of GIST/malignancy

Suggested scoring: Score 10 points for FNH,
5 points for FNH with differential of adenoma,
0 points for other diagnoses
Scoring agreed at meeting.

Case I1/429 Age 60, Female

Original diagnosis: focal nodular hyperplasia.

Comment: It is good practice to include a statement on the absence of recurrent GIST, but insufficient consensus to include this in the scoring.

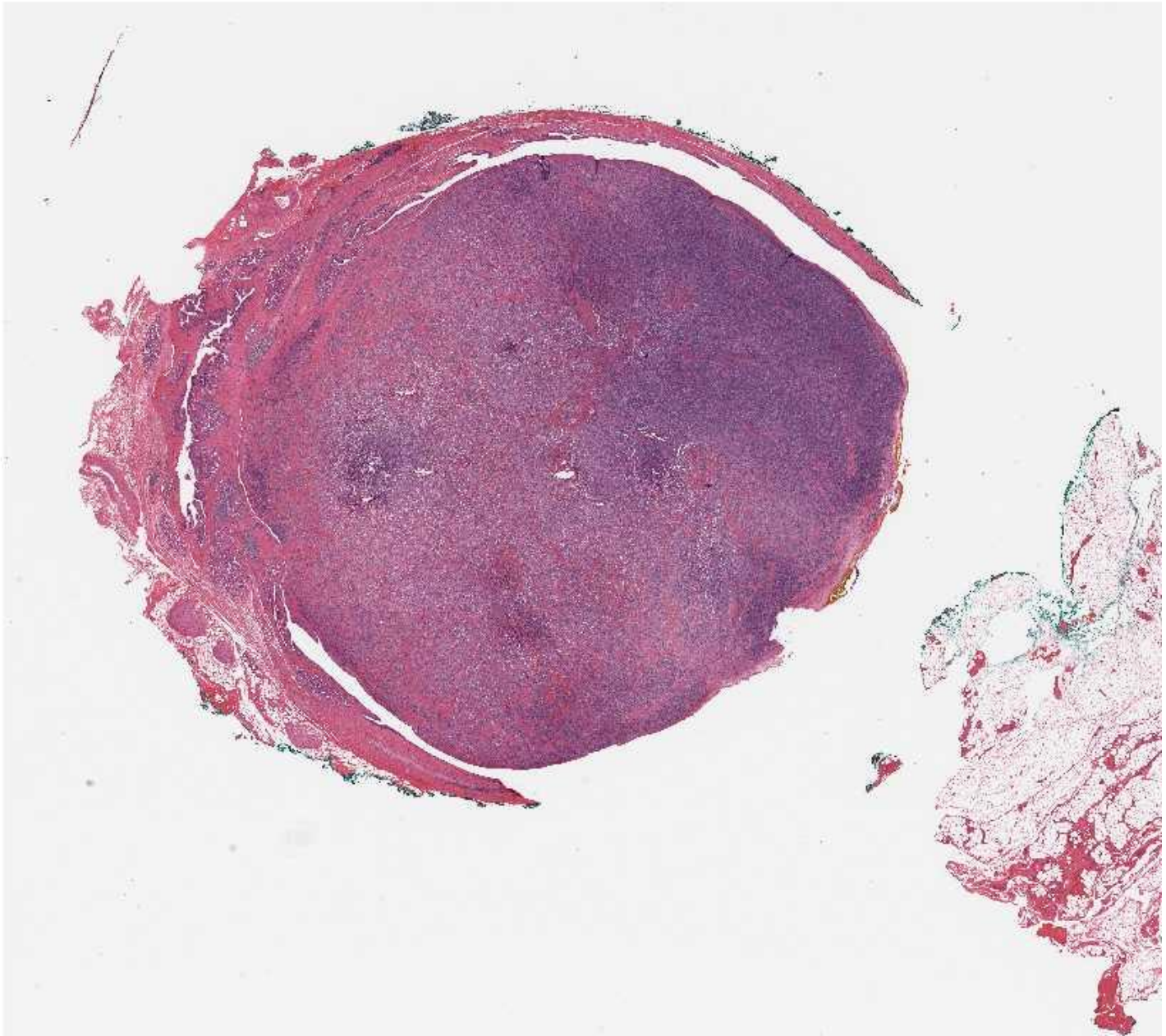
Case I1/430

Age 70, Male

Tumour mid CBD

27mm segment of bile duct
up to a diameter of 13mm

430



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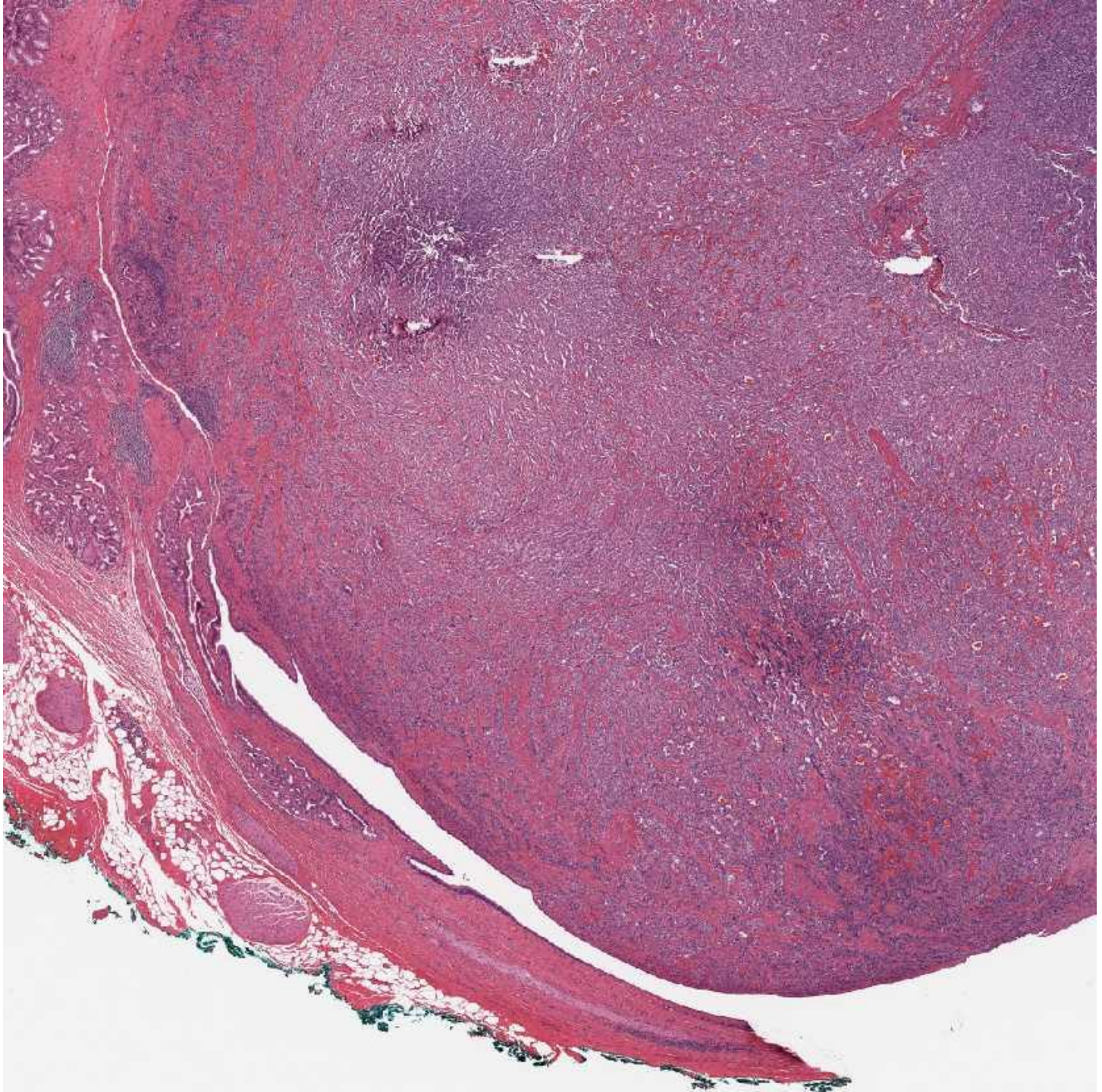

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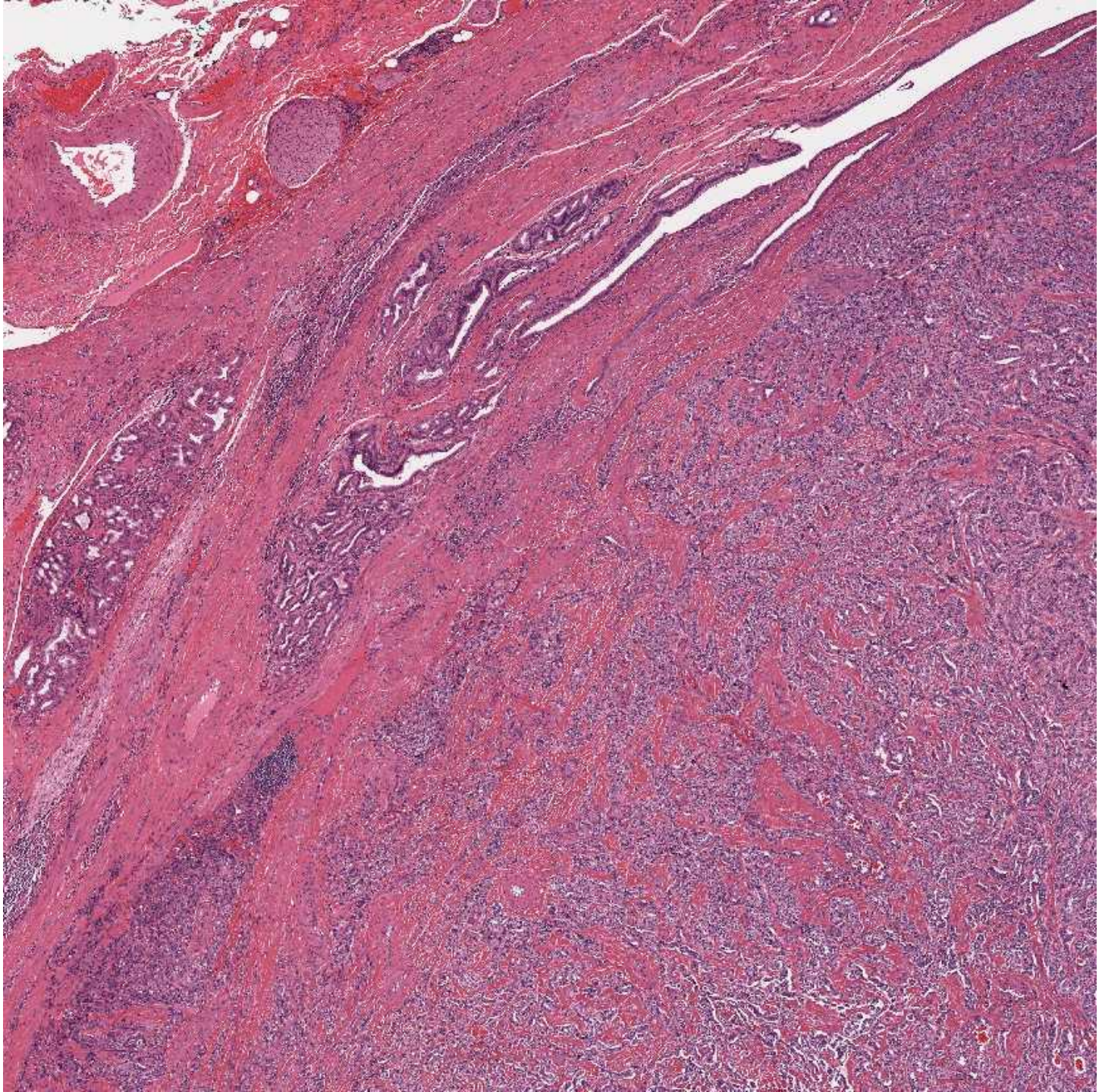

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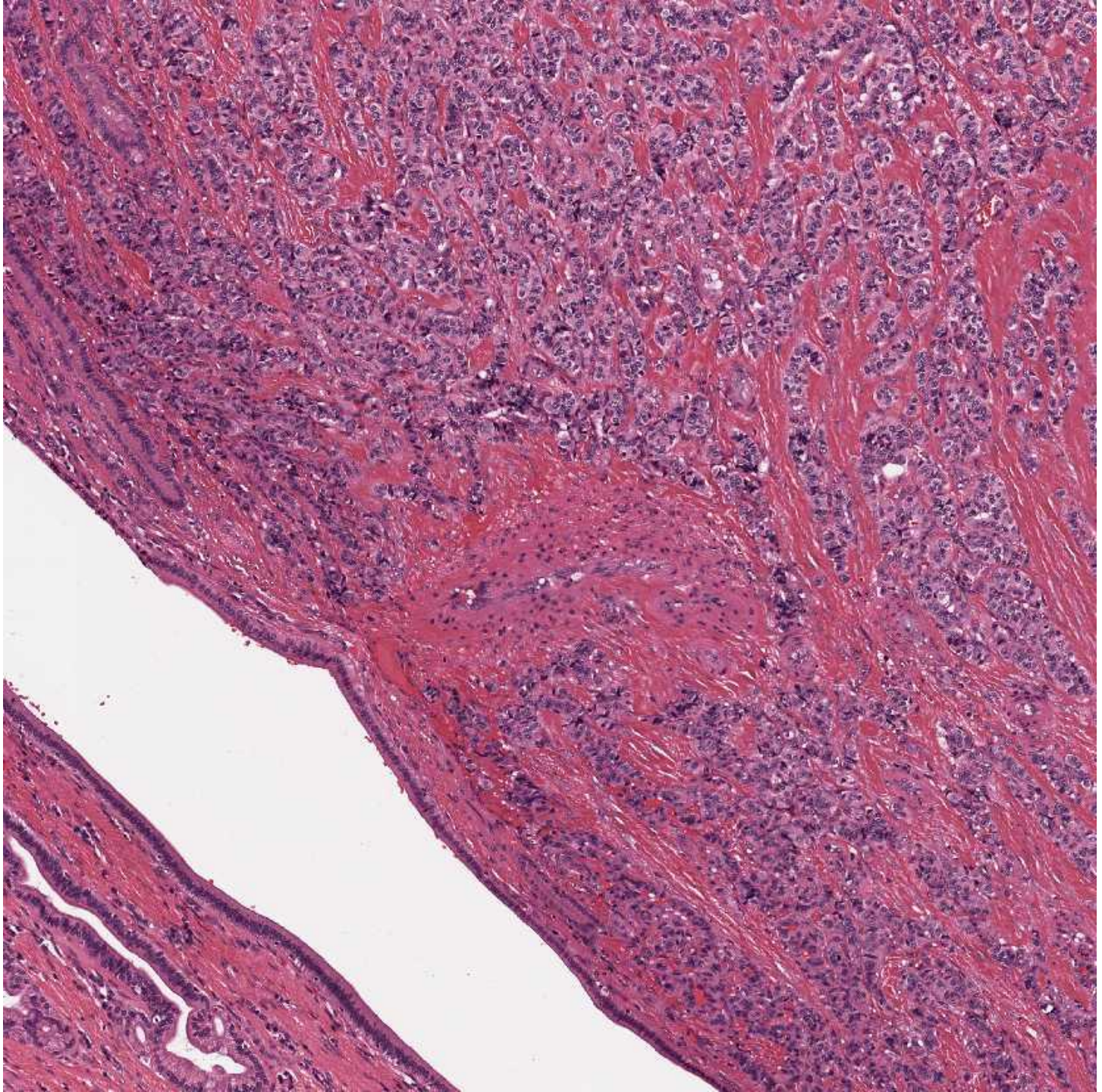

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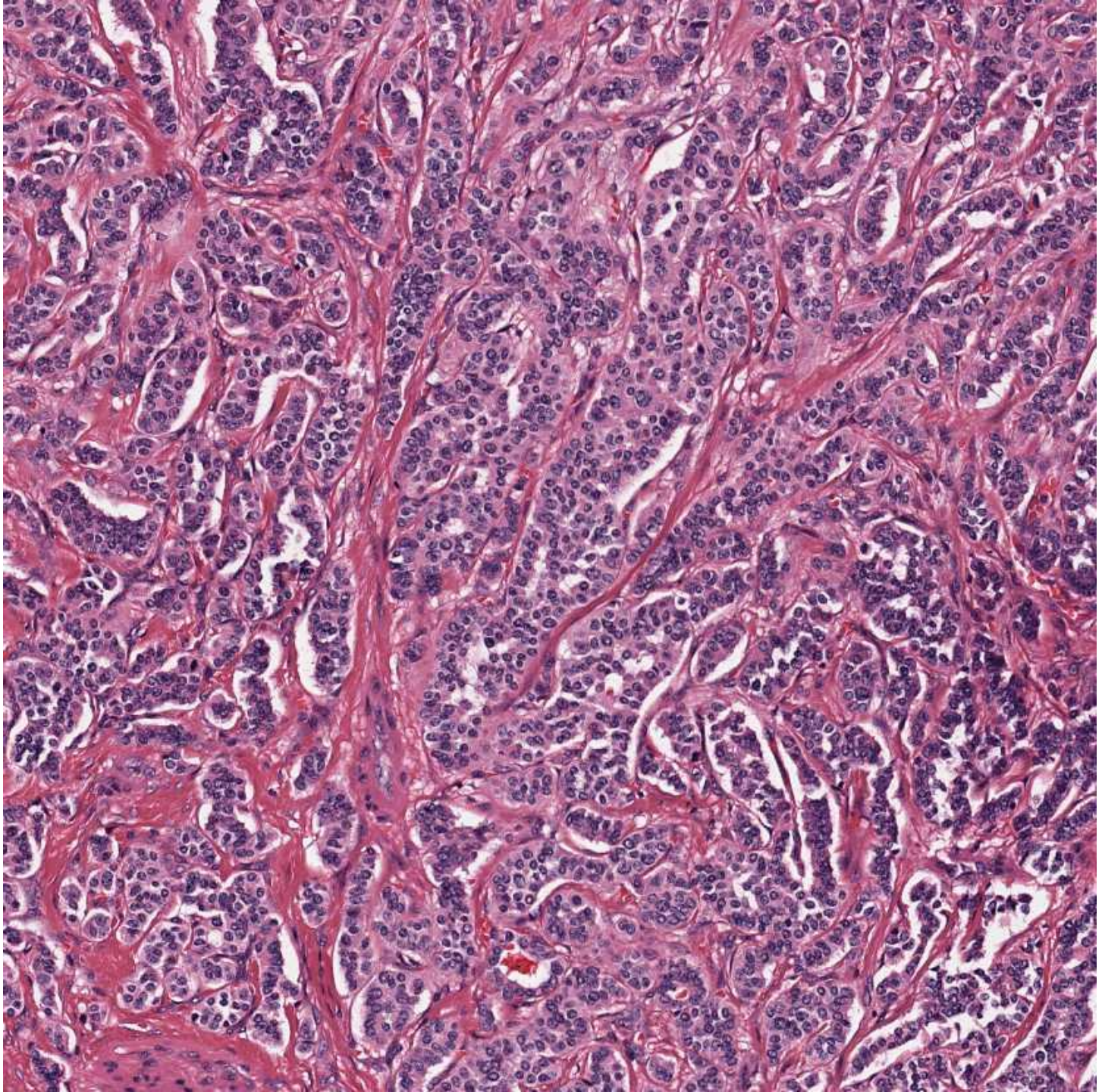

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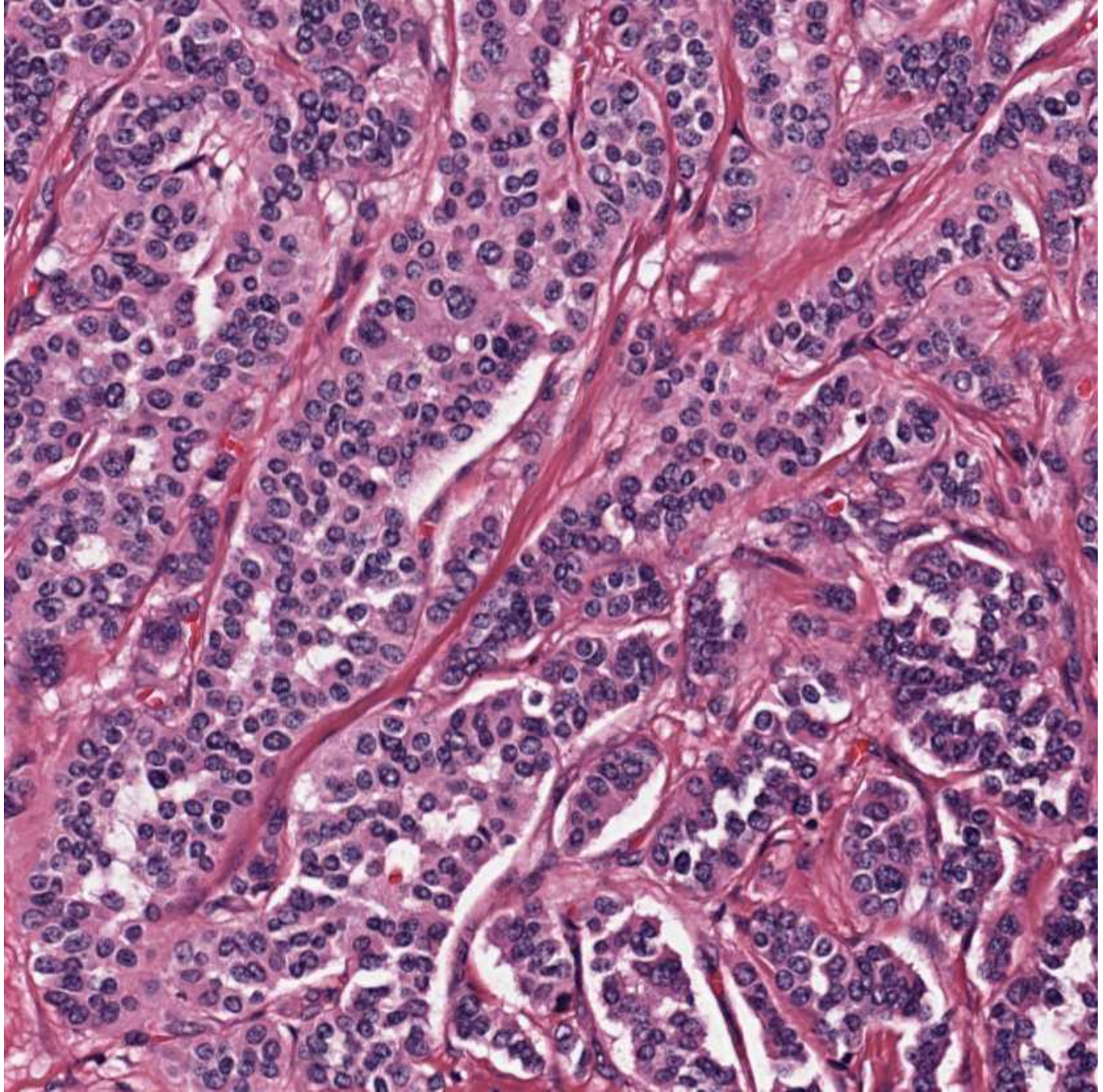


Case I1/430 Age 70, Male

72 Neurendocrine lesion of any terminology:

4 carcinoid

6 neurendocrine neoplasm

58 neurendocrine tumour

4 neurendocrine carcinoma

60 needs immuno confirmation

9 immunos not mentioned

18 could be primary or secondary

1 most likely secondary

1 history of MEN? Unusual site

Other:-

7 cholangiocarcinoma/bile duct Ca

3 cholangioCa – neurendocrine markers needed

1 differential – NET or tubular adenoma (immunos not mentioned)

1 bile duct adenoma

1 intraductal papillary adenoma, no dysplasia

1 intraductal papillary neoplasm of bile duct

1 ? Paraganglioma, needs S100, neurendocrine markers

1 metastatic e.g. germ cell tumour/yolk sac tumour

Suggested scoring: score 10 points for any response of neurendocrine lesion (for discussion – appropriate terminology). Score 5 points for cholangioCa, neurendocrine markers needed. Other responses score 0 Scoring agreed at meeting.

Case I1/430 Age 70, Male

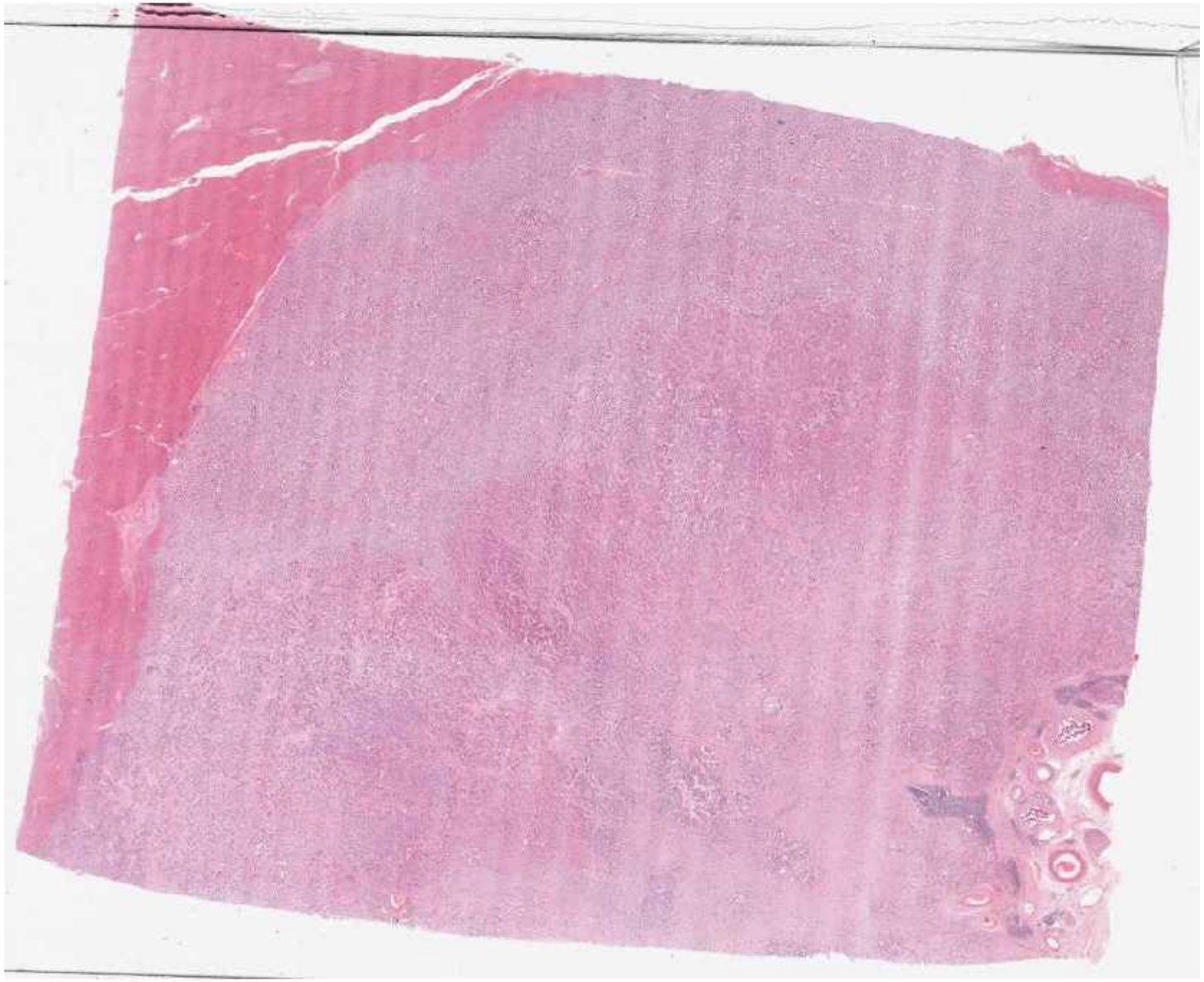
Original diagnosis: Bile duct carcinoid (well differentiated neuroendocrine …..)

Case I1/431
Age 67, Female

Past medical history of chondrosarcoma.
Segment IV&V lesion? Metastatic disease

40mm homogeneous white lesion
with gritty cut surface

431



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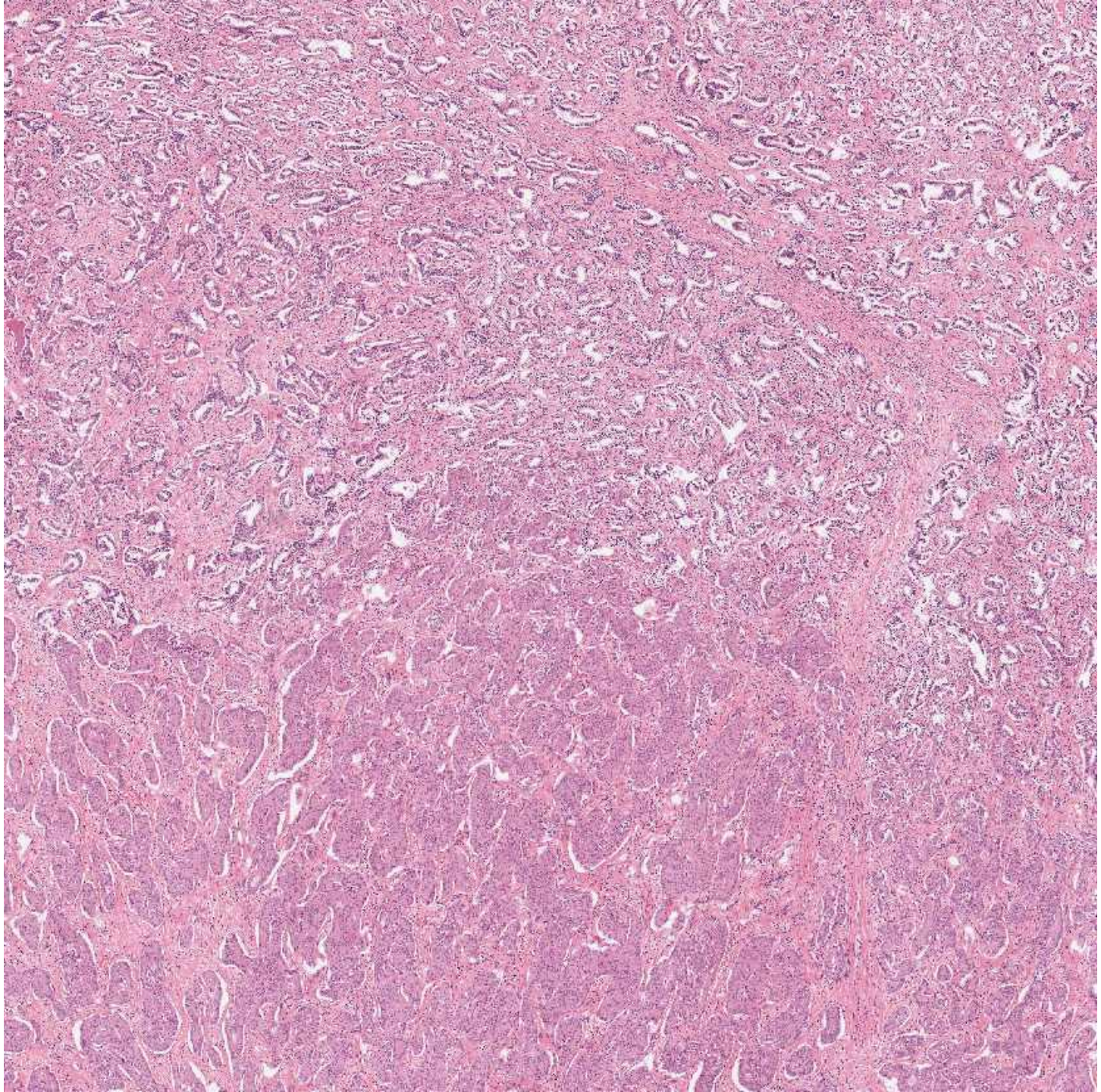

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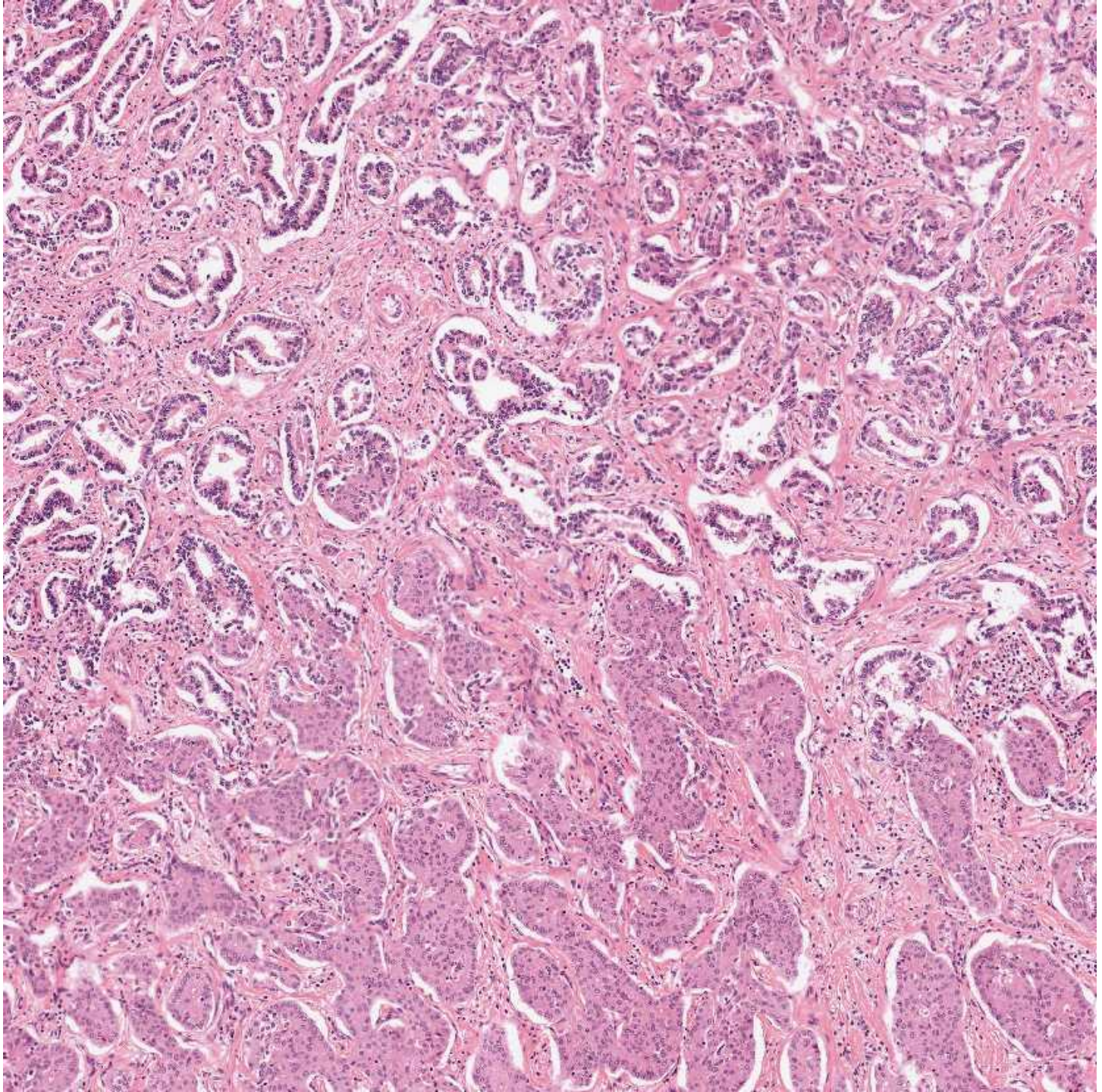

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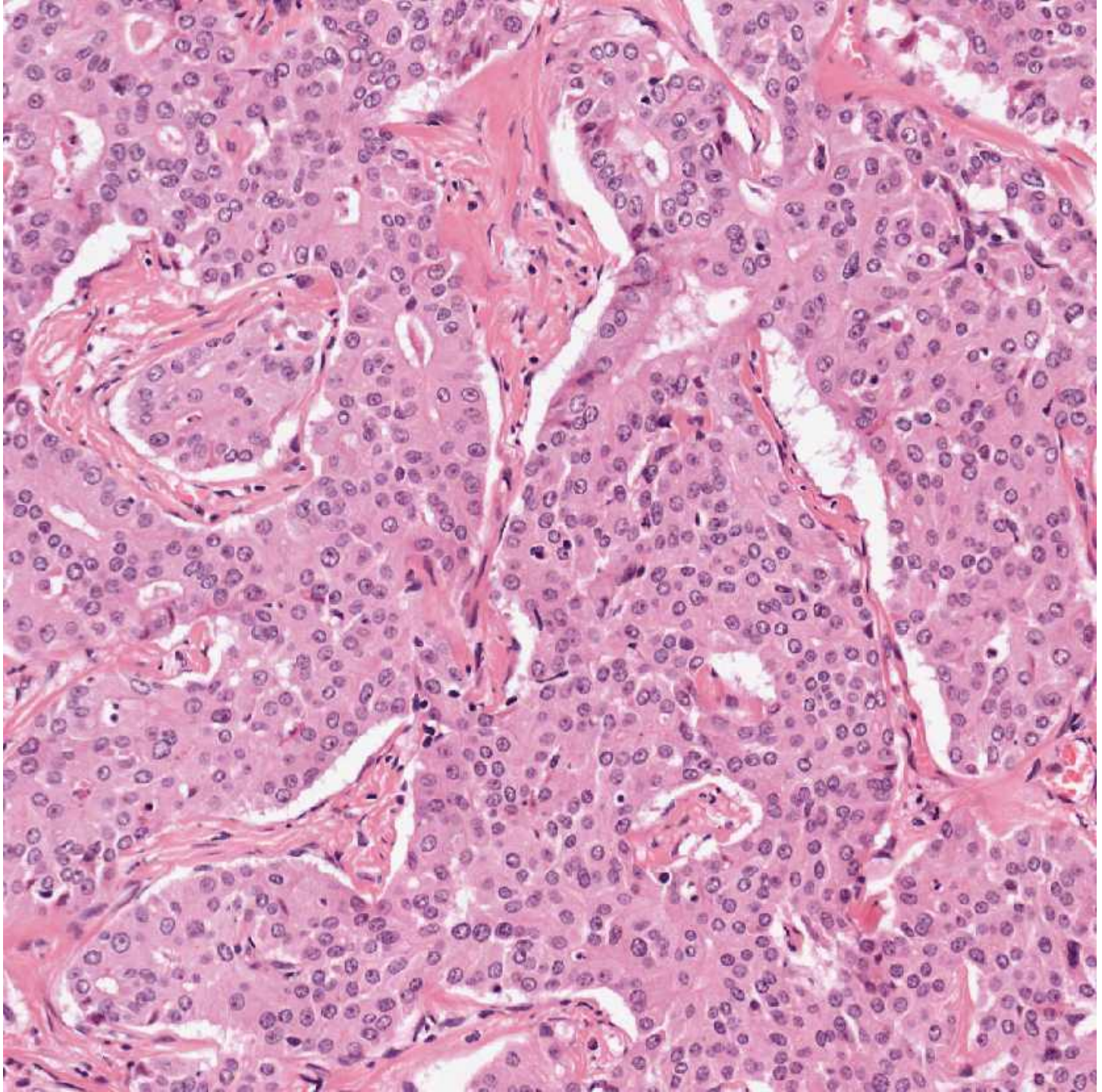

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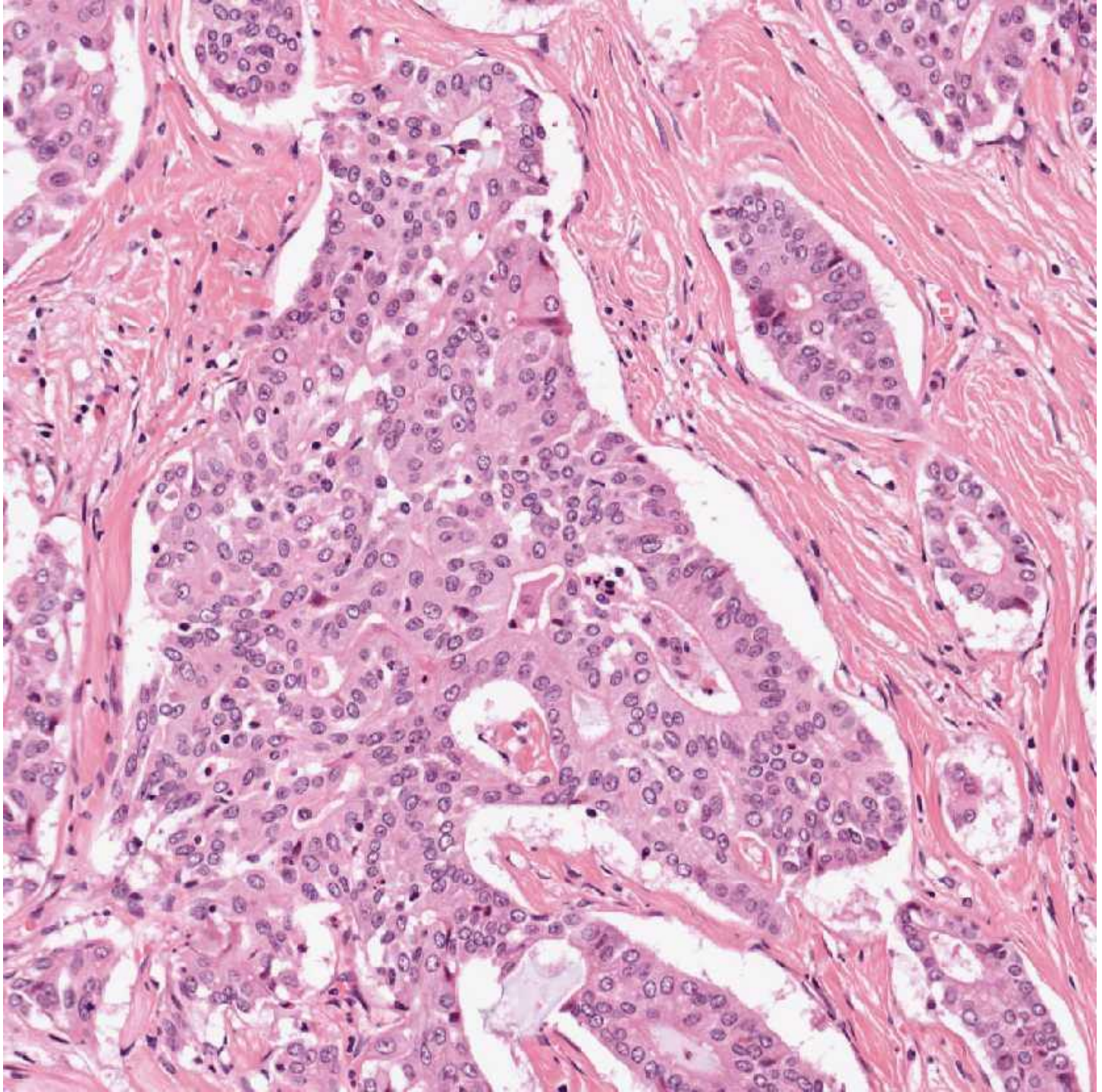

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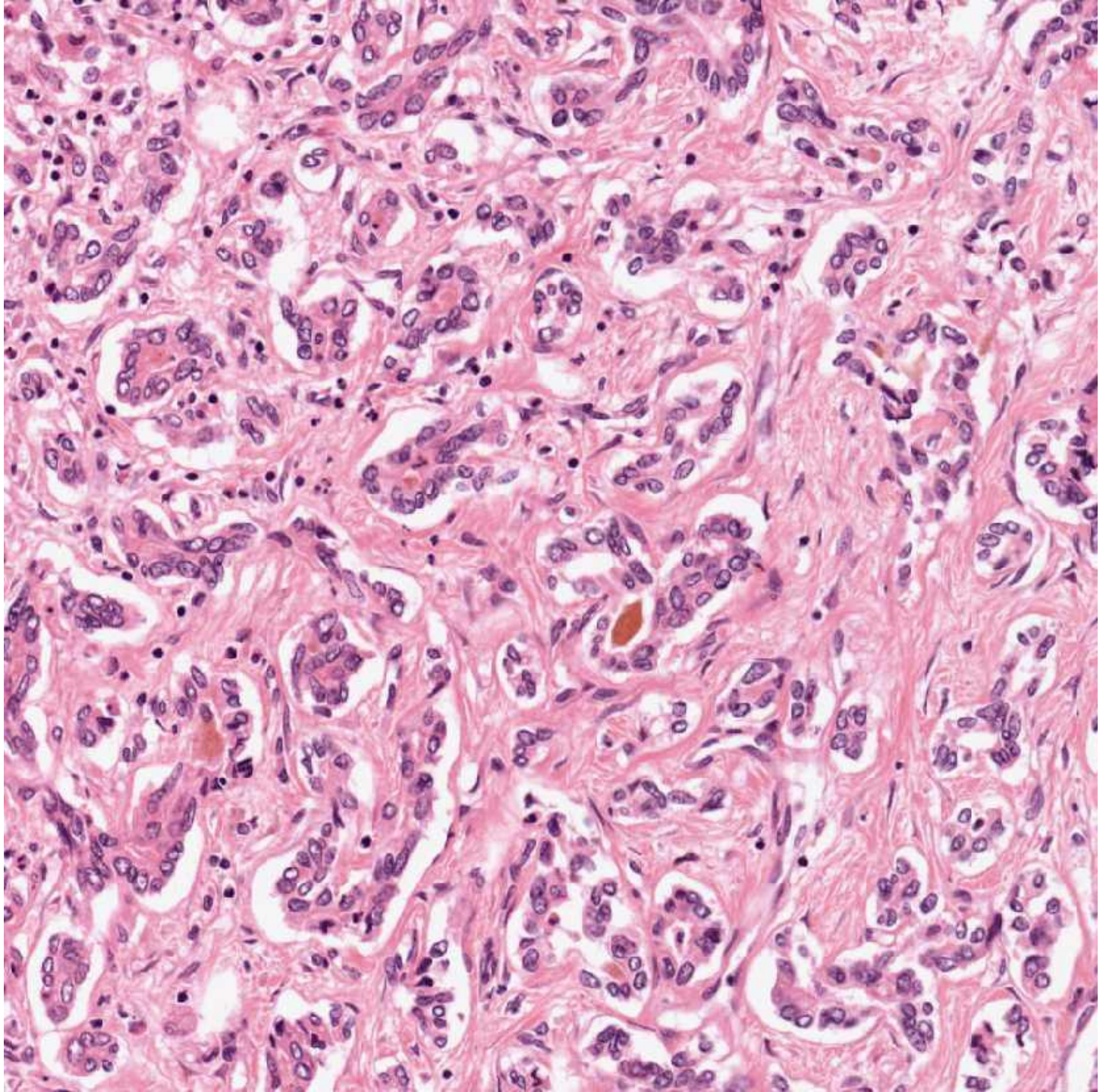

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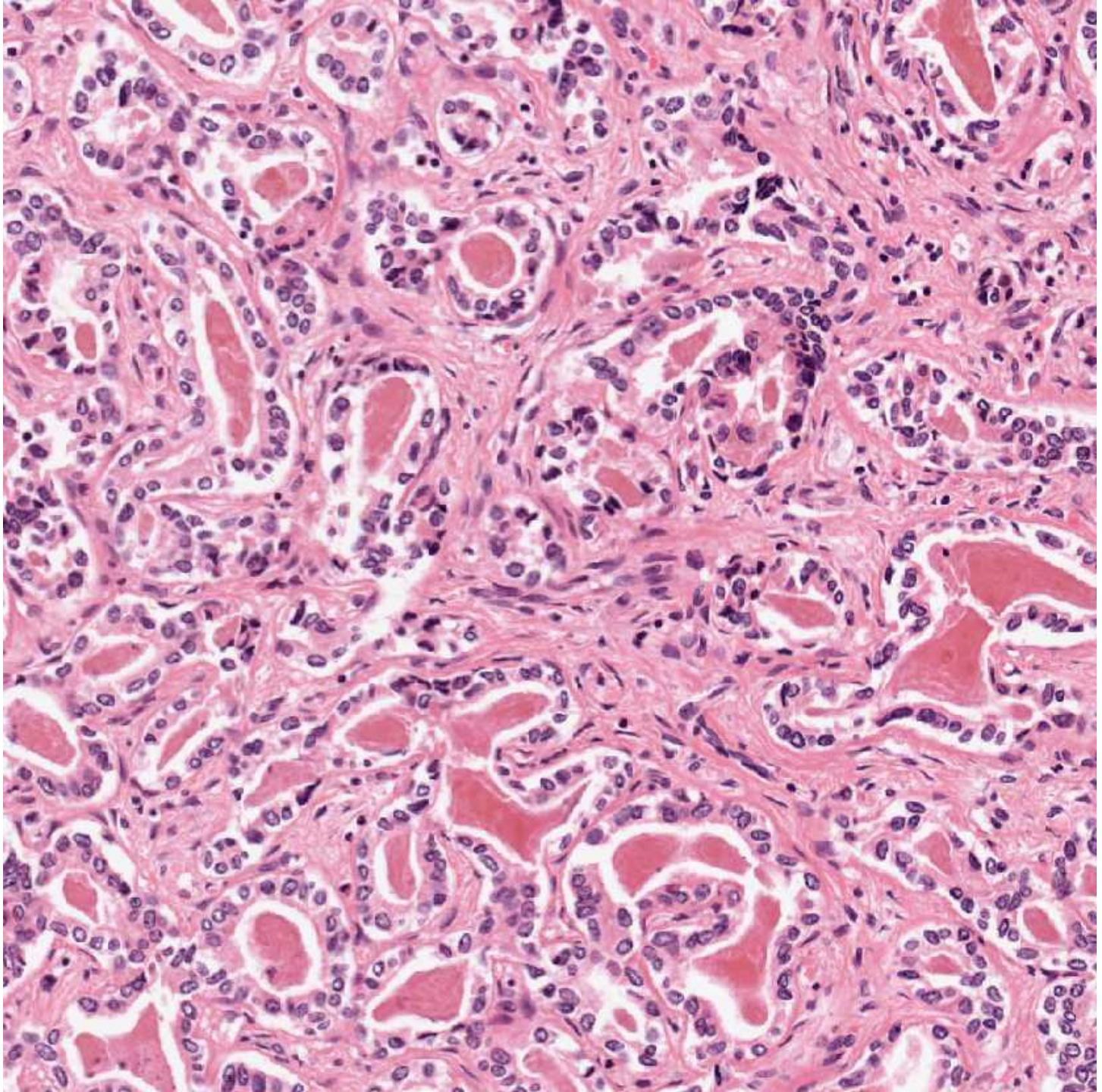

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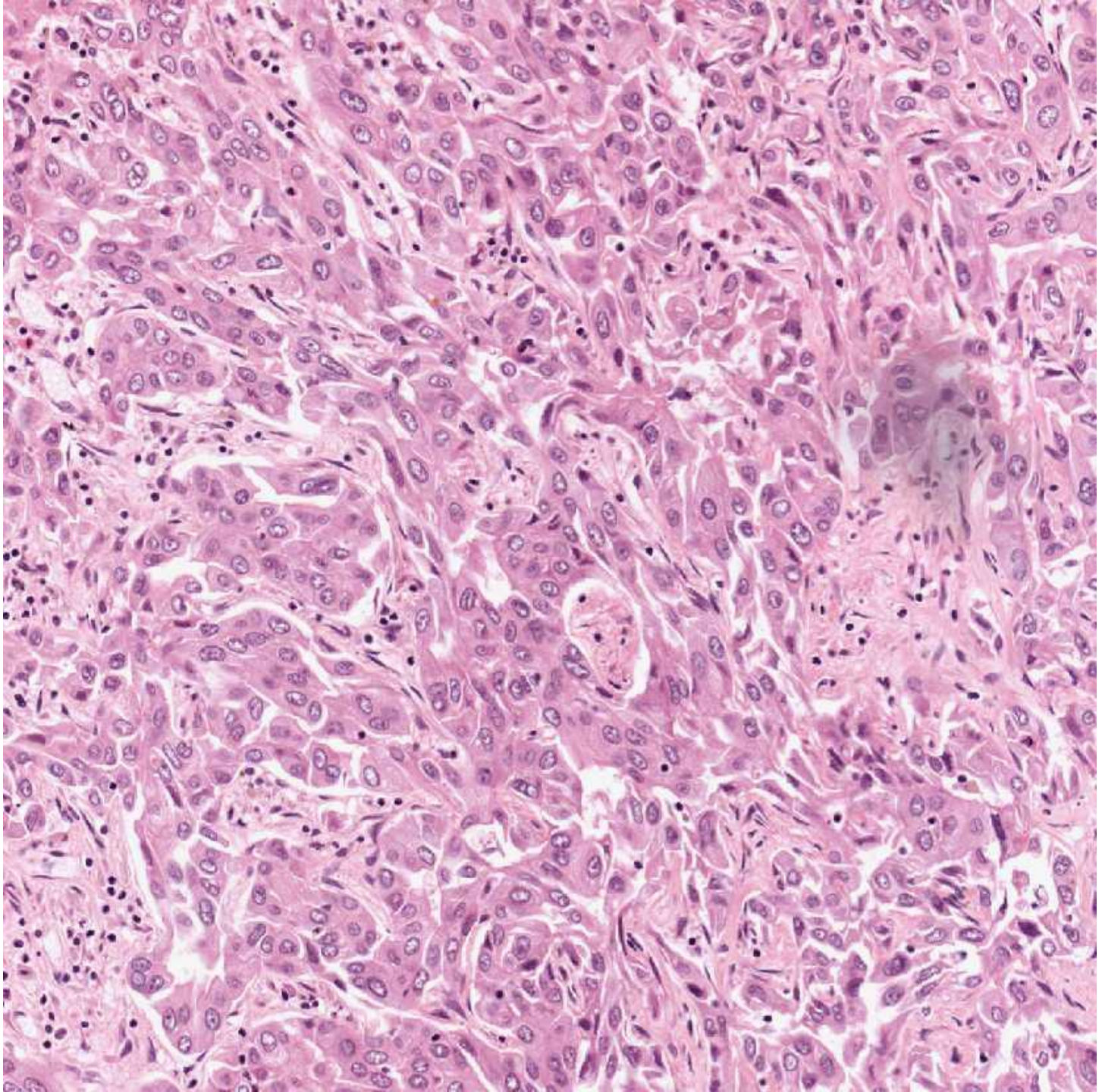


Case I1/431 Age 67, Female

Primary liver tumour:

36 Cholangiocarcinoma +/- differential diagnosis

17 Mixed cholangio/ hepatocellular carcinoma

(11 – mixed CC/HCC included in differential of other responses)

1 hepatocellular carcinoma

1 fibrolamellar carcinoma

1 Bile duct adenoma, no malignancy.

12 comment - ? Arisen from adenoma

Metastatic or either:

9 Adenocarcinoma - favours metastatic

2 Metastatic neurendocrine carcinoma

2 mixed adenoCa and carcinoid

1 Brenner tumour of ovary metastatic to liver

15 Primary or metastatic – can't distinguish

2 adenoCa, needs immunos

1 can't report on H&E

Comments: 34 not chondrosarcoma

10 - Mix up with case 428?

Suggested scoring:

Unsuitable for scoring

= Agreed at meeting.

Case I1/431 Age 67, Female

Original diagnosis: combined hepatocellular – cholangiocarcinoma

Comment: this is an example of a showing mixed features of hepatocellular carcinoma and cholangiocarcinoma. These tumours are increasingly recognised and reflect the origin of at least some primary liver cell cancer from a common progenitor cell. These are staged as for cholangiocarcinoma. Immunohistochemistry should be performed to demonstrate features of both tumour types (AFP, HepPar1 and CK7, CK19).

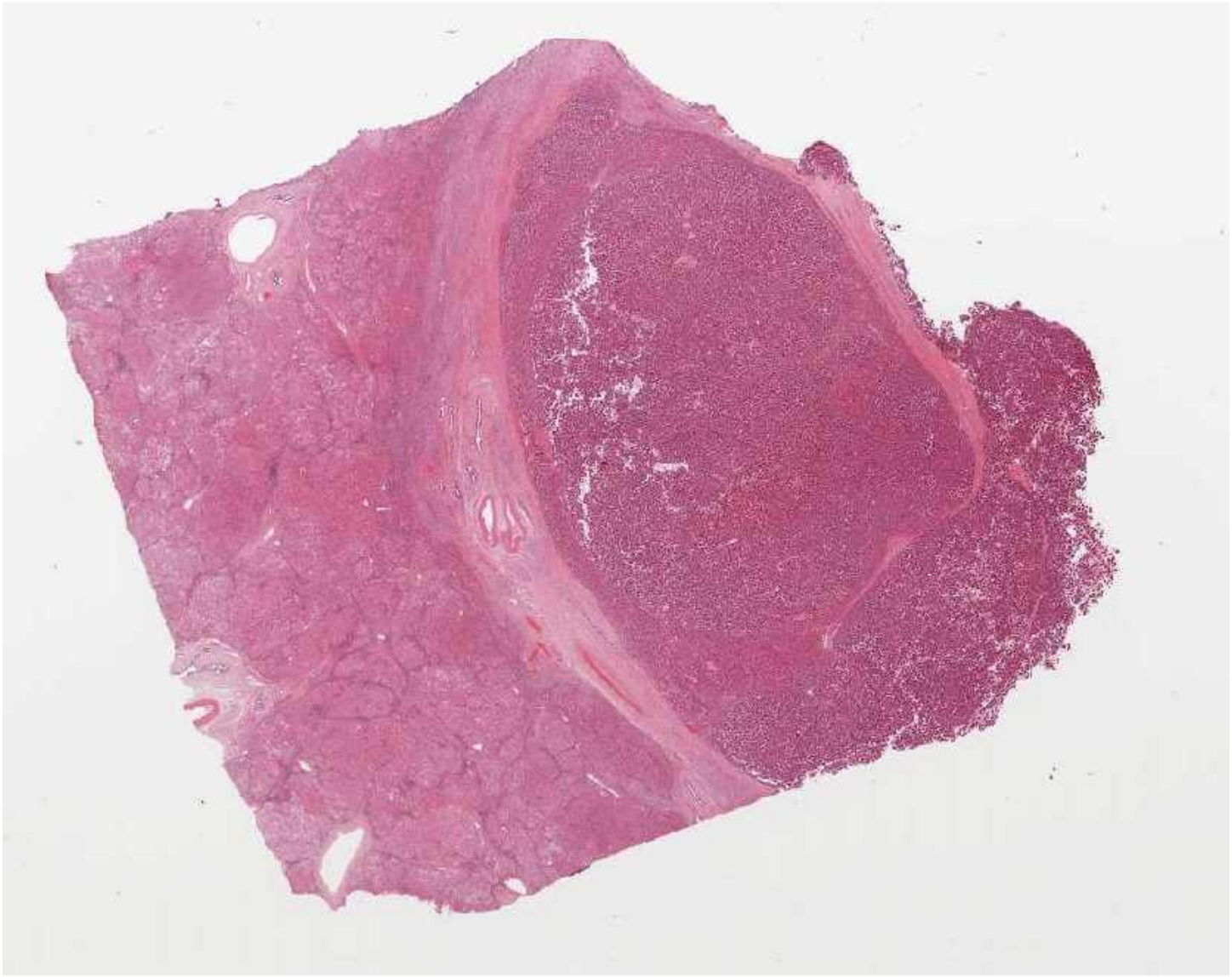
Case I1/432
Age 72, Male

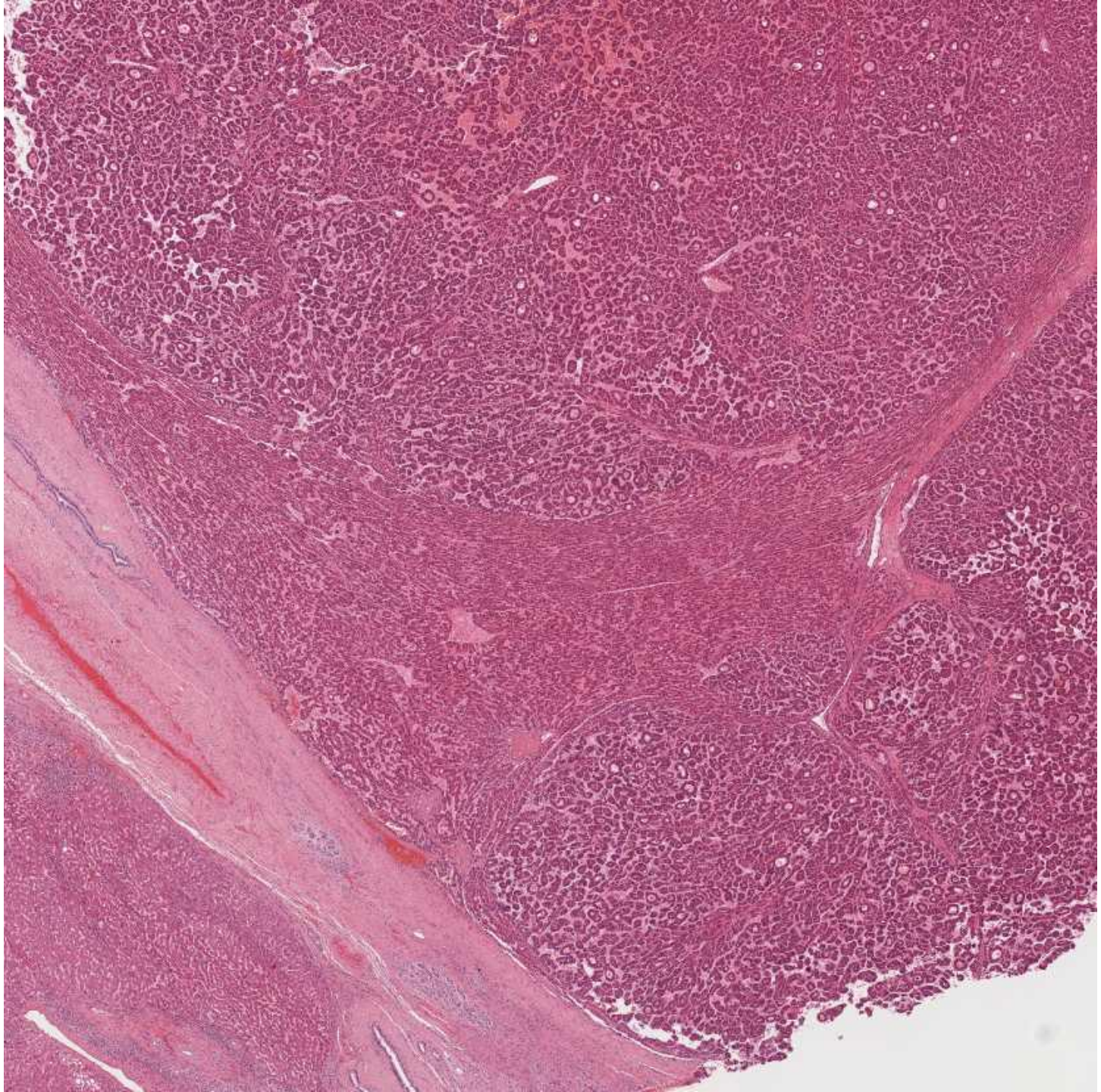
4.5cm lesion in seg 2/4 ? HCC,
background liver fibrotic

Left Hepatectomy 473g, 140x115x60mm
circumscribed soft tan tumour 45mm across

(please also see EVG and PASD on website)

432





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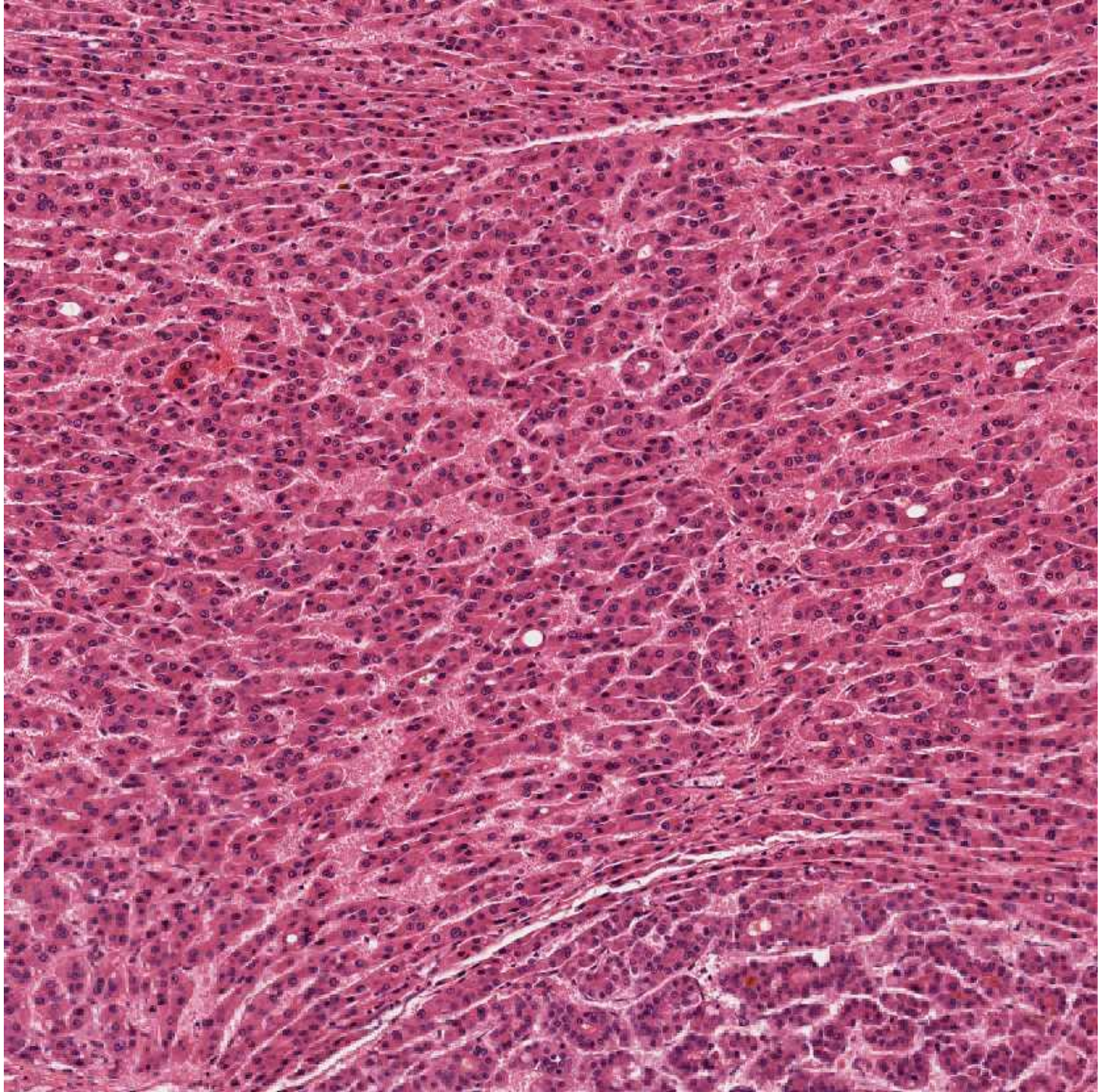
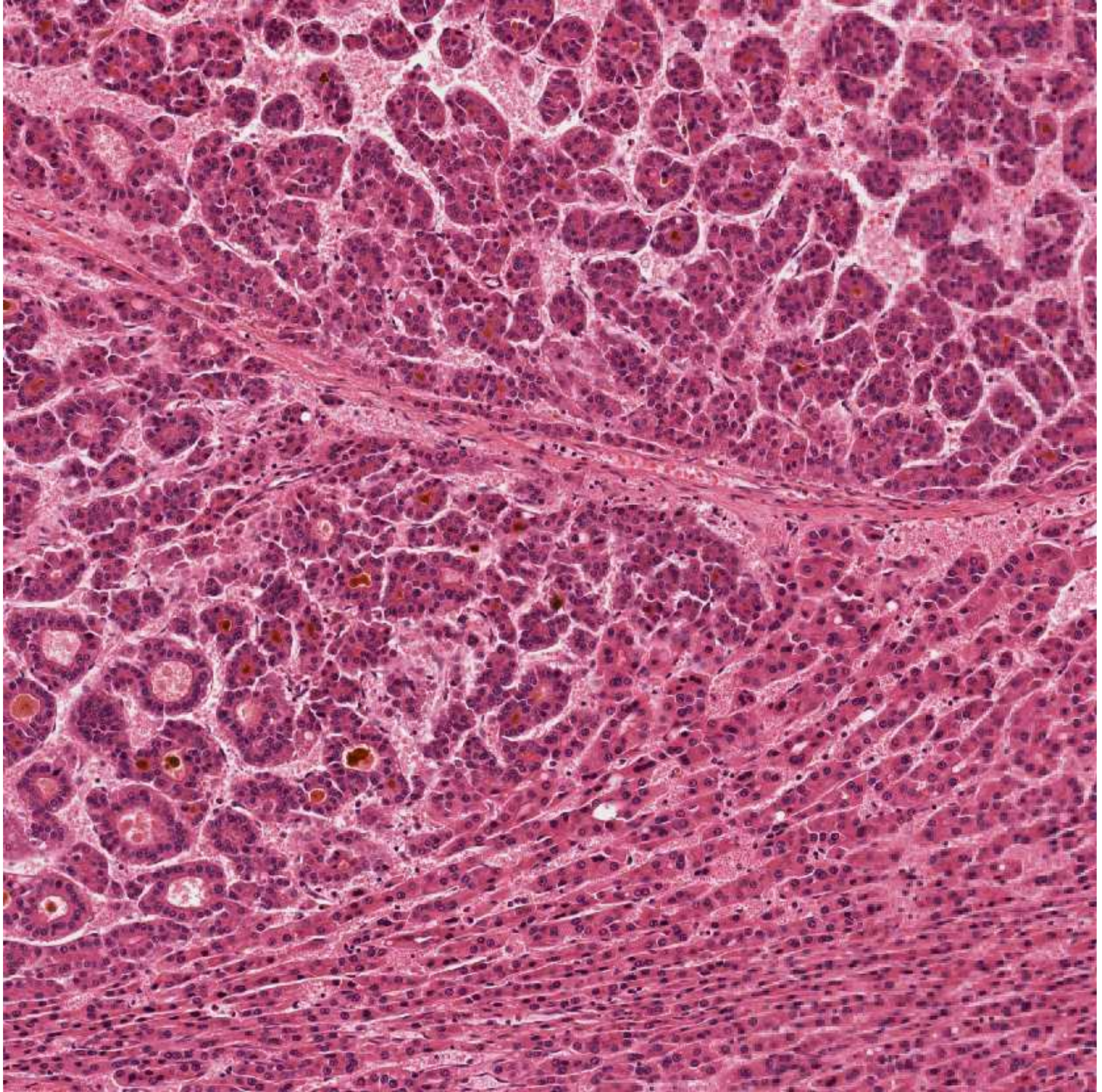
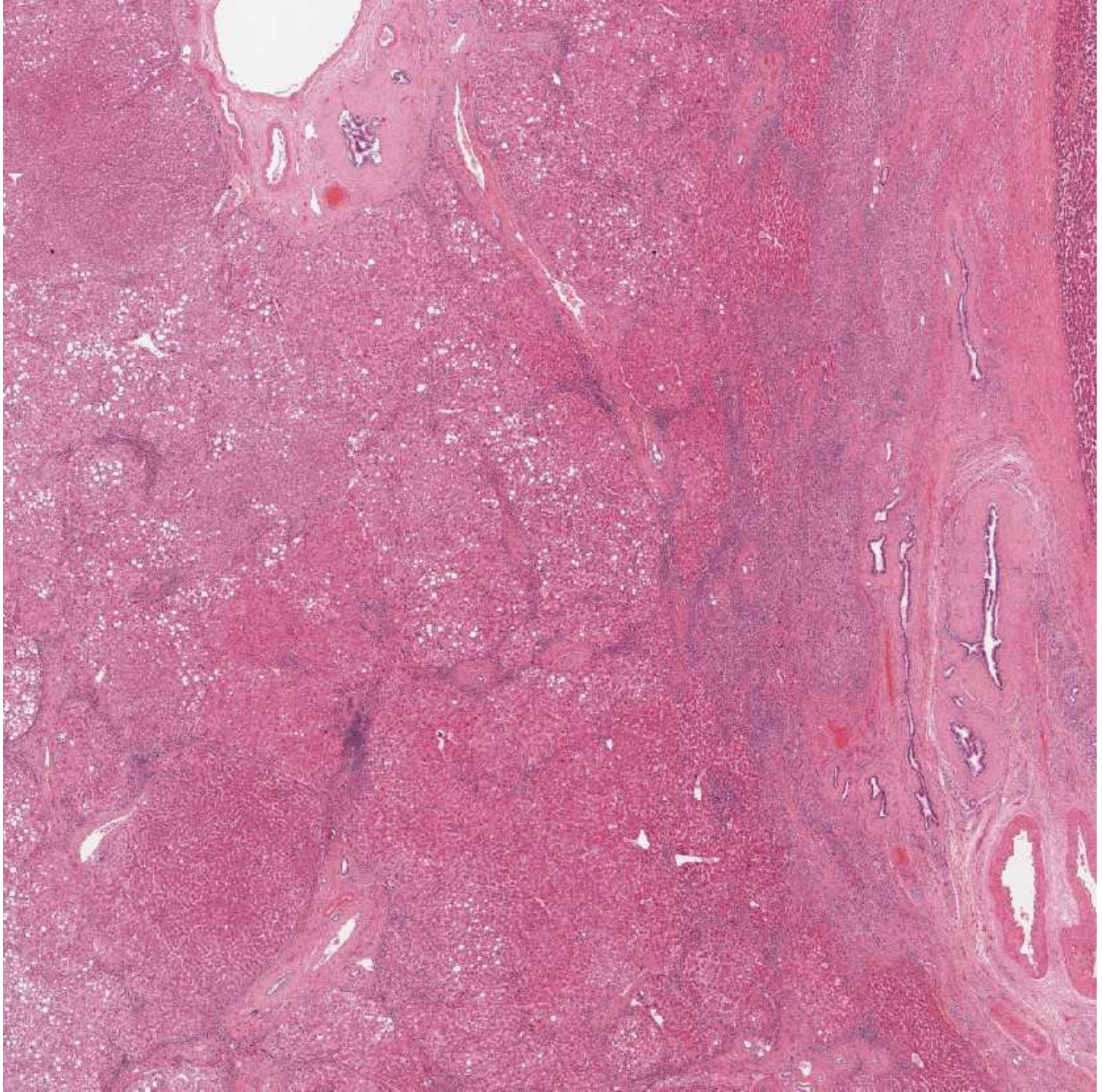
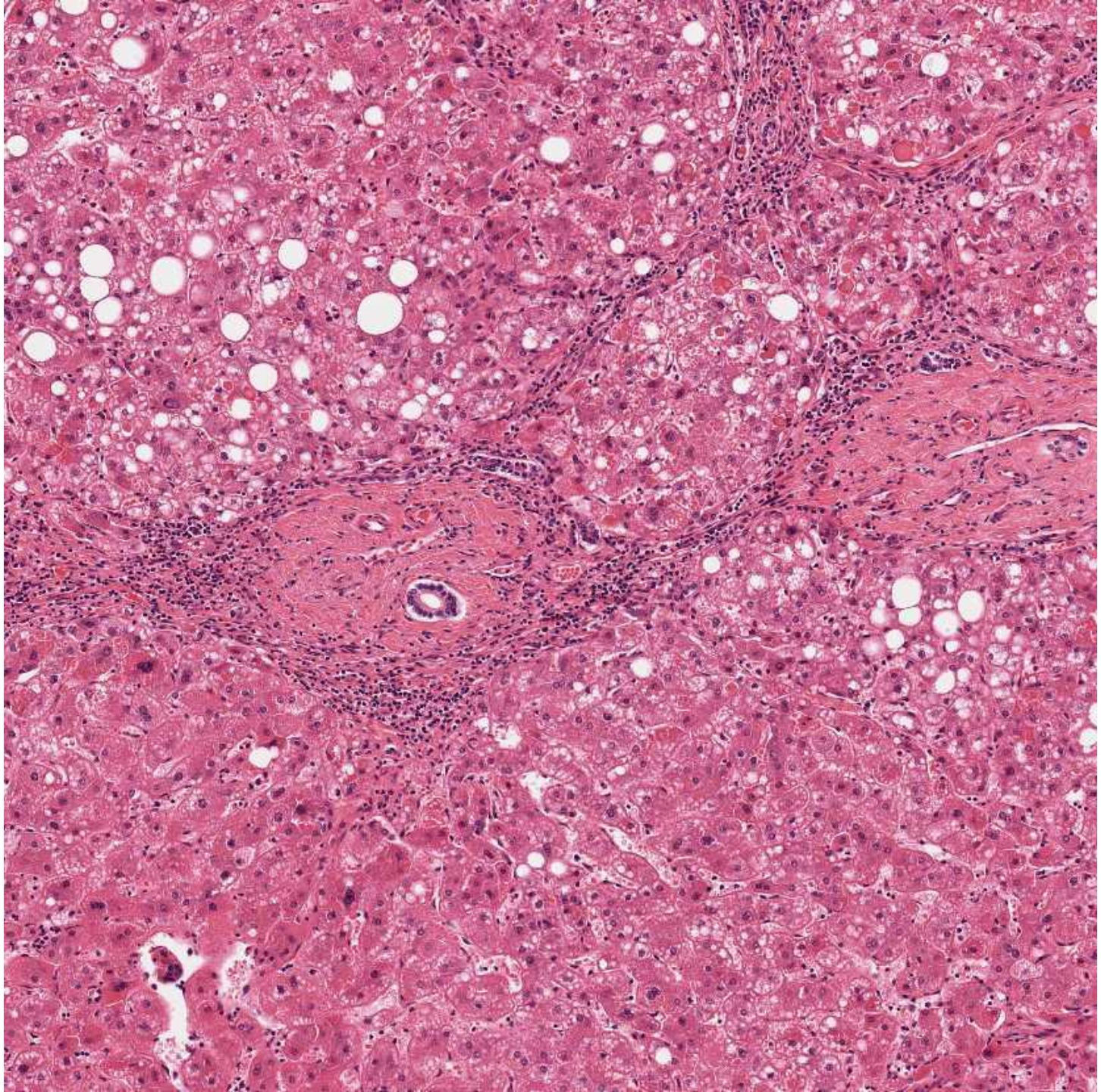
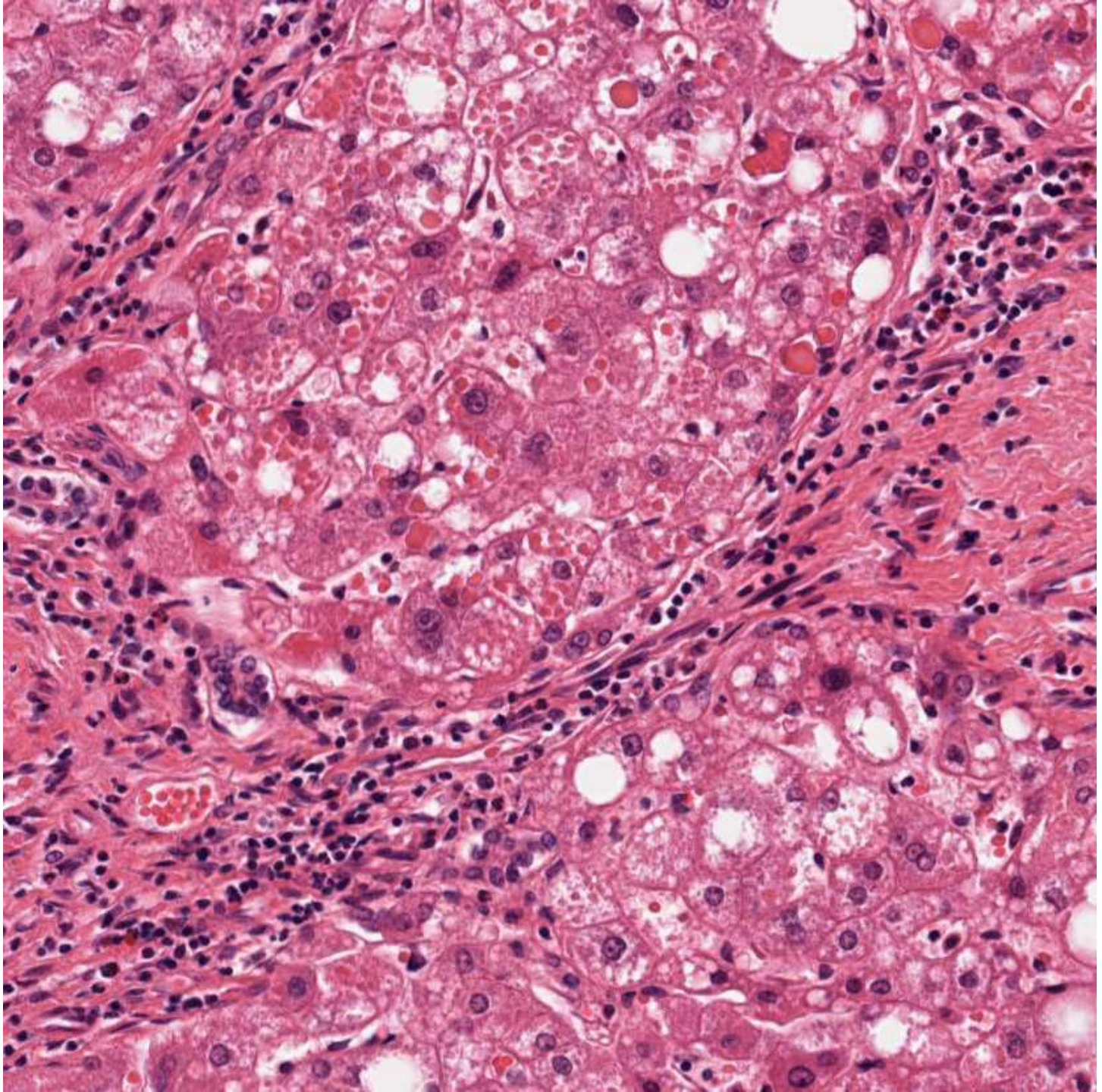
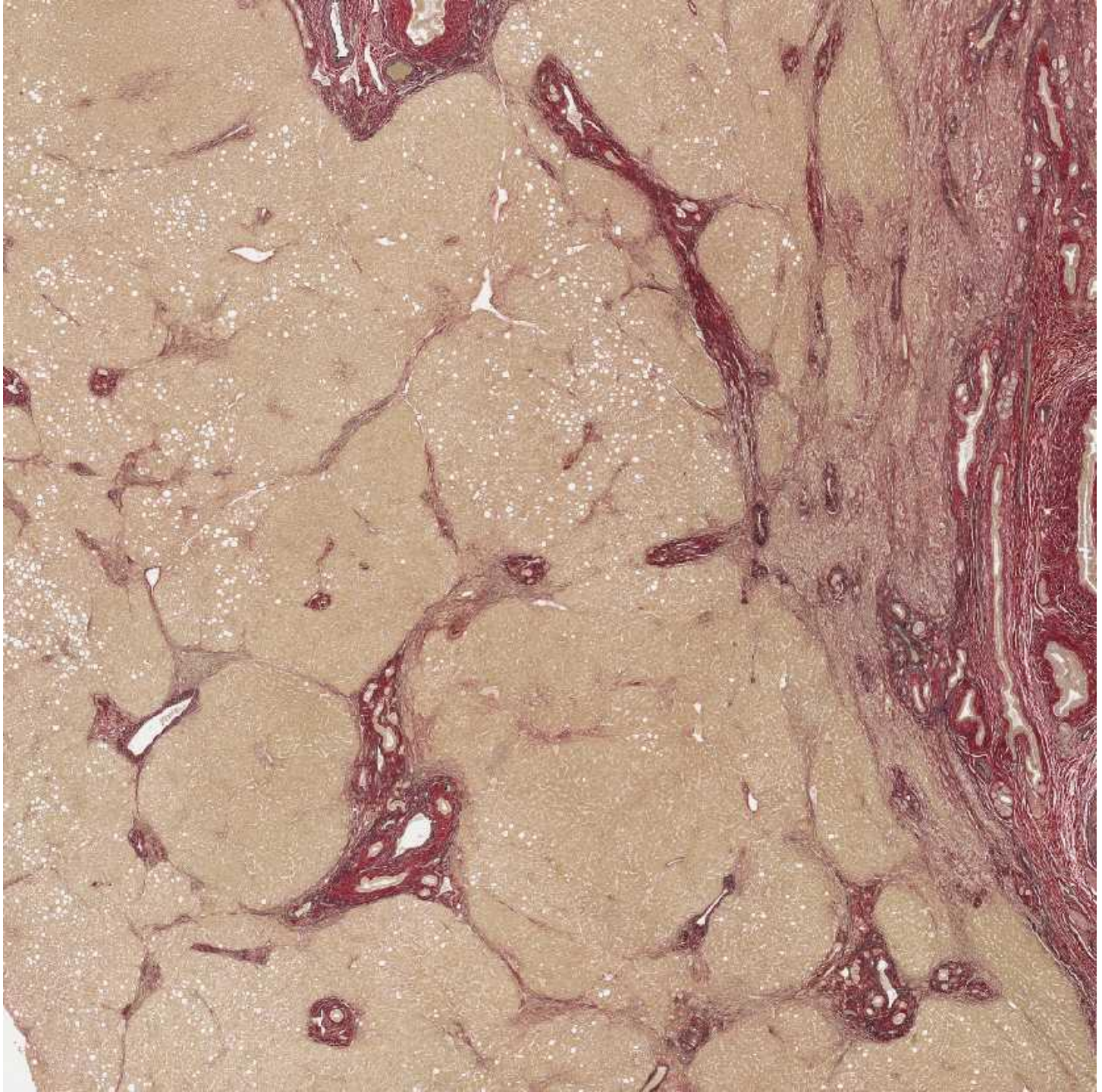


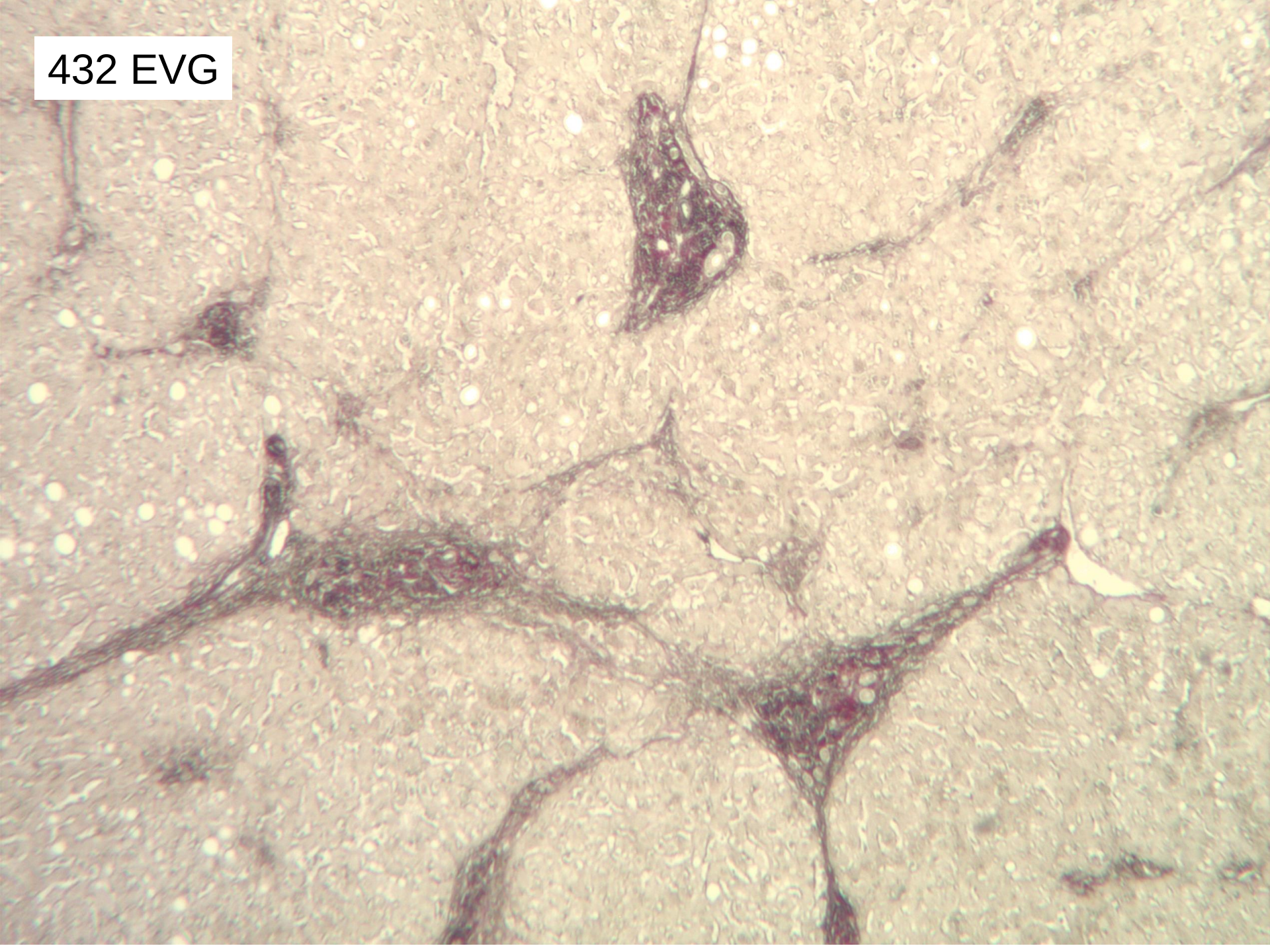


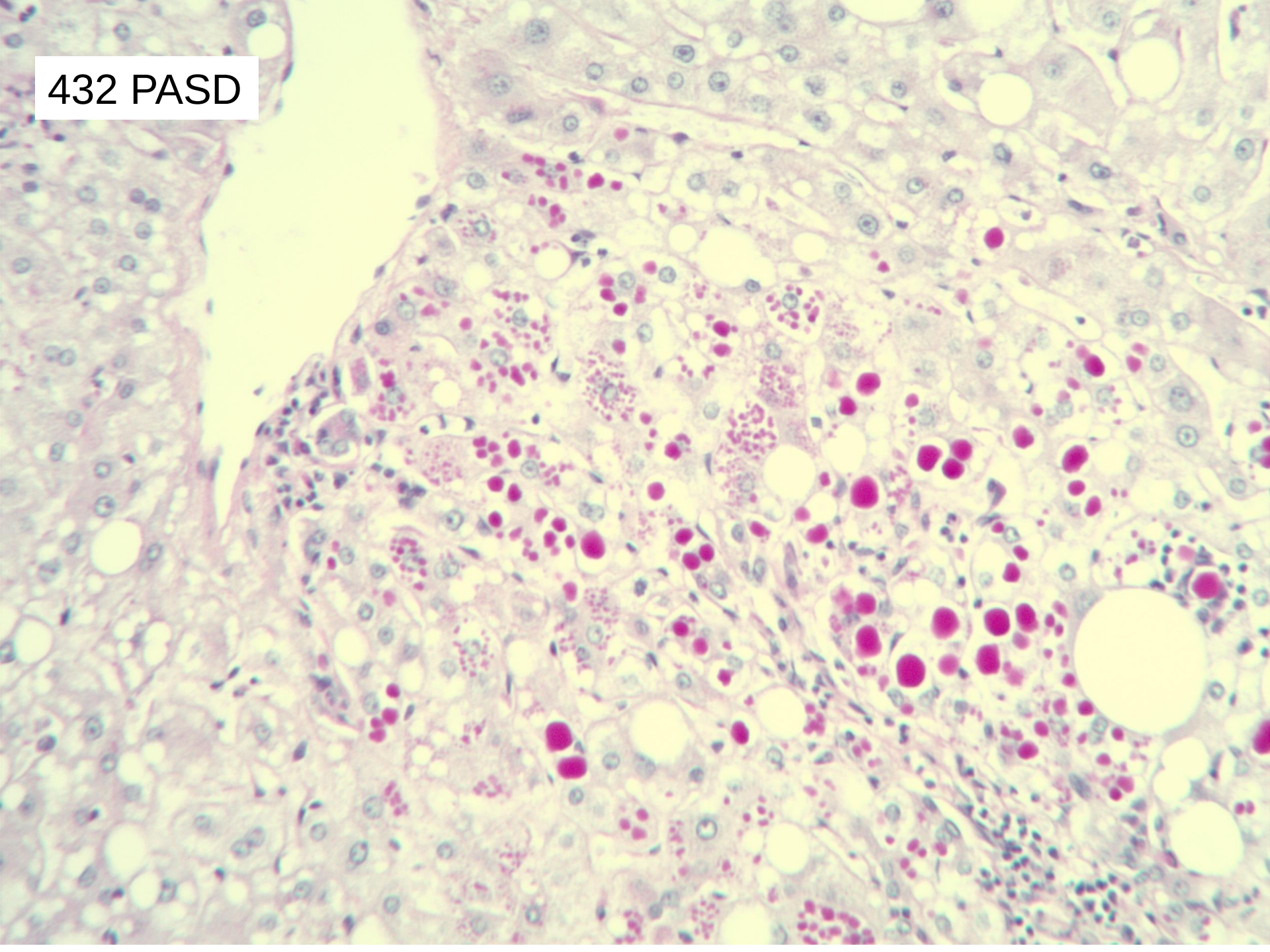









432 EVG


432 PASD

Case I1/432 Age 72, Male

85 Hepatocellular carcinoma

1 low grade dysplastic nodule

1 HCC – immunos to exclude adenocarcinoma

1 well differentiated adenocarcinoma – cholangio or met

9 commented on vascular invasion present

Background liver:

60 Cirrhosis

24 fibrotic, not cirrhotic

4 Stage not mentioned

77 alpha 1 antitrypsin deficiency

11 alpha 1 antitrypsin not mentioned (1 'PASD globules')

36 Background fatty liver disease

Suggested scoring: for 10 points – HCC, plus comment on background fibrosis and alpha 1 ATD. Lose 5 points if background comments are missing. Scoring agreed at meeting.

Case I1/432 Age 72, Male

Original diagnosis: Hepatocellular carcinoma on a background of cirrhosis, steatohepatitis and alpha 1 antitrypsin deficiency. Later found to be piZ homozygous serum alpha 1 antitrypsin level 0.27g/L (normal range 1.1-2.1)

Case I1/433

Age 52, Female

Right hepatectomy for slowly enlarging rt lobe lesion and GB. Clinically ? Benign.

Liver measuring 14.8 x 11 x 7cm weighing 550g

Well defined rounded lesion measuring 5.5cm in maximum dimension.

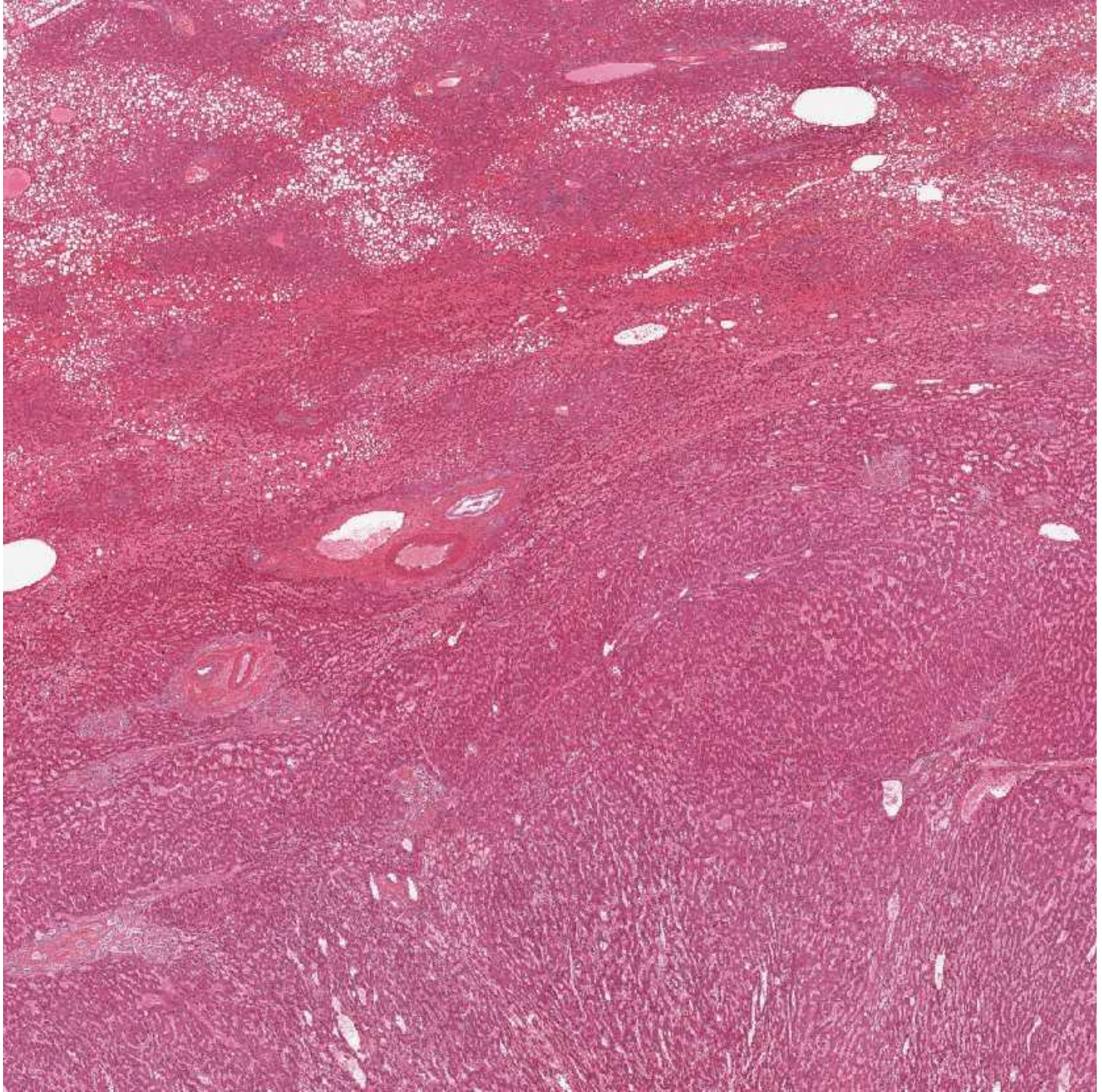
The inner part of the lesion appears congested where as the outer part is lined by a rim of pale tissue with an irregular inner border and a smooth outer border.

Background liver appears normal.

(please also see reticulin on website)

433

433



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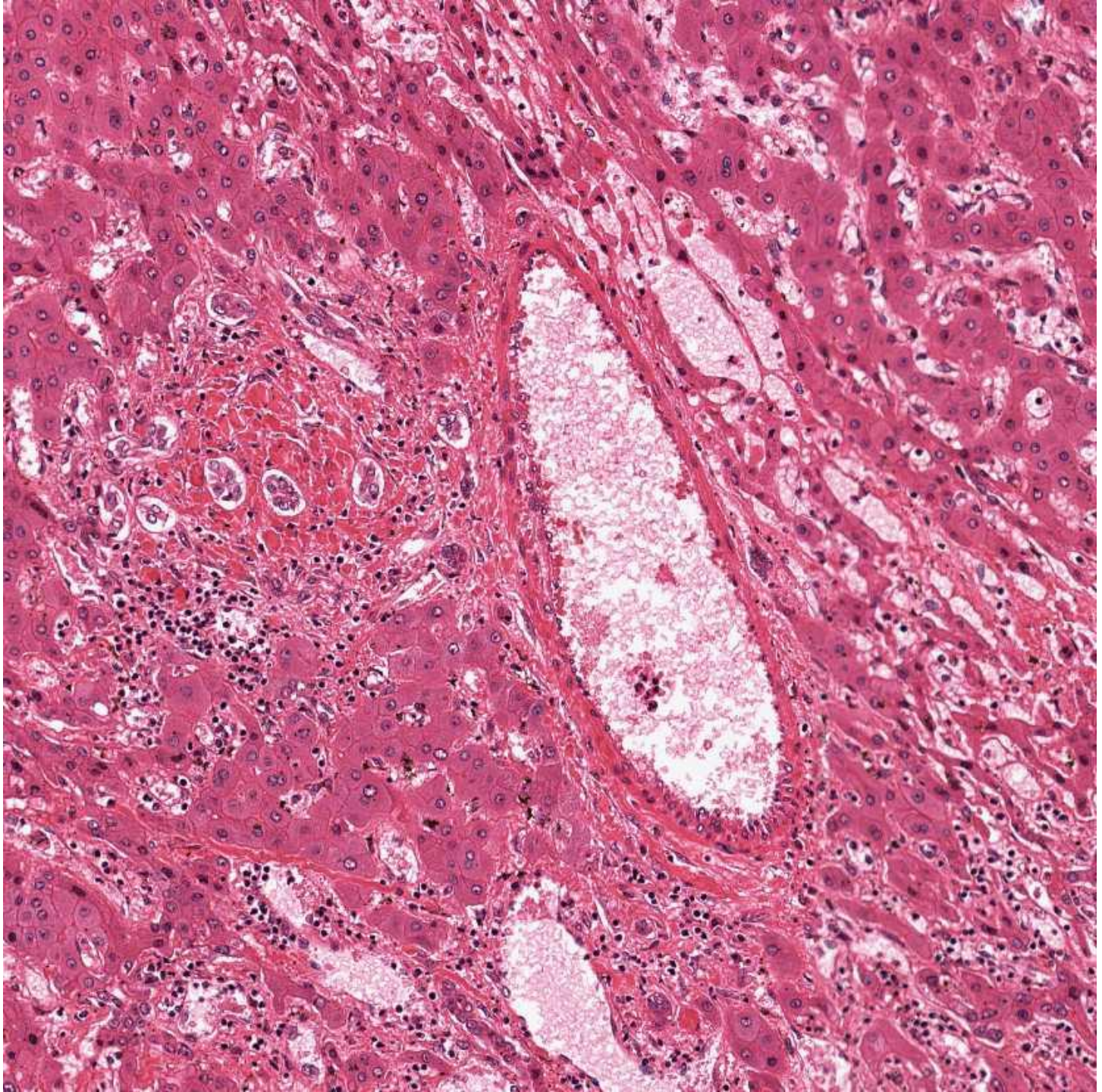

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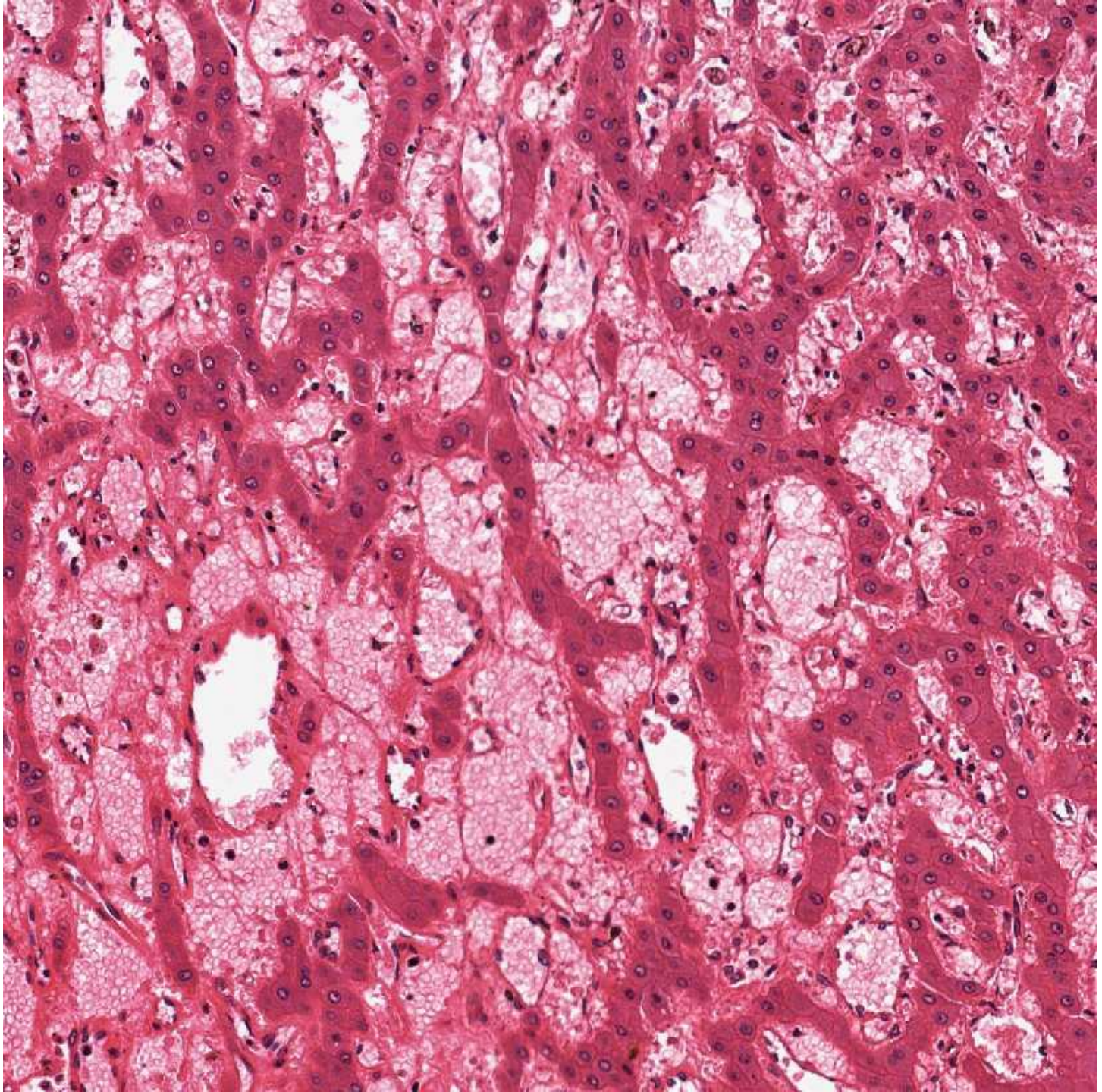

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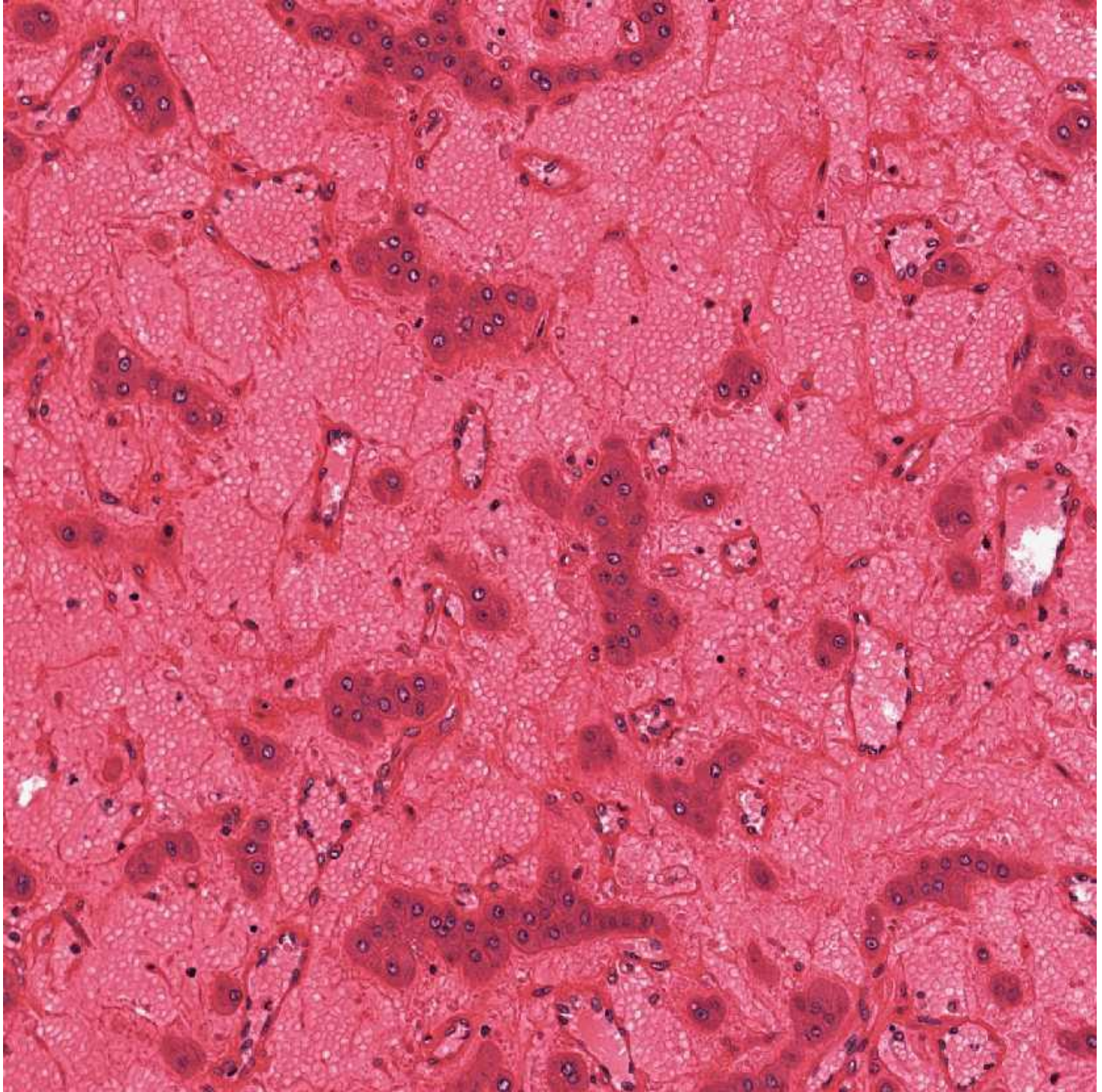

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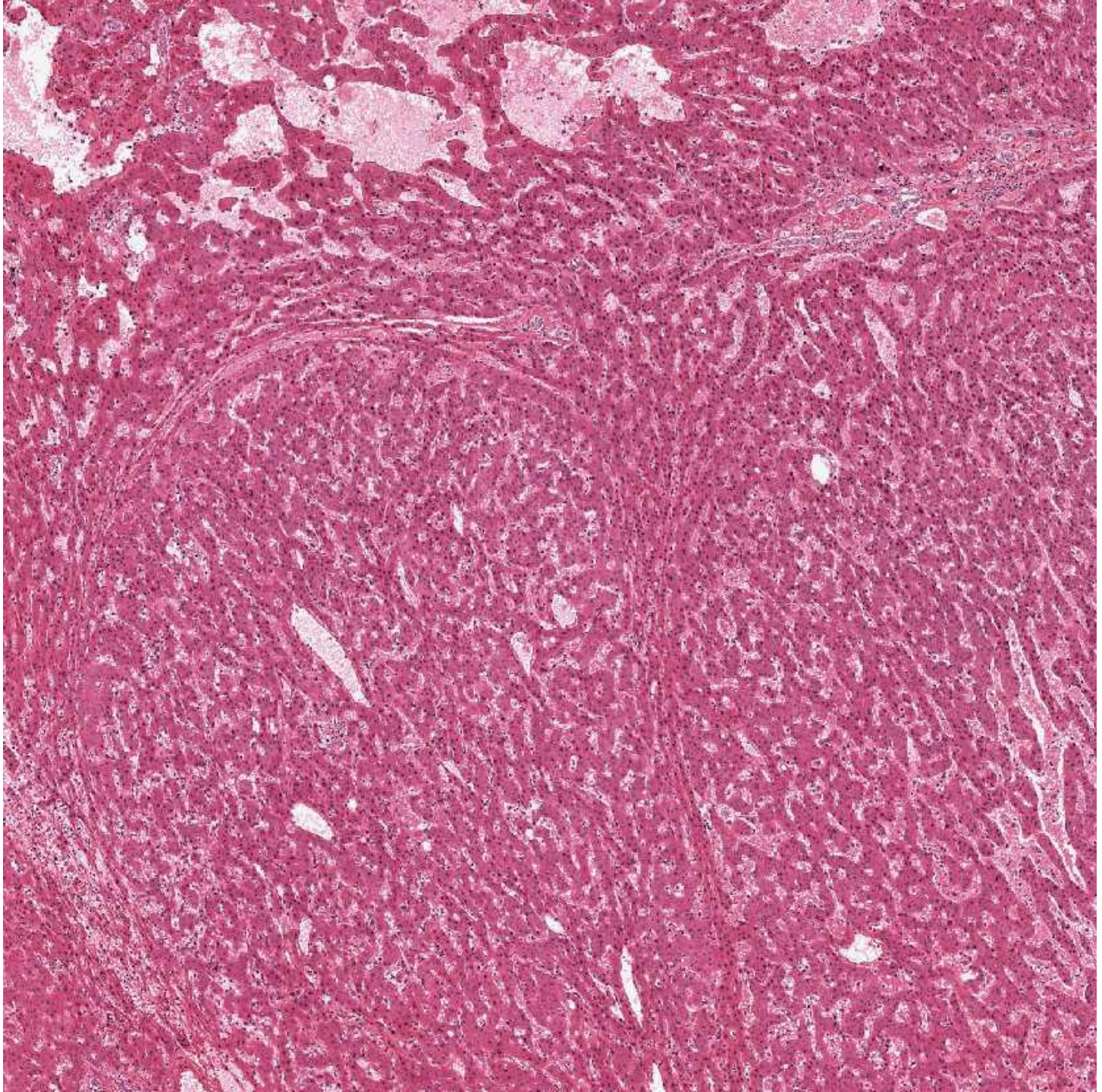

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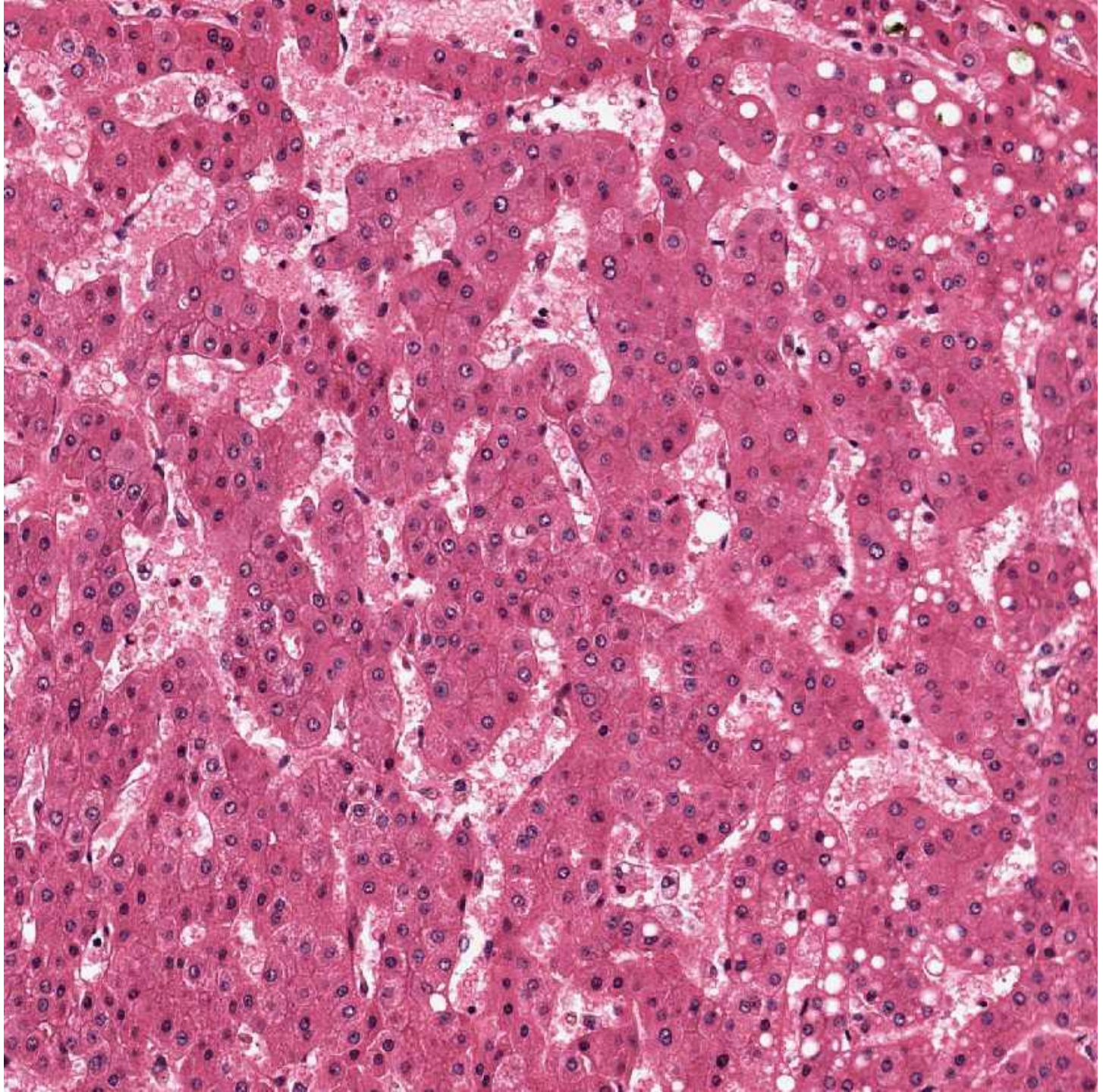
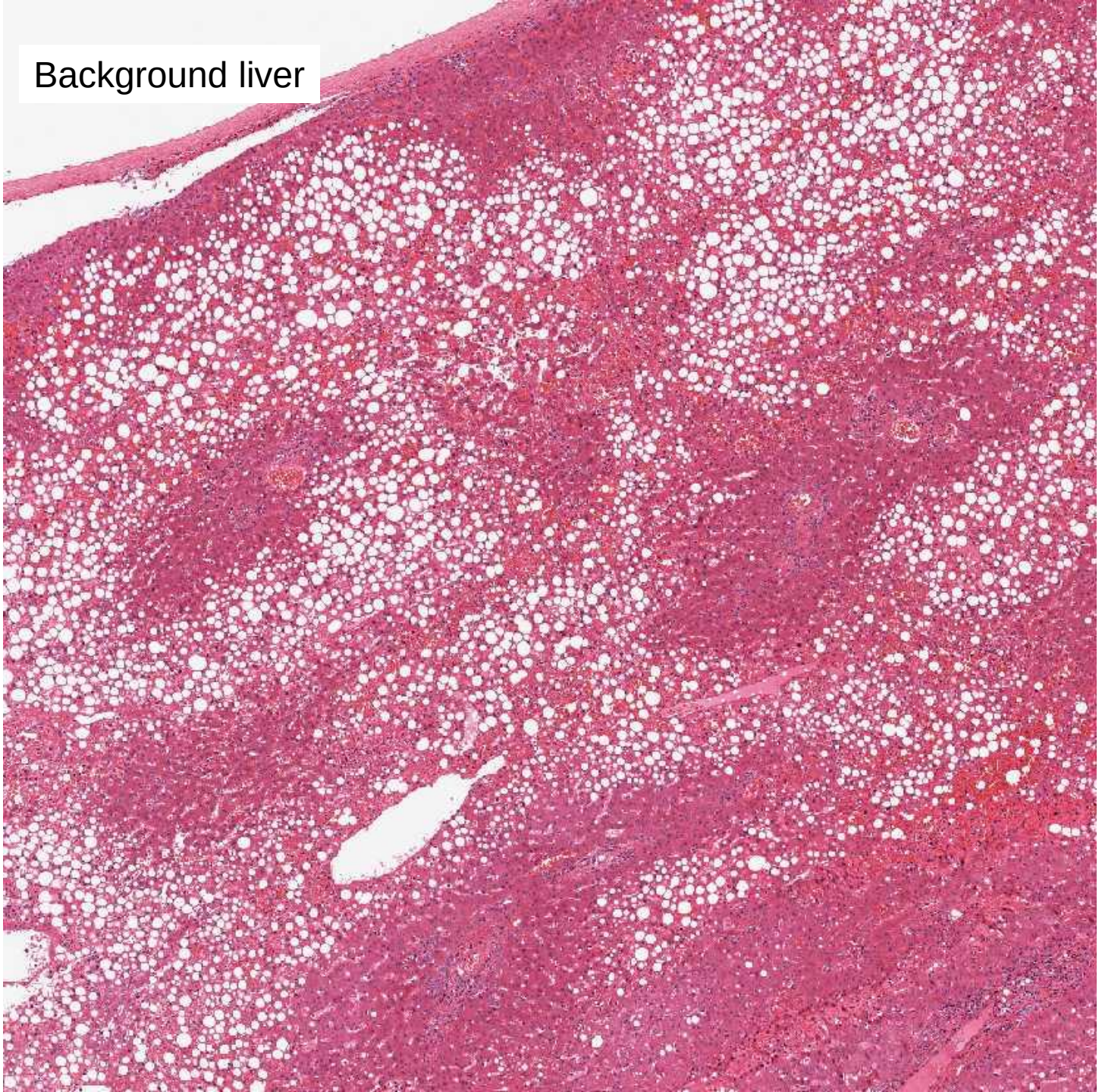


433

Background liver



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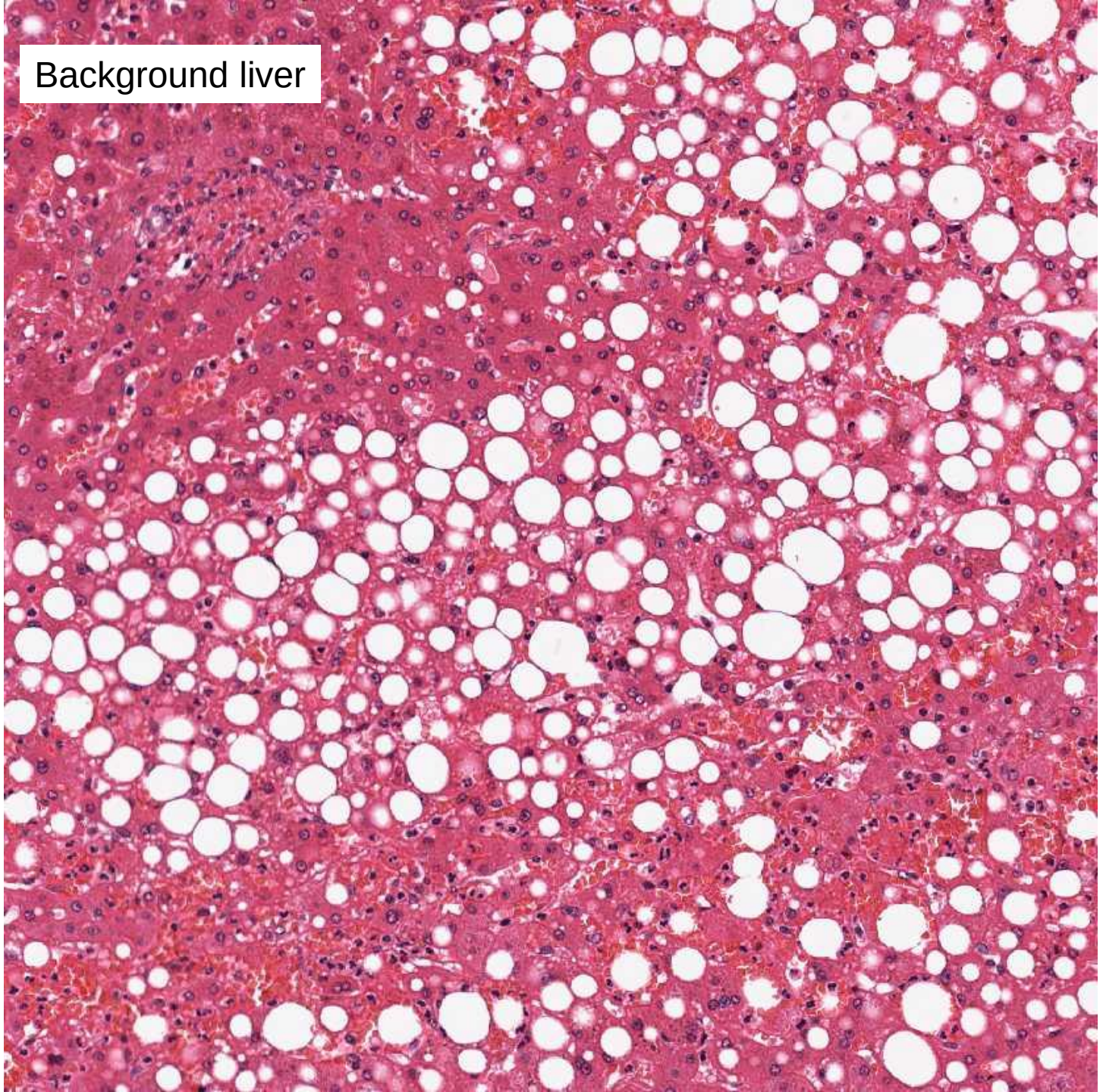
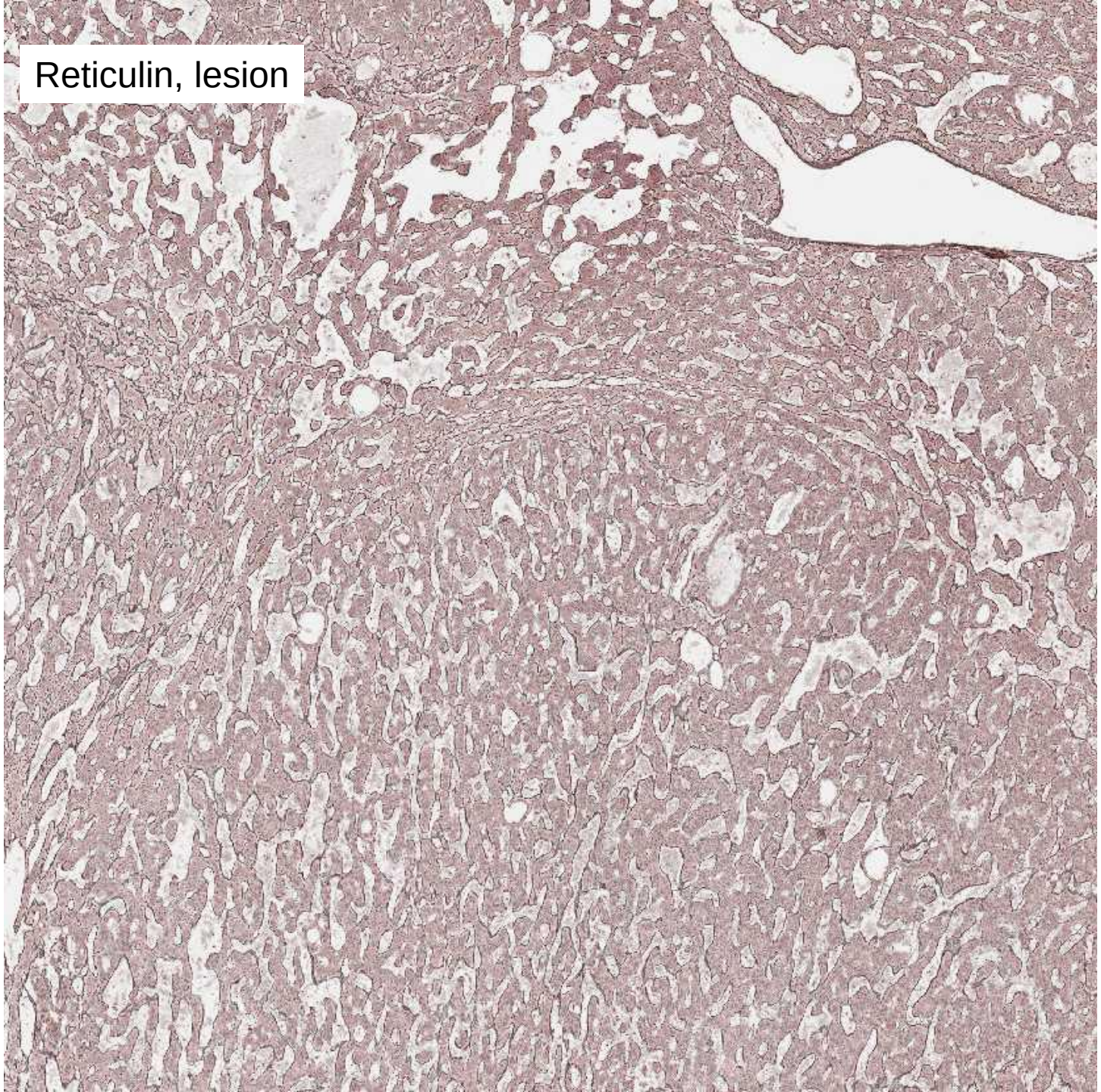


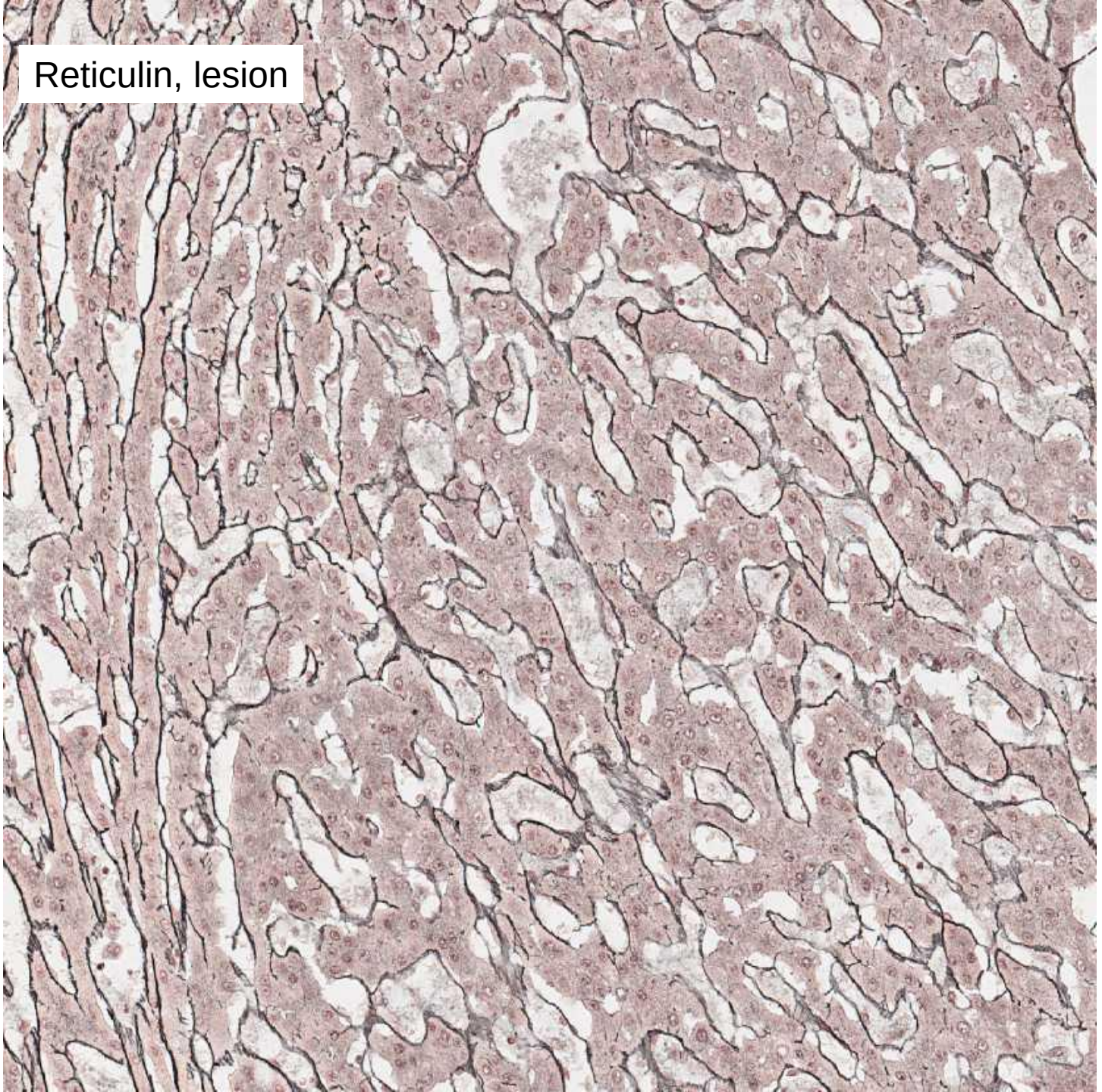
433

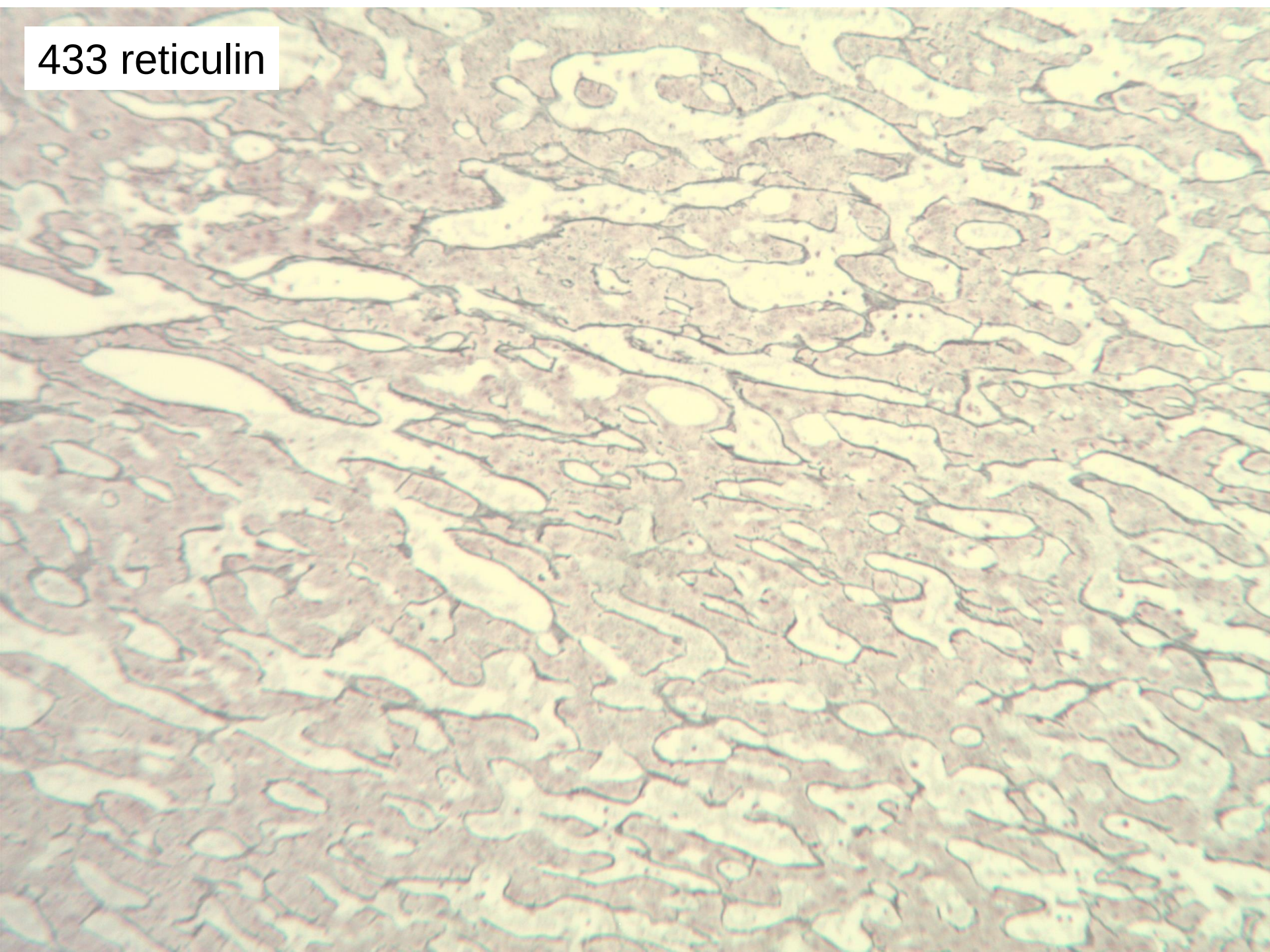
Reticulin, lesion



433

Reticulin, lesion




433 reticulin

Case I1/433 Age 52, Female

66 Liver cell adenoma, of which:

32 adenoma NOS

14 inflammatory adenoma

10 telangiectatic adenoma

10 adenoma or HCC

of adenoma: 22 request immunos

9 well differentiated HCC

of which 3 request immunos

Others:

5 peliosis

2 haemangioma

1 nodular regenerative hyperplasia

1 focal nodular hyperplasia

1 macroregenerative nodule type 1

1 shock liver/venous outflow obstruction

1 Haemorrhagic infarction of adenoma or haemangioma or venous outflow obstruction

Background liver:

55 steatosis

32 background not mentioned

1 background 'unremarkable'

Suggested scoring:

Accept all with focal hepatocellular neoplasm, either adenoma or well differentiated HCC with confirmatory immunos

If accept adenoma only, insufficient consensus for scoring

Discussion at meeting: not suitable for scoring

Case I1/433 Age 52, Female

Original diagnosis: hepatocellular adenoma, steatosis with mild fibrosis.

Comment: this case had a benign/malignant split in diagnosis and so was considered unsuitable for scoring. However, hepatocellular tumours that are histologically borderline are increasingly recognised, and this lesion is probably best regarded as an example, see presentation in the main meeting by Alastair Burt.

The end of circulation I1