



## **Liver Case Presentations**

***New York Path Society, November 9, 2017***

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**Department of Pathology**  
**New York University School of Medicine**  
**New York City**

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## Case 1

54 year old woman

Alkaline Phosphatase 276 (nl 30-145)

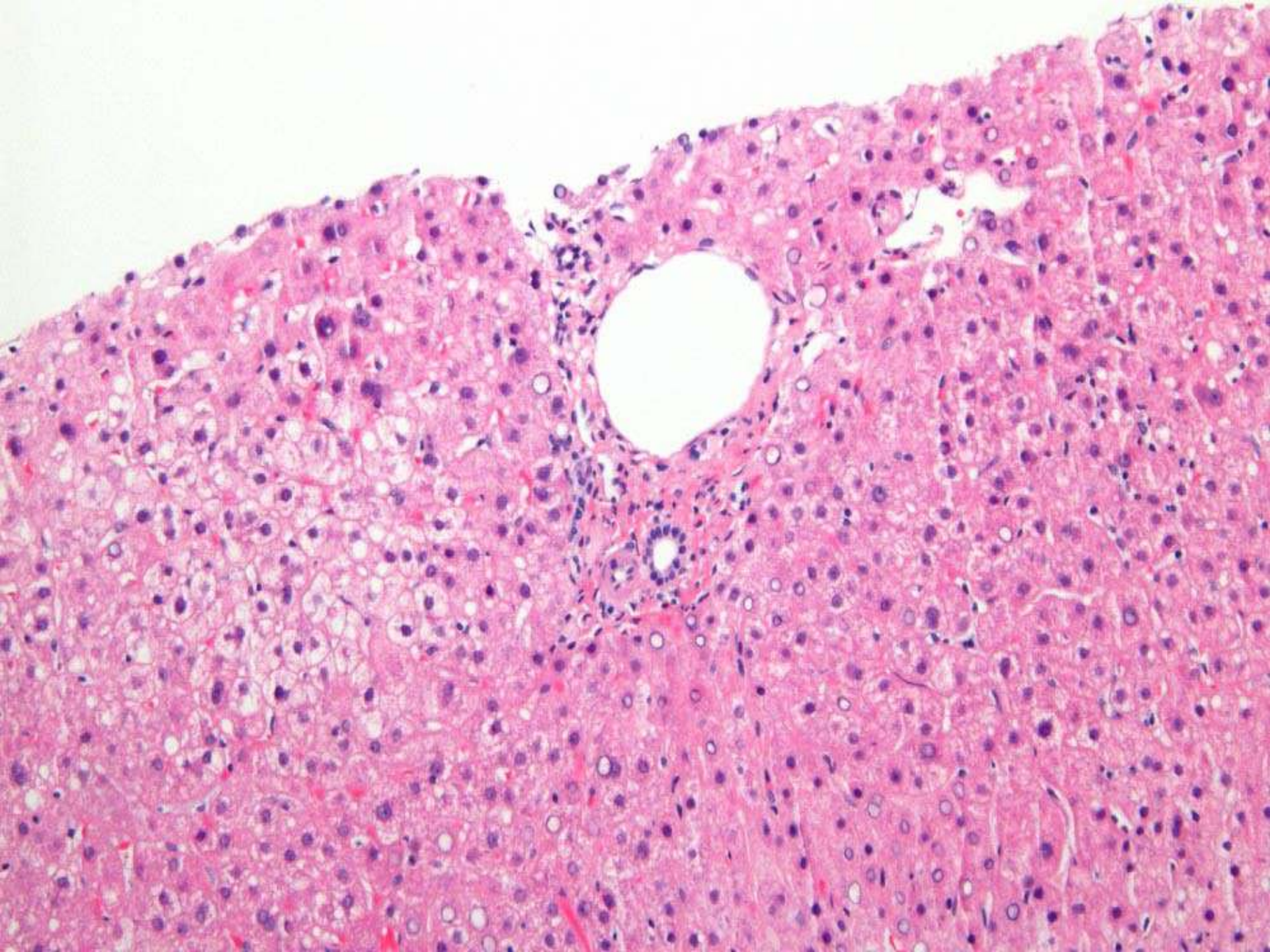
ALT: 53 (nl 10-45)

AST: 36 (nl 10-45)

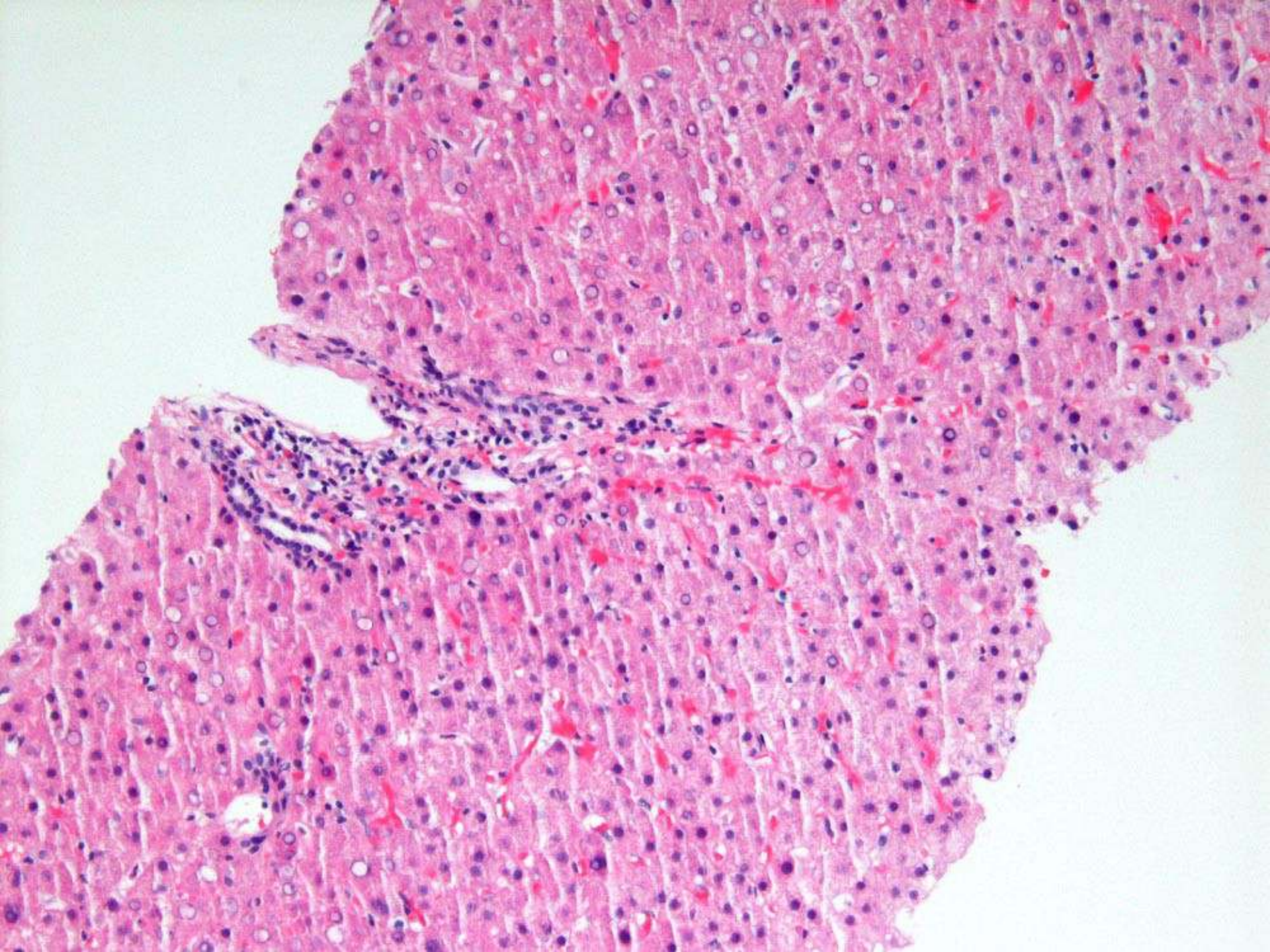
AMA positive 1:250

ANA, ASMA negative

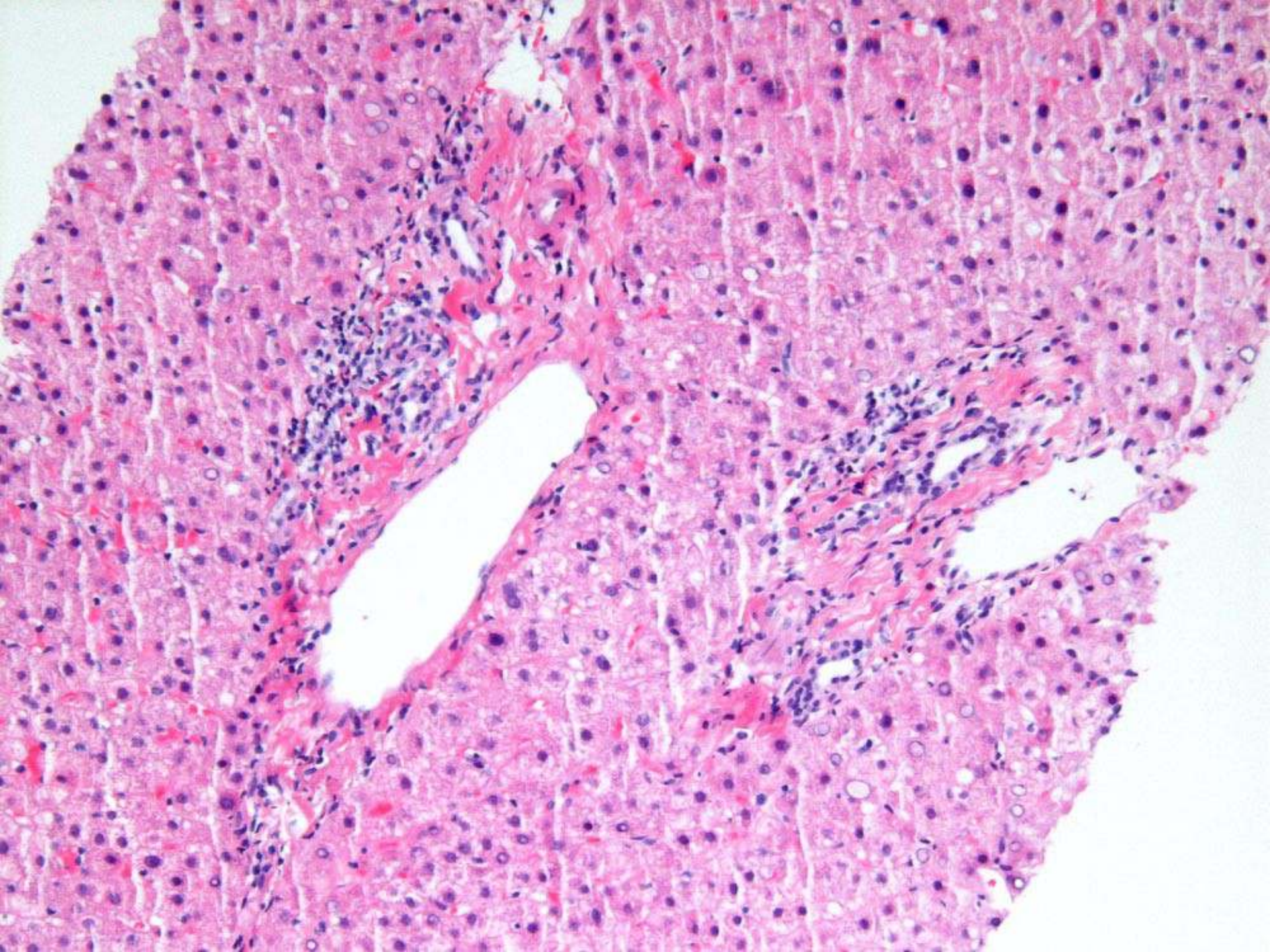
Liver Biopsy: Primary Biliary Cholangitis?



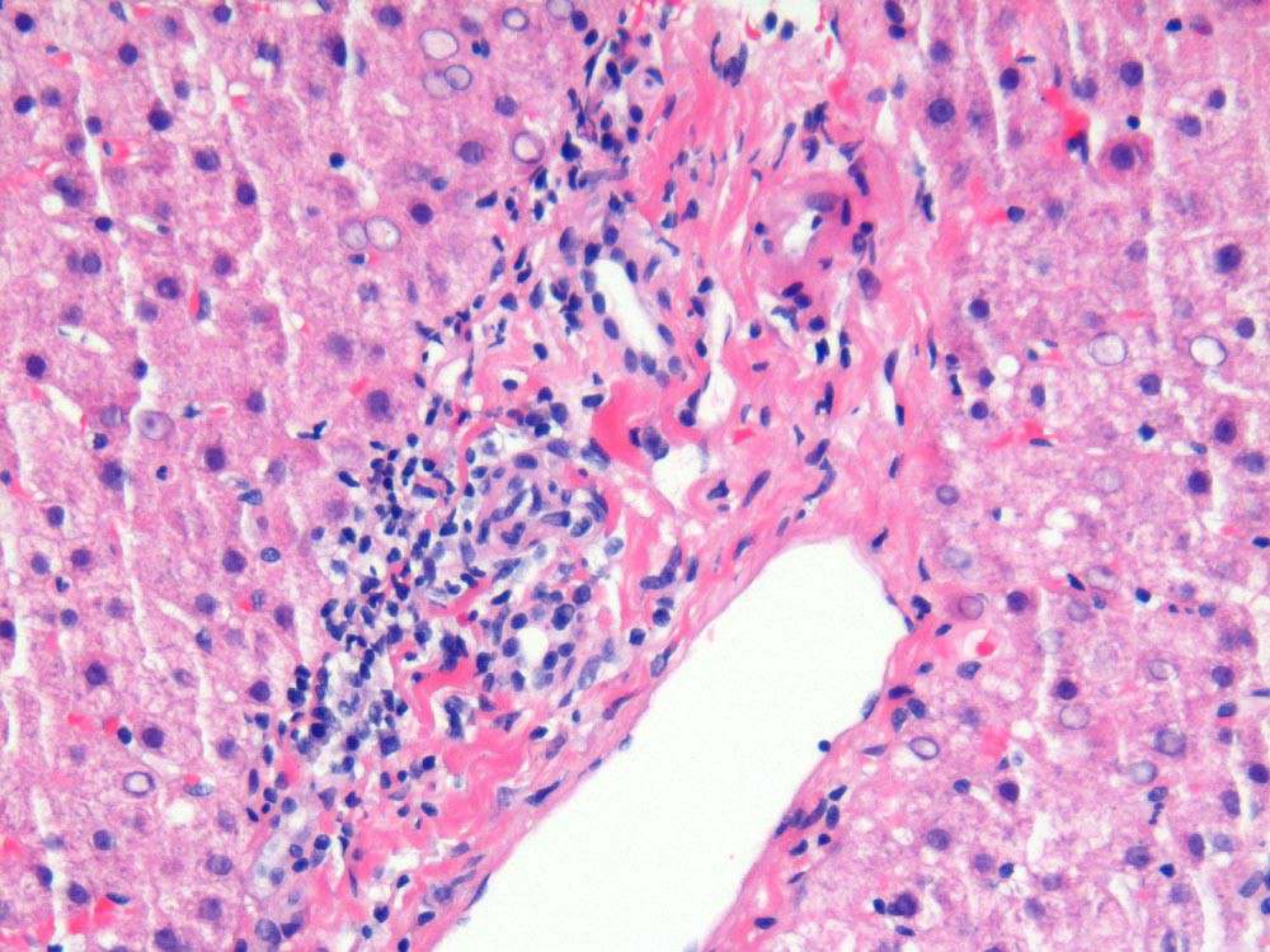












**What do I do now?**

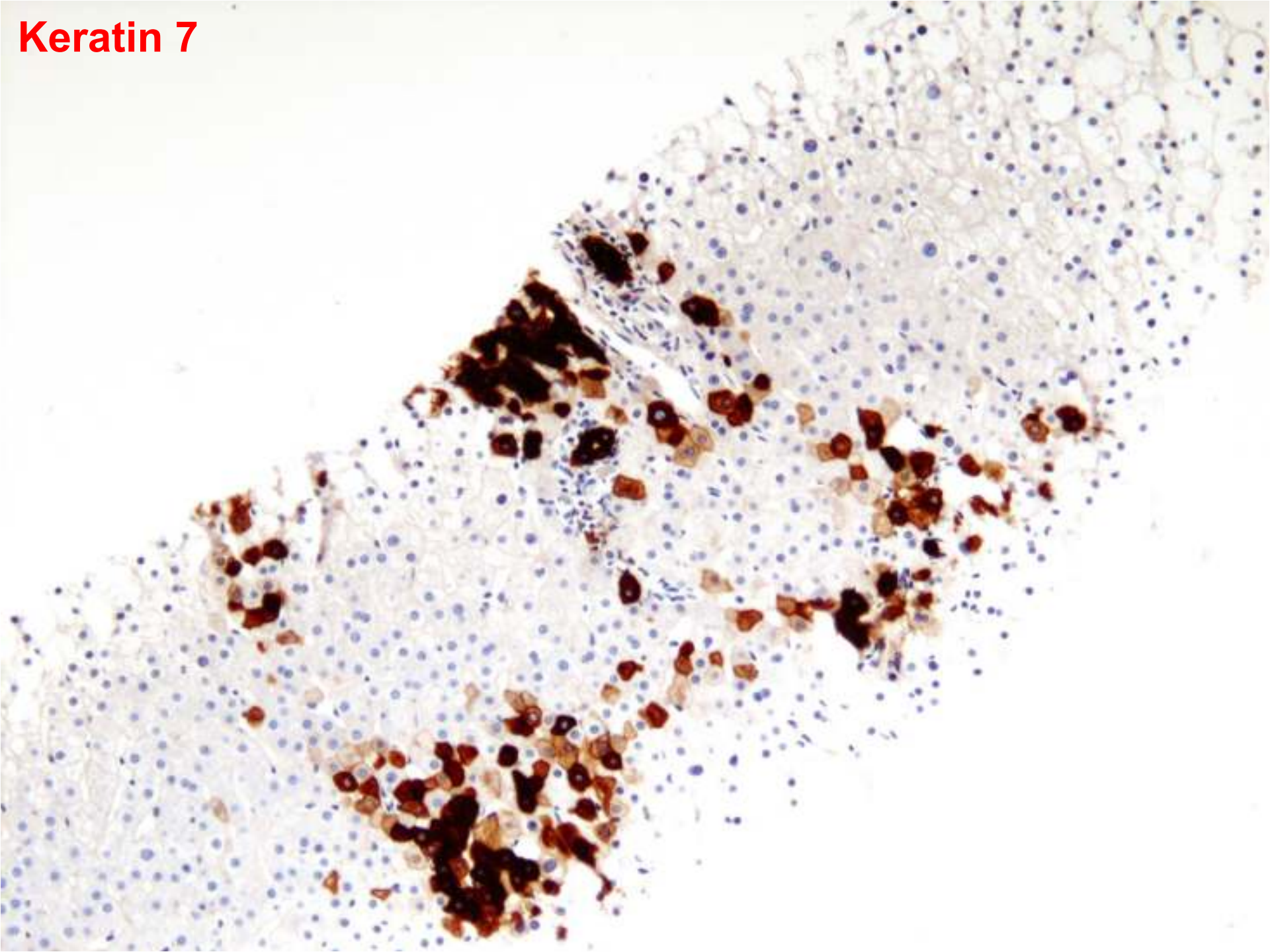
**What do I do now?**  
**IHC for K7 and K19**



# Keratin 7



**Keratin 7**

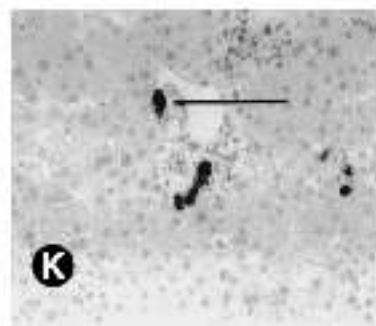
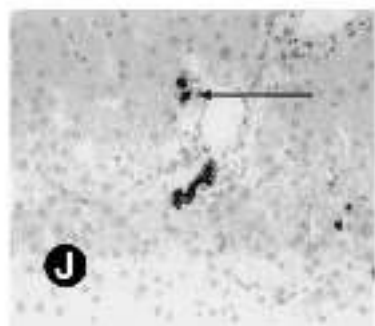
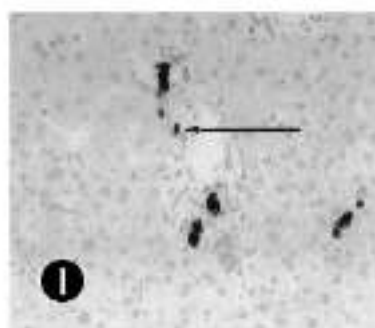
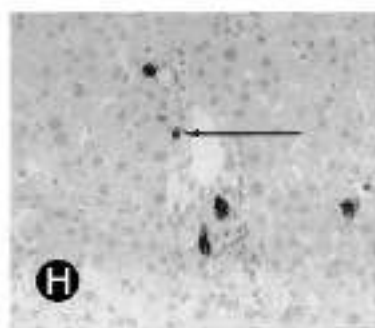
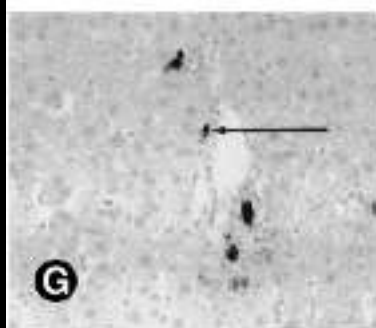
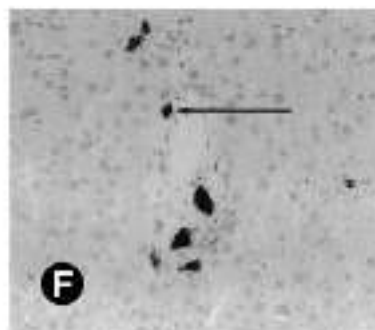
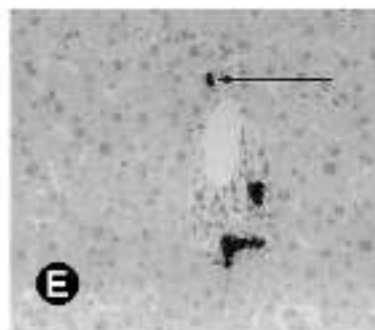
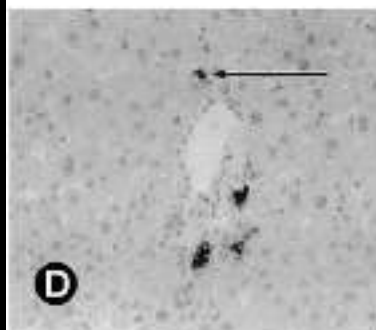
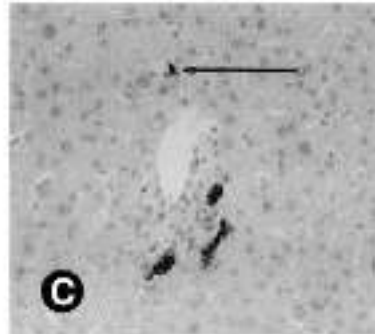
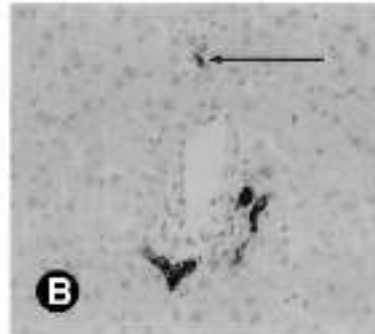
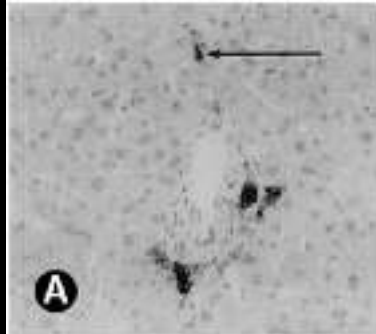


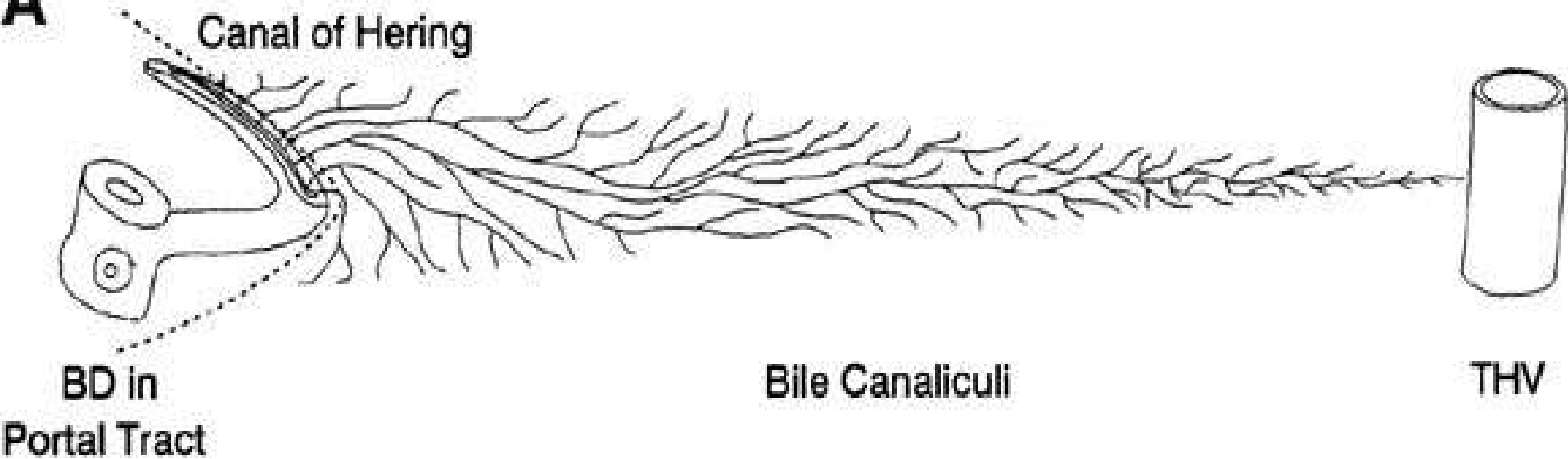


**What do I do now?**  
**IHC for K7 and K19**

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**IHC for K7 and K19**





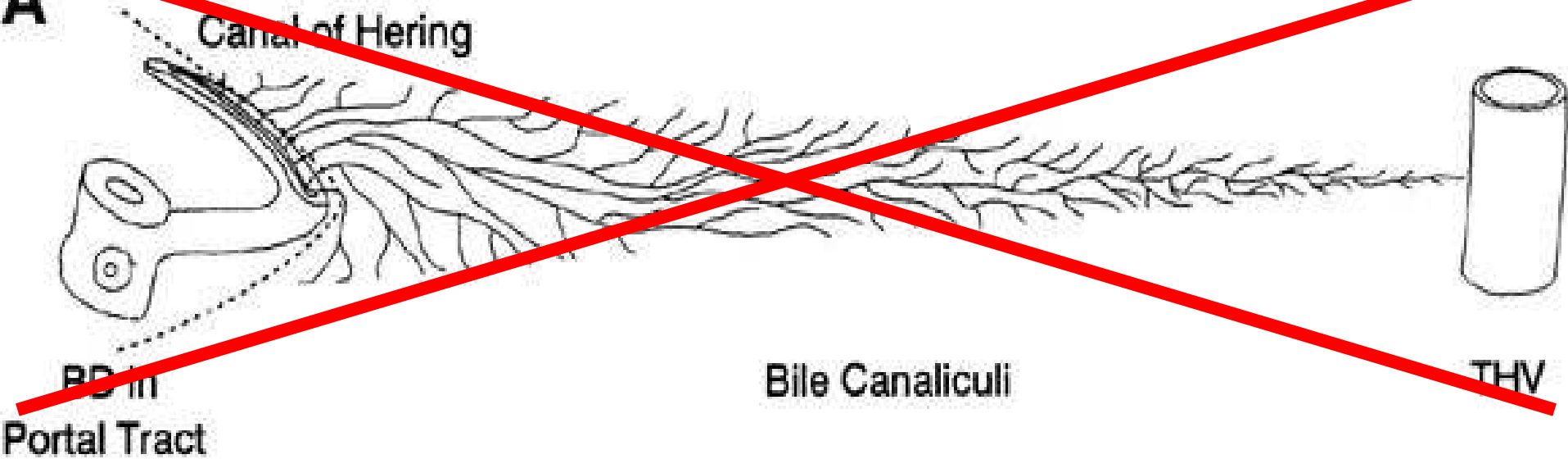
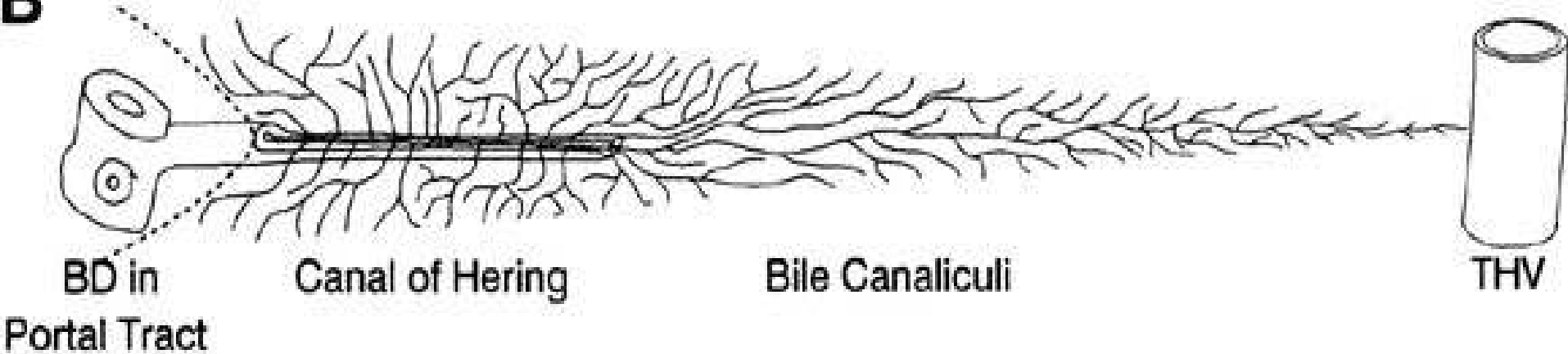
**A**

**Aleta and James Crawford**  
*for* Theise et al., *Hepatology*. 1999; 30: 1425.

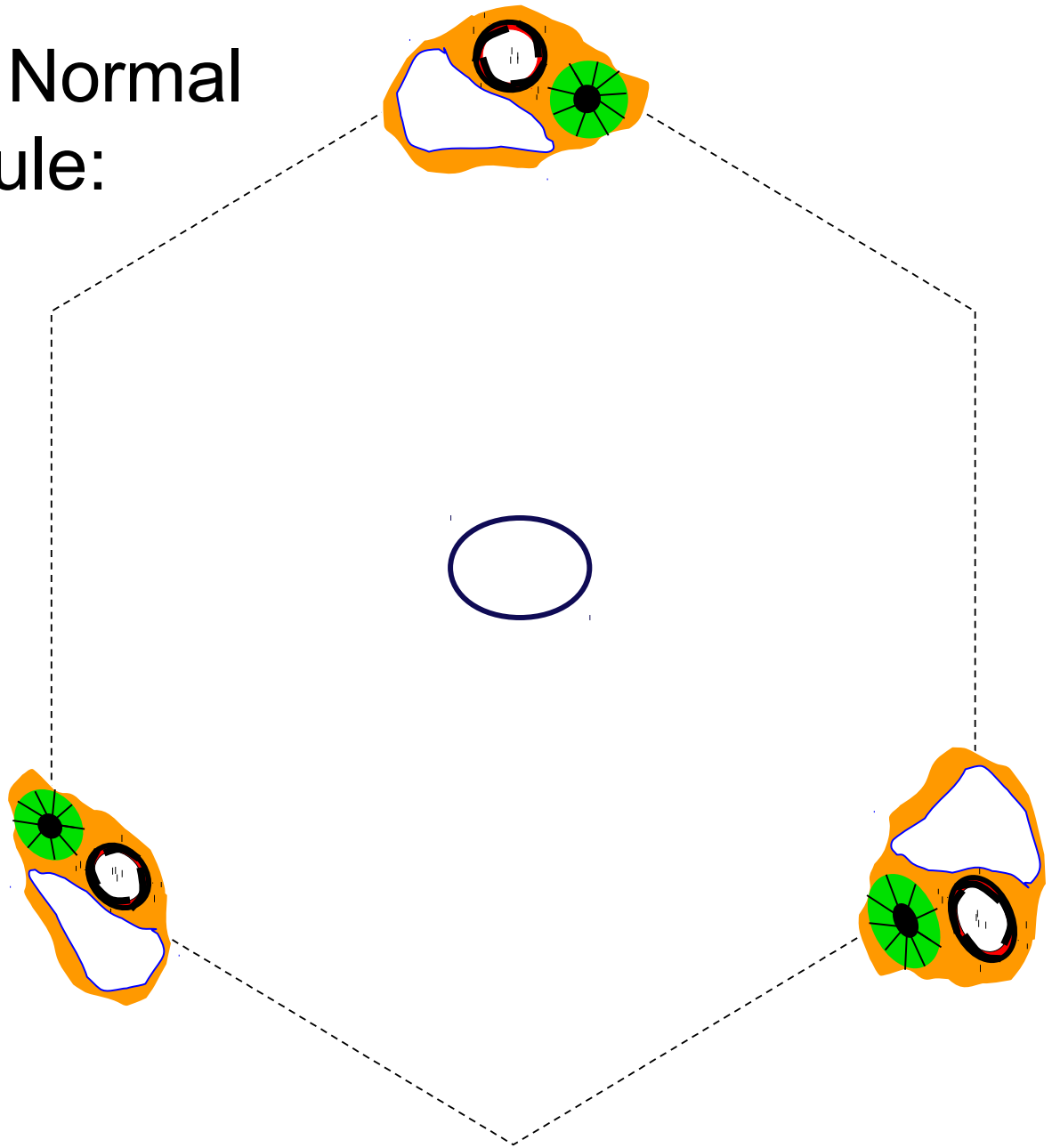
**Definitions according to:**

**Roskams, Theise et al., *Hepatology* 2004; 39: 1739-45.**



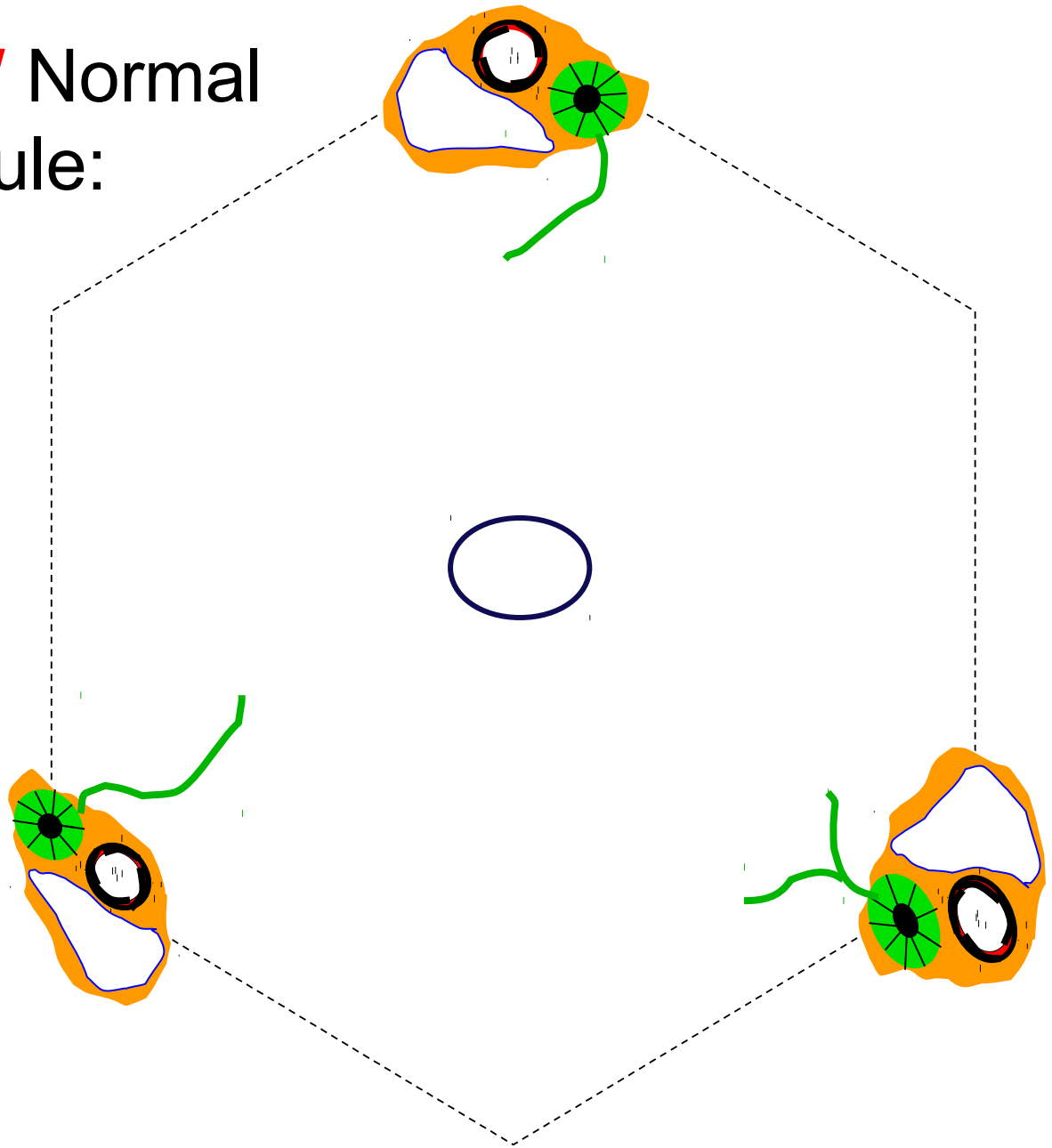
**A****B**

The **OLD** Normal  
Liver Lobule:





The **NEW** Normal  
Liver Lobule:

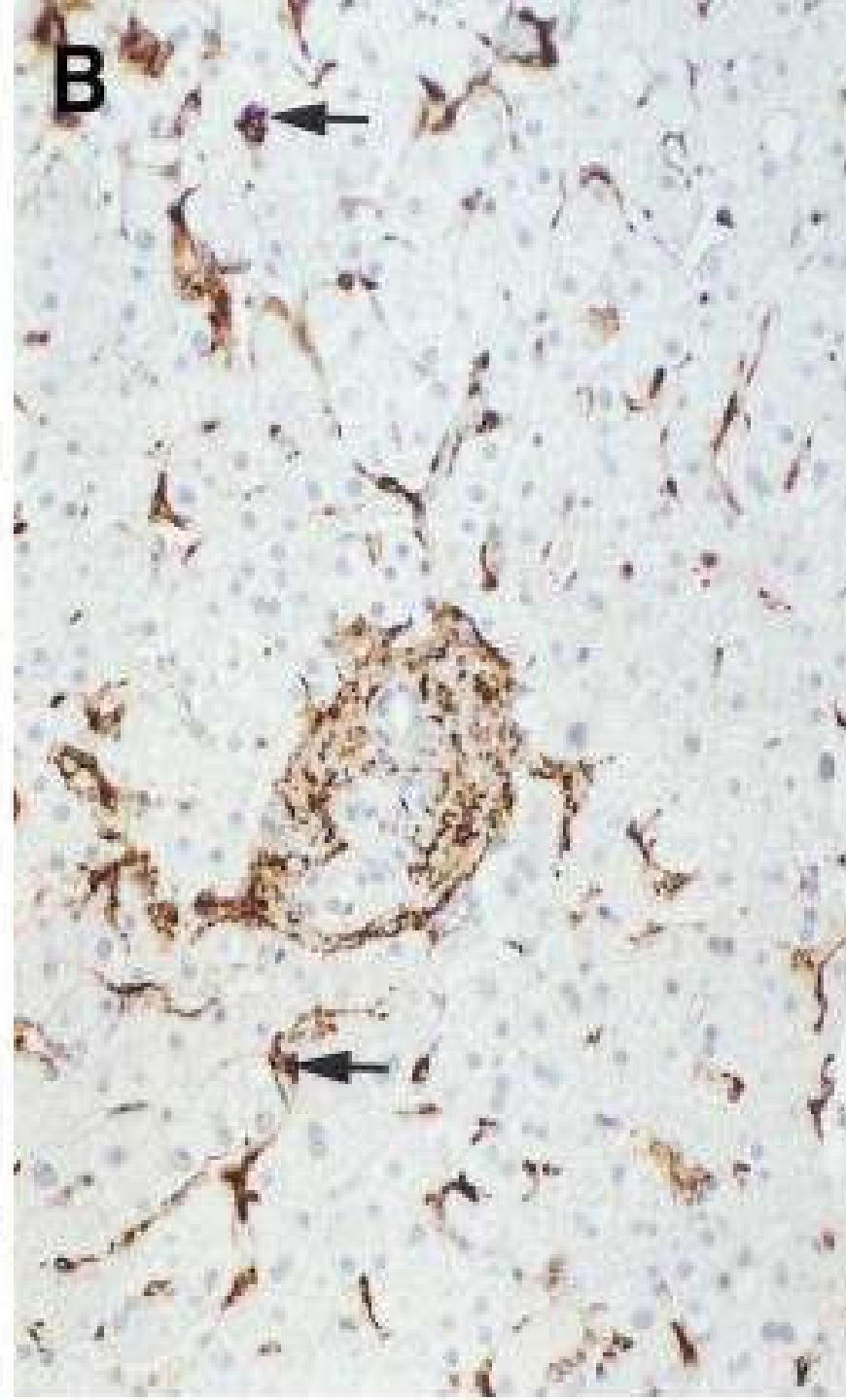
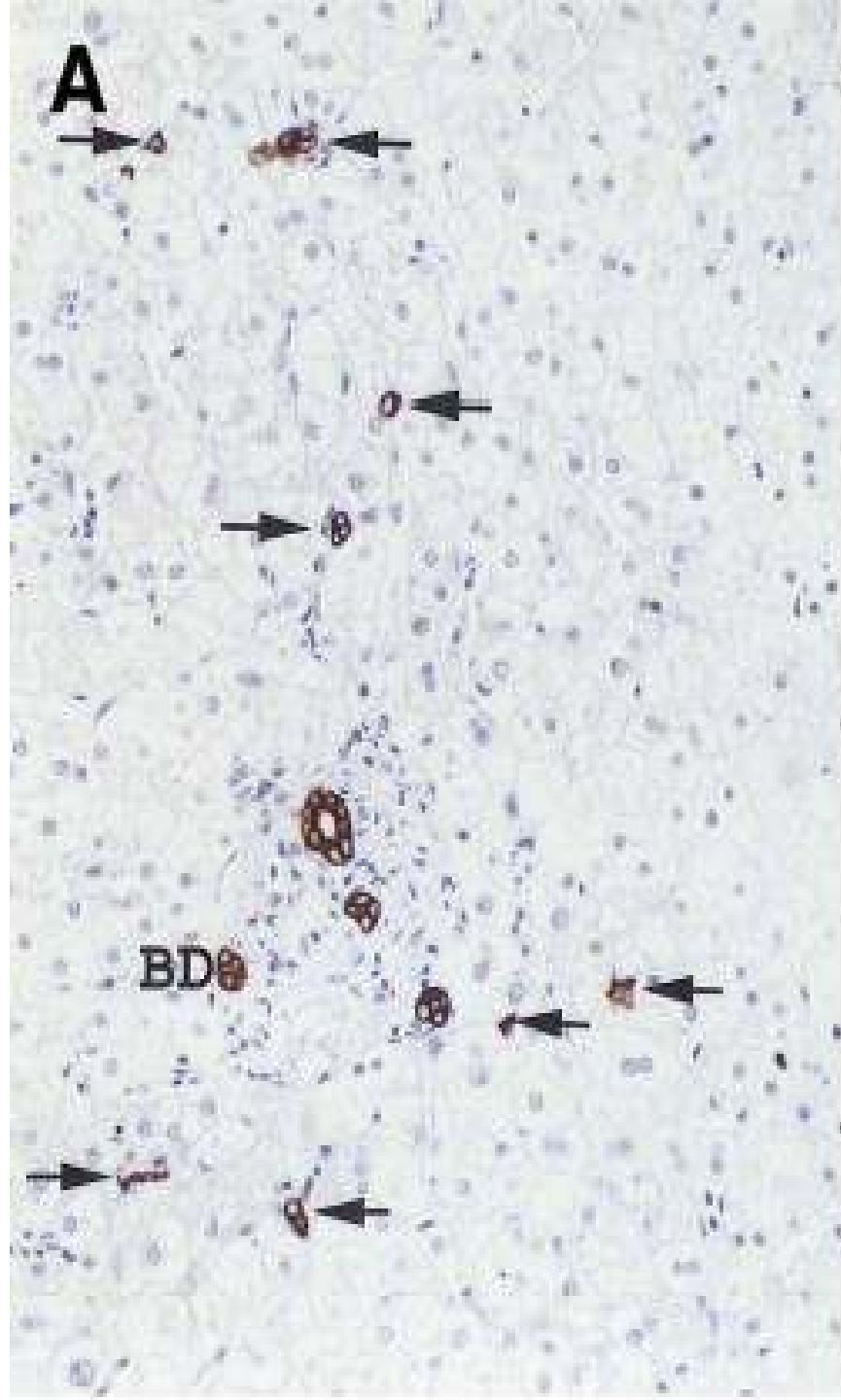


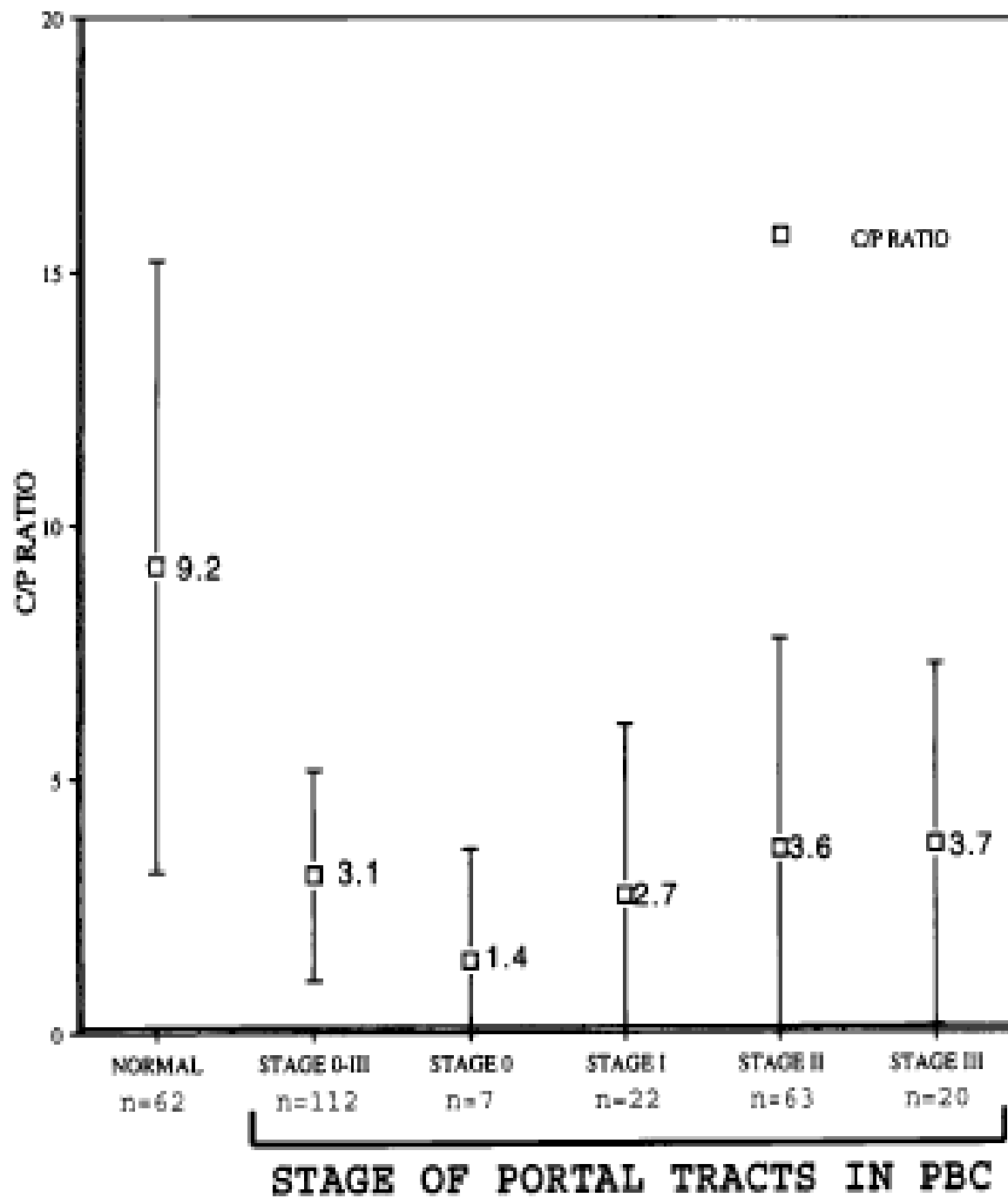
# Destruction of Canals of Hering in Primary Biliary Cirrhosis

ROMIL SAXENA, MD, FRCPATH  
PRODROMOS HYTIROGLOU, MD  
SWAN N. THUNG, MD  
NEIL D. THEISE, MD

HUMAN PATHOLOGY 2002; 33: 983



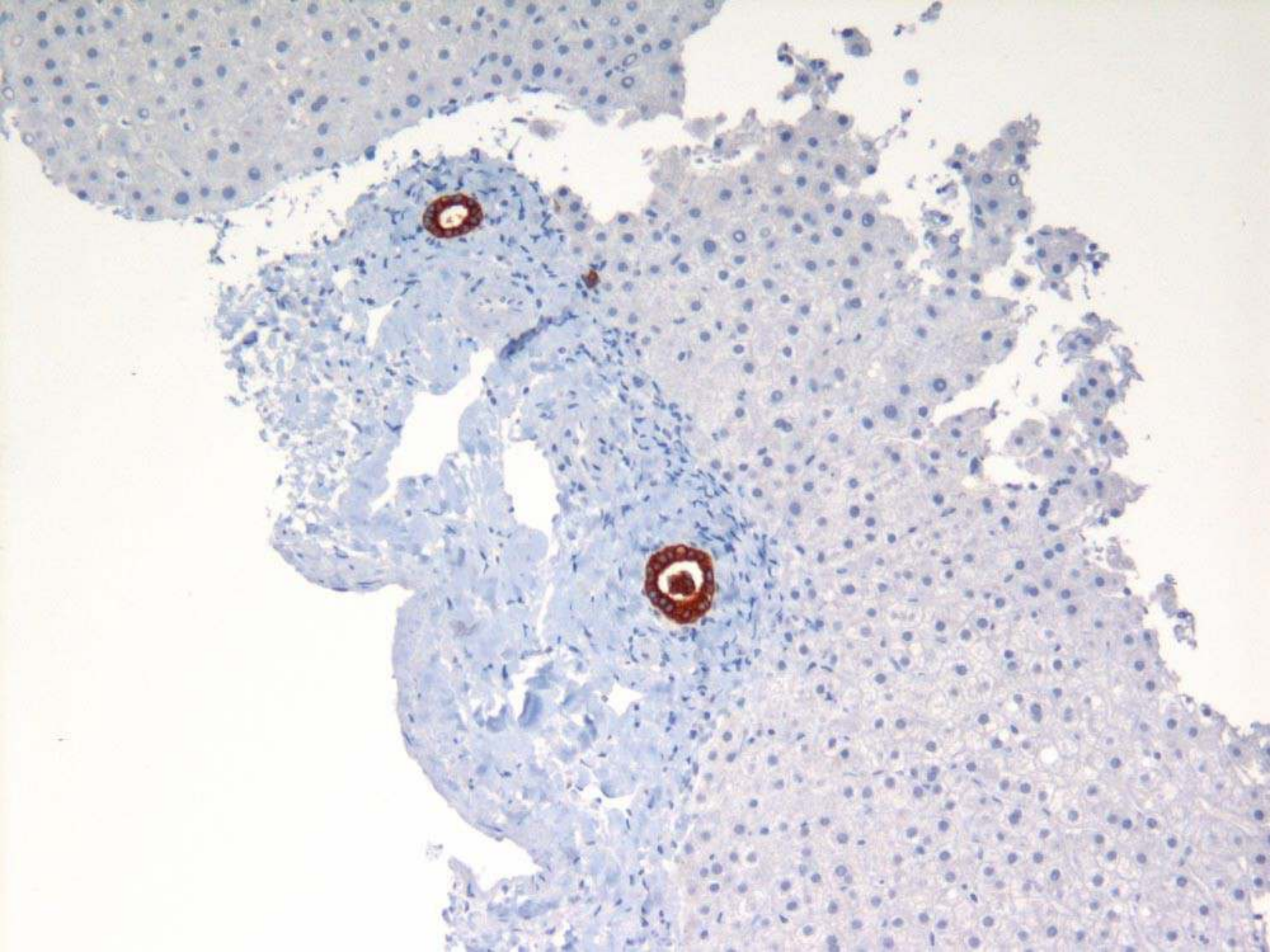




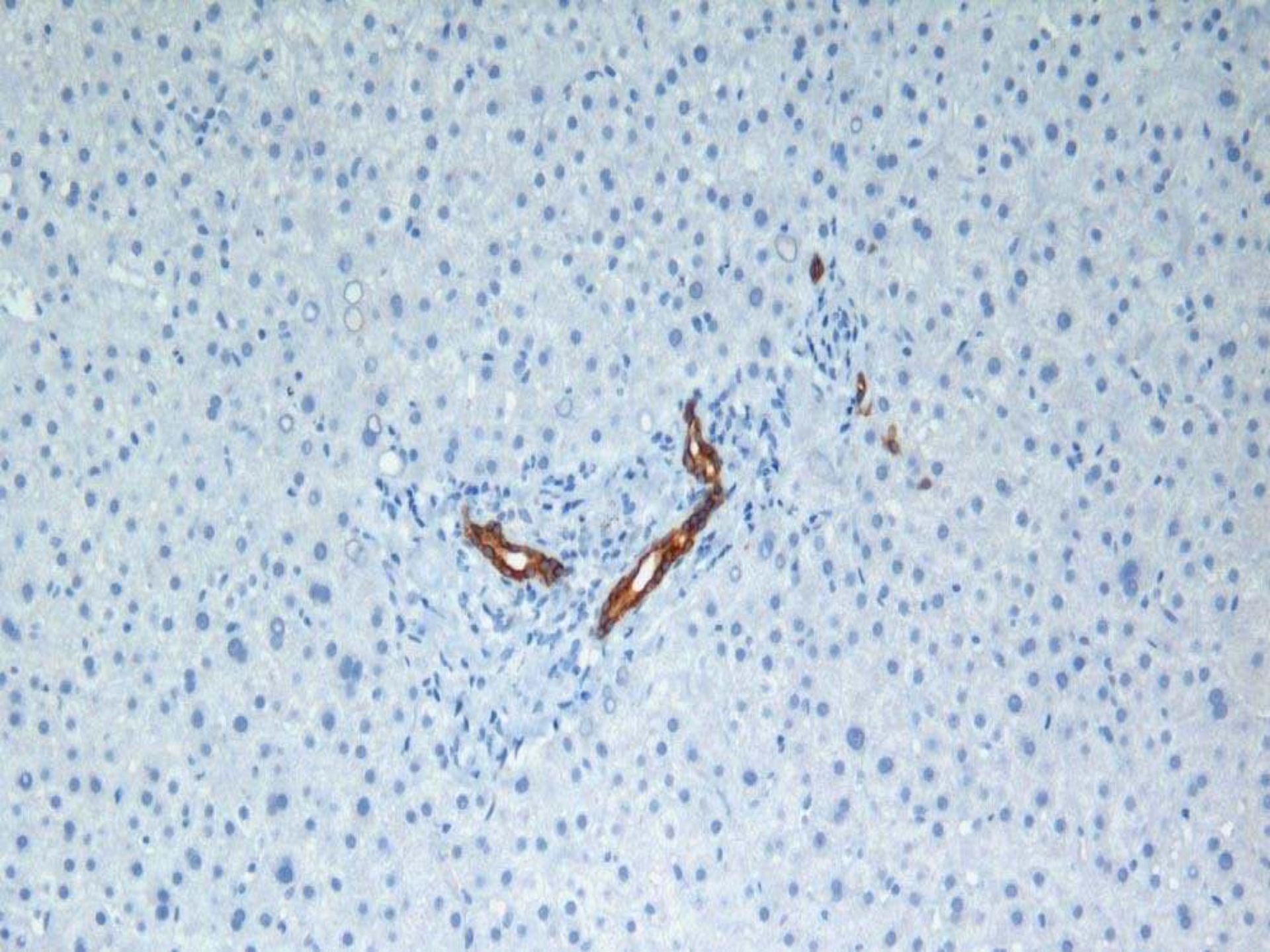
**Reminder: NORMAL**



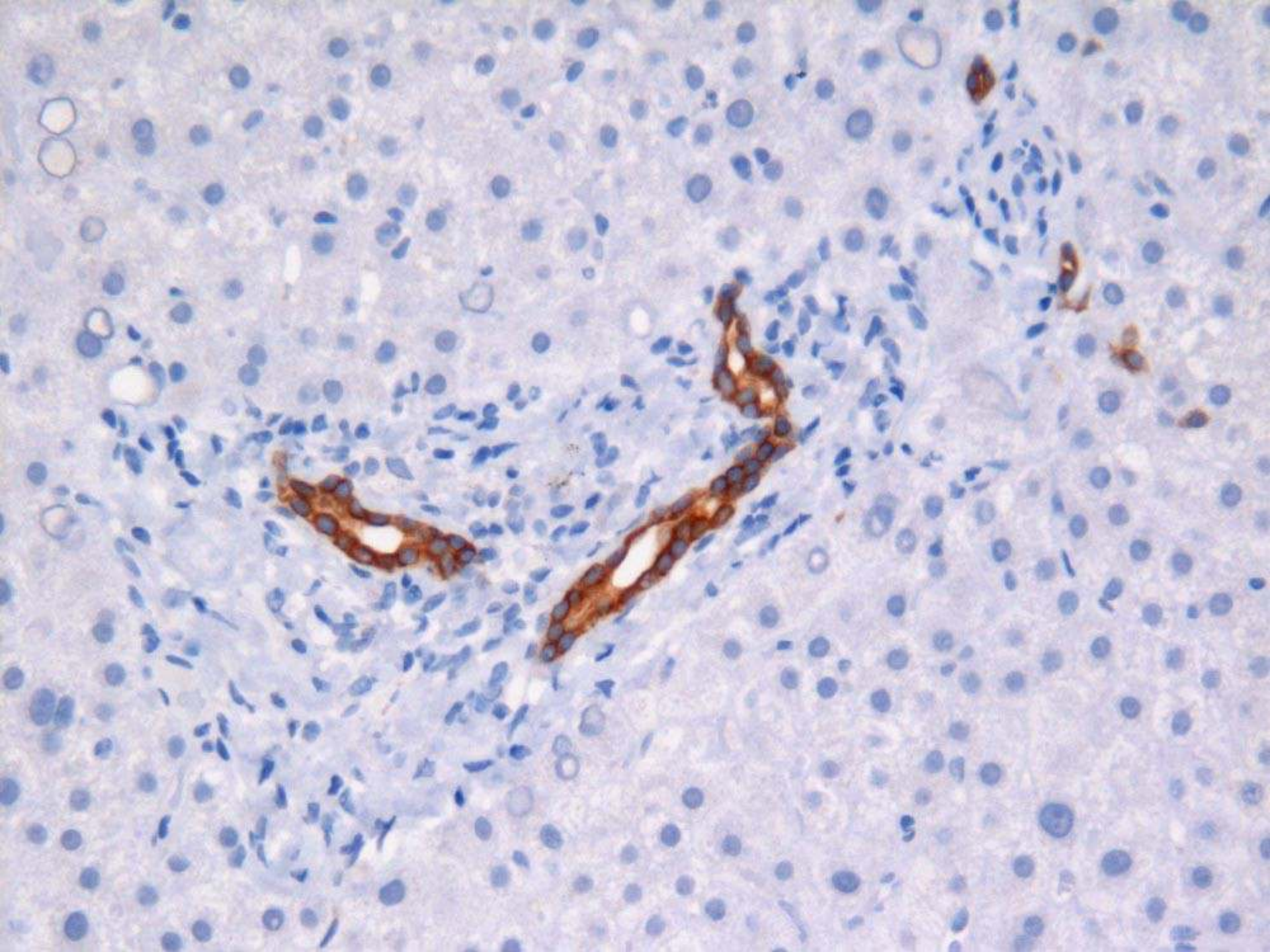




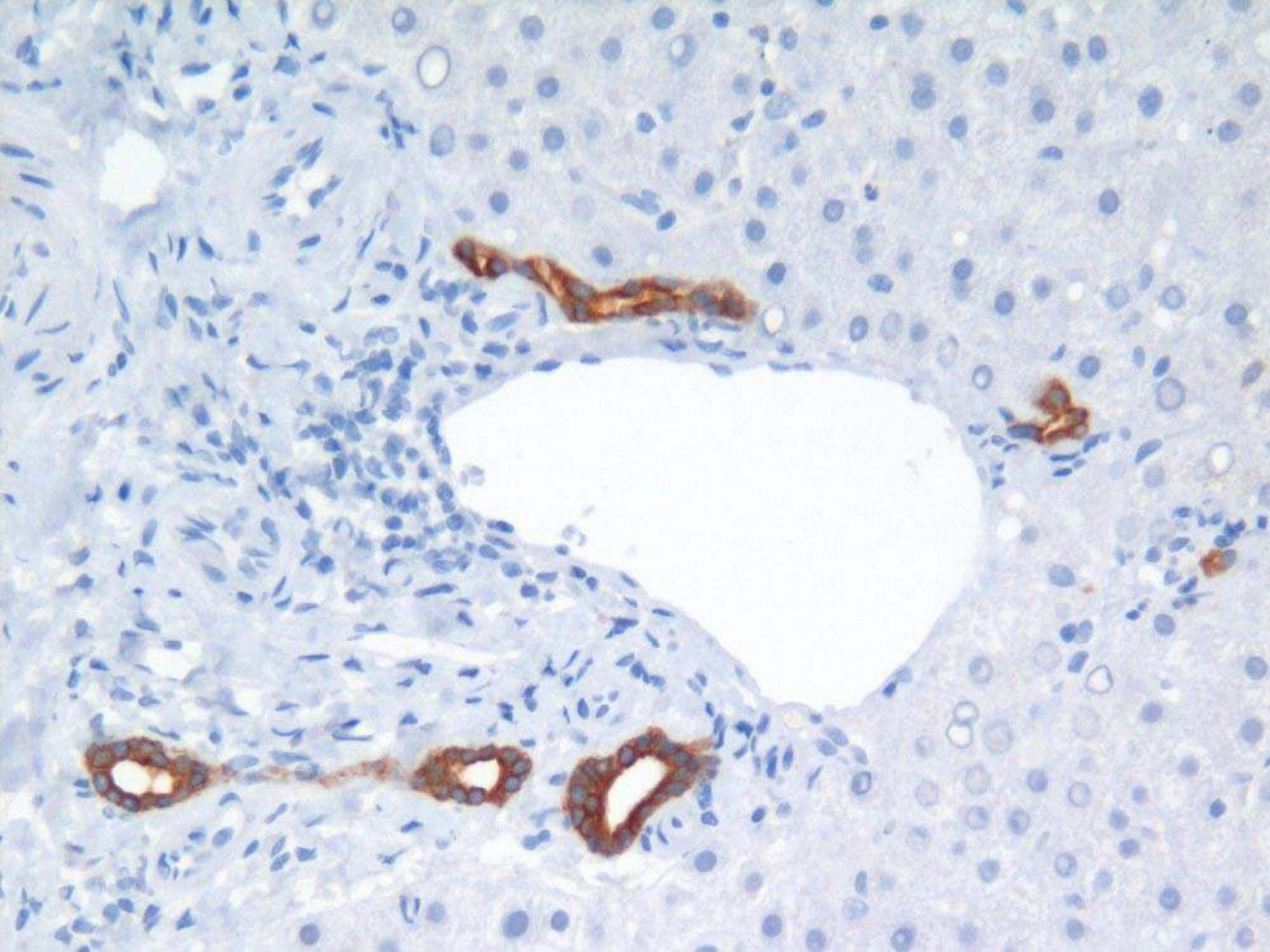




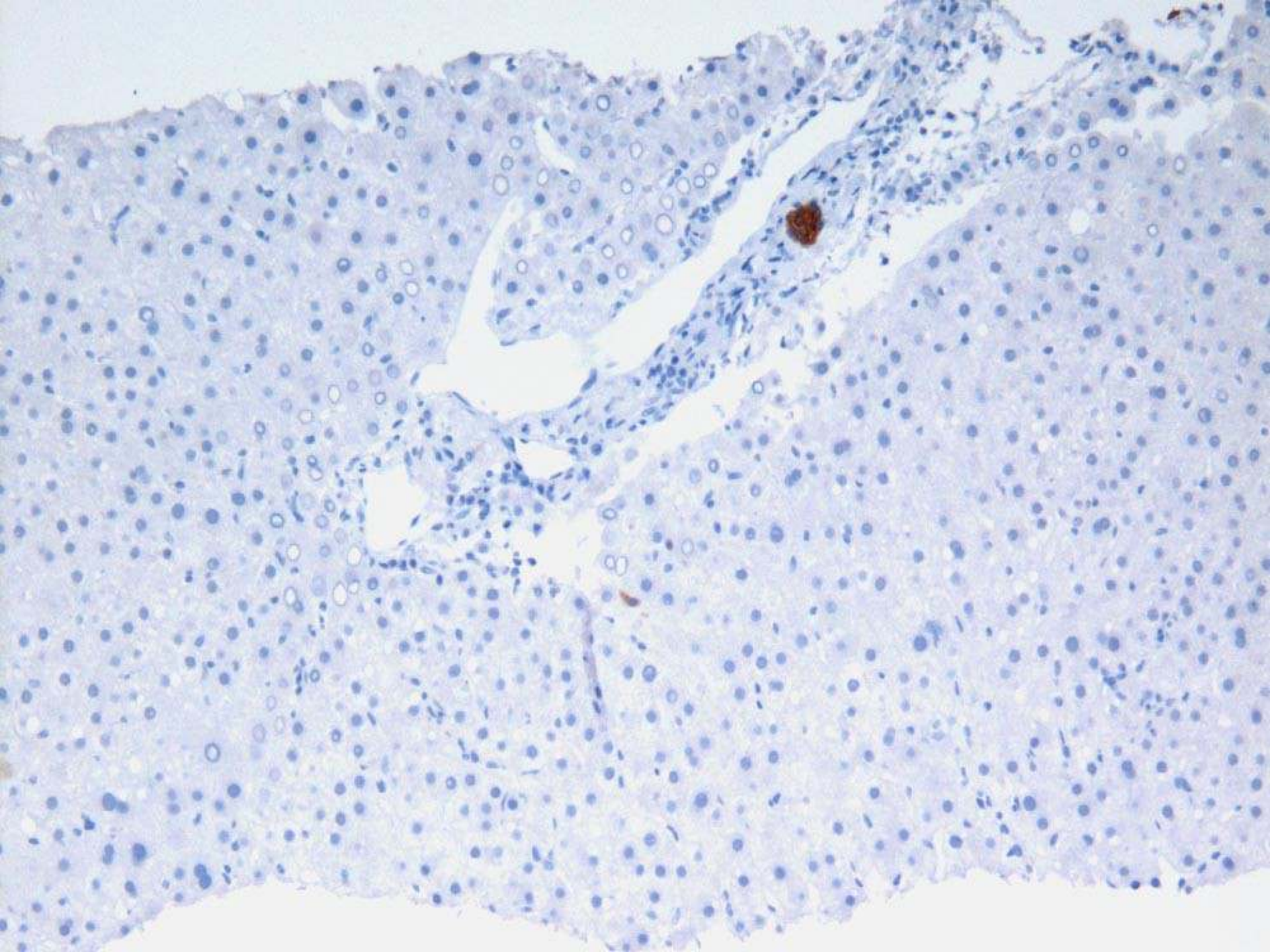




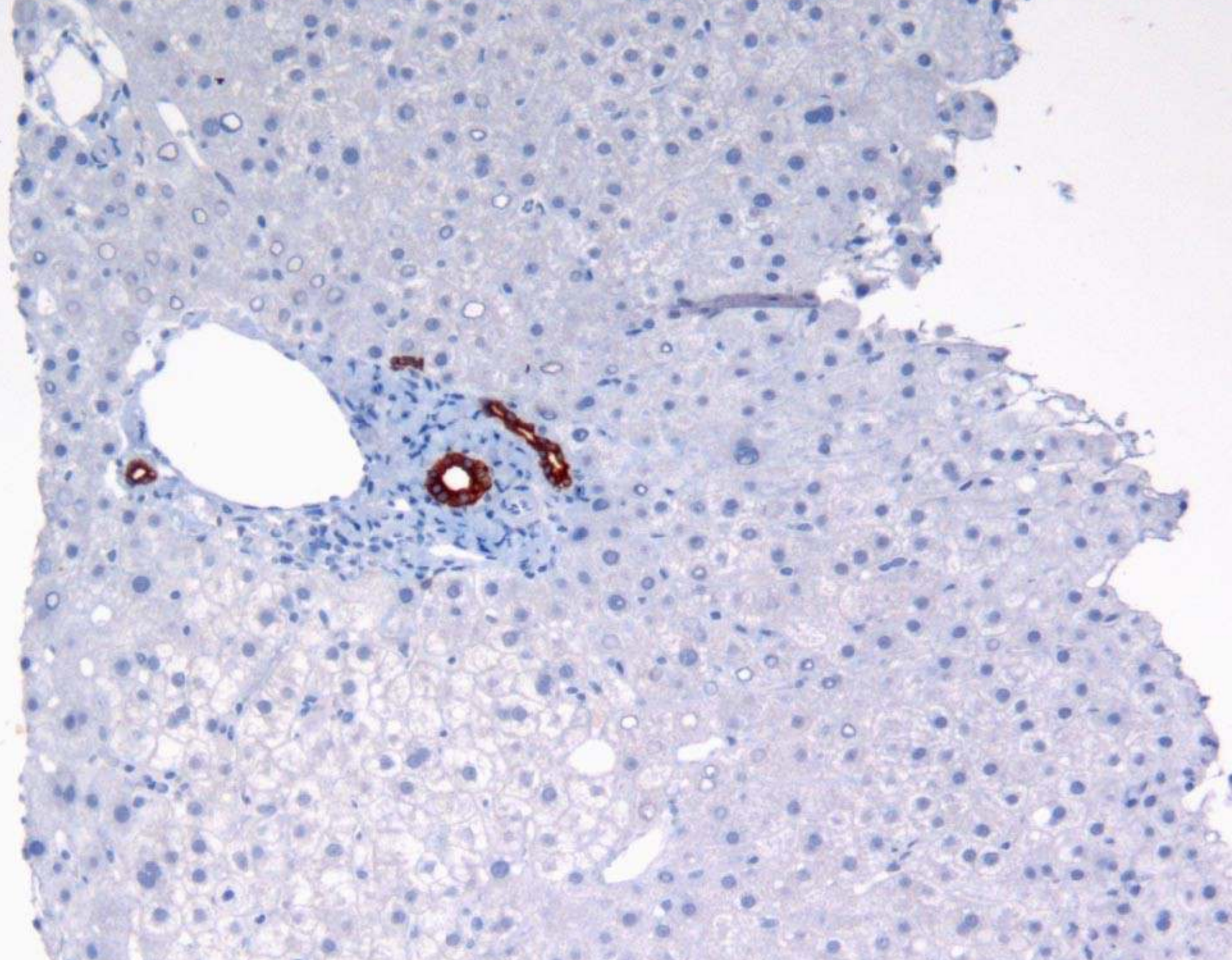












## Case 1

Final Diagnosis:  
Paucity of Canals of Hering/Ductules  
Compatible with “Minimal Change”  
Primary Biliary Cholangitis.



# **Autoimmune hepatitis**

## **Histology:**

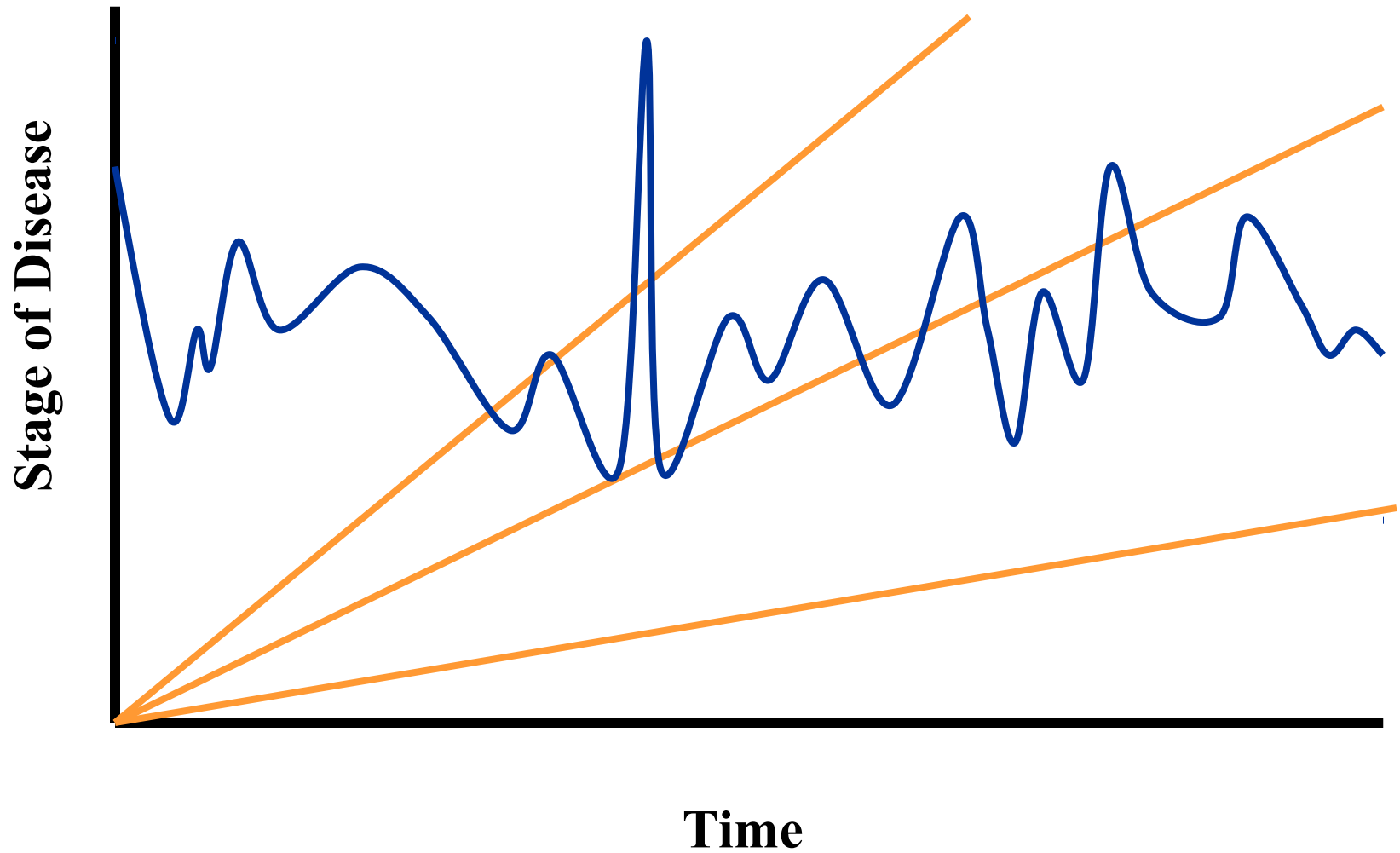
**Fibrosis like viral hepatitis staging**

**Activity: different from viral hepatitis...**

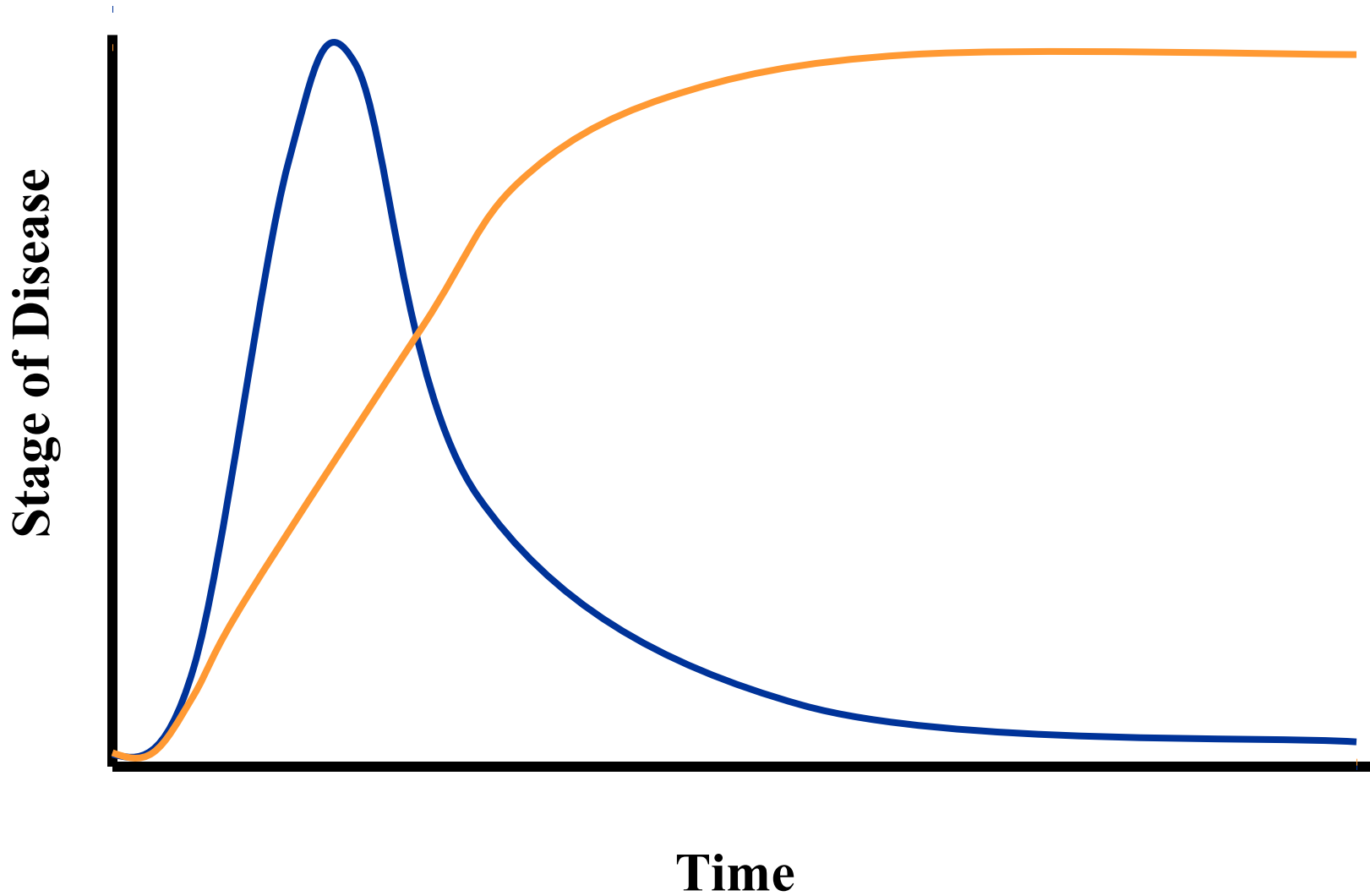
# **Dynamics of Activity and Progression of Autoimmune Hepatitis over Time**

**Assessment is NOT like chronic viral hepatitis!**

# Viral hepatitis: Progression vs. activity over time

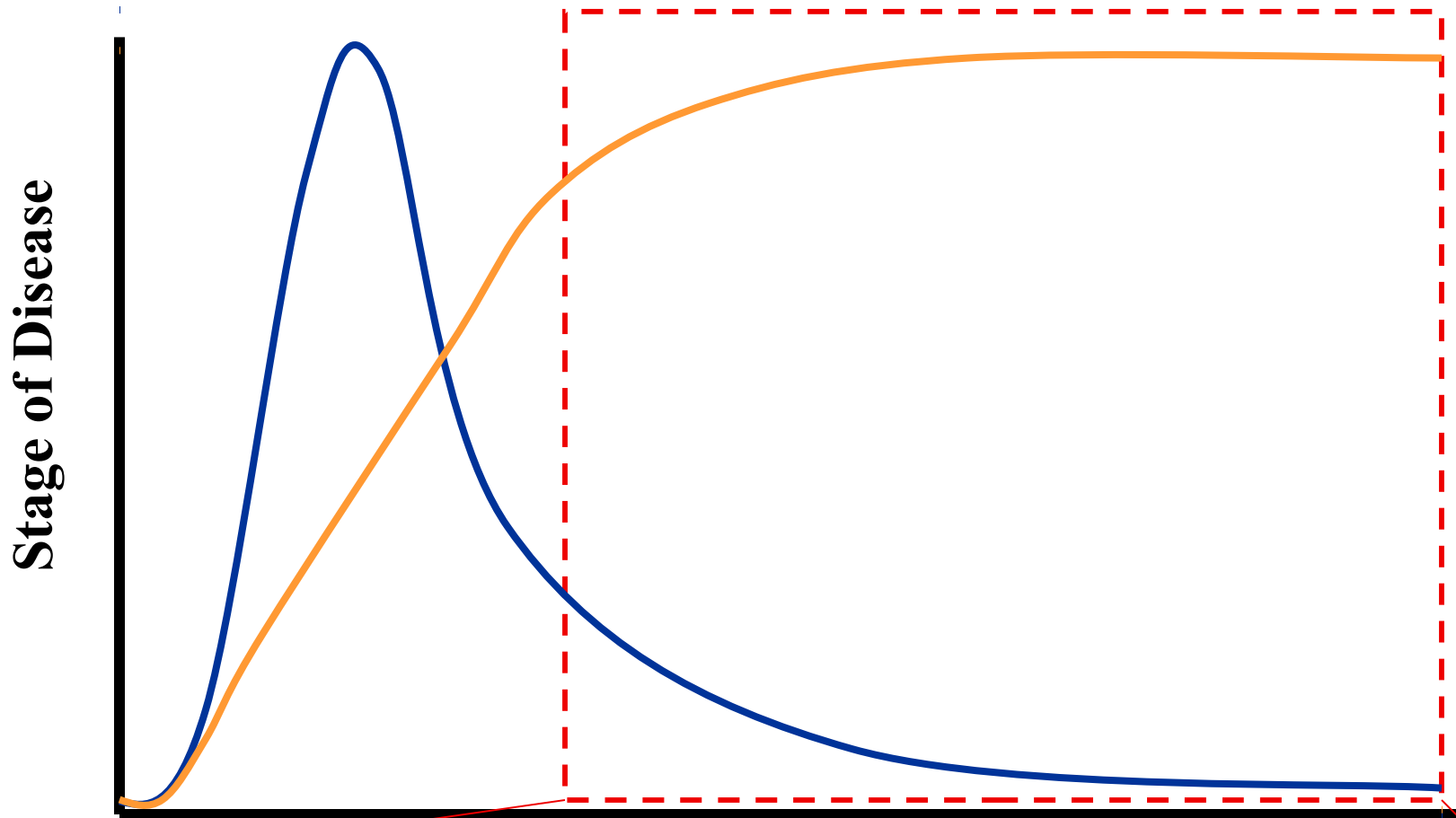


# Autoimmune hepatitis: Progression vs. activity over time



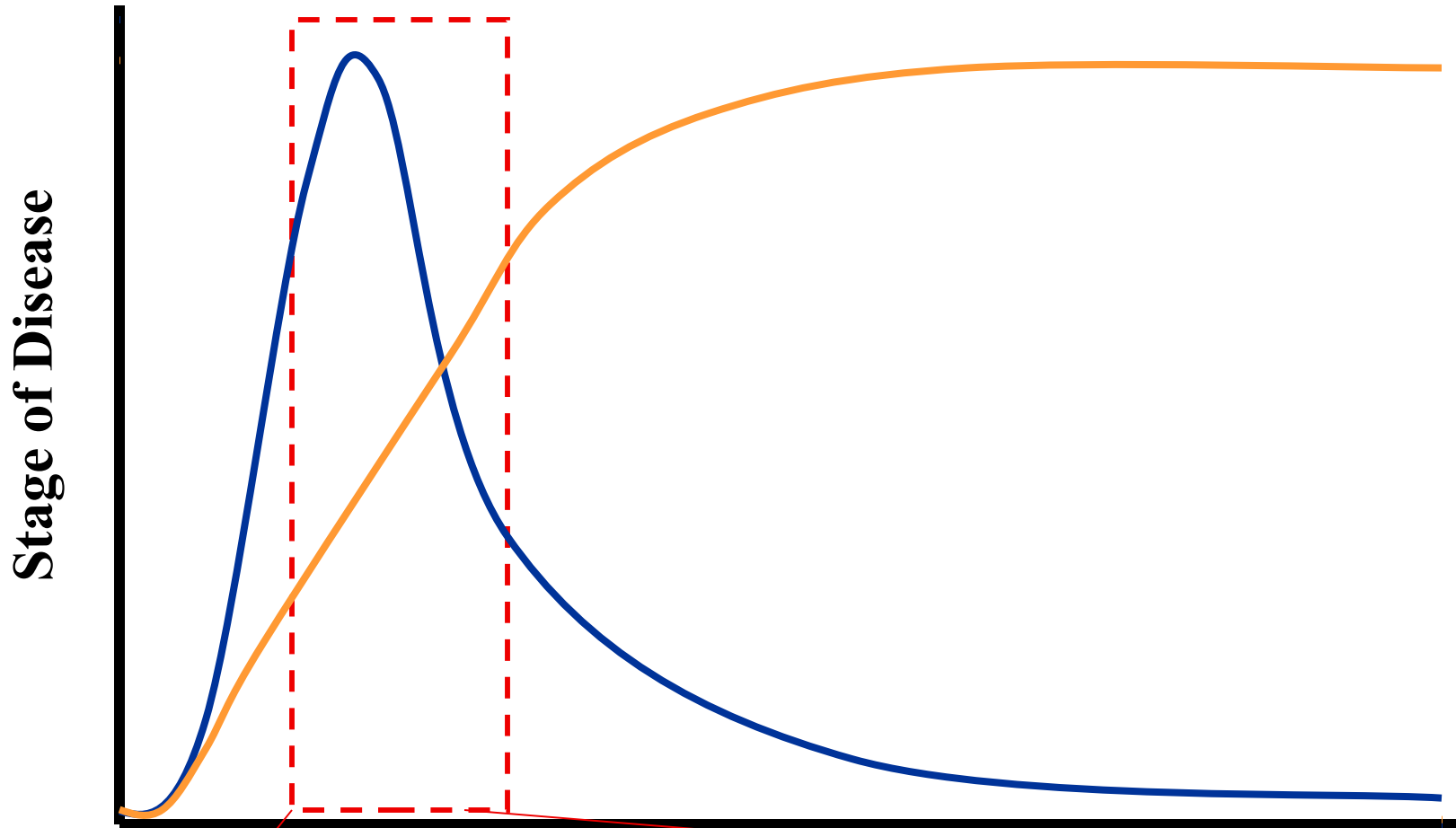


## Autoimmune hepatitis: Progression vs. activity over time



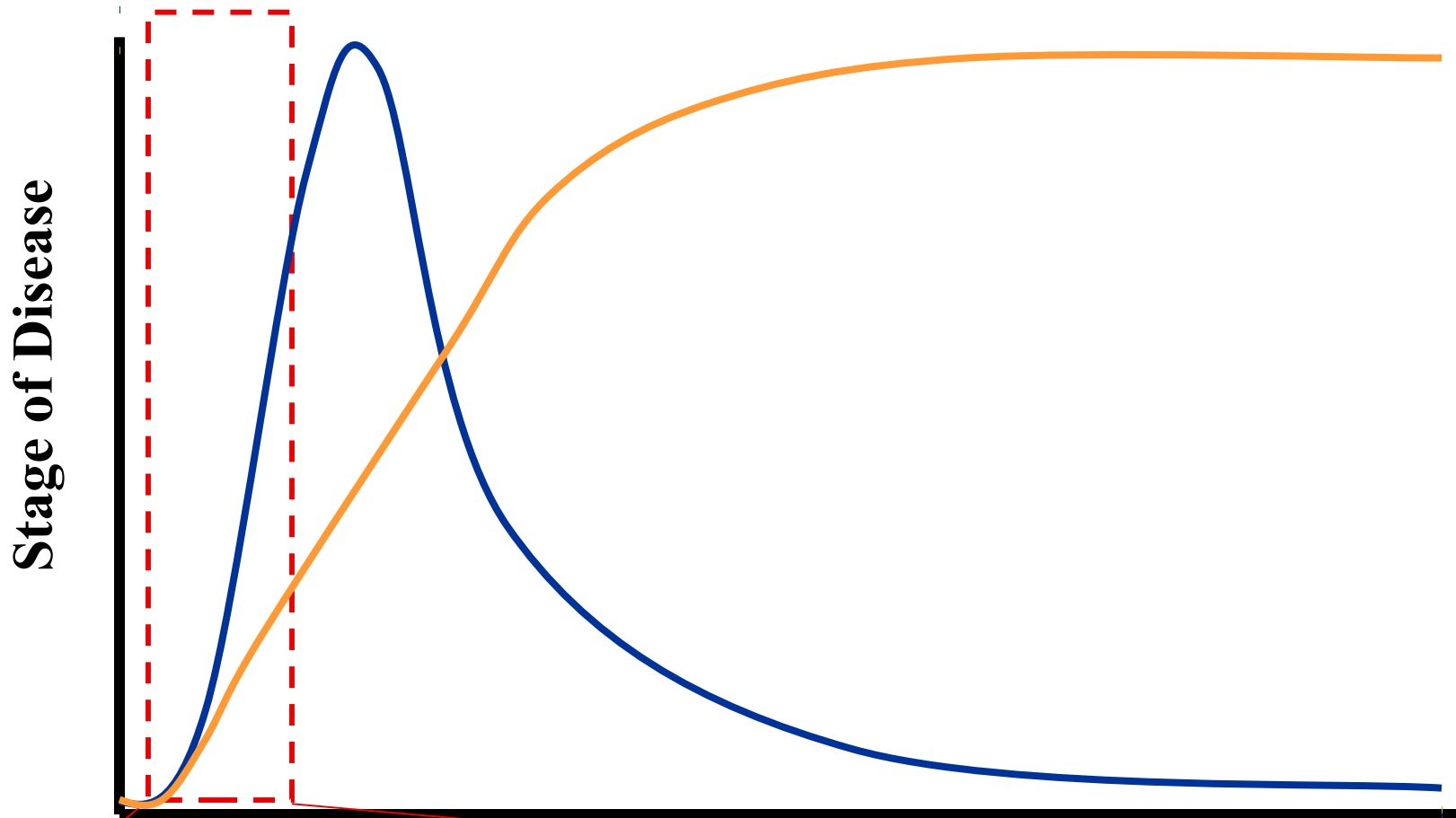
**Biopsy: Advanced disease, but mild or “burned out hepatitis”**

# Autoimmune hepatitis: Progression vs. activity over time



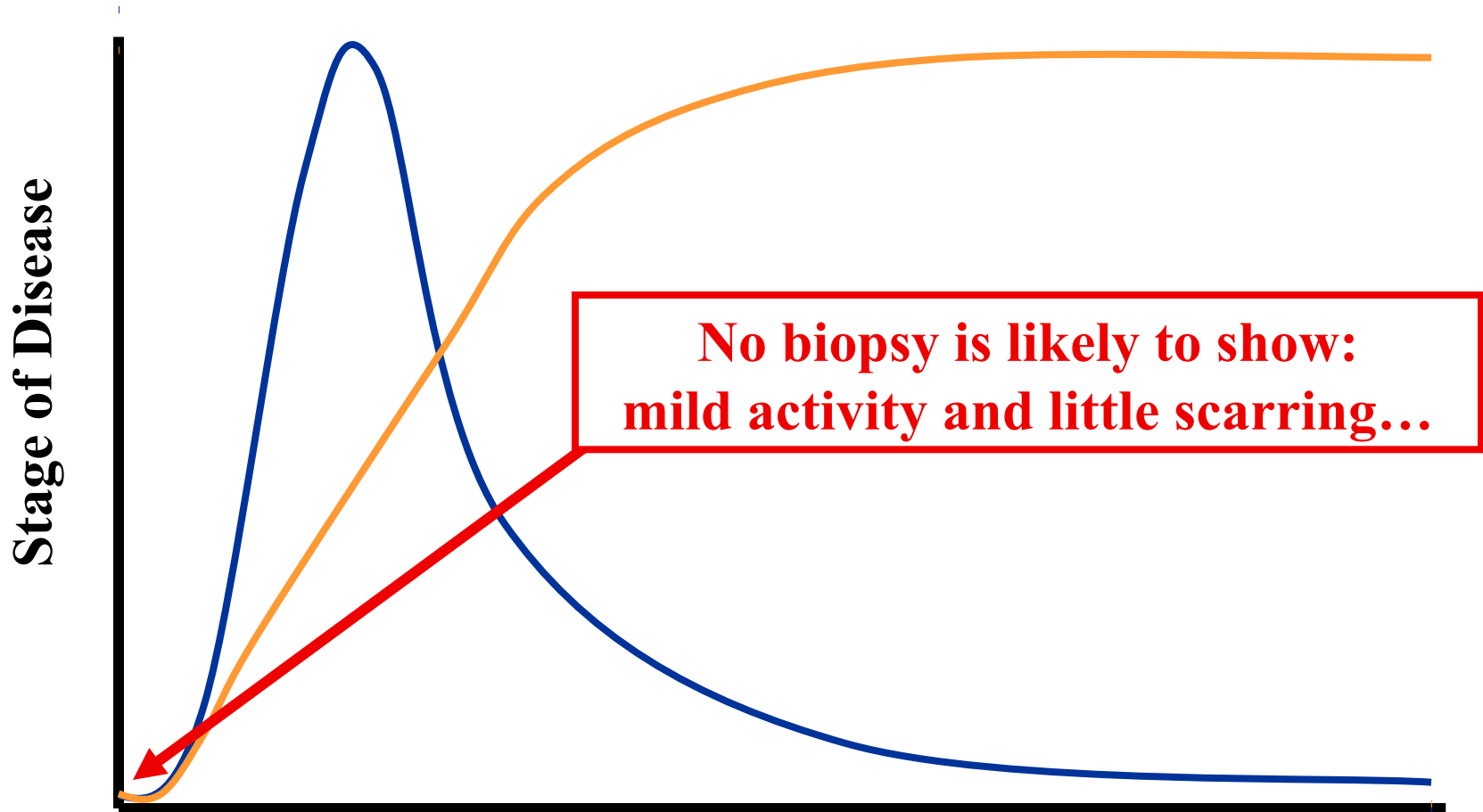
**Biopsy: Advancing disease and severe activity**

# Autoimmune hepatitis: Progression vs. activity over time



**Biopsy: Little scarring, but severe activity**

## Autoimmune hepatitis: Progression vs. activity over time





## Case 2

78 year old man with a hx of spontaneously resolving hepatitis of unknown etiology 15 years ago and single isolated mildly elevated ALT of 70 a year ago. Now presents with progressive weight loss, anorexia but no abdominal pain, and a newly dilated bile duct to 11 mm (6 mm last yr on a normal Ct) with mildly nodular liver on MRI/MRCP last week.

LFTs: ALT 1545, AST 1200+, alk phos 254, Bilirubin 3.7.

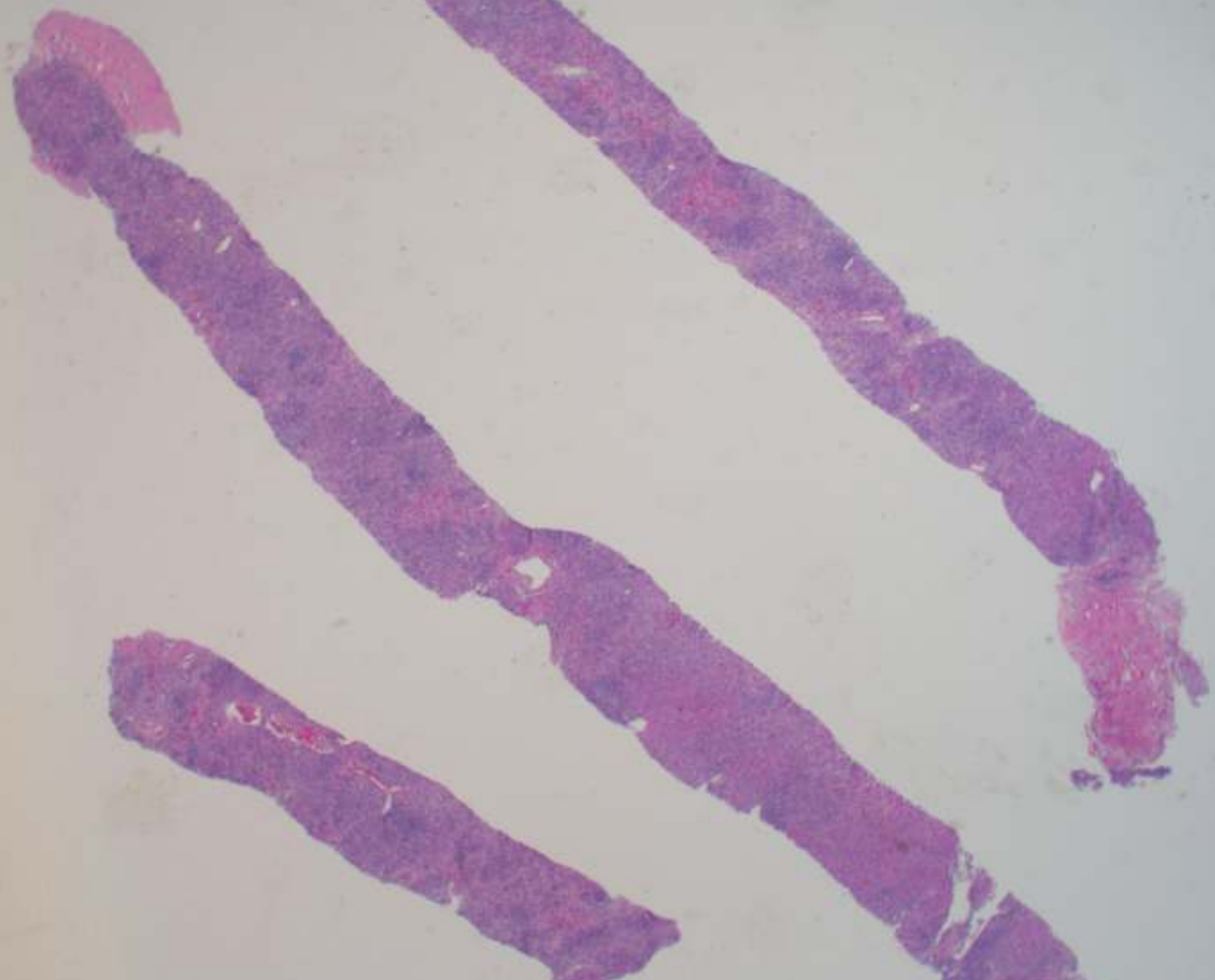
Neg Hepatitis A, B, C, E

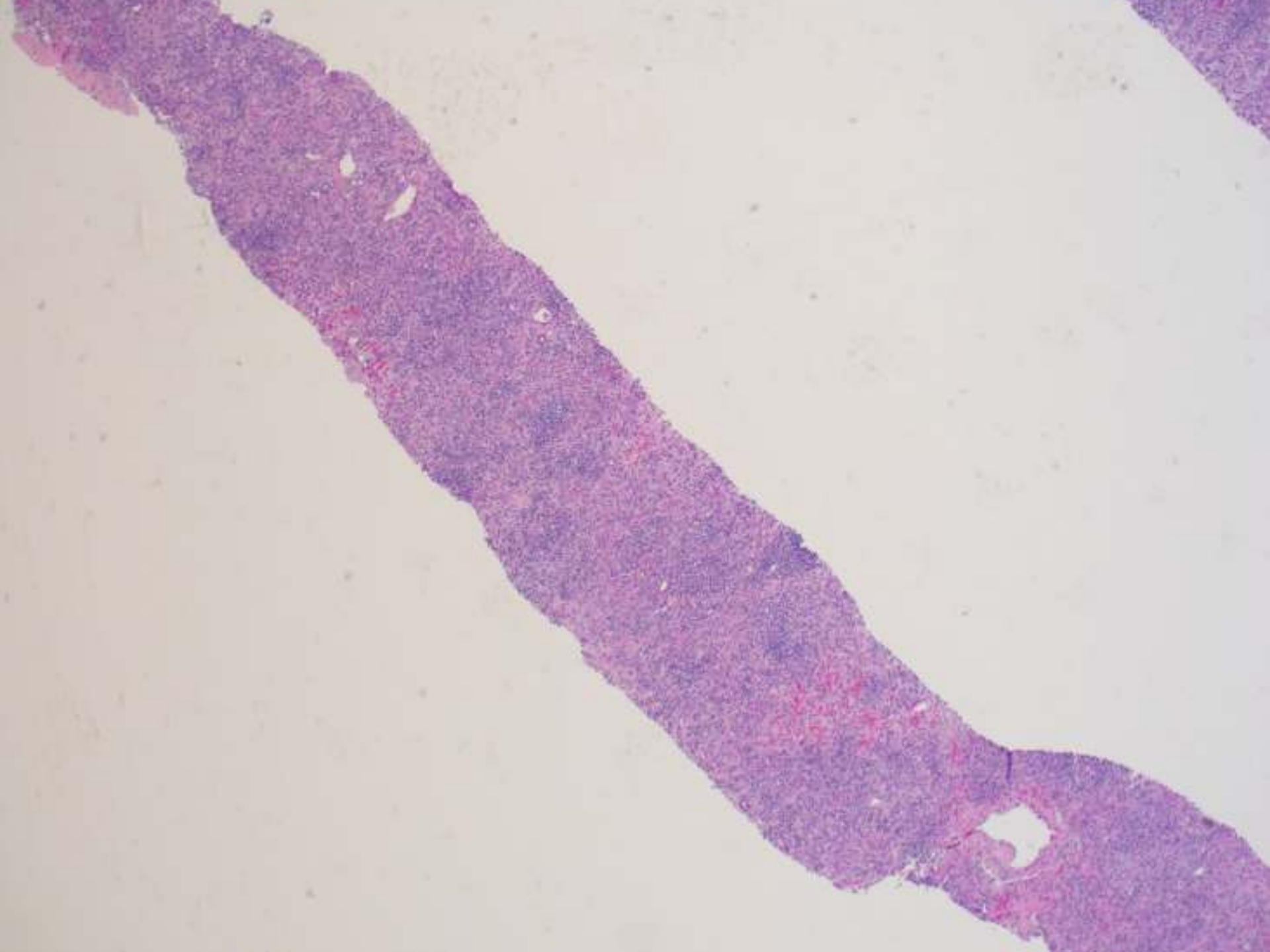
Normal Ceruloplasmin

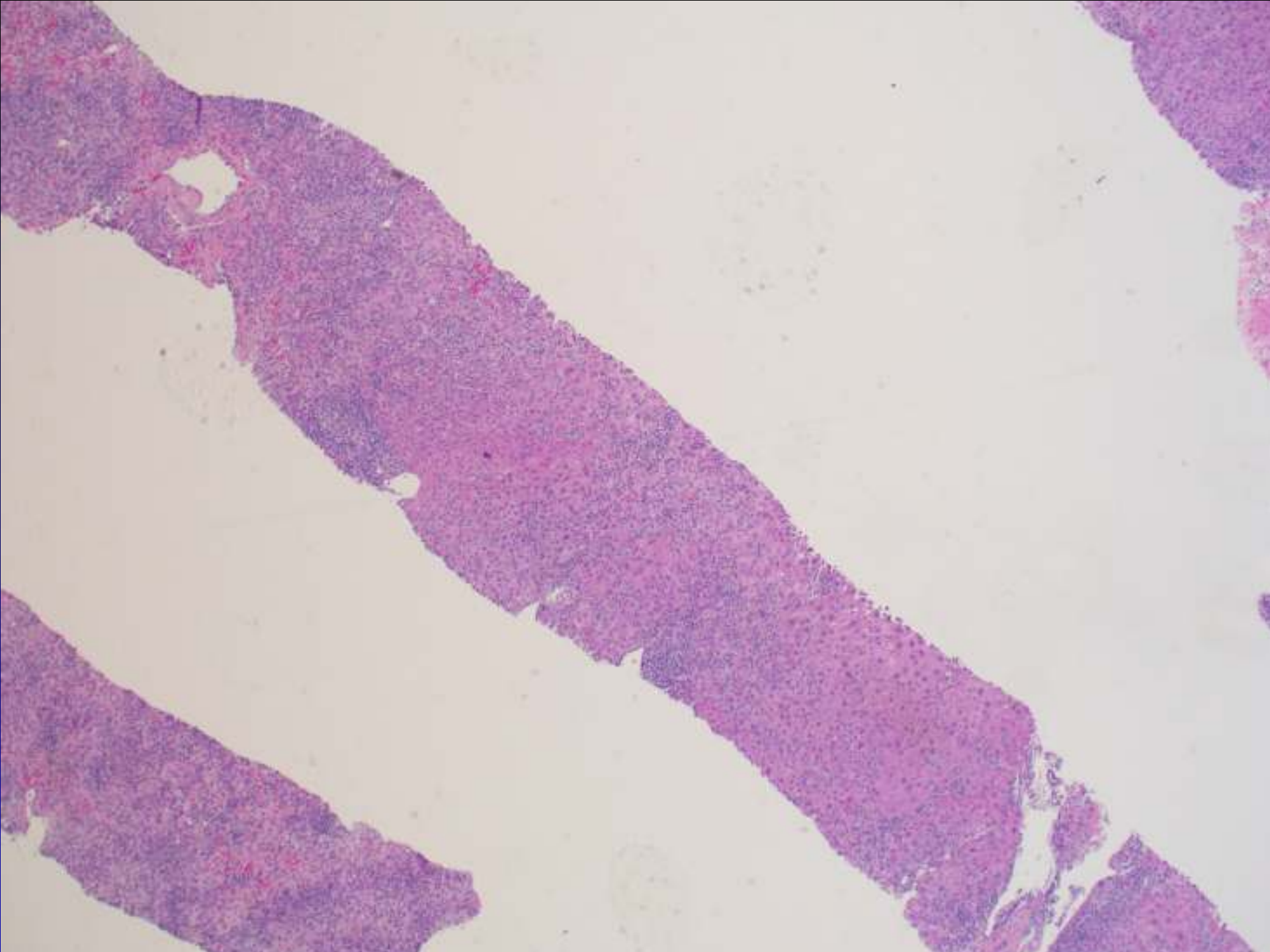
*ANA, 1:320, ASMA 1:320*

*Neg: anti-LKM1, AMA*

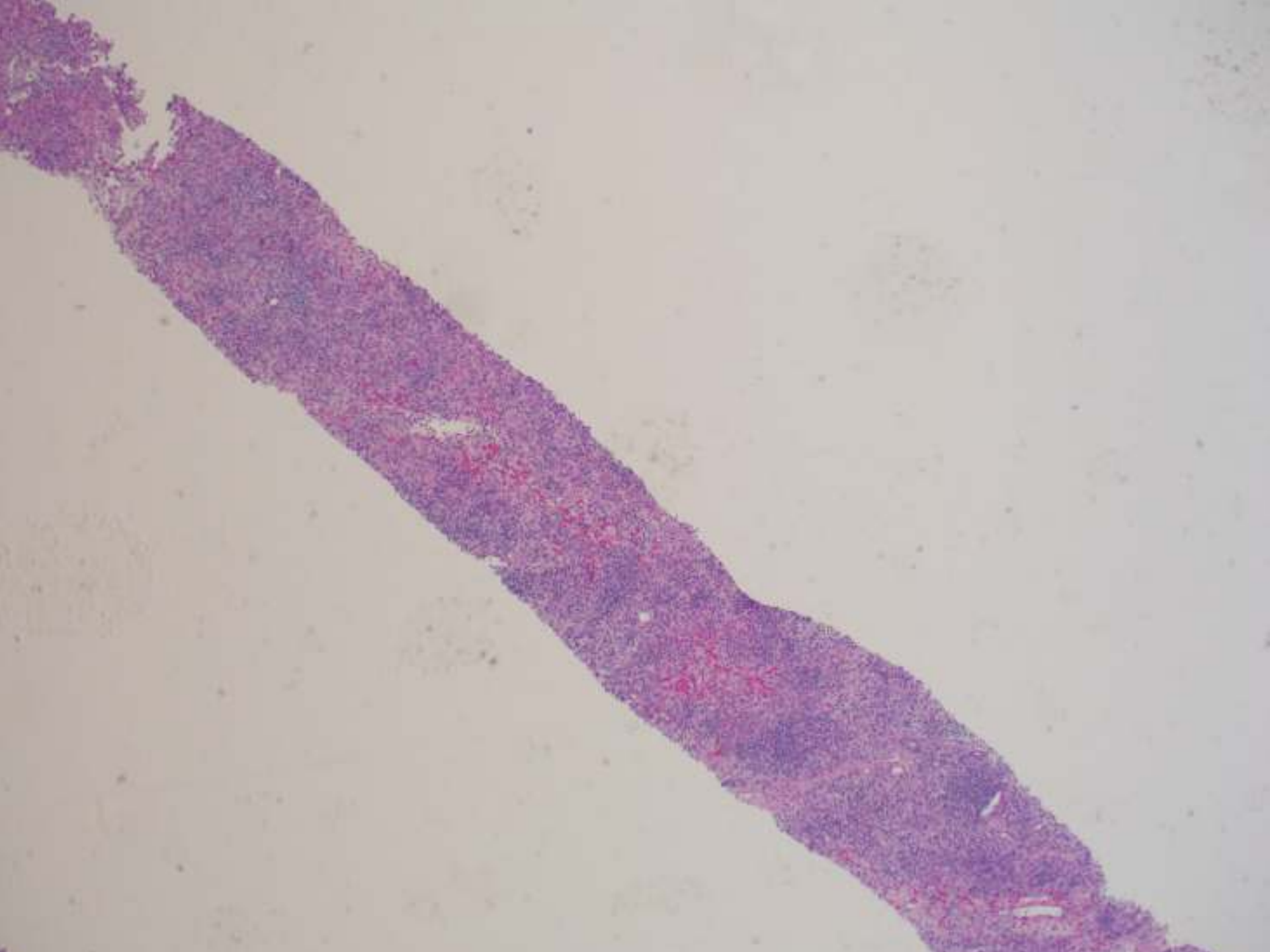
*IgG 2x normal*



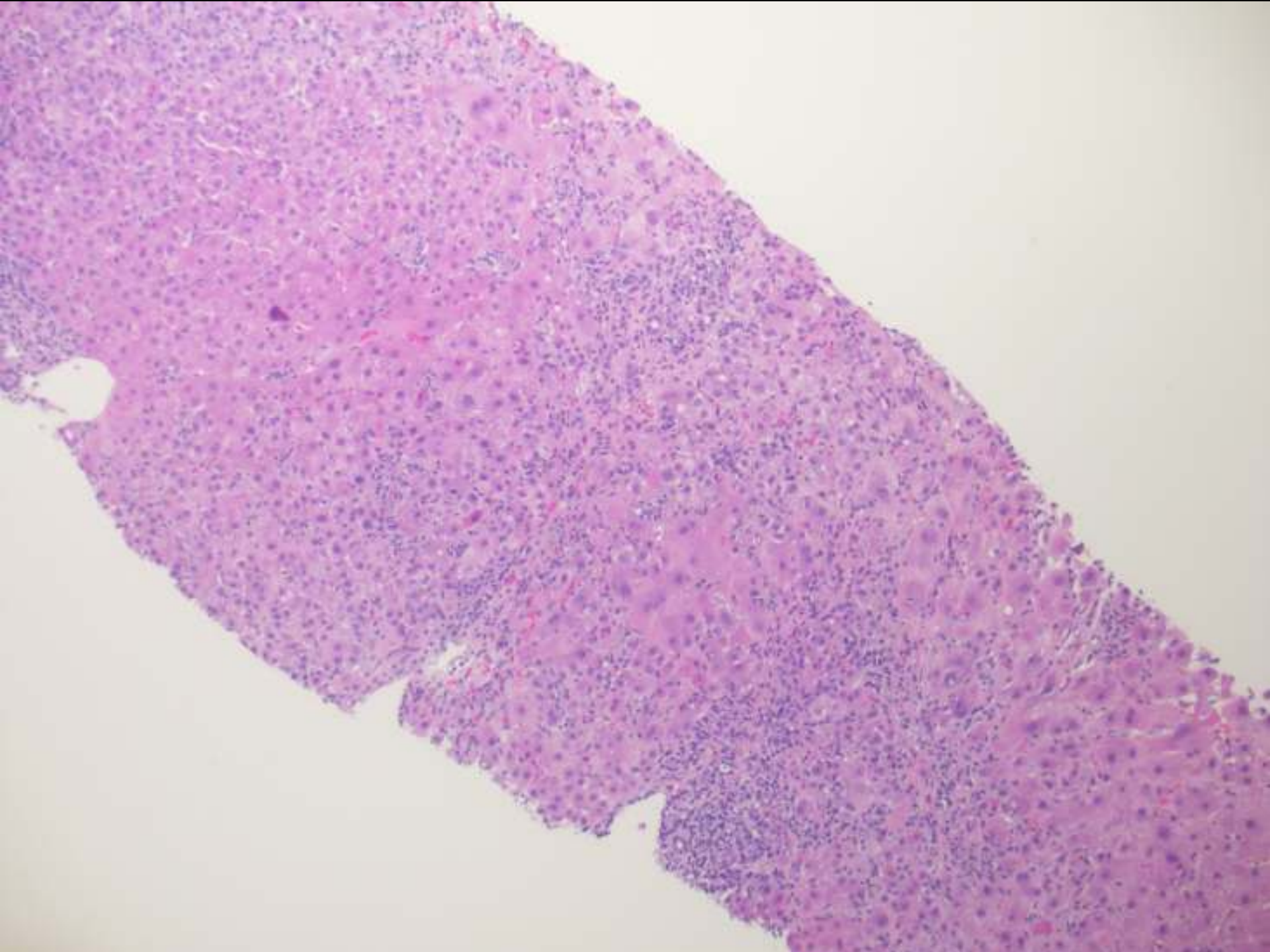


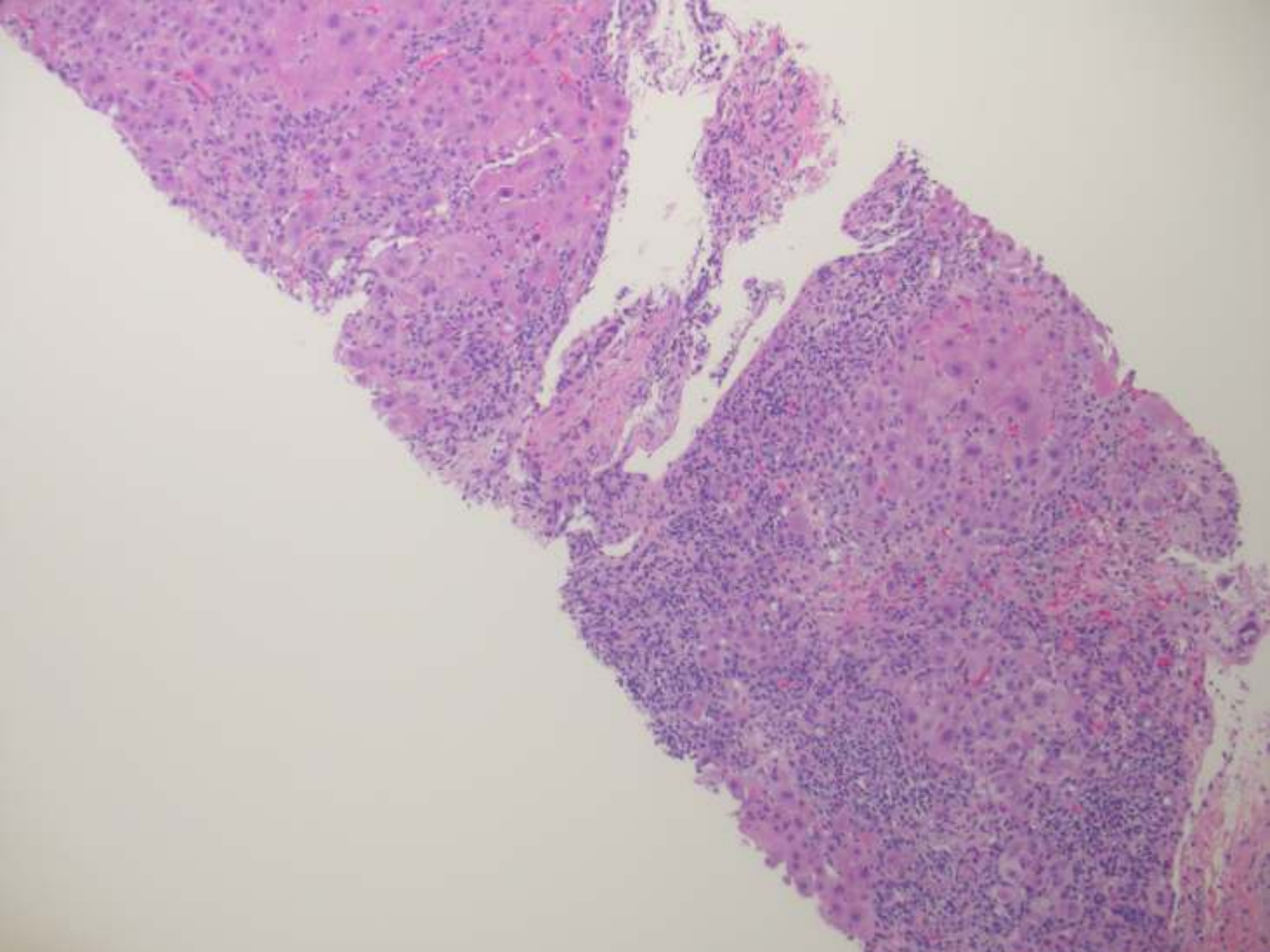




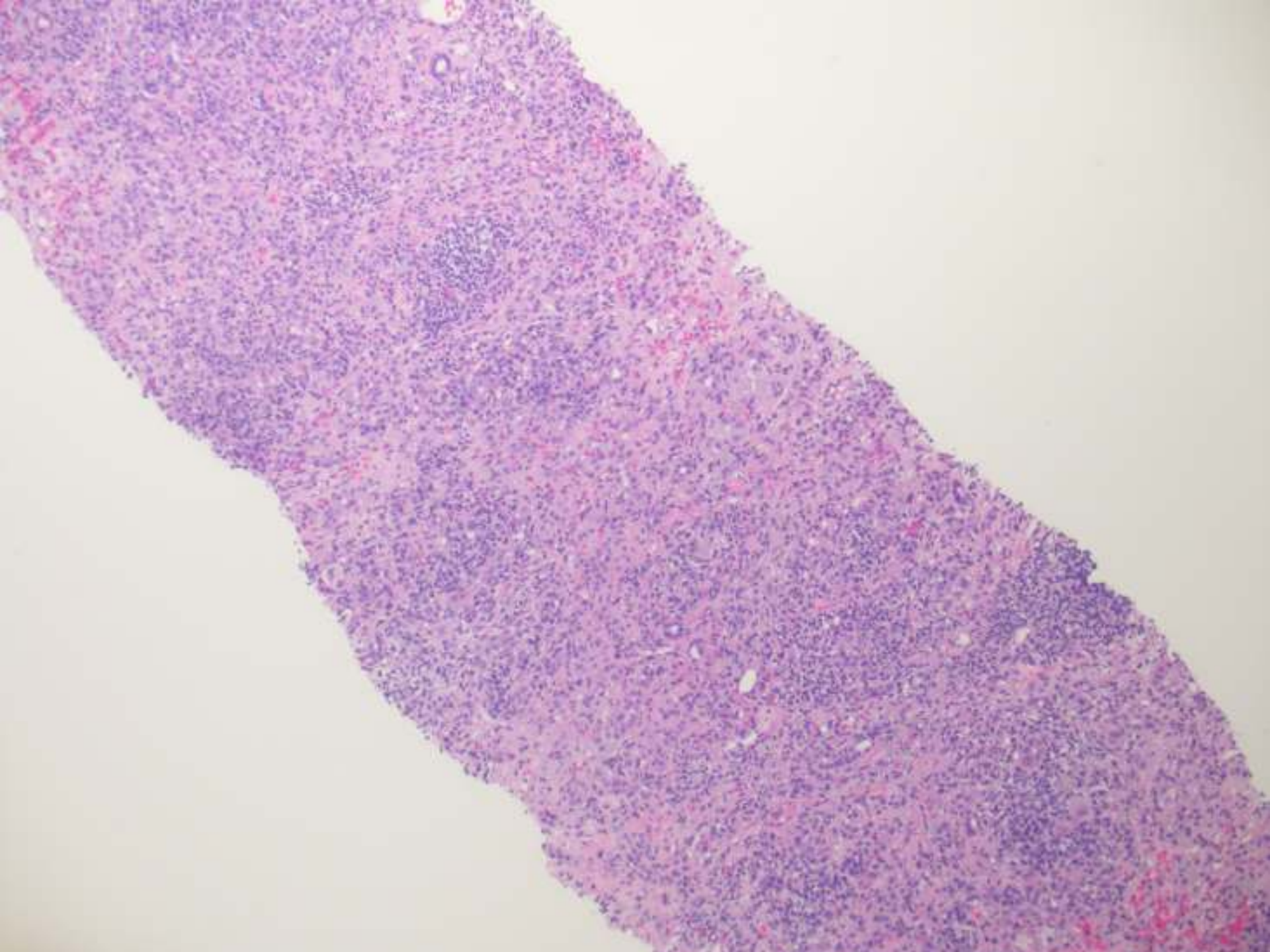




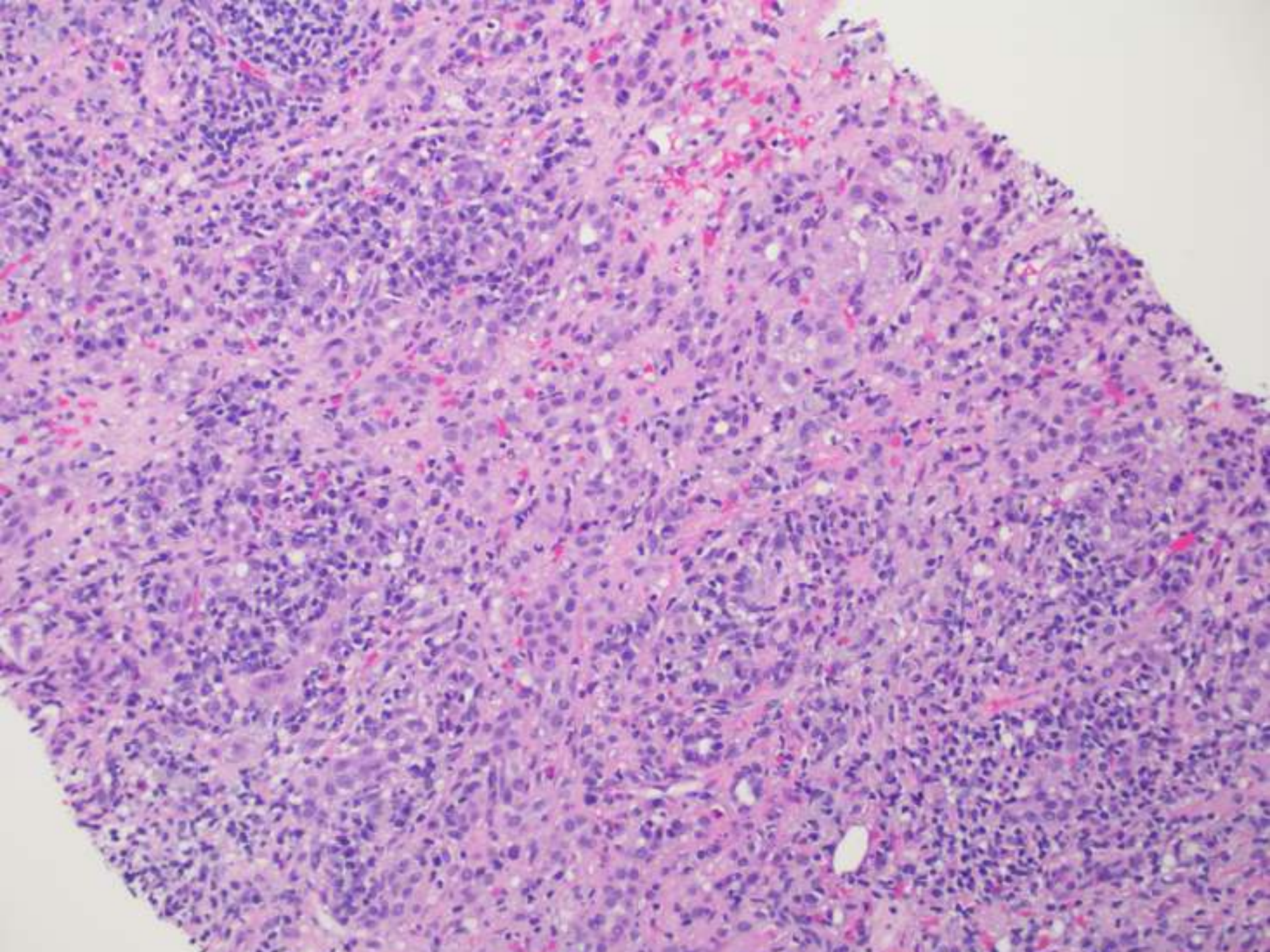




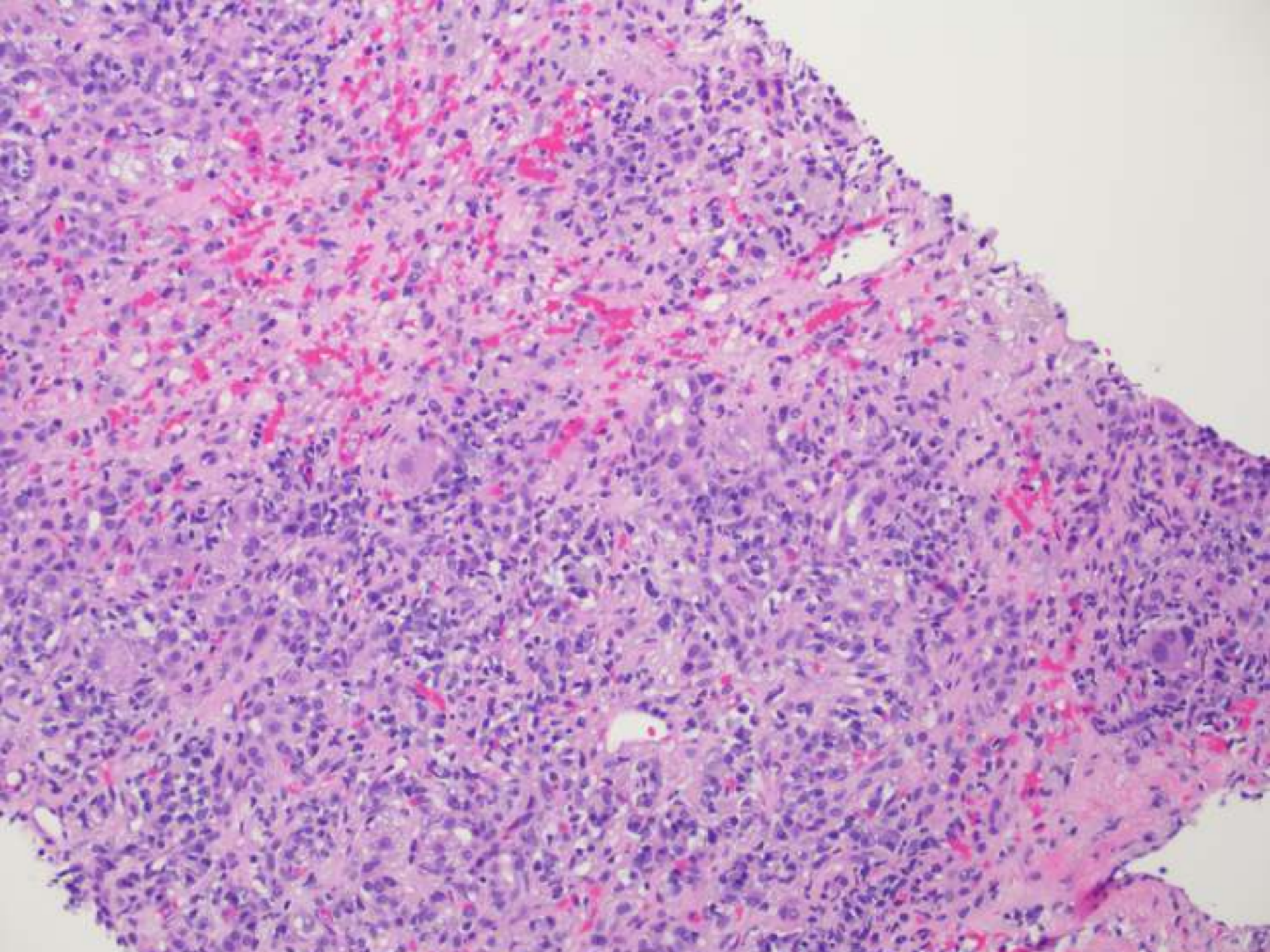




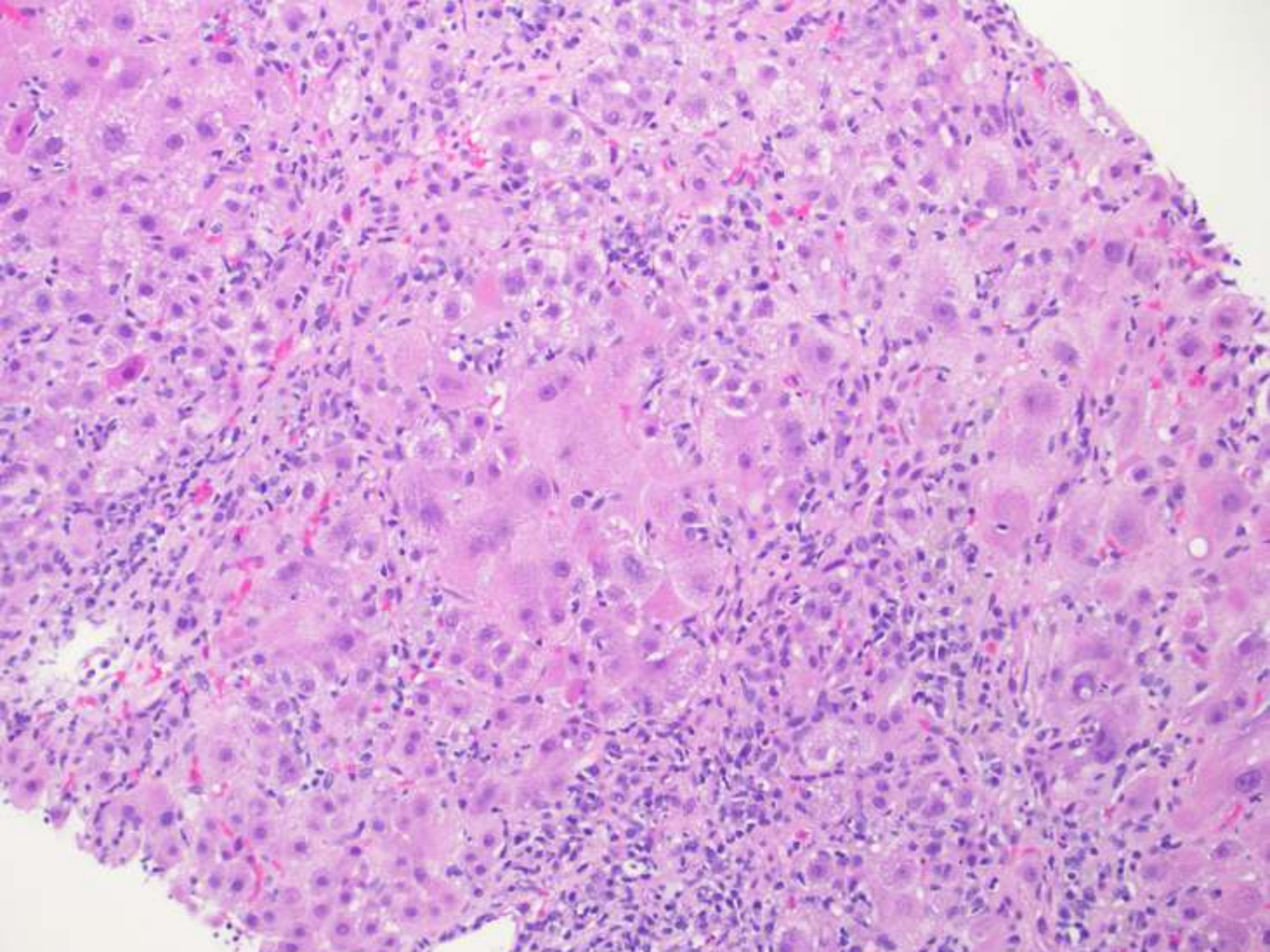




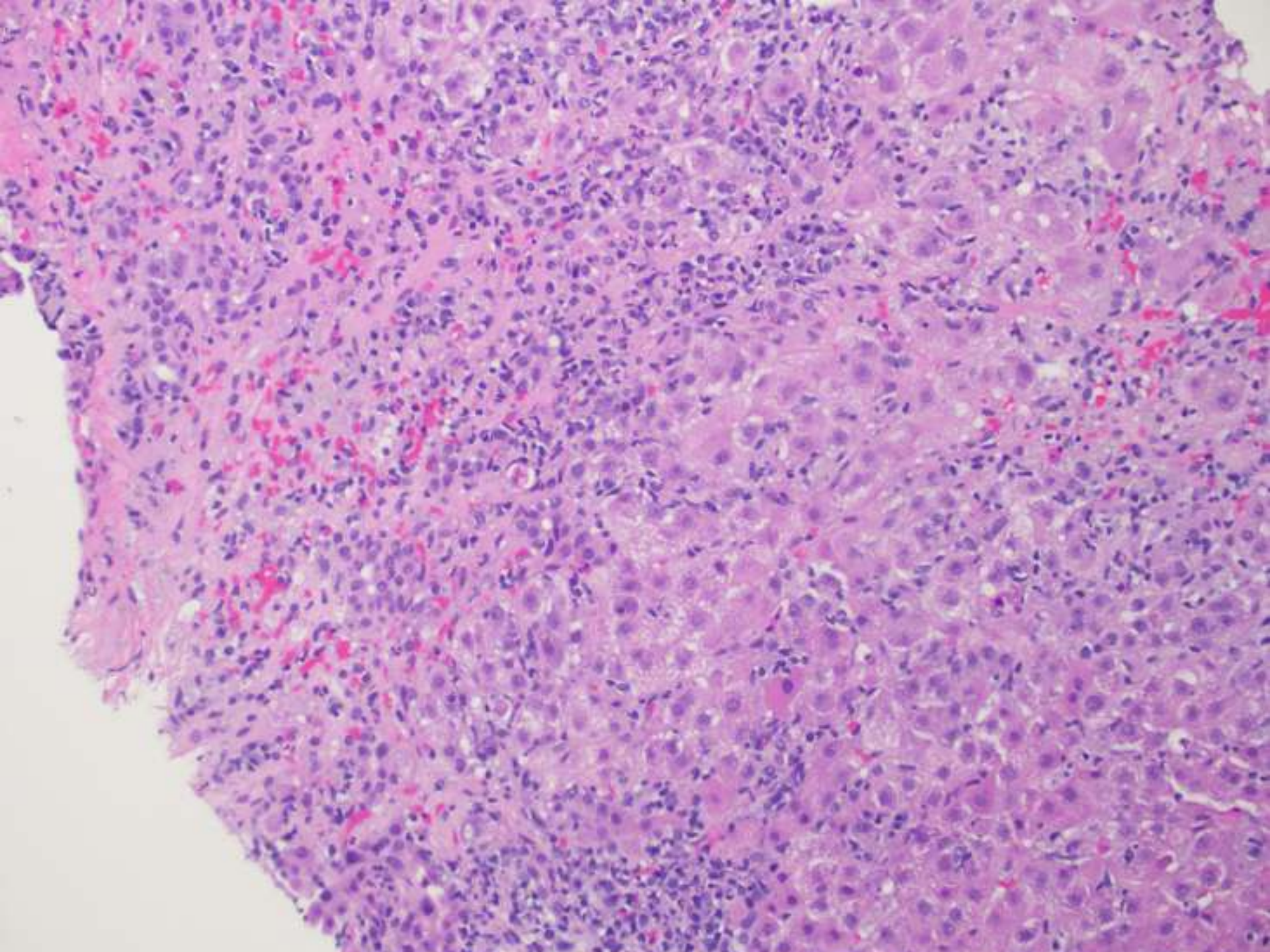




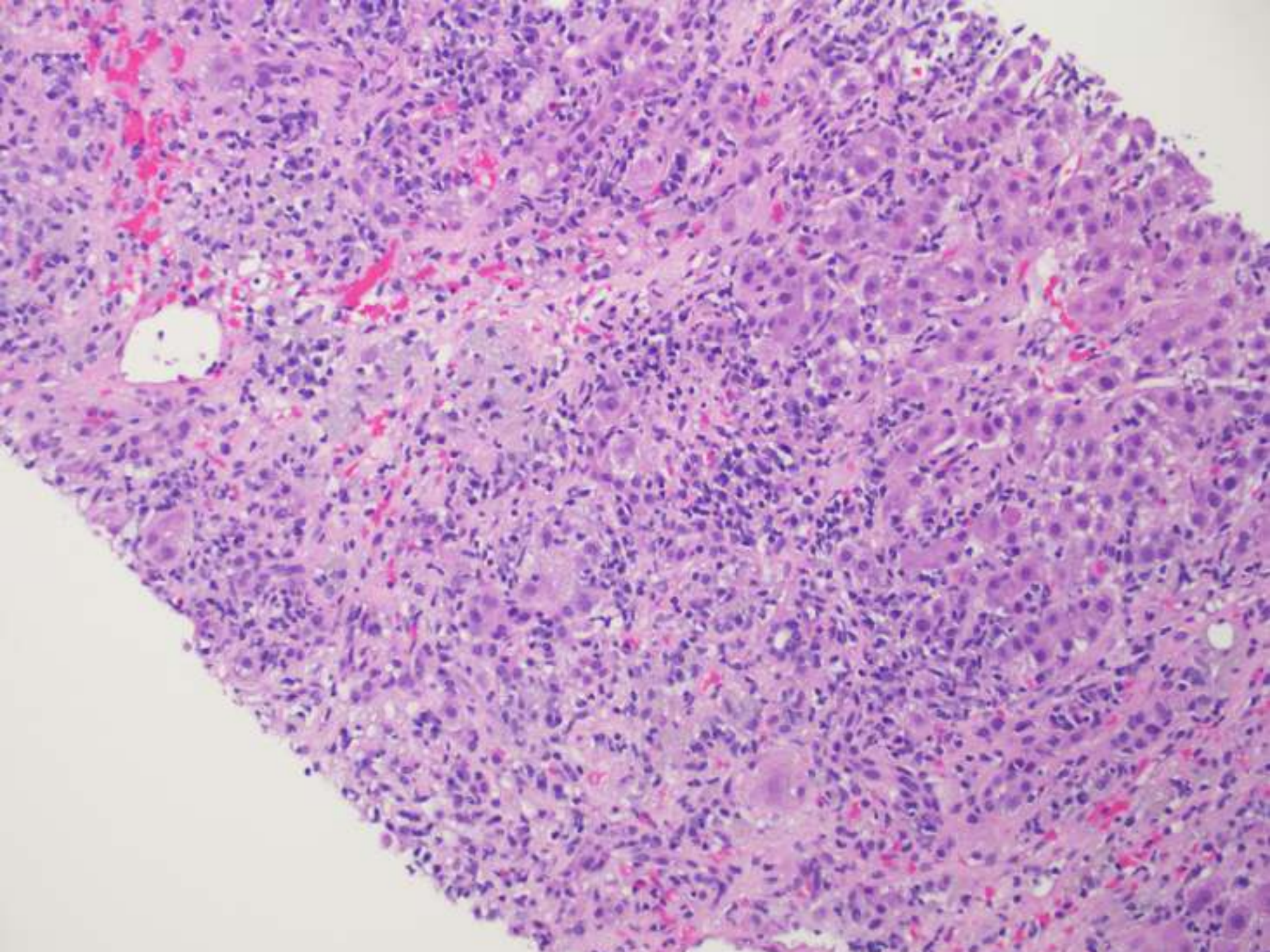




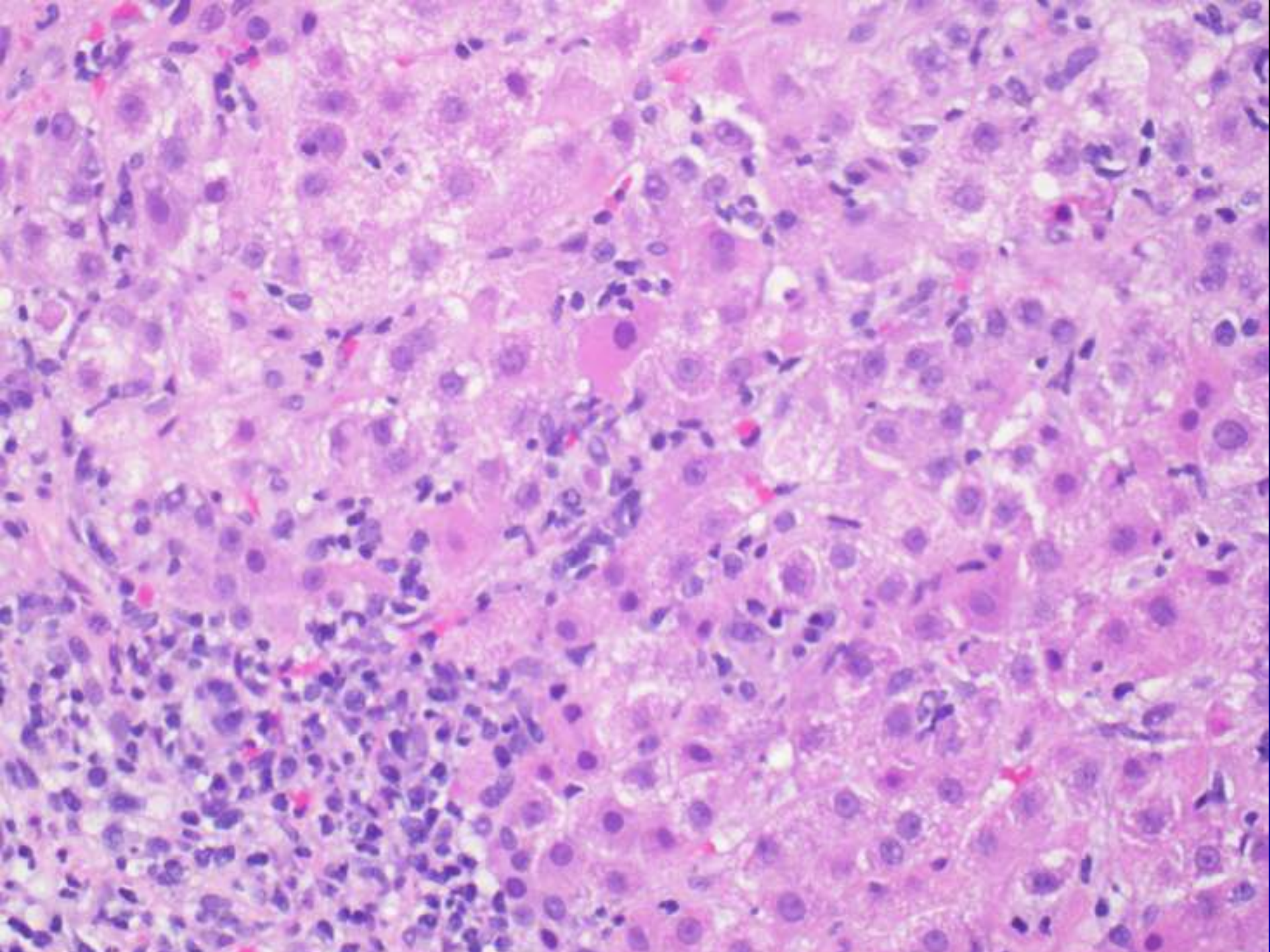




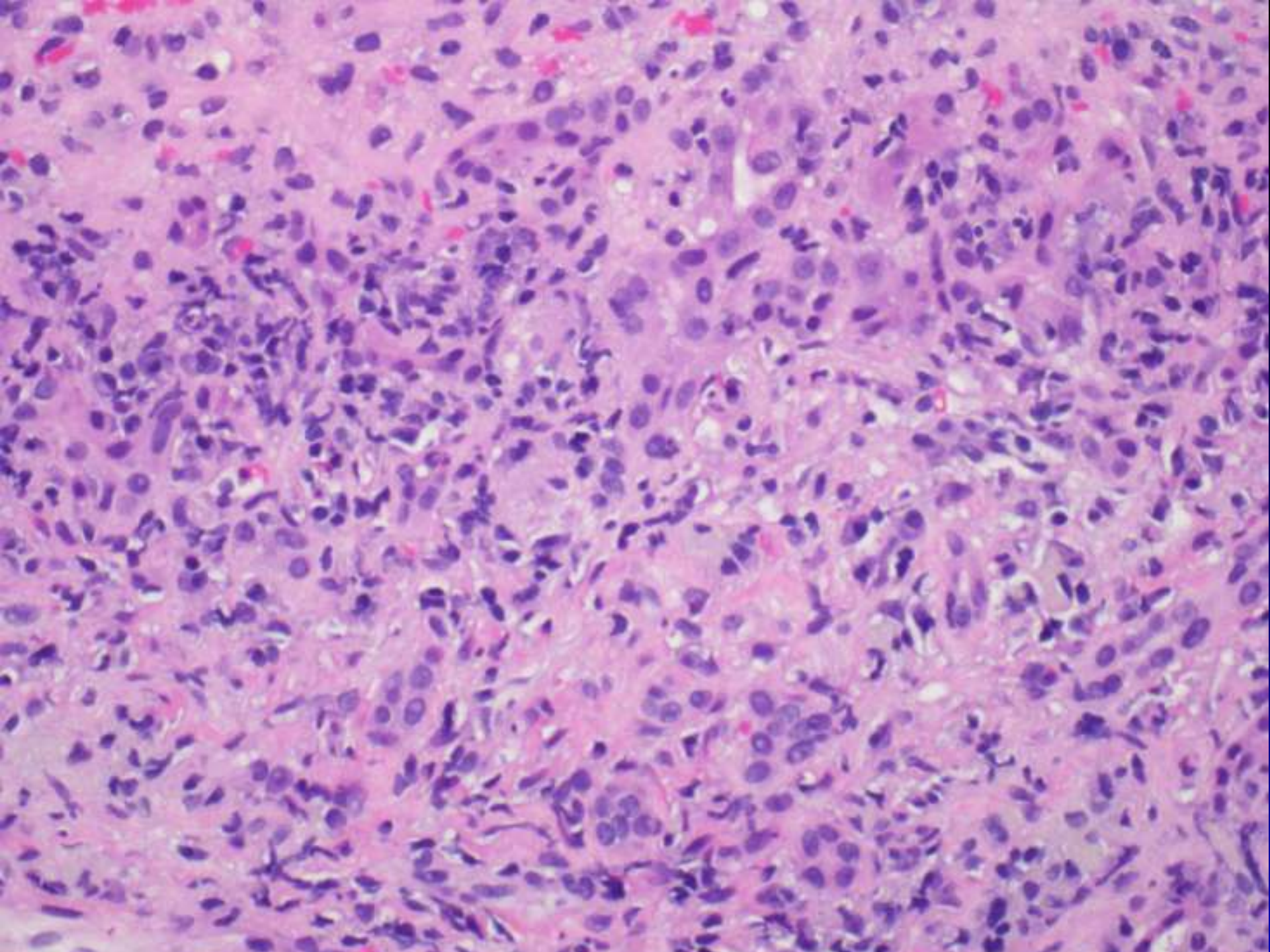




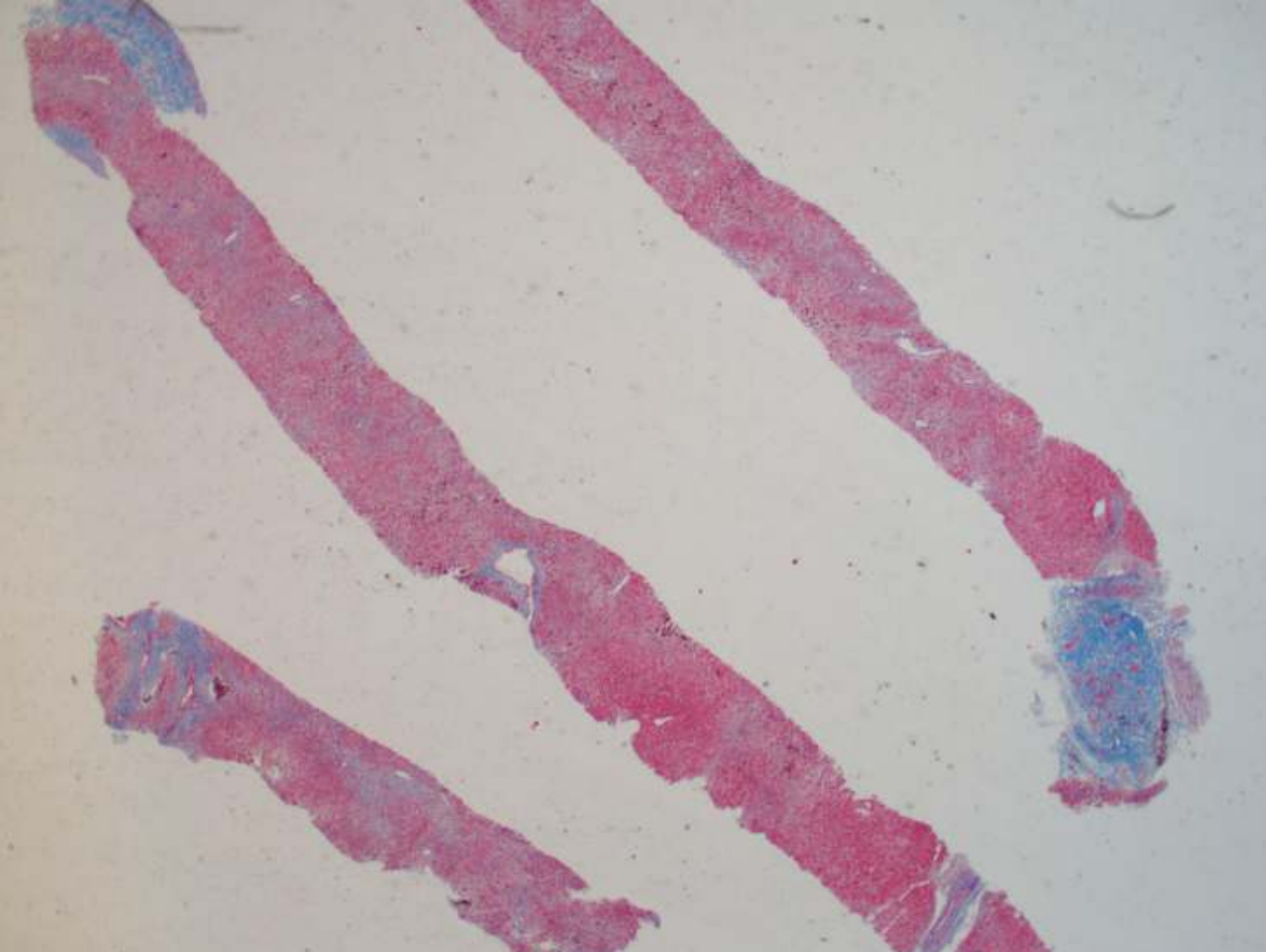


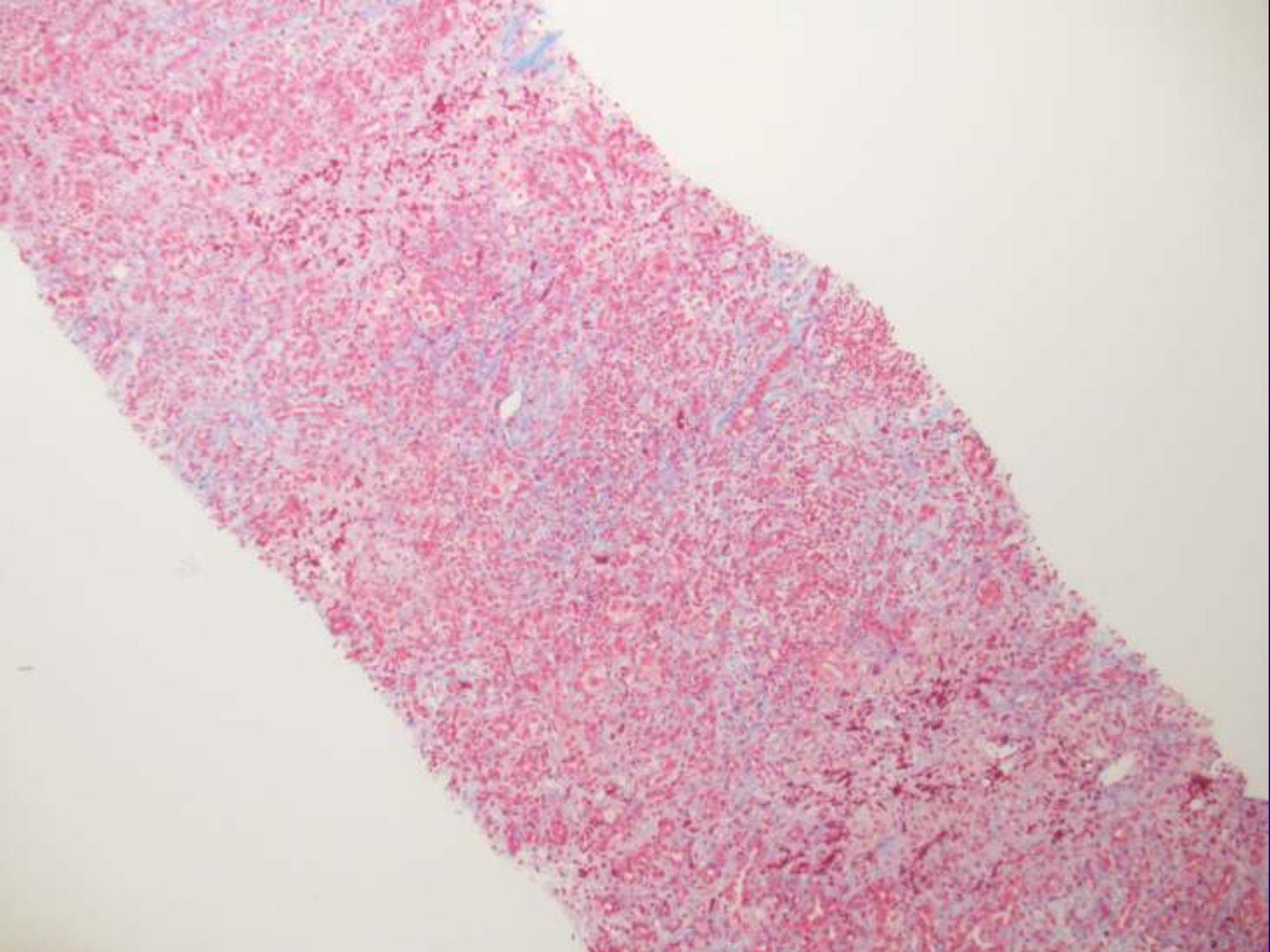




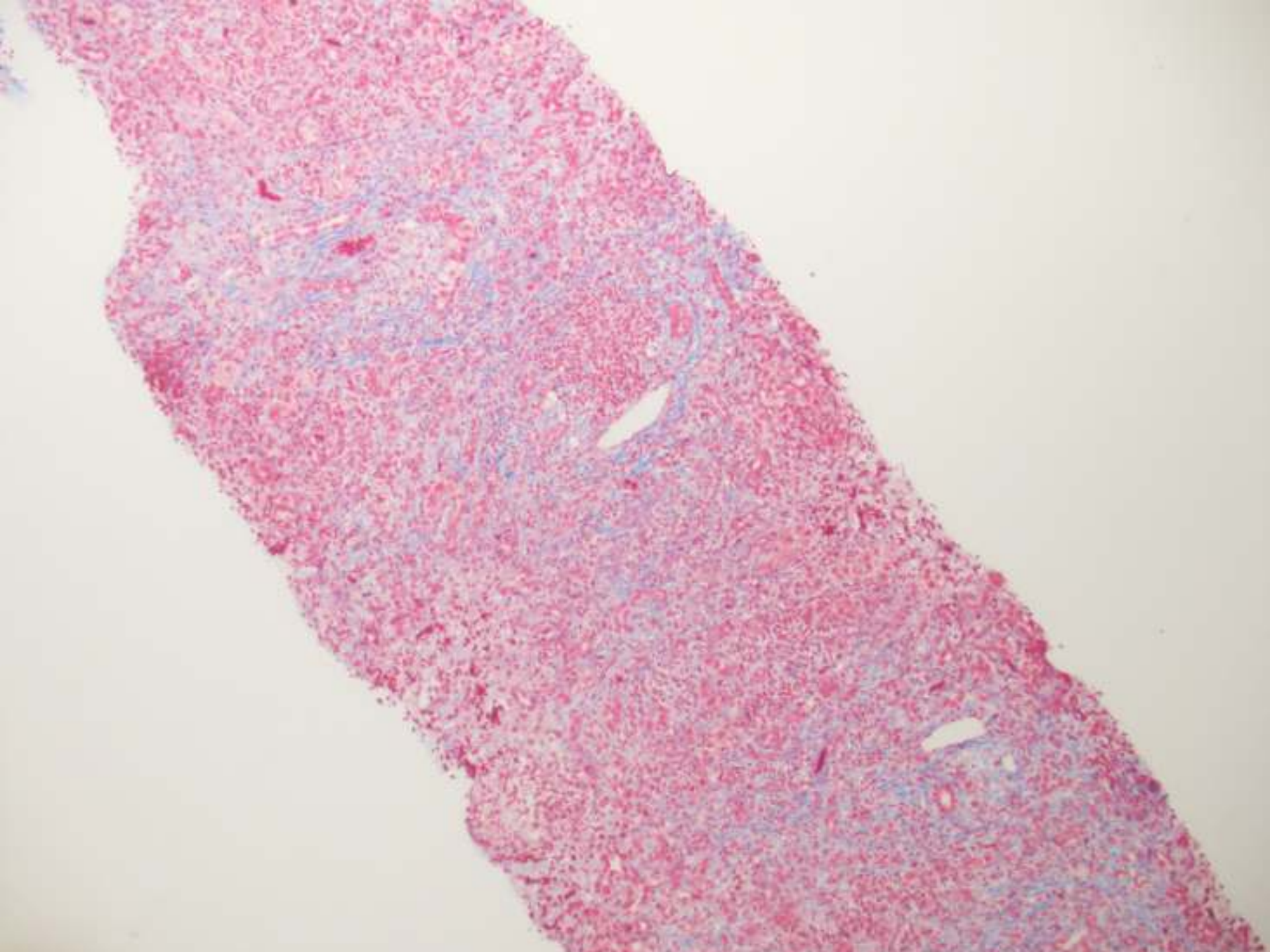












## Case 2

Final Diagnosis:

-CHRONIC HEPATITIS, MARKEDLY ACTIVE (PARENCHYMAL COLLAPSE), WITHOUT SIGNIFICANT SCARRING COMPATIBLE WITH AUTOIMMUNE HEPATITIS.



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Final Diagnosis:

-CHRONIC HEPATITIS, MARKEDLY ACTIVE (PARENCHYMAL COLLAPSE), WITHOUT SIGNIFICANT SCARRING COMPATIBLE WITH AUTOIMMUNE HEPATITIS.

**Comment: yada yada yada, etc etc etc.**

**Numerical assignment for the above stage of disease:**

**Modified Ishak scheme: stage 0/4**

**Metavir scheme: F0**

**Beijing classification: Early stage**

## Case 3

50 year old woman

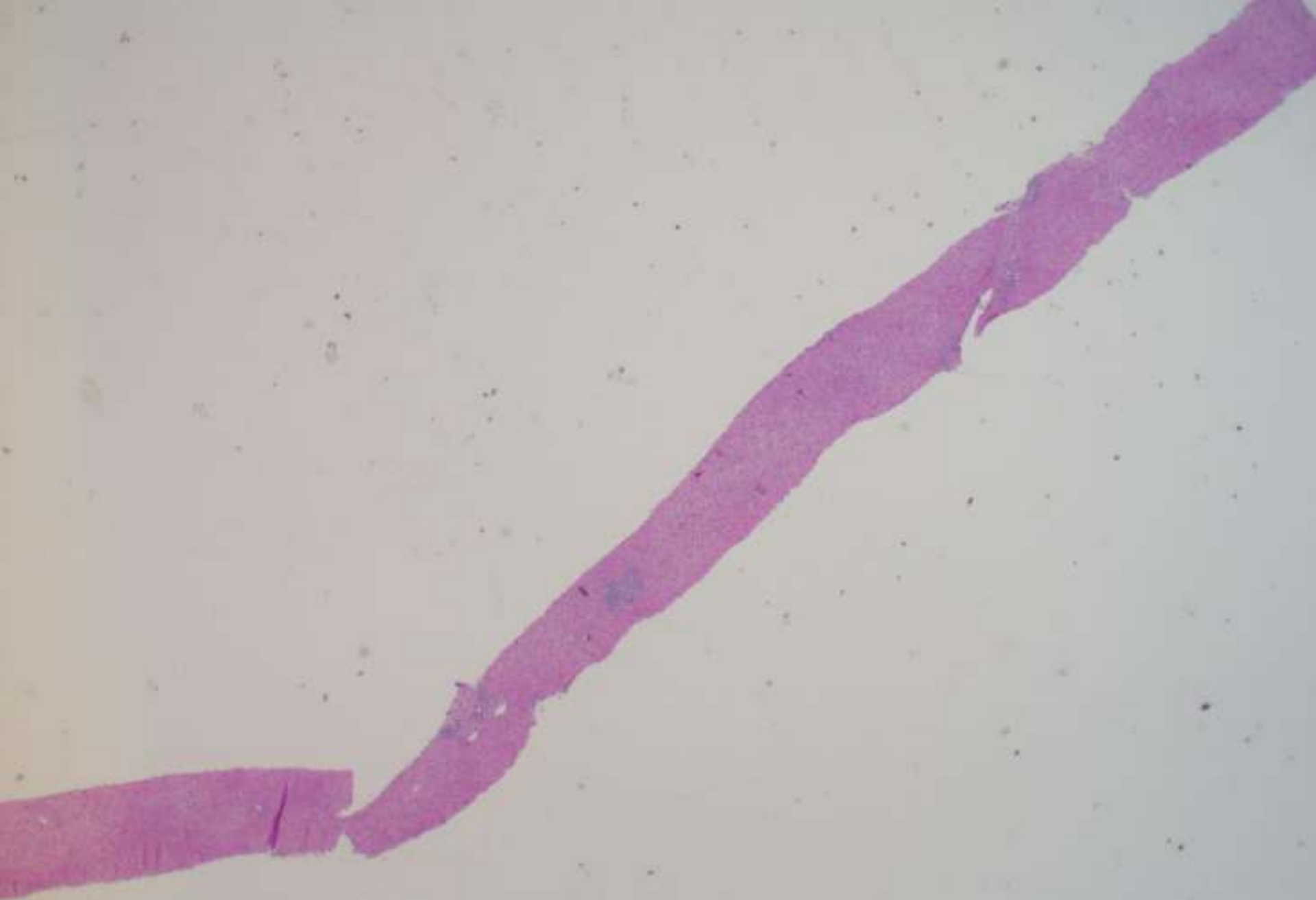
Alkaline Phosphatase 61 (nl 30-145)

ALT: 77 (nl 10-45)

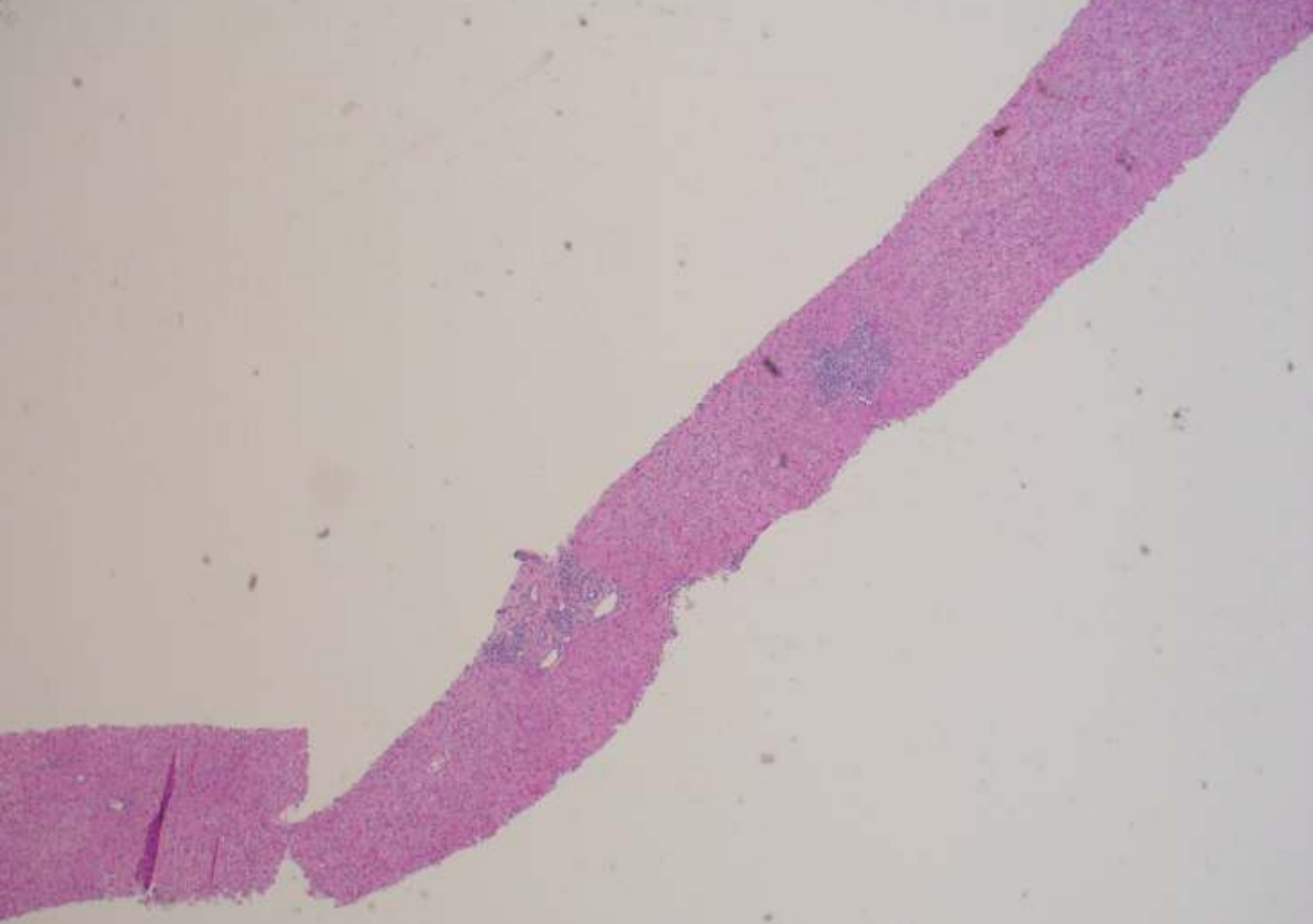
AST: 43 (nl 10-45)

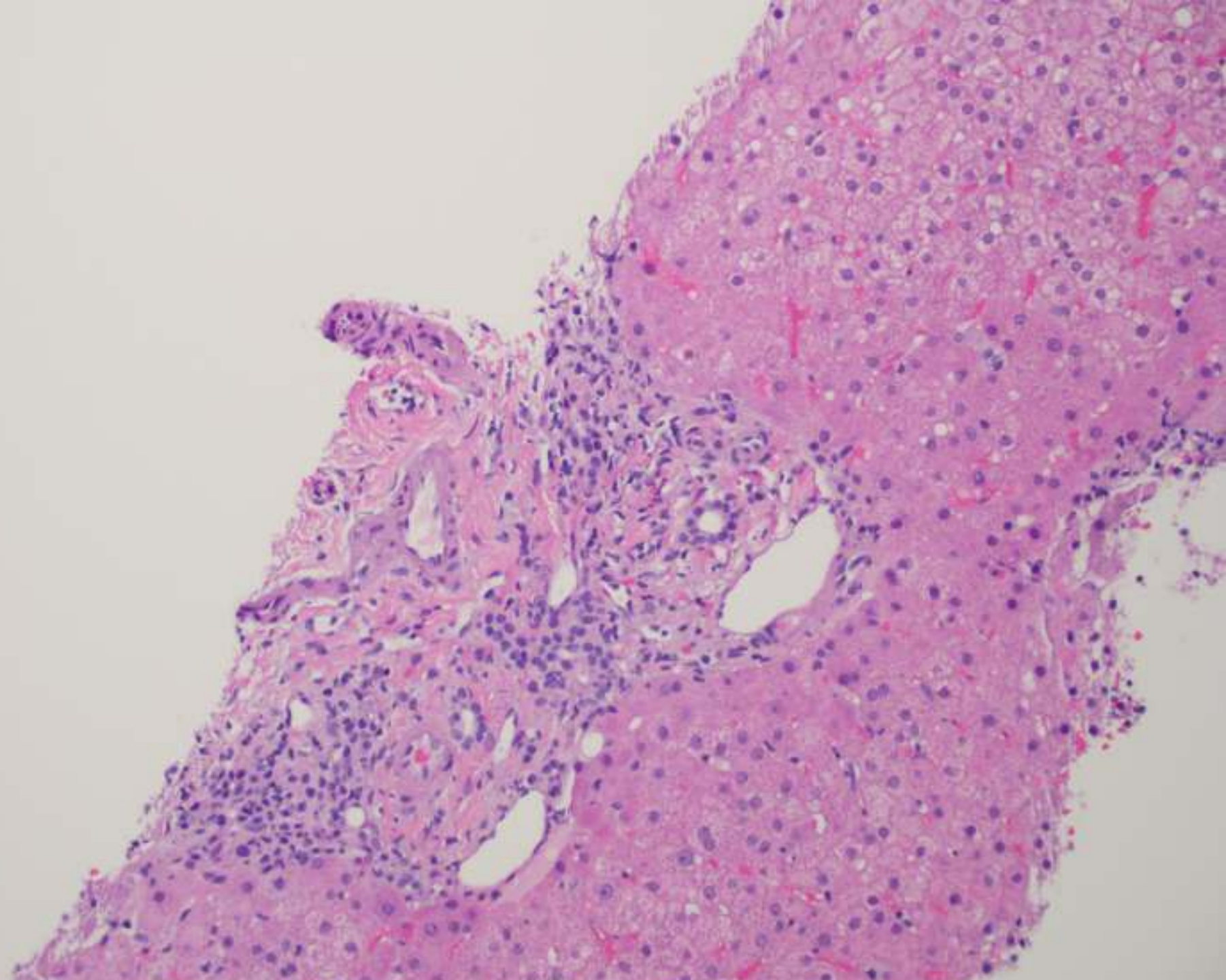
ANA 1:160, ASMA, AMA, anti-LKM1 negative

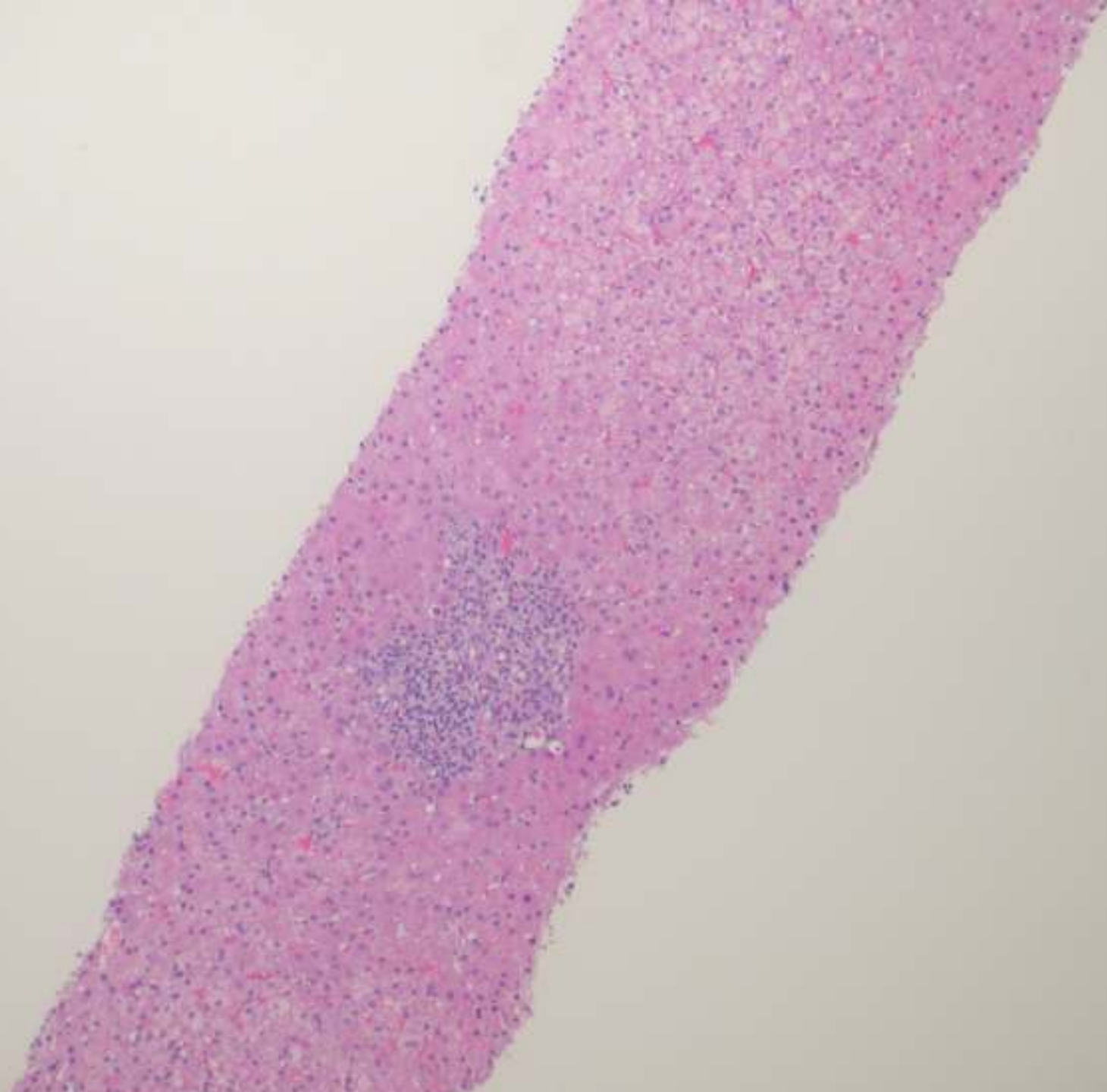
Hepatitis A, B, C negative



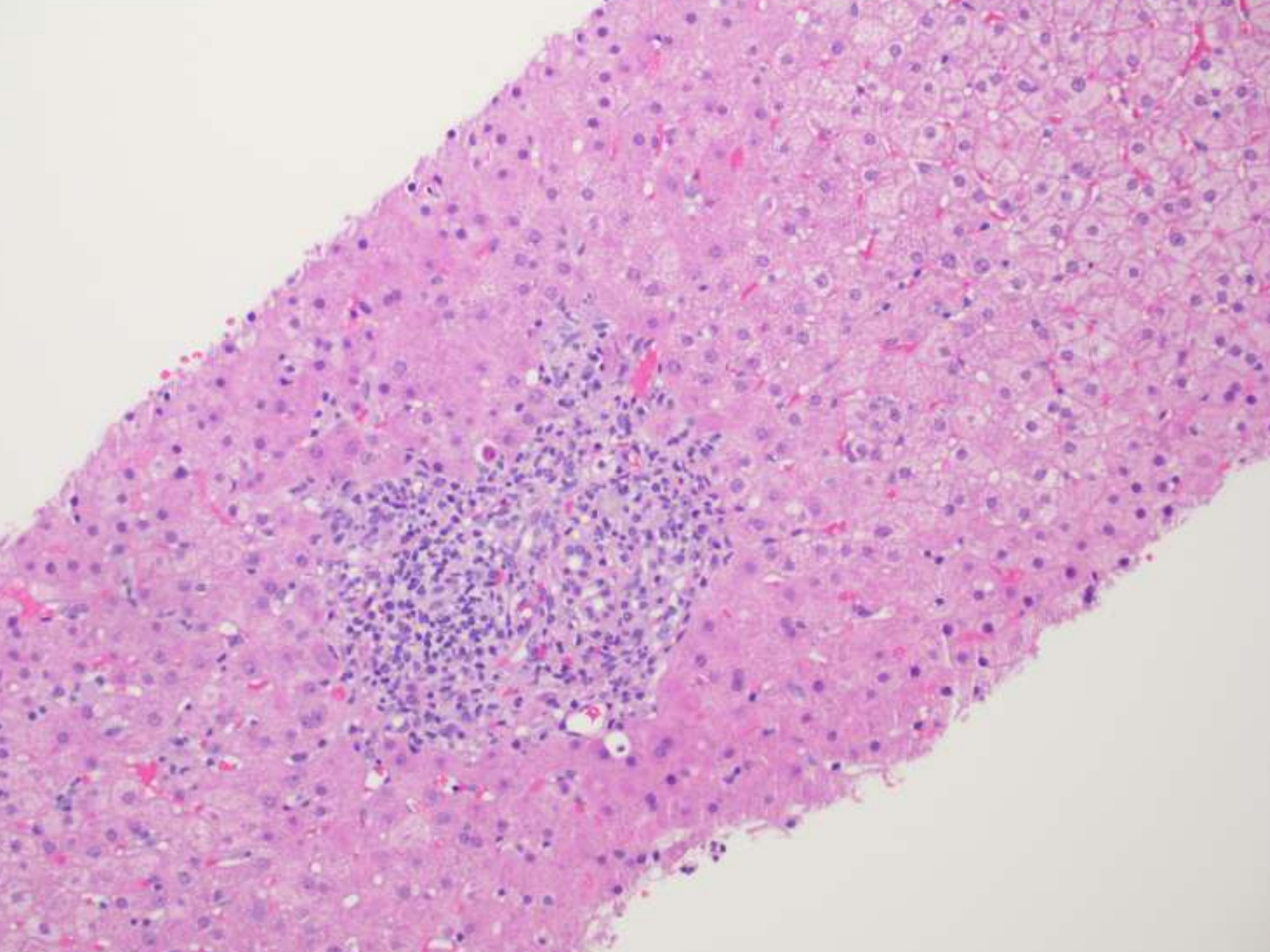




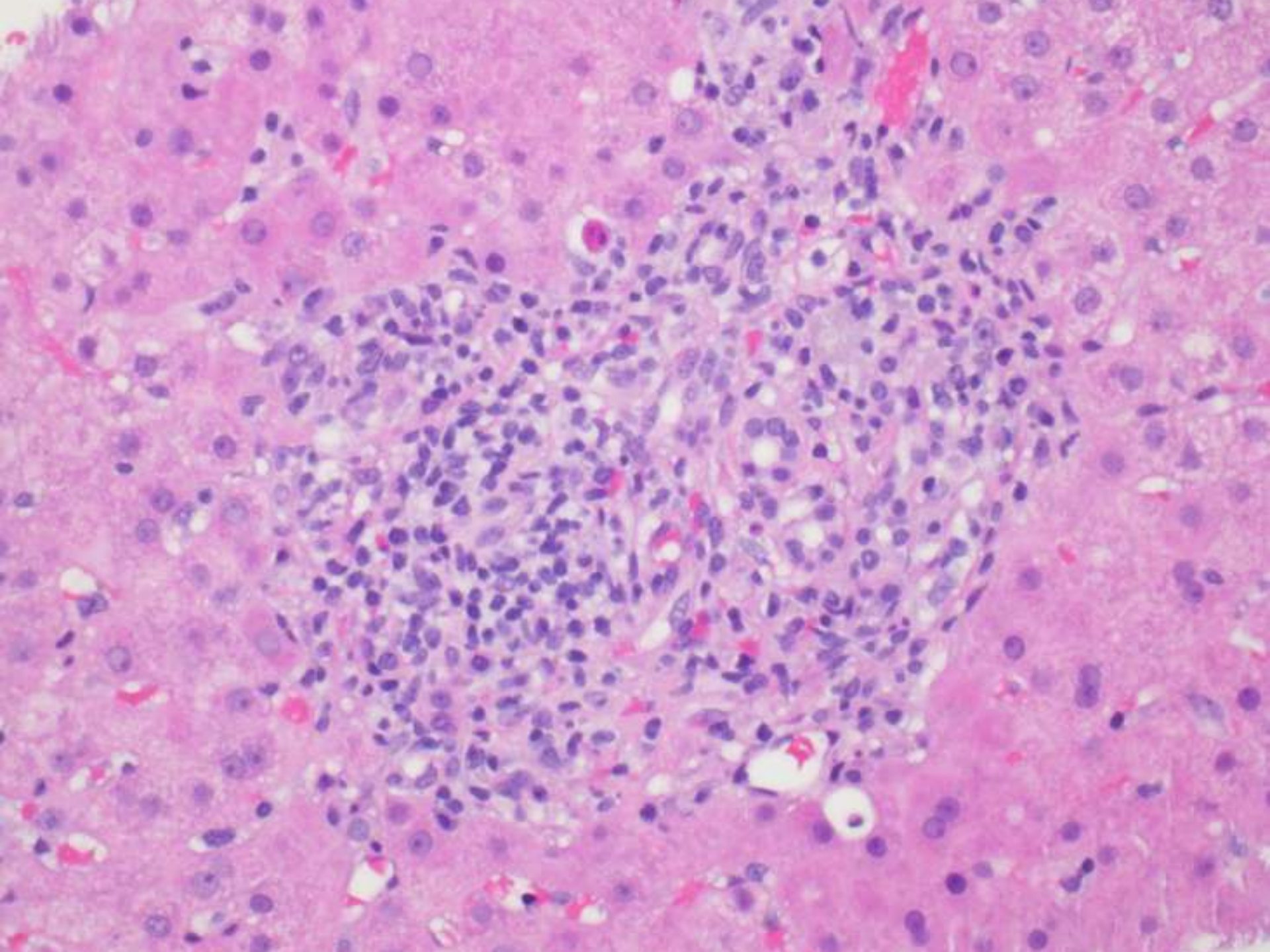




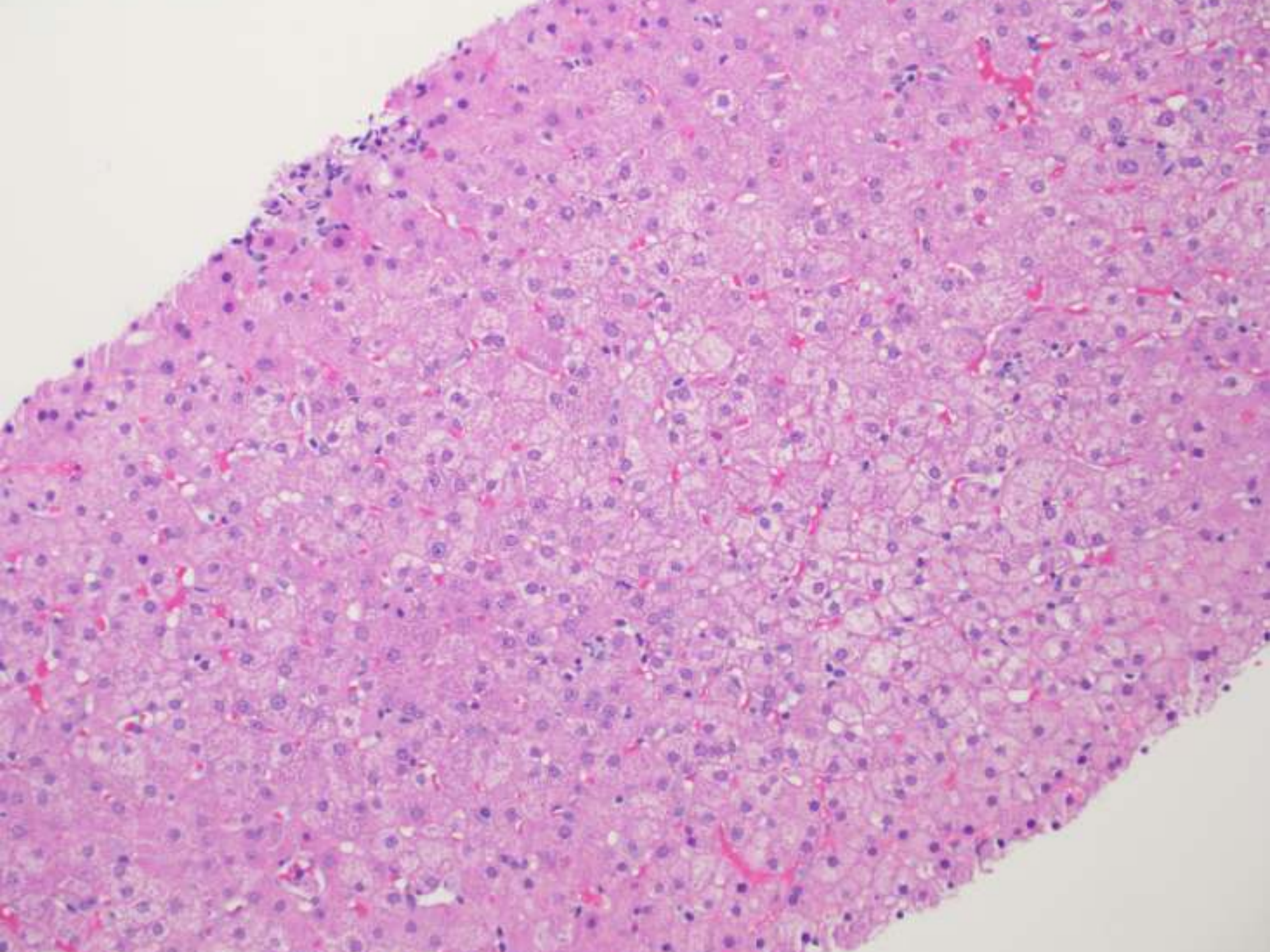




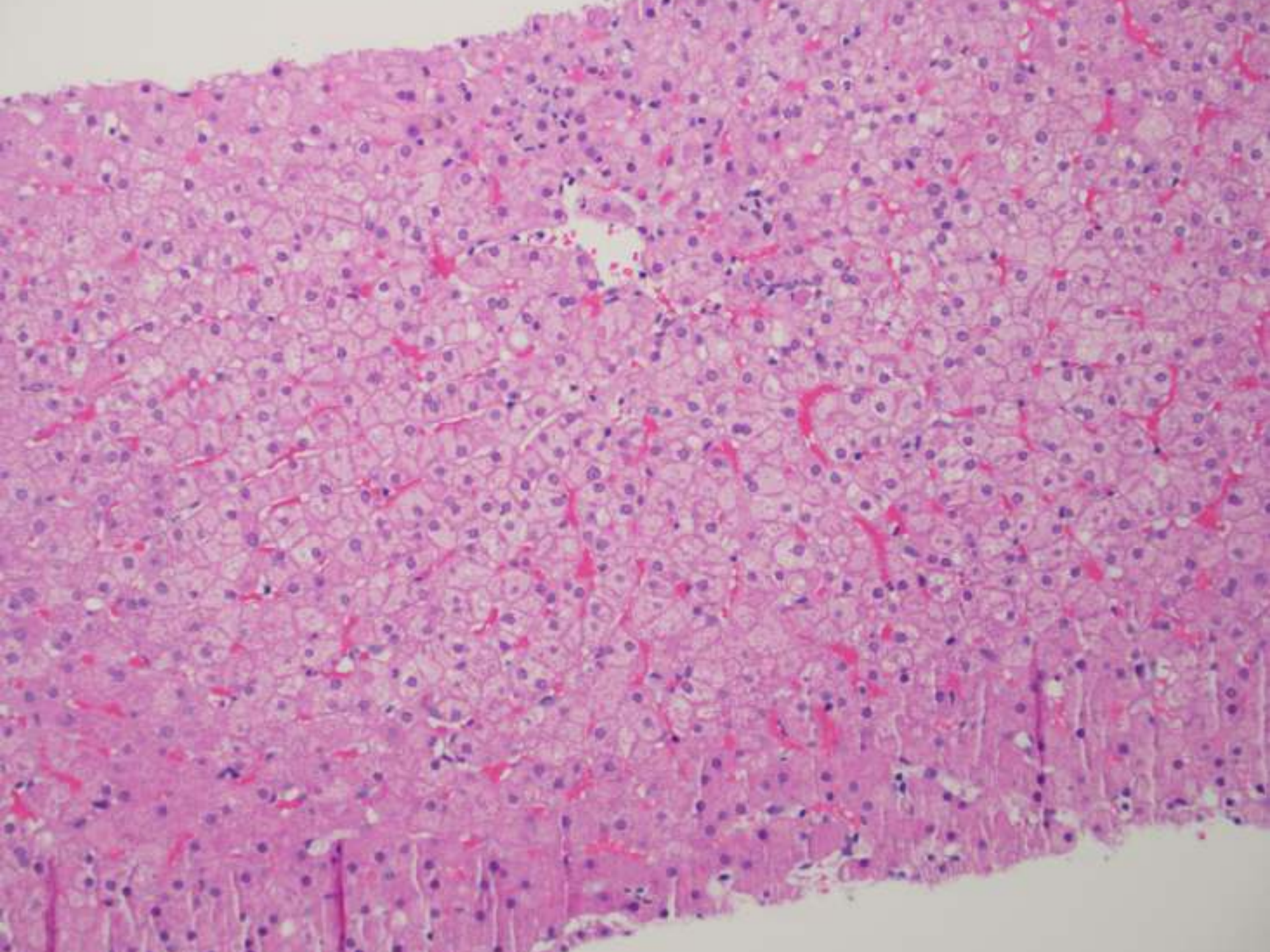




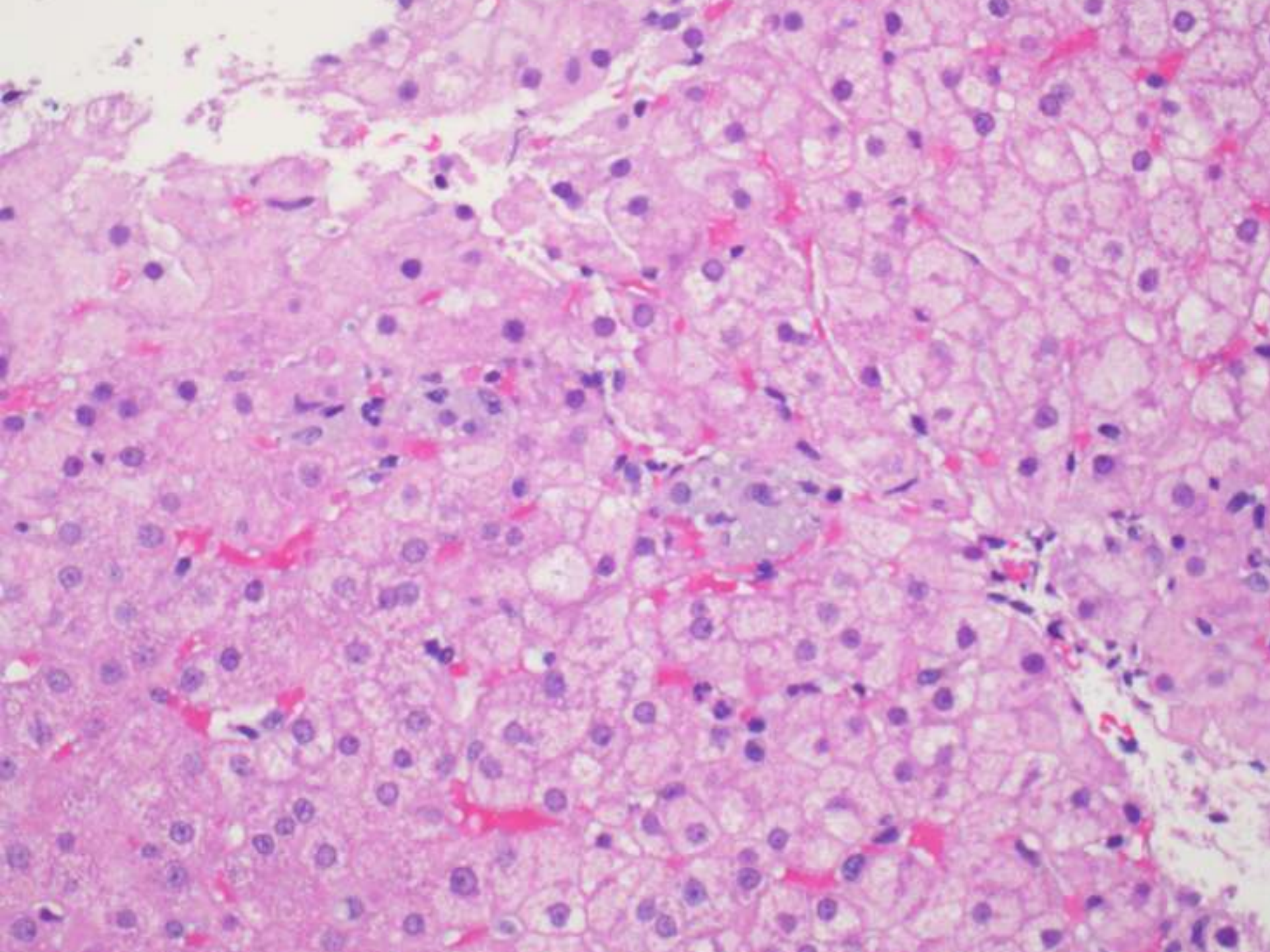




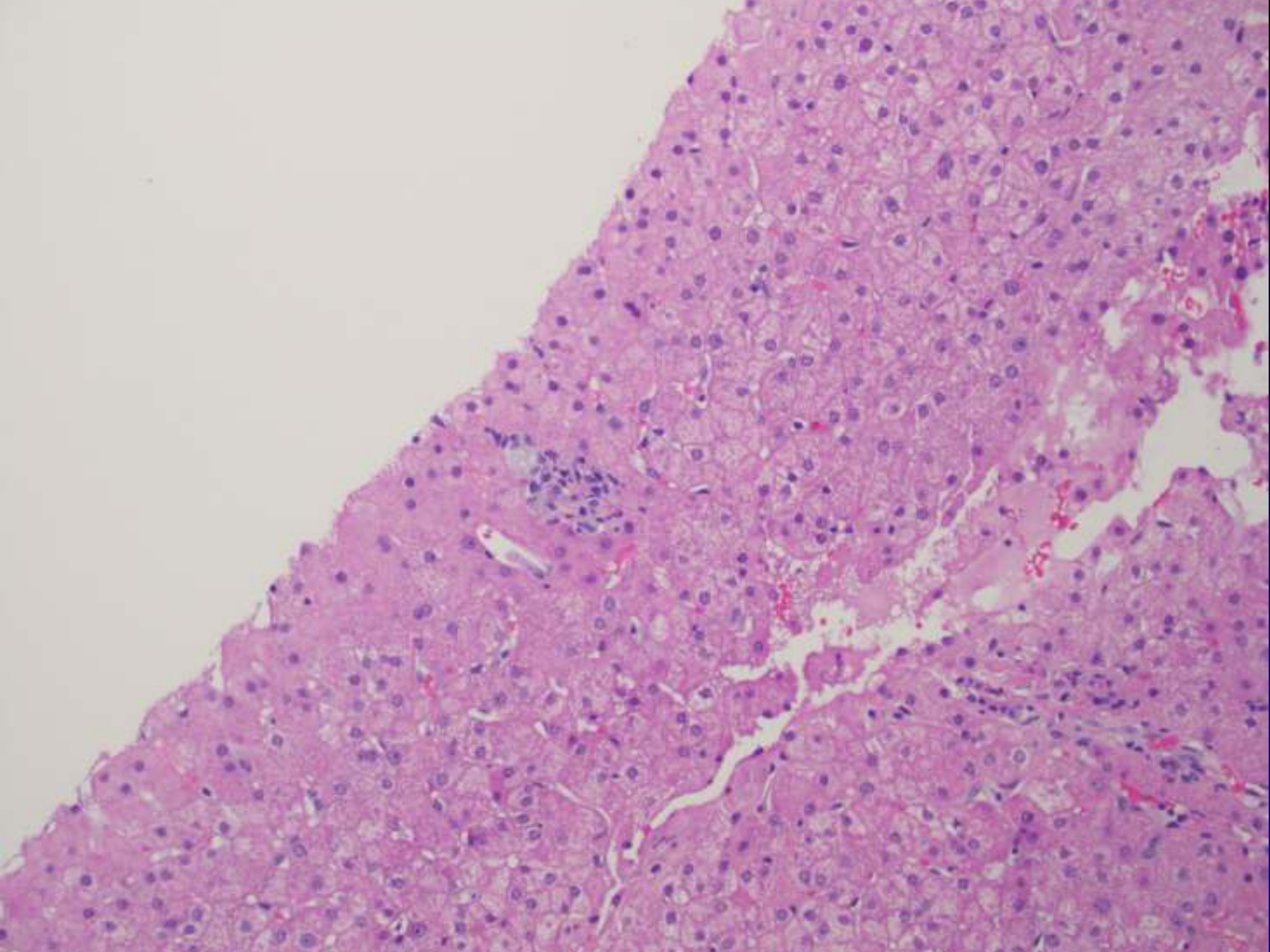




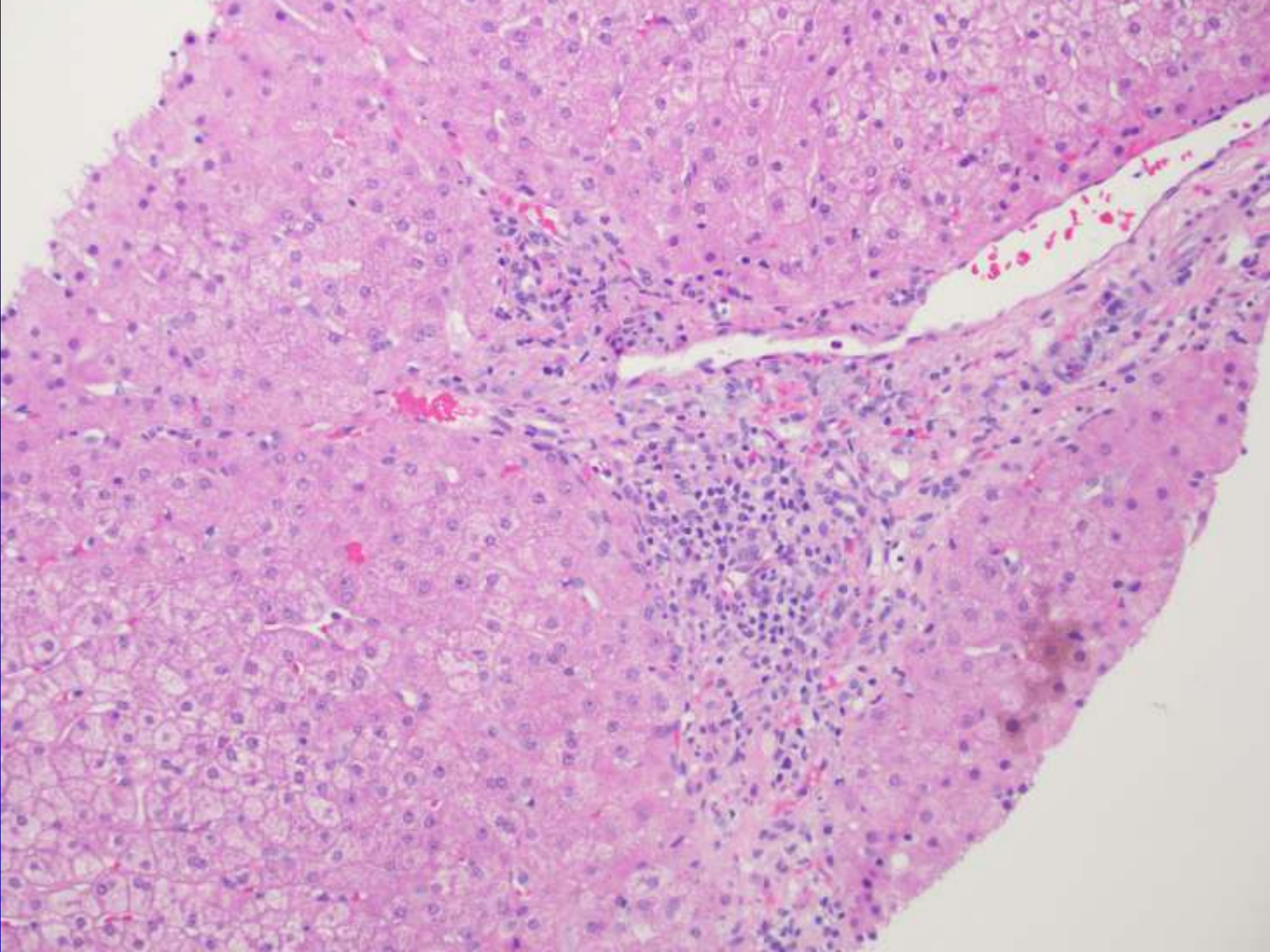


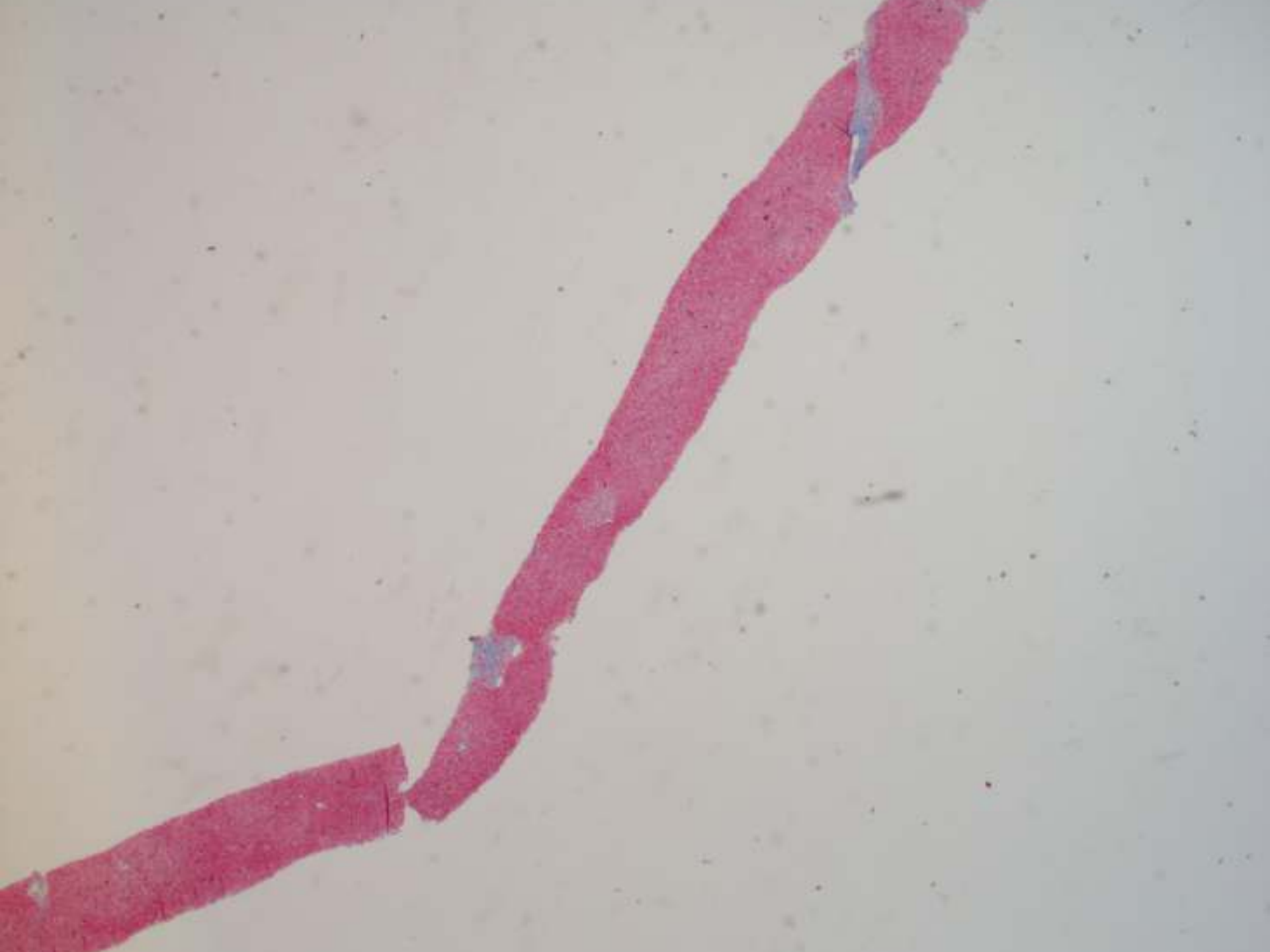




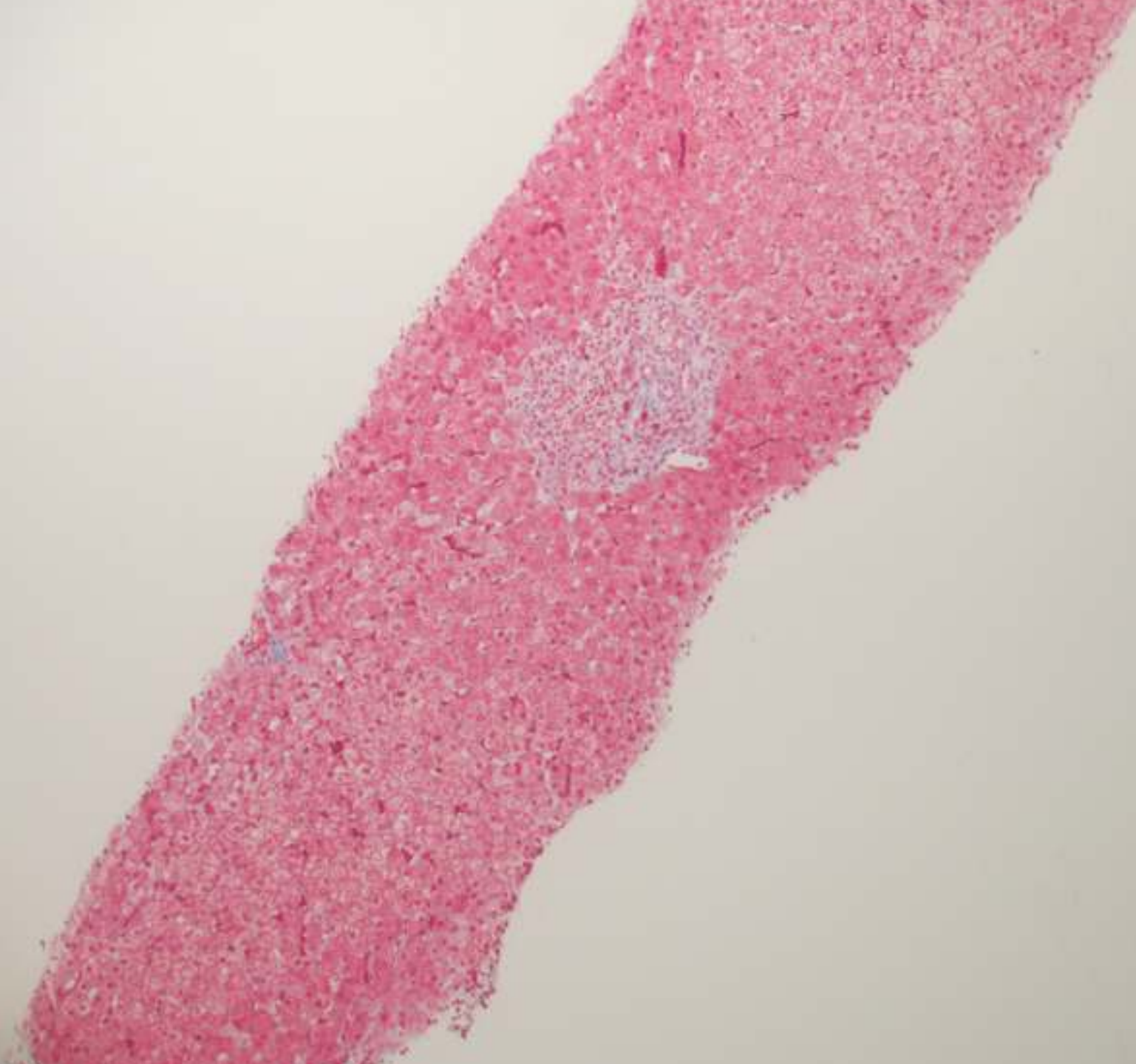




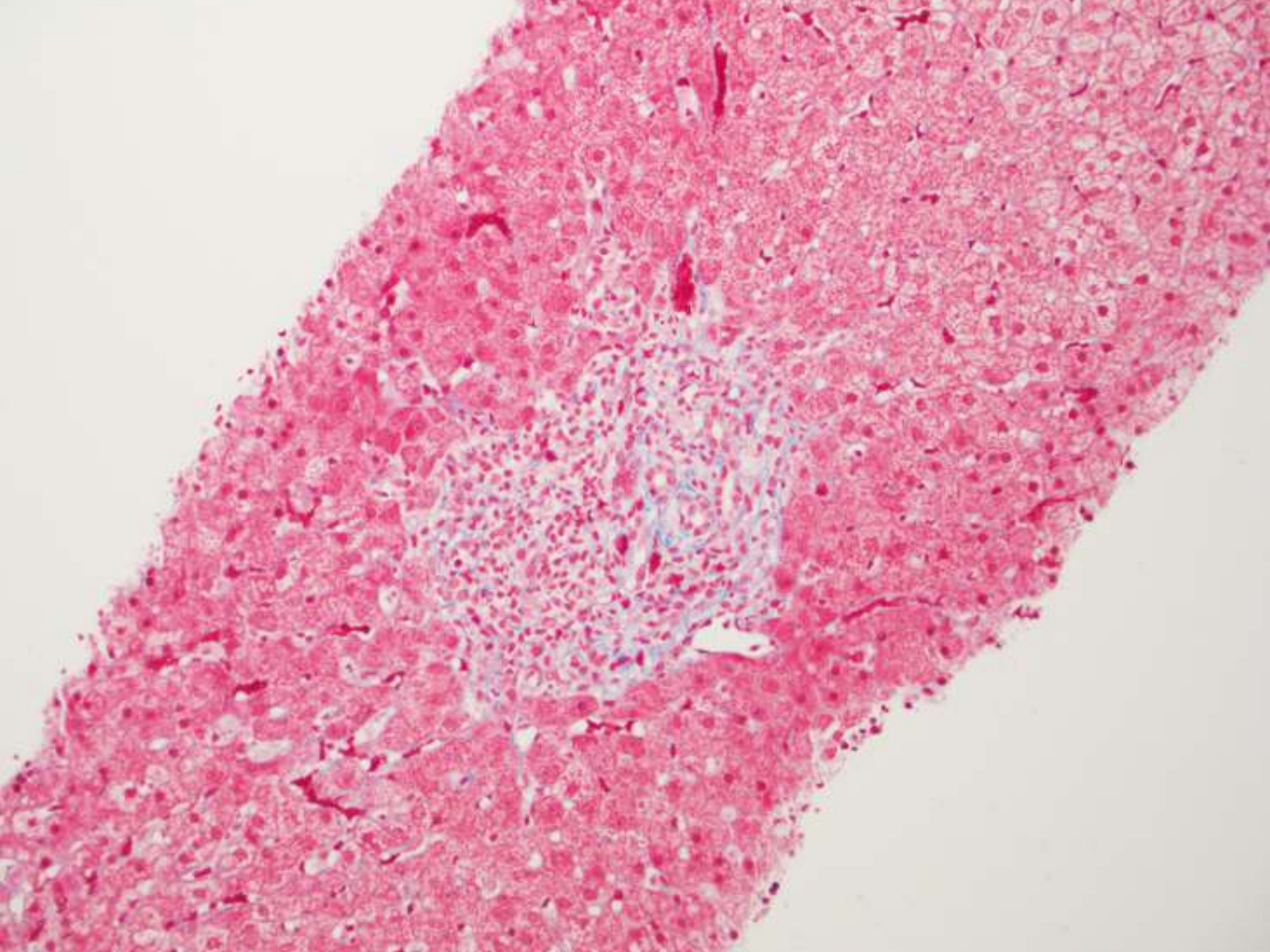








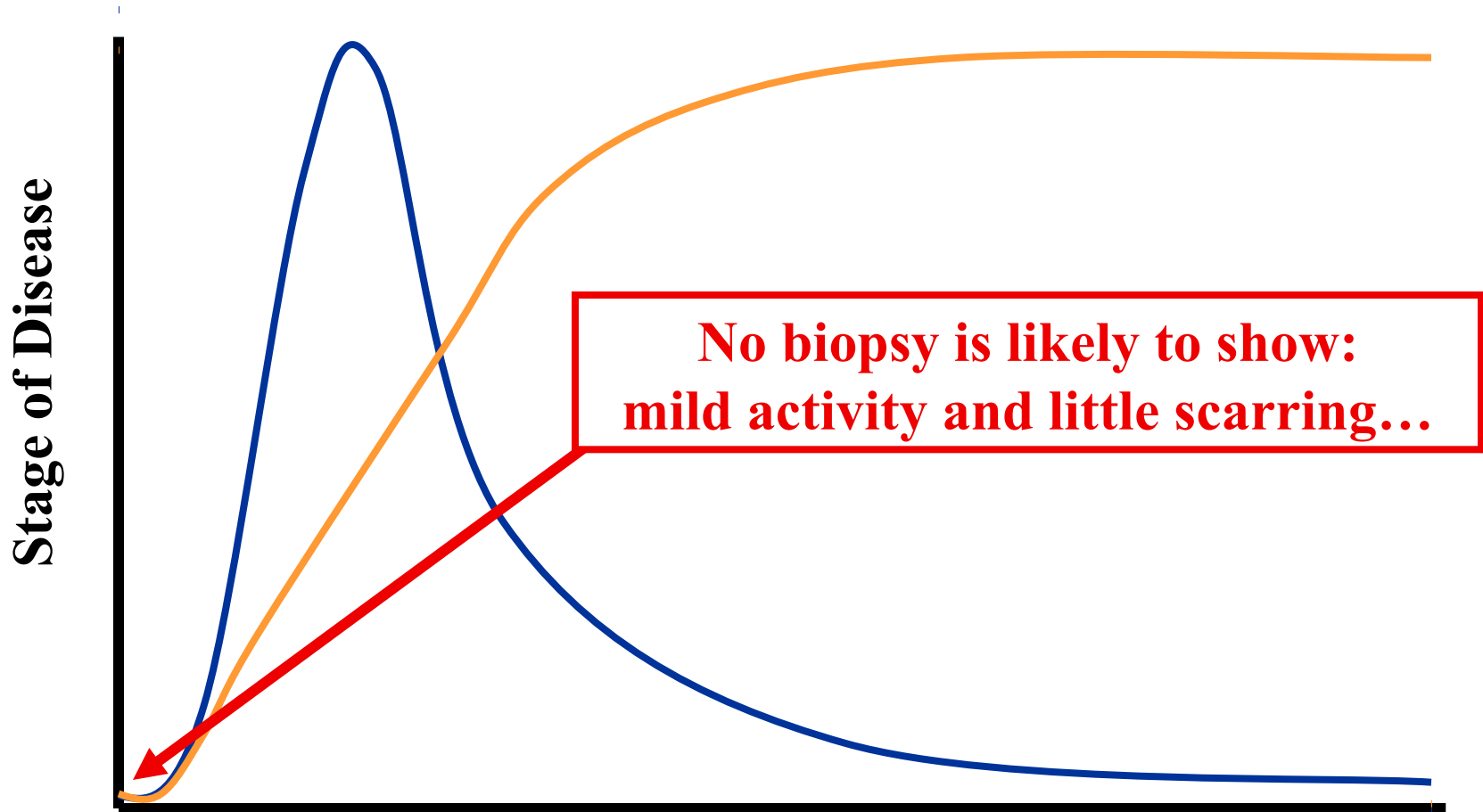




## **Case 3**

Is this autoimmune hepatitis...?

## Autoimmune hepatitis: Progression vs. activity over time





## Case 3

Is this autoimmune hepatitis...?

History as given: NO!!!!

## Case 3

Is this autoimmune hepatitis...?

**BUT!!!!**

## Case 3

Is this autoimmune hepatitis...?

**BUT!!!!**

The patient has been on immunosuppressive therapy for 5 years  
for autoimmune hepatitis.

Would like to attempt coming off meds.

Biopsy to see if any activity...



## Case 3

Final Diagnosis:

**-CHRONIC HEPATITIS, MILDLY ACTIVE, WITHOUT SIGNIFICANT SCARRING COMPATIBLE WITH PARTIALLY TREATED AUTOIMMUNE HEPATITIS.**

**Comment: yada yada yada... mild portal infiltrates associated with mild, focal interface hepatitis, etc etc etc.**

**Numerical assignment for the above stage of disease:**

**Modified Ishak scheme: stage 0/4**

**Metavir scheme: F0**

**Beijing classification: Early stage**

## Case 4

2004: 18 year old woman presents to emergency room with nausea, vomiting, fatigue and jaundice; ALT/AST >9000

Serologically negative for:

HAV, HBV, HCV

ANA, AMA, ASMA, anti-LKM1

Drugs or over the counter medications, etc.

Ceruloplasmin and iron indices all normal.

Clinical impression of fulminant failure of unknown cause.  
Receives supportive care while awaiting liver transplant.

No donor organ available, but patient recovers completely  
and goes home well.

## Case 4

2008: Now 22 years old, returns to emergency room with identical clinical picture: nausea, vomiting, fatigue and jaundice; ALT/AST >8000

Again, negative for:

HAV, HBV, HCV

ANA, AMA, ASMA, anti-LKM1

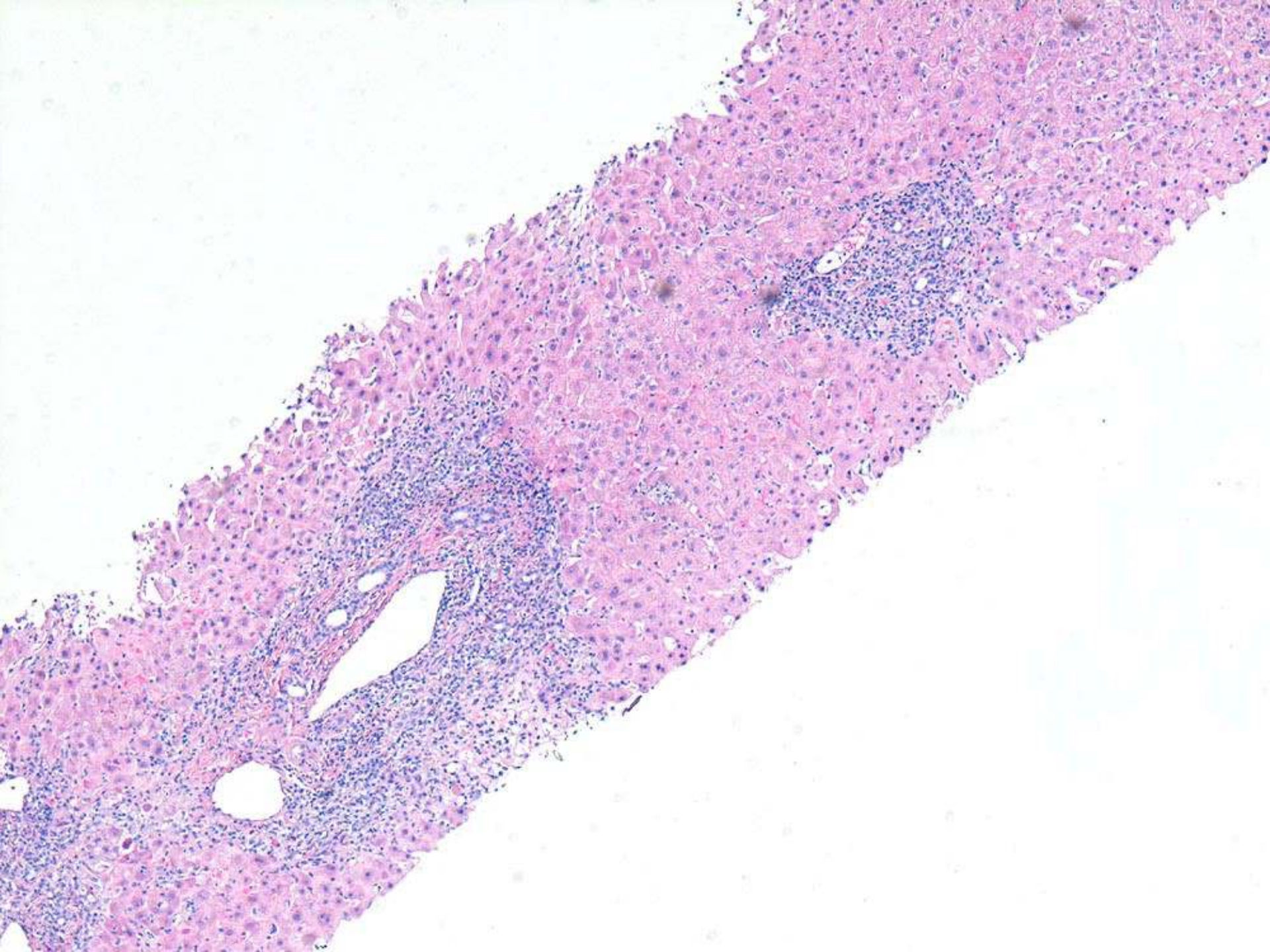
Drugs or over the counter medications, etc.

Again, ceruloplasmin and iron indices all normal.

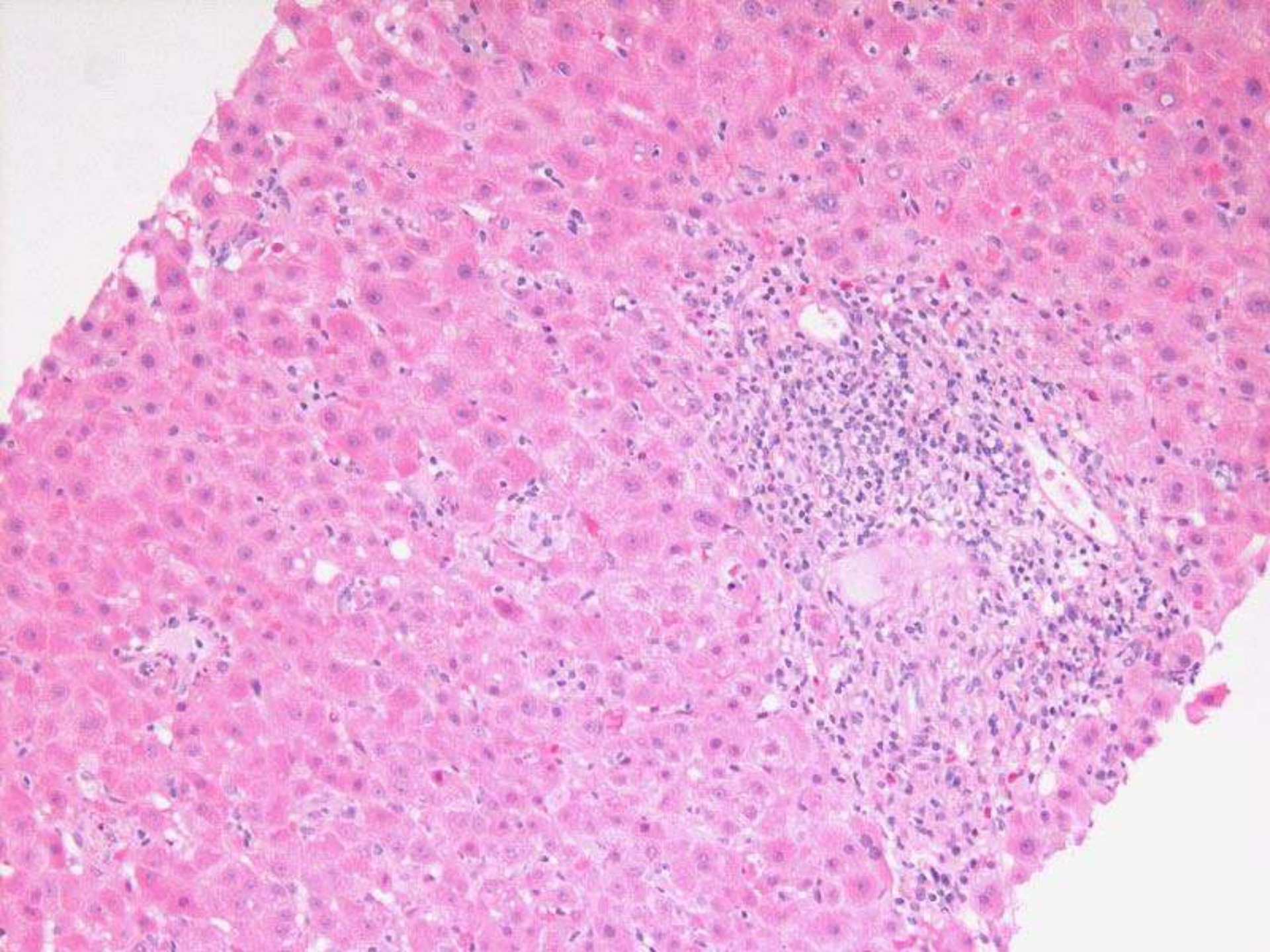
Again, clinically: Fulminant failure of unknown cause. Receives supportive care AND a liver biopsy to define what now appears to be a second flare of a chronic liver disease.

Again, patient recovers completely and goes home well.

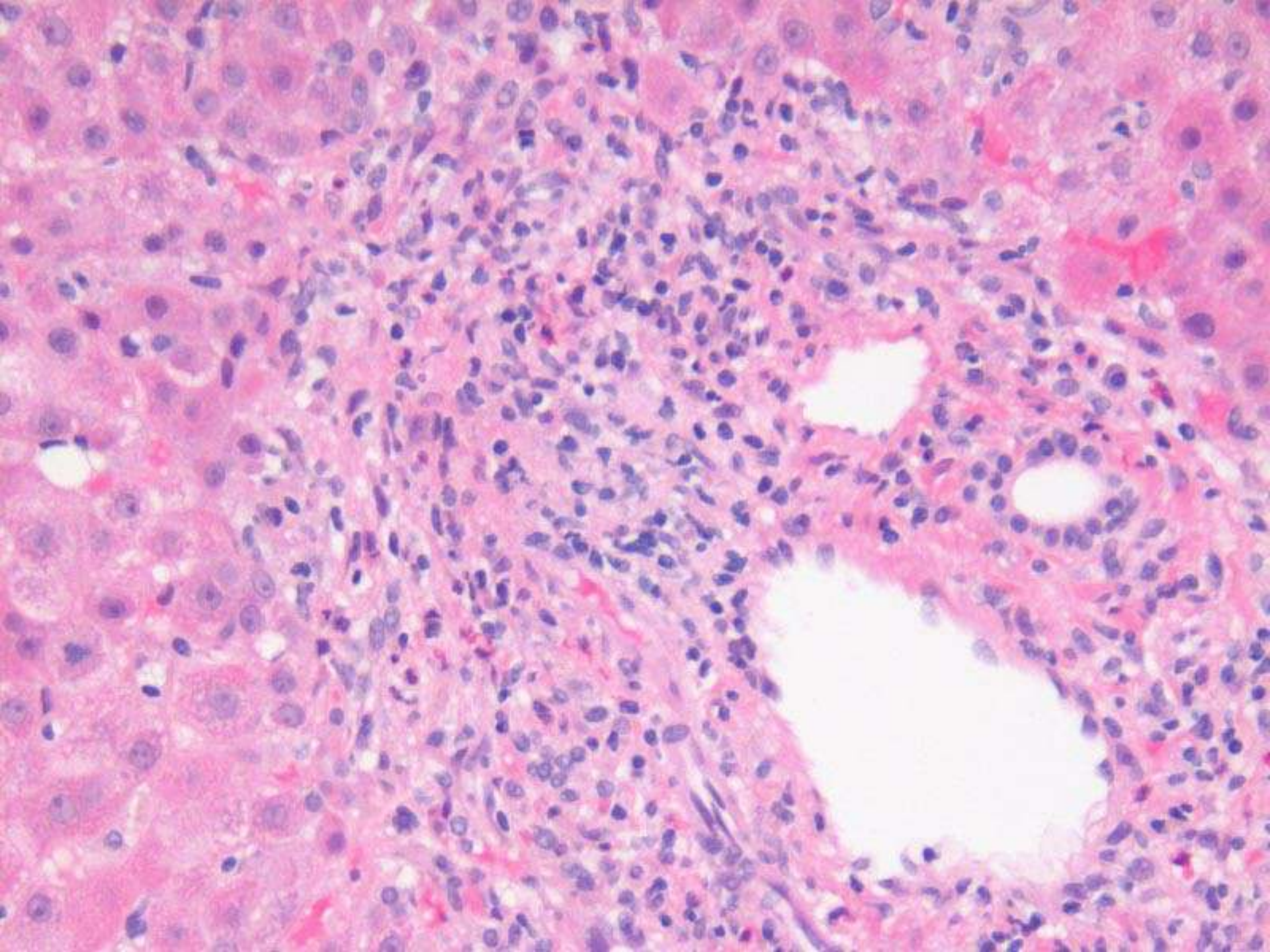




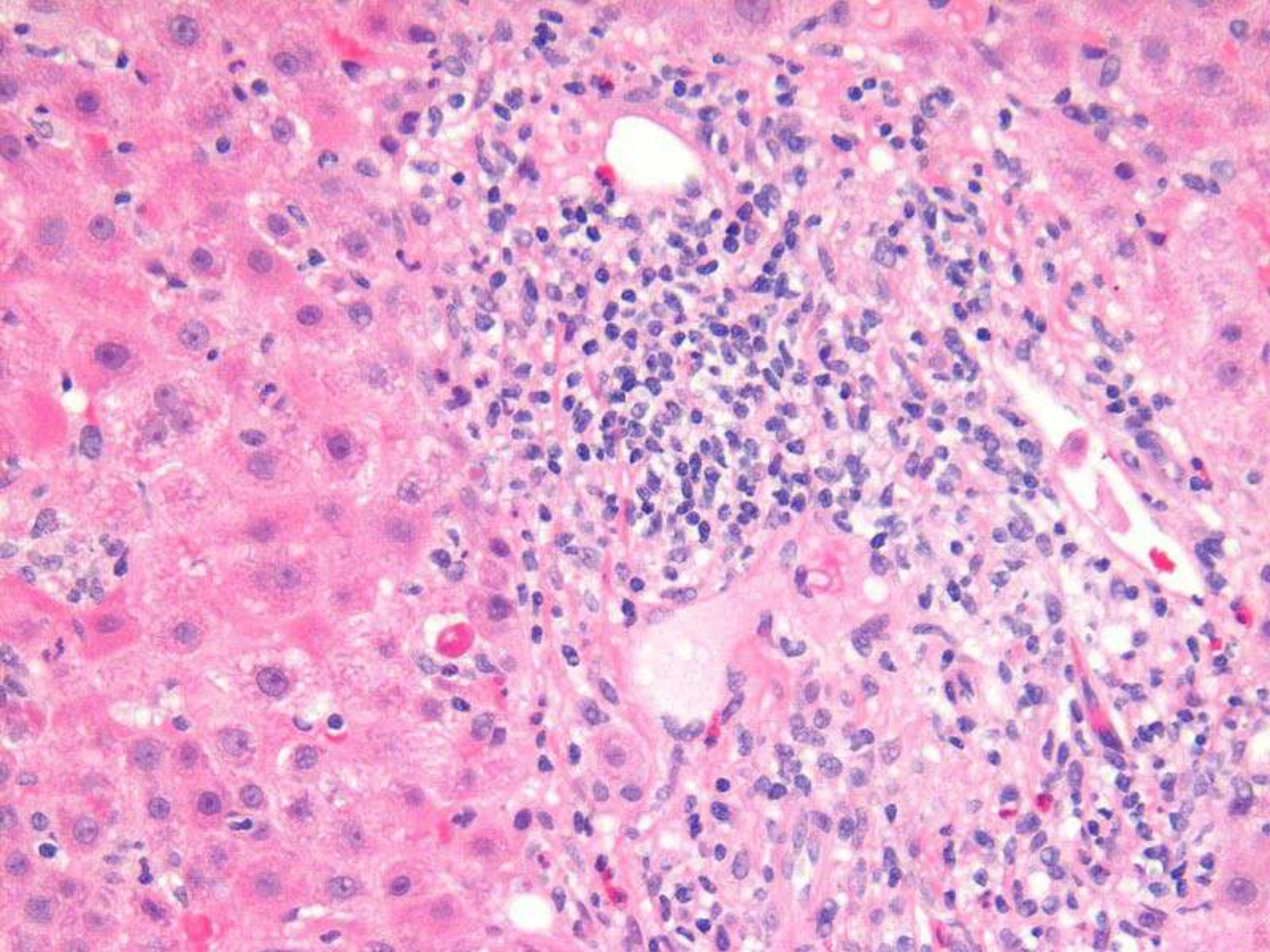




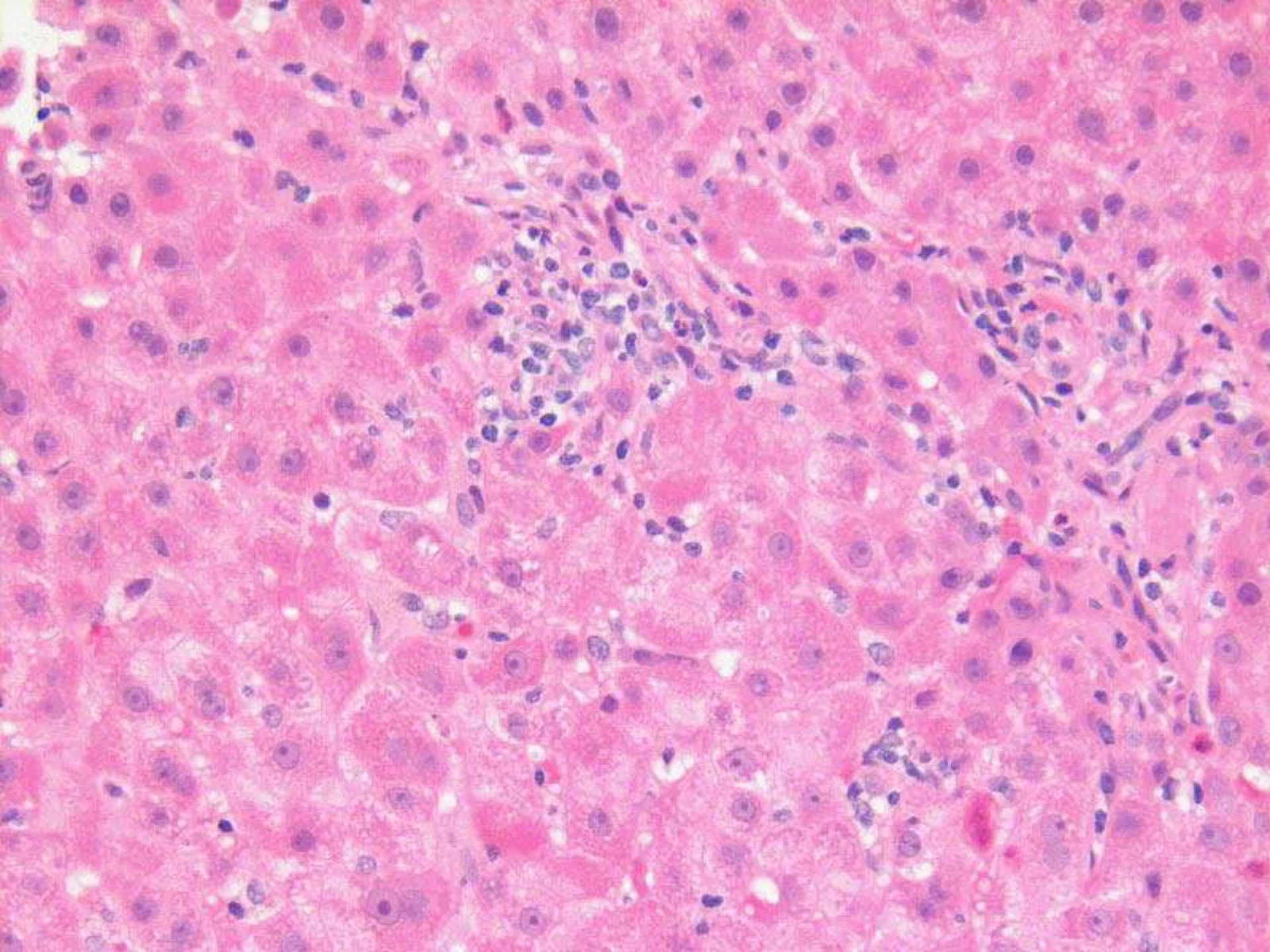




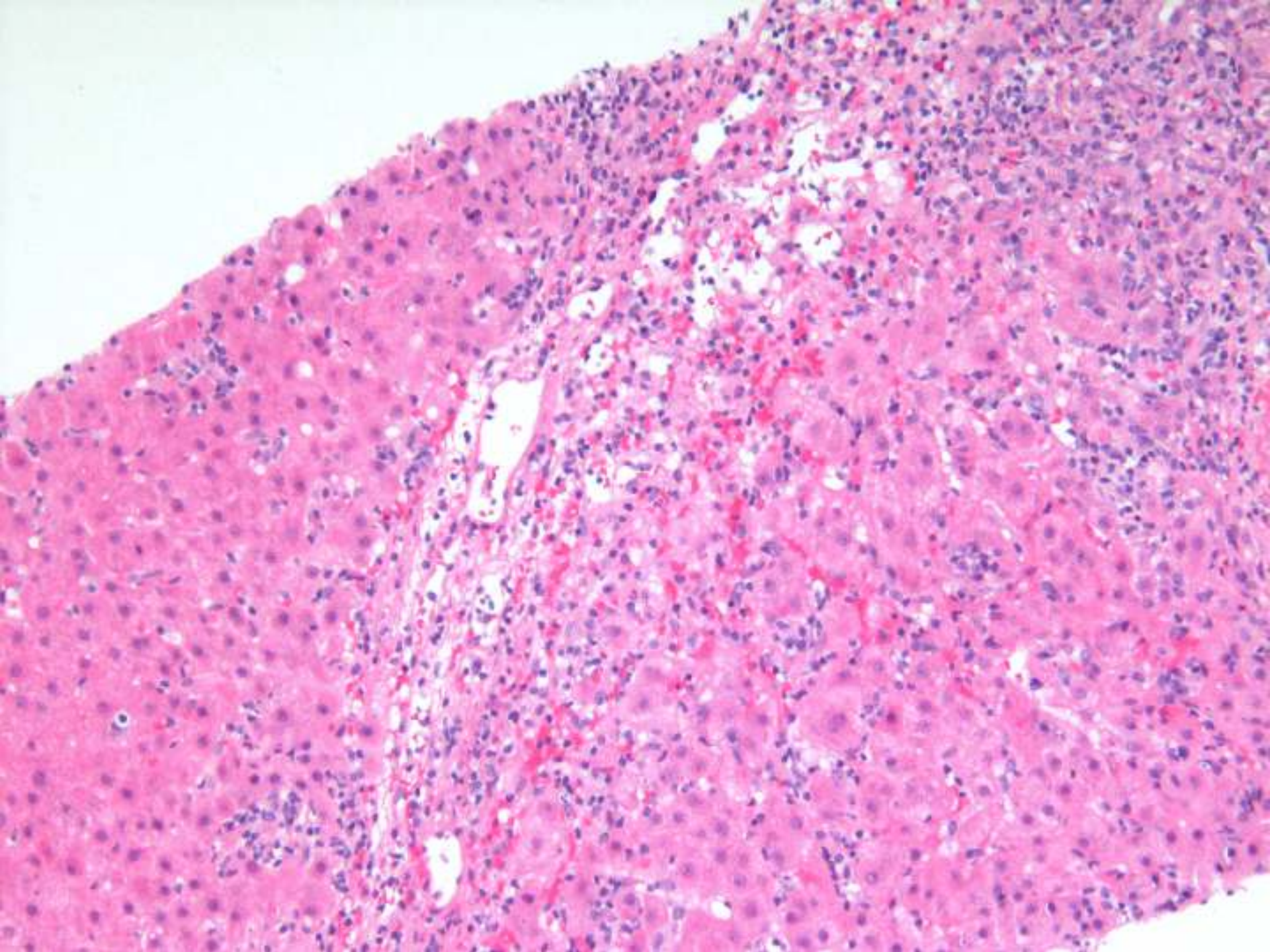




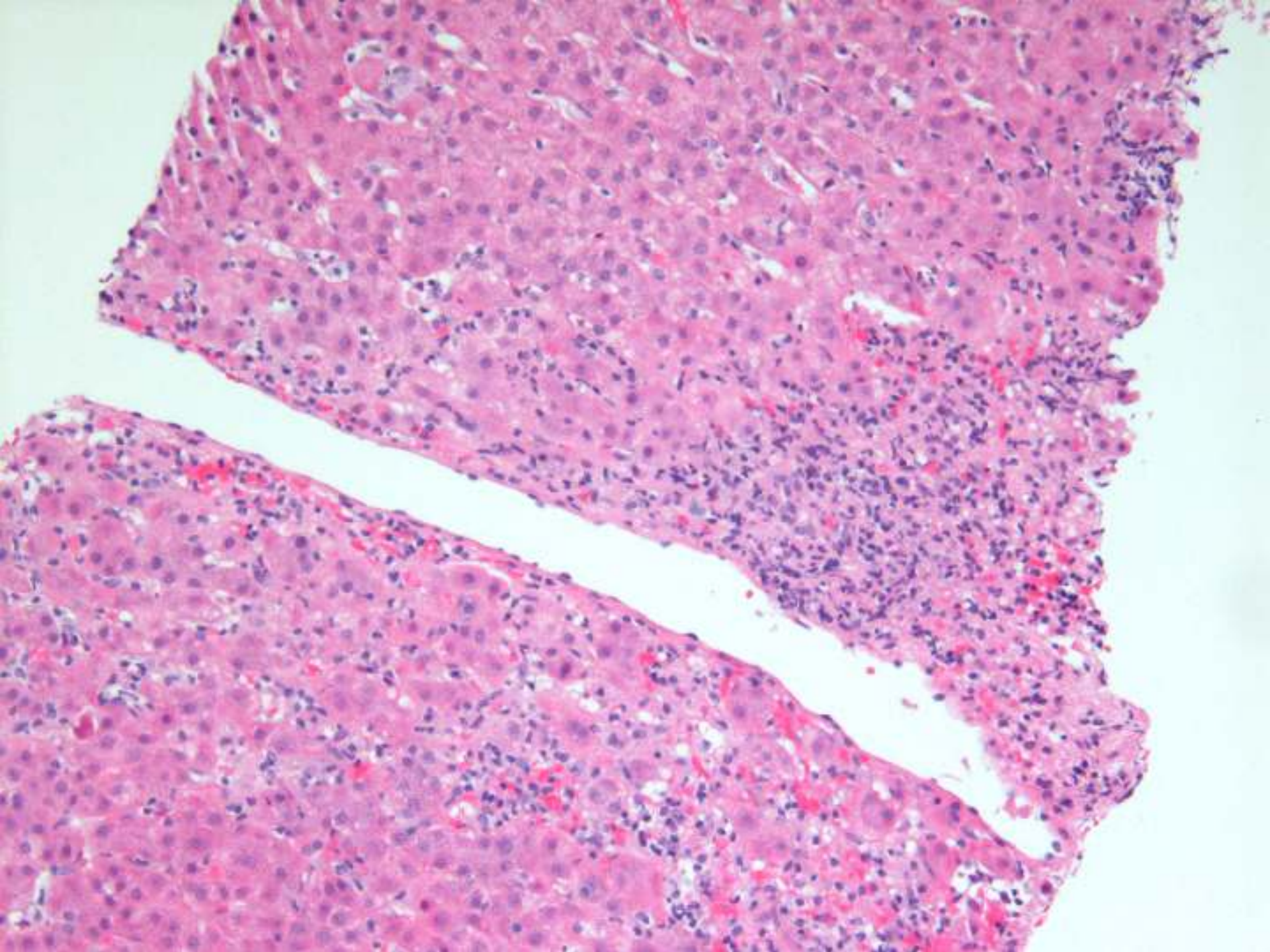




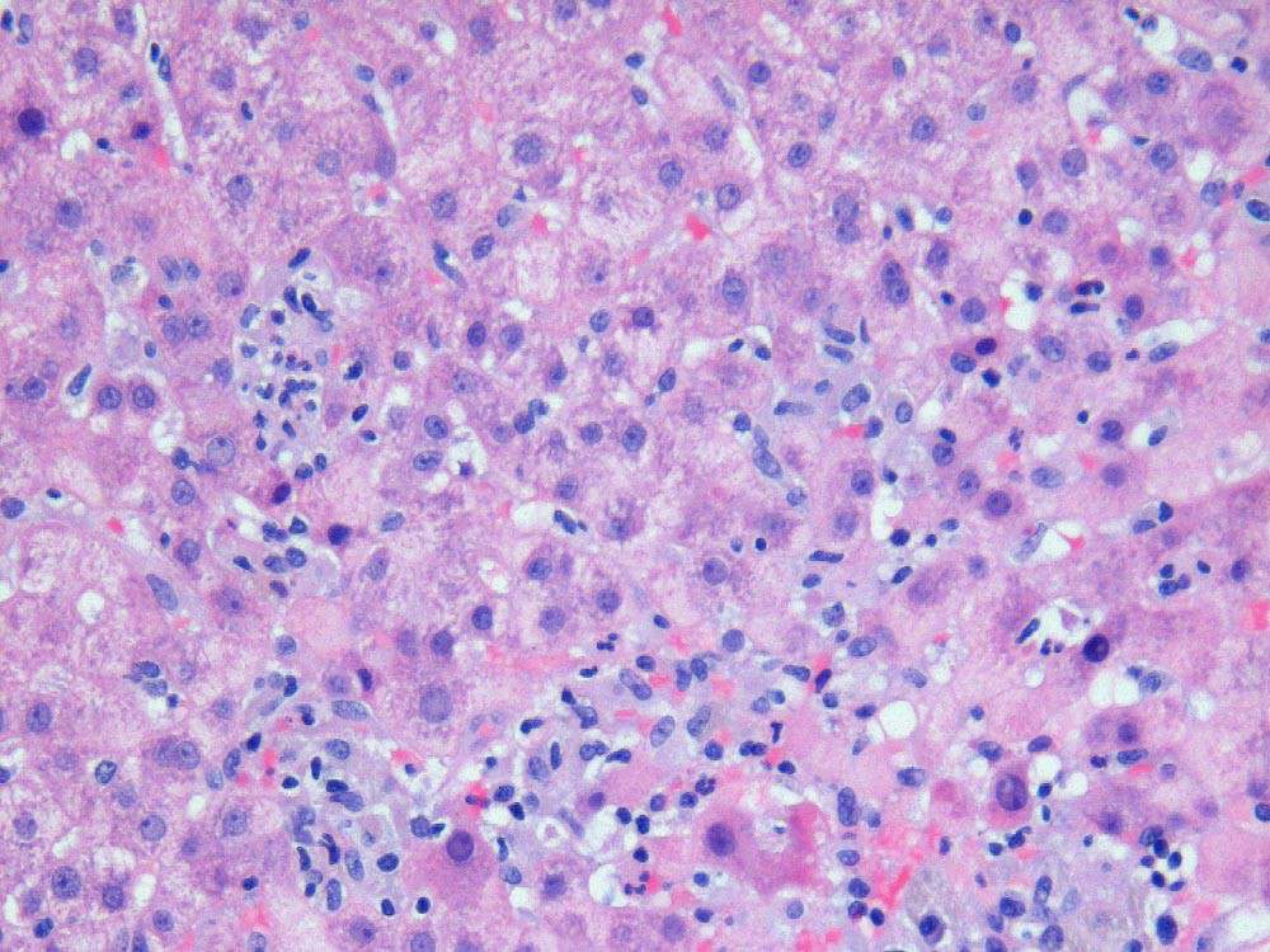




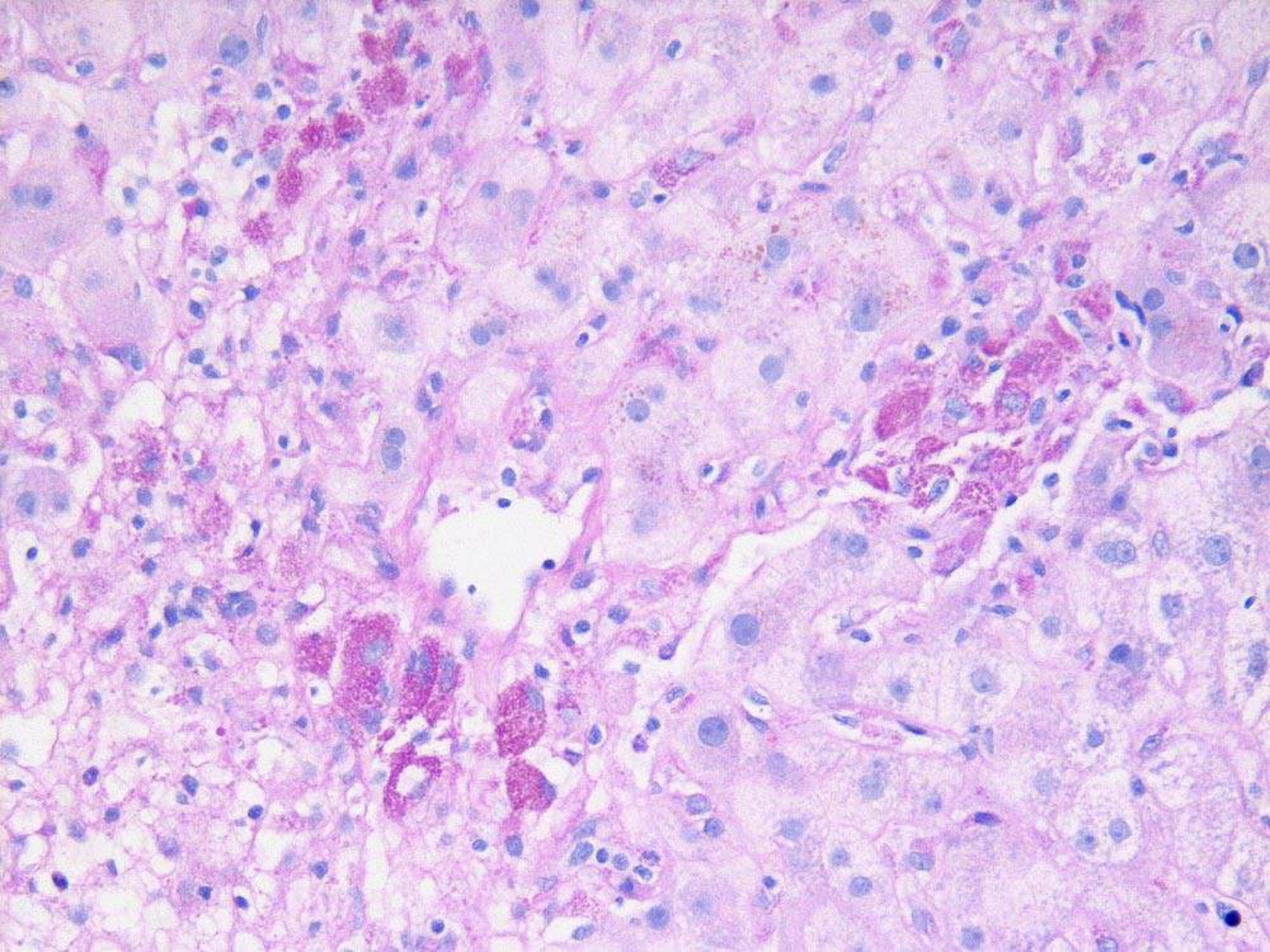














## Histologic findings:

Dense mononuclear portal infiltrates, not plasma cell rich,  
rare eosinophils

>>> “chronic hepatitis”

Confluent necrosis: perivenular and focal bridging necrosis

>>> “severe activity”

Moderate, focal portal fibrosis:

>>> modified Ishak stage 1/4

Histologic findings:

Dense mononuclear portal infiltrates, not plasma cell rich,  
rare eosinophils

>>> “chronic hepatitis”

Confluent necrosis: perivenular and focal bridging necrosis

>>> “severe activity”

Moderate, focal portal fibrosis:

>>> modified Ishak stage 1/4

Differential diagnosis:

Chronic viral hepatitis

Autoimmune hepatitis

Drug/toxin induced chronic hepatitis

Wilson’s disease



## Histologic findings:

Dense mononuclear portal infiltrates, not plasma cell rich,  
rare eosinophils

>>> “chronic hepatitis”

Confluent necrosis: perivenular and focal bridging necrosis

>>> “severe activity”

Moderate, focal portal fibrosis:

>>> modified Ishak stage 1/4

## Differential diagnosis:

~~Chronic viral hepatitis~~

~~Autoimmune hepatitis~~

~~Drug/toxin induced chronic hepatitis~~

~~Wilson's disease~~

## Histologic findings:

Dense mononuclear portal infiltrates, not plasma cell rich,  
rare eosinophils

>>> “chronic hepatitis”

Confluent necrosis: perivenular and focal bridging necrosis

>>> “severe activity”

Moderate, focal portal fibrosis:

>>> modified Ishak stage 1/4

>>> Metavir F1

>>> Beijing classification: Early stage

Differential diagnosis:





Histologic findings:

Dense mononuclear portal infiltrates, not plasma cell rich,  
rare eosinophils

>>> “chronic hepatitis”

Confluent necrosis: perivenular and focal bridging necrosis

>>> “severe activity”

Moderate, focal portal fibrosis:

Differential diagnosis:

Maybe not chronic...?

Maybe repetitive acute injury...?

## Case 4

FINAL DIAGNOSIS:

- CHRONIC HEPATITIS, MARKEDLY ACTIVE (BRIDGING NECROSIS), WITH MODERATE PORTAL FIBROSIS, ? CAUSE



FINAL DIAGNOSIS:



Intern Med. 2003; 42: 1104-6.

**Drug-induced hepatitis due to repeated use of hair dye.**

Tokumoto Y, et al.

**A 27-year-old Japanese man with no past history of liver disease was admitted to our hospital due to liver abnormalities. The patient was diagnosed with drug-induced hepatitis, as the three episodes of hepatitis occurred just after repeated use of hair dye. After cessation of the hair dye use, abnormal liver function tests improved to within the normal range. Although hair dyes contain various hepatotoxic compounds, hair dye is not known to cause drug-induced hepatitis. Thus, in cases of liver abnormality of unknown origin, the history of hair dye use should be investigated.**





## Case 4

### FINAL DIAGNOSIS:

- HEPATITIS, MARKEDLY ACTIVE (BRIDGING NECROSIS), WITH MODERATE PORTAL FIBROSIS, COMPATIBLE WITH DRUG/TOXIN INDUCED LIVER INJURY (DILI).



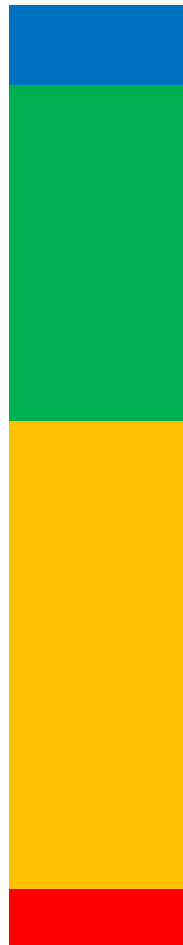


-  **Viral hepatitis**
-  **NAFLD/ALD**
-  **Autoimmune Diseases**
-  **Drug/Toxin (DILI)**





**2012**



**2012**

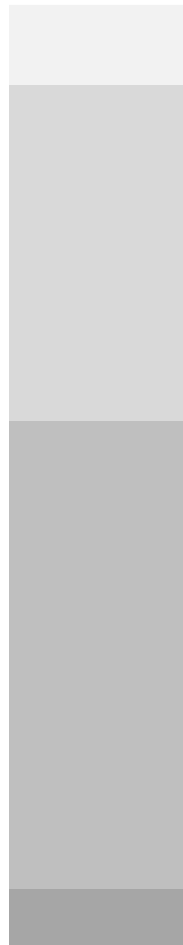


**Hypothetical  
2017**

-  **Viral hepatitis**
-  **NAFLD/ALD**
-  **Autoimmune Diseases**
-  **Drug/Toxin (DILI)**







Hypothetical  
2017



Actual  
2017



-  **Viral hepatitis**
-  **NAFLD/ALD**
-  **Autoimmune Diseases**
-  **Drug/Toxin (DILI)**



## Typical DILI statement:

In the absence of... etc etc, the observed changes may relate to drug/toxin induced liver injury (DILI), including prescription and over the counter medications, herbal remedies, dietary supplements, “vitamins” and topical or environmental exposures; clinical correlation required.

