

# Medikamentös-toxische Leberschädigungen

- Breites Spektrum von Minimalveränderungen, Fettleberhepatitis, autoimmune hepatitis, akute und chronische Leberentzündung, cholestatische Veränderungen, akutes Leberversagen und Zirrhose
- Schwierige differentialdiagnostische Abgrenzung, da keine spezifischen morphologischen Schädigungsmuster
- Allein histologisch keine Abgrenzung von viral oder autoimmun bedingten Hepatitiden möglich
- Bildung von Autoantikörpern möglich (z.B. ANA,SMA)

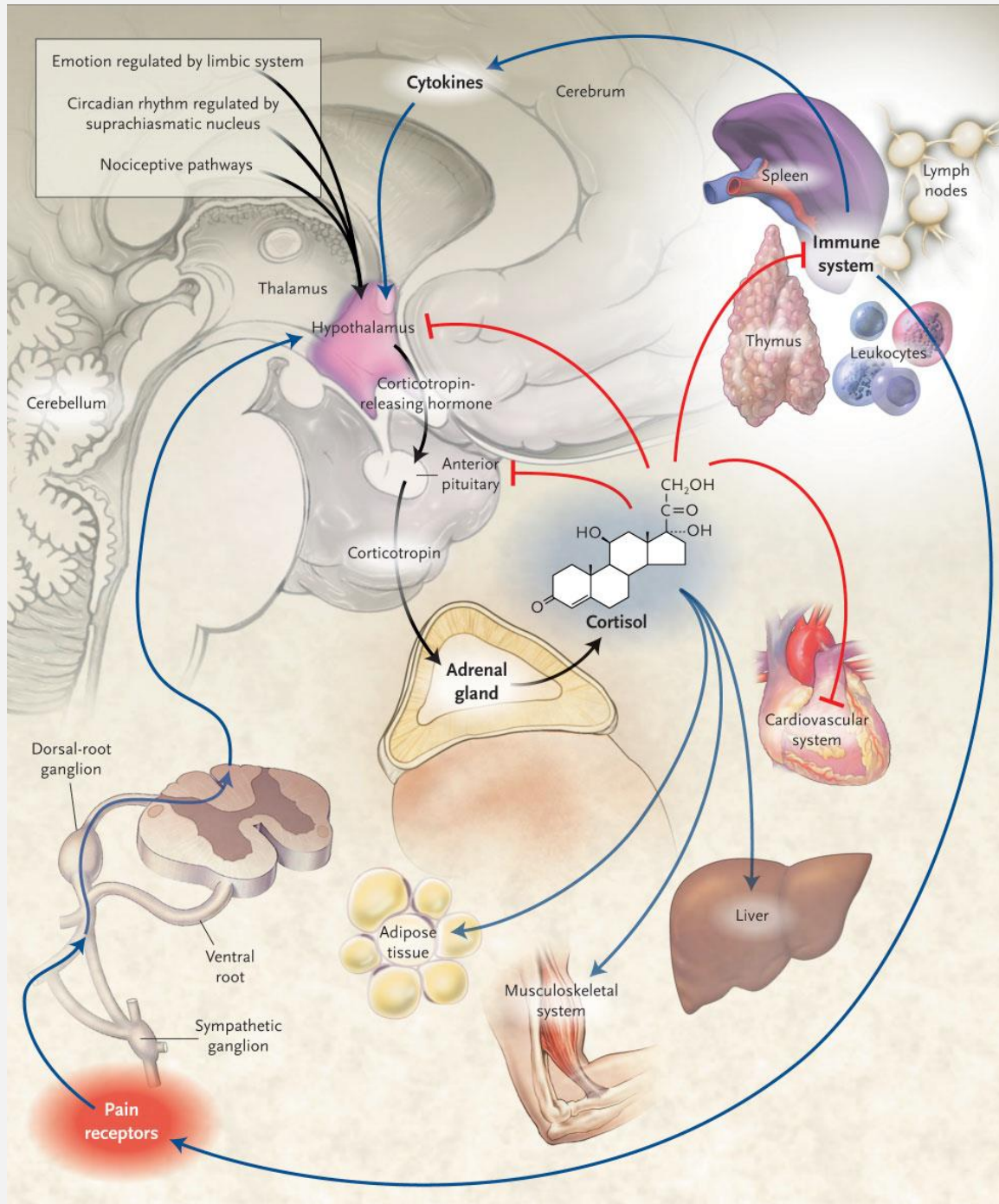
# Drug-induced liver injuries

Very variable changes of liver tissue

- Minimal changes in portal tracts or intralobular
- Non-alcoholic steatohepatitis
- Autoimmune hepatitis
- Acute and chronic inflammation of the liver
- Cholestasis
- Acute liver failure
- cirrhosis

# Drug-induced liver injuries

- No specific pattern of injury of the liver tissue
- Difficult differential diagnosing
- Histologically great resemblance to viral induced hepatitis
- Occasional occurrence of antibodies (e.g. ANA, SMA)



from:  
 Rhen T, Cidlowski JA  
 N Engl J Med (2005)  
 353, p 1713

# Einteilung der medikamentös-toxischen Leberschädigungen nach Pathogenese

1. Intrinsischer Mechanismus
  - a. Direkt (dosisabhängig, direkte Hepatozytenschädigung)
  - b. Indirekt (dosisabhängig, indirekte Hepatozytenschädigung)
2. Idiosynkratischer Mechanismus
  - a. Immunologischer Mechanismus - allergische Reaktionen, Fieber, Exantheme, Eosinophilie
  - b. Metabolischer Mechanismus – meist über kovalente Bindungen von Arzneimitteln an Proteine, gegen die immunologische Reaktionen ausgelöst werden können

# Pathogenetical classification of drug-induced liver injury

## 1. Intrinsic mechanism

- Direct injury of hepatocytes (dosis-dependent)
- Indirect injury of hepatocytes (dosis-dependent)

## 2. Idiosyncratic mechanism

- Immunologic mechanism – allergic reaction, fever, exanthema, eosinophilia
- Metabolic mechanism – mostly via covalent bindings to proteins induce an immunological reaction

# Morphological classification of drug-induced liver injury

## 1. Injury of hepatic type

- Acute : necroses mostly centrilobular, apoptoses, collapsed fields hemorrhage, swelling of hepatocytes, inflammatory infiltration of portal tracts by lymphocytes and histiocytes, ceroid-containing macrophages, granulomas
- Chronic : inflammatory infiltration of peri-portal regions and portal tracts by lymphocytes and histiocytes, plasma cells, eosinophilic granulocytes, interface hepatitis, intralobular hepatitis, fibrosis

## 2. Injury of cholestatic type

## 3. Fibrosis

## 4. Damage of vessels

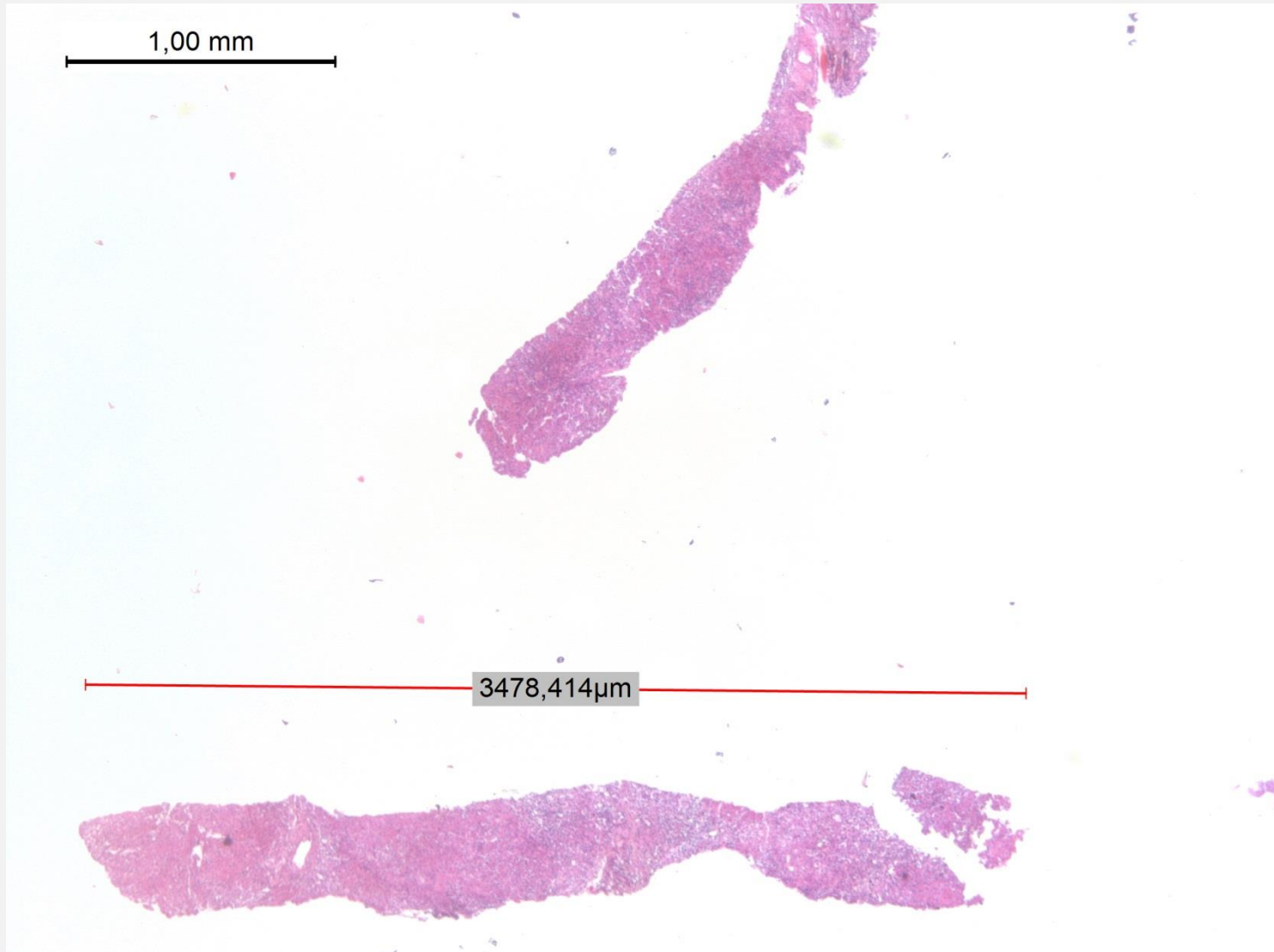
## 5. Neoplasia

# Einteilung der medikamentös-toxischen Leberschädigungen nach Morphologie

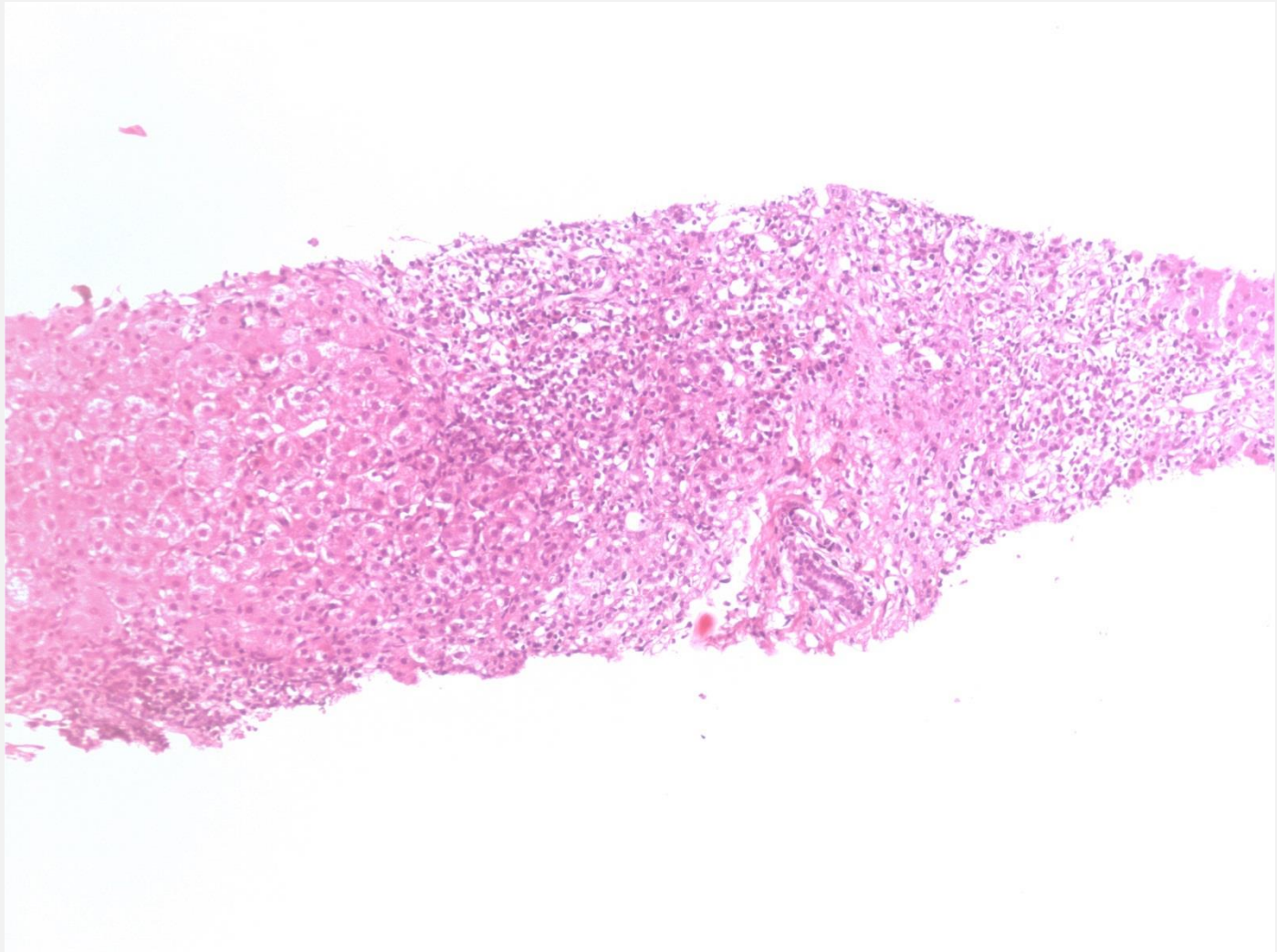
1. Schäden vom hepatitischen Typ
  - a. akut: Nekrosen - meist zentrolobulär, Apoptosen, Gerüstkollaps, Einblutungen, Ballonierung der Hepatozyten, lympho-histiozytäre Entzündung, Ceroid-beladene Makrophagen, Granulome
  - a. Chronisch: betont periportale Infiltrate aus Lymphozyten, Plasmazellen, eosinophilen Granulozyten, Histiozyten, Interface hepatitis, intralobular hepatitis, Fibrose
2. Schäden vom cholestatischen Typ
3. Fibrose
4. Gefäßschäden
5. Neoplasien



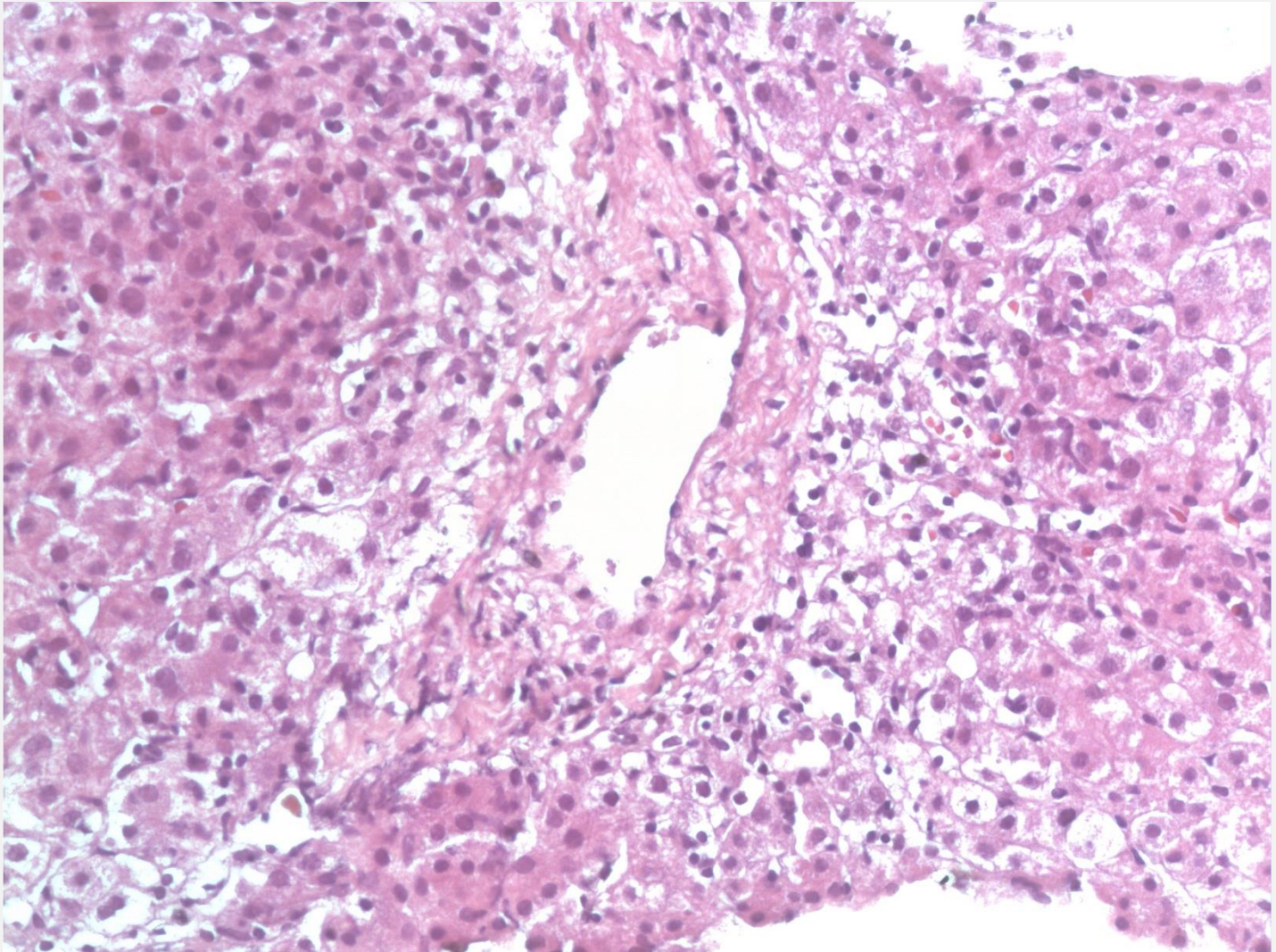
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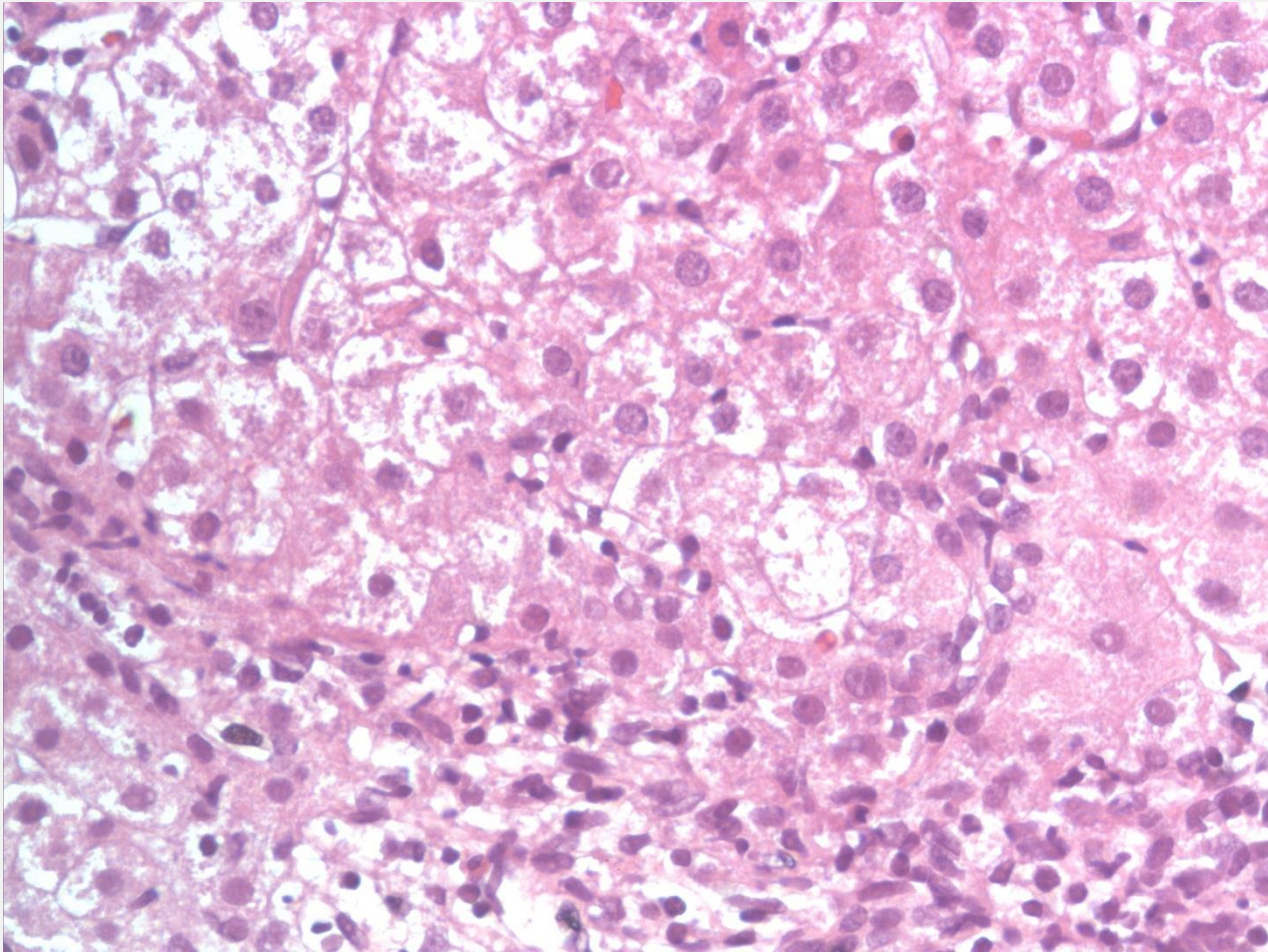
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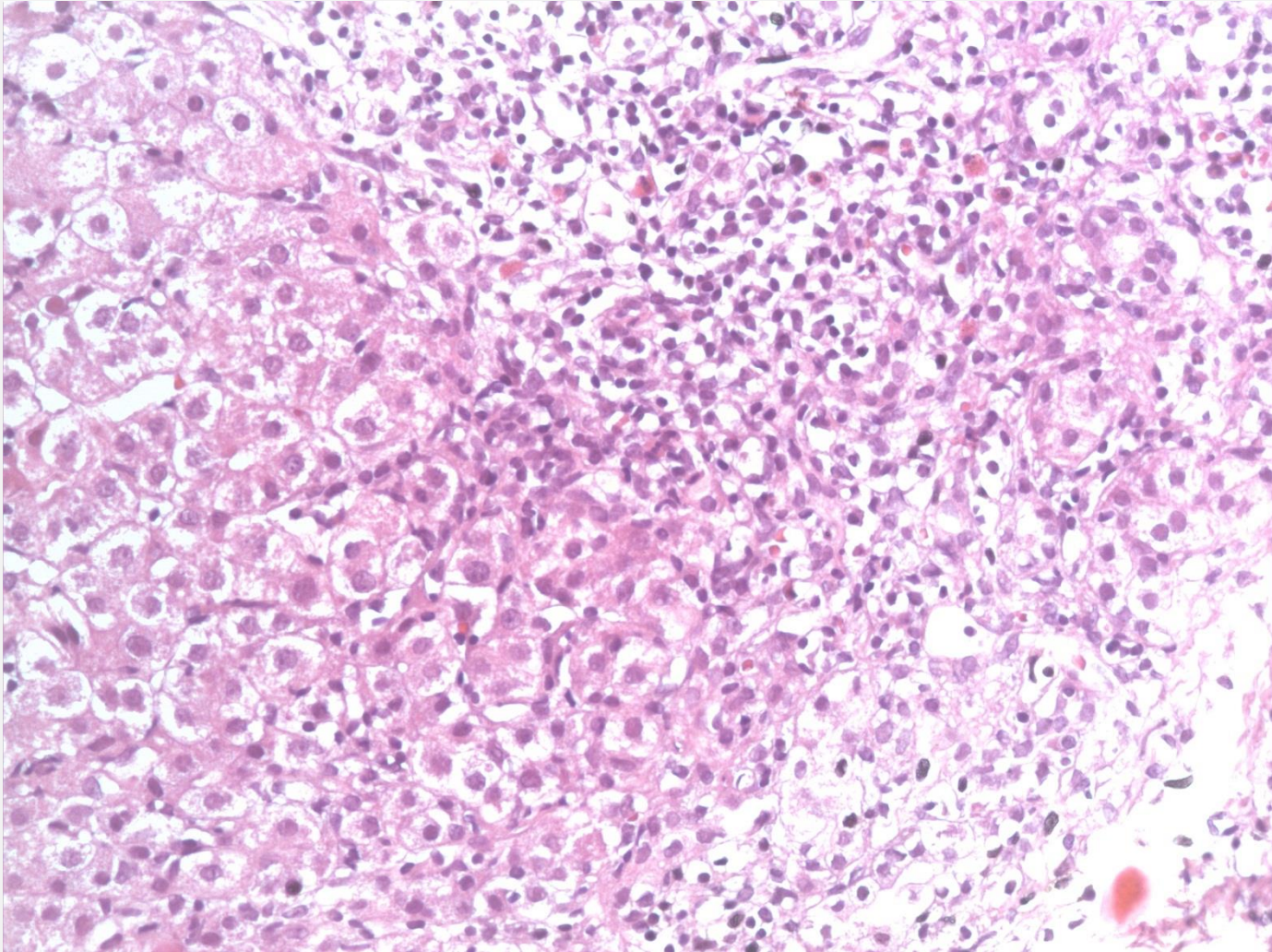
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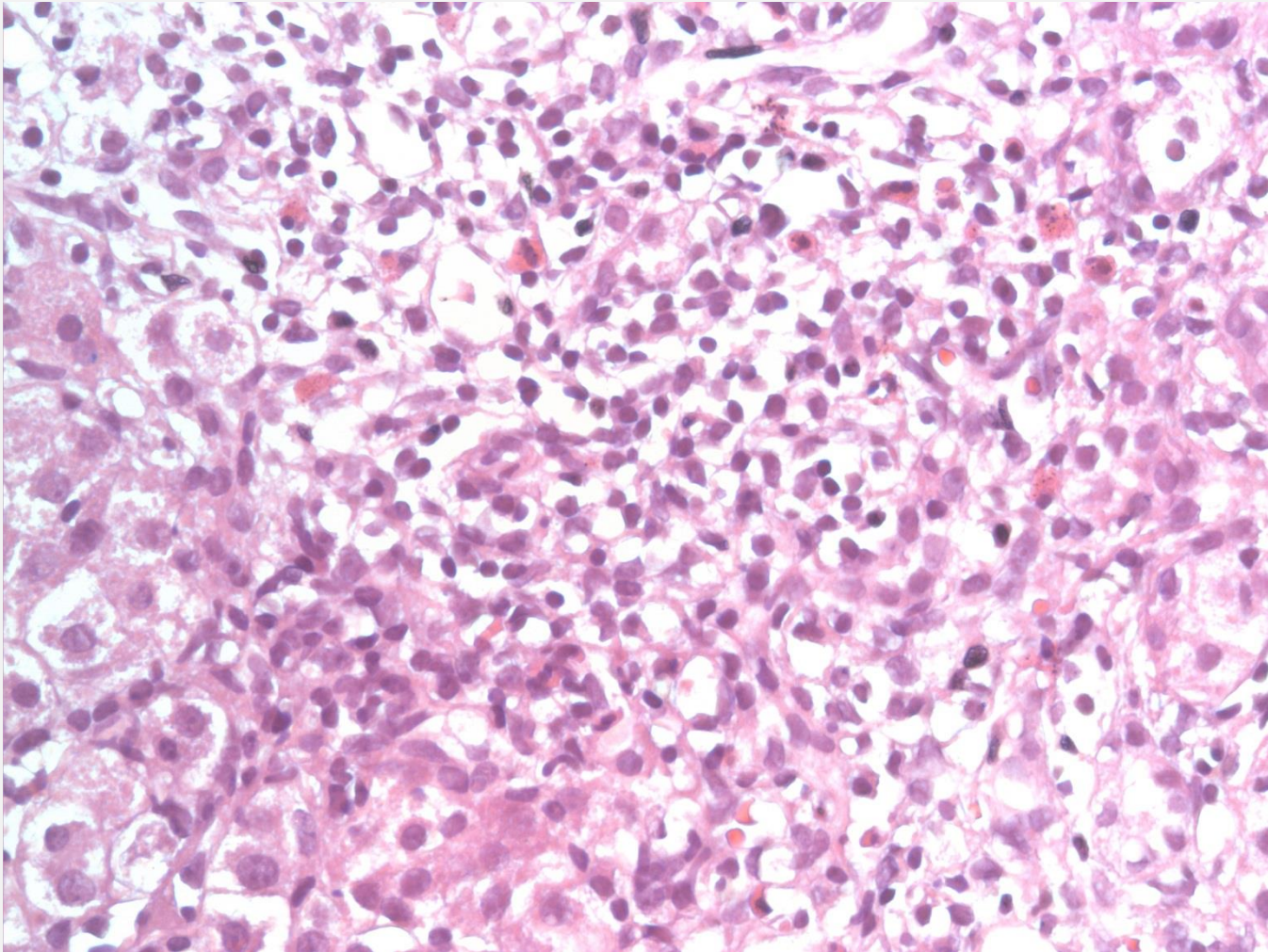
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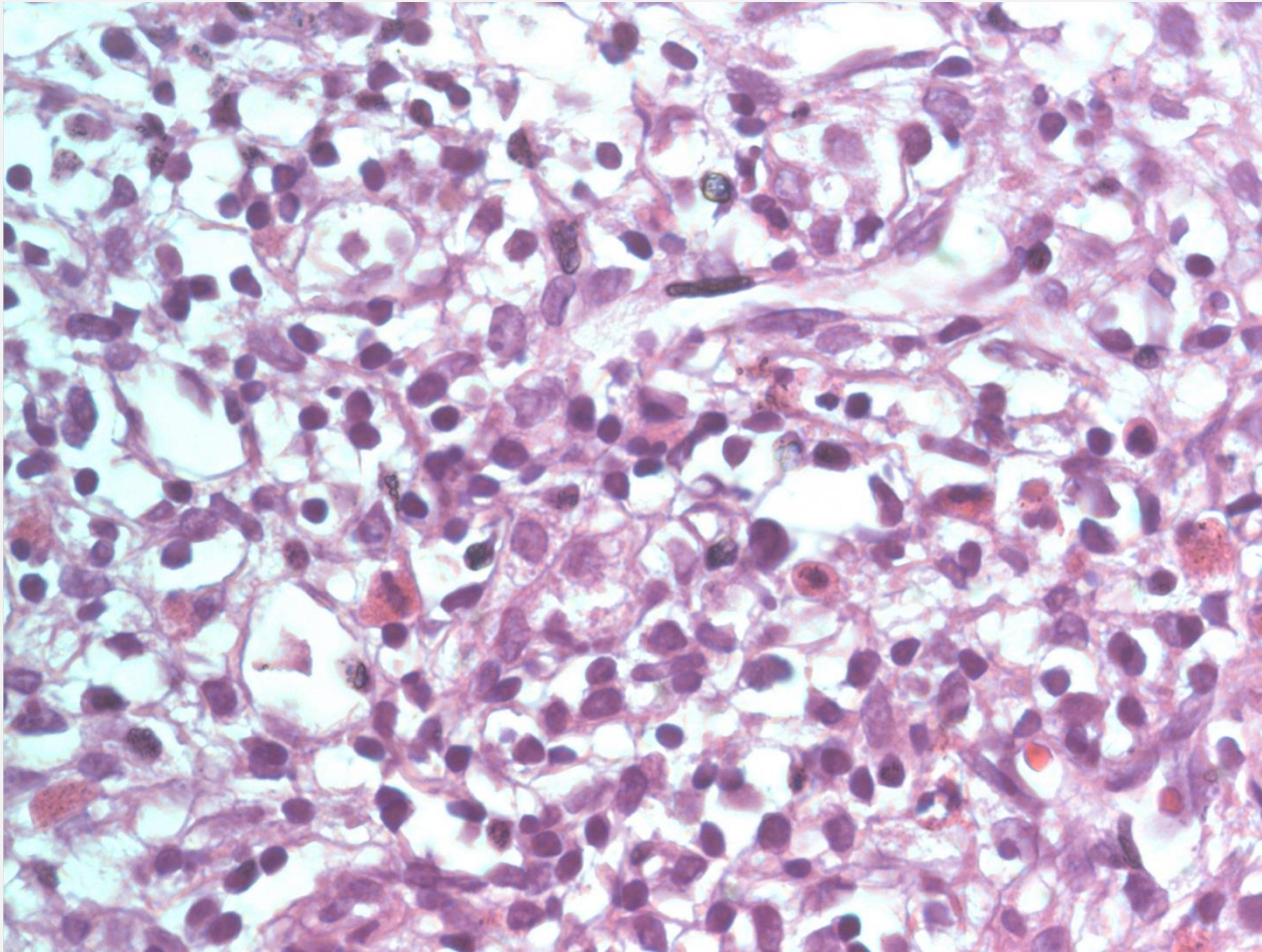
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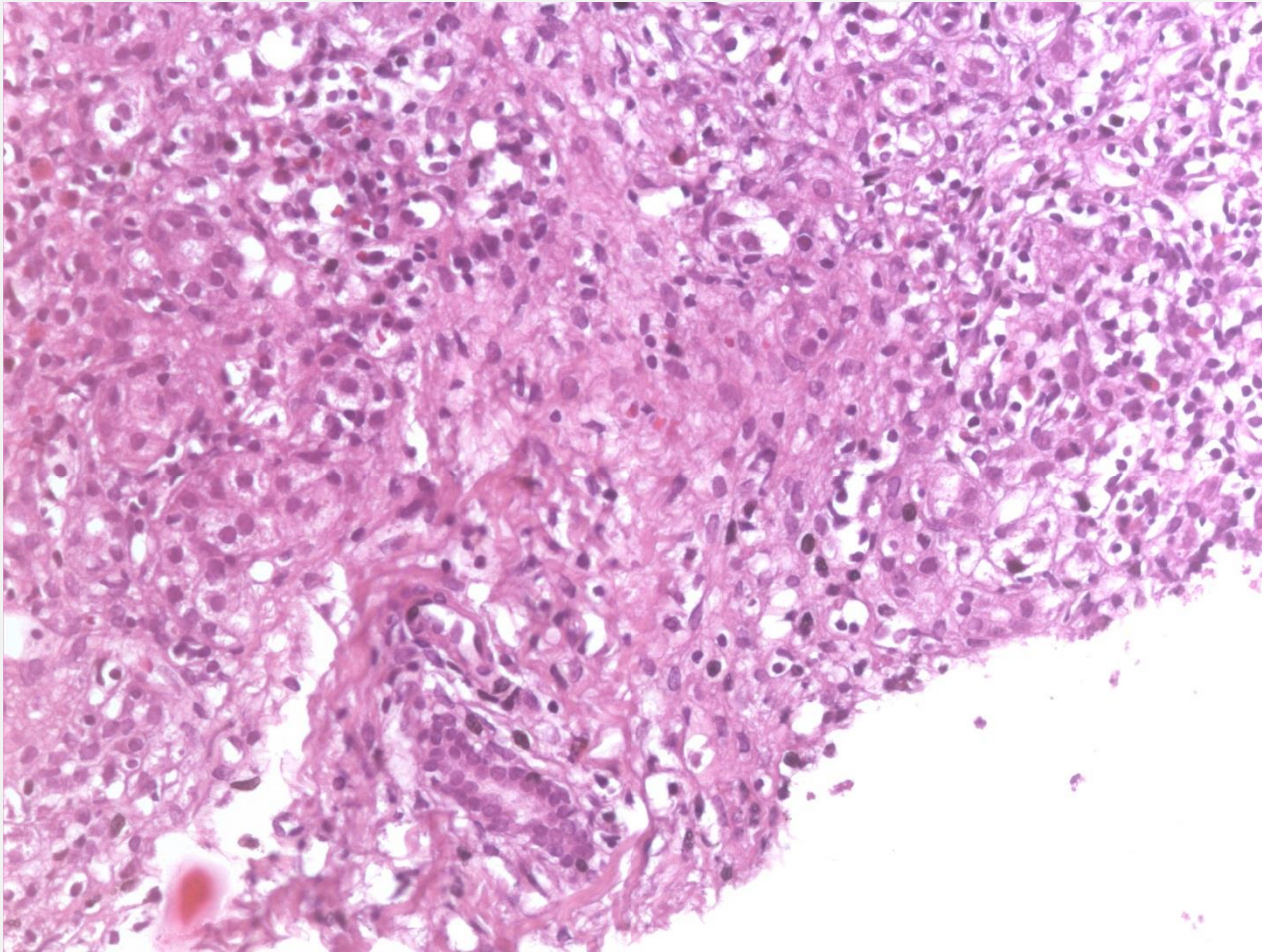
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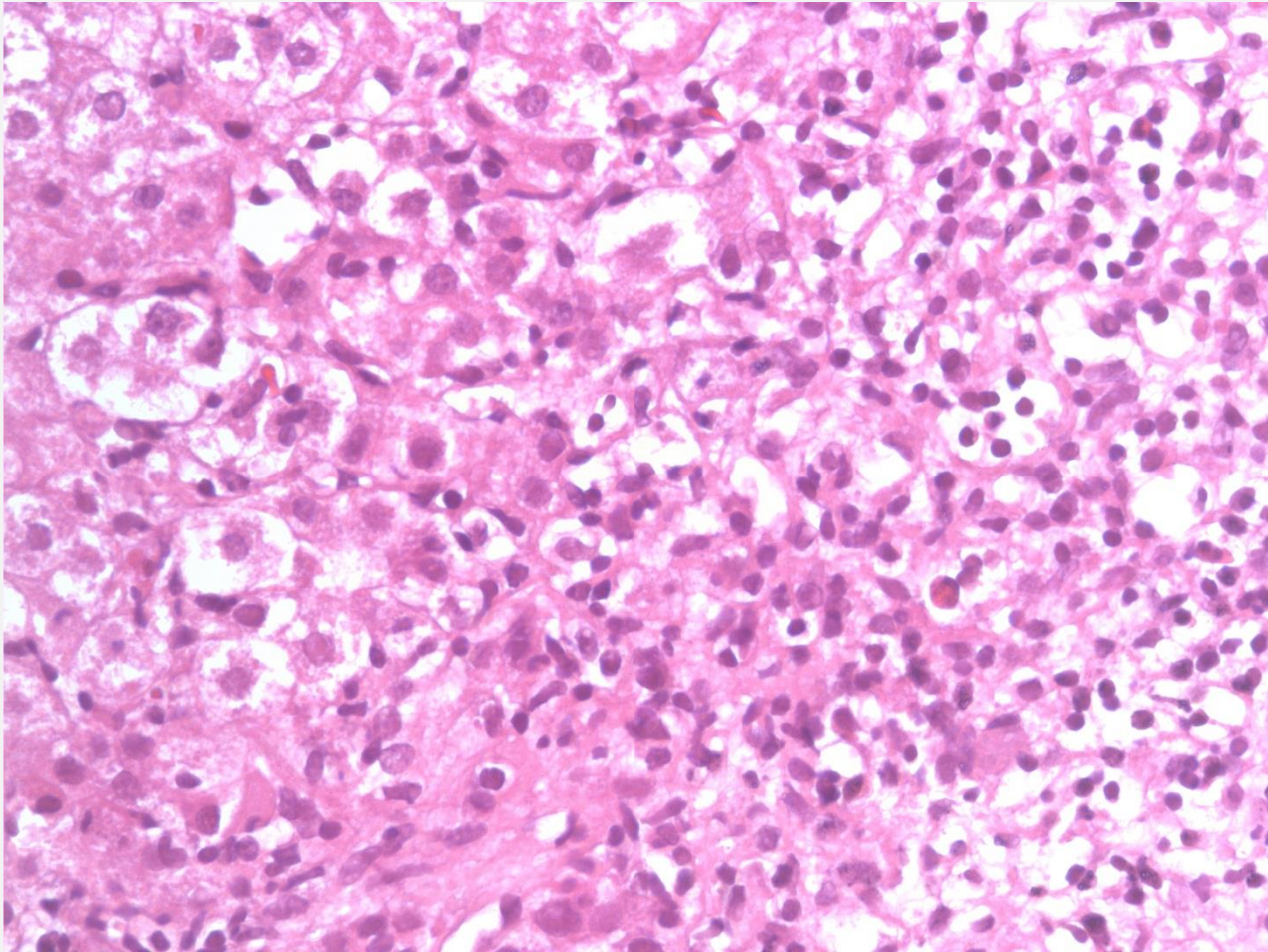


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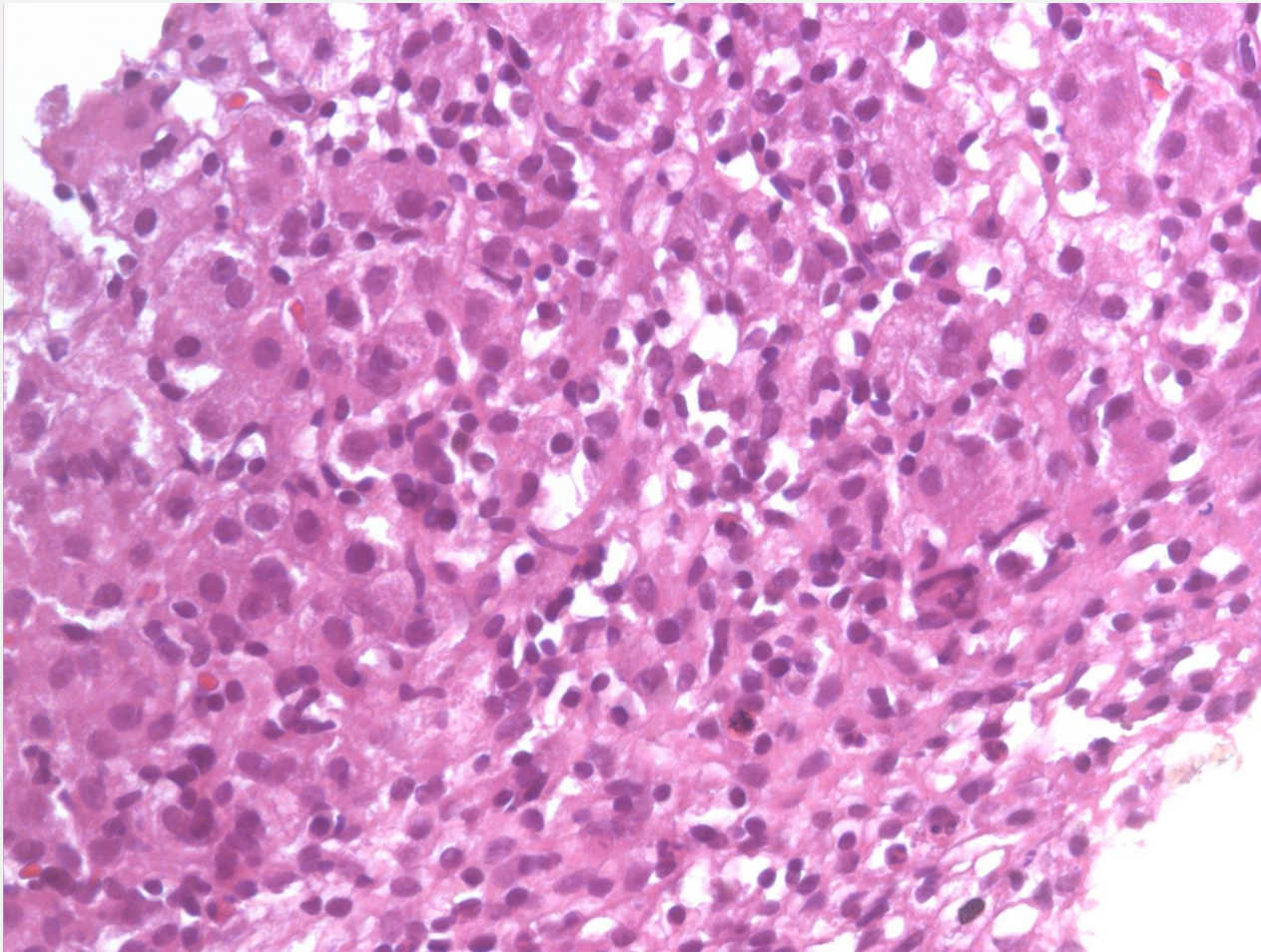




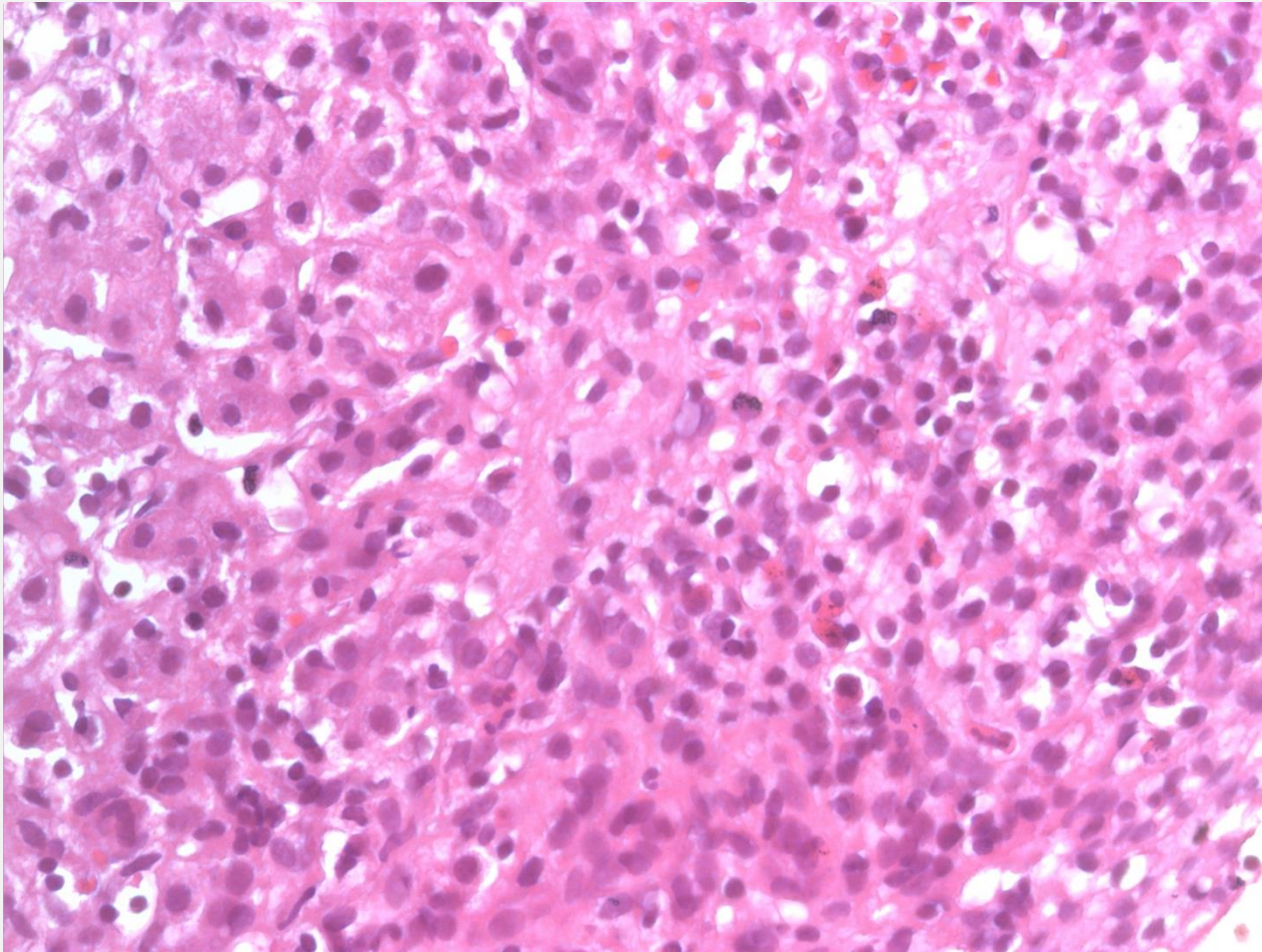
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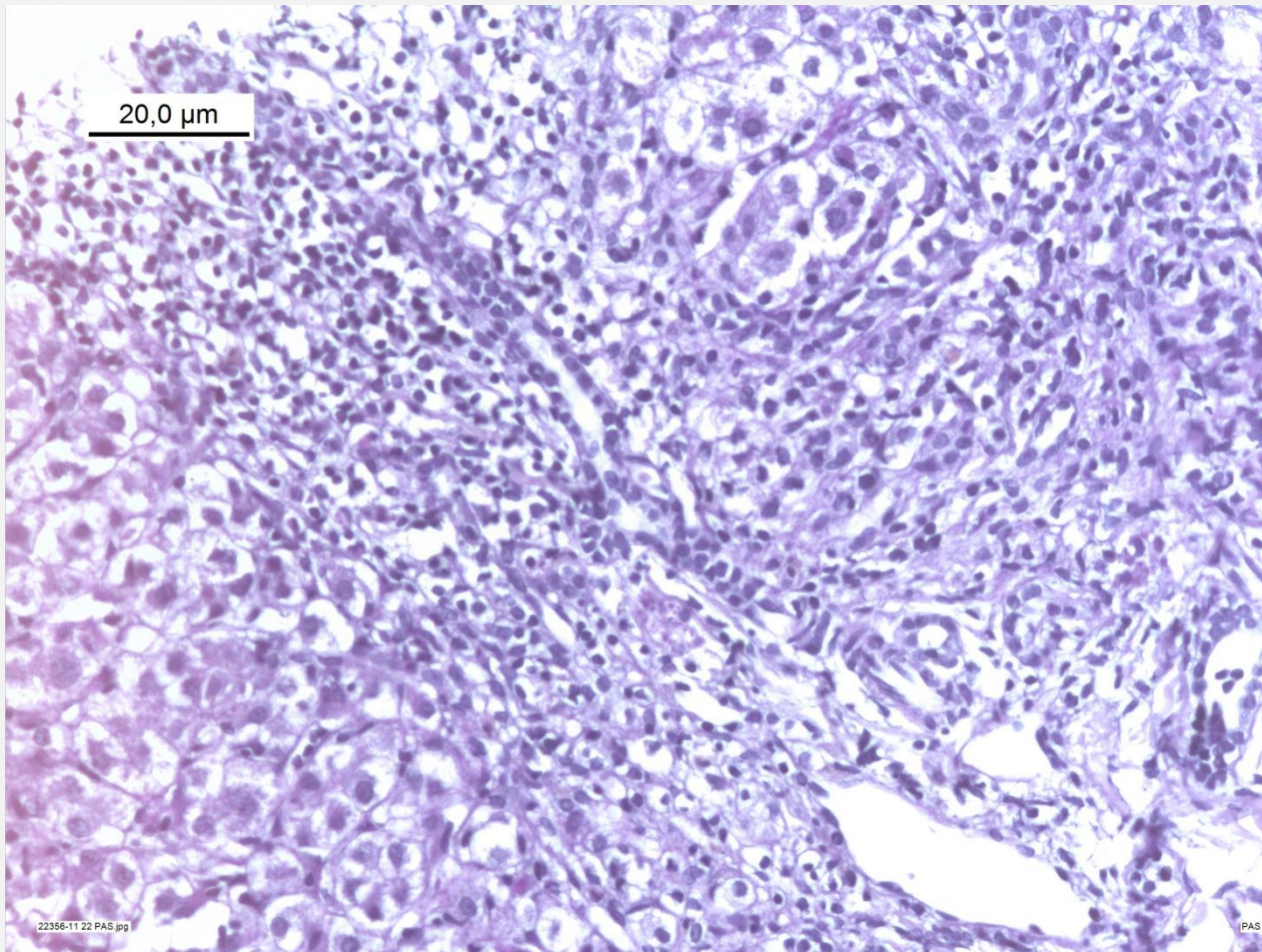
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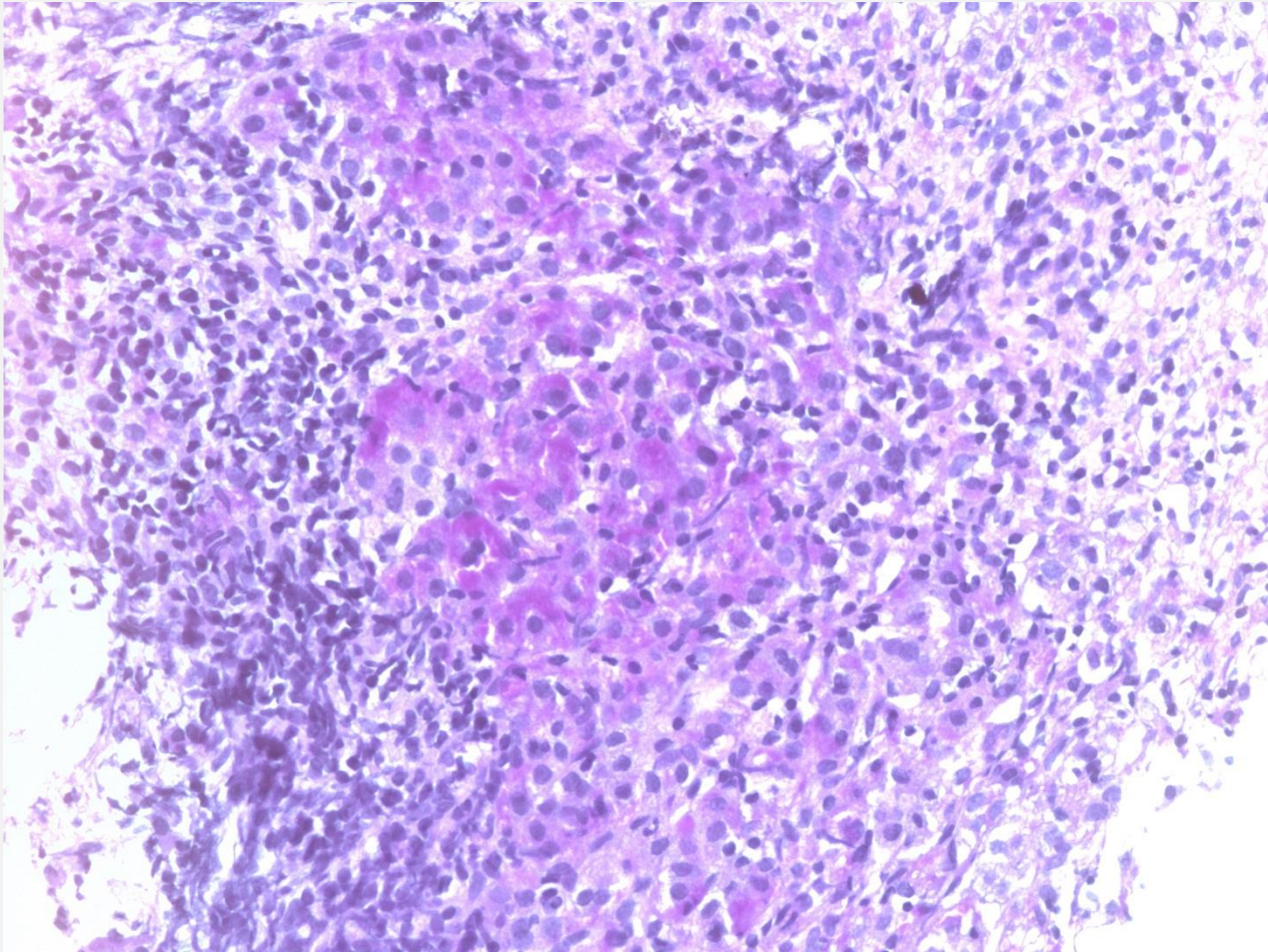
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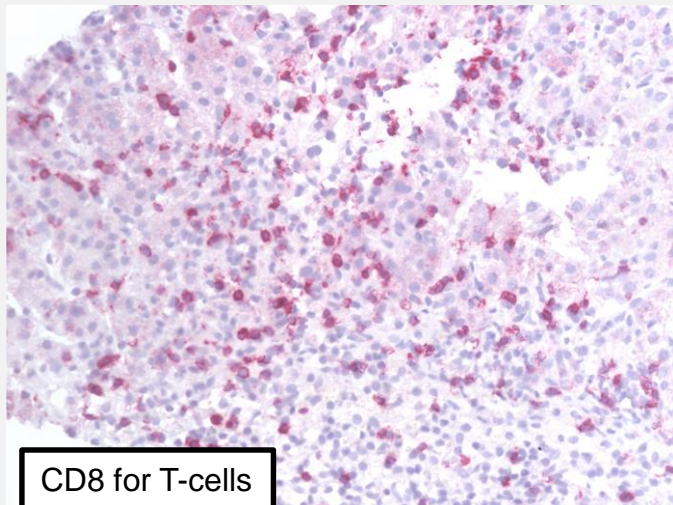
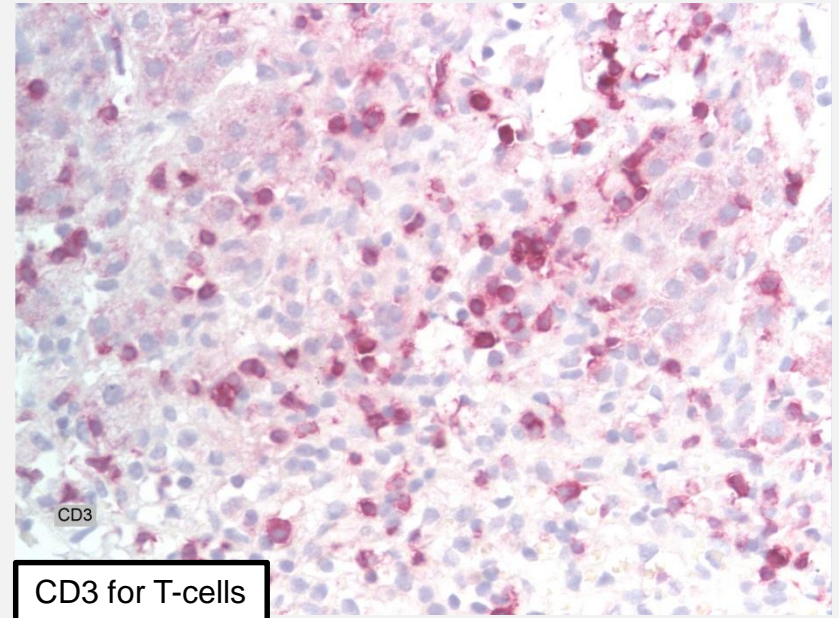
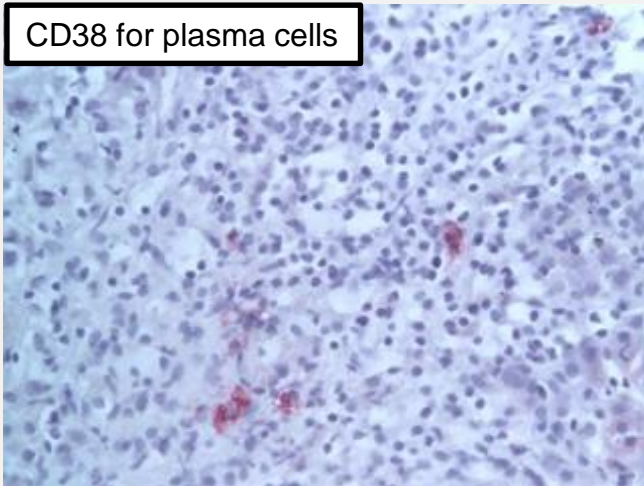
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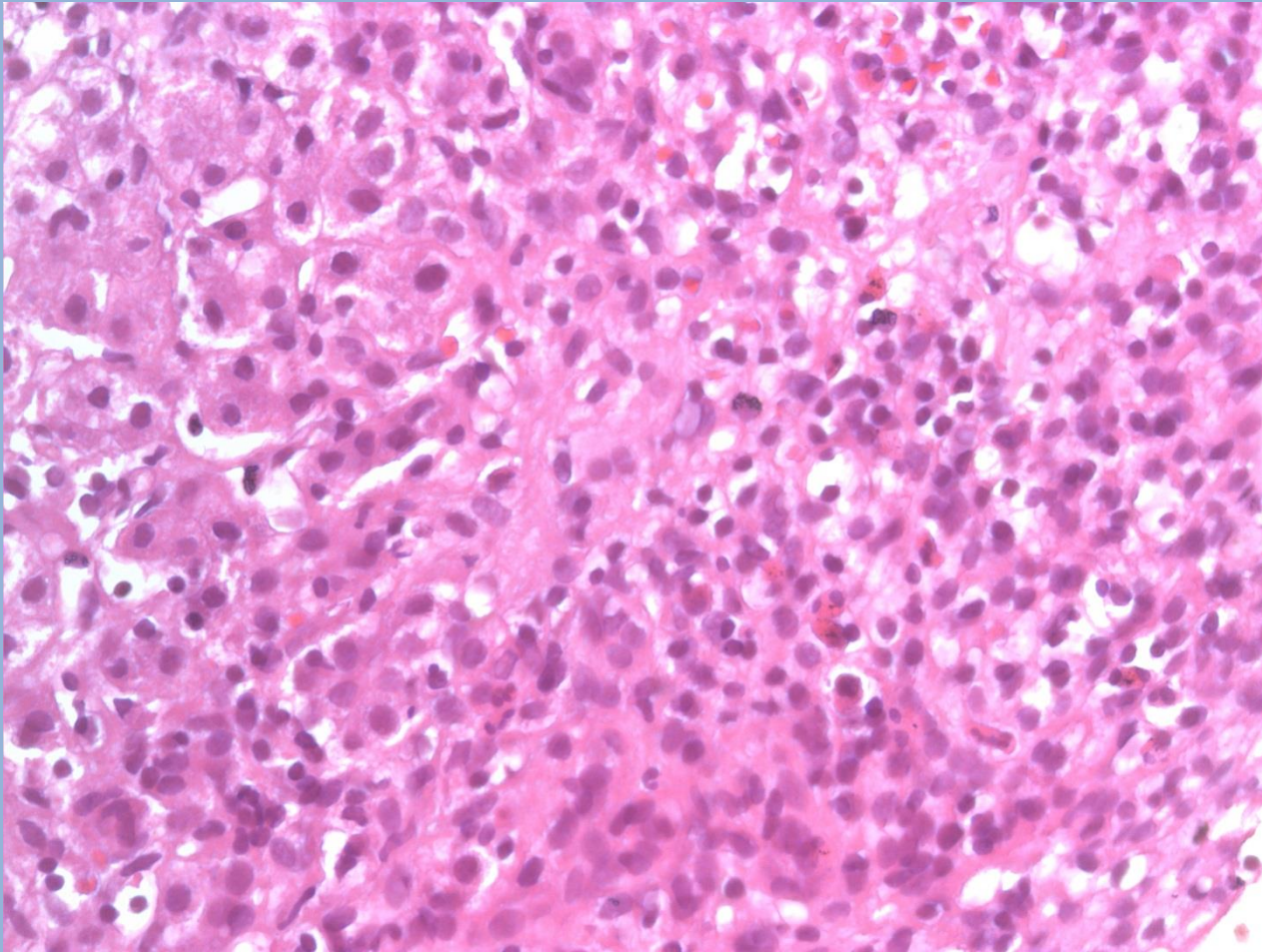
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# Immunohistochemistry for CD38-positive plasma cells and CD3-positive and CD8-positive T-cells



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