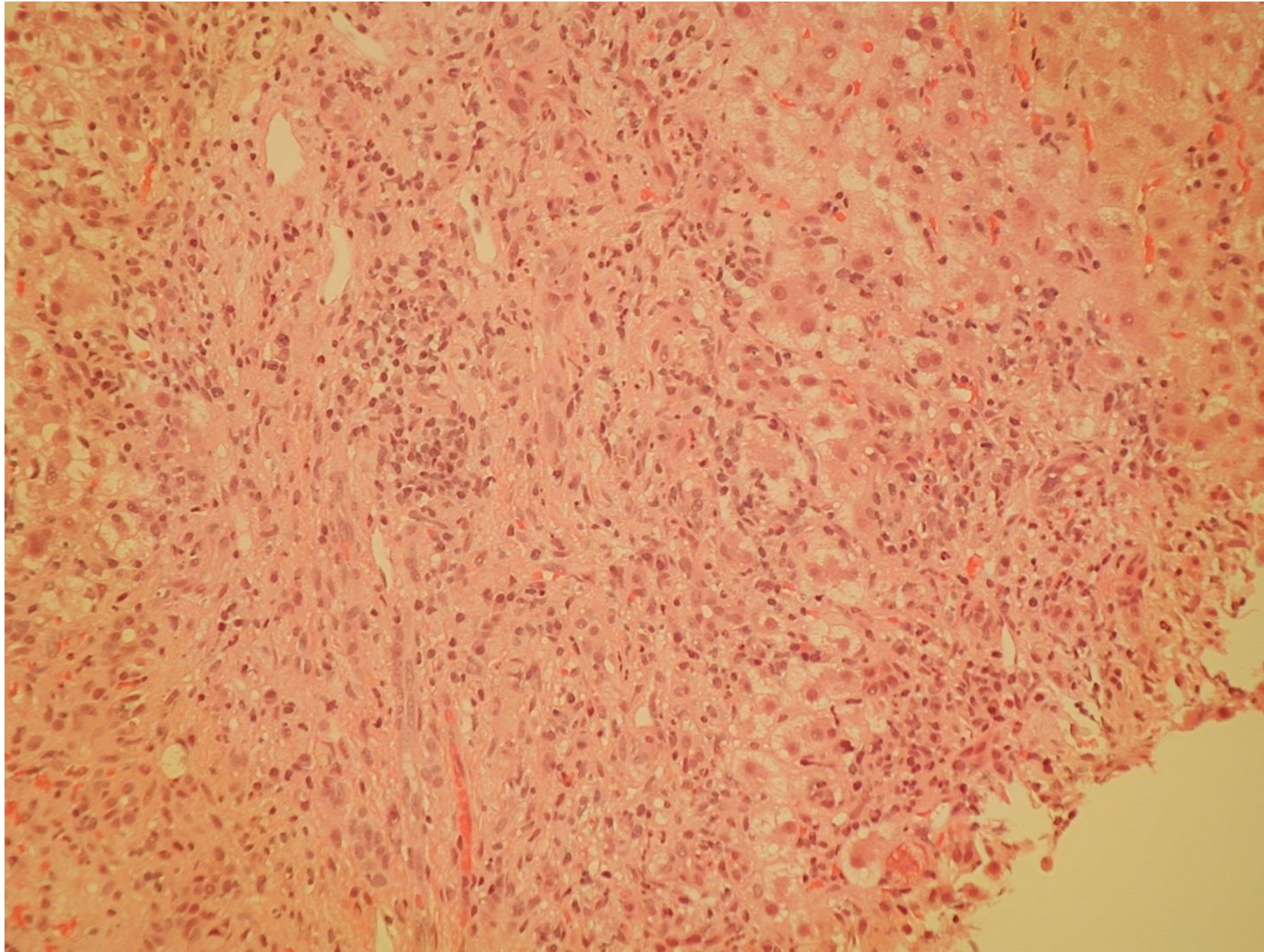
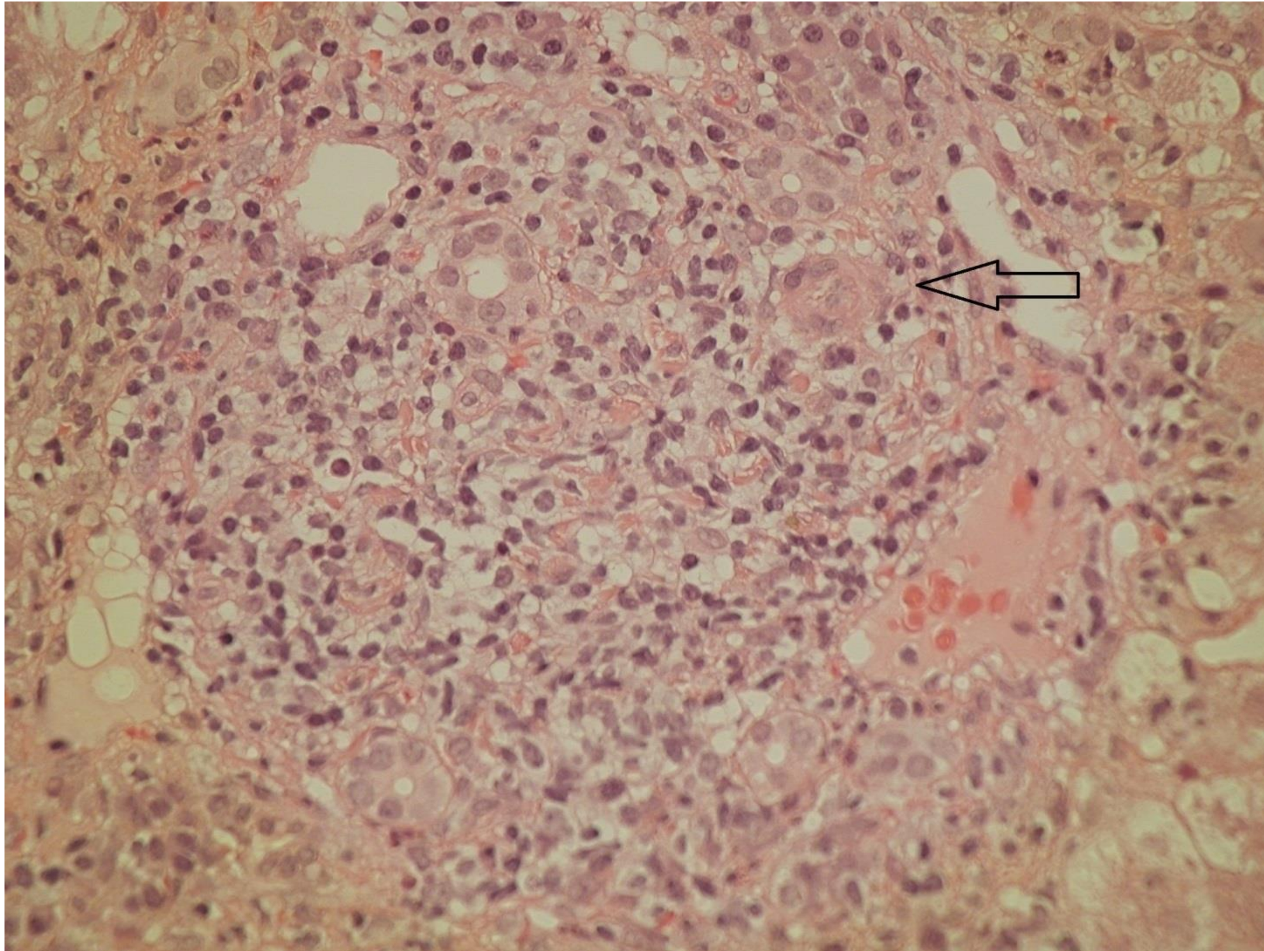
LO8 and LO9

- Similar cases.
- Lot of inflammation with cellular ballooning – appearance of an acute hepatitis.
- Lots of cell loss with collagen deposited on the Sirius Red stain.

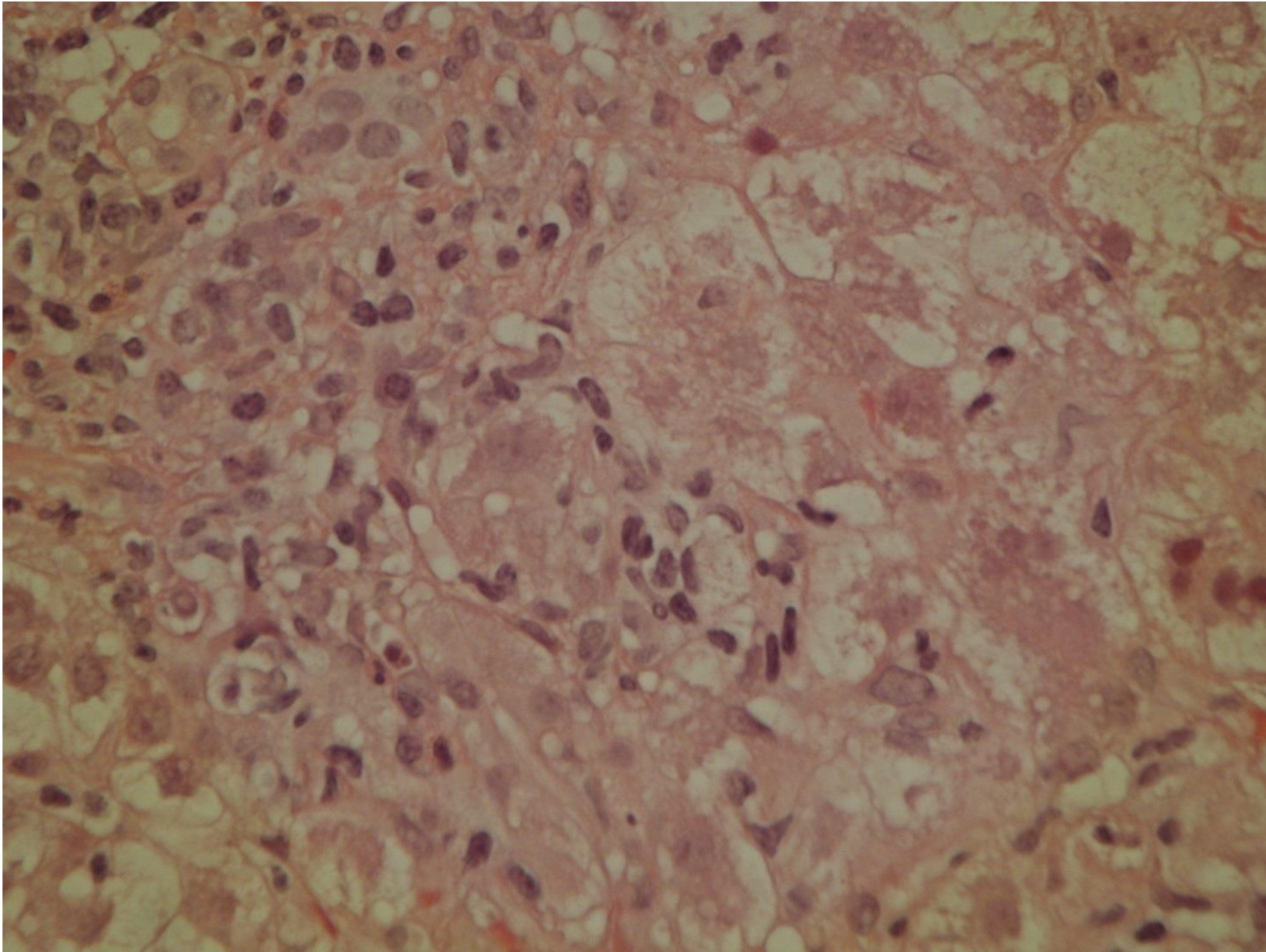
Both slides very busy on low power



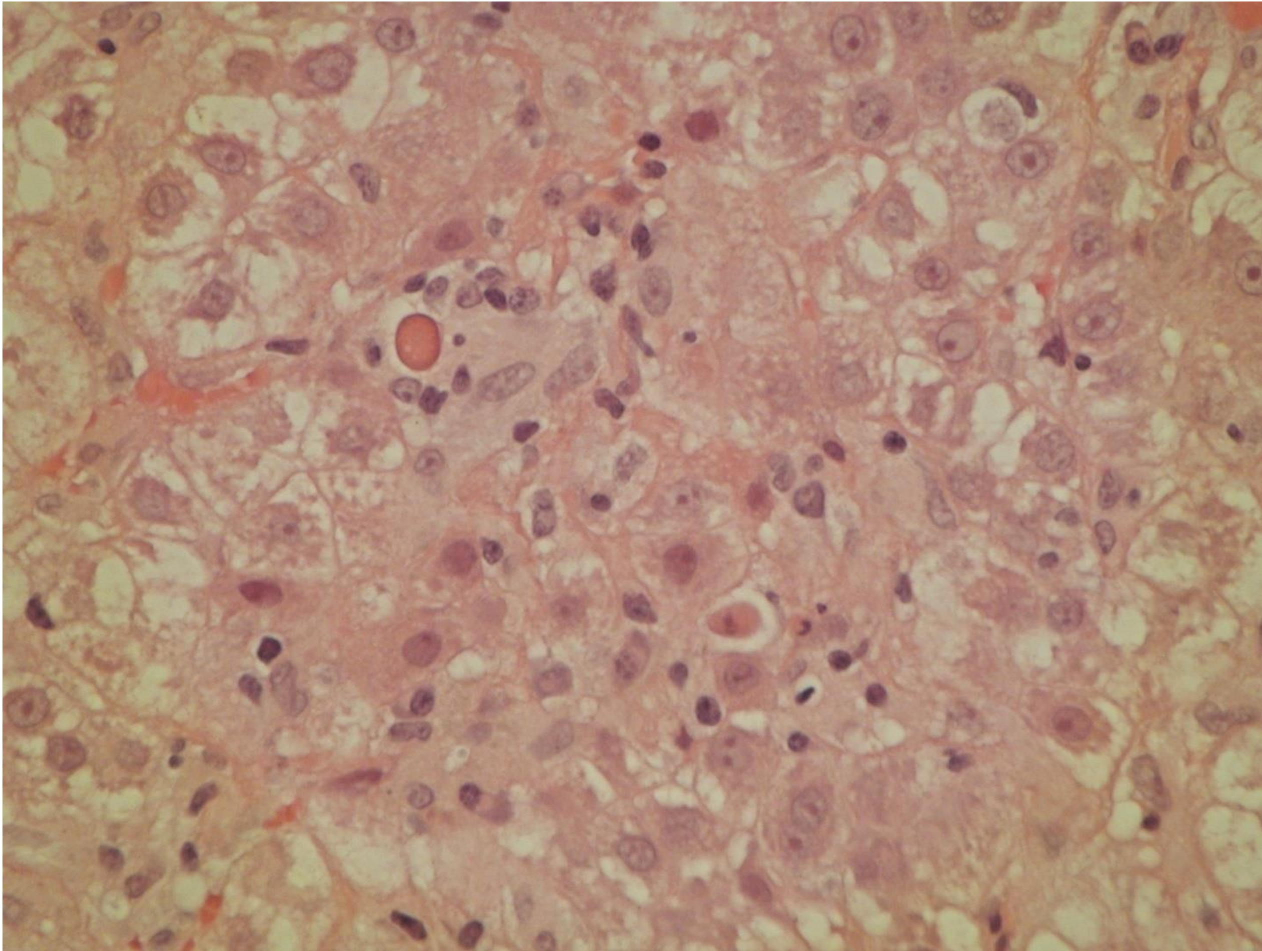
How do I identify the portal tract ?



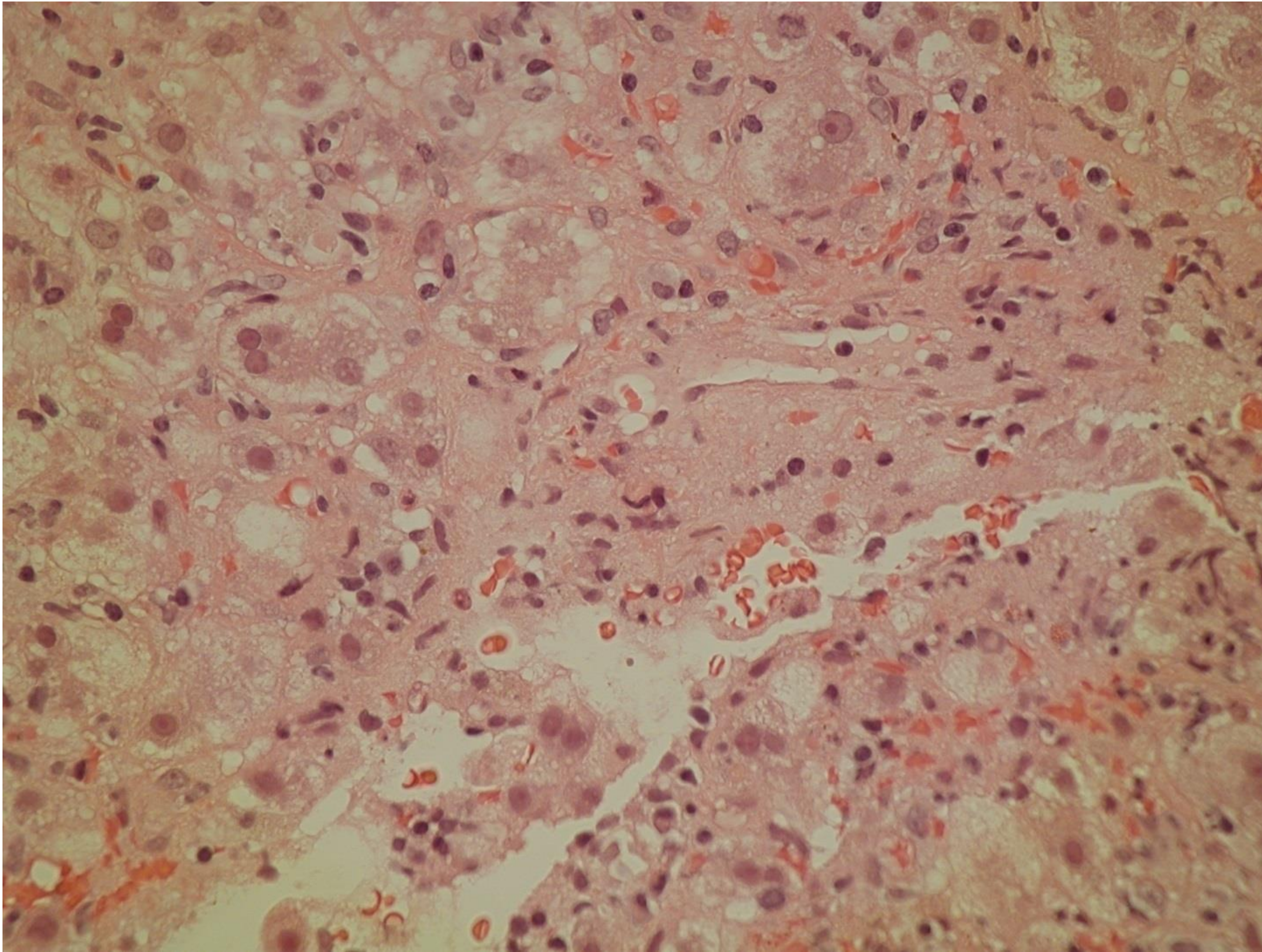
At the interface



Lobular injury



Central area



Reaching a diagnosis

- Histological constellation of features suggesting an acute hepatitis.
- Plasma cells and rosettes a feature of AIH.
- Lot of inflammation, marked interface hepatitis and pericentral necrosis – severe.
- Both middle aged females.
- ANA+ and one SMA+ consistent with type 1 AIH.

LO8 LFTs at biopsy

ALT	496	(9-55)
AST	1040	(10-45)
AlkPhos	153	(30-130)
GGT	144	(4-35)
Bilirubin	79	(0-20)
IgG	15.8	(6-16)
IgA	normal	
IgM	normal	

LO9 LFTs at diagnosis

ALT	948	(9-55)
AST		
AlkPhos	169	(30-130)
GGT	185	(4-35)
Bilirubin	228	(0-20)
IgG	29.7	(6-16)
IgA	normal	
IgM	normal	

Atypical features

- Given in clinical details.
- Possibly the reason for biopsy.
- One had progressive jaundice.
- The other sounds like a partial remission and relapse.
- RUQ pain – can get this with capsular distension in acute hepatitis.

Differential diagnosis pre-biopsy

- NAFLD – not in this case.
- Acute viral hepatitis
- Drug-induced liver injury (DILI)

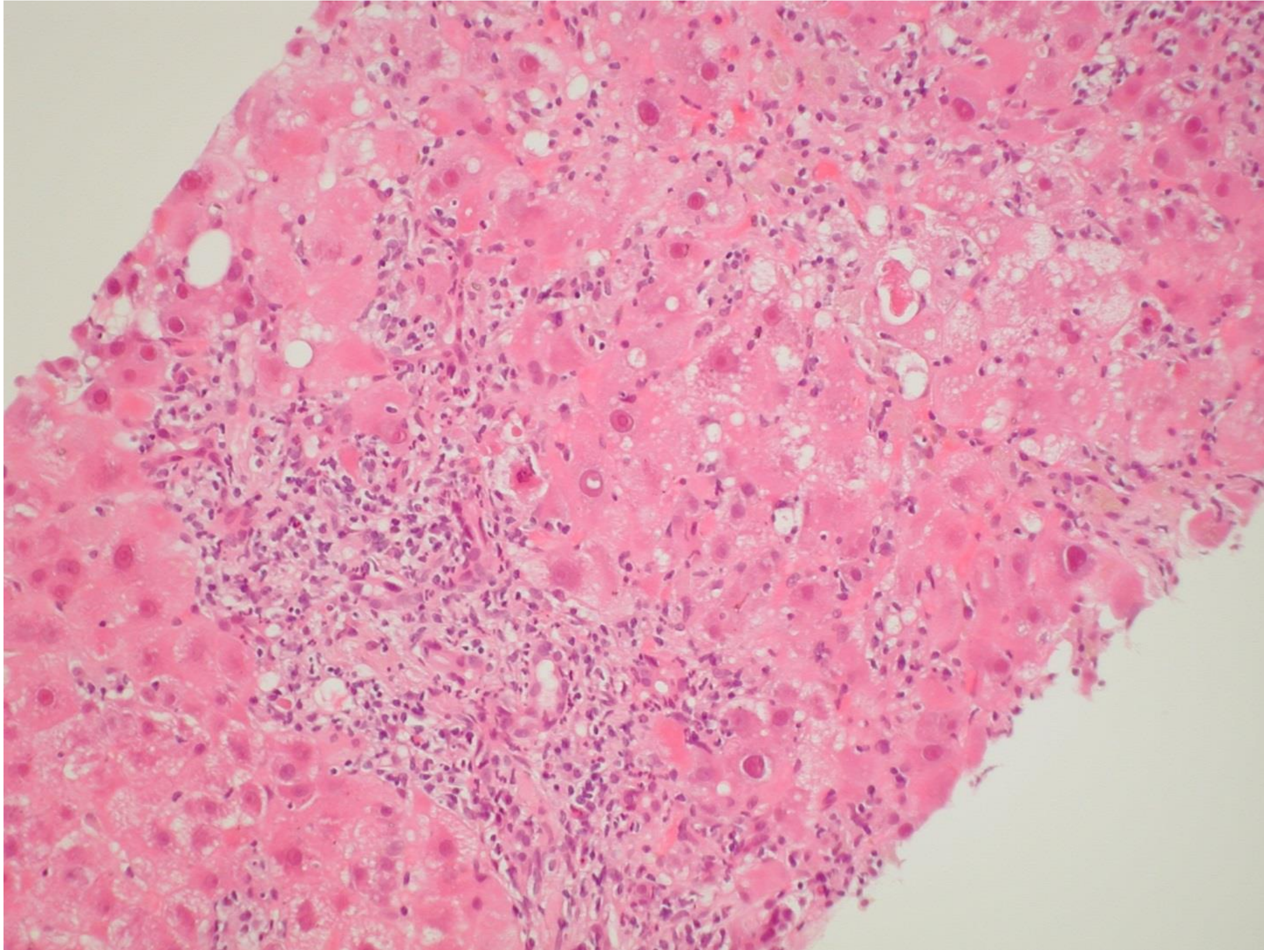
Differential diagnosis - NAFLD

- Very different clinical scenarios.
- May be raised transaminases if NASH.
- May be weakly ANA positive.
- Characteristic liver biopsy findings if steato-hepatitis present.
- Only really clinically considered if ANA+ and raised LFTs.

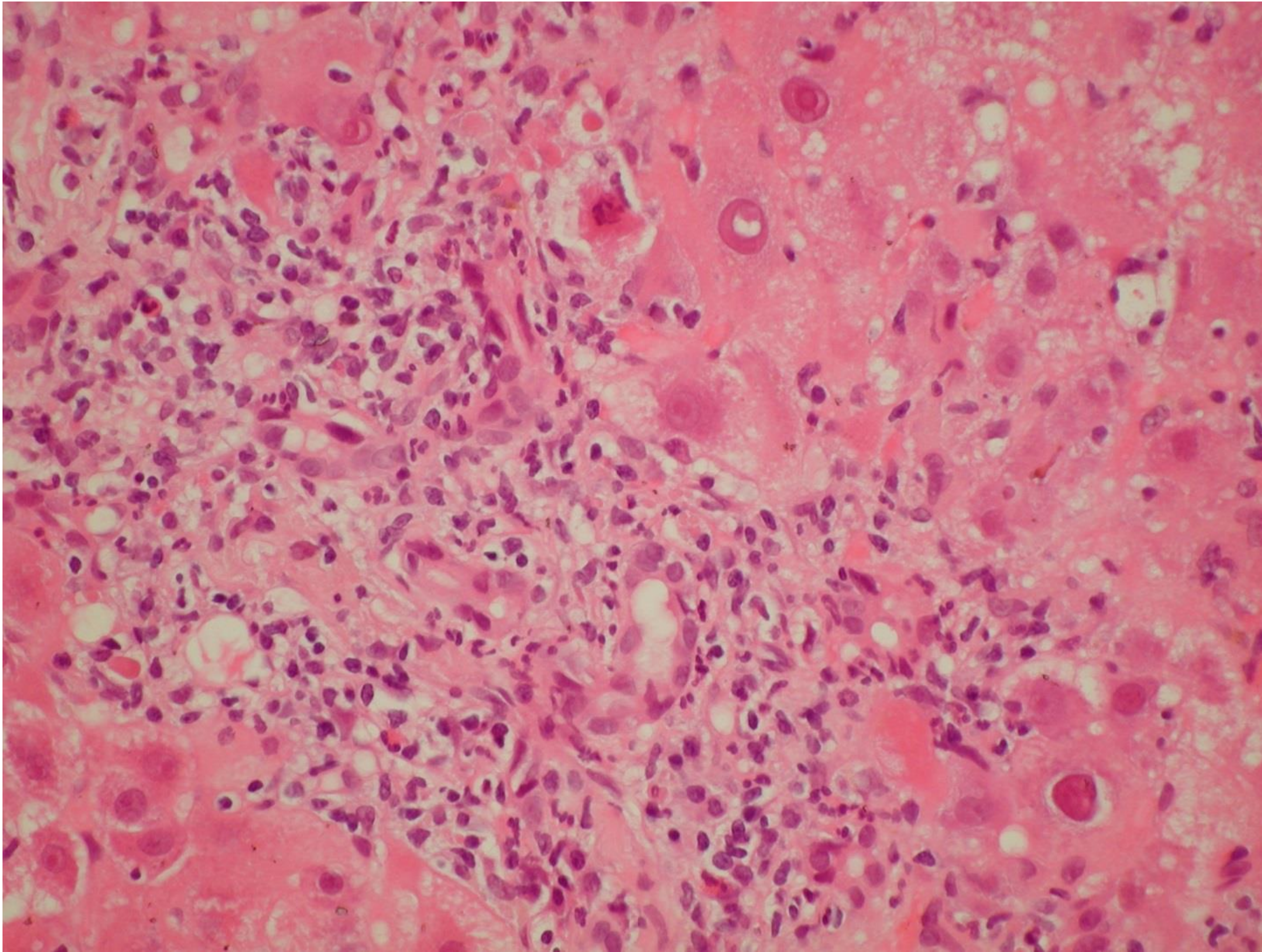
Differential diagnosis – acute viral hepatitis

- Acute presentation can be similar.
- Most acute viral hepatitis is not biopsied.
- Serology available if thought of.
- Most likely to be seen on biopsy is Hepatitis E.
- Superficially similar features on biopsy.
- Viral may have a more mixed inflammatory infiltrate, less interface hepatitis and fewer plasma cells and rosettes.
- Serology for autoantibodies negative.

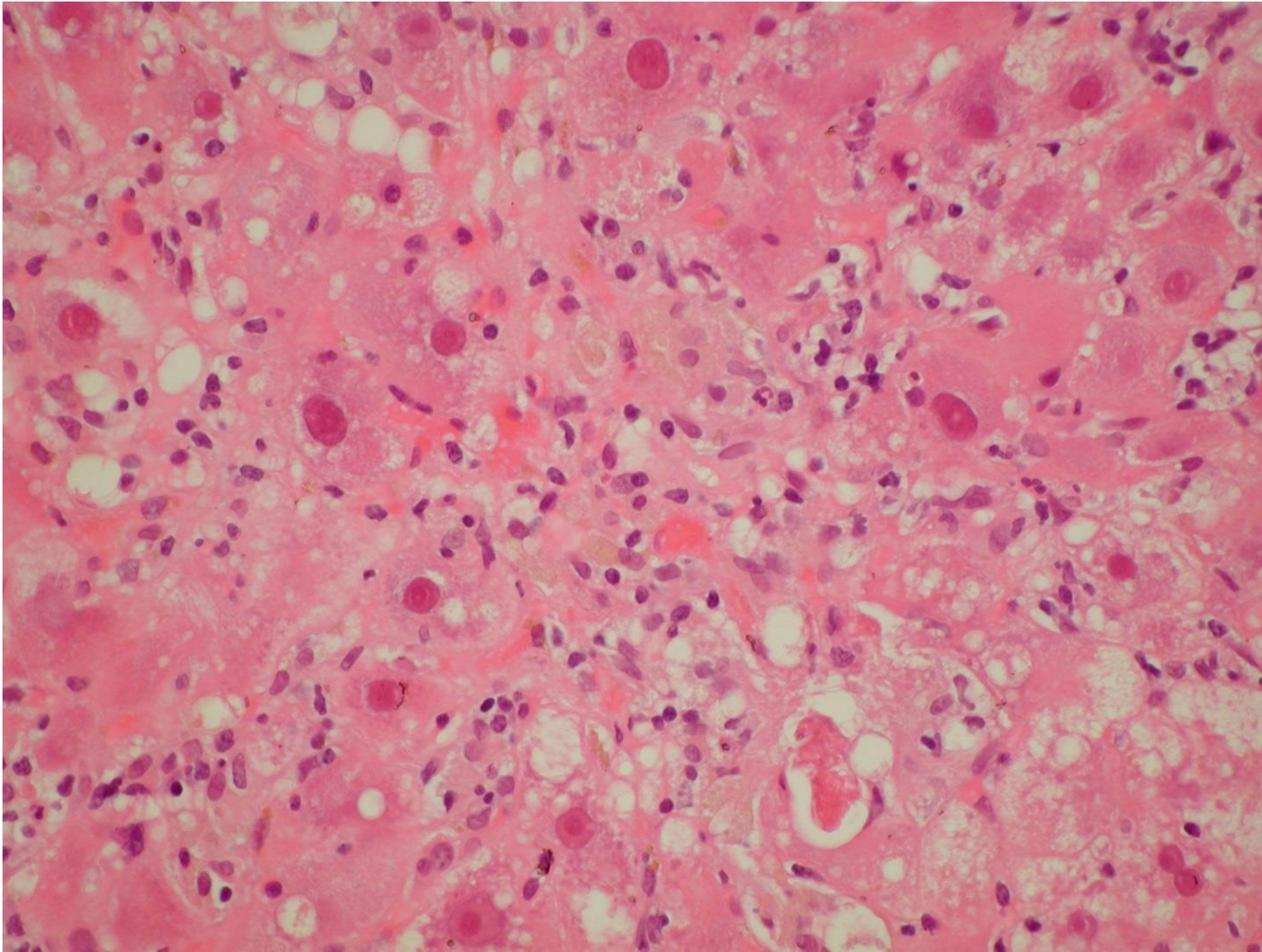
Acute hepatitis E



Acute hepatitis E



Acute hepatitis E



Differential diagnosis – drug-induced liver injury

- Acute onset.
- May have previous history of acute liver injury.
- Drug/ complementary medicine history not always immediately forthcoming.
- Hepatocellular, cholestatic or mixed.
- May be related or spurious autoantibodies (usually ANA, +/- ASMA).

Differential diagnosis – drug-induced liver injury

- Includes patients who have AIH already and in whom an exacerbation is triggered by a drug/ herbal medication.
- Includes patients whom the drug/ herbal medication triggers AIH in those with a predisposition to developing it.
- Some patients will develop progressive disease if not treated.

Drug-induced AIH – commonly implicated preparations

- Retrospective study of 82 patients with AIH.
- 13.4% had drug-induced AIH. Clinically similar.
- 4 nitrofurantoin, 4 statins, 2 herbal medications, 1 diclofenac.
- More likely to be ≥60yrs age and take longer to relapse after stopping medication.
- Nitrofurantoin – older, longer duration of use, higher fibrosis stage and relapse less likely.

Yeong et al. Heptol Res 2016 46:E79- 88

Drug-induced AIH – commonly implicated preparations

- α-methyldopa
- Fibrates
- Hydralazine
- Minocycline
- Nitrofurantoin
- HMG-CoA reductase inhibitors (Statins)
- Black Cohosh
- Iplimumab
- TNF alpha antagonists
- Mesalazine

- Prevalence >15% (large international registry). If recurs on stopping steroids consider idiopathic AIH.

Stine & Northup Expert Opin Drug Metab Toxicol 2016 1- 11

Drug-induced AIH – commonly implicated preparations

- Also consider:
  - Khat (catha edulis) – Somalia and Yemen
  - Dydrogesterone during fertility treatment
  - Azathioprine and metabolite-related hepatitis

Riyaz et al. World J Hepatol 2014 6: 150- 4

Altinaş Turk J Gastroenterol 2004 15: 49- 52

Chertoff et al. BMJ Case Rep 2014 doi:a0.1136/bcr-2014-206859

Drug-induced AIH – commonly implicated preparations

- 88 patients 2004- 2014, 91% female.
- 74% hepatocellular injury.
- 25% severe.
- 39% ↑ IgG, 72% ↑ANA, 60% ↑ SMA, 0% SLA.

Drugs studied - Nitrofurantoin 82%

- Minocycline 73%
- Methyldopa 55%
- Hydralazine 43%

- Decrease in positive serology after stopping.
- Similar HLA type distribution.

De Boer et al. Clin Gastroenterol Hepatol 2016 (E-pub)

Histological diagnosis

- Features consistent with active autoimmune hepatitis.
- Features of chronicity (i.e. fibrosis) lend more weight to this diagnosis.
- Drug and herbal medication history should be considered in case this is drug-induced injury.

Follow-up

LO8 Good response to steroids LFTs returned to normal, on maintenance azathioprine

LO9 Responding to steroids, LFTs' improving but still abnormal raised AlaAT (70) and GGT (347) and raised IgG (16.5)