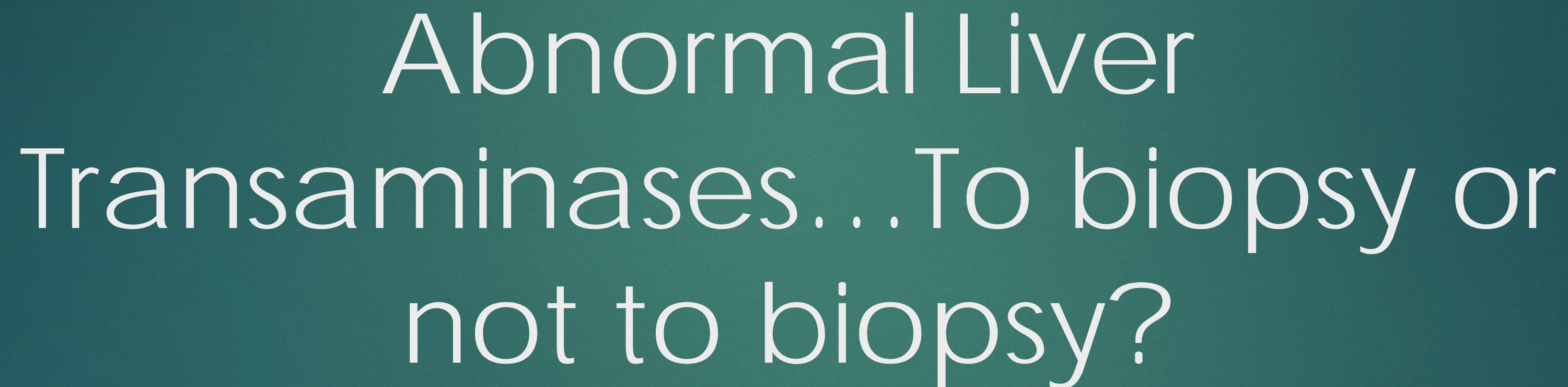

Abnormal Liver Transaminases…To biopsy or not to biopsy?

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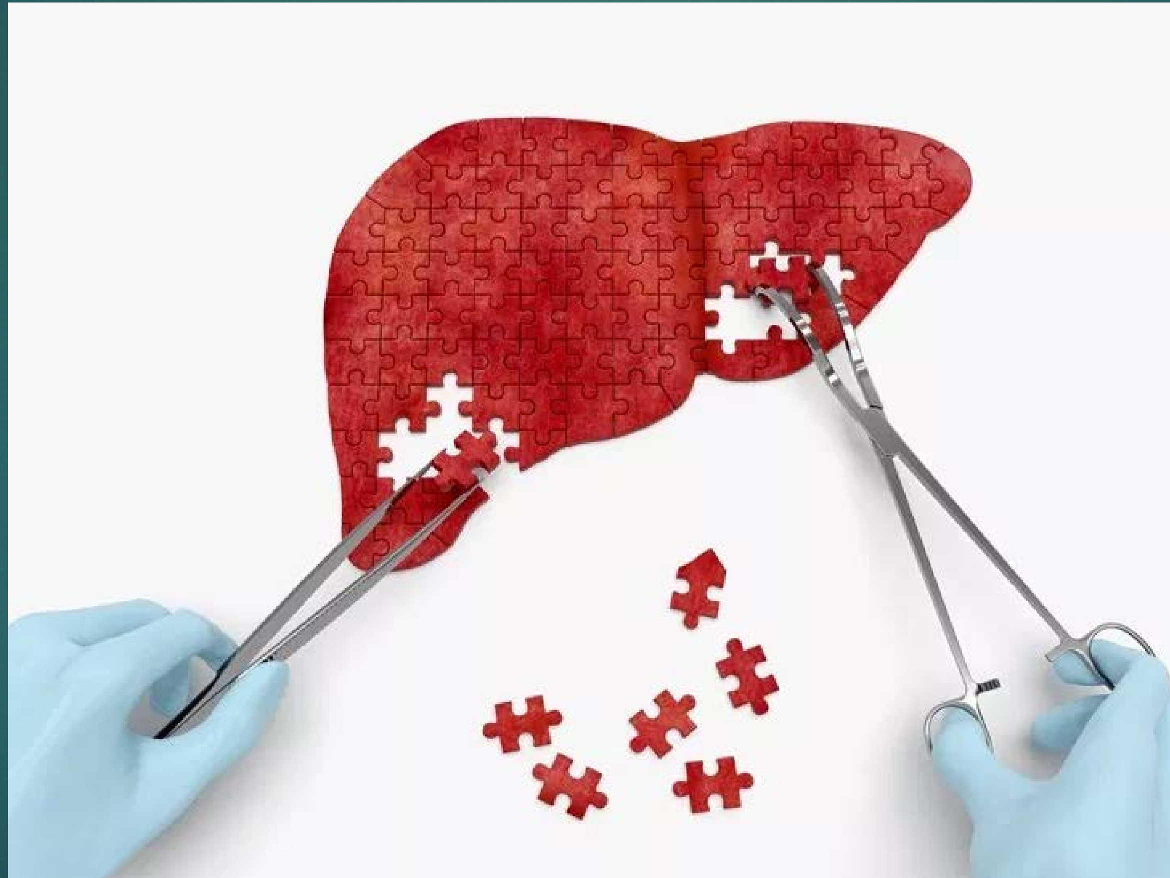
Disclosures

- Dr. Gilmour
  - Clinical trials, site PI Abbvie, Mirum

Biopsy: Completing the picture or just adding to it?



Case Study

- 20 year old male referred to your GI practice because of elevated liver transaminases on pre-isotretinoin screening
- Labs from family physician:
  - AST 105 u/l [6-35 u/l]
  - ALT 98 u/l [6-45 u/l]
  - ALP 275 u/l [53-128 u/l]
  - GGT 50 u/l [7-50 u/l]
  - Tbili 18 µmol/l [1.7-18.9 u/l]

Case Study (con't)

- 20 year old male previously healthy, no oral antibiotic therapy for acne, no colitis symptoms, no family history of liver disease or IBD
- Patient is not sure why he is in a GI office, he states he feels well and he HATES needles

Further Investigations?

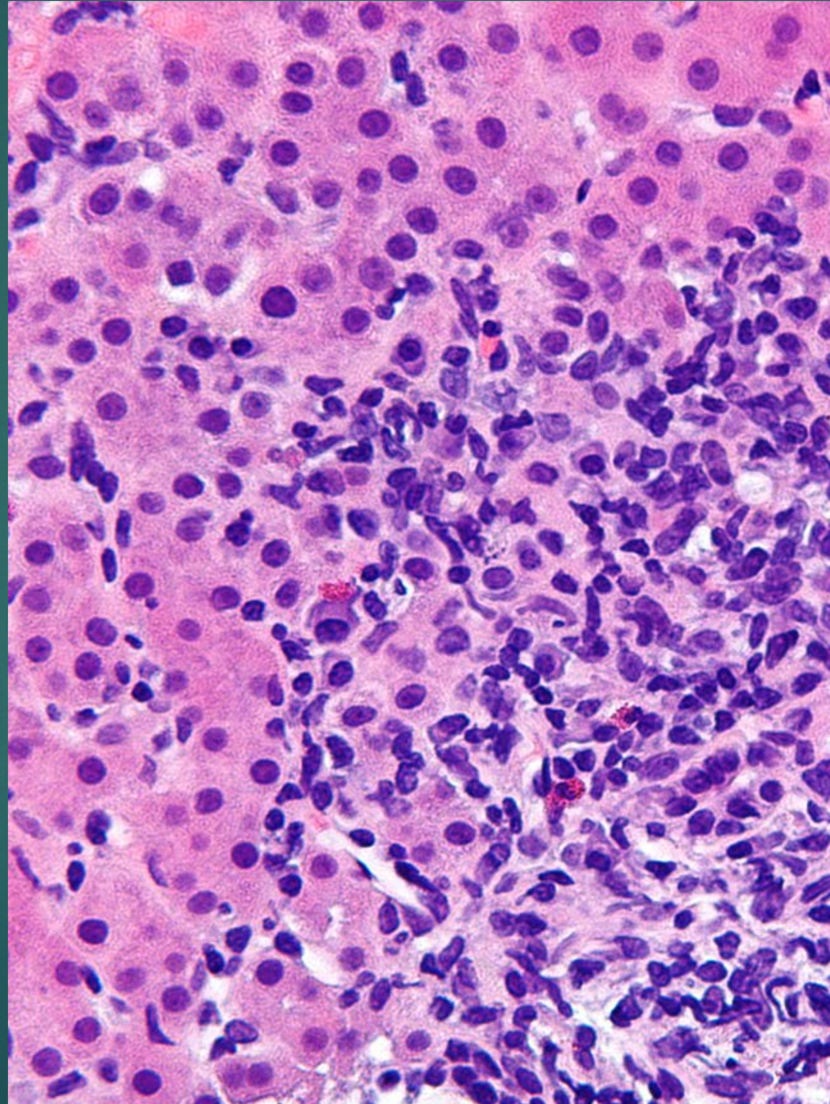
Further Investigations

- ANA 1:80; IgG 18 g/l [7-15 g/l]
- SMA neg; AMA neg; LKM neg
- Cu; ceruloplasmin; ferritin, alpha 1 all normal
- EBV old infection; Hep A, B, C negative and reflect immunization for HBV
- Ultrasound: very mild heterogeneity ; no hepatosplenomegaly; normal portal flow
- Radiology did an ultrasound shear wave: "mild fibrosis score"

Treat based on biochemistry?

Liver biopsy then decide on therapy?

Histology



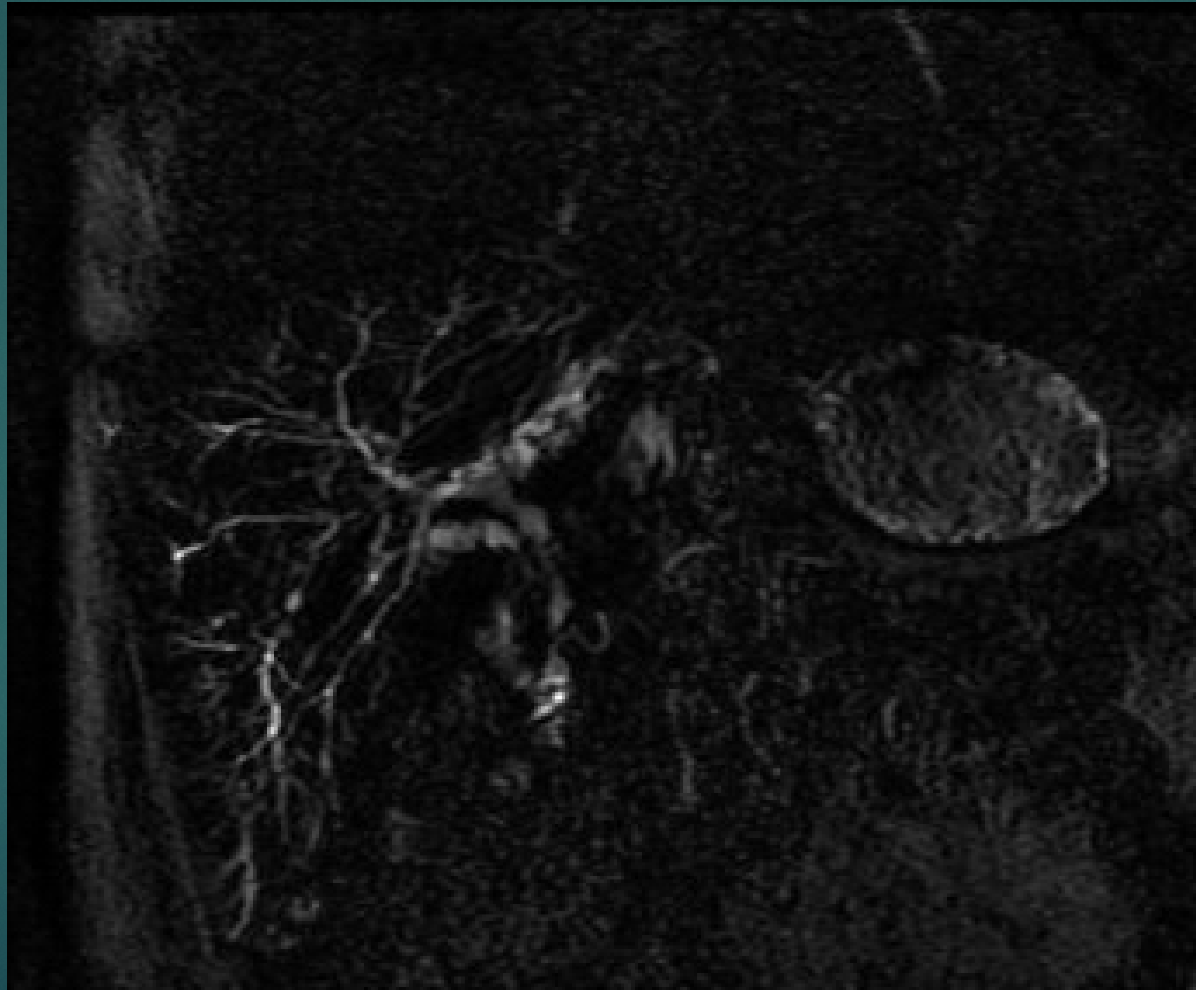
Case Study (con't)

- Prednisone 50 mg po q daily was started, and then azathioprine 100 mg daily was added
- Transaminases trend down but do not normalize
- When the prednisone was weaned the transaminases increase to more than initial presentation
- Patient very clear that they are adherent with medications (and patient is mildly Cushingoid; 6 TGN levels in therapeutic range)

Next Steps

- ? Change pharmacotherapy
- ?Rebiopsy
- ?MRCP
- All of the above
- None of the above

MRCP: “attenuated intrahepatic ducts”



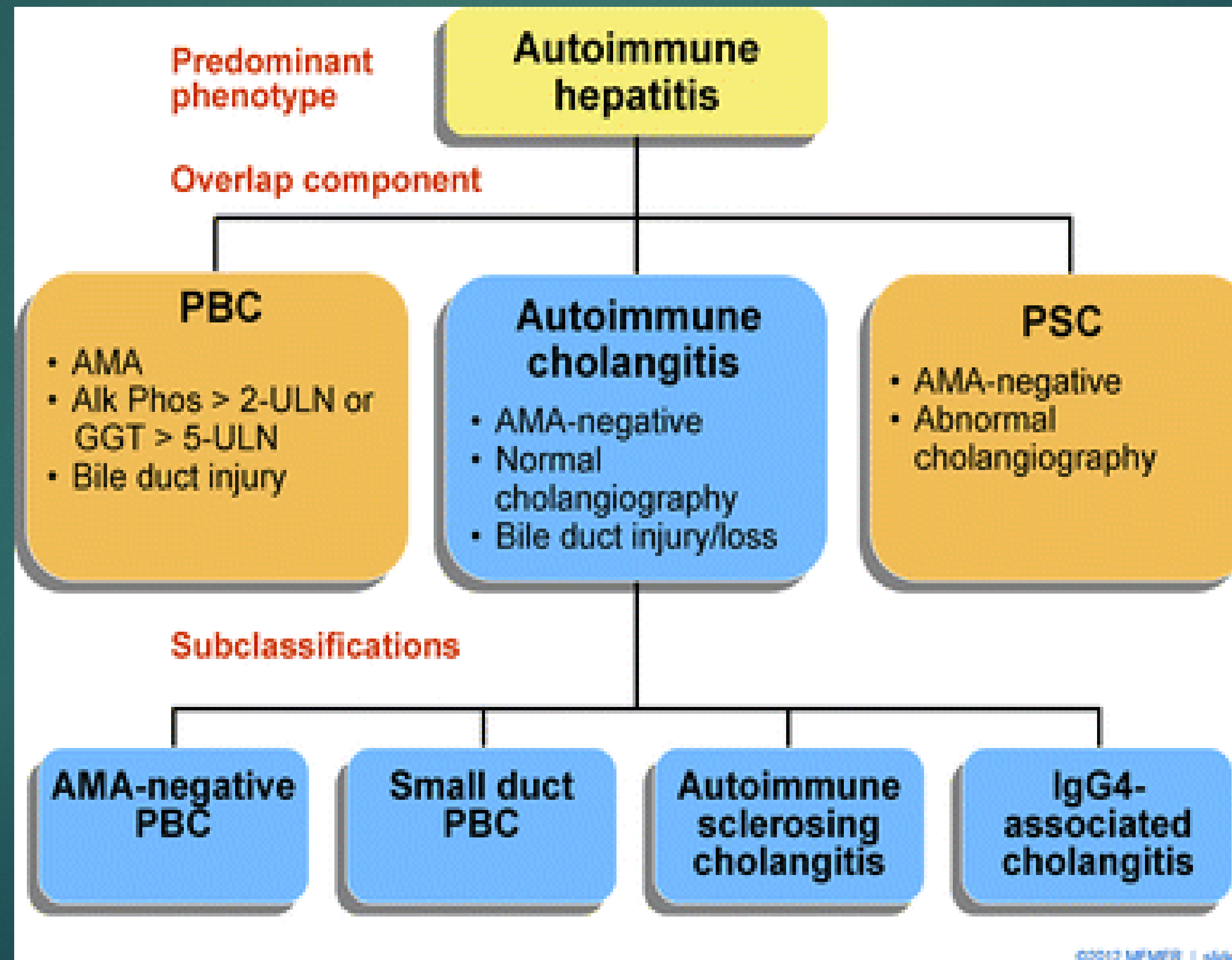
Overlap Syndrome: Entity or
Evolution

Dilemma

- AIH, PBC, PSC have emerged as distinct clinical entities
- But none of these have known distinct etiological agents, or distinctive pathogenic pathways to definitively define them
- These are all clinical syndromes with clinical, lab, serological, genetic and histological features that can be shared.
- We define by the clustering of the above

AIH with Secondary Features = Overlap Syndromes

Czaja Dig Dis Sci 2013



Overlap Syndrome

- AIH has been described in overlap with cholangiopathies:
  - AIH and Primary biliary cirrhosis
  - AIH and Primary sclerosing cholangitis
- No validated criteria for the diagnosis of AIH/PBC or AIH/PSC
- Literature describes the two entities being diagnosed at the same time, AIH first or PBC/PSC first diagnosed

AIH/PBC

- Frequency of overlap AIH/PBC 7 to 13% of AIH patients (adult)
- Retrospective studies have found that these patients have:
  - Higher AST/ALT to PBC alone
  - Higher δ-globulin levels
  - Higher prevalence of other autoimmune disorders
    - Efe et al Eur J Gastroenterol Hepatol 2012
    - Heurgue et al J Gastroenterol Hepatol 2010

Paris Criteria

- Require the presence of 2/3 clinical hallmarks of each disease, AIH and PBC
  - AIH
    - ALT 5 X ULN
    - IGg 2 X ULN
    - + SMA
    - Histology of interface hepatitis
  - PBC
    - ALP 2 X ULN
    - GGT 2 X ULN
    - AMA +
    - Histology of duct lesions

AIH/PSC

- Frequency of overlap is 6 to 11% of AIH patients
- Less female prevalence vs AIH alone
- More likely to be associated with IBD than AIH alone
- Pediatric study found that 31% of AIH patients had histological evidence of biliary damage
    - Czaja Dig Dis Sci 2013
    - Gregorio et al Hepatol 2001

Diagnostic Criteria AIH/PSC

- No specific criteria
- Clinically these are patients with:
  - AIH predominantly
  - Cholestatic labs
  - Absence of AMA
  - Histological and/or radiographic findings of bile duct injury or loss
  - Concurrent IBD (+/-)
  - Non-responsive to conventional corticosteroid therapy

Discussion!