Special stains in liver pathology

Which, why, how......Really?

Sanjay Kakar, MD
University of California, San Francisco

Outline

• Which stains
• Why the stain is done
• How the stain is interpreted
  Pitfalls, technical aspects
• Really
  Reflex use of special stains

Special stains: liver pathology

• Trichrome
• Iron
• PAS-diastase
• Reticulin
• Copper
• Other: elastic, PAS, bile

<table>
<thead>
<tr>
<th>Process</th>
<th>Role</th>
<th>Principle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron hematoxylin</td>
<td>Nuclear stain</td>
<td>Works well in acidic solutions</td>
</tr>
<tr>
<td>Red dye: Acid fuchsin</td>
<td>Stains cytoplasm, muscle</td>
<td>Intermediate molecular weight, stain both collagen and muscle</td>
</tr>
<tr>
<td>Acid fuchsin (Biebrich scarlet) chromotrope 2R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyacid (phospho-tungstic acid)</td>
<td>Removes red dye from collagen</td>
<td>Large molecules</td>
</tr>
<tr>
<td>Blue/green dye: Methyl green Fast Green Aniline Blue</td>
<td>Stains collagen</td>
<td>Large molecule dye: stains only collagen</td>
</tr>
</tbody>
</table>

Masson: sequential staining, Gomori: single step
Trichrome stain

- Why
  - Staging: viral hepatitis, steatohepatitis
  - Diagnosis of steatohepatitis
  - Regression of cirrhosis
  - Fibrosis vs. necrosis
  - Recognizing unsuspected amyloidosis
- How
  - Interpretation and pitfalls

Steatohepatitis: essential features

AASLD/NASH Clinical Research Network

- Steatosis
- Inflammation
- Hepatocellular injury
  - Ballooned hepatocytes
  - Pericellular fibrosis
Steatosis vs. steatohepatitis

- Disease progression
- Treatment

Steatohepatitis guidelines

The Diagnosis and Management of Non-alcoholic Fatty Liver Disease: Practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association

Recommendation
20. Pioglitazone can be used to treat steatohepatitis in patients with biopsy-proven NASH. However, it should be noted that majority of the patients who participated in clinical trials that investigated pioglitazone for NASH were non-diabetic and that long-term safety and efficacy of pioglitazone in patients with NASH is not established. (Strength - 1, Evidence - B)

Recommendation
21. Vitamin E (α-tocopherol) administered at daily dose of 800 IU/day improves liver histology in non-diabetic adults with biopsy-proven NASH and therefore it should be considered as a first-line pharmacotherapy for this patient population. (Strength - 1, Quality - B)
Overstained trichrome

Chronic venous outflow obstruction

Trichrome stain
- Staging: viral hepatitis
- Steatohepatitis
- Regression of cirrhosis
- Fibrosis vs. necrosis
Cirrhosis regression

- Thin fibrous septa with perforations
- Prominent vessels and ductular reaction disappear
- Nodularity may persist

Wanless, Arch Pathol Lab Med, 2000
Friedman, Hepatology 2006
Chang, Hepatology, 2010

Alcoholic cirrhosis with regression

Thin septa: no shunting vessels or ductular reaction

Regression: perforated fibrous septa
42 M with jaundice, hepatomegaly x 4 wks

ALT, AST >1000 U/L

Ultrasound: cirrhosis

Repeat trichrome

Dark: portal collagen, Light: necrosis
Orcein stain: no elastic fibers in necrotic area

Amyloid: pale deposits

Globular amyloid deposits: subtle on HE stain

Globular amyloid: highlighted by trichrome
Special stains: liver pathology

- Trichrome
- Iron
- PAS-diastase
- Reticulin
- Copper
- Other: elastic, PAS, bile

Perls iron stain (not Perl’s)

- K ferrocyanide + HCl
- Ferric ferrocyanide (Prussian blue)
- Max Perls: German pathologist

Entombment of Christ: Peter van der Werff, 1709

Starry Night: van Gogh
Iron stain

- **Why**
  - Distinguish from other pigments
  - Semiquantitative analysis
- **How**
  - Patterns of hepatic iron overload
  - Grading of iron overload

Hepcidin

- **Activity** depends on iron stores
- **Binds** ferroportin

Normal iron regulation

- **Blocks Iron Absorption**
- **Blocks Iron Release**
- **Hepatocyte**

**Hepcidin**

- **Genetic/acquired**
  - Hepcidin
  - Ferroportin
  - Transferrin
- **Increased iron**
- **Dietary**
- **Hemolysis**

Fig: Textbook of Liver Pathology: Kakar, Ferrell, Eds. Chapter by M Torbenson
### Primary Pattern of siderosis Mechanism

<table>
<thead>
<tr>
<th>HFE hemochromatosis</th>
<th>Hepatocellular</th>
<th>HFE gene mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-HFE hemochromatosis</td>
<td>Mostly hepatocellular</td>
<td>Non-HFE mutations</td>
</tr>
<tr>
<td></td>
<td>Some: macrophages</td>
<td></td>
</tr>
</tbody>
</table>

### Secondary Pattern of siderosis Mechanism

<table>
<thead>
<tr>
<th>Hemolysis, multiple transfusions</th>
<th>Macrophages</th>
<th>Excess iron from RBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic diseases</td>
<td>Macrophages</td>
<td>Excess iron in macrophages</td>
</tr>
</tbody>
</table>

### Iron storage

<table>
<thead>
<tr>
<th>Storage form</th>
<th>Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ferritin</strong></td>
<td>Virtually all cells Trace amounts in the plasma</td>
</tr>
<tr>
<td><strong>Hemosiderin</strong></td>
<td>Reticuloendothelial system including Kupffer cells</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ferritin blush</th>
<th>Hemosiderin</th>
</tr>
</thead>
</table>

### Iron stain: interpretation

- Grading of iron overload
- Patterns of hepatic iron overload
### Modified Scheuer grading scheme

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 0</td>
<td>Granules absent or barely discernible at 400x</td>
</tr>
<tr>
<td>Grade 1</td>
<td>Granules discernible at 250x</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Granules discernible at 100x</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Granules discernible at 25x</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Masses visible at 10x or naked eye</td>
</tr>
</tbody>
</table>

### Deugner-Turlin grading scheme

<table>
<thead>
<tr>
<th>Iron grading: simple method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>Minimal</td>
</tr>
<tr>
<td>Mild</td>
</tr>
<tr>
<td>Moderate</td>
</tr>
<tr>
<td>Marked</td>
</tr>
</tbody>
</table>

- Separate grade: hepatocellular, Kupffer cell
- Hepatocellular: periportal vs. random

### Iron: quantitative analysis

- Can be performed from paraffin embedded tissue
- Allows correlation with H&E morphology

<table>
<thead>
<tr>
<th>Iron: quantitative analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal iron</td>
</tr>
<tr>
<td>Mild increase</td>
</tr>
<tr>
<td>Moderate</td>
</tr>
<tr>
<td>Marked</td>
</tr>
</tbody>
</table>

**Hepatic iron index**

\[
\text{Hepatic iron index (µg iron per gram dry weight of liver/55.846 patient's age)}
\]

>1.9: suggests hemochromatosis (non-cirrhotic)
Iron stain: interpretation

- Grading of iron overload
- Patterns of hepatic iron overload

History

- 35/M with obesity
- Elevated serum ferritin
- Liver biopsy: steatohepatitis

Periportal hepatocellular siderosis
Iron overload in NASH

- 20-50% serum ferritin elevated
- 15-60% increased hepatic iron

<table>
<thead>
<tr>
<th>Distribution</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kupffer or hepatocellular mild/moderate, random</td>
<td>Secondary</td>
</tr>
<tr>
<td>Hepatocellular, periportal</td>
<td>HH or secondary</td>
</tr>
</tbody>
</table>

Periportal siderosis

- *HFE* hemochromatosis
- Non-*HFE* hemochromatosis
- Secondary iron overload
  - Steatohepatitis
- Rare conditions
  - Porphyria cutanea tarda
  - Hereditary aceruloplasminemia

Diagnosis

*HFE* 282Y homozygous
- Steatohepatitis
- *HFE* hemochromatosis with mild periportal hepatocellular siderosis, no portal based fibrosis

Significance of iron overload or *HFE* mutations in progression of steatohepatitis is not clear

History

- 55/M with cirrhosis
- No *HFE* mutation
- No known etiology
HII>2, heterogeneous iron overload

Cirrhosis with siderosis

- Non \( HFE \) hemochromatosis
- Secondary siderosis in cirrhosis of another etiology

Hemochromatosis

<table>
<thead>
<tr>
<th>Type 1 (HFE HH)</th>
<th>Genotype</th>
<th>Liver biopsy</th>
<th>Clinical presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autosomal recessive</td>
<td>C282Y homozygous, C282Y /H63D</td>
<td>Hepatocytes</td>
<td>3(^{rd}) or 4(^{th}) decade Liver, pancreas, heart, skin, joints</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type 2 (Juvenile HH)</th>
<th>Genotype</th>
<th>Liver biopsy</th>
<th>Clinical presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autosomal recessive</td>
<td>Hemojuvelin (2A) or hepcidin (2B)</td>
<td>Hepatocytes</td>
<td>1(^{st}) three decades More severe disease than HFE HH</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type 3</th>
<th>Genotype</th>
<th>Liver biopsy</th>
<th>Clinical presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autosomal recessive</td>
<td>Transferrin receptor type 2 mutation</td>
<td>Hepatocytes</td>
<td>Similar to HFE HH Intermediate between HFE HH and juvenile HH</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type 4</th>
<th>Genotype</th>
<th>Liver biopsy</th>
<th>Clinical presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autosomal dominant</td>
<td>Ferroportin mutation</td>
<td>1(^{st}) subtype: hepatocytes 2(^{nd}) subtype: Kupffer cells</td>
<td>4(^{th}) or 5(^{th}) decade Severity varies with type of mutation</td>
</tr>
</tbody>
</table>

Siderosis in cirrhosis

<table>
<thead>
<tr>
<th>Ludwig, Gastroenterology, 1997 (n=447, HII&gt;1.9)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hereditary hemochromatosis</td>
<td>100%</td>
</tr>
<tr>
<td>Alpha-1-antitrypsin deficiency</td>
<td>28%</td>
</tr>
<tr>
<td>Cryptogenic cirrhosis</td>
<td>19%</td>
</tr>
<tr>
<td>Alcoholic cirrhosis</td>
<td>14%</td>
</tr>
<tr>
<td>Chronic hepatitis B, hepatitis C</td>
<td>18%, 7%</td>
</tr>
<tr>
<td>PBC, PSC</td>
<td>1% each</td>
</tr>
</tbody>
</table>

- Marked siderosis can occur in the absence of HH
- Siderosis rare in biliary diseases
- Siderosis is an adverse risk factor*

*Brandhagen, Hepatology, 2000
**HFE HH: Homogeneous distribution**

Image: Dr. Linda Ferrell

**Siderosis: periseptal, stroma, endothelial cells**

**Bile duct siderosis**

**Cirrhosis: HH or secondary siderosis**

<table>
<thead>
<tr>
<th>Hereditary hemochromatosis</th>
<th>Cirrhosis with marked secondary siderosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homogeneous distribution</td>
<td>Heterogeneous</td>
</tr>
<tr>
<td>Siderosis in bile ducts, stroma, endothelial cells</td>
<td>Generally absent</td>
</tr>
<tr>
<td><em>HFE</em> mutation (in <em>HFE</em> HH)</td>
<td>Not present</td>
</tr>
</tbody>
</table>

Diagnosis: Cryptogenic cirrhosis with secondary iron overload
16

**Iron stain: role of the pathologist**

<table>
<thead>
<tr>
<th>Clinical setting</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HFE C282Y homo C282Y/H63D</td>
<td>Extent of iron, Extent of fibrosis</td>
</tr>
<tr>
<td>HFE other mutations</td>
<td>Extent of iron, No risk for HFE HH</td>
</tr>
</tbody>
</table>

**Iron stain: role of the pathologist**

<table>
<thead>
<tr>
<th>Clinical setting</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HFE not known</td>
<td>Raise possibility of HH, Periportal siderosis, or moderate to marked hepatocellular iron</td>
</tr>
<tr>
<td>Chronic viral hepatitis Steatohepatitis Cirrhosis</td>
<td>Recommend HFE testing, Possible disease progression, Possible poor prognosis</td>
</tr>
</tbody>
</table>
Special stains: liver pathology

- Trichrome
- Iron
- PAS-diastase
- Reticulin
- Copper
- Other: elastic, PAS, bile

PAS-diastase stain

Glycogen, other carbohydrates
- Periodic acid converts –OH component to aldehyde
- Combines with Schiff reagent: magenta complex
- Diastase digests glycogen

PAS-D stain

- Why
  - Alpha-1-antitrypsin deficiency
  - Highlight macrophages
  - Glycogen (with PAS stain)
  - Highlights basement membrane
- How
  - Pitfalls
  - Interpretation

A1AT deficiency

Mallory hyaline
A1AT deficiency

Giant mitochondria

A1AT deficiency

Incomplete digestion

Immunohistochemistry: alpha-1-antitrypsin

50/F with cirrhosis, obese, serum A1AT normal
Alpha-1-antitrypsin deficiency

- Normal allele PiMM
- Homozygous state (PiZZ)
  - Chronic hepatitis and cirrhosis
- Heterozygous state (PiMZ)
  - Significance unclear
  - Progression of fibrosis in other liver diseases

Challenges in diagnosis (clinical)
- Uncommon disease
- Can occur in the absence of childhood symptoms and lung disease
- Serum levels unreliable

Challenges in diagnosis (pathologic)
- Cytoplasmic globules can be subtle
- PAS-D: periportal location
- Globules not specific for diagnosis
  - Vascular etiologies
  - Acute hepatitis
- PiZZ vs. PiMZ cannot be distinguished on biopsy

Gold standard for diagnosis: Protease inhibitor phenotyping
Mild portal inflammation

Resolving hepatitis: PAS-D stain highlights macrophages

History

- 40/M with renal transplant
- Persistent elevation of ALT, AST 5-6x
- No history of viral hepatitis

Cytoplasmic inclusions
`Ground glass’ appearance

- Hepatitis B
- Drugs: Barbiturates, cyanamide
- Metabolic diseases
  - Glycogen storage IV
  - Lafora disease
  - Hypo(a)fibrinogenemia

Wisell, AJSP, 2006; Bejarano, Virchow Arch, 2006

Glycogen inclusions (‘pseudo ground glass’)

- Often on multiple immunosuppressive medications
- No correlation with any specific drug

Wisell, AJSP, 2006; Bejarano, Virchow Arch, 2006

PAS-D stain: partial digestion

Special stains: liver pathology

- Trichrome
- Iron
- PAS-diastase
- Reticulin
- Copper
- Other: elastic, PAS, bile
**Reticulin stain**

Argyrophilic reaction
- Sensitization: heavy metals
- Ammoniacal silver
- Reducing agent (formaldehyde)
- Toning: gold
- Removal of unreacted silver

**Gomori reticulin**

- 1928: Pathologist, Budapest
- 1932: Surgeon, Budapest
- 1943: Internal Medicine, Chicago
- 1956: Research in histochemistry, Palo Alto

**History**

- 60/F with long history of rheumatoid arthritis
- Portal hypertension
- Ultrasound: cirrhosis

**Reticulin stain**

- Why
  - Collapse of reticulin fibers: necrosis
  - Nodular liver architecture (NRH)
  - Abnormal reticulin network (HCC)
- How
  - Interpretation
  - Pitfalls
Biopsy
- Normal portal tracts
- Hepatocellular damage: none
- No inflammation
- No fibrosis

Nodular regenerative hyperplasia

Wanless criteria
- Hepatocellular nodules, often <0.3 cm
- Often diffuse involvement of the liver
- Fibrosis absent or minimal

Wanless IR, Hepatology, 1990

Nodular architecture: reticulin

Nodular regenerative hyperplasia
Reticulin Loss in Benign Fatty Liver: An Important Diagnostic Pitfall When Considering a Diagnosis of Hepatocellular Carcinoma

Aastur D. Singh, MD, PhD; Dhanpat Jaisi, MD, PhD;† Sanjay Kakar, MD;‡ Tsungh-Fuh Wu, MD, PhD;§ Matthew M. Yeh, MD, PhD;¶ and Michael Torbenson, MD#

Special stains: liver pathology

- Trichrome
- Iron
- PAS-diastase
- Reticulin
- Copper
- Other: elastic, PAS, bile
Copper stain

• Why
  Chronic biliary disease
  Wilson disease: not reliable

• How
  Interpretation
  Pitfalls

Copper stain

• Orcein: black granules
• Rubeanic acid: black granules
• Rhodanine: red granules

Rubeanic acid: copper in periportal hepatocytes

40/F with positive ANA, SMA
Biopsy diagnosis of AIH
Clinical picture and liver enzymes favored biliary disease
Hepatocellular injury mild, bile duct damage can be patchy

Periportal copper
Periportal CK7+

Autoimmune cholangiopathy (AMA-negative PBC)

A Sunday on La Grand Jatte: George Seurat (pointillism)
Copper stain

Hepatitic vs. biliary etiology not clear
- Careful review in periportal region
- Conjunction with CK7
- Not useful in advanced disease
- Negative results do not exclude biliary disease

Wilson disease: quantitative copper reliable

Survey

Which stain(s) should be performed up front for every liver biopsy?

<table>
<thead>
<tr>
<th></th>
<th>Trichrome</th>
<th>PAS-D</th>
<th>Iron</th>
<th>Retic</th>
<th>Copper</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=15</td>
<td>100%</td>
<td>40%</td>
<td>40%</td>
<td>20%</td>
<td>0</td>
</tr>
<tr>
<td>Univ (n=10)</td>
<td>100%</td>
<td>60%</td>
<td>60%</td>
<td>30%</td>
<td>0</td>
</tr>
<tr>
<td>UCSF (n=5)</td>
<td>100%</td>
<td>40%</td>
<td>20%</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

- PAS-D: Globules of A1AT
- Iron: Mild periportal siderosis in early HH
Mean stage 1.0 with H&E, 1.69 with trichrome
Trichrome stage was higher in 53.3%
Fibrosis stage was raised by 2 or more points in 17.8% with trichrome stain
The hepatic fibrosis score is significantly underestimated by H&E stain in the posttransplant setting in hepatitis C

Special stains: liver pathology
- Trichrome
- Iron
- PAS-diastase
- Reticulin
- Copper
- Other: elastic, PAS, bile
**Glycogenic hepatopathy**

- Type 1 diabetes
- Elevated transaminases
- Hepatomegaly
- Glycogen storage disease
  - More swelling, fibrosis
  - Clinical setting

**Two common errors**

- Portal inflammation is not equivalent to chronic hepatitis
- Lobular inflammation does not necessarily indicate hepatitis disease
HFE hemochromatosis

<table>
<thead>
<tr>
<th>HFE gene involved</th>
<th>Manifestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>C282Y homozygous</td>
<td>Iron overload: 30-50%</td>
</tr>
<tr>
<td></td>
<td>Hemochromatosis: 10-30%</td>
</tr>
<tr>
<td>C282Y/H63D</td>
<td>Iron overload</td>
</tr>
<tr>
<td></td>
<td>Hemochromatosis</td>
</tr>
<tr>
<td>C282Y heterozygous</td>
<td>No or minimal iron overload</td>
</tr>
<tr>
<td>H63D homo/heterozygous</td>
<td>No risk of hemochromatosis</td>
</tr>
<tr>
<td>H63D homozygous</td>
<td></td>
</tr>
<tr>
<td>C282Y/H65C</td>
<td></td>
</tr>
</tbody>
</table>

Hepatocellular siderosis
A1AT immunohistochemistry

Mild lobular inflammation

PAS-D stain

...Really

• All biopsies with unexplained liver dysfunction
• All nonneoplastic liver biopsies

Nodular regenerative hyperplasia
Nodular regenerative hyperplasia

• Asymptomatic for prolonged period of time
• Liver function and liver enzymes normal
• Present with portal hypertension

Portal hypertension without cirrhosis

• Nodular regenerative hyperplasia
• Sarcoidosis
• Portal vein thrombosis
• Idiopathic portal hypertension (noncirrhotic portal fibrosis)

Idiopathic portal hypertension

• Portal vein thrombosis which has recanalized
• Portal vein changes
  Obliteration (small veins)
  Intimal thickening (large veins)
• Portal fibrosis, thin bridging septa
• Normal or nonspecific changes
Nodular regenerative hyperplasia

- Rheumatologic diseases: RA, SLE
- Vascular disorders:
  - BC syndrome, PV thrombosis
- Hematological diseases
  - Leukemia, lymphoma
  - Myeloproliferative diseases
- Drugs: azathioprine, oxaliplatin
- Other: PBC, celiac disease

NRH: portal vein obliteration

Kleiner, Hepatology, 2006
Fig 8.1

Portal inflammation, no bile duct injury
Is this primary biliary cirrhosis?

- Significance of histologic findings
- Specificity of positive AMA

Diagnostic dilemma

Is this primary biliary cirrhosis?

- Significance of histological findings
  The findings are nonspecific
- Specificity of positive AMA

Mild lobular inflammation

PBC: bile duct damage, florid duct lesion
Specificity of AMA

- High specificity for PBC
- Autoimmune hepatitis
- Infections like TB
- ELISA-based assay more specific

Positive AMA: asymptomatic, normal ALP

Bx: Classic 12/29, consistent 12/29, N=2

Most progressed to symptomatic PBC
50% at 5 years, 95% at 20 years

Diagnosis

- Diagnosis:
  Mild portal and lobular inflammation, suggestive of PBC; see note

Note:

- Patchy bile duct involvement in early PBC can be missed on biopsy
- Majority of AMA+ develop features typical of PBC on follow-up
- AMA+ and periportal copper suggest early PBC
Case 2

• 40/F with nonspecific abdominal symptoms
• “Elevated LFTs”
• ANA, SMA positive
  AMA negative
• Work up for other liver diseases negative (viral, drug, Wilson, A1AT deficiency)

Diagnosis

• ANA, SMA+
• Biopsy: interface activity foci of lobular inflammation
• Diagnosis: Autoimmune hepatitis

Do you agree with the diagnosis?

AIH: role of liver biopsy

• Acute hepatitis
• Chronic hepatitis with varying degree of activity
• Cirrhosis
• Typical histologic features:
  High necroinflammatory activity
  Numerous plasma cells

Serial liver enzymes

<table>
<thead>
<tr>
<th></th>
<th>1-2009</th>
<th>9-2009</th>
<th>1-2010</th>
<th>4-2010</th>
<th>6-2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT (30)</td>
<td>58</td>
<td>62</td>
<td>83</td>
<td>159</td>
<td>133</td>
</tr>
<tr>
<td>AST (30)</td>
<td>40</td>
<td>38</td>
<td>65</td>
<td>100</td>
<td>110</td>
</tr>
<tr>
<td>ALP (130)</td>
<td>192</td>
<td>210</td>
<td>288</td>
<td>324</td>
<td>308</td>
</tr>
</tbody>
</table>
Diagnosis

Portal and interface inflammation with focal bile duct damage, most c/w AMA negative PBC
• Moderate interface activity present
• Mild elevation of ALT/AST and absence of prominent hepatocellular injury does not provide definite evidence of AIH component
• If ALT/AST rise >400-500, overlap syndrome can be considered