Basic patterns of liver damage – what information can a liver biopsy provide and what clinical information does the pathologist need?

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FATTY LIVER DISEASE

Clinical Liver Disease Volume 2, April 2013, Pages 64–67
Clinical Liver Disease Volume 1, September 2012, Pages 108–111
(http://onlinelibrary.wiley.com/doi/10.1002/cld.31/full)
Types of fatty change:
Large droplet

“mesovesicular fatty change”
Types of fatty change:
Small droplet
Fatty liver disease:

- Ballooning and inflammation
Recognising ballooning

(B) Normal hepatocytes, ballooning, grade 0. Cytoplasm is pink and granular and liver cells have sharp angles.

(C) Ballooning, grade 1. Hepatocytes have rounded contours with clear reticular cytoplasm. Size is quite similar to that of normal hepatocytes.

(D) Ballooning, grade 2. Cells are rounded with clear cytoplasm and twice as large as normal hepatocytes.
Differences between ASH and NASH

• The following are commoner in ASH:
  diffuse microvesicular steatosis,
  cholestasis
  neutrophilic satellitosis of Mallory–Denk body-containing balloon cells
  dense networks of perisinusoidal fibrosis

• Only ASH shows a significant incidence of veno-occlusive lesions and sclerosing hyaline necrosis.

Clinical Dilemmas in NAFLD Elsevier 2016 p 72
Nuclear vacuolation
## Alcoholic hepatitis Histological Score

<table>
<thead>
<tr>
<th>Points</th>
<th>Stage of fibrosis</th>
<th>Bilirubinostasis</th>
<th>PMN infiltration</th>
<th>Megamitochondria</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No fibrosis or portal fibrosis</td>
<td>No</td>
<td>No/Mild</td>
<td>No megamitochondria</td>
</tr>
<tr>
<td>0</td>
<td>Expansive fibrosis</td>
<td>Hepatocellular only</td>
<td>Severe</td>
<td>Megamitochondria</td>
</tr>
<tr>
<td>+3</td>
<td>Bridging fibrosis or cirrhosis</td>
<td>Canalicular or ductular or ductular plus hepatocellular</td>
<td>No/Mild</td>
<td>No megamitochondria</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Megamitochondria</td>
</tr>
</tbody>
</table>

The AHHS categories are as follows: mild, 0–3; intermediate, 4–5; severe, 6–9.
Histologic features independently associated with 90-day survival included in the Histologic AHHS:
(A) Hepatocellular and canalicular bilirubinostasis (arrow).
(B) Ductular bilirubinostasis (arrow).
(C) Megamitochondria (arrows).
### NAFLD Activity Score

<table>
<thead>
<tr>
<th>Steatosis grade</th>
<th>Lobular inflammation</th>
<th>Hepatocellular ballooning</th>
</tr>
</thead>
<tbody>
<tr>
<td>0: &lt;5%</td>
<td>0: None</td>
<td>0: None</td>
</tr>
<tr>
<td>1: 5-33%</td>
<td>1: &lt;2 foci/20x field</td>
<td>1: Mild, few</td>
</tr>
<tr>
<td>2: 34-66%</td>
<td>2: 2-4 foci/20x field</td>
<td>2: Moderate – marked,</td>
</tr>
<tr>
<td>3: &gt;66%</td>
<td>3: &gt;4 foci/20x field</td>
<td>many</td>
</tr>
</tbody>
</table>

**NAFLD activity score (NAS): 0-8**

- Steatosis (0-3) +
- Lobular Inflammation (0-3) +
- Ballooning (0-2)

CHRONIC HEPATITIS
• Assess disease severity:
  Grade (necro-inflammation)
  Stage (fibrosis)
  ? Score (using modified Histological Activity Index / METAVIR)

• Assess disease progression or response to treatment

• Exclude co-existing liver diseases
Laennec Subclassification of Cirrhosis
Stage:
Laennec Subclassification of Cirrhosis

<table>
<thead>
<tr>
<th>Stage</th>
<th>Name</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>F0</td>
<td>No definite fibrosis</td>
<td></td>
</tr>
<tr>
<td>F1</td>
<td>Minimal fibrosis</td>
<td>No septa or rare thin septum; may have portal expansion or mild sinusoidal fibrosis</td>
</tr>
<tr>
<td>F2</td>
<td>Mild fibrosis</td>
<td>Occasional thin septa; may have portal expansion or mild sinusoidal fibrosis</td>
</tr>
<tr>
<td>F3</td>
<td>Moderate fibrosis</td>
<td>Moderate thin septa; up to incomplete cirrhosis</td>
</tr>
<tr>
<td>F4A</td>
<td>Cirrhosis, mild, definite or probable</td>
<td>Marked septation with rounded contours or visible nodules. Most septa are thin (one broad septum allowed)</td>
</tr>
<tr>
<td>F4B</td>
<td>Moderate cirrhosis</td>
<td>At least two broad septa, but no very broad septa and less than half of biopsy length composed of minute nodules</td>
</tr>
<tr>
<td>F4C</td>
<td>Severe cirrhosis</td>
<td>At least one very broad septum or more than half of biopsy length composed of minute nodules (micronodular cirrhosis)</td>
</tr>
</tbody>
</table>

Liver Int. 2016; 36: 847–855
CHRONIC VIRAL HEPATITIS

Clinical Liver Disease Volume 1, April 2012, Pages 32–35
(http://onlinelibrary.wiley.com/doi/10.1002/cld.30/full)
Clinical Liver Disease Volume 2, February 2013, Pages 49–51
HBV: Ground glass hepatocytes

Orcein
HCV:
Lymphoid aggregate/follicle
HCV: Hepatitic bile duct damage
HCV genotype 3: Fatty change
HDV
AUTOIMMUNE HEPATITIS
Autoimmune hepatitis

• Help in making the diagnosis
• Help in assessing the response to treatment
Simplified histological criteria for the diagnosis of AIH

• “Typical”
  1. Interface hepatitis
  2. Lymphocytic / lympho-plasmacytic infiltrates in portal tracts and extending into the lobule
  3. Rosetting of liver cells

• “Compatible” a chronic hepatitis with lymphocytic infiltration without all the above features

• “Atypical” for AIH when showing signs of another diagnosis.
DRUG INDUCED LIVER INJURY
• “Any kind of liver disease can be caused by a drug”

• Histological features suggesting a drug reaction:
  Eosinophils, plasma cells, granulomas, sharply demarcated necrosis, cholestatic hepatitis
Drug reaction
Drug reaction
Drug reaction
Histological predictors of severity in drug-induced liver disease.

• **More severe disease associated with:**
  1. necrosis
  2. fibrosis stage
  3. microvesicular steatosis
  4. cholangiolar cholestasis
  5. bile duct damage

• **Milder disease associated with:**
  1. granulomas
  2. increased eosinophils
http://livertox.nih.gov/
Biliary tract disease: Orcein stain
Biliary tract disease: CK7
PBC
Primary Biliary Cholangitis

= the new name for Primary Biliary Cirrhosis
IgG4 Disease

IgG4+ plasma cells (>10/hpf)
IgG4+/IgG+ cell ratio >40%

Causes of Disappearing Bile Ducts

- PBC* (and its variants)
- PSC (and its variants)
- Drugs and Toxins
- Chronic transplant rejection
- Graft Vs. Host
- Hodgkin’s Disease, Histiocytosis X
- Sarcoid
- Paucity of interlobular bile ducts
- HIV
- Idiopathic
Grading and Staging of Biliary Duct Disease

• Grading: hepatitis and cholangitis
• Staging: fibrosis, copper binding accumulation and duct loss

VASCULAR DISEASE
Nodular regenerative hyperplasia
Causes of Nodular Regenerative Hyperplasia

• Connective tissue disorders
• Myeloproliferative disorders
• Chronic vascular congestion
• Drugs e.g. steroids, anticancer drugs, anticonvulsants, immunosuppressive agents

DISCREPANCY RATES IN LIVER BIOPSY REPORTING
• fibrosis staging
• recognising and interpreting bile duct disorders
• misdiagnoses of autoimmune hepatitis

J Clin Pathol 2014;67:825-827
Histopathology 2016;69:315-21
WHAT CLINICAL INFORMATION DOES THE PATHOLOGIST NEED?
• A decent clinical history!
• Look at the biopsy and write the description without knowing any clinical information
• Only write the conclusion when you have the information
Rare example of a full drug history

The remedies are:

Bacillium 200c weekly boosts immune system
Narayani cold mix - which contains aconite, allium sepia Euphrasia - for when you feel a cold coming on or when you have a cold.

For the aching of the body when you have a cold I gave you Gelsemium 30c/200c
Winter tonic to boost immunity has Emerald 12c, Echinacea 6c, Earthworm 6c, thymus gland 6c, tissue salts 6x Ferrum phase 6c and Narayani immunity mix 86 Cm which contains gunpowder, interferon, kali phos, thymus, virus bacteria.

And

Tonsils and glands mixes. which I prescribed for you to take when throat was sore.

Diptherinum 30c, Penicillin nosode, phytolacca, Streptococci nosode.

glands mix - belladonna, glandular fever nosode, lymph organ remedy, mercurious, virus bacteria.