Chronic Biliary Disease

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Chronic Biliary Disease

• Terminology – can be confusing
• Disease processes are heterogeneous in distribution
• Abnormalities can be subtle
• Can be problematic
  – Early biliary changes missed in 1/3 referrals
  – High discrepancy rate between referral interpretation and specialist opinion
Terminology

- Biliary piecemeal necrosis
- Cholestatic liver disease
- Ductular proliferation
- Ductopenia
- Biliary interface
- Extrahepatic cholestasis
- Cholangiopathy
- Bilirubinostasis
- Cholate stasis
- Vanishing bile duct syndrome
- Ductular reaction
Chronic Biliary Disease

- Cholestatic liver disease / LFTs - cholestasis
- Intrahepatic / extrahepatic cholestasis
Chronic Biliary Disease

- Cholestatic liver disease / LFTs - cholestasis
- Intrahepatic and / or extrahepatic bile ducts
- Cholangiopathy
Chronic Biliary Disease

- Cholestatic liver disease / LFTs - cholestasis
- Intrahepatic and / or extrahepatic bile ducts
- Cholangiopathy
- Biliary interface activity (cholate stasis, ductular reaction, fibroplasia)
Ductular reaction
CK7 immunohistochemistry
Ductopenia
Biliary Disorders

- Cholestatic liver tests – ALP, GGT, Bilirubin

- Key questions
  - Pain
  - Pruritus
  - Associated disorders
  - Family history
  - Drug history

- Ultrasound of biliary tree / MRCP
Cases
Case 1 A.B.

Female 56 yrs
Presented to GP general malaise, fatigue
Abnormal LFTs

Dec 2016:
ALP 183, ALT 36, GGT 158
Elevated IgG and IgM, AMA +
USS – fatty liver
Case 1 A.B.

- Portal granulomatous inflammation with duct destruction
- Ductopenia
- Minimal periportal copper associated protein
- Mild fibrosis

- Diagnosis – Primary Biliary Cholangitis
### Historical Staging of PBC (&PSC)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Ludwig system</th>
<th>Scheuer system</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Portal</td>
<td>Florid duct lesion</td>
<td>Bile duct damage and portal inflammation</td>
</tr>
<tr>
<td>2</td>
<td>Periportal</td>
<td>Ductular proliferation</td>
<td>Expanded portal tracts with bile ductular reaction, periportal inflammation, and biliary interface activity</td>
</tr>
<tr>
<td>3</td>
<td>Septal</td>
<td>Fibrosis</td>
<td>Periportal fibrosis with portal – portal bridging; loss of bile ducts</td>
</tr>
<tr>
<td>4</td>
<td>Cirrhosis</td>
<td>Nodular cirrhosis</td>
<td>Irregular parenchymal nodules with bridging fibrous scars</td>
</tr>
</tbody>
</table>
Stages 1-4
# Japanese system

*Nakanuma Histopathology 2006*

<table>
<thead>
<tr>
<th>Histological staging</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fibrosis (F)</strong></td>
<td></td>
<td></td>
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<tr>
<td>Absent or limited in portal tracts</td>
<td>Periportal fibrosis (incomplete septa)</td>
<td>Bridging fibrosis</td>
<td>Cirrhosis</td>
<td></td>
</tr>
<tr>
<td><strong>Bile duct loss (B)</strong></td>
<td>Absent</td>
<td>&lt;1/3 portal tracts</td>
<td>1/3–2/3 portal tracts</td>
<td>&gt;2/3 portal tracts</td>
</tr>
<tr>
<td>**Chronic cholestasis (C) (orcein +ve) *</td>
<td>Absent</td>
<td>&lt;1/3 periportal areas</td>
<td>1/3–2/3 periportal areas</td>
<td>&gt;2/3 of periportal areas</td>
</tr>
</tbody>
</table>
Biopsy in PBC

• Diagnosis unclear, though extended serology panel may help

• Non-response to UDCA (more likely if young):
  ? Ductopenic variant
  ? AIH/PBC overlap
  ? additional aetiology such as NASH
Case 2 M.S.

- 35 yr old female
- Known PBC, AMA+
- IgG 11.4  IgM 3.4
- Developed worsening pruritis and jaundice after drug trial for PBC (anti CXCL10 MAb)
- Imaging did not suggest cirrhosis
- Biopsy performed
Widespread cholestasis

ductopenia

Widespread cholestasis
Case 2 M.S.

- Ductopenia, cholate stasis and profound cholestasis, unusual for stage of disease
- No improvement
- Bil 154   ALP 543   ALT 112
- Listed for liver transplant – bilirubin & pruritis
- Transplanted 2013
Typical PBC with cirrhosis at transplant
2838g
bile stained; scattered small nodules; smooth capsule
EPSR- occasional septa
Different sized ducts
Copper-associated protein = massive

Orcein

Victoria blue
Case 2 M.S.

- Diagnosis - ‘ductopenic variant of PBC’

Possibly exacerbated by a drug
Case 3 S.P.

- 55 yr old female
- Type 2 DM, HTN, dyslipidaemia
- Abnormal LFT - ALP 210, ALT 75
- ? NASH with significant fibrosis
- Liver biopsy
Case 3 S.P.

- Predominantly portal / periportal non-necrotising granulomatous inflammation with fibrosis
- Numerous epithelioid and multinucleate cells
- Bile ducts displaced
Case 3 S.P.

- Most in keeping with hepatic sarcoidosis
Case 4 J.P.

- 70 year old female
- Asymptomatic, central adiposity, HTN
- Incidental finding of abnormal LFT
- ALP 250, GGT 270
- Liver USS normal
- Negative autoantibodies and Ig’s
- Unusual pattern of LFT for NAFLD
Case 4 J.P.

- Duct destruction with periductal oedema
- Dutopenia
- Cholate stasis
Case 4 J.P.

- Diagnosis primary sclerosing cholangitis
Primary Sclerosing Cholangitis
Case 5 M.T.

- 34 year old male
- Incidental finding of some peripheral dilated ducts on CT for appendicitis late 2014
- MRCP confirmed cholangiopathy
- Asymptomatic, normal LFTs
- Not clear if PSC or congenital
- Proceeded to liver biopsy
Abnormal biliary tree with focal dilatation and widespread strictures. Possibilities would include a cholangiopathy related to PSC, ischaemia, parasitic infection - congenital syndromes such as Caroli's seem less likely.
Victoria blue - elastic, no CAP
Case 5 M.T.

- Irregular, rounded map-like fibrosis, with abnormal ductules
- Little inflammation
- No cholestasis or cholate stasis
Case 5 M.T.

• Ductal plate malformation; Congenital Hepatic fibrosis
Ductal plate malformation

• Choledochal cyst
• Caroli’s
• Polycystic Liver Disease
• Congenital Hepatic Fibrosis
• Von Meyenburg Complex

Increasing size of affected Bile duct
Case 6 J.A.

- 73 yr old female
- 6 months intermittent upper abdo pain
- 1.5 stone weight loss + jaundice
- CT showed biliary dilatation and ampullary lesion
- Whipples resection for ampullary adenocarcinoma
- Intra-operatively ? Cirrhotic
- Liver biopsy
CASE 6 J.A.

- Biliary pattern fibrosis
- Oedema and acute inflammation
- Ductular reaction
- Cholate stasis
- No significant duct damage or ductopenia
CASE 6 J.A.

- Secondary biliary fibrosis
Summary – Biliary disease

- Challenging and can be subtle
- Discussed terminology and key features of biliary disease
- Clinical and radiological correlation is crucial
- Not usually required for diagnosis of PBC / PSC
- Ductular reaction
- Ductopaenia – unaccompanied arteriole
- Copper associated protein
- CK7 immunohistochemistry
Thank you