National Liver Pathology EQA Scheme

Open Meeting, July 1\textsuperscript{st} 2003. Bristol
Case 171 - history

Female, 35 years. Abnormal LFTs

Three cores of liver tissue
Case 171-Diagnoses

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steatohepatitis</td>
<td>142</td>
</tr>
<tr>
<td>Steatosis (fatty change, fatty liver)</td>
<td>223</td>
</tr>
<tr>
<td>steatosis/minimal steatohepatitis</td>
<td>10</td>
</tr>
<tr>
<td>fatty change + mild chronic hepatitis</td>
<td>30</td>
</tr>
<tr>
<td>non-specific</td>
<td>25</td>
</tr>
<tr>
<td>PBC</td>
<td>10</td>
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</tbody>
</table>
Case 171 comments

Steatohepatitis minimal or mild: 5 people
?NRH: 5 people
need VG, retic, Ubiquitin: several
More history: most
?circulatory disturbance, ?portal hypertension: 3
some thought steatosis + mild chronic hepatitis

Follow up?

*Not discussed with pathologist. Reported as non-specific hepatitis. No relevant clinical details available*
Case 171 Discussion

• Accept first four diagnoses

Fibrosis is important – need connective tissue stain before recognizing steatohepatitis.
No consensus over criteria for steatohepatitis amongst members.
In some centres ballooning +/- Mallory bodies, +/- neutrophils, +/- fibrosis are criteria that are required for steatohepatitis, but not all use this.

Fatty liver disease is an American umbrella term to encompass any of these. There is very little evidence on the clinical significance of these various changes, on which to base diagnosis.

A role for a discussion group in forming a consensus on terminology amongst UK liver pathologists was discussed.
Case 172 - History

- A 65 year old man. Liver biopsy performed at the time of colectomy (for colorectal carcinoma).
Case 172- Diagnoses

Metastatic adenocarcinoma, consistent with CRC: 397.8
Primary adenocarcinoma: 0.2
Cholangiocarcinoma: 2
Adenocarcinoma: primary or secondary not stated: 10
No slide received: 30
Case 172- Comments

CK7&20, and/or review primary  7
consider upper GI primary        1
+ features due to adjacent SOL:      5
with granulomas:           1
with secondary sclerosing cholangitis  1

Follow-up: *Dr Sherwood:*  metastatic
  adenocarcinoma biopsied at time of colectomy
Case 172 – Discussion:

Clear consensus agreed to accept only metastatic adenocarcinoma (+/- consistant with CRC). Most would only do further investigation – cytokeratin etc – if clinical uncertainty of origin of metastasis.
Case 173 - History

Hepatitis C carrier for 5 years.
Case 173 (Educational)- Diagnoses

Normal/within normal limits: 118
Almost normal, no significant abnormality: 110
Minimal/mild steatosis: 100
Ductopaenia: 20
Minimal/mild chronic hepatitis: 42
Don’t know: 10
?oncocytic metaplasia, ?amyloid,
  focal cytoplasmic granularity: 30
Case 173 comments:

Special stains: several
Foam artefact 1
Follow up: Dr Prescott: PCR +ve, LFTs normal
Case 173  Discussion

Educational case therefore not included on EQA scoring. Several in audience had seen normal biopsies after years of infection with hepatitis.
Case 174 History

? Lymphoma

Liver biopsy
Case 174 - Diagnoses

Lymphoma 30
Biliary disease NOS 69
Cholestasis, probably lymphoma: 139
Lymphoma not excluded 64
LCH 20
Malignant infiltrate 20
Clear cells ?what in portal tracts 50
Chronic hepatitis 1
Metastatic clear cell carcinoma 4
Changes of nearby mass lesion 10
Infection 5
Venous outflow obstruction 4
Drug reaction 2

(lymphoma mentioned somewhere in comments, but not in main diagnosis: 3 people)
Case 174: comments

Everyone!

Most asked for immunos, more clinical details

‘Educational case – would be clinically irresponsible to report this on one H&E with no clinical information’

People wondered about: HD, T cell lymphoma, mastocytosis, histiocytosis, hairy cell leukaemia, other leukaemia,

Most also commented on features of biliary obstruction

Some also saw features of venous outflow obstruction
Case 174

Follow up: Dr Kennedy

On sabbatical but report faxed from St Vincent’s

Clinical details: hairy cell leukaemia. ALD
Case 174 – Discussion

Comment from Dr Roberts – clinical inflammation available at time of reporting original biopsy to be circulated with EQA cases. This case is therefore excluded from scoring. It is nevertheless a valuable educational case.

Overall, suggestion of lymphoma/leukaemia of some sort was raised by 37/44 respondents. A further 6 commented on odd cells without speculating what they were.
Case 175 History

F45. History of acute hepatitis.
Negative for Hepatitis A, B, and C, on viral screen.
Positive ANA titre 1/6000.
On Vioxx – Cox2 inhibitor.
Case 175 Diagnoses

Acute hepatitis, attributed to drug, autoimmune not mentioned in main diagnosis: 140
Autoimmune hepatitis 60
Acute hepatitis +/- BHN;
neither or both causes mentioned 180
Acute on chronic autoimmune 20
CMV hepatitis 10
No section 20
Case 175, comments:

Several: ?acute presentation of autoimmune, need more information on autoantibodies

Viral/CMV inclusions  2

Don’t think drugs cause giant cells  2

Focal haematopoiesis  2

Follow up: Dr Kennedy: reported as: acute severe hepatitis on a background of fibrotic change (stage 3/6). The aetiology is in keeping with autoimmune type
• Case 175, Discussion
  Accept all responses except CMV hepatitis.

See discussion of 176
Case 176 History

F44. Transaminitis, ALT>650, alk phos 188, positive SMA. ? AIH.

Further details: history of hypothyroidism – on thyroxine replacement therapy. Rh factor +ve, EBV +ve (Report: evidence of recurrent EBV infection).

History of blood transfusion 4 years ago (hysterectomy for fibroid).

Recent history of treatment with amoxycillin and ciprofloxacin for ? UTI
Case 176 Diagnoses

Acute hepatitis, ? or probably drug, autoimmune not mentioned in main diagnosis 157
Autoimmune hepatitis 79
Hepatitis, neither or both causes mentioned in main diagnosis: 138
Chronic active hepatitis in keeping with drugs 30
Chronic autoimmune 20
Hepatitis, probably acute, ?drug or hepatitis C 10
EBV 4
?biliary disease 2
Case 176 comments

Eosinophils: several
Viral hepatitis needs exclusion by serology: several
?variant syndrome of AIH/PBC
LBDO like or cholangiolitis element: 5 people

Follow up: Dr Guha, at meeting: clinical diagnosis was AIH, treated with steroids Azathioprine improved. Liver function test normalized, still taking low dose steroids.
Case 176 Discussion

All diagnoses accepted.

Comment is that even this does not confirm the diagnosis of autoimmune hepatitis, since drug hepatitis would also have resolved with steroids.

Considerable debate over role of histopathology in acute hepatitis, and what constitutes acute hepatitis.
Summary of discussion

- Role of histology is to exclude chronicity and comment of severity of acute hepatitis.

In chronic hepatitis, plasma cells, interface hepatitis and rosetting are characteristics favouring autoimmune aetiology, while in acute hepatitis, histological features do not help in determining the aetiology. In acute liver damage, there may be transient liver autoantibodies; therefore raised IgG and smooth muscle autoantibodies high titer of liver autoantibodies are required to accept autoimmune hepatitis as the cause.

Discussion on terminology of acute-v-chronic hepatitis.

To diagnose chronic hepatitis needs clinical history duration >6 months or presence of elastic fibres in septa. In absence of evidence of chronicity, it is not possible to determine duration of hepatitis on histology. The diagnosis autoimmune hepatitis is usually made without indication of acute or chronic, since it is accepted that this is always a chronic disease.
Case 177 History

F 50. Cholestatic jaundice on atorvastatin. Also nephrotic
Case 177 Diagnoses

Cholestasis associated with drug: 128
Hepatitis – drug related: 33
Biliary obstruction 116
Portal reaction consistent with drug but exclude duct obstruction 40
Chronic obstructive Biliary disease 20
Biliary disease – drugs or obstruction 45
?chronic hepatitis+drug induced Cholestasis 10
<table>
<thead>
<tr>
<th>Condition</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis ?cause</td>
<td>5</td>
</tr>
<tr>
<td>Sepsis</td>
<td>12</td>
</tr>
<tr>
<td>Ductopaenia and cholangiolitis, ?PBC</td>
<td>10</td>
</tr>
<tr>
<td>Ductopaenia and cholangiolitis ?drugs/PBC</td>
<td>10</td>
</tr>
<tr>
<td>Cholangiolitis and paucity of ducts ?drugs</td>
<td>10</td>
</tr>
<tr>
<td>Difficult – no answer</td>
<td>10</td>
</tr>
</tbody>
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Case 177 comments:

Several: Biliary features
   ?does atorvastatin cause LBDO like changes
several: ?ductopaenia
Few – advise imaging, looks like ?PSC/PBC

Follow up: *Dr Ansell:* – *no duct obstruction found but still had high alkaline phosphatase 9 months later. Nephrotic syndrome reduced to minimal change nephropathy.* *Investigation of biliary tree shows no obstruction*
Case 177 Discussion

- Role of statin in cholestatic liver disease.
- The statins recognised to cause hepatitis, although low risk, not associated with cholestatic injury. This biopsy shows features suggestive of biliary disease; clinicians know the patient is on statin.
- Response to this biopsy should be to recommend investigation to exclude large duct obstruction or chronic biliary disease.
• Accepted diagnoses are any that mention need for investigation of biliary tree; attributing these features to the drug without raising the possibility of duct obstruction or some form of (non-drug related) chronic biliary disease is not an accepted diagnosis.
Case 178 History

Male 61.
Known UC for 2 years
Recent episode of jaundice
Case 178 Diagnoses

PSC

? PSC mentioned in main diagnosis  340

60

Cholestasis – PSC mentioned in secondary diagnosis  20

Cholestatic hepatitis, ? drug.

No mention of PSC anywhere  20
Several: needs imaging for PSC
In view of severe cholestatis, ? dominant stricture, exclude malignancy,
? sepsis
Follow up: Dr Ansell: *much copper associated protein.*

*ERCP failed. Diagnosis of PSC accepted on this biopsy and clinical data.*
• Case 178 discussion
  Accepted diagnoses equals = any that mention PSC somewhere.
Case 179 History

F 48. Large tumour in liver.

Immuno: HMB45 positive.
Angiomyolipoma

Comments:
association with renal AMLs, tuberous sclerosis in 5-10%
Lipomatous type: 2 people
Case 179 Discussion
Full consensus.
Accept all diagnoses
Case 180  History

Female aged 56.
Generally unwell.

Abnormal LFT’s.  Raised Alk Phos, Gamma GT, and AAT
Anti mitochondrial Ab Positive 1:160.
Nti Nuclear +ve 1:1640
Anti smooth muscle negative
Case 180 Diagnoses

PBC 336
PBC/AIH overlap 54
Chronic active hepatitis, ?PBC, ?Autoimmune 10
Chronic Biliary disease – periductal fibrosis ?PSC but AMA favours PBC 10
Granulomatous hepatitis,, ?PBC, ?Sarcoid 10
Case 180: comments:

35% PBC have ANA
No interface here to indicate overlap with AIH
Overlap in view of lobular hepatitis component
Parenchymal activity part of PBC
Autoimmune cholangiopathy, also known as immune cholangitis, in view of wide distribution of chronic inflammation
ANF red herring – not hepatitic enough for overlap
Need ERCP/ultrasound  4 people
Case 180: comments:

Follow up:

Dr Sheehan, ANF was membranous and therefore due to anti lamin and not anti-ds DNA, therefore not autoimmune hepatitis.

This was first diagnosis of PBC, commenced treatment with ursodeoxycholic acid.
Case 180 Discussion
Accept all as correct results.

Criteria for diagnosing overlap with autoimmune hepatitis vary.
Case 181  History

Male aged 62 years. Recently diagnosed with recto-sigmoid carcinoma. Nodules seen on surface of liver at operation.

Wedge biopsy of liver, 13mm diameter. Multiple dark nodules on surface – cystic appearance, ? metastases
Case 181 Diagnoses

Von Meyenberg complexes/ Biliary microhamartoma
390

Polycystic disease/VMCs 20
Bile duct hamartoma 30
Case 181: comments

Part of polycystic if macroscopic cysts present
Steatosis 4 people

Follow up: Dr Sheehan,
incidental finding during surgery for CRC
• Case 181 Discussion
  Full consensus. Accept all diagnoses