Circulation T

Manchester

July 5th 2006
Case 242

- 8 year old female with polycystic disease
- Section from explanted liver.
Case 242

31 Congenital hepatic fibrosis
13 Autosomal recessive polycystic kidney disease
11 in the spectrum of polycystic disease
3 ductal plate malformation
3 ?caroli’s
Case 242

**Scoring: Accept all diagnoses**

**Discussion:** The dilatation of large ducts against the background of congenital hepatic fibrosis indicates that this is an example of Caroli’s syndrome (dilatation of intra-hepatic ducts + congenital hepatic fibrosis), rather than congenital hepatic fibrosis alone.
Case 242

Follow up:

The clinical details received with this liver were 'polycystic disease'.

The patient had one episode of early acute rejection at which time we were also told that there had been a combined liver and kidney transplant performed as there had been previous bilateral nephrectomy in another hospital for cystic kidneys.

No further biopsies have been received and therefore the patient is presumed to be doing well.
Case 243

• 58 female
• Liver nodule noted at time of organ transplantation
• Liver wedge biopsy
• 4mm pale tan nodule on wedge
Case 243
Case 243
Case 243
Background liver
Case 243

41 adenoma
4 FNH or benign ? FNH
3 benign ? adenoma or FNH
3 regenerative or hyperplastic nodule
2 regenerative nodular hyperplasia
2 focal fatty change or adenoma
3 focal steatosis

comments:
steatosis in the adenoma  13
mild hepatitis in background liver  4
Case 243

**Scoring:** Accept responses that indicate this is a focal benign hepatocellular lesion (see comment)

**Discussion:** perhaps best characterized as a focal benign hepatocyte lesion – this lacks characteristics of adenoma (because it is encapsulated, with no unaccompanied arteries in the lesion) as well as lacking characteristics of focal nodular hyperplasia. Responses that did not indicate the focality of the lesion were rejected. Regenerative nodular hyperplasia is a diffuse change without fibrosis and focal steatosis is seen as a patch of fatty change within a group of liver cells with no architectural alteration.
Case 244

• 52 female
• Alcoholic liver disease, ? Cirrhosis

• 2 cores of tissue up to 10mm long
• (H&E and HVG slides)
Case 244
Case 244

50  Alcoholic steatohepatitis
6   alcoholic liver disease, not otherwise specified
1   no mention of alcohol

20  severe fibrosis
18  developing/incomplete cirrhosis
3   early cirrhosis
11  Cirrhosis

2   central sclerosing hyaline necrosis

Comments: ? sickle cells  2
Case 245

Scoring: for full marks, answers require alcohol, steatohepatitis and at least marked fibrosis to be included in response; half marks if part is missing

Discussion around one use of alcohol in diagnosis – most diagnose alcoholic liver disease when there is a history of excessive alcohol consumption supplied, and suggest alcoholic aetiology if no history of alcohol is given. Anecdotally, this has caused problems where a given history of alcohol on the request form was subsequently found to be erroneous. However, pragmatically a case can be reported as consistent with alcohol if the alcohol history is supplied.
The criteria for steatohepatitis – Ballooned hepatocytes, Mallory bodies, and sinusoidal fibrosis in this case indicate that steatohepatitis is appropriate terminology even though there is no inflammatory cell component either in portal tracts or parenchyma. It was commented that as steatohepatitis resolves, the order of disappearance of features is polymorphs then fat then ballooning then Mallory’s then fibrosis. As the lesion evolves over time, it is accepted to diagnose steatohepatitis without requiring the presence of inflammatory cells.
Case 244

Discussion contd:
Fibrosis – As long as vascular relationships appear preserved, as in this case, a diagnosis of established cirrhosis was probably not appropriate. Developing cirrhosis or severe fibrosis is more accurate here. Clearly there can be portal hypertension as a result of sinusoidal fibrosis without implying that cirrhosis has developed.

Sclerosing central hyaline necrosis, as answered by 2, is the most appropriate terminology in this case.

Follow-up information – Clinical history was of high alcohol (4 bottles of wine per night for the last 18 months), admitted with jaundice and liver failure and bleeding varicies. Varicies banded difficult to manage and eventually died from variceal haemorrhage.
Case 245

• 65 male

• History of SLE and sarcoidosis

• abnormal LFTs – alk phos 164, gamma GT 326,

• IgG 17.4, ANA 1:640, dsDNA >300, smooth muscle b ++

• Needle core 28mm long
Case 245

51 granulomas/granulomatous inflammation
3 granulomas not mentioned
2 slide missing

50 most likely sarcoidosis
3 sarcoidosis and/or SLE
1 sarcoidosis and AIH
1 sarcoidosis and AIH/SLE/PBC
1 sarcoidosis and veno-occlusive disease

exclude TB/request ZN 27
needs AMA 3
need copper-protein 4
comment that granulomas are a feature of SLE – several
Case 245

- **Scoring:** Accept all diagnoses mentioning granulomas and sarcoidosis
- **Discussion:** The auto-antibodies may be associated with the separate clinical diagnosis of SLE, but there is thought to be insufficient histological evidence to suggest a component of autoimmune hepatitis.
Follow up –

- Diagnosis: granulomatous hepatitis, most likely sarcoidosis
- Evidence for diagnosis of sarcoidosis:
  - Clinical diagnosis sarcoidosis and SLE
  - 1 year after this biopsy, developed granulomatous skin lesion, diagnosed as sarcoid
  - AMA –ve
- LFTs currently normal apart from mildly raised GGT
Case 246

- 55 M
- Hep C RNA positive genotype 1
- ? For treatment
Case 246
Case 246

53  HCV
2  hepatitis C not mentioned
3  steatohepatitis, lacking usual features of hepatitis C

33  Also steatosis
3  Also steatohepatitis

Additional clinical cause for steatosis: 12
Histology would indicate treatment if clinically appropriate 13
Case 246 contd.

Severity:
No comment on grade or stage – 2

Mild chronic hepatitis 2
Moderate chronic hepatitis 1
inflammation

Rest – not possible to assess fibrosis without connective tissue stain

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Case 246

Scoring: Reject answers that do not mention hepatitis C, or suggest the liver disease is other than due to hepatitis C; half marks if there is no comment on severity.

Discussion: The table of degrees of severity included so that individuals can place themselves amongst their peers. Some of the spread in severity may be due to the widely variable amount of tissue in the slides.
Case 246

- Follow up Dr Finlayson
- Ex-IVDU, was also drinking 2 bottles wine per day 4 months before biopsy, macrocytosis
- ALT 238
- USS coarse texture,
- HCV combination therapy started.
Case 247

- 40 M
- 6cm tumour in segment 8. probable focal nodular hyperplasia on imaging. Incidental finding.

- Laparoscopic tumour resection
- Several pieces of granular brown tissue up to 1.5cm
Case 247
Case 247

55  Focal nodular hyperplasia
2  ? telangiectatic FNH
1  ? cholangiocarcinoma

? state of background liver  7
Case 247

Scoring: Accept all except cholangiocarcinoma.
Case 248

- 77 M
- Jaundice. Special stains are negative for HBsAg, alpha 12 antitrypsin, copper, copper associated protein an haemosiderin.

- Core of brown tissue, 17x1mm
Case 248
Case 248

Morphology/only diagnosis:
33 Cholestasis ± inflammation/cholestatic hepatitis
4 cholestasis and cholangiolitis
11 PSC
4 large duct obstruction
1 PSC or large duct obstruction
1 chronic hepatitis with biliary features
2 no mention of cholestasis or biliary disease anywhere in answer

As main/most likely/only cause:
20 ?Drug reaction
10 ?PSC
4 ?large duct obstruction
1 ?ascending cholangitis

differential diagnosis including:
13 drugs
12 PSC
1 PBC
4 large duct obstruction

comments:
autoantibodies 6
ERCP 16
Several mentioned periductal fibrosis
No copper associated protein
therefore not PSC/PBC 2
Case 248

**Scoring:** Insufficient concensus for scoring.

**Discussion:** This was a cholestatic liver biopsy in which the changes appeared recent, and suggested of drugs.

Because of periductal fibrosis in one portal tract, several responses were PSC with no qualification. In practice, in view of the absence of any fibrosis, ductopaenia, or copper associated protein, this case lacks sufficient histological features to allow an unqualified diagnosis of PSC. Canalicular cholestasis would also be unusual in early stage PSC.
Case 248

Follow up –

• Diabetic, treated for foot ulcer with penicillin, then admitted with painless jaundice.
• US and CT negative.
• Fibrosis surrounding duct, so booked for MRCP. Autoantibodies and viral serology negative
• responded to prednisolone but developed perforated DU, surgically treated but died. No PM.
• Conclusion: painless jaundice most likely drug related.
Case 249

- 37 F
- Liver biopsy – presented with non-specific illness/malaise. US – multiple lesions in liver, hydatid cysts, mets. Also has lesions in spleen
- Wedge biopsy – piece of tissue measuring 2.5x1x1cm. The cut surface shows irregular white foci.
Cased 249
Case 249
Case 249

49  abscess with actinomycosis
2  abscess with aspergillus
1  hydatid (saw hooklets)
4  abscess with no organisms mentioned
1  abscess with possible bacterial colonies

Comments:
? primary source of infection  7
? immunocompromised  8
? IUCD  7
Case 249

Scoring: reject responses that do not include actinomycosis

Discussion: Sufficiently characteristic for diagnosis of actinomycosis, although in real life would require confirmation by Gram and Grocott stains. The importance of mentioning actinomycosis was underlined by experience of a different case where this had been overlooked in original biopsy, resulting in multiple resections for unrecognized disseminated disease.
Case 250

- 58M
- Patient with ulcerative colitis on mesalazine (long term).
- Recent history of jaundice, AAT 1212; alk phos 230; total bilirubin 29;
- anti-smooth muscle antibody +++; antinuclear antibody 1:640; ferritin>2000; viral screen negative,
- no alcohol,
- no increase in collagen on connective tissue stains.
Case 250

58 hepatitis, of which:
   16 Hepatitis NOS
   6 cholestatic hepatitis
   14 acute hepatitis
   4 subacute hepatitis
   18 chronic hepatitis

7 no evidence of PSC
7 PSC a possibility
2 PSC/AIH overlap
2 alpha 1 antitrypsin deficiency
   (both also diagnosed autoimmune hepatitis)

Aetiology:

31 autoimmune most likely or only diagnosis
16 drugs most likely or only diagnosis
5 drugs/AIH equal
2 viral/drugs/autoimmune equal
1 viral or drug
8 autoimmune included in differential
13 drugs included in differential
9 autoimmune not mentioned
21 drugs not mentioned

8 answer implies awareness of association of autoimmune hepatitis in long term users of mesalazine
   (ref: Gut 99;44;886-8)

needs ERCP: 6
needs orcein  8
needs Perls  4
Case 250

**Scoring:** Responses that included hepatitis, aetiology of autoimmune and/or drug related accepted

**Discussion:** Terminology for Hepatitis as acute versus chronic – in this case there is no fibrosis and the inflammation is predominantly lobular, and the history is acute – therefore acute hepatitis would seem more appropriate. However, current terminology for autoimmune hepatitis is not to designate either acute or chronic, since these cannot be reliably be determined from histology, and acute presentations of autoimmune hepatitis are becoming well recognized.
Case 250

Discussion contd.

Aetiology – The presence of appropriate autoantibodies associated with hepatitic histology is sufficient for diagnosis of autoimmune hepatitis.

In this case portal tracts eosinophils are readily identified, whereas interface hepatitis with plasma cells is more difficult to find. Mesalazine is reported as causing chronic hepatitis with autoantibodies; whether Mesalazine had caused the hepatitis, could not be known, as steroids were given and mesalazine withdrawn at the same time.

(Ref: Deltenre et al. Mesalazine (5-ASA) induced chronic hepatitis. Gut 99;44;886-8).
Follow up

- Patient had been taking mesalazine for several years prior to presentation.
- The mesalazine was stopped after presentation.
- No other hepatotoxic drugs.
- ERCP not done.
- Perls stain negative.
- Good response to steroids, LFTs normal and have remained so.
Case 251

- 76 M

- Previous Dukes’ B carcinoma of transverse colon, 1 year earlier. Now has recurrence at ileo-sigmoid anastomosis. Site resected and solitary nodule ? metastasis seen in gallbladder bed and resected.

- Segment 5 liver: 62g wedge of liver measuring 7x4.5x3.5cm. WShite nodular lesion on cutting this measuring 2cm diameter. Firm white appearance.
Case 251
Case 251
Case 251

43  solitary necrotic nodule
6   infarcted nodular lesion ? metastasis
1   chemotherapy induced necrosis of metastasis
1   consistent with metastatic adenocarcinoma
1   fibrous nodule
1   infarcted pseudotumour
1   inflammatory pseudotumour
1   nodule with pigmented ghost cells ?? melanoma ?? adenoma
2   infarction , no malignancy

and steatosis  18
and steatohepatitis  2

differential includes post treatment metastasis  10
no evidence that this was a metastasis  19
? previous surgery (gall bladder)  4
? previous chemotherapy  13
lymphoma possible  2
needs ZN  2
needs reticulin  4
needs cytokeratin IHC  6
Case 251

**Scoring:** insufficient concensus for scoring

Discussion; Solitary necrotic nodule as originally described was a small hyalinised nodule with some surrounding pallisading histiocytes, believed to be attributed to parasitic infection. Thus different from the histology in this case, which is larger with clearly central necrosis that was originally cellular.

Participants have seen examples of post-chemotherapy metastases with this histology, although in the absence of any identifiable tumour morphology, an origin as metastatic carcinoma could not be confirmed. The history of previous chemotherapy was not available when slides were circulated.

Although the correct answer was tumour regression following chemotherapy, there was not sufficient consensus to allow scoring.
Case 251

Follow up

- Diagnosis: solitary necrotic nodule
- Dukes B adenocarcinoma resected 1 year previously, liver mets seen at that time.
- Oxaliplatin chemotherapy prior to liver resection;
- (the cholecystectomy was at the time of this liver resection, not previously)
- All of the nodule was blocked – no viable adenocarcinoma, subsequently immunohistochemistry shows no positivity for epithelial markers.
Case 252

- 58 F
- Abnormal liver function tests, alp phos 253, GGT 395.
- Autoantibodies negative apart from smooth muscle antibodies +++
- History of rheumatoid arthritis and thyroid disease. ?autoimmune hepatitis.
- -ve ZN on biopsy

- 3 fragments of liver, combined length 14mm
Case 252
Case 252

49 granulomas/granulomatous hepatitis, with further comment about aetiology
4 granulomatous hepatitis, no further comment
4 granulomas and ductopaenia
3 PBC as main diagnosis, with differential
1 PBC as only diagnosis without qualification

Aetiology:
32 sarcoidosis
21 TB must be excluded (stated in diagnosis box)
12 TB not mentioned anywhere or implied in comments
8 sarcoid/TB/PBC/drug with no preference
6 AMA –ve PBC a possibility
11 differential diagnosis includes drugs
4 granulomas associated with rheumatoid arthritis

Further information required:
ZN – lots
AMA 4
Orcein 4
CXR 3
Drug history 3
Case 252

**Scoring; Reject PBC as only diagnosis without qualification**

Discussion: Correct answer required recognition of granulomas, with some discussion of differential. The biopsy was not considered diagnostic of PBC without qualification. There are no mitochondrial antibodies. Definitive clinical diagnosis not yet available.
Case 252

Follow up:

• Diagnosis: Granulomatous hepatitis

• Multiple levels through the biopsy showed no evidence of bile duct damage associated with the granulomas

• Anti mitochondrial antibodies were negative
Case 253

- 56 M
- Hepatomegaly, GGT 450, alcoholic history
- 3 tan cores of tissue, from 7-20 mm
Case 253
Case 253

57 amyloid
1 no answer

(number of words in answer varies from 0 to 81!)

differential of light chain deposition disease, if Congo red negative 4
some comment on clinical differential diagnosis 25
Follow up:
Further investigation showed normal renal and cardiac function, no paraprotein or Bence Jones but there was immunoparesis and 10% plasma cells in marrow.
Referral to national amyloid centre for SAP scan confirmed uptake in Liver and Spleen and a high level of free AL light chain in blood.
He has been started on high dose chemo.