Liver Pathology Symposium
- medical livers

BDIAP meeting
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Case 1 sed

- 65/F Diabetic. Raised ALT, USS fatty. Fibroscan ? cirrhosis
- Retic, CAB
Diagnosis case 1

- Steatohepatitis
- Mild fibrosis
- In keeping with Non-Alcoholic Fatty Liver Disease
Case 2

- 52/M Background liver (sic).
- From records; Albumin 35, Bili 12, Alk Phos 173, ALT 58.
- Retic, EPSR, vic blue
Victoria Blue
Diagnosis case 2

- Cirrhosis
- Steatohepatitis with minimal steatosis
- F/I obese and diabetic
- C/W Non-alcoholic fatty liver disease
Scoring NASH

First up – *Brunt Am J Gastro* 1999, 0-3 for steatosis, inflammation and fibrosis.

Large USA group, *Kleiner Hepatology* 2005, **NAS score**, on 14 categories, with borderline cases. Problems – cries of misuse (*Hepatology* 2011) when tried to be used diagnostically – for **trails** and long term follow-up of NASH only.
Scoring NAFLD

• French group *Bedossa Hepatology* 2012, for spectrum of NAFLD, (when >5% steatosis), designed in morbid obesity.

• Algorithm to separate normal, NAFLD and NASH; validated in metabolic syndrome

**SAF score** – steatosis (0-3), activity (0-4; ballooning & inflammation), fibrosis (0-4)

• Correlated with diagnosis of NASH (activity >2) and ALT levels
SAF algorithm

Steatosis
(0,1,2,3)

0 → 0, 1, 2

1, 2, 3 → 1

0 ->

1

2

Ballooning
(0,1,2)

Lobular inflammation
(0,1,2)

0, 1, 2 →

0

1

2

0 → NAFLD

1 → NAFLD

2 → NAFLD

0 → NAFLD

1 → NASH

2 → NASH

0 → NAFLD

1 → NASH

2 → NASH

Diagnosis

No NAFLD
Our cases...

• Case 1 – S 2, A 3 (2+2), F 1

• Case 2 – S 0, A 3 (2+1) F 4
Case 3

• 53/M Jaundiced 2-3 weeks, ascites, bilirubin 354. TJ biopsy.
• CAB, orcein, PASD, Retic
PASD

Orcein
Diagnosis case 3

• Cirrhosis

• Steatohepatitis, cholestasis, regeneration (6 weeks abstinence)

• First presentation of Alcoholic liver disease with decompensation.
Case 4

• 42/F HCV. Clinically cirrhotic. Tissue confirmation please.

• EPSR, orcein
EPSR
Diagnosis case 4

• Cirrhosis
• Overall mild chronic hepatitic activity in keeping with chronic HCV infection
• With mild steatohepatitis
• F/I – patient also diabetic
Case 5

• 65/M Cryptogenic cirrhosis; nodules marked variation in size.
• All stains—apart from perls
PASD

Alpha-1 antitrypsin

PiZ antigen
Diagnosis case 5

• Cirrhosis
• Steatohepatitis, presumed NAFLD
• Abnormal phenotype for Alpha-1-antitrypsin (serum level in normal range)
Case 6

- 42/F known ALD ? AIH.
- Retic, orcein, EVG, EPSR
Diagnosis case 6

• Severe fibrosis, central hyaline sclerosis, regeneration
• Florid Steatohepatitis, with little steatosis
• Alcoholic liver disease
• No features of AIH

• F/I - IgG 14.2 (6.0-13.0g/l), IgA 4.4 (0.8-3.7g/l), IgM 1.1 (0.4-2.2g/l)
• ANA +ve weak, ANCA, SMA, AMA neg
Assessment of ASH

• Histology score to predict short term mortality, Altamarino Gastroenterology 2014

• Fibrosis – bridging/cirrhotic, bile in hepatocytes, canaliculae and ductules - poorer outcome; steatosis, MDB and ballooning – no affect; prominent PMNs and megamitochondria – positive affect.
Case 7

- 32/M Deranged LFT's. Hx of ETOH abuse, however more hepatitic picture. CLD screen -ve. Hx of anabolic steroid use.
- Retic, CAB, PASD
Diagnosis case 7

- Microvesicular steatosis, probably alcohol
- Cholestasis, probably drug.
- F/I – seizures with acute detox 3yrs later
Why biopsy in ALD?

- Anything to treat? A 2\textsuperscript{nd} diagnosis
- ASH or decompensation or sepsis or drug reaction when jaundiced?
- ? Evidence of drinking in transplant setting
Case 8

- 61/M Abnormal LFTs. Recently on Methotrexate, for rheumatoid arthritis. ??Primary Biliary cirrhosis.
- EPSR, orcein, perls, PASD
Perls

PASD
Diagnosis case 8

• Incipient cirrhosis, with little fat but ongoing steatohepatitis – possible alcohol of NAFLD

• Focal biliary features ? Risk factors

• F/I – Alk phos 225, ALT 31; denies alcohol, hi BMI, AMA pos, IgG, A & M up.

• Bx taken as USS fatty but AMA positive!

• ?dual diagnosis
Role of MTX as anti-rheumatic

• BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the BAD. *Chakravarty Rheumatology 2008.*

• Typical dose MTX 7.5-25mg per wk; possible toxicity related to cumulative doses > 1.5g

• Different with psoriasis – risk factor for metabolic syndrome
Case 9

- 67/M Deranged LFTs. ?NAFLD, heterogenous liver on US. Raised Alk phos.
- Retic, CAB, PASD, orcein
Diagnosis case 9

• Granulomatous cholangiopathy – probable Primary Biliary Cirrhosis

• No sig NAFLD features

• AMA negative

• AP 385 Alt 95, IgM 3.4 IgG 13.6 ACE Normal
AMA negative PBC

• Overall natural history is similar to AMA pos
• AMA +ve >90%, with specificity of 95% and non-specific ANA ~30% PBC
• Second order serology may be helpful if AMA -ve, nuclear and envelope antigens - anti-Sp100 and anti-gp210
Staging of PBC

• Related to ducts and fibrosis – Scheuer 1976, Ludwig 1978
• But biliary disease very irregular – staging not appropriate
• Recent Japanese proposal (also grade) Nakanuma pathol Int 2010, Histopathology 2014
  – Bile duct loss
  – Fibrosis
  – Copper associated protein *
Case 10

• 66/F Abnormal LFTs  Bili 25, Alk Phos 574, ALT 148, AMA weakly +ve, SMA -ve
PBC diagnosed 20yrs ago elsewhere.

• Retic, EPSR, orcein, vic blue, PASD, IHC CK7 CK19
orcein
Diagnosis case 10

- Primary Biliary Cirrhosis/ Autoimmune Hepatitis overlap, with cirrhosis

- F/I recently unwell, weight loss; IgG 29.6. Initial biopsy not available – biopsy
PBC/AIH overlap

• May be synchronous or metachronous; biochemical, serological and histological diagnosis – uncommon to rare

• Two out of 3 major criteria for both diagnoses need to be present (EASL guidelines)

• Florid interface activity

• Newer guidelines and 2nd order antibodies may help clarify.
Case 11

• 32/F Mass in liver ? cholangiocarcinoma. Wedge biopsy of non-lesional liver at time of laparoscopic staging.

• EPSR, orcein vic blue
Diagnosis case 11

- Primary Sclerosing Cholangitis with large sclerosed ducts

- F/I - Biopsy at time of diagnosis of cholangiocarcinoma near normal.

- Apparent history of PSC diagnosed several years previously but not being followed up...
Case 12

- 56/FAbdo pain, nausea, hepatosplenomegaly, ascites. Previous cholecystitis.
- Retic, CAB, PASD IHC PiZ
Diagnosis case 12

• Secondary biliary cirrhosis, with Alpha-1 Antitrypsin abnormal phenotype

• Cholecystectomy complicated by complex stricturing at 10yrs, with biliary sludge and stones i.e., an ischaemic cholangiopathy

• MZ phenotype
Case 13

• 30/M previous high alcohol intake, Coeliac disease ?cause of hepatosplenomegaly.

• EPSR, orcein,
orcein

EPSR
Diagnosis case 13

- Granulomatous cholangiopathy – possibly Sarcoidosis
- Coeliac diagnosis – secure; responded to gluten free diet
- Raised Alk Phos and severe pruritis. AMA negative
- Mediastinal lymphadenopathy, ACE >120 IU/l (20-70)
Spectrum of sarcoid in liver

• Predominantly portal involvement with fibrosis, +/- lobular granulomata
• Cholestatic – can be PBC like or PSC, about 1/3 with ductopenia (58%)
• Inflammatory – lobular +/- portal (41%)
• Vascular – granulomatous phlebitis portal or hepatic – NRH like, v rare BCS (20%)
• Mass forming – sarcoidoma (6%)

*Devaney Am J Surg Pathol 1993*
Case 14

• 51/F Laparotomy for portacaval shunt. Established cirrhosis - previous bx suggested Budd Chiari syndrome.

• EPSR, orcein, EVG, PASD
Diagnosis case 14

• Chronic Budd-Chiari Syndrome – hepatic vein and portal vein thrombosis with secondary biliary obstruction due to choledochal varices

• F/I Alk phos 679, ALT 54; previous bilirubin >100; ERCP, slight narrowing without stones = stented
Key Points

• Fatty Liver Disease is common – both alcohol and NAFLD

• Either may be an important secondary, or even primary pathology in patients being investigated for abnormality of liver function

• Liver biopsies may be tricky – are all features explicable by one diagnosis; does your report address the clinical query?
Key Points

• Biliary disease can be subtle, (and is frequently missed), but a raised Alkaline Phosphatase is a massive clue

• Less typical cases are increasingly being biopsied

• You need good quality histochemistry and Clinical Input to generate a helpful report.