LABORATORY TESTS AND DIAGNOSTIC PROCEDURES IN LIVER DISEASE

Adventures in Liver Land

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Prometheus
Serum Aminotransferases Levels Exceeding 500 IU/L

- Acute viral hepatitis
- Drug or toxic liver injury
- Ischemic hepatitis
- Severe C.A.H.
- CBD stone
- Budd Chiari and V.O.D.
- Acute Fatty Liver of Pregnancy and HELLP
- Wilson’s disease
Serum Aminotransferases

- AST : ALT greater than 2
- Both less than 300 IU/L

Characteristic of alcoholic liver disease
Serum Aminotransferases
Normal or Minimal Elevations Despite
Advanced Liver Disease

• Chronic HCV

• Idiopathic genetic hemochromatosis

• NAFLD
Serum Aminotransferases

AST and ALT elevated

Comprehensive blood work-up unrevealing

Liver biopsy normal

Muscle Source
A Quiz!

1. 42 year old “social drinker” with hepatomegaly
   A. AST = 2700 IU/L
      ALT = 3874 IU/L

2. 48 year old alcoholic with a recent history of headaches
   B. AST = 88 IU/L
      ALT = 41 IU/L

3. 26 year old with WPW syndrome and a prolonged bout of palpitations
   C. AST = 19,420 IU/L
      ALT = 16,748 IU/L
Celiac Sprue Can Cause Chronic “Unexplained” ALT Elevations

• 140 consecutive patients with a comprehensive negative serologic work-up studied.

• 13 patients (9.3%) had positive antigliadin and antiendomysial antibody tests. Duodenal biopsies consistent with sprue.

• Liver biopsies revealed non-specific changes.

• ALT and AST usually normalize on a gluten free diet.

Four Causes of “Unexplained” ALT (SGPT) Elevations

1. Muscle Disease/Injury (CPK)
2. Celiac Sprue (TTG antibody)
3. Adrenal Insufficiency (Cortisol)
4. Thyroid Dysfunction (TSH)
Very Low ALT Levels

A 57 year old male has a serum ALT of 4 IU/L. It is repeated and found to be 1 IU/L.

Choose the correct answer(s).

He likely has:
A) Chronic Renal Failure
B) Pyridoxine Deficiency
C) B12 Deficiency

Correct answer is A and B
Serum Alkaline Phosphatase Sources

1. Liver
2. Bone
3. Small intestine
4. Placenta
5. Other, e.g., Regan isoenzyme
What does cholestasis mean?
Serum Alkaline Phosphatase

- Patients with cholestasis have increased levels
- Level not helpful in distinguishing intrahepatic from extrahepatic cholestasis
- Rarely patients with hypernephroma and Hodgkin’s have elevated levels in absence of liver involvement
- Patients with Wilson’s disease often have normal or below normal values
Cholestasis may be seen rarely in patients with hypernephroma as part of a paraneoplastic syndrome. This is referred to as nephrogenic hepatic dysfunction syndrome or Stauffer’s syndrome. The cause is unknown but may relate to secretion of IL-6.
Rare Causes of Jaundice in Adults

1. Hypernephroma
2. Hodgkin’s (paraneoplastic phenomenon)
3. Amyloid
4. Hemobilia
5. Hepatic Artery Aneurysms
6. Bile Duct TB
7. Bile Duct Lymphoma
8. BRIC Syndrome
Serum Bilirubin

- Indirect, direct, delta
- “Isolated” hyperbilirubinemia
- Prognostic indicator
  - Alcoholic hepatitis
  - Halothane hepatitis
  - PBC
When Is Jaundice An Emergency?

1. Severe unconjugated hyperbilirubinemia in the newborn.

2. When patient has fulminant hepatic failure.

3. When patient has cholangitis.

4. When patient has massive hemolysis.
Alcoholic Hepatitis

Discriminant Function Value
Prothrombin time - Control x 4.6
plus
Serum bilirubin (in mg/dl)
Value > 32, mortality 50%!
Causes of low serum Albumin

1. Malnutrition
2. Liver disease
3. Nephrotic syndrome
4. Protein losing enteropathy
Serum Globulins

1. Increased IgG
   A. A young woman with abnormal LFT’s and arthralgias

2. Increased IgA
   B. A 42 year old salesman with hepatomegaly, spider nevi and AST of 112 IU/L

3. Increased IgM
   C. A 57 year old white woman with hypothyroidism and pruritis
Increased Serum Globulins

Answers

1. Increased IgG  Autoimmune Hepatitis

2. Increased IgA  Alcoholic Liver Disease

3. Increased IgM  Primary Biliary Cirrhosis
Serum Ferritin Elevated

1. Idiopathic genetic hemochromatosis
2. Hepatocellular necrosis
3. Hodgkin’s
4. Leukemia
5. Hyperthyroidism
6. Uremia
7. Rheumatoid arthritis
Cirrhosis is Very Unlikely in a Patient with Hemochromatosis If:

1. Patient <40 years old
2. No Hepatomegaly
3. Ferritin <1000
4. Normal AST and ALT
Remember

- Serum ferritin **may be normal** in pre-cirrhotic hemochromatosis.

- A patient with a ferritin in excess of 10,000 may turn out **not to have hemochromatosis**.
Liver Ultrasound

Hepatic lesions
Ascites
Gallstones
Jaundice
Gallstones: Ultrasound
Computed Tomography

Hepatic lesions

Jaundice

Budd-Chiari syndrome

Iron overload
Utility of CT: Liver Abscess
Utility of CT: Liver Abscess
The Roles of Imaging

- Detect
- Diagnose
- Stage
- Plan treatment
- Treat
Contemporary CT scanning helps plan surgical approach
CT: Virtual hepatectomy
“Ominous” imaging features

- Tumor thrombus
- Caval extension
Magnetic Resonance Imaging (MRI)

- Hepatic metastases
- Vascular lesions, e.g., hemangioma
- Hepatic and portal vein
- Iron overload
MRI: Hepatic Hemangioma
MRI: Clarity of Vascular Structures
Stigmata of Chronic Liver Disease
Stigmata of Chronic Liver Disease
A Medical Limerick!

An older Miss Muffett
Decided to rough it
And lived upon Whiskey and Gin
Red hands and a spider
Developed outside her
Such are the wages of sin

Dr. Bean
Continued …

But in spite of the teacher, physician and preacher, She could not be made to believe Icteric, anemic and hyperlipemic She developed the syndrome of Zieve!
Rupture of Umbilical Hernia
That one, with his swollen belly, is pregnant with his own death.

St. Jerome, c. 347 - 419 C.E.
34 year old woman

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<th>Date</th>
<th>Serum Alk Phos</th>
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Each lab value is…

WHAT’S THE DIAGNOSIS?
Eye Findings in Wilson’s Disease
Sunflower Cataract in Wilson’s Disease
Liver biopsy has been considered to be the Gold Test.

However, it is invasive, subject to sampling and on rare occasions there can be serious complications.

Is there a non-invasive alternative to evaluating the degree of hepatic fibrosis?
Sampling error of liver biopsy

Fibrosis area: 65%

Fibrosis area: 15%

Courtesy of M. Pinzani, Florence
Fibrotest (fibrosure)

Alpha 2 macroglobulin, haptoglobin, gammaglobulin, GGT, total bilirubin, apolipoprotein A1

The severity of disease was correctly identified in 46% of patients.

Am J Gastroenterol

Fibrosure. I am not so sure!
Fibroscan

Examination time < 5 minutes

Median value of 10 successful acquisitions

Sampling error
- Biopsy – 1/50,000
- Fibroscan – 1/500

Courtesy of N. Afdhal, MD
Hepatic Elastography

- Fibroscan is a rapid and non-invasive measure of hepatic stiffness
- Hepatic stiffness correlates with fibrosis

The probe induces an elastic wave through the liver

The velocity of the wave is evaluated in a region located from 2.5 to 6.5 cm below the skin surface

Sampled volume: 1: 500
Sampling

- Liver biopsy samples only $1/50,000^{th}$ of whole liver.

- Fibroscan samples $1/500^{th}$ of whole liver.
Advantage of Fibroscan

- Liver transient elastography obviates the need for inaccurate and invasive liver biopsies.
- The actual stiffness score can provide us with an accurate glimpse of staging cirrhosis on a continuum.
Emerging Scenario

Patients with suspected Liver Disease

Biomarkers and Fibroscan

Low likelihood of fibrosis
- No liver biopsy
- Follow or treat

Grey zone
- Liver biopsy

High likelihood of fibrosis
- No liver biopsy
- Screen HCC, varices
Deadly Mushroom

Amanita phalloides (Death Cap)
What did Big Ben say to the Leaning Tower of Pisa?

If you have the inclination, I have the time!