Evaluation of a Child with Elevated Transaminases

Linda V. Muir, M.D.
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Disclosures

• *I do not have a financial interest, arrangement or affiliation with medical/pharmaceutical/equipment companies.*
Liver Function Tests

- **Liver cell injury or inflammation**
  - AST, ALT, LDH
- **Synthetic function**
  - PT, PTT, INR, Albumin, clotting factors VII & V
- **Bile flow or cholestasis**
  - GGT and alkaline phosphatase, plus 5’ nucleotidase
- **Hepatic excretory function**
  - Bilirubin, serum bile acids
Case Study

- 17 year old male presented with 3 week history of fatigue, no jaundice, nausea, and malaise.
- Evaluation by his primary care provider revealed normal bilirubin, but elevated transaminases in the 900 - 1100 iu range.
- PT and INR were normal as was GGT
History

• Previously well, excellent student
• Dropped back in athletics due to fatigue
• Few pounds of wt loss attributed to poor appetite

• No family history of liver disease
• No exposures such as prior transfusions or travel outside the US
• Denied use of IV drugs
• No chronic medications or herbal use
Evaluation- Physical

• Physical exam
  – Normal vitals
  – Mildly icteric
  – Normal body habitus; no sign of chronicity
  – No K-F rings
  – Liver edge down 1.5 cm below RCM, normal texture, slightly tender; no splenomegaly
  – No skin lesions
Evaluation – Initial Laboratory

- CBC without anemia or evidence of hemolysis
- Platelets slightly elevated
- AST – 900, ALT – 1100
- Total protein 8.9, albumin 3.1
- PT and INR normal
- Alkaline phos & GGT were normal
- Bilirubin total and direct slightly elevated
Evaluation – Imaging

– Liver slightly enlarged for age, homogeneous and normal appearing texture
– Doppler of hepatic vessels was normal
– Spleen – no abnormality seen
Evaluation—Further Labs

- Serum copper and ceruloplasmin were normal
- Alpha 1- antitrypsin phenotype MM
- Viral screen was negative for hep A, B, C
  - EBV titers showed past infection
  - CMV screen negative
  - No hx of URI to warrant nasal swab
- Tylenol level normal
- Anti-bodies for LKM (liver, kidney microsomes) were normal, as was celiac screen
- Smooth muscle antibodies: 1:320
- IgG total was 2 times normal
Biopsy of Liver

- Many plasma cells & mononuclear cells
- Active hepatitis extending beyond the limiting plate
- No bridging fibrosis
- No viral inclusions seen
- No evidence of metabolic disorders
Therapy

- Immunosuppression
- Close monitoring
- Protection from future hepatic infections
Differential Diagnoses

- Autoimmune disorders
- Viral - hepatitis A, B, C, EBV, CMV
  - Adenovirus, coxsackie, varicella, HSV, HIV
- Metabolic – alpha 1- antitrypsin, Wilson’s
- Toxins – Tylenol, herbals, minocycline
- Non- alcoholic steatohepatitis (NASH)
- Vaccination induced - Synergis
Autoimmune hepatitis

– Two main types
  • Type I or classic with antibodies to smooth muscle
  • Type II with antibodies to liver-kidney microsomes

– Third type with antibodies against soluble liver antigens has been proposed
  • Some consider this as subset of AIH-I.

– There is also overlapping syndrome between AIH and sclerosing cholangitis.
Other Autoimmune Disorders -> Elevated Liver Transaminases

• Celiac disease
• Rheumatoid arthritis
• Inflammatory bowel disease
• Systemic lupus erythematosus
• Thyroiditis
Case II

• 12 year old boy presents to peds gi clinic with jaundice, weight loss, fatigue, intermittent fevers

• No family history of liver disease

• No unusual exposures – travel, meds, toxins, IV drugs, herbals or tattoos
Laboratory Evaluation

- Total and direct bilirubin mildly elevated
- High GGT and alkaline phosphatase
- Normal IgG total and antibody studies
- Normal coagulation studies
- Transaminases slightly elevated
- CBC notable for slight anemia
- Normal serum copper and ceruloplasmin
- Normal alpha1-antitrypsin phenotype
- Viral studies all negative, no prodrome
Evaluation- Physical

- Thin, small in height for age, and low wt for ht.
- Jaundiced
- Mildly tender over the RUQ and RLQ, no hepatosplenomegaly; no fluid wave
- No spider telangectasias
Further Evaluation

• Imaging- no hepatosplenomegaly by ultrasound, and normal vessel flow. No ductal obstruction or dilatation

• Liver biopsy – neutrophils in ductules, with profound expansion in the portal triads. No fibrosis.
Endoscopy and Colonoscopy

- Severe inflammation in the terminal ileum
- Biopsies confirmed Crohn’s disease
Therapy

- Treated for inflammatory bowel disease with steroids, Imuran and Pentasa
- Treated for bacterial cholangitis with antibiotics
Case III

- 8 year old hospitalized for malaise, nausea
- Found to have elevated AST and AST in 3000 range, mildly elevated bilirubin
- Coagulopathy

- No family hx of liver disease
History tells all

Medication – 2 months into therapy for TB

INH
Rifampicin
Streptomycin

Resolved with supportive care and modification of TB medication regimen
Evaluating Child with Elevated Transaminases

• History is critical for exposures
  – Medications
  – Herbals
  – Travel
  – Drug abuse
  – Tattoos
Obtain clear medication history

- Chronic Tylenol, especially if taking other medication such as phenytoin
- Minocycline/erythromycin
- Isoniazid esp when taken with rifampicin, streptomycin or ethambutal
- Vitamin A in excess
- Herbals – bush teas, comfrey,(alkaloids), kava kava, chaparral leaf, echinacea has some hepatotoxic potential.
Screening Priorities

- Viral- hepatitis A, B, C, CMV, EBV titers
  - Other viral studies as warranted, HSV, adenovirus, HIV
- Autoimmune – total IgG, antibodies to smooth muscle & LKM, IgA total & TTG
- Metabolic- Alpha 1- AT phenotype, ceruloplasmin & serum copper
- Toxin/medication- Tylenol level
- Ultrasound