

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 ALT 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