Liver Enzyme Elevation

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Case Presentation

- **NAFLD**
- **Other Causes**

  -hepatic

  -extra hepatic

NAFLD

- Hepatic steatosis
- Absence of secondary causes of hepatic steatosis
  - medication
  - alcohol consumption
  - parenteral nutrition
  - inborn errors of metabolism
- Absence of coexisting chronic liver disease

NAFLD

- ***Highly prevalent liver disease in children***
- ***The most common cause of liver disease in children***
- ***Not always benign form***
- **Usually after nine years of age**
- **Case reports ,as young as two years and cirrhosis as early as eight years**

Prevalence

- **Indirect evidence (ALT,imaging)**
  - **- indirect estimate of NAFLD**
  - **-poor sensitivity and specificity**
- **Definite Diagnosis**
  - **-approximately 7 % in the general population**
  - **-up to 34 % among obese children**

NAFLD Categories

- **Nonalcoholic fatty liver (NAFL)**
  without hepatocellular injury
- **Nonalcoholic steatohepatitis (NASH)**
  with inflammation , with or without fibrosis
- **Cirrhosis**

Clinical Presentation

- **Asymptomatic(the most)**
- **RUQ pain or nonspecific symptoms**
- **Obesity-associated comorbidities**
- **Rarely signs of ESLD**

SCREENING(NASPGHAN)

- All children with obesity
- Overweight children with other risk factors
- Between 9 and 11 years
- Measurement of ALT

Laboratory Evaluation

- **ALT elevation :*the best screening test for NAFLD in children***
- **Can also be normal, even with NASH**
- **limited sensitivity and specificity**
- **resolve with improve weight status**
- **only moderately helpful for presence or severity of NAFLD**

Measurement of ALT

- **ULN of 22 units/L for girls and 26 units/L for boys ?**
- ***Normal ALT***

  - repeat in 2-3 years (or sooner)
- ***Moderate ALT***

  -repeat within a few months, diet and exercise

Further Evaluation

- **Persistent elevation of ALT(>2 × ULN)**
- **Marked ALT elevations (ALT >80 units/L)**
- **Symptoms suggesting acute liver disease**
- **Red flags for advanced liver disease**

Red Flags

- Chronic fatigue
- GI bleeding
- Jaundice
- Splenomegaly
- Firm liver on examination
- Enlarged left lobe of the liver
- Low platelets, low WBC
- Elevated direct bilirubin
- Elevated INR
- Long history of elevated liver enzymes (>2 years)

- ***AST and GGT***

  -not independently tests as screening

  -higher AST (AST/ ALT ratio >1)

  and GGT with worse histology

- ***Elevated AST or GGT in the context of normal ALT***

Testing for additional comorbid conditions

- **Dyslipidemia**
- **Type 2 diabetes**
- **Hypertension**
- **Renal impairment**
- **Obstructive sleep apnea**
- **Vaccination**

- ***Increased prevalence of chronic kidney disease***
- ***Pediatric patients with NAFLD yearly with serum BUN, creatinine, urine albumin-to-creatinine ratio***

Not recommended for screening

Ultra sonography

- **Poor sensitivity and specificity**
- **severe abdominal adiposity can interfere with sonographic quality.**

Ultrasonography

- **Determination or quantification of steatosis ?**
- **Assessing other causes of liver disease (masses, gallbladder disease, PHT)**
- **Use of CT for determination or quantification of steatosis ?**

MRI

-More accurate quantitative measure of steatosis

-Not useful for screening

-Severity of hepatic steatosis does not correlate with clinical features of advanced NAFLD

Ultrasound Elastography

- For grading of fibrosis based on liver stiffness
- For grading of hepatic steatosis
- Closely correlation with significant fibrosis in pediatric patients with NAFLD
- High technical failure rates in patients with obesity

MRE

- **Noninvasive screening for liver stiffness**
- **Effective for advanced fibrosis (accuracy of >90%) including in severely obese patients**
- **Not able for no fibrosis versus mild fibrosis**
- **?? For detection of inflammation**
- **High cost, lack of widespread availability, and need for further validation**

Magnetic Resonance Spectroscopy

- **Quantification of hepatic fat**
- **Particularly helpful with small amounts of hepatic steatosis**
- **Not routinely used**

Liver biopsy

- **Definitive diagnosis of NAFLD**
- **The most accurate approach for severity , extent of inflammation and fibrosis**
- **Other causes of liver disease other than NAFLD**
- **Not always necessary for clinical management**

Liver biopsy

- **Increased risk of NASH**
- **Advanced fibrosis**

  -Higher ALT (>80 U/L)

  -AST/ALT >1

  -GGT elevation

  - Red flags (splenomegaly)

Liver biopsy

- **More severe or progressive liver disease**
  - **-ALT persistently >80 units/L**
  - **-splenomegaly**
  - **-thrombocytopenia**
  - ***- serum ferritin >1.5 times ULN(suggestive of NASH and advanced fibrosis)***
  - **-increased liver stiffness by elastography**
- **Alternate cause of the liver disease**

MANAGEMENT

- **Weight loss**
- **The only established treatment**
- **The primary treatment recommendation in guidelines**
- **Lifestyle modification**

MANAGEMENT

- ***Physical activity may improve NAFLD (ALT), independent of weight loss.***
- **Limit screen time to no more than two hours per day.**

Pharmacotherapy

- No medication for routine treatment of NAFLD
- Vitamin E:may has beneficial effects on some serologic and histologic markers
- No data on long-term outcomes
- Some concerns about long-term safety

Vitamin E

- **Steatosis alone (minimal inflammation) : against treatment**
- **Biopsy-proven NASH (with or without fibrosis)**
- **No response to lifestyle intervention**
- **Suggest to treat**
- ***Monitoring with ALT every 3 months***
- ***significant sustained decline in ALT (eg, at least a 50 percent decline in ALT during the first three to six months)***
- **Repeat liver biopsy at the end of a two-year**
- **Do not recommend treating for more than two years**

Pharmacotherapy

- **Ursodeoxycholic acid**
- **Probiotic supplements**
- **Omega-3 fatty acid supplements**
- **Metformin**
- **…**
- **Follow-up**


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