AN INTERESTING CASE OF LIVER FAILURE

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HISTORY

• Ms. A, a 9 year old girl,
• First born of non consanguineous marriage
• From Tripura
• Intermittent fever for 15 days and yellowish discoloration of the sclera for 10 days
• No history of diarrhoea
• No history of abdominal pain
• No history of high grade fever with chills, anemia, vomiting, abdominal distension
• No history of seizures
• No history of TB contact
• No history of encephalopathy/ sleep disturbances
• No history of GI bleeds(hematemesis/ melena)
• No history of edema
• No history of any treatment (herbal supplements) given outside

• No history of recent blood transfusion, needle stick injury
• She was the first born of non consanguineous parents
• No family history of liver diseases/ deaths.
• Antenatal period / Perinatal period was uneventful
• Vaccination as per the national immunisation program
ON EXAMINATION

- Alert, GCS-15/15
- Icteric
- No stigmata of chronic liver disease
• Liver palpable 4cm below the right costal margin, firm, smooth surface, margins well felt
• Spleen palpable 1 cm below the left costal margin
• No KF ring (s/b ophthalmologist)
SYNOPSIS

• 9 year old girl with fever and jaundice of recent onset, with mod Hepatomegaly with no overt bleeds or encephalopathy
INVESTIGATIONS

- Hb-13.1
- TC-8600
- PLt-3.29
- PT-31/11
- INR-2.8
**LIVER FUNCTION**

- **Total bili** - 26.5 (upto 1mg/dl)
- **Direct bili** - 18.2 (upto 0.2mg/dl)
- **Total protein** - 6 (6-8g/dl)
- **Albumin** - 3.6 (3.8-5.4g/dl)
- **SGOT** - 975 (15-55U/L)
- **SGPT** - 725 (5-45U/L)
- **ALP** - 376 (<300U/L)
**WORK UP TOWARDS ETIOLOGY**

- Hepatitis A IgM - negative
- Hep B surface Ag - negative
- Hep E IgM - negative
- Hep C RNA PCR - negative
- CMV/ EBV/ Lepto IgM - negative
- Serum copper - 96.9 (90-190)
- IgG was elevated - 1930 (400-1590)
• USG abdomen – mildly enlarged liver, prominence with thickening of intra hepatic biliary radicles in both lobes. Multiple, enlarged peripancreatic and periportal LN noted, s/o active hepatitis

• Bilateral renal pelvic prominence, rest normal
- Cultures: no growth
- ANA: negative
- ANCA: negative
- ASMA: negative
- Liver biopsy: deferred in view of high PT /INR
THE DIAGNOSTIC INVESTIGATION??

Liver

Immunity
• DCT - positive
• Anti LKM - positive
• Anti LC-1 - positive
• Anti M2-PDH - negative
• Anti SLA - negative
DIAGNOSIS

- AUTO IMMUNE HEPATITIS
DEFINITION

chronic hepatic inflammatory process
• elevated serum aminotransaminase concentrations
• liver associated serum autoantibodies
• hypergammaglobulinemia
EPIDEMIOLOGY

- INCIDENCE: 1.9 cases per 100,000 persons per yr
- PREVALENCE: 16.9 cases per 100,000 persons per yr
- Females account for 70% of cases, 50% ≤ 40 years
- Cause of chronic liver disease: 11-23%
- AIH accounts for 2.6% and 5.9% of liver transplants in Europe and U.S. respectively
NATURAL HISTORY

- Severe disease (untreated)
  - 40% die within 6 months of diagnosis
  - 40% of survivors develop cirrhosis
  - 54% of cirrhotics develop varices within 2 years of diagnosis of cirrhosis
  - 20% of patients with varices will bleed
PATHOGENESIS

AIH

- Triggering factors
- Genetic factors
- Autoantigens
- Immuno-regulatory
- Genetic factors
  - Antigen presentation/immunocyte activation
  - DRB1 encodes for MHC II antigen binding grooves (antigen presentation to T cells)
- Triggering factors
  - Infections (HAV, HBV, HCV, HSV, EBV, measles)?
  - Medications (ABX, statins, NSAIDs etc.)?
- **Antibody-dependent cellular cytotoxicity**
  - Antibodies directed against ASGPR
  - Suppressor T cell defect
  - Binding of NK cell to antigen-antibody complex followed by hepatocyte destruction

- **Cell-mediated cytotoxicity**
  - IL-12 and IL-2 released
Biochemical

Gamma globulin
Autoantibody

Histological

Interface hepatitis
Portal plasma cell
# INTERNATIONAL AUTO IMMUNE HEPATITIS GROUP CRITERIA

- Gender
- AP/AST, ALT ratio
- Serum globulins/IgG
- ANA, ASMA, LKM-1
- AMA positive
- Viral serologies
- Drug history/Alcohol intake
- Liver histology
- Other autoimmune diseases
- HLA DR3/DR4
SIMPLIFIED CRITERIA

- Autoantibodies
  - ANA, ASMA, LKM-1, SLA

- IgG
  - Typically elevated in autoimmune hepatitis

- Histology
  - Interface hepatitis, lymphocytic or lymphoplasmacytic infiltrate, rosettes
AIH TYPE 1

- Age: 10-20yrs
- Female: 78%
- γ-globulin elevation: marked
- Autoantigen: asialoglycoprotein receptor?
- Autoantibodies: ANA, ASMA
  - Others: pANCA, actin, ASGPR, SLA/LP
- HLA: A1, B8, DR3 or HLA DR4 serotypes
- Extrahepatic autoimmune disease: 15-40%
AIH TYPE 2

- Age: 2-14 years
- Female: 90%
- γ-globulin elevation: Mild
- Autoantigen: CYP450 IID6
- Autoantibodies: LKM-1
  - Others: LC-1, SLA/LP

Extrahepatic autoimmune disease: 40%

Severity: more severe than type 1?
HISTOLOGY

- Piecemeal necrosis *(interface hepatitis)*
- Panacinar inflammation or collapse
- Lymphoplasmacytic infiltrates
- Eosinophils
- Rosette formation
- Fibrosis or cirrhosis
- Absence of portal lymphoid aggregates and steatosis
SEVERE DISEASE

- AST ≥ 10 NORMAL
- AST ≥ 5 NORMAL + IgG >2 NORMAL
- Bridging necrosis
- Multilobular collapse
- HLA B8, DR3
- African American males

MORTALITY WITHOUT LIVER TRANSPLANTATION

- 50% at 3 years
- 90% at 10 years
HITOLOGY AND PROGNOSIS

- Interface hepatitis
  - 17% risk of cirrhosis at 5 years
  - Normal survival

- Bridging or multilobular necrosis
  - 82% risk of cirrhosis at 5 years
  - 45% 5-year mortality

- Cirrhosis
  -
TREATMENT OPTIONS

IMMUNOSUPPRESSANTS

- STEROIDS
- AZATHIOPRINE
• Prednisone
• initial dose of 1-2 mg/kg/24 hr - UNTIL aminotransferase values return to less than twice the upper limit of normal.
• The dose should then be lowered in 5 mg decrements
• over 2-4 mo until a maintenance dose of 0.1-0.3 mg/kg/24 hr is achieved.
SECOND LINE AGENTS (CENTRE BASED PROTOCOL)

- Mycophenolate
- Cyclosporine
- Tacrolimus
- Budesonide
- Methotrexate
- Cyclophosphamide
REMISSION

- Disappearance of symptoms
- Normalization or near normalization of AST to < 2 normal
- IgG and bilirubin: normal
- Minimal or no hepatic inflammation
- 65% and 80% of patients within 18 months and 3 yrs of initiation of Rx, respectively

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TREATMENT END POINTS

- Disease remission
- Relapse after treatment withdrawal
- Treatment failure
- Incomplete response
- Drug toxicity
LIVER TRANSPLANTATION

- In End-stage liver disease
- In Fulminant liver disease

- Results
  - 5 yr pt and graft survival: 80-90%
  - Recurrence: 15-40%
COURSE OF MS A.

- Clinically well
- Started on 2mg/kg prednisolone – slowly tapered and is on 0.2mg/kg/day dose
- On follow up for 9 months now.
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<th>Test</th>
<th>Value</th>
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<td>Total bili</td>
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<tr>
<td>Direct bili</td>
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<td>Albumin</td>
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TAKE HOME MESSAGE

- Clinical presentation is variable
- Diagnosis based upon LFTs, serology, gamma globulins, and histology
- Early diagnosis is crucial (death if undiagnosed)
- Timely referral to the specialist (esp acute liver failure or coag not correcting with vitamin k)
THANK YOU