



Pathology of Autoimmune Liver Diseases

Autoimmune Liver Diseases-

- √Autoimmune Hepatitis -
- √Primary Biliary Cirrhosis -
- √Primary Sclerosing Cholangitis -
- √Overlap Syndrome -

Autoimmune Hepatitis-

Chronic progressive inflammatory liver disease characterized histologically by interface hepatitis, the presence of circulating liver-related autoantibodies in the serum and increased levels of IgG in the absence of unknown etiology

Classification of AIH -

- Type 1 AIH (SMA/ANA-
- Type 2 AIH (LKM-1-
- Type 3 AIH (anti-LA/LP-

Diagnostic Criteria for AIH -.

Exclusion of genetic diseases -

A1ATD, Wilson's Ds, Iron overload

Exclusion of viral infection -

No bl. Transfusion, -ve anti-HCV(HCV-RNA)

-ve HBsAg, -ve IgManti-HBc, anti-HAV, EB, CMV -

Exclusion of toxic injury

No exposure to drugs or chemicals

Limited daily alcohol < 35g in men, 25g in w

Inflammatory indices -

Predominant s. aminotransferase abnormalities -

Immunoglobulins IgG>1.5 normal -

Autoantibodies titre>1:80 adults, 1:20 children -

Histological features: absence of biliary injury -

Type 1 AIH -.

Circulating auto antibodies -

Smooth muscle antibody SMA

&/or antinuclear antibody ANA

Hypergammaglobulinaemia -

Concurrent immune disease

Human leucocyte antigen

HLA DR3or DR4

Type 2 AIH -.

Circulating autoantibodies

Liver/kidney microsome type 1

Occur in younger age (children 2-14y

adults may be affected

Concurrent immune disease: vitiligo, IDDM, AI-thyroiditis, Rhd arthritis, ulcerative colitis

Hypergammaglobulinaemia is less pronounced

Progress more rapidly to cirrhosis

Type 3 AIH -.

Circulating autoantibodies -

Soluble Liver antigen/liver pancreas

(anti SLA/LP)

Female: Male 9:1 -

Mean age 37y (17-67y)

Have no difference with type 1 AIH regarding

HLA phenotyoe, Clinical, lab. Findings, Response to corticosteroids

May be a variant of type 1 AIH

Histological Diagnosis-.

Interface hepatitis: a constant feature -

Lymphoplasmacytic inflammation -

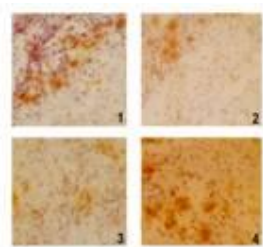
Spotty necrosis -

Panlobular necrosis -

Bridging necrosis -

Other histological features -

Perivenular necrosis Giantcell multinucleated hepatocytes

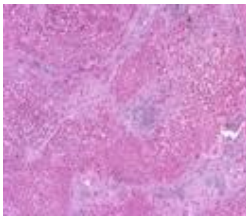
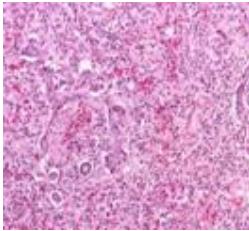
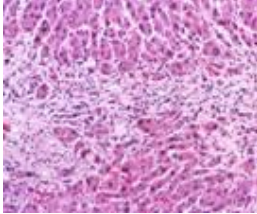


:interface hepatitis (interferon gamma -

: lymphoplasmacytic infiltrate (Th2 cytokines -

:Fibrosis (TGF bet -

: spotty necrosis (TNF alpha -



Value of Needle liver biopsy in AIH -.

To establish the diagnosis -

To assess severity of the disease -

To examine response following treatment -

To exclude Wilson's disease -

To test for HBV markers -

To determine whether cirrhosis is present -

To predict prgnosis-

IH 17% develop cirrhosis in 5 y -

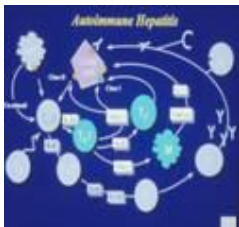
Bridging necrosis 82% develop cirrhosis in 5y -

CD4 +ve T cells recognising a self antigenic peptide, The peptide must be embraced by HLA class II and presented to uncommitted T h cells

Costimulatory molecules on APC interaction activation of uncommitted T h cells

differentiation of T cells to functional phenotypes Th1 cytokines activation of macrophage, NK

Th2 cytokines activation of plasma cells



Characterized by progressive destruction of small intrahepatic bile ducts, chronic cholestasis, biliary fibrosis & cirrhosis

Seropositive for AMA -

Female: Male 9:1 -

Age range 20-80 y -

Family predisposition -

HLA-DR8-

Stage 1: florid duct lesion -

Random, florid focal destruction of septal and interlobular bile ducts, surrounded by dense infiltrate of lymphocytes, plasma cells, histiocytes. Granulomas +/- ,Cholestasis

Stage 2: ductular proliferation -

bizzare shaped ducts, infl. Infiltrate extends to parenchyma, IH, Cholestasis, Mallory bodies

Stage 3: Fibrosis -

infl. Infiltrate is less prominent, replaced by fibrosis -

Stage 4: Cirrhosis -

Fibrous septa have bridged portal areas enclosing micronodular cirrhosis -

Autoimmune basis of PBC-

**Bile duct epithelium express increased amount of HLA-A,B,C,DR antigens making them the prime targets for the immune reaction
Circulating autoantibodies**

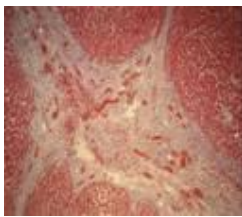
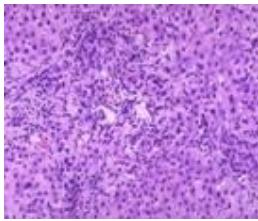
AMA (95% of pts

Increased level of circulating immune complexes -

Increased levels of serum immunoglobulins -

Decreased number of circulating T cells (h, c-

Chronically activated complement system -



PBC: florid duct lesion

ductular proliferation

Primary Sclerosing cholangitis -

Chronic autoimmune disease of the biliary tree with abundant periductular fibrosis with shrinkage and subsequent loss of bile ducts

Extrahepatic and large intrahepatic bile ducts are encircled and collapsed by periductular fibrosis

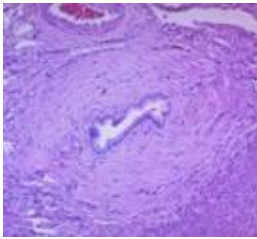
Portal tract show edema, bile stasis -

Cholestatic biochemical changes -

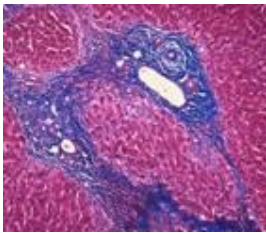
Usually associated with ulcerative colitis -

Male predominance 2-3:1 -

Circulating antibodies against cytoplasmic constituents of neutrophils (ANCA-



Sclerosing cholangitis



Sclerosing cholangitis

AIH-PBC overlap syndrome -.

Characterized by clinical features of AIH with PBC like features -

AMA +ve -

Cholestatic biochemical findings -

Histology: -

infl. infiltrate around hepatocytes and bile ducts

portal & periportal lymphoplasmacytic infiltrate

bile duct loss, destructive cholangitis

AIH-PSC overlap syndrome -.

Characterized by SMA/ANA +ve, interface hepatitis, hypergammaglobulinaemia

Cholestatic biochemical findings -

Inflammatory bowel syndrome (ulcerative colitis-

Histology: -

fibrous obliterative cholangitis

portal tract edema, bile stasis

bile duct loss

Resistant to corticosteroid therapy

AIH-chronic viral hepatitis overlap syndrome -.

Characterized by SMA/ANA +ve, titre > 1:320 with a true viral infection (most common HCV

Corticosteroids enhance viral replication -

Interferons intensify immune reactivity -

Histological examination direct treatment against the predominant manifestation

- (virus versus autoimmune

Autoimmune cholangitis -.

Characterized by SMA/ANA +ve -

Histological evidence of bile duct injury and cholestatic picture -

Absence of AMA -

Normal cholangiogram

Nermine A. Ehsan

Assistant Professor of Pathology

National Liver Institute

Menoufiya University

