AUTOIMMUNE CHALLENGES IN HEPATO BILIARY MEDICINE

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- Auto immune hepatitis
- Epidemiology
- Clinical Presentation
- Diagnostic Evaluation
- Treatment
- Prognosis

DEFINITION

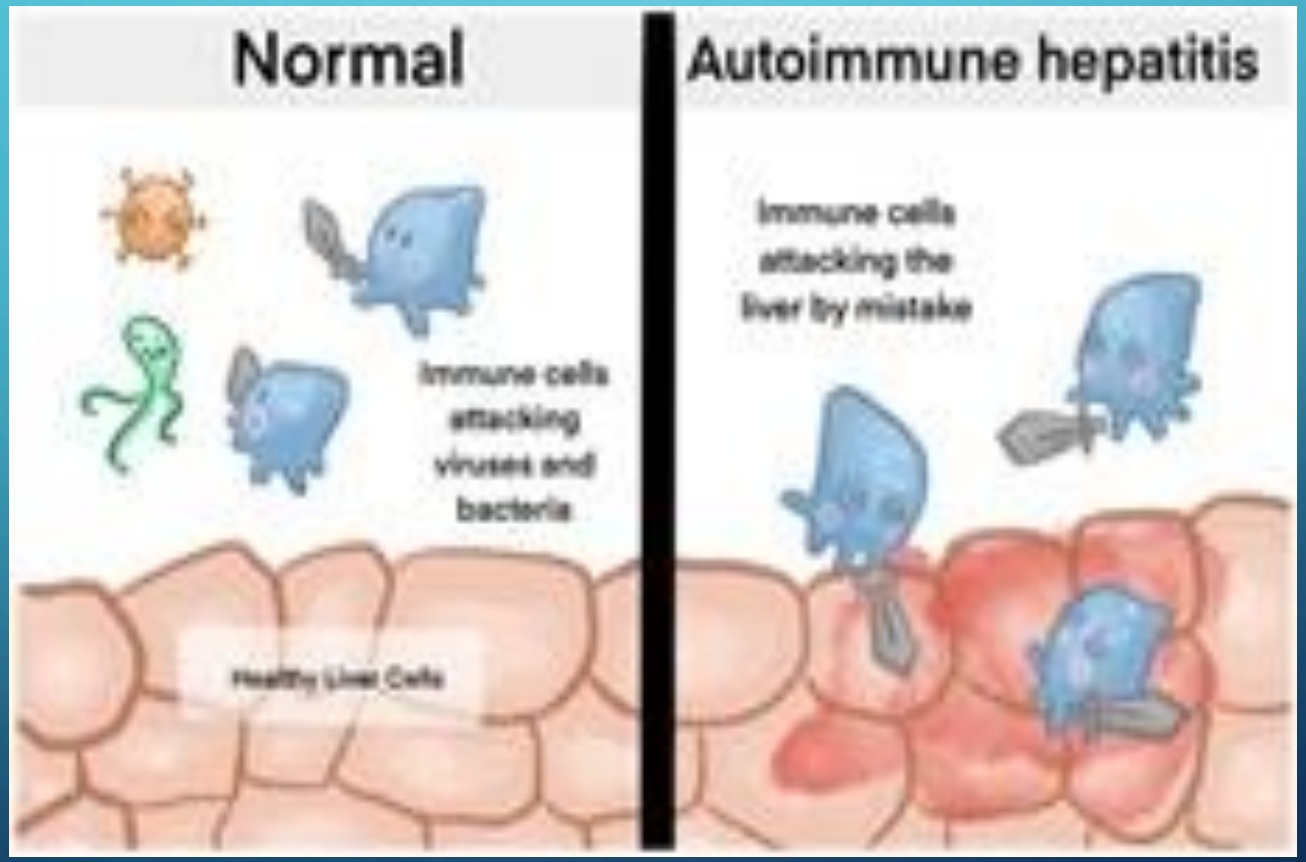
- Autoimmune hepatitis is a chronic inflammatory disease,generally characterized by circulating autoantibodies and elevated serum globulin level.
- The disease may start as acute hepatitis and may progress to chronic liver disease and Cirrhosis.
- Can occur at any age and ethnic group, predominantly affects female.

EPIDEMIOLOGY

- Mostly Females are affected (F : M = 4–10 : 1
- Worldwide incidence of AIH is 0.7 – 2.0 per 100,000
- Prevelence is 4 – 25 per 100,000

- AIH can occur at any age , however
- The age of presentation is bimodal

  2nd Decade and 5th to 6th Decade

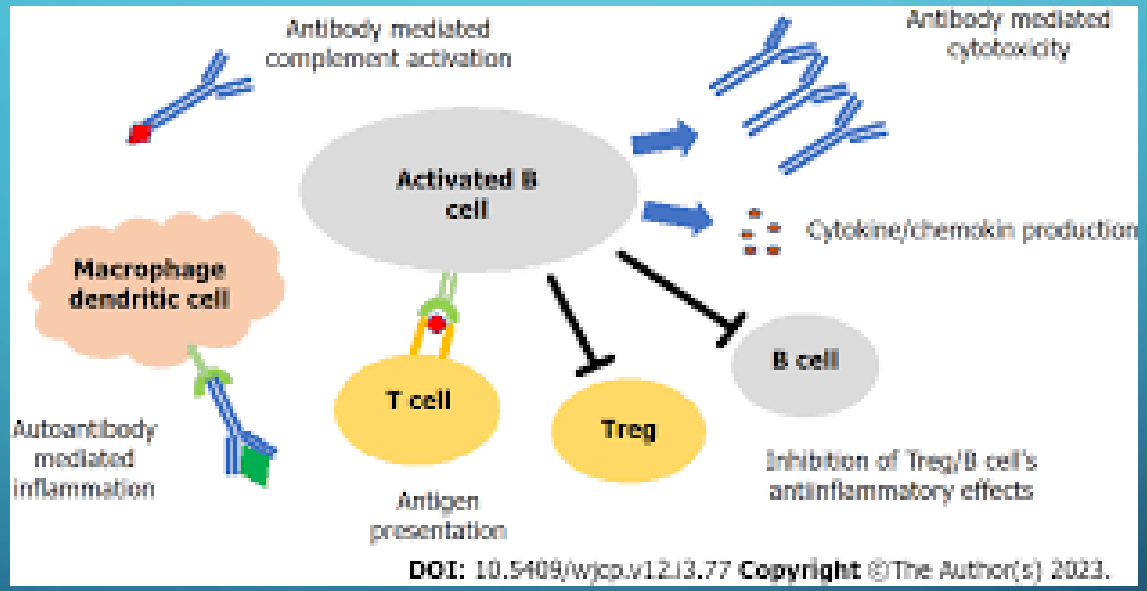

Normal
Autoimmune hepatitis
Immune cells attacking viruses and bacteria
Immune cells attacking the liver by mistake
Healthy Liver Cells

Classification

is based on type of autoantibodies:

- Type 1
  - positive ANA and ASMA (classic form, responds well to steroids)
- Type 2
  - positive LKM-1 (typically female children and teenagers; disease can be severe), LKM-2 or LKM-3;
- Type 3
  - positive antibodies against soluble liver antigen(anti-SLA)
- Type 4
  - No Autoantibodies detected (~20%)

- Mainly Two types of AIH – Type 1 and Type 2.
- Type 1 AIH is associated with ANA, ASMA, AAA, other autoantibodies like p-ANCA,
- Type 2 AIH is associated with AKLM-1 and or ALC-1.
- Overlap syndromes can occur with features of both autoimmune hepatitis and primary biliary cholangitis or primary sclerosing cholangitis.



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- AIH is caused by environmental trigger in a genetically predisposed individual.
- At molecular level it is thought to be the antigen,MHC complex and T cell receptors.
- Viruses drugs ,herbs and immunization have been suggested as triggering agents.

- Most evidence suggests a central role for an alteration in T cell function , alteration in B cell function is also important.
- Escape from normal suppression of self reactive T cells, which results in ongoing inflammation and necrosis.

CLINICAL FEATURES

- AIH may present as

  Acute Hepatitis

  Cirrhosis

  Acute Liver Failure

  Acute or Chronic Liver disease with fluctuating Pattern

  Some pt asymptomatic, vague ill health.


Risk Factors for Autoimmune Hepatitis
TYPE 1 DIABETES
SCLEROSING CHOLANGITIS
RHEUMATOID ARTHRITIS
ULCERATIVE COLITIS

- AIH may present with some Extra hepatic disease Like

  Autoimmune Thyroiditis

  Rheumatoid Arthritis

  Type I DM

  Ulcerative Colitis, Celiac Disease

  SLE

- Skin Lesions associated with AIH
- Can occur anytime in the course of disease
- Rashes seen 8-17% of patients

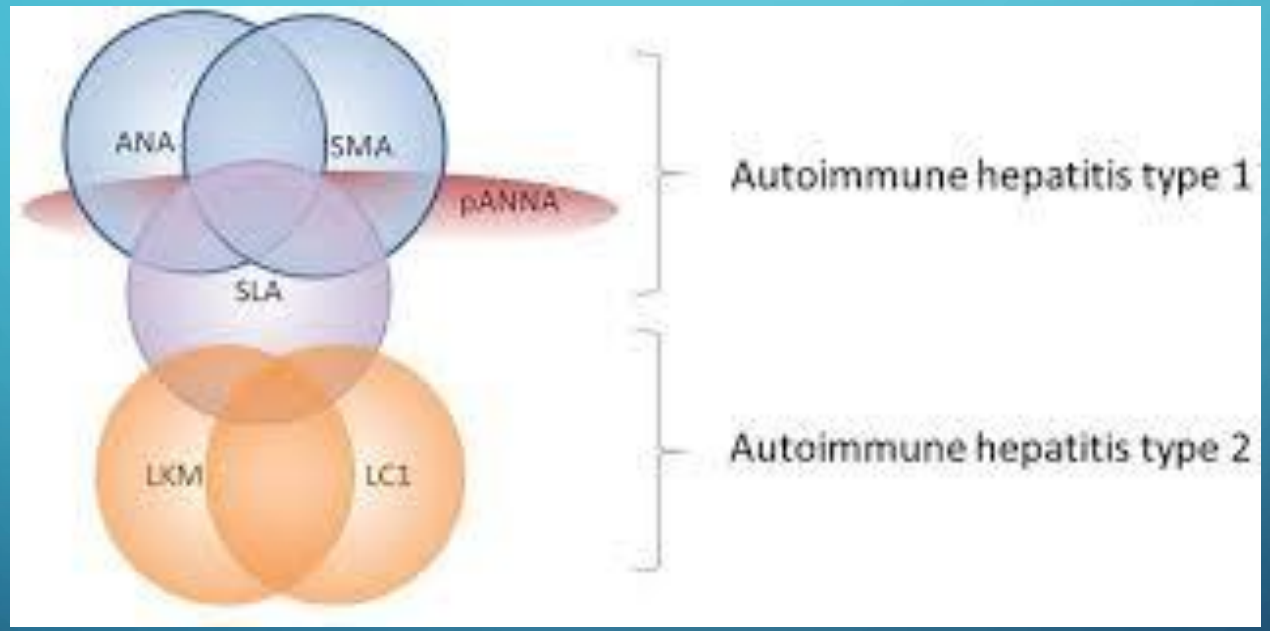
Most Commonly as transient and nonspecific Maculo popular rash

over the Face ,Trunk, Upper arm.

Associated Skin Lesion may be Psoriasis,Vitiligo,Urticaria,Acne,Lichen Planus,Erythema Nodosum and Pyoderma Gangrenosum.

INVESTIGATIONS

- Liver Enzymes
- In Acute Presentation ALT,AST may exceed 10 to 20 times
- Ratio of Alp to ALT/AST 1.5 to 5 times
- Gamma globulins Increase in gamma globulins
- Auto Antibodies
- ANA titre of 1:80 to 1: 100 or more is significant.


ANA
SMA
pANNA
SLA
LKM
LC1
Autoimmune hepatitis type 1
Autoimmune hepatitis type 2

- ASMA in the titre 1:80 or more is significant
- ASMA more than 1:320 reflects presence of AAA.
- Anti SLA/LP found in 10- 30% pts.
- ANCA found in some patients.
- AMA found in 8-12% cases
- Anti DNA antibodies can be found in some pts.

- Histology: Portal Mononuclear cell infiltrate

  Periportal lesion(piecemeal or Interface hepatitis)

  Bile duct changes Ductal injury or ductal destraction

>80% pt.

  Plasma cell infiltrate,rosettes of hepatocytes

  Some degree of fibrosis.

DIAGNOSTIC CRITERIA

- In a pt with compatible clinical presentation
- AST and/ALT at least 2 times the upper limit.
- A minimum of one +ve lab test, Increased IgG and or ANA,ASMA at a titre of at least 1: 40.
- Exclusion of disease that have similar clinical presentation like Acute viral hepatitis,drug induced liver injury and Alcoholic liver disease.
- Liver biopsy

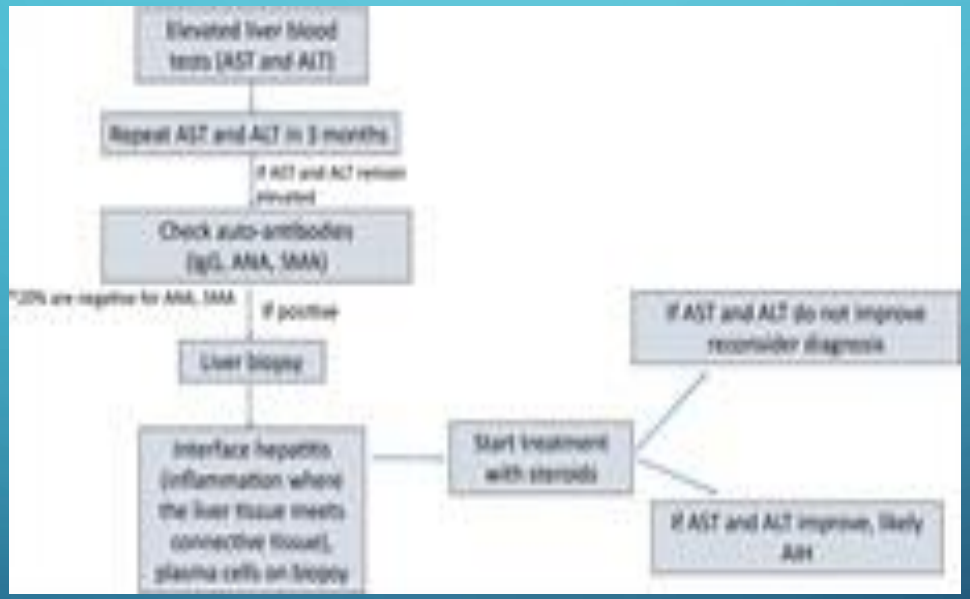
Feature/parameter	Discriminator	Score
ANA or SMA+	≥1:40	+1*
ANA or SMA+	≥1:80	+2*
or LKM+	≥1:40	+2*
or SLA/LP+	Any titer	+2*
IgG or γ-globulins level	>upper limit of normal >1.1x upper limit	+1 +2
Liver histology (evidence of hepatitis is a necessary condition)	Compatible with AIH Typical of AIH Atypical	+1 +2 0
Absence of viral hepatitis	No Yes	0 +2

DIAGNOSTIC SCORING SYSTEM

- Based on
- Autoantibodies ANA/ASMA 1:40 Point 1. Titre 1:80 point 2.
- IgG titre > 1:10 Point 2.
- Liver histology Histologic features compatible with Auto immune hepatitis Point 1. Auto immune hepatitis typical histologic pattern Point 2.
- Absence of viral hepatitis: Absence of viral hepatitis Point 2.

- Probable Diagnosis if scoring is 6.
- Definitive diagnosis is if scoring is equal or more 7.


Autoimmune Hepatitis: Tenets of Dis
AIHA

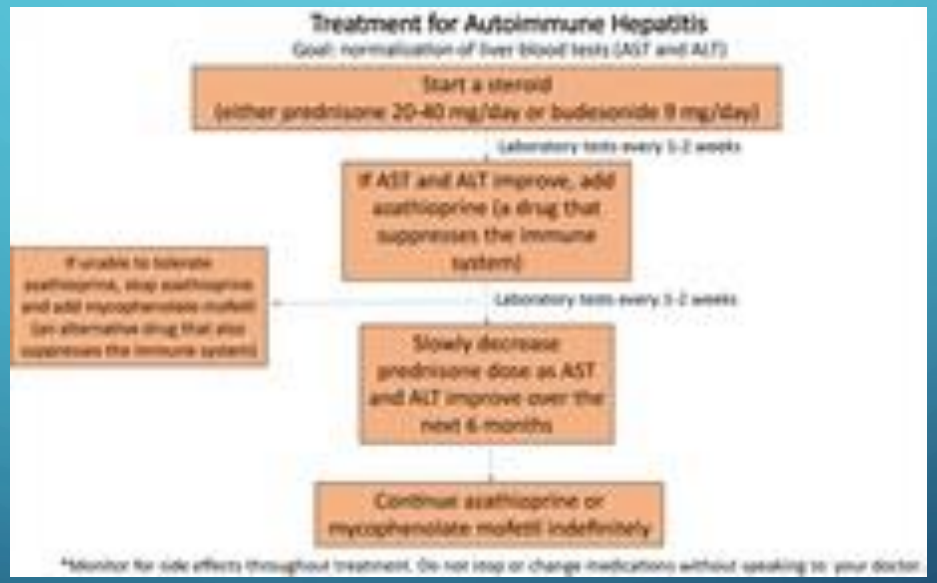

Elevated liver blood tests (AST and ALT)
Repeat AST and ALT in 3 months
Check auto-antibodies (IgG, ANA, SMA)
If positive
Liver biopsy
Interface hepatitis (inflammation where the liver tissue meets connective tissue), plasma cells on biopsy
Start treatment with steroids
If AST and ALT do not improve reconsider diagnosis
If AST and ALT improve, likely AIH

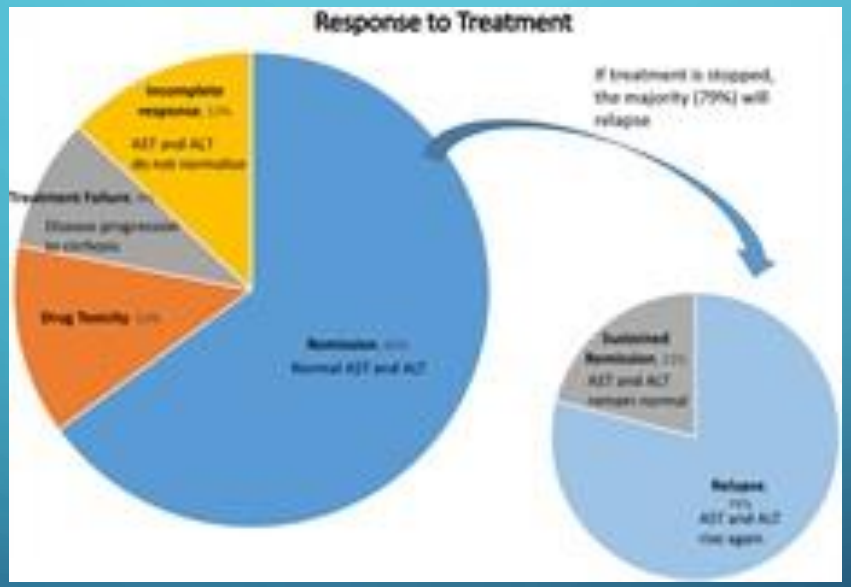
DIFFERENTIAL DIAGNOSIS

- Primary biliary cholangitis
- Overlap syndrome
- Other causes of Hepatitis ; Viral Hepatitis, Drug Induced liver injuryNASH,SLE associated liver disease. Acute Liver Failure, Iron overload.

TREATMENT

- Most patients with AIH respond well to steroids and AZA, with the liver blood tests becoming normal within several months. However, in some patients, the inflammation is more difficult to treat. In these cases, mycophenolate is usually tried next and then tacrolimus.


Treatment for Autoimmune Hepatitis
Goal: normalization of liver blood tests (AST and ALT)
Start a steroid
(either prednisone 20-40 mg/day or budesonide 9 mg/day)
Laboratory tests every 1-2 weeks
If AST and ALT improve, add azathioprine (a drug that suppresses the immune system)
Laboratory tests every 1-2 weeks
Slowly decrease prednisone dose as AST and ALT improve over the next 6 months
Continue azathioprine or mycophenolate mofetil indefinitely


Response to Treatment
If treatment is stopped, the majority (79%) will relapse

PROGNOSIS

- The chances for success are higher if the enzymes and IgG are normal for 2 years first.
- Up to 80% of patients will have their immune disease become active after medications are stopped .
- It is not easy to predict when this will occur, although it often happens in the first year. Because it could occur months to years after treatment has been stopped, liver blood tests to check for relapse must be done at regular intervals forever.


THANK
YOU!