

PEDIATRIC AUTOIMMUNE HEPATITIS

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INTRODUCTION

- a chronic inflammatory condition of the liver
- complex interaction among genetic factors, immune response to antigens present in hepatocytes, and immune regulation alterations
- Depending on the serological profile, AIH is divided into two subtypes:
 - type 1, positive for smooth muscle antibodies (SMA) and/or antinuclear antibodies(ANA)
 - type 2, positive for liver kidney microsomal antibody type 1 (antiLKM-1) and/or anti-liver cytosol type 1 (anti-LC-1)

- AIH distribution is global
- there is a female predominance, with a ratio of 3:1 for type 1 and up to 9:1 for type 2
- Incidence peaks are between 10 and 11 years old for AIH type 1 and between 6 and 7 years old for AIH type 2
- The course of AIH is progressive and advances to cirrhosis with end stage liver failure if left untreated

PATHOPHYSIOLOGY

- individuals with a genetic predisposition, exposure to triggering factors leads to an imbalance between effector and regulatory immunity
- overcome self-tolerance making autoimmune aggression in the liver to persist even in the absence of the initial trigger
- This is due to the existence of “molecular mimicry” mechanisms and a reduction in the number and function of regulatory T cells
- Genetic susceptibility is determined by the presence of (MHC II) molecules, more specifically (HLA) DR

- Depending on the ancestry or geographic region, HLA susceptibility varies
- Alleles conferring susceptibility to type 1 AIH are HLA-DR3 and DR4 among European and North American
- type 2 AIH, the most common allele among German Caucasian is DRB1
- The inflammatory reaction is caused by T cells (mainly T helper cells), B cells, macrophages, and natural killer (NK) cells
- The triggering factor of the inflammatory response is still unclear

- several viral agents included as potential triggers:

hepatitis A, B, C and E viruses

measles virus

Epstein-Barr virus

herpes simplex virus

DIAGNOSIS

- The diagnosis of AIH is focused on a combination of clinical, biochemical, immune and histological findings and the exclusion of other causes of liver disease

CLINICAL MANIFESTATIONS

- In the pediatric, AIH may present in different ways and be more aggressive than in adults
- The most common presentation is acute hepatitis (~ 40%), including loss of appetite, nausea , vomiting, and arthralgia, followed by jaundice , choluria and/or acholia
- it may start as acute liver failure (~3% and 25%) of patients with AIH-1 and AIH-2, respectively
- Other less common presentations include insidious AIH with
 - predominantly non-specific symptoms (25-40%)
 - complications of cirrhosis(10%)
 - asymptomatic AIH, diagnosed incidentally(abnormal liver function tests, hepatosplenomegaly)

- Regardless of the presentation, nearly one third of patients have cirrhosis at the time of diagnosis, which evidences the long course of this disease
- patients may have a fluctuating periods of remissions and recurrences, which may delay diagnosis and treatment initiation
- It is critical to suspect AIH, confirm the diagnosis immediately, and start an early treatment
- During physical examination, patients may not have signs of underlying liver disease or show jaundice and the signs typical of chronic liver disease, including telangiectasis, palmar erythema, hepatosplenomegaly, and collateral blood flow

- A family history of autoimmune disease is common in 40% of cases
- ~20% of patients show associated autoimmune alterations , at the time of diagnosis or during the course of the disease

thyroiditis

inflammatory bowel disease

hemolytic anemia

vitiligo

celiac

insulin-dependent diabetes

LAB TESTS

- high aminotransferase levels (2 to 50 times normal values)
- hypergammaglobulinemia (an increase of IgG secondary to non-specific B cell proliferation)
- direct hyperbilirubinemia
- normal or slightly increased gamma-glutamyl transferase (GGT)
- Up to 45% of AIH-2 and 9% of AIH-1 have IgA deficiency
- C4a levels may be reduced in up to 69% of cases
- In patients with cirrhosis and portal hypertension, pancytopenia secondary to hypersplenism
- Patients with acute liver failure usually have a prolonged prothrombin time (PT) that does not respond to vitamin K administration.

AUTO ANTIBODIES

- A key element in AIH diagnosis is autoantibody detection
- they may also be present in other conditions
- their isolated finding is not enough to confirm the diagnosis
- Standard serology includes autoantibody detection by immunofluorescence, allows to differentiate between both types of AIH:

AIH-1 is characterized by ANA and/or SMA

AIH-2 is characterized by anti LKM-1 and/or anti-LC-1 antibodies

- there is a third group characterized by the presence of antibodies to soluble liver antigen (SLA) or liver pancreas antigen, which are currently included in AIH-1
- Overall, 40% of AIH-1 cases and 80% of AIH2 cases are diagnosed before 18 years old
- In the pediatric population, $\geq 1:20$ dilutions for ANA and SMA, and $\geq 1:10$ dilutions for antiLKM-1 are indicative of disease
- There is a seronegative form of AIH, present in $\sim 10\%$ of cases, which should be taken into consideration once other potential etiologies are ruled out based on patient age

**THANKS FOR YOUR
ATTENTION**