Autoimmune hepatitis type 2 triggered by hepatitis A in a child: First case described in our context.

ABSTRACT:

The pathogenesis of autoimmune hepatitis (AIH) remains unknown. However, some viral infections seem to be triggers for AIH in patients with a genetic predisposition.

We report a case of a child with type 2 AIH following acute viral hepatitis type A (HAV) that has never been described in our Moroccan context.

This is an 8-year-old child who suffered from hepatitis A at the age of 5 years, which was cured after 3 months. During the following months, she presented with jaundice associated with epistaxis. Complementary exams showed; polyclonal hypergammaglobulinemia and antinuclear and anti-LC1 antibodies associated with the presence of necrotico-inflammatory lesions of hepatocytes in liver biopsy. A diagnosis of autoimmune hepatitis type 2 was retained. The evolution was favorable under treatment with corticosteroid and azathioprine.

KEYWORDS: Autoimmune hepatitis; Hepatitis A; Antibodies.

Introduction:

Autoimmune hepatitis (AIH) is a chronic inflammatory liver disease, characterized by positive circulating autoantibodies, with inflammatory liver histology, including lymphocytic infiltrates and interface hepatitis. Occurring most often in female patients with a genetic predisposition (1).
The pathogenesis of AIH remains unknown. However, many viruses in particular hepatitis viruses may be involved in triggering an autoimmune process causing AIH in a genetically predisposed subject (2).
In this article we report a case of a child with type 2 AIH triggered by hepatitis A that has never been described in our Moroccan context.

Case Presentation :

This is an eight-year-old child with a history of hepatitis A infection at the age of 5 years (HAV serology type IgM positive), heal spontaneously after 3 months, who has presented for 6 months hypogastric pain, jaundice with normal stool/urine color, and epistaxis. The child was hospitalized for

3 days in a peripheral hospital where she has received injections of vitamin K and then was referred to the pediatric department of the military hospital in Rabat for additional investigations and management.
In the clinical examination the child was conscious, subicteric and apyretic. The abdomen was supple. The rest of the examination was without particularity.
On biological tests:
Normochromic, normocytic anemia with hemoglobin=9.7g/dL, MCV =80.3 fL, MCHC=33.4 g/dl, MCH=26.8 pg , Platelets=241000 /µl, WBC=8800/µl, Neutrophils=4593/µL, lymphocytes =3379/µL.
Fasting blood glucose at 0.82g/l.
Cholestatic hepatitis, with total bilirubin at 64 mg/L predominantly conjugated at 60 mg/L, hepatic cytolysis with AST (aspartate aminotransferase) at 614 U/L and ALT(alanine aminotransferase) at 515 U/L and high rates of ALP(alkaline phosphatise) = 488 U/L and GGT(Gamma-glutamyl transferase)=127 U/L, The prothrombin time (PT) was low at 56%, as well as albumin at 29 g/l and Factor V at 48%.
Viral serologies had found anti-HAV-IgM negative, anti-HAV-IgG positive, other viral serology was negative (anti-EBV IgM & IgG, HBs-Ag, anti-HBs and anti-HBc, anti-HCV and anti-HIV). A
Polyclonal hypergammaglobulinemia at 30g/l was found at serum protein electrophoresis.
Autoantibody screening revealed: a positive Coombs-Test and antinuclear > 1/ 320, anti-LC1 to 78 UA. But negativity of anti-DNA, IgA anti-tissue transglutaminase, Anti-gliadin IgA, anti-endomysium, anti-LKM1, antimitochondrial, anti-smooth muscle, anti-neutrophil cytoplasmic.

Abdominal ultrasound and angiography, magnetic resonance cholangiopancreatography were all normal.

Drug-induced liver injuries, acute viral hepatitis, primary sclerosing cholangitis, Wilson's disease, alpha-1 antitrypsin deficiency were eliminated.

Liver histology showed: chronic hepatitis (clarified and distended hepatocytes with acinar metaplasia at hepatic parenchyma) associated along cholangitis lesions with portal dense lymphocytic infiltrate, severe interface hepatitis, and mild to moderate lobular necrosis with moderate portal fibrosis, consistent with autoimmune hepatitis. The IAIHG (International Autoimmune Hepatitis Group) score was 17.

The basis of treatment was a combination of azathioprine 1.5 mg/kg and corticosteroids 2mg/kg for 1 month. The evolution was favorable with a remission of clinical signs (regression of jaundice and gastrointestinal symptomatology) and biological (normalization of ALT rates at 38 U/L and AST at 58 U/L and PT at 70%). The regression of corticosteroids dose was initiated with no signs of relapse.

Discussion:

The diagnosis of AIH in our patient was retained on clinical and biological criteria revealing liver damage, the presence of polyclonal hypergammaglobulinemia, anti-nuclear and anti-LC1 antibodies as well as by the presence of necrotic inflammatory responses of hepatocytes on histological analysis of liver and after having eliminated the other causes of chronic hepatitis.

The classification of AIH into AIH types 1 and 2 is recognized according to seropositivity for circulating antibodies: antinuclear and/or smooth muscle antibody (anti-actin or anti SLA) in type 1 AIH, LKM1 and/or hepatic cytosol (LC1) in type 2 (3, 4).

Anti-nuclear antibodies are most often found in AIH type 1 but are non-specific, however it can be said that our patient has AIH type 2 in the presence of anti-LC1 antibodies which are more specific even if LKM1 antibodies are absent (5,6).

Hepatitis A is the most common cause of acute viral hepatitis in children, its evolution is most often spontaneously favorable, however in our patient the hepatitis A virus seems to be involved in triggering of AIH. (7, 8)

The induction of type 1 AIH following hepatitis A and B infections or Epstein - Barr virus (EBV) has been described (2). Viral infection could modify or release cell antigens, and represent the first step in an autoimmune process. In the serum of patients with chronic hepatitis C virus, an autoantibody type LKM1 can be observed, but the antigenic sites recognized by this autoantibody are different from those recognized in the type 2 AIH (9). As with other hepatotropic viruses, HCV could induce the appearance of anti-LKM1 antibodies by modification or release of proteins, or by molecular similarity between HCV proteins and cytochrome P450 proteins. This phenomenon of cross-recognition between autoantigens and viral proteins would explain why a viral infection can trigger an AIH in a particular genetic predisposition. In these patients an immune response, programmed to be limited in time, would be sustained due to the existence of cross-reactivity between viral antigens and self-proteins.

There is a clear female predominance in AIH in type 2 (90%) which is attenuated in type 1 (75%), thus elective to the human leukocyte antigen (HLA) B8 DR3 or DR4 and a deficiency of the complement C4. These genetic factors explain why 30 to 40% of patients with AIH also have another autoimmune disease at diagnosis or in the years since diagnosis (10).

However, in our patient, the old infection with hepatitis A seems to induce an autoimmune process causing type 2 and not type 1.

HAV vaccination is strongly recommended for patients with chronic liver disease to prevent decompensation due to HAV superinfection. In addition, combined vaccination against hepatitis A/B is both safe and highly immunogenic against HAV and HBV in HCV-infected patients with well-compensated liver disease. Patients with AIH are also a risk group for disease exacerbation or relapsing hepatitis A or B. Therefore, this group of people should be protected against both HAV and HBV, hence the interest of vaccination (11).

Conclusion:

Our patient appears to be an example in which hepatitis due to HAV might lead to AIH.
Hence, we suggest in cases of persistent liver disease following HAV contamination, AIH should be sought systematically in order to start treatment early.
In another perspective, patients with AIH should also be vaccinated against both hepatitis viruses HBV and HAV to prevent serious progression.

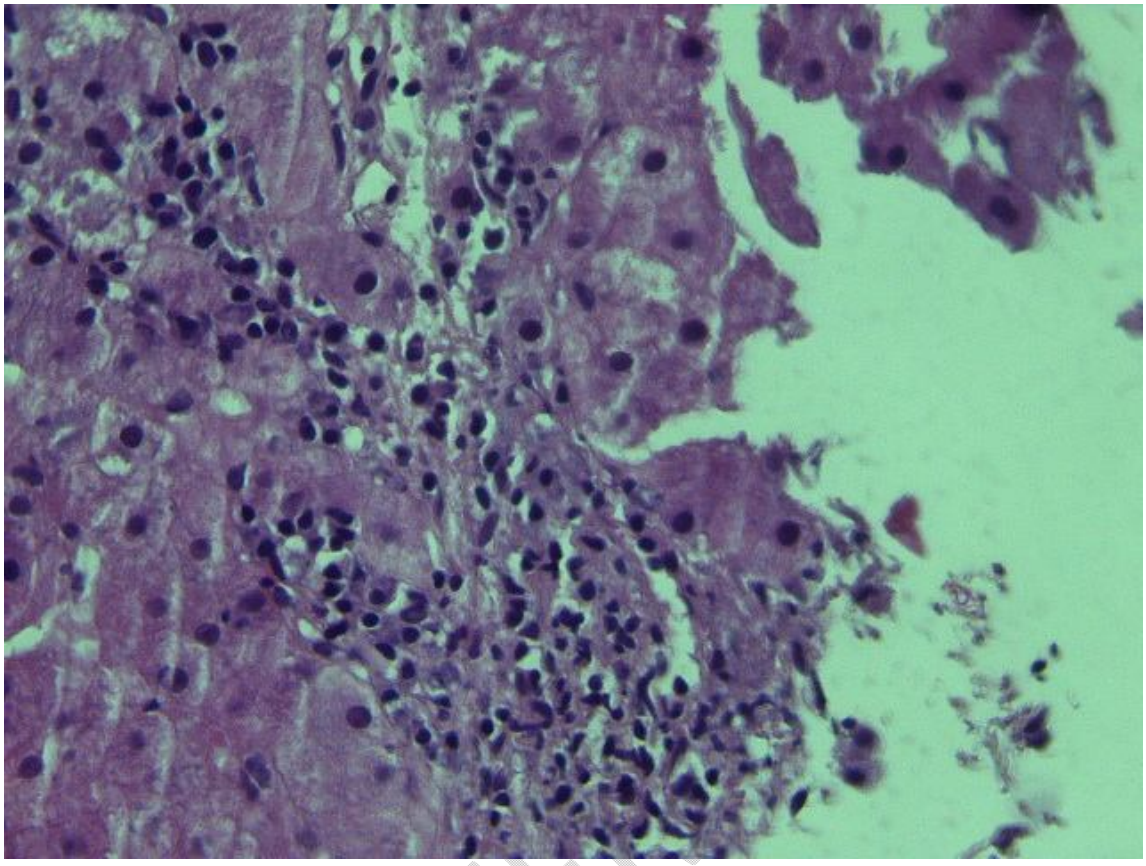

Figure 1: Intralobular necrotic foci (enlargement x 40)

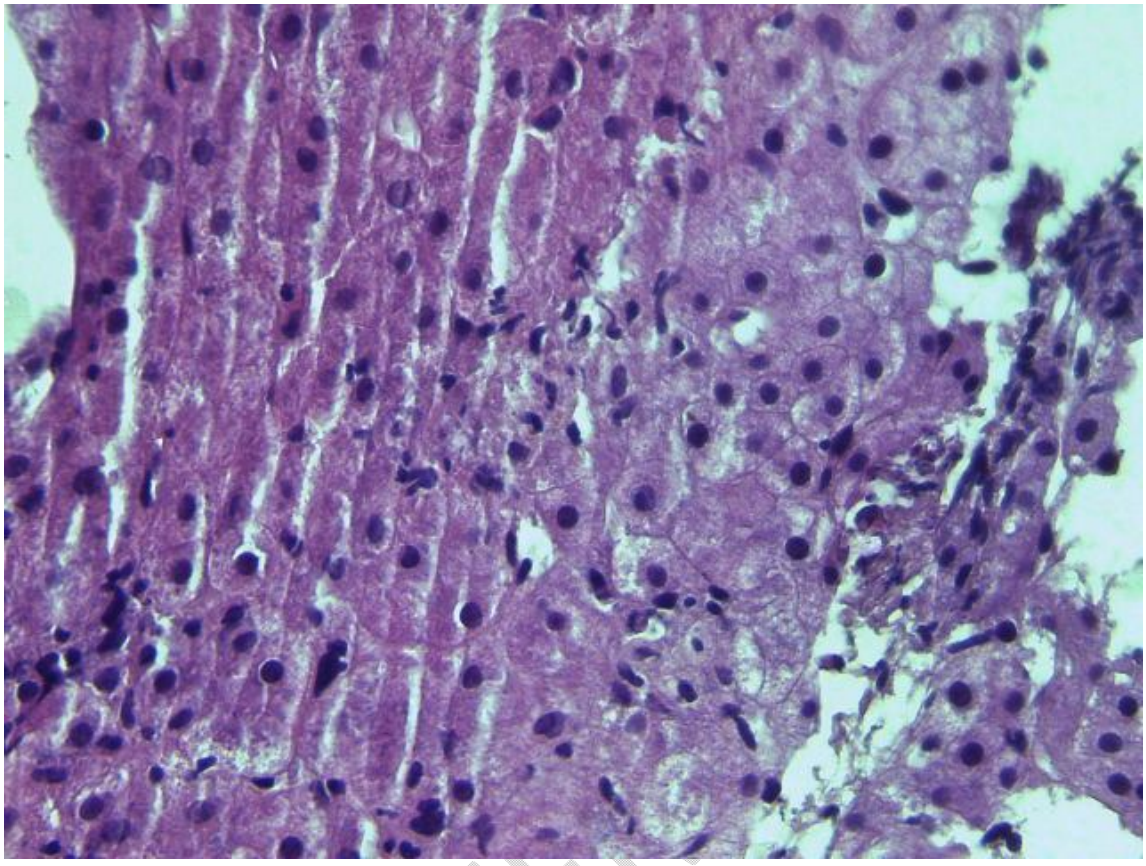

Figure 2: Intralobular microgranulomas with hepatocellular necrosis (enlargement x 40)

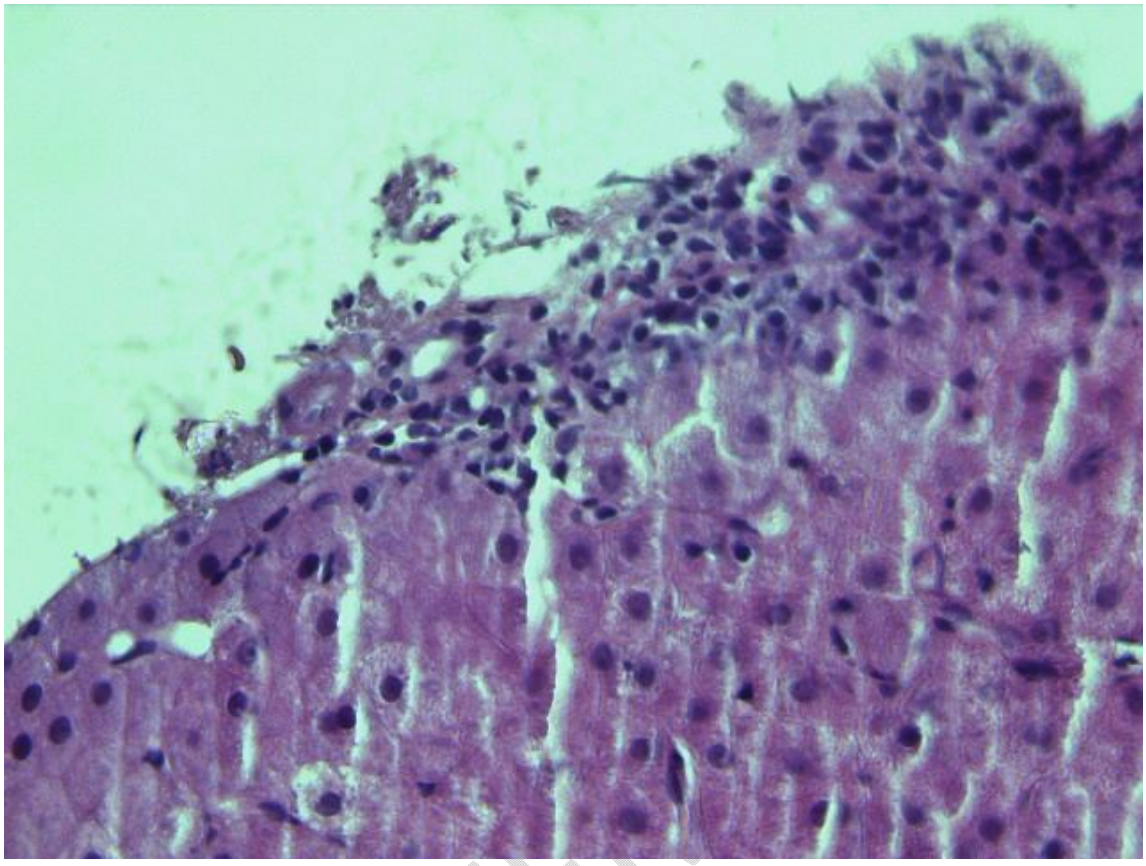

Figure 3: piecemeal necrosis of moderate interface hepatitis

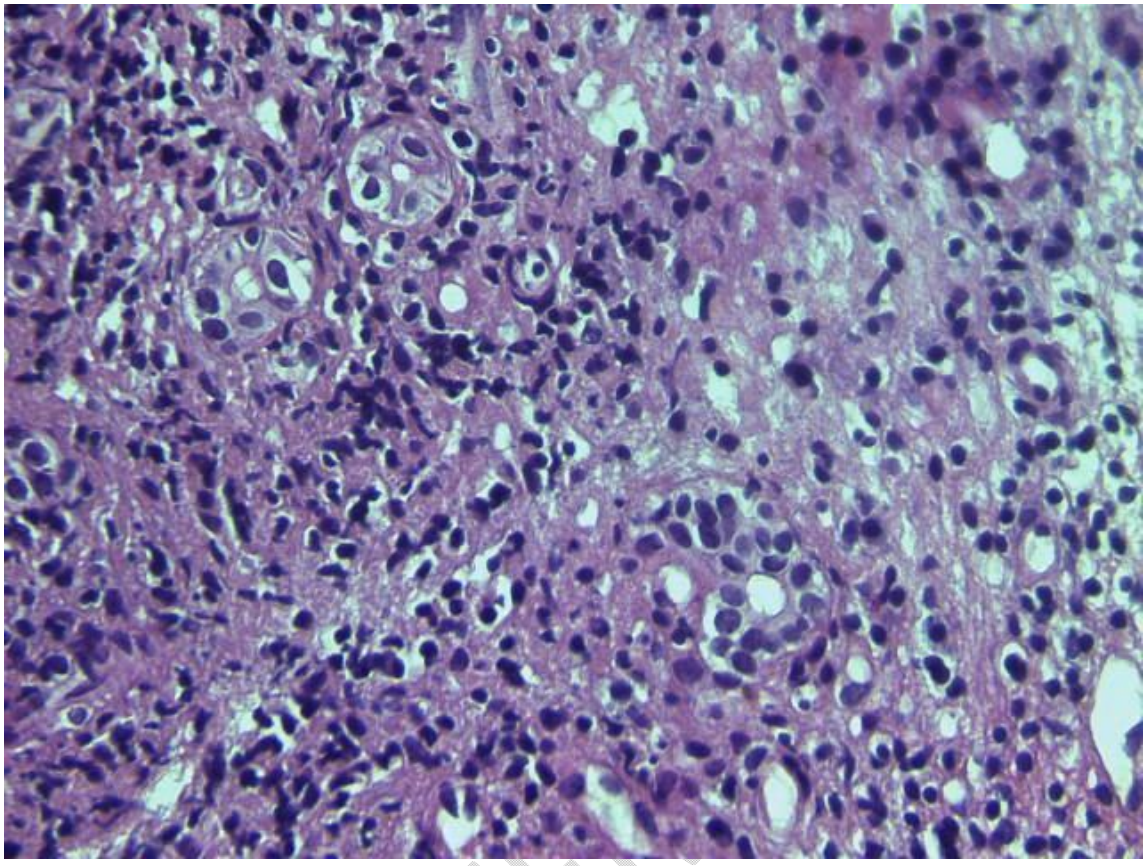

Figure 4: inflammatory infiltrate of the portal space rich in lymphocytes with cholangitis lesions

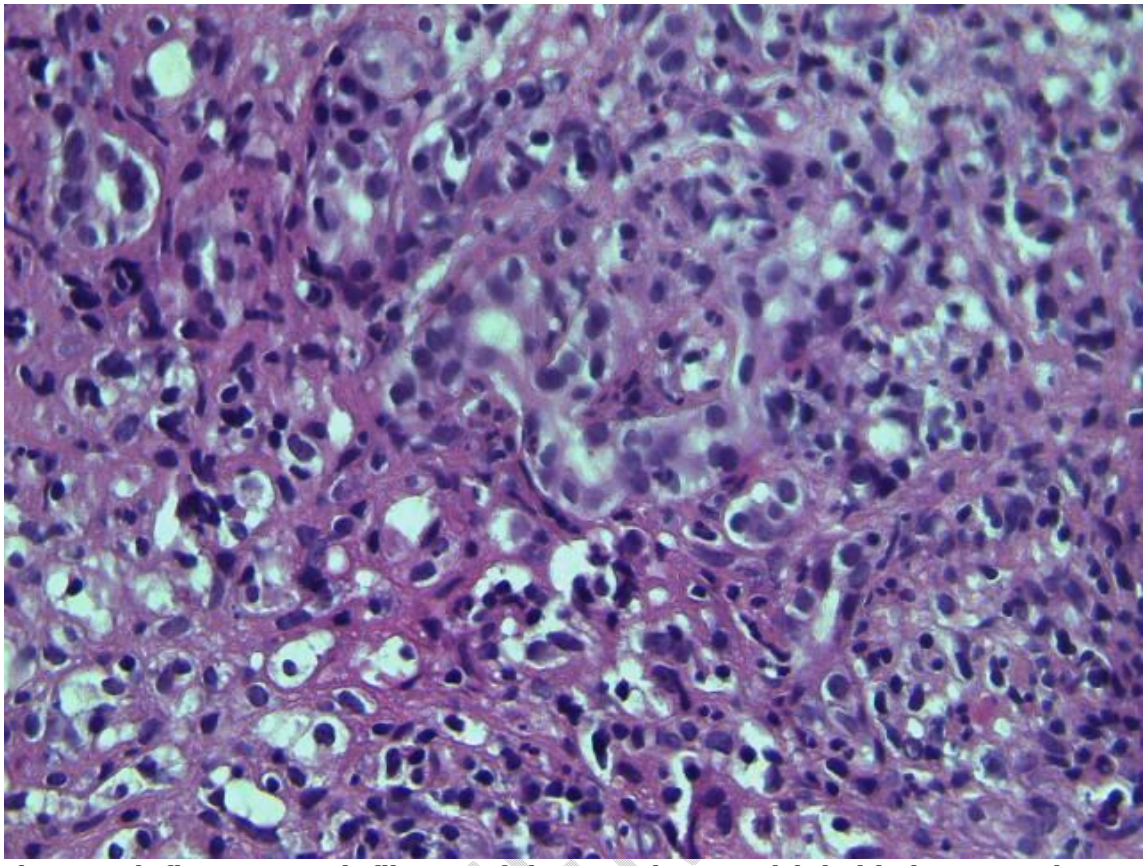

Figure 5: inflammatory infiltrate of the portal space rich in histiocyte and eosinophiles

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