Autoimmune Hepatitis with anti SLA antibodies

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To the Editor,

Autoimmune hepatitis (AIH) is a chronic progressive liver disease characterized by female predominance, hypergammaglobulinemia, specific autoantibodies, an association with HLA DR3 & DR4 and a favourable response to immunosuppressive treatment. The diagnosis of AIH includes a combination of clinical, laboratory and histological features (1).

Three subtypes of AIH have been proposed based on the different immunomarkers. Type I AIH, the most common form of the disease is associated with antinuclear (ANA) and anti smooth muscle (SMA) antibodies, affects all age group and is associated with HLA DR3 and DR4 (2). Type 2 AIH characterized by the presence of anti-liver kidney microsomal-1(LKM1) antibodies, is associated with HLA DRB1 and has a poorer outcome (2,3). Type 3 AIH defined by the presence of anti-soluble liver antigen/liver pancreas antibodies (anti-SLA/LP), is a rare condition, representing less than 10% of all AIH (4-6). According to recent clinical, genetic and serological findings it has been suggested that anti-SLA seropositive patients do not define a separate group of AIH but rather a subgroup of type 1 AIH. The target of anti-SLA has been identified by several groups as a ~50 kDa UGA serine tRNA-associated protein complex called (tRNP (Ser) Sec), through the screening of cDNA libraries. It is a complex associating tRNA and selenocysteine (7,8). This disease is associated with a more severe course and has been associated with a more frequent recurrence of AIH after liver transplantation (9).

We describe the case of a 20 year old male patient who had a diagnosis of AIH made at age of 13 based on positive anti-SMA and anti-SLA antibodies, high titre of ANA (1/320), and perinuclear anti-neutrophil cytoplasmic (pANCA) antibodies (1/160). Liver biopsy showed severe piecemeal necrosis as well as severe portal fibrosis with a METAVIR (10) score of A3F3 (Fig. 1). He was treated with steroids 2 mg/kg/day and azathioprine (50 mg/day) was added after 3 months allowing weaning of steroids. Five years later, since his AIH was in clinical and biochemical remission and the repeated liver biopsy had only shown mild signs of activity (A1) with absence of fibrosis (F0), (Fig. 2), it was decided to stop azathioprine. At that time, US elastography was normal (3.9 kPA).

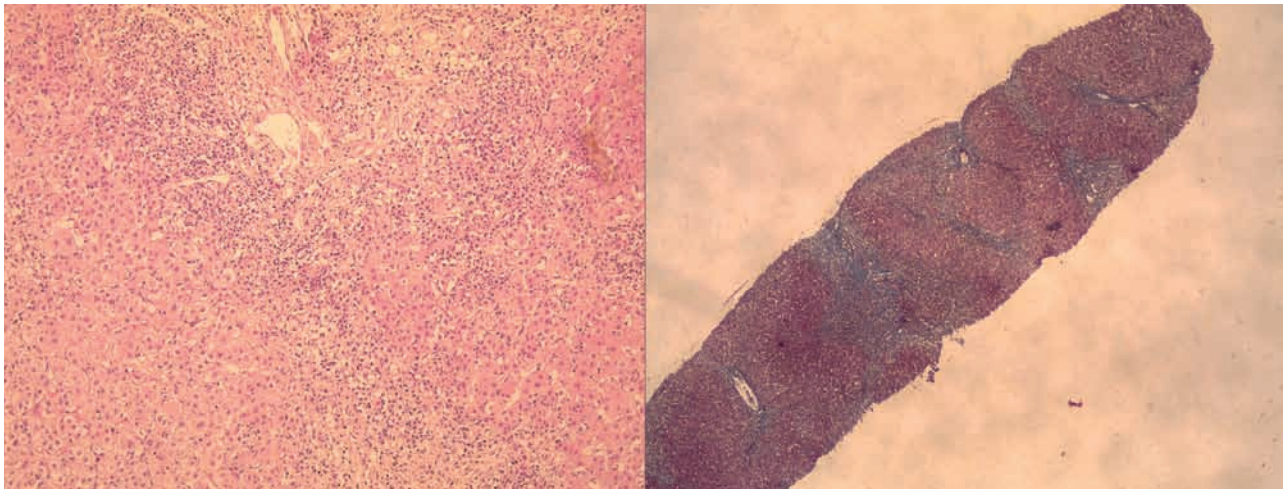

Fig. 1. — Liver biopsy 2004 showing high grade activity (A3) on the left panel, severe fibrosis (F3) on the right panel.

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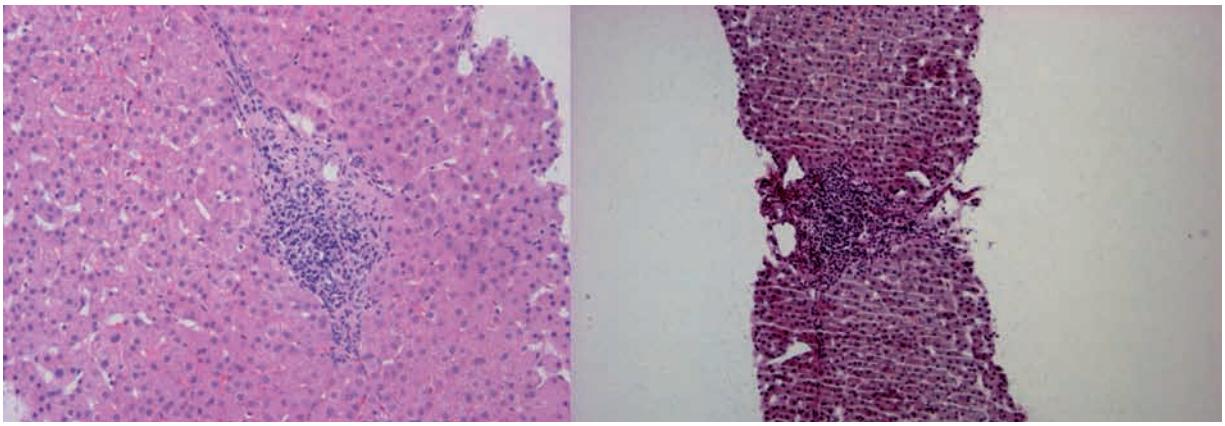

Fig. 2. — Liver biopsy 2010 after 5 years of immunosuppressive therapy showing low grade activity (A1) on the left panel and absence of fibrosis (F0) on the right panel.

After three months of follow up the patient develops a transaminase flare (ALT : 109 IU), together with an increase of p-ANCA titre (1/2560) as well as the presence of anti SLA antibodies. He was then put again on azathioprine and budenoside with the diagnosis of recurrent AIH. After six weeks, ALT levels went back to normal values (33 IU).

This observation illustrates several points regarding anti-SLA AIH : 1/ its potential occurrence in pediatric patients 2/ its potential severe course and reversibility under immunosuppressive therapy 3/ its recurrence after stopping immunosuppressive therapy thus implying probably lifelong treatment with its potential complications 4/ the search for pANCA and anti-SLA can act as an additional pointer toward the diagnosis of AIH.

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