Autoimmune hepatitis-primary sclerosing cholangitis overlap syndrome complicated by inflammatory bowel disease

The term "overlap syndrome" is used to describe variant forms of autoimmune hepatitis (AIH) which present with characteristics of AIH and primary biliary cirrhosis (PBC) or primary sclerosing cholangitis (PSC) [1]. The overlap syndrome between AIH and PSC is a rare condition and only few cases have been published, partly associated with ulcerative colitis, or with Crohn's disease [1-6]. AIH-PBC overlap syndromes have been reported in almost 10% of adults with AIH or PBC, whereas AIH-PSC overlap syndromes were found in 6 to 8% of children, adolescents, and young adults with AIH or PSC [1].

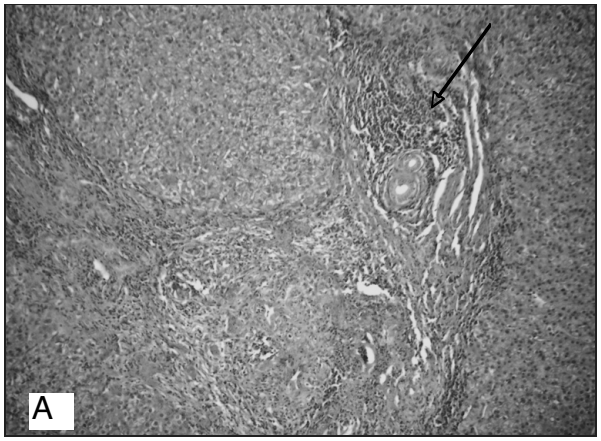
We report the case of one boy with AIH and PSC complicated by non specific inflammatory bowel disease.

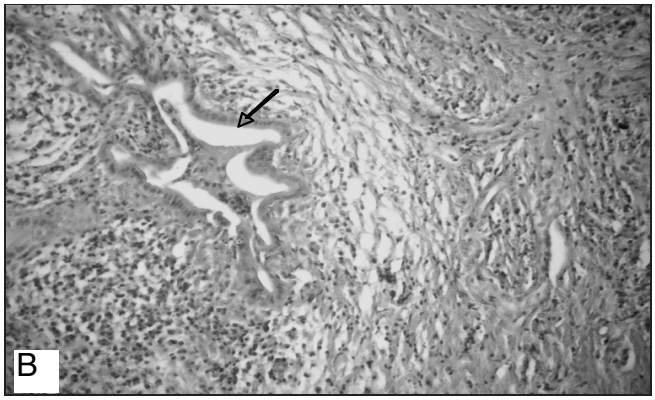
Case report

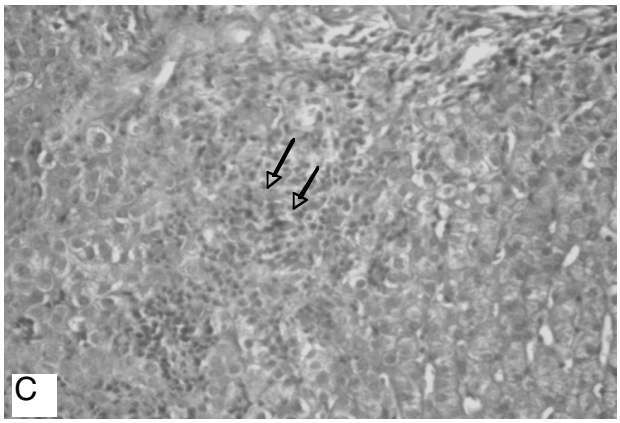
Clinical history: A 4-year-old boy was admitted in our pediatric department to investigate an hepatosplenomegaly discovered fortuitously by a medical examination at his Children garden . there is no history of jaundice, but the parents reported a history of chronic diarrhea since 4 months. His parents are first cousin. The father is followed up for vitiligo and hypothyroidism.

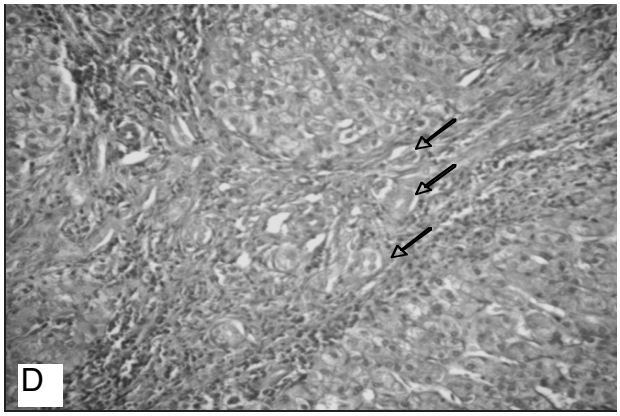
Laboratory investigations: hemoglobin: 10,8 g/dl, white blood cell count: 14900/mm^3, platelet count: 340 000/mm^3, sedimentation rate: 76 mm/h, alanine transaminase (ALT): 187 U/l, aspartate transaminase (AST): 280 U/l, alkaline phosphatase (ALP): 1785 U/l gamma-glutamyl transpeptidase (GGT): 280 U/l total bilirubin: 7.1 mg/dl, direct bilirubin 5 mg/dl, albumin: 36 g/dl, globulin 19,7 g/l, IgG: 16,2g/l, IgM: 1,33g/l; IgA: 2,22g/l and serological markers for all hepatotropic viruses such as A, B, C, cytomegalovirus, Epstein–Barr virus were negative.

Figure 1: A liver biopsy
A: showed a portal inflammation, periductal fibrosis with infiltration of lymphocytes and plasmocytes(long arrow);
B: ductular cholangiectasia (short arrow);
C: periportal piecemeal necrosis (double arrow);
D: ductular proliferation (triple arrow)









We detected high levels of anti-nuclear antibody (ANA) 1:160, smooth muscle antibody (SMA) > 1/40, and perinuclear antineutrophil cytoplasmic antibodies (pANCA) was positive.

Histological examination of liver biopsy revealed portal inflammation with infiltration of lymphocytes and plasmocytes in the bile ducts and ductular proliferation. Periductal fibrosis. and periportal piecemeal necrosis (Fig.1).

Magnetic resonance cholangiography showed intra- and extrahepatic biliary dilation with scattered biliary strictures indicating primary sclerosing cholangitis (Fig. 2).

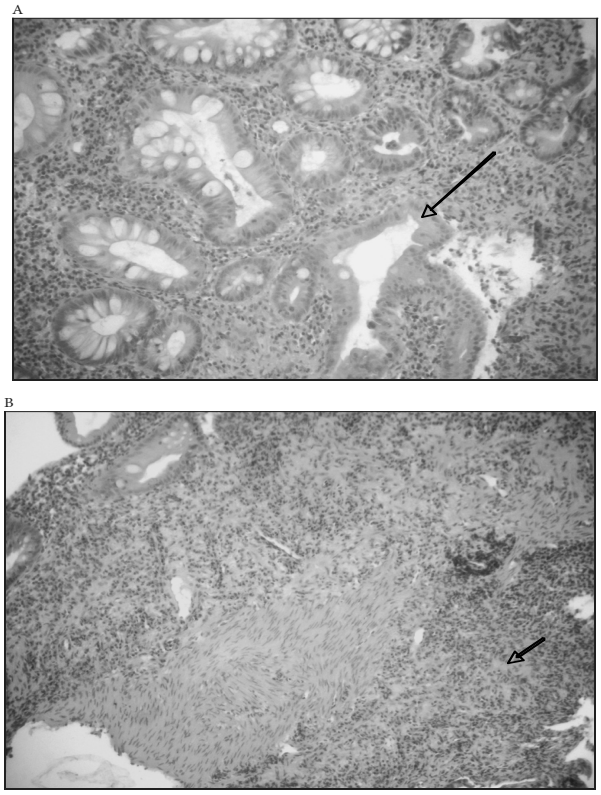
A colonoscopy was made but didn't show any anomalies. However, a biopsy should have been carried out to make sure that there no abnormalities.

Figure 2: Magnetic resonance cholangiography showed intra- and extrahepatic biliary dilation with scattered biliary strictures indicating primary sclerosing cholangitis

Using the revised diagnostic criteria for AIH [2], our patient scores were: ALP:AST ratio <1.5; +2, serum globulin; +3, ANA > 1:80; +3, viral hepatitis markers negative; +3, drug history negative; +1, no alcohol intake; +2, liver histology; interface hepatitis +3, lymphoplasmacytic infiltrate +1, biliary changes ≥3, response to therapy +3 (relapse). Aggregate score post-treatment: 18 regarding definite AIH. Elevated levels of alkaline phosphatase, pANCA positive, histological and magnetic resonance cholangiography findings made up us to diagnose the overlap syndrome between AIH and PSC in our patient.

Immediately, we began to give prednisolone (2mg/kg per day), azathioprine (1, 2 mg/kg per day) and Ursodeoxycholic acid (UDCA) orally. The evolution was favorable within 2 days: disappearance of diarrhea. Serum aminotransferase becomed normal in 2 weeks. Then we decrease the dose of prednisolone slowly, but the evolution was marked by the relapse of diarrhea after 10 months when we decrease the dose of prednisolone to 0,5 mg/kg/day. Laboratory investigations showed a high level of Á-globulins (19g/dl), sedimentation rate: 6 mm/h, ALT: 18 U/l; AST: 37 U/l, ALP: 292 U/l. Colonoscopy revealed segmentaire patchy mucosal inflammation throughout the colon. Mucosal biopsies demonstrated some crypt distortion, focal cryptitis, increased chronic inflammation, and a rare micro abscess of crypt establishing a diagnosis of non specific inflammatory colitis (fig.3). We increase the dose of prednisolone to 2 mg/kg/day and azathioprine to 1, 84 mg/kg per day. The patient improved rapidly: disappearance of diarrhea after 24 hours. Currently, the patient is in remission since 8 months with a lower dose of prednisone (10 mg per day), azathioprine and UDCA.

Figure 3: Biopsy of colonic mucosa. A: crypt distortion and dedifferentiation (long arrow). B: chronic inflammatory changes in the mucosa and sub mucosa (short arrow) represented by increased lymphocytes and plasma cells.



Conclusion

AIH- PSC overlap syndrome is rarely encountered in clinical practice. It can be associated with inflammatory bowel disease. Its treatment includes anticholestatic therapy with ursodeoxycholic acid (UDCA) of the cholestatic component and immunosuppressive therapy with corticosteroids and azathioprine of the hepatitic component of these disorders. Liver transplantation is the treatment of choice for end stage disease.

References

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