A case of primary biliary cirrhosis with high titers of antinuclear antibody and distal ulserative colitis in remission

Antinükleer antikor titresi yüksek primer siroz ve remisyonda distal ülseratif kolit (olgu sunumu)

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ÖZET: *Bu yazıda remisyonda dital ülseratif kolit ve primer biliyer sirozlu (PBS) semptomatik erkek hasta takdim edilmiştir. Serum alkalen fosfataz (AP), gama-glutamyl transpeptidaz (GGT), aspartat aminotransferaz (AST), alanın aminotransferaz (ALT) ve bilirubin seviyeleri yüksektir. Serum anti mitokondrial (AMA), M2 bant ve antinükleer antikor (ANA), immunfloresans tekniği ile yüksek titrelerde pozitif bulunurken, düz kas antikoru (SMA), negatif bulunmuştur. Laparoskopik wedge biopsy incelemesi devre II-III primer biliyer sirozla uyumlu olarak gelmiştir. Hastaya 3 ay süreyle UDCA 15 mg/kg/günbaşlanmış ve tedaviye kolşisin 0.6 mg (2x1) + UDCA ile devam edilmesine karar verilmiştir.*

Anahtar kelimeler: **Primer biliyer siroz, ülseratif kolit**

SUMMARY: *This article reports a male patient, diagnosed as symptomatic primary cirrhosis (PBC) with distal ulcerative colitis in remission. Serum biochemical study showed increases in alkaline phosphatase (AP) gama-glutamyl transpeptidase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT) and bilirubin levels. Serum anti-mitochondrial antibody (AMA), M2 band and antinuclear antibody (ANA) were positive in high titers on immunoflourescence (IF). Smooth muscle antibody (SMA) was negative. Laparoscopic wedge biopsy specimen examination was compatible with stage II-III PBC. The patient was treated with 15 mg/kg/day UDCA for three months and planned to go on with colchicine 0.5 mg twice a day + UDCA for two years.*

Key words: **Primary biliary cirrhosis, ulcerative colitis**

A 27 year old male patient was admitted to hospital with severe itching, fatigue and jaundice. His complaints started 8 months ago with itching first and episodes mostly disturbed him at nights. Jaundice had begun only 3 weeks ago and never resolved spontaneously. It showed progression since then. He could not go to his office because of unbearable fatigue. From the history as we learned, he had been hospitalised for bloody diarrhea and corampy colics at lower abdominal area, when he was 12 years old. Biopsy taken from rectum (At Gülhane Hospital, 15 years ago) was compatible with ulcerative colitis and X-ray lower series of other colonic segments were normal. Fresh stool examinations and stool microbial cultures were negative. He was diagnosed as distal ulcerative colitis and medicated with sulfasalazine (3x1) and prednisone enema (20 mg 2x1) He had had 3 episodes of activation when he was taking sulfasalazine at maintenance dose. The patient was not on therapy now for 10 years.

Physical Examination :

There was marked jaundice in sclera. Other systemic investigation revealed no abnormality.

Biochemical Investigations Were As Follows:

Hb: 14g/dL, WBC: 8500, Htc: 45, ESR: 33 mm/hr, peripheric blood smear: normal PLT: 40400, BUN: 13 mg/dL, glucose: 86 mg/dL, AST: 120 U/L (0-220), ALT: 215 U/L (0-41) GGT: 415 U/L (11-49), ALP: 1629 U/L (98-279), amilase: 146 U/L (0-220), lipase: 50 U/L (0-190), total protein: 8.9 g/L, albumin: 4.5 g/L, total bilirubine: 3.5 mg/dL (0-1), direct bilirubin: 2.8 mg/dL (0-0.3), cholesterol: 380 mg/dL (112-250), trigliserid: 198 mg/dL (50-200), AMA: (+) 1/5120, ANA: (+) 1/2560 speckled type,

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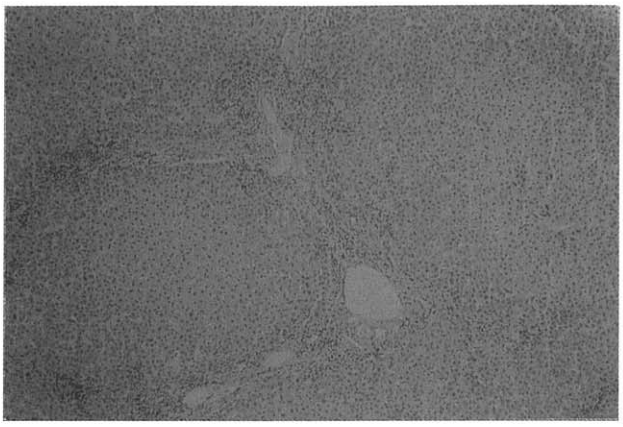

Figure 1. Forming of granuloma in zone I.

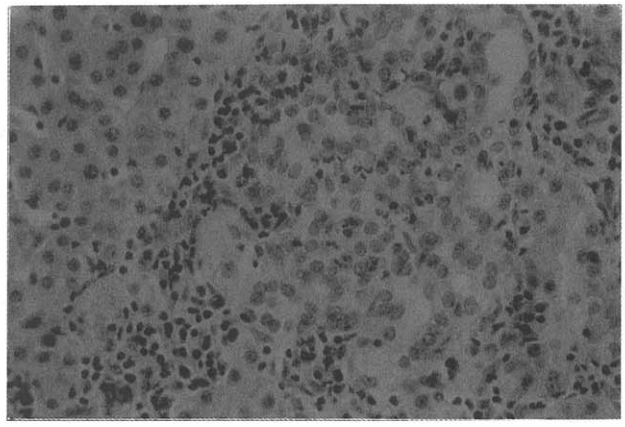

Figure 2. Cellular reaction surrounding the damaged duct including lymphocytes, plasma cells, eosinophils and histiocytes.

SMA: (-), M2 band: (+)>7 (<0.1), IgA: 2.8 g/L (0.8-4), IgG: 20.9 g/L (7-15), IgM: 6.5 g/L (0-3), HbS Ag: (-), Anti HbS (-), Anti-HAV IgM: (-), Anti-HCV (-), HCV RNA PCR: (-).

Abdominal USG: normal, ERCP: normal, Rectoscopy: normal, Rectal biopsy: Compatible with ulcerative colitis in remission (plasmocytosis at lamine propria, cryptic distorsion), Colonscopy: normal, Eosophagogastroduodenoscopy: normal Laparoscopic wedge biopsy of liver: Fibrous tissue proliferation and lymphocytic infiltration in portal areas, piece meal necrosis, destruction of interlobuler bile ducts, damaged bile ducts infiltrated and surrounded by lymphocytes, ductular proliferation in one area. There was no bile retention in hepatocytes.

Comment: Stage II-III primar biliary cirrhosis:

HLA subtyping: HLA ABC: A3, A11, B21, B, BW, CW4, CW6, HLA DR: DR1, DR7, DRW8, DQW8, DQW1, DQW2.

DISCUSSION

We presented a male patient with primary biliary cirrhosis and distal ulcerative colitis in remission. In our case, the presence of inflammatory bowel disease, suggested primary sclerosing cholangitis (PSC). İndeed PSC may be clinically indistinguishable from PBC. However characteristic bile duct beading and irregulatirites were absent on endoscopic retrograde cholangiopancreatic (ERCP) examination. Besides AMA and M2 band in primary sclerosing cholangitis. Unlike studies in primary biliary cirrhosis, most studies have found the presence of classic antibodies to be unusual in primary sclerosing cholangitis and in a study ANA was found in 6% AMA in 5%, SMA in 11%. Studies from other centers have found some what a higher incidence of autoantibodies in PSC patients (2,3). In children with PSC the incidence of ANA seems to be similar to that reported in patients with autoimmune chronic active hepatitis (CAH) (4). Although ANA titers was also high in our case, the presence of high titers of M2 band has strognly suggested the diagnosis of PBC rather than CAH.

Hypergamaglobulinemia occurs in about 30% of patients with PSC and IgM levels were increased in 40% to 50% (1). In addition it was found that 5% of patients with PSC have eosinophilia which in some patients may be striking (5,6). IgM levels were also high in our patient but there was no eosinophilia on peripheric blood smear. If we consider the high titers of M2 band, the high levels of IgM was compatible with PBC but not PSC.

Primary biliary cirrhosis is a chronic progressive cholestatic liver disease of unknown cause and characterised by the destruction of intrahepatic bile ducts (5). The relation between PBC and genetic markers is unclear. Several studies have shown no relation between PBC and human leucocyte antigens (HLA) (6-8). Others have indicated a relation o HLADR3 and HLADRW8 (9, 10). There was six fold increase in frepuency of HLADRW8 in 118 consecutive white patients with PBC referenced to the Mayo Clinic and a three fold increase in frequency of HLADRW8 in a group of 35 patients referenced to the University of California Los Angeles for liver transplantation (10,11). In our patient HLA subtyping, also

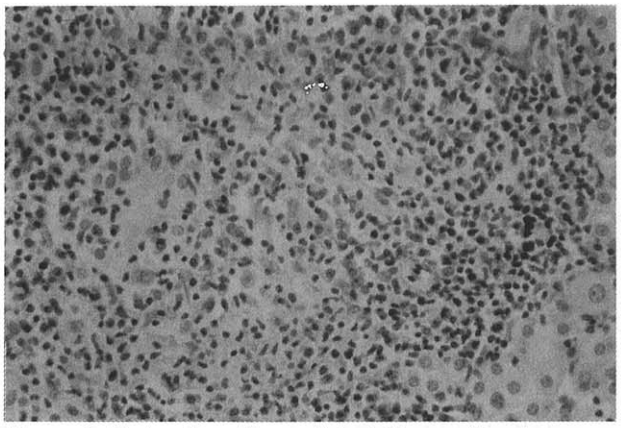

Figure 3. Destruction of a small ductuli, granulomatous reaction in portal area and piecemeal necrosis. (40x1)

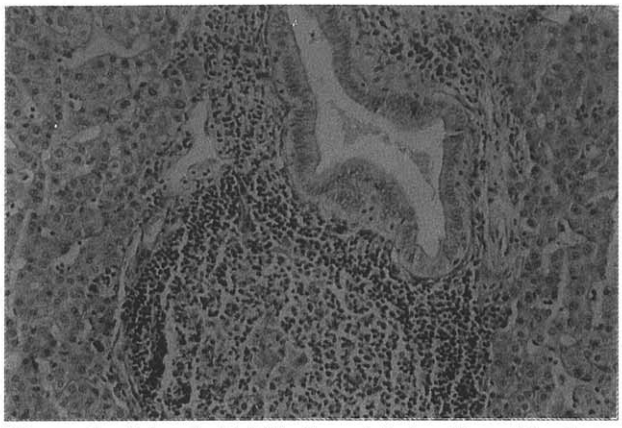

Figure 4. A lymphoid follicule and destruction of the basement membrane of a bile duct are seen in PAS stain. (40x1)

revealed a HLADRW8 pattern, which was also compatible with PBC.

On the other hand, the PBC patients are 90% female. The reason for the female prepondarence is not known. Survival is the same for men and women (12). In men the disease is marked with less common pruritus at initial diagnosis, also less skin pigmentation, less autoimmune features, especially the Sicca Syndrome (12).

Non hepatic disorders are found in 69% of patients (13). Rheumatoid arhtritis systemic lupus eritematosis, mixed connective tissue disease, dermatomyositis, scleroderma, CREST (Calsinosis, Raynoud phenomenon, Eosophageal spasm, scledactly, telengiectasia), autoimmune thyroiditis, jejunal villous atrophy, autoimmune trombocytopenia, insulin, receptor antibodies are frequent in PBC but ulcerative colitis is a rare accompaniment (13,14).

Extraintestinal biliary complications of ulcerative colitis are fatty liver sclerosing cholangitis, chronic active hepatitis, cirrhosis, pyogenic liver abscess.

In conclusion, we presented a male patient with distal ulcerative colitis and primary biliary cirrhosis which we believe is a rare association.

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