A Rare Case of Anti-SLA/LP Positive Autoimmune Hepatitis Presenting with Acute Severe Hepatitis

Akut Şiddetli Hepatitle Prezente Olan Anti-SLA/LP Pozitif Nadir Bir Otoimmün Hepatit Olgusu

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ABSTRACT Autoimmune hepatitis is a rare chronic liver disease of unknown etiology. The disease predominates among women and is characterized by hypergammaglobulinemia, characteristic autoantibodies, association with a favorable response to immunosuppressive treatment. The spectrum of presentation is wide, ranging from no symptoms to acute liver failure. In this report, we present a rare case of anti-SLA/LP antibody positive autoimmune hepatitis with acute severe hepatitis in a male patient.

Key Words: Hepatitis, autoimmune; hepatitis antibodies

ÖZET Otoimmün hepatit, etiyolojisi tam olarak bilinmeyen kronik bir karaciğer hastalığıdır. Otoimmün hepatit sıklıkla kadınlarda görülür ve hipergamaglobulinemi, belli otoantikorların varlığı, immünosupresif tedaviye iyi yanıt vermesi gibi karakteristik özelliklere sahiptir. Otoimmün hepatitin klinik spektrumu geniş olup; hiç semptom olmayabilir veya akut karaciğer yetersizliğine kadar değişen bir klinik seyir gösterebilir. Bu olgu sunumunda, nadir rastlanan bir durum olarak anti-SLA/LP otoantikor pozitif otoimmün hepatiti olan bir erkek hastada gelişen akut şiddetli hepatit sunulmuştur.

Anahtar Kelimeler: Hepatit, otoimmün; hepatit antikorları

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Autoimmune hepatitis (AIH) is necroinflamatory disorder with unknown etiology. The detection of liver related auto-antibodies with exclusion of other causes of chronic liver disease such as viral, toxic, metabolic and genetic causes constitute the hallmark of the diagnosis. Autoantibodies can be absent in about ten to thirty percent of patients. Certain autoantibodies (anti-SLA/LP) in autoimmune liver disease have prognostic implications. Anti-SLA is specific for autoimmune liver diseases, in which it is associated with a more severe disease course. The onset of AIH disease is usually insidious, with unspecific symptoms, such as, fatigue, malaise, arthralgias, and fluctuating jaundice, right upper quadrant pain or lethargy. However, a substantial proportion of patients may have no obvious signs or symptoms of liver disease, while occasionally the presentation may be severe and almost identical to an acute or fulminant episode of viral. We present here an unusual case of anti-SLA/LP antibody positive autoimmune

hepatitis with acute severe hepatitis in a male patient.

CASE REPORT

A 23-year-old man presented with abnormal liver function tests. He had also jaundice, anorexia, itching and weight loss. He had no significant past medical history and denied blood transfusion, IV drug abuse, intake of potential hepatotoxic drugs. There was no family history of hepatitis. On physical examination, he had icteric sclera, no palmar erythema, no shifting fullness and no abdominal tenderness. The laboratory data showed WBC: 7100/mm^3, hemoglobin:13.7 g/dL, hematocrit: %39, MCV: 80 fl, platelet: 204 000/mm^3. His serum level of alanine aminotransferase (ALT): 168 U/L, aspartate aminotransferase (AST):156 U/L, alkaline phosphatase (ALK-P): 107 U/L, GGT: 40 U/L and total bilirubin: 44 mg/dL, direct bilirubin: 33 mg/dL. Prothrombin timewas 17.3 seconds, with international normalized ratio of 1.2 (1.0-1.2). Anti-hepatitis A immunoglobulin M (anti-HAV IgM), hepatitis B surface antigen (HBsAg), anti-hepatitis B core IgM (anti-HBc IgM), anti-hepatitis C virus (HCV) antibody, anti-Epstein Barr virus IgM, anti-cytomegalovirus IgM, and antimitochondria antibody (AMA) were negative. ANA, ASMA, Anti-LKM, AMA and ANCA were negative.

Anti SLA/LP antibody was found positive (titer: +++). Immunglobulin G (IgG) was 3116 mg/dL (normal 540-1822 mg/dL). The Autoimmune Hepatitis Scoring System score was 19. Abdominal sonography revealed thickening of the gallbladder wall, other findings were compatible with hepatitis. Magnetic resonance cholangiopancreaticography revealed hepatosplenomegaly (Figure 1) and no other pathological finding was defined.

Liver needle biopsy was performed and biopsy showed lobular necrosis, portal and lobular inflamation, interphase hepatitis, plasma cell infiltration, rosett formation (Figure 2-5). All these findings were compatible with autoimmune hepatitis. Steroid therapy (1 mg/kg/day 60 mg) was

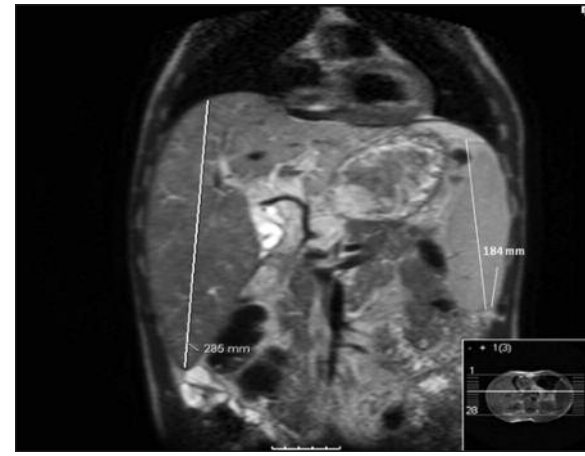

FIGURE 1: Shows hepatoslenomegaly.

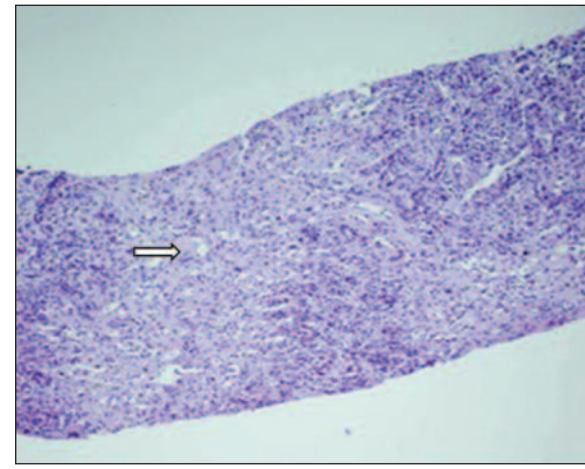

FIGURE 2: Low-power photomicrograph of the liver biopsy sample (stained by hematoxylin and eosin, magnification x 100) shows confluent necrosis in hepatocytes

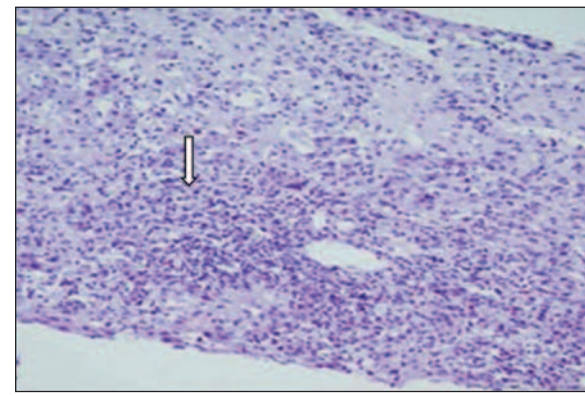

FIGURE 3: Low-power photomicrograph of the liver biopsy sample (stained by hematoxylin and eosin, magnification x 100) shows interphase hepatitis which is found in autoimmune hepatitis

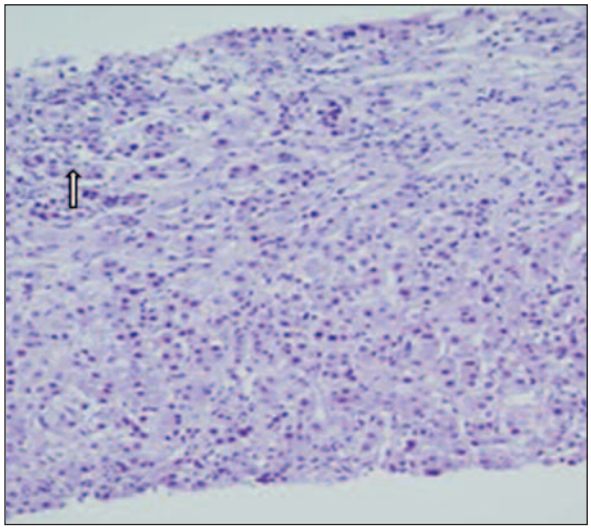

FIGURE 4: Low-power photomicrograph of the liver biopsy sample (stained by hematoxylin and eosin, magnification x 100) shows plasma cell infiltration which is also seen in autoimmune hepatitis.

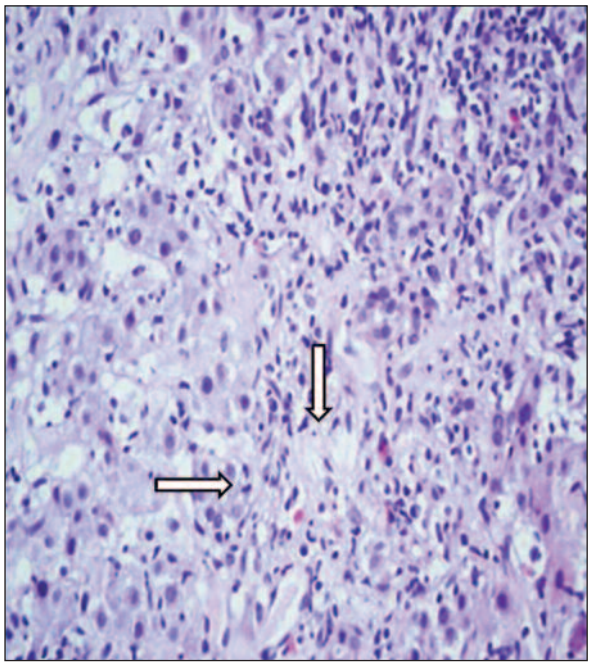

FIGURE 5: High -power photomicrograph of the liver biopsy sample (stained by hematoxylin and eosin, magnification x 200) shows hepatocyte rosette formation which is found in autoimmune hepatitis.

given after liver biopsy. One week later liver function tests began to decline and symptoms of the patient dissappeared. All autoantibodies were found negative. After two months of treatment remission of hepatitis was achieved. He is on follow-up for 2 years.

DISCUSSION

The diagnosis of AIH is based on a combination of clinical, laboratory, and histological findings.[1,2]

The clinical features of autoimmune hepatitis vary from asymptomatic, in which the disease is discovered when abnormal serum enzyme levels are detected during a screening examination, to a severe, acute, and even fulminant hepatitis.[3] The clinical features and prognosis of patients with fulminant-type autoimmune hepatitis have remained uncertain, and only a few adult cases have been reported in detail.[4,5]

AIH is a common cause of chronic hepatitis, and acute presentation is thought to be uncommon.[6] An acute or abrupt onset occurs in 40% of patients with autoimmune hepatitis, whereas an acute severe presentation is rare.[7]

The acute form can be seperated from the the chronic form by laboratory features (higher serum AST and ALT levels, total serum bilirubin concentration, and serum γ-glutamyl transpeptidase level) and by histological findings (more frequent centrilobular zone 3 necrosis with plasmacytic infiltration and bile duct injury), but its recognition in individual cases relies mainly on an awareness that acute severe autoimmune hepatitis is possible.

The presence of autoantibodies is an important component of the diagnosis but the most commonly detected autoantibodies, antinuclear antibodies (ANA) and smooth muscle antibodies (SMA), are not specific for the disease.[8] Antibodies to liver-kidney microsome type 1 (anti-LKM1) occur in a small subgroup of patients with AIH but they are also found in chronic hepatitis C and in severe rejection after liver transplantation.[9-12] In contrast, antibodies to soluble liver antigen (SLA) and liver-pancreas antigen (LP) have been described a specific for autoimmune liver disease.[13,14] Several reports have shown that many patients with AIH negative for ANA and SMA show positive SLA reactivity or LP reactivity,making these antibodies an important diagnostic marker.[14]

Certain autoantibodies in autoimmune liver disease have prognostic implications that are under-

utilized and under-developed. Antibodies to soluble liver antigen, actin, liver cytosol type 1, asialoglycoprotein receptor, chromatin, cyclic citrullinated peptide, and uridine glucuronosyltransferases have been associated with the occurrence, severity, and progression of autoimmune hepatitis.[15]

Antibodies to soluble liver antigen identify individuals who have more severe histological changes, require longer durations of treatment, invariably relapse after drug withdrawal, and have a higher frequency of liver transplantation or death from liver failure than patients without these antibodies.[15]

Their high specificity for autoimmune hepatitis, frequent occurrence in cryptogenic chronic hepatitis, and close association with HLA DRB1*0301, severe histological disease, and treatment dependence have made anti-SLA the most promising serological markers of prognosis in autoimmune hepatitis.

In this case, patient presented with high levels of transaminases and bilirubins. Only anti SLA and LP antibodies were positive and autoimmune hepatitis with acute severe presentation is considered. This was a rare clinical presentation of autoimmune hepatitis. Although this disease mostly affects women, our patient was male.

Anti-SLA is occasionally found in patients with AIH who are negative for ANA,SMA, and anti-LKM1. Anti-SLA are highly specific for the diagnosis of autoimmune liver disease and their detection may identify patients with more severe disease and worse outcome.[16] Although other types of autoimmune hepatitis are associated with acute severe form of presentation, this form of acute severe autoimmune hepatitis has not been reported.

We described a male patient with anti-SLA/LP antibody positive autoimmune hepatitis presenting with acute severe hepatitis, whose jaundice and abnormal liver function test results resolved following steroid therapy.

As a result, the key to recognizing acute severe autoimmune hepatitis is to remember it in the differential diagnosis and to make the designation after viral, drug induced, toxic and metabolic disorders have been systematically excluded. Absence of the autoantibodies conventionally used for diagnosis (ANA, SMA or LKM) at presentation should not exclude the diagnosis of AIH. Anti-SLA/LP positive autoimmune hepatitis is a rare form of the disease. Anti-SLA antibodies denote patients with a more severe course of AIH and a propensity for relapse after corticosteroid withdrawal compared to their negative counterparts. Rapid response to immunosuppressive therapy, such as prednisolone, is characteristic. Early diagnosis and therapy are essential for the patients prognosis. Liver transplantation is indicated in advanced disease.

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