Progressive hepatobiliary autoimmune diseases and cyclic citrullinated peptide antibodies

İlerleyici hepatobiliyer otoimmun hastalıklar ve siklik sitrülinize peptit antikorları

Dear editor,

Overlap syndrome is used to define the variant forms of autoimmune hepatitis (AIH) which presents with characteristics of AIH and two cholestatic syndromes, i.e. primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC). The AIH-PBC overlap syndrome is the most common form, affecting 5% of patients with AIH (1). Overlap syndromes may show a progressive course towards liver failure and cirrhosis (2). As other autoimmune diseases, AIH-PBC overlap syndrome may be complicated with types of autoimmune disorders. Currently, the data related with overlap syndromes and other autoimmune disorders are scarce. We had a patient that presented with AIH-PBC, amyloidosis, and Sjogren syndrome.

We present a 66-year-old female patient with previous history of essential hypertension. She was referred to Gastroenterology clinic from General Internal Medicine out-patient clinic with increased transaminases and normal sonographic imaging. Laboratory tests of the patient were as follows: alanine transaminase, 400 IU/L (normal range, 0-40 IU/L); alkaline phosphatase, 247 IU/L (range, 30-120 IU/L); gamma-glutamyl transpeptidase, 255 IU/L (range, 5-36 IU/L); and creatinine, 1.9 mg/dL (range 0,5-1.2 mg/dL). Serologic tests were as follows: ANA, 1/320 positive; ASMA, negative; anti-LKM 1, negative; AMA, 1/320 positive; anti-CCP, 5.73 positive (laboratory normal is below 1); anti-ENA, positive; IgM, 257 mg/dL (range 46-304 mg/dL); and Ig G, 1720 mg/dL (range 884-1912 mg/dL). The pathological findings in liver biopsy were consistent with AIH (Figure). Two years later, during the routine follow-up, urine protein testing was found to be positive. The 24-hour urine protein level was 1108 mg per day. The rectal biopsy sampling was consistent with amyloidosis. The patient had signs of keratoconjunctivitis sicca and therefore underwent Schirmer's test and salivary gland biopsy. The histo-pathological findings were consistent with Sjogren disease.

As mentioned above, the patient status was progressively complicated by amyloidosis and Sjogren disease. Sjogren syndrome has been previously reported to be associated separately with AIH and PBC. However, to our knowledge, no association was reported with AIH plus PBC, i.e. overlap syndromes (3). In addition, no data could be found regarding the association between amyloidosis and overlap syndrome. The positivity of anti-CCP antibodies in the index case can be mentioned as an interesting finding. Although anti-CCP antibodies were reported to be related to severe disease course in type 1 autoimmune hepatitis, its association with progression to overlap syndrome including amyloidosis and Sjogren disease is not known (4). Therefore, further studies are needed for the possible effect of anti-CCP on the progressive overlap syndrome. In conclusion, it should not be forgotten that overlap syndrome may also present with other types of autoimmune diseases which may not be coexisting, but may emerge later during routine follow-up.

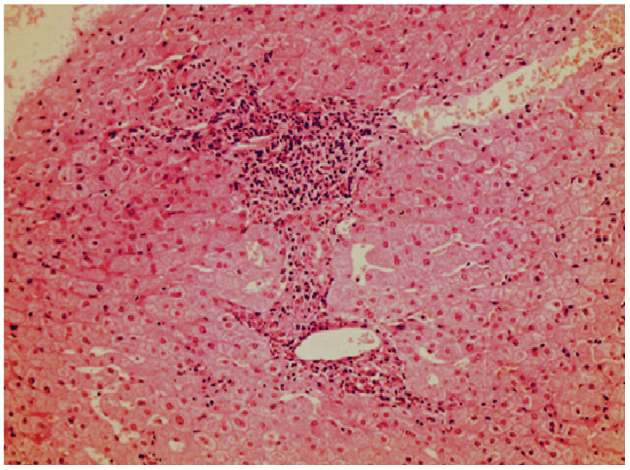

Figure 1. Hematoxylin-Eosin dye, 1x100 HPF: Infiltration of mononuclear cells to portal/periportal zones and bridging necrosis.

Address for correspondence: Mehmet Sait BUGDACI
Konya Meram Education and Research Hospital,
Gastroenterohepatology Clinic, Konya, Turkey
E-mail: msbugdaci@gmail.com

Manuscript received: 19.01.2012 **Accepted:** 30.03.2012

doi: 10.4318/tjg.2013.0514

REFERENCES

1. Heurgué A, Vitry F, Diebold MD, et al. Overlap syndrome of primary biliary cirrhosis and autoimmune hepatitis: a retrospective study of 115 cases of autoimmune liver disease. Gastroenterol Clin Biol 2007; 31:17-25.
2. Rust C, Beuers U. Overlap syndromes among autoimmune liver diseases. World J Gastroenterol 2008; 14:3368-73.
3. Ebert EC. Gastrointestinal and hepatic manifestations of Sjogren syndrome. J Clin Gastroenterol 2012; 46:25-30.
4. Montano-Loza A, Czaja AJ, Carpenter HA, et al. Frequency and significance of antibodies to cyclic citrullinated peptide in type 1 autoimmune hepatitis. Autoimmunity 2006; 39:341-8.

Mehmet Sait BUĞDACI[1, 2], Hakan AKIN[2], Ahmet DANALIOĞLU[2], Hakan ŞENTÜRK[2]

Department of [1]Gastroenterohepatology, Konya Meram Education and Research Hospital, Konya

Department of [2]Gastroenterohepatology, Bezmi Alem Vakıf University, School of Medicine, İstanbul

Identification of rodent common biliary tract

Rodentlerde ortak safra kanalının saptanması

To the Editor,

In recent years, increasing interest surrounding islet replacement therapies in human has provided the drive for advances in the methods used to isolate islets from humans as well as a host of animal research models (1). Although there are many published islet isolation protocols specific to mouse and rat, few provide the necessary details for researchers to successfully perform the complex procedures (1). The one of the most prevalent approaches for isolating islets from rodent pancreatic tissue differ, primarily, in the way digestive enzymes are introduced to the pancreatic tissue surrounding the islets. In the first approach, collagenase is injected into the common bile duct of an animal. However, it is not easy to identify the rodent common biliary tract, because the tract is observed in enriched fat tissues anatomically.

We infused indocyanine green (ICG) (1.0 ml/body of 10 mg/ml) to the rats during about one minute through the femoral vein before surgery. Araki et al. (2) previously described a method for enhanced visualization of the common biliary tract using ICG and reported its use in 54 patients undergoing cholecystectomy. We have chosen ICG because of its rapid hepatic uptake, efficient biliary excretion, lack of toxicity, and prompt fecal elimination (3). Male Sprague-Dawley rats, weighting 400 to 450 g, were housed in a certified animal care facility and handled according to the *Guide for the Ca-*

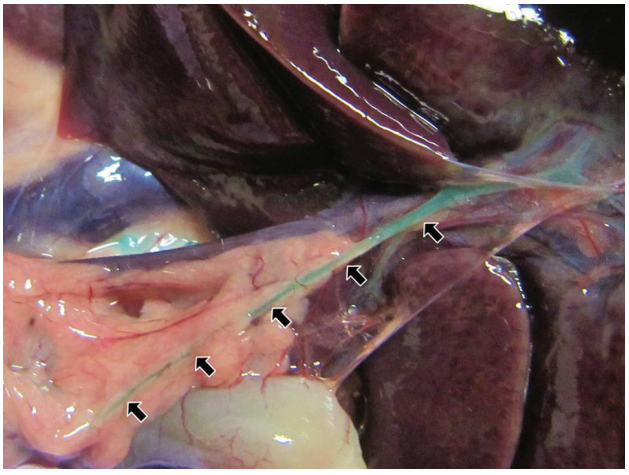

Figure 1. Enhanced visualization of the common bile duct by indocyanine green (arrows).

Address for correspondence: Takayoshi KIBA
National Hospital Organization Kure Medical Center, Division of Modern Medical Technology, Institute for Clinical Research, Hiroshima, Japan
Phone: +81 823 223111
E-mail: takkiba@hotmail.com

Manuscript received: 27.03.2012 **Accepted:** 21.05.2012

doi: 10.4318/tjg.2013.0535