Vanishing bile duct syndrome in a patient with Hodgkin's lymphoma and asymptomatic hepatitis B virus infection

Hasan Umit[1], Gulbin Unsal[1], Ahmet Tezel[1], Ali Riza Soylu[1], Gülsüm Emel Pamuk[2], Burhan Turgut[2], Muzaffer Demir[2], Dilek Tucer[1], Nilay Ermantas[1], Ugur Cevikbas[3]

(1) Department of Gastroenterology and (2) Department of Hematology, Trakya University Medical Faculty, Edirne, Turkey ; (3) Department of Pathology, Istanbul University, Istanbul Medical Faculty, Istanbul, Turkey.

To the Editor,

45-years-old male patient presented with jaundice, dark urine and white stool. He has presented with lumps in the right groin, fever, drenching night sweats and weight loss 3 years ago, been diagnosed as Hodgkin's lymphoma (HL), nodular sclerosing type. He has received 8 courses of adriamycin, bleomycin, vinblastine, dacarbazine (ABVD) chemotherapy and 24 sessions of radiotherapy and has been followed up as in remission for 6 months.

Physical examination was normal except for jaundice and bruises due to itching. Lymphadenomegaly or hepatosplenomegaly were absent. In his laboratory analysis, Hemoglobin was 14 g/dL, hematocrite 39.7%, leucocytes 17,300/µL and platelets 410,000/µL. The erythrocyte sedimentation rate was 31 mm/h, and protrombine time 13.2 seconds. The transaminase levels were, AST : 85 U/L, ALT : 91 U/L, ALP : 123 U/L, GGT : 93U/L, while total bilirubin was 20,3 mg/dL and conjugated bilirubin 20 mg/dL. Serology showed HBsAg and anti-HBe positive, while anti-HBc IgM, HBV-DNA, hepatitis Delta antibody, and anti HCV were negative. Autoantibodies such as antinuclear antibody (ANA), liver kidney microsomal antibody-1 (LKM-1), anti-smooth muscle antibody (ASMA) and anti-cytoplasmic antibody were negative. Ultrasonography showed multiple small calculi in the gallbladder while both intrahepatic and extrahepatic bile ducts were normal at MRCP. Gallium-67 scintigraphy did not show any signs of relapse of the Hodgkin's lymphoma. Liver biopsy showed absence of the normal bile ducts, ductular proliferation and the patient was diagnosed as Vanishing Bile Duct syndrome (Fig. 1). The bilirubin levels decreased rapidly after treatment of corticosteroids (Prednisolone, 1 mg/kg/day). Lamivudine (100 mg/day) was started in order to prevent reactivation of his currently inactive HBV infection. Symptoms and laboratory findings rapidly improved and the doses of the corticosteroids have been reduced gradually and discontinued while the patient has been asymptomatic for 5 months.

The diagnosis of VBDS in a patient with HL presenting with jaundice depends on the exclusion of other causes of cholestasis. Most probable causes are HL infiltration, viral hepatitis, and stones in the biliary tract.

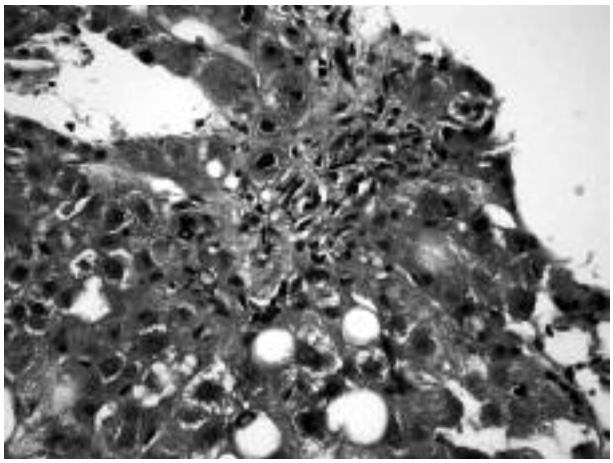

Fig. 1. — Microscopic examination of the liver demonstrating bile duct loss within the portal area, bile accumulations within the hepatocytes and the canaliculus, macrovesicular steatosis (H&E, original magnification).

In our patient, active HBV infection was excluded (undetectable HBVDNA), and the absence of abdominal pain and normal bile ducts observed by MRCP excluded a possible extrahepatic cholestasis. The HBsAg positivity has been considered as low replicative asymptomatic HBV infection and the present condition as independent from HBV infection. The pathological examination of liver biopsy excluded the infiltration of lymphoma.

To establish a diagnosis in a patient with HL presenting with jaundice is quite challenging. It may still be harder with the presence of other possible causes of jaundice as in our patient. If VBDS is diagnosed in a patient with HL, jaundice is usually the initial symptom which leads also to the diagnosis of HL itself. VBDS with HL has been reported as highly mortal but fortunately our patient has been cured with corticosteroids.

Correspondence to : Assist. Prof. Hasan Umit, M.D., Trakya Universitesi Tip Fakultesi, Gastroenteroloji BD, Edirne, 22030 Turkey.
E-mail: hasanumit@ttmail.com ; drhumit@gmail.com

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The clinical course of this syndrome remains a mystery because of its infrequency. There are reports of reversible and irreversible cases (1-3). The major factor to adjust the prognosis is to achieve a remission state if an active HL is certain. In patients with HL in remission, corticosteroids and ursodeoxycholic acid treatment have been suggested (4). Patients should be closely followed up for possible relapses in HL or liver disease. In conclusion, the possibility of VBDS should be considered in the differential diagnosis of unexplained intrahepatic cholestasis in patients with HD. Corticosteroids may be beneficial in such patients.

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