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A Case Report of Primary T-Cell Lymphoma of the Liver

The patient was a 50-year-old woman who presented intermittent mild fever with elevated liver enzymes for 12 years. The liver biopsy showed diffuse portal and sinusoidal involvement of lymphoid cells with minimal atypia and epithelioid histiocytic granuloma formation. Subsequent bone marrow biopsy showed lymphomatous involvement. The lymphocytes infiltrating the liver were reactive for T-cell marker and showed TCR γ gene rearrangement. The patient was diagnosed as primary peripheral T-cell lymphoma of the liver. Indolent clinical course and resemblance with hepatitis were considered to be a rare and unique feature of this case.

Key Words: *T-cell Lymphoma; Liver*

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INTRODUCTION

Primary lymphoma of the liver is a rare disease with about 100 cases reported (1). Due to the rarity of this disease, the working diagnosis before the liver biopsy was invariably one of metastatic carcinoma, hepatoma or cholangiocarcinoma.

Most primary lymphomas of the liver are B cell type, and only 15 cases of primary T-cell lymphoma were reported in the literature (2-8). Unusual non-Hodgkin's lymphoma with diffuse involvement of the liver without lymphadenopathy were reported in three patients (9). Their clinical manifestations suggested hepatitis but each patient had aggressive lymphoma, involving primarily the liver and spleen. Our case showed a unique feature of an indolent clinical course with hepatitis-like manifestations and diffuse involvement of the liver.

CASE REPORT

A 50-year-old woman presented with a 12-year history of intermittent fever and chill. She had no significant family or medical histories. There were no evidence of lymphadenopathy, anemia or peripheral blood lymphocytosis. Abdominal computer tomographic scan showed hepatosplenomegaly without mass lesion in the liver (Fig. 1). Bone marrow biopsy showed granulomatous inflammation. Exploratory laparoscopy finding was a diffuse enlargement of the liver without any identifiable mass, and enlarged spleen. The lymph nodes surrounding the liver were slightly enlarged. Biopsy was done from the right and left lobes of the liver and periaortic lymph node. The initial diagnosis of the liver biopsy was idiopathic granulomatous hepatitis. The periaortic lymph node showed reactive hyperplasia. Diffuse lymphomatous involvement was detected in the second bone marrow biopsy. The liver biopsy was re-examined with immunocytochemical and molecular studies with PCR and revised as low-grade T cell lymphoma of the liver, primary peripheral-T cell lymphoma (unspecified) of the liver accord-

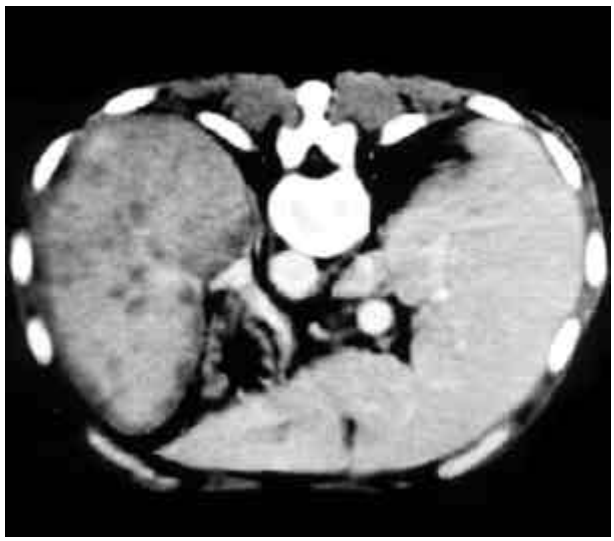

Fig. 1. Abdominal CT scan shows enlarged liver and spleen.

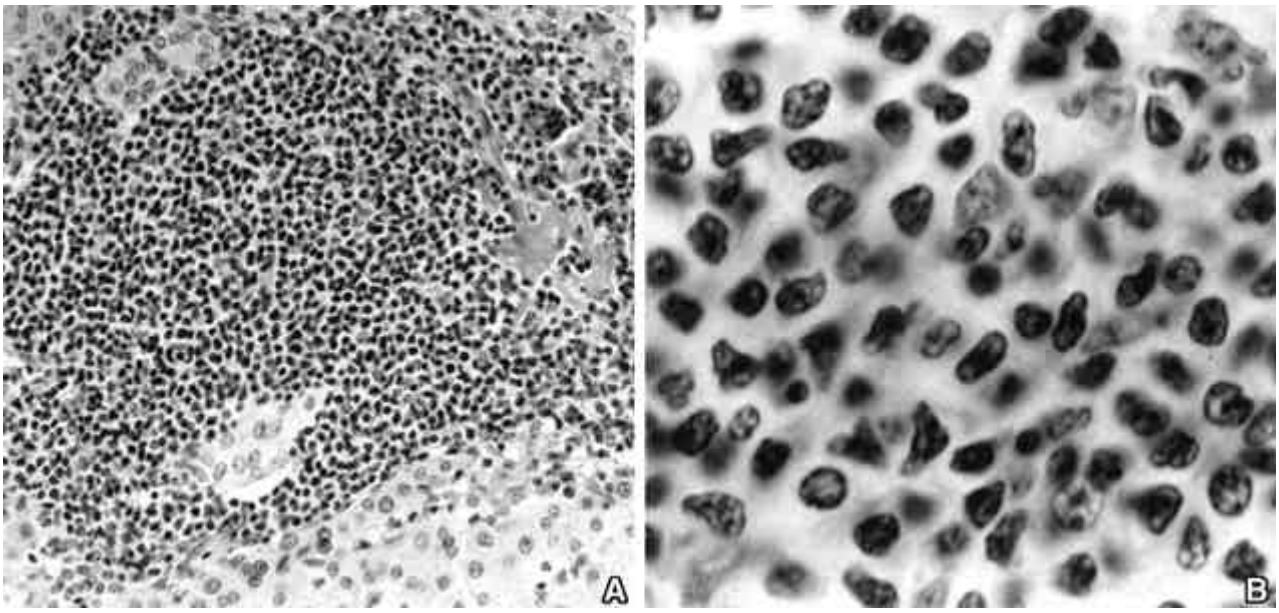

Fig. 2. Histologic findings of liver wedge biopsy. A: Widening of portal spaces due to atypical lymphoid infiltration admixed with some histiocytes are noted (H&E, ×100). B: Lymphocytes shows minimal to mild nuclear atypia (H&E, ×1,000).

ing to the REAL classification.

Microscopically, some portal spaces were widened with lymphocytic infiltration. A few portal spaces were compactly packed by lymphoid cells. Hepatic parenchymal infiltration with occasional coalescence of the tumor was found (Fig. 2A). Hepatic sinusoids were dilated by the infiltration of lymphoid cells. The tumor cells were mostly small and the nuclear diameter was same as or slightly larger than those of normal lymphocytes. Nuclear atypia was difficult to distinguish from reactive lymphocytes. High magnification demonstrated mild nuclear pleomorphism and atypia with lobulation (Fig. 2B). Small amounts of epithelioid histiocytes, plasma cells and reactive lymphocytes were admixed with tumor cells. The changes in hepatocytes were unremarkable. The second bone marrow biopsy showed well circumscribed lymphohistiocytic nodules in the interstitium. Granulomas consisting of epithelioid histiocytes were found. Immunostaining showed that more than 75% of the infiltrated lymphocytes were positive for CD3 (Dakopatts, Copenhagen, Denmark, polyclonal, 1:80) and TIA-1 (Coulter, monoclonal, 1:50) (Fig. 3), and negative for CD20 (Dakopatts, Copenhagen, Denmark, monoclonal, L-26, 1:100). Monoclonality in TCR γ gene rearrangement was observed with polymerase chain reaction using outer primer of Vγ5'-AGGGTTGTGTGGAATCAGG-3' and Jγ5'-CGTCGACAACAAGTGTTGTTCCAC-3' and inner primer of Jγ5'-GGATCCACTGCCAAAGAGTTTCTT-3' (Fig. 4).

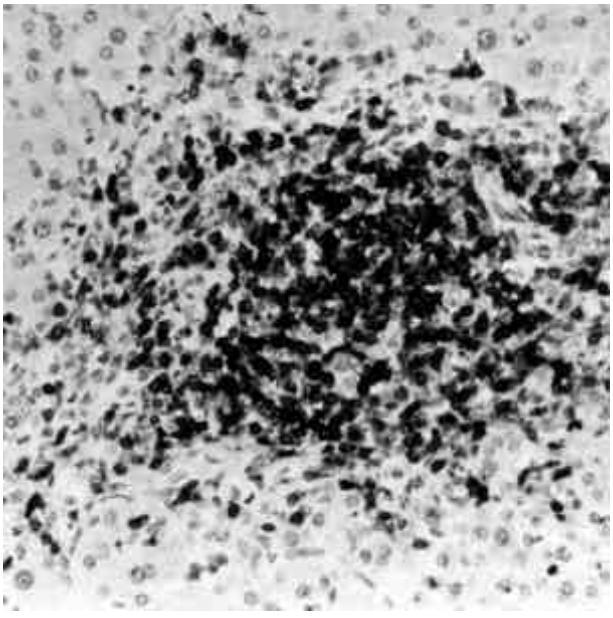

Fig. 3. Immunostaining for CD3 is positive in almost of the tumor cells (×100).

The patient achieved complete remission at 12 months and is alive with no evidence of disease at 15 months.

DISCUSSION

Primary lymphoma of liver is usually presented with abdominal pain, hepatomegaly, and palpable mass. However, diffuse tumor infiltration or long history without fulminant progress and bland histologic feature is a unusual feature (2). Because the present case showed no

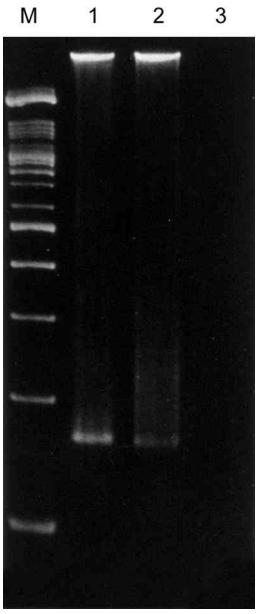

Fig. 4. Molecular studies with PCR shows a monoclonal band of TCR γ gene rearrangement. M, size marker; 1, positive control; 2, liver of this patient; 3, negative control.

other possible primary focus under the clinical work-up, the possibility of secondary involvement of lymphoma could be excluded. Another possibility is a hepatosplenic $\gamma\delta$ T-cell lymphoma. Nearly all of those patients are young adult males, with a median age at presentation of 20 years. The clinical course is aggressive, and despite multiagent chemotherapy, the median survival duration is less than 1 year (10). Histologically those tumors are characterized by a mixture of small to medium sized atypical lymphocytes (11). Our case lacks the characteristic features of hepatosplenic $\gamma\delta$ T-cell lymphoma, so we could rule out.

Fifteen cases of primary T cell lymphoma of the liver have been previously reported (2-8). Ten patients showed diffuse enlargement of the liver without mass formation. Initial diagnoses included chronic active hepatitis, "granulomatous cholangitis", inflammatory pseudotumor, and anaplastic carcinoma. Suspecting the lymphoma early is important because clinical diagnosis can be confused by unusual presentation resembling inflammatory hepatobiliary disease and by the absence of enlarged peripheral lymph nodes. The present case showed indiscernible nuclear atypia of neoplastic lymphocytes and the presence of granuloma, which led to the confusion of a non-neoplastic condition such as granulomatous hepatitis. Although abnormal cytological features are helpful in distinguishing lymphoma from reactive disorders of the liver, the small lymphoid cells with minimal atypia often represent apparent neoplastic cell components as in the current case.

In conclusion, although peripheral lymphadenopathy may be absent, lymphoma should be considered in the differential diagnosis of a patient whose course is atypical for hepatitis.

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