Co-occurrence of hepatocellular cancer and non-Hodgkin lymphoma

To the editor Hepatocellular cancer (HCC) accounts for 85% to 90% of all primary liver tumors and is the eighth most common cancer. High-risk groups for the development of HCC are hepatitis B, C, and D carriers as well as patients with alcoholic liver disease, genetic hemochromatosis, tyrosinemia, and cirrhosis from any cause. The clinical presentation of HCC may vary; in some patients, the disease is detected during asymptomatic period. However, in half of the patients, the disease manifests itself with right upper quadrant pain, abdominal mass, or worsening of clinical condition.[1]

Lymphomas represent a group of solid tumors of the lymphoid cells and are divided into Hodgkin and non-Hodgkin lymphomas (NHL). NHL account for approximately 4% of new cancers in men and are among the top causes of cancer--related deaths in adults in most industrialized countries.[2]

An overlap syndrome involving HCC and NHL is rare. In the United States cohort of 952 cirrhotic patients, lymphomas were found in less than 1%.[3] There have only been a few case reports of hepatitis B-related HCC coexisting with NHL.[4,5] We desribe yet another case of such coexistence.

A 50-year-old male patient with a primary diagnosis of HCC was admitted to our hospital for further evalution of a newly detected mass in the left inguinal lymphadenopathy. He also reported fatigue, low-grade fever (37.6°C), and night sweats. The diagnosis of hepatitis B-related HCC was made 2 years earlier. He had consumed alcohol weekly. Medications included lamivudine, sorafenib, spironolactone, and lactulose.

A physical examination on admission showed nonspesific pain on the right upper quadrant with moderate ascites and splenomegaly (18 cm in the craniocaudal dimension; upper limit of the normal range, 12–13). There was no rebound or guarding. There were prominent inguinal lymph nodes of up to 3 cm in diameter on the left inguinal region. There were also tenar muscle atrophy and venous collaterals on the periumbilical region. The remaining measurements were within the normal ranges.

Laboratory tests on admission showed the following results (with the reference values in brackets): hemoglobin, 10.3 g/dl (11–18 g/dl), hematocrit, 31.1% (35%–55%); white blood cells, 8700 mm^3 (4000–11,000 mm^3); platelet count, 114,000/mm^3 (150,000–400,000/mm^3), prothrombin time, 18 s (13 s); aspartate transaminase 163 U/l (0–37 U/l); alanine transaminase 51 U/l (0–41 U/l); total bilirubin, 1.81 mg/dl (0-1 mg/dl); direct bilirubin, 0.8 mg/dl (0–0.2 mg/dl); alkaline phosphatase, 594 U/l (0–270 U/l); total protein, 5.68 g/dl (6.6–8.7 g/dl); albumin 2.13 g/dl (3.5–5.2 g/dl); and γ-glutamyltransferase, 182 U/l (8–61 U/l).

Viral serologic tests were as follows: anti-hepatitis C virus negative, surface antigen of the hepatitis B virus (HBsAg) positive, anti-HBs antibody negative, anti-HBe antibody positive, and delta antibody negative. The AFP level was 1110 ng/ml.

Magnetic resonance imaging (MRI) of the abdomen revealed a liver mass 10 × 10 cm in diameter, which was consistent with known HCC (FIGURE 1). Positron emission tomography – computed tomography (PET-CT) showed hypermetabolic lymph nodes on the left external inguinal region (FIGURE 2). A lymph node biopsy also revealed diffuse large B-cell lymphoma (FIGURES 3A and 3B).

The adjuvant chemotherapy with cyclophosphamide, anthracycline doxorubicin, vincristine, and prednisone (CHOP protocol) was started. Constitutional symptoms resolved during treatment. The patient is currently in remission with the CHOP regimen.

We presented an interesting case of HCC associated with NHL. Patients with hepatitis B virus infection are at an increased risk of HCC and other extrahepatic malignancies.[3] Hepatitis B-related cancers other than HCC have been well-documented. In a recent Taiwanese study, the incidence rate of NHL in HBsAg-seropositive women was 3.18 per 100,000 person-years.[4] In a Korean cohort study, HBsAg-positive participants were at an increased risk of NHL, particularly for diffuse large B-cell lymphoma.[5] To date, fewer than 20 cases of HCC-associated NHL have been reported.[6] Most of them have been linked to hepatitis C infection.[7,8]

Our case report suggests that HCC may be associated with the development of NHL.

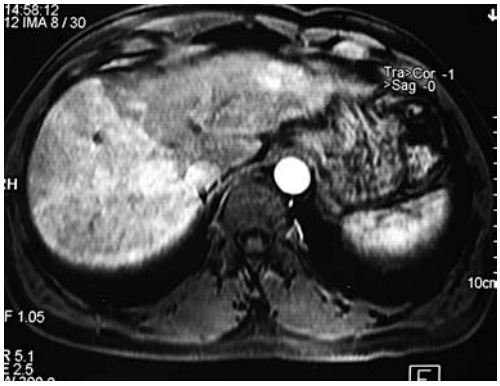

FIGURE 1 Magnetic resonance imaging shows a liver mass consistent with hepatocellular carcinoma

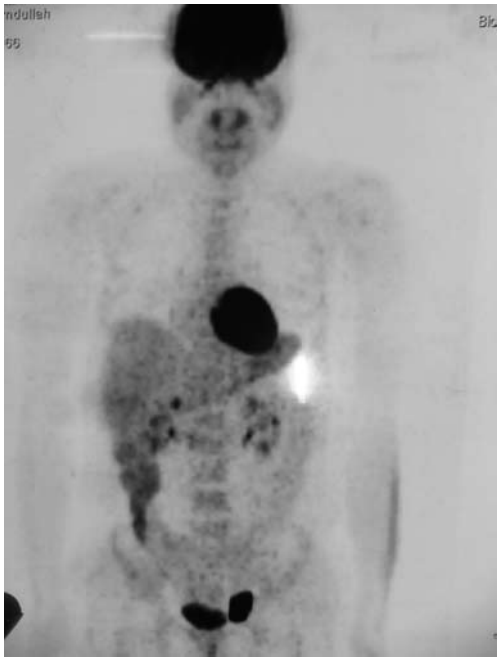

FIGURE 2 Positron emission tomography – computed tomography shows abnormal uptake on the left inguinal lymph nodes that were likely pathological

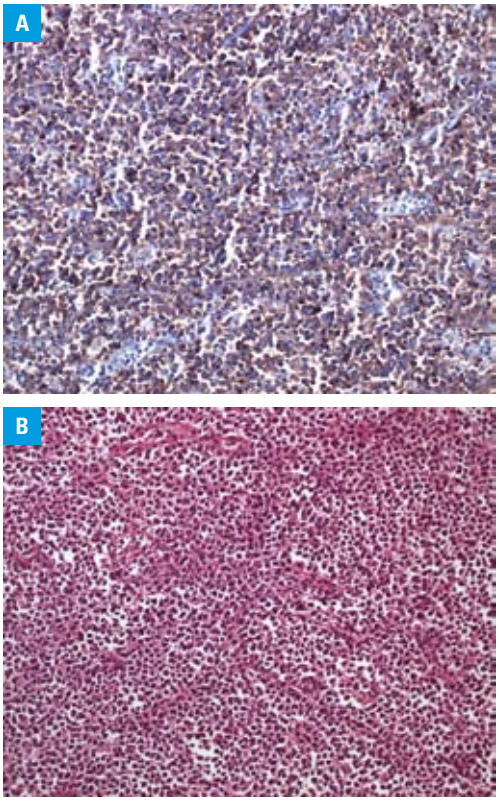

FIGURE 3 Histological and immunohistochemical photographs of diffuse B-cell lymphoma; hematoxylin and eosin staining in the low-power field view (A); anti-CD 20 staining (B); the photograph shows diffuse infiltration of lymphoma cells

Paraneoplastic manifestations of HCC include fever, portal vein thrombosis, hypoglycemia, polycythemia, hypercalcemia, and porphyria. However, peripheral lymphadenopathy is rarely reported.[1] Therefore, the differential diagnosis of lymphadenopathy is narrow in the case of HCC, and some patients may have coexisting diseases. Moreover, NHL can manifest itself as inguinal lymph node enlargement accompanied by constitutional signs as observed in our case.[9] In our patient, we were able to differentiate diffuse-type B-cell lymphoma from HCC-related lymphadenopathy using PET-CT and histologic examination of lymph node biopsy specimens.

In conclusion, we reported an extremely rare case of HCC associated with diffuse large B-cell lymphoma. A combination of PET-CT with lymph node biopsy may help detect the disease at an early stage.

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