Turk J Gastroenterol 2004; 15 (2): 94-96

Hepatic lymphoma metastasis presenting with severe acute liver failure: A rare case

Ağır akut karaciğer yetmezliği ile seyreden karaciğer lenfoması

Mehmet KANBAY[1], Gürden GÜR[2], Murat KORKMAZ[2], Beyhan DEMİRCİ[3], Sedat BOYACIOĞLU[2]

Başkent University Medical School Department of Internal Medicine[1], Department of Gastroenterology[2], Department of Pathology[3], Ankara

Hepatic lymphoma metastasis is rare, and should always be considered in the differential diagnosis of hepatic malignancy. A 52-year-old man presented with a four-day history of fever, fatigue, yellowish skin and nausea. His past medical history was unremarkable. There was no history of alcohol intake or medications. His physical examination revealed generalized jaundice and hepatomegaly. His blood tests showed liver failure and coagulopathy. Abdominal ultrasonography illustrated hepatomegaly. A further work-up included bone marrow and liver biopsy. The pathology report was B-cell lymphoma. He was treated with chemotherapy, and his laboratory findings during follow-up showed steady improvement. In conclusion, lymphoma metastasis to liver can be a cause of liver dysfunction. A high index of suspicion is required for the diagnosis. We emphasize the importance of obtaining tissue sample in all patients with suspicious lesion in any organ to avoid missing the rare but curable pathologies.

Key words: Lymphoma, liver metastasis, acute liver failure

Karaciğer lenfoması nadir görülen bir hastalık olup nedeni açıklanamayan karaciğer hastalıklarının ayırıcı tanısında düşünülmesi gereken bir tablodur. Hastanemize 4 gündür olan ateş, terleme, bulantı ve sağ üst kadranda ağrı şikayetleri ile başvuran 52 yaşında erkek hastanın fizik muayenesinde sarılık, ateş ve hepatomegali dışında bir özellik olmayıp saptanmadı. Laboratuar analizinde, karaciğer yetmezliği ve koagulopati bulguları rastlandı. Abdominal ultrasonografisinde hepatomegali ve hepatosteatoz dışında bir özellik saptanmadı. Takibinde karaciğer enzimlerinde yükselme ve genel durumunda kötüleşme gözlendi. Tanı amaçlı yapılan karaciğer ve kemik iliği biyopsi sonucu B-hücreli lenfoma olarak rapor edildi. Kemoterapi sonrası hastanın kliniğinde ve laboratuar değerlerinde düzelme gözlendi. Şiddetli akut karaciğer hastalığı ile seyreden karaciğer hastalıklarının ayırıcı tanısında özellikle ateş,terleme, kilo kaybı ve sağ üst kadranda ağrı şikayeti olan hastalarda karaciğer lenfoması da düşünülmelidir.

Anahtar kelimeler: Lenfoma, karaciğer metantazı, akut karaciğer yetmezliği

INTRODUCTION

Hepatic lymphoma metastasis is rare. Most of these patients present with right upper quadrant pain or discomfort, hepatomegaly, and symptoms of B-cell lymphoma (fever, night sweats, weight loss). In addition, the majority of patients are male and most are in the fourth decade of life. The prognosis of hepatic lymphoma metastasis is more favorable than primary or secondary epithelial malignancies of the liver. Hepatic lymphoma metastasis should always be included in the differantial diagnosis for patients who present with the above-mentioned symptoms. Chemotherapy often yields good results.

CASE REPORT

A 52-year-old man was admitted to the Department of Internal Medicine with the complaints of fever, fatigue, yellowish skin and nausea. The problems had existed for the previous four days. The patient's medical history was unremarkable. On examination, he appeared well nourished, and was mildly icteric. His vital signs were blood pressure 120/70 mmHg, heart rate 108/min, respiratory rate 28/min, and body temperature 40°C. On physical examination, there was no evidence of lymphadenopathy. The patient exhibited mild tenderness in the right upper quadrant and the liver was palpable below the right costal margin. Labo-

Address for correspondence: Mehmet KANBAY
35. Sokak 81/5 Bahçelievler, Çankaya-Ankara, Turkey
Phone: +90 312 222 03 98
Fax: +90 312 215 42 16
E-mail: drkanbay@yahoo.com

Manuscript received: 23.12.2003 **Accepted:** 25.05.2004

ratory testing on admission showed normal serum levels of hemoglobin, leukocyte, blood urea nitrogen (BUN), creatinine (Cre), and electrolytes and nothing abnormal on a peripheral blood smear. The following parameters were elevated: lactate dehydrogenase (LDH): 990 U/L (225-450), aspartate aminotransferase (AST): 152 U/L (0-40), alanine aminotransferase (ALT): 174 U/L (0-41), alkaline phosphatase (AP): 480 U/L (15-250), GGT: 270 U/L (8-61), total bilirubin (T-Bil): 6.91 mg/dl (0.2-1.2), direct bilirubin (D-Bil): 4.26 mg/dl (0-0.25), and C-reactive protein (CRP): 122 mg/L (0-10). The prothrombin time was prolonged at 34 s (11-14.5s), and arterial blood gas analysis showed mild metabolic acidosis. Posterior-anterior and lateral lung radiographs revealed a nodule in the lung posterior to the heart. Based on the initial findings, the patient was referred to the Gastroenterohepatology Department. Computed tomography (CT) of the thorax and abdomen revealed hepatomegaly (170 cm), massive ascites, hydrophilic gall bladder due to ascites and a nodule in the left lower lobe basal segment of the lung (Figure 1). The patient's clinical condition grew progressively worse and his liver function deteriorated further each day (Table 1). The fever and elevated CRP suggested possible sepsis. After collecting samples of blood, urine, sputum, and ascites fluid for culture, we initiated empirical treatment with wide spectrum combination of piperacillin-tazobactam. An extensive serological work-up for infectious agents was done, which revealed that the patient was negative for HbsAg, anti-HbsAb, anti-Hbc immunoglobulin-M (Ig M), anti-hepatitis C virus, anti-HAV Ig M, cytomegalovirus Ig M, and Epstein-Barr virus Ig M. A Brucella agglutination test was also negative. Even with the antibiotic therapy, the patient's temperature remained at 380C or higher. Biopsies of liver and lung and bone marrow biopsy were performed.

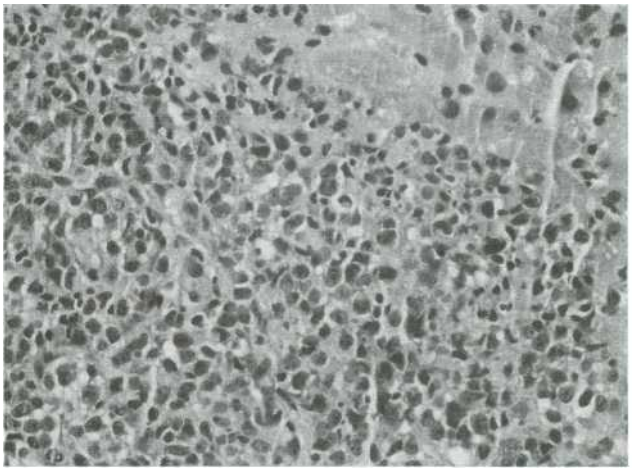

Figure 1. Histopathologic examination of liver showed B-cell lymphoma

Histological examination of the liver specimen revealed diffuse sinusoidal infiltration with medium to large atypical lymphocytes. Immunohistochemical staining of the tissue demonstrated CD20- and CD3-positive B-lymphocytes (Figure 2). The bone marrow biopsy featured marked hypercellularity; special immunohistochemical staining showed sinusoidal infiltration of CD20 positive B-cells. The patient was diagnosed with hepatic B-cell lymphoma metastasis. He tolerated chemotherapy well, and laboratory findings during follow-up showed steady improvement (Table 1).

DISCUSSION

The most common causes of acute liver failure are viral hepatitis and drug-induced liver injury (1, 2). Hepatic lymphoma metastasis is rare (3, 4). Patients are usually diagnosed in the fourth decade of life, and this type of neoplasm is more common in males than females (ratio 3:1). At present, neither the etiology nor the pathogenesis of hepatic

Table 1. The consecutive laboratory analysis of the patient

Parameter	On admission	3rd day	6th day	4th day AC	21st day AC
Hb (g/dl)	15.9	14.3	13.3	13.2	12.9
WBC (/mm^3)	6400	4400	8700	7200	9400
PLT (/mm^3)	126000	108000	168000	189000	192000
ALT (U/L)	174	448	662	247	70
AST (U/L)	152	342	378	127	56
AP(U/L)	480	423	370	242	386
GGT (U/L)	270	224	157	96	68
Cre (mg/dl)	0.6	0.8	1	0.9	1
BUN (mg/dl)	26	18	16	23	18
PTZ (s)	34	36	32	24	16
Albumin (g/dl)	2.7	2.6		2.3	3,6

AC: After Chemotherapy

lymphoma is clear; however, some evidence suggests chemical carcinogens (propane, petrol and others) and viruses (e.g., hepatitis B virus, human immunodeficiency virus, Epstein-Barr virus) as possible etiologic factors. Hepatic involvement is usually nodular (solitary or multiple), and only a few cases feature diffuse infiltration of the liver tissue (3). Our patient exhibited diffuse infiltration.

Clinically, most patients with hepatic lymphoma metastasis exhibit right upper quadrant pain or discomfort, hepatosplenomegaly without peripheral lymphadenopathy and symptoms of B-cell lymphoma (weight loss, fever and night sweats) (6). The latter combination of symptoms is a hallmark of this disease. Other clinical and laboratory findings include fatigue, jaundice, thrombocytopenia, elevated LDH and liver parameters and, as in our case, metabolic acidosis.

There are many treatment options for liver lymphoma, including chemotherapy, surgery and radiation therapy, either alone or combined (7, 8). At present, there is no standard optimal treatment for this disease. Our patient was treated with chemotherapy and responded well. This case of hepatic lymphoma metastasis is unusual in a number of respects. The clinical course was particularly aggressive. Acute severe liver disease with progressive deterioration is not the typical scenario for hepatic lymphoma metastasis. Also, in contrast to previously reported cases, our patient did not exhibit splenomegaly or thrombocytopenia even though there was bone marrow involvement. The reason our patient developed ascites without splenomegaly is the rapid clinical progression. The cause of ascites is most probably portal hypertension due to diffuse liver involvement very much like the acute alcoholic hepatic insufficiency. Benign cytology of the ascites, albumin gradient greater than 1.2, absence of peritoneal thickening during radiological evaluations, and decrease in ascites after chemotherapy all make portal hypertension secondary to liver metastasis of lymphoma as the likely cause of the ascites.

In conclusion, hepatic lymphoma metastasis can be a cause of liver dysfunction, and should be taken into account in the differential diagnosis of fever of unknown origin associated with acute liver dysfunction. A high index of suspicion is required for the diagnosis. We emphasize the importance of obtaining tissue sample in all patients with suspicious lesion in any organ to avoid missing the rare but curable pathologies.

REFERENCES

1. Stewart KS, Gordon MC. Non-Hodgkin lymphoma in pregnancy presenting as acute liver failure. Obstet Gynecol 1999; 94: 847.
2. Lee WM. Acute liver failure. N Engl J Med 1993; 329: 1862-72.
3. Aghai E, Quitt M, Lurie M, et al. Primary hepatic lymphoma presenting as symptomatic immune thrombocytopenic purpura. Cancer 1987; 60: 308-11.
4. Adeodu O, Nwosu S. Hepatic Burkitt lymphoma: presentation with extremely rapid growth. Clin Pediatr 1990; 29: 529-31.
5. Shabab N, Rowena L. Hepatosplenic T-cell lymphoma. Am S Clin Oncol 2003; 176: 1889-90.
6. Yasin M, Hartranft T. Primary hepatic lymphoma: unusual presentation and clinical course. Am J Surg 1997; 63: 951-3.
7. Daniel SJ, Attiyeh FF, et al. Primary lymphoma of the liver treated with extended left hepatic lobectomy. Cancer 1985; 55: 206-9.
8. De Ment SH, Mann RB, Staal SP, et al. Primary lymphoma of the liver. Report of six cases and review of literature. Am J Clin Pathol 1987; 88: 255-63.