Cumhuriyet Tıp Derg 2011; 33: 97-100
Cumhuriyet Med J 2011; 33: 97-100

Case report-Olgu sunumu

Acute myeloblastic leukaemia in a patient with liver cirrhosis due to chronic hepatitis B during lamivudine therapy

Kronik hepatit B'ye bağlı karaciğer sirozu olan ve lamivudin tedavisi alan bir hastada akut miyeloblastik lösemi

Hilmi Ataseven, İlhami Yüksel, Mehmet İbiş, Mehmet Arhan, Mehmet Demir, Nurgül Şaşmaz

Department of Gastroenterology (H. Ataseven, MD), Cumhuriyet University, School of Medicine, TR-58140 Sivas, Gastroenterology Clinic (İ. Yüksel, MD), Dışkapı Yıldırım Beyazıt Teaching and Research Hospital TR-06110, Anakara, Department of Gastroenterology (M. İbiş, MD, M. Arhan, MD, N. Şaşmaz, MD), Turkey Yüksek İhtisas Hospital, TR-06100 Ankara, Department of Gastroenterology (M. Demir, MD.), Erzurum Teaching and Research Hospital, TR-25000 Erzurum

Abstract
There are several causes resulting in decompensation of compensated cirrhosis and disturbing ascites regulation. Besides, hematologic disorders including anemia, thrombocytopenia, leucopenia and coagulation disorders may also accompany cirrhosis. In this case, we discuss a patient with liver cirrhosis on lamivudine treatment with refractory ascites and pancytopenia, who developed acute myeloblastic leukemia during the course of the disease.
Keywords: Hepatitis B, liver cirrhosis, acute myeloblastic leukemia, lamivudine

Özet
Kompanze sirozun dekompanze olmasının ve asit regülasyonunun bozulmasının farklı nedenleri vardır. Ayrıca, anemi, trombositopeni, lökopeni ve pıhtılaşma bozuklukları gibi hematolojik bozukluklar da siroza eşlik edebilir. Bu vaka sunumunda, lamivudin kullanan karaciğer sirozlu bir hastada hastalığın seyri sırasında akut miyeloblastik lösemi gelişen refrakter asit ve pansitopenili bir vakayı tartıştık.
Anahtar sözcükler: Hepatit B, karaciğer sirozu, akut myeloblastik lösemi, lamivudine

Geliş tarihi/Received: April 17, 2010; **Kabul tarihi/Accepted:** November 22, 2010

Corrosponding address:
Dr. Hilmi Ataseven, Gastroenteroloji Anabilim Dalı, Cumhuriyet Üniversitesi Tıp Fakültesi, TR-58140 Sivas. E-posta: hilmiataseven@yahoo.com

This study was presented as a poster in 5th APASL Single Topic Conference in İstanbul.

Introduction

Liver cirrhosis is the last stage of a complex process resulting from hepatocyte damage. As a chronic and progressive liver disorder, cirrhosis may develop in response to several etiologic factors. It may develop particularly following chronic viral hepatitis, which is a vital public health problem. Serious, sometimes life-threatening complications including portal hypertension and secondary gastrointestinal bleeding, ascites, spontaneous bacterial peritonitis, encephalopathy, hepatocellular carcinoma, hypersplenism and hematological disorders may develop during the course of the disease. Anemia, thrombocytopenia, leucopenia and coagulation disorders may accompany cirrhosis. Hematologic malignancies such as leukemia and/or lymphoma have also been reported in patients with liver cirrhosis. This, however, mostly relates with activation of hepatitis and decompensation of cirrhosis due to immunosuppression following chemotherapy or bone marrow or solid organ transplantation procedures targeting these malignancies [1-3]. In

this report, we present a case with acute myeloblastic leukemia (AML) developed during follow-up in a patient with liver cirrhosis secondary to hepatitis B virus who was on lamivudine treatment and who did not underwent any immunosuppressive treatment.

Case report

A 45-years old male patient who is pending to liver transplantation presented with recent complaints of weight gain, swelling in the abdomen, weariness and fatigue. He had been on follow-up for two years for liver cirrhosis due to hepatitis B. Physical examination revealed typical findings of chronic liver diseases, as well as tense ascites, umbilical hernia and bilateral pretibial edema. Medical history included esophageal varices and treatments with lamivudine 100 mg 1x1, propranolol 20 mg 2x1, lansoprazole 30 mg 1x1, spironolactone 100 mg 1x1. Abdominal ultrasonography demonstrated undersized liver, coarse structure, irregular borders, oversized spleen and generalized ascites. Serum HBV DNA was negative. Baseline laboratory values at admission are presented in (Table 1). The patient was hospitalized for management of ascites. No infection findings were observed in ascitic fluid analysis. Ascites regulation could not be achieved in the patient despite appropriate diuretic and paracentesis treatments. Besides, decreases in hemoglobin and hematocrit levels were detected in the patient although there were no findings of bleeding (Table 2). Therefore, two units of erythrocyte suspension were administered. The patient with dizziness during follow-up demonstrated further decreases in hemoglobin and hematocrit levels in the repeat whole blood count and therefore peripheral smear (PS) was carried out and consultations with hematology department were performed. PS demonstrated 20-30% blast formation (Figure 1). Increased leukocyte level count also noted in control hemograms and the patient developed fever during follow-up. He was transferred to the hematology clinic with the diagnosis of AML.

Table 1. Baseline laboratory values at admission

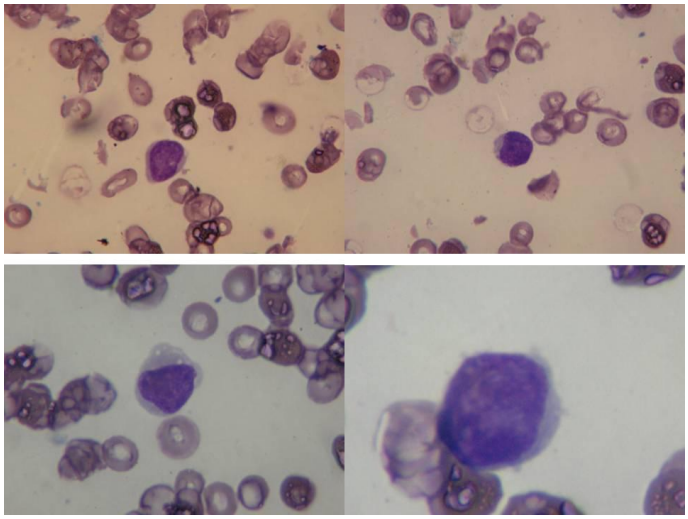
FPG (mg/dl)	92
AST	94 (normal range 0-38) U/L
ALT	39 (normal range 0-41) U/L
ALP	435 (normal range 0-270)
GGT	53 (normal range 8-61) U/L
Serum albumin	2.2 g/dl
Total bilirubin	5.14 (0-1.1) mg/dl
Direct bilirubin	2.68 (0-0.3) mg/dl
Alpha fetoprotein	0.5 IU/ml
PT	21.5 Sec
INR	1.72
HBsAg	(+)
Anti HBe	(+)
Anti HCV	(-)
Ascites liquid	Leucocytes: 300 /uL (neutrophils 100, lymphocytes 200), Albumin: 0.6 g/dl, density: 1016, lactic dehydrogenase: 152 U/L, serum ascites albumin gradient (SAAG): 1.6 (>1.1)

FPG: fasting plasma glucose AST; aspartate aminotransferase, ALT; alanine aminotransferase, GGT; gamma-glutamyl transpeptidase, ALP; alkaline phosphatase, PT; prothrombin time

Table 2. Whole blood follow-up counts

	Hemoglobin g/dl	Leukocyte/uL	Hematocrit %	Platelet /uL
20.09.06	7.0	1400	19.8	34000
25.09.06	5.9	2900	17	29000
27.09.06	7.3	4900	20.9	42000
28. 09.06	6.6	4600	18.7	26000

Figure1. Blast cells visible on peripheral smear (HE X 1000).



Discussion

Development of liver cirrhosis during the course of chronic viral hepatitis and consequent portal hypertension in advanced stages is well-known. Development of ascites, on the other hand, is the most common complication of the liver cirrhosis and is acknowledged as a reliable indicator of progression from the compensated to decompensated phase. Development of malignancies (such as Hepatocellular Carcinoma HCC) should be considered in cases who develop ascites or who become refractory to treatment while being regulated with treatment or those non-responsive from the beginning. Anemia is a frequent disorder in liver cirrhosis which may be associated with several factors including malnutrition, vitamin deficiency, hemorrhage, hypersplenism, immunity and hemolysis. Destruction and sequestration of blood elements in the spleen are promoted by splenomegaly secondary to portal hypertension and consequent anemia, leucopenia and thrombocytopenia is observed [1-4].

Our patient was hospitalized for management of ascites. The patient with no significant findings on blood and ascetic fluid analysis underwent ultrasonography which did not demonstrate any findings except liver cirrhosis and generalized ascites. Alpha fetoprotein was also normal. Intensive diuretics treatment was administered and therapeutic paracentesis was performed when the patient did not respond to diuretics. Full relief could not be achieved with this treatment either. Reductions particularly in hemoglobin and hematocrit levels were observed in the patient who initially had pancytopenia. Because there were no bleeding events, this was first associated with hypersplenism. However, blast cells were observed in PS performed upon persistence of this reduction

Failure to achieve adequate ascites management was associated with acute myeloblastic leukemia which may have amplified decompensation due to development of malignity but may also be due to development of ascites secondary to leukemia as ascites may occur at the onset and/or during the progress of leukemias [4-7]. We think that AML, along with hypersplenism may have contributed to the development of peripheral blood disorder in a similar manner. To the best of our knowledge, contribution of AML to decompensation has not been reported previously. Although concurrence of liver cirrhosis with hematologic malignancies has been presented before, this coexistence primarily relates to activation of viral hepatitis and decompensation of cirrhosis to a degree that may result in a fatal outcome in immunosuppressed patients [8-10] or development of hematologic malignancy in some way in a patient with cirrhosis following an immunosuppressive treatment [11].

Lamivudine is effective not only in chronic hepatitis B but also in patients who have undergone liver transplantation and in those receiving chemotherapy. It is also indicated in preventing development of decompensation and HCC in patients with cirrhosis secondary to HBV and in reducing pre-transplantation staging. No serious adverse effects during development of resistance have been reported. However, Chien et al. [12] have claimed that risk of AML increased in a population using lamivudine. Our patient pending to transplantation has been using this drug for 2 years. Definitely, it may not be appropriate to associate development of AML to treatment with this drug. Nevertheless, we think that caution should be exercised in this regard.

Hematologic malignancies not commonly seen with cirrhosis such as leukemia should also be considered and relevant assessments should be performed in cases where ascites regulation is inadequate and/or unexpected abnormalities are observed in peripheral blood, particularly if lamivudine is being administered.

References

1. Doti CA, Gondolesi GE, Sheiner PA, Emre S, Miller CM, Aledort LM. Leukemia after liver transplant. Transplantation 2001; 72: 1643-6.
2. Yeung LT, Petric M, Cutz E, Roberts EA. Histological improvement with lamivudine therapy for de novo hepatitis B occuring in an anti-HBs-positive child after bone marrow transplantation. Bone Marrow Transplant 2002; 30: 459-62.
3. Lin PC, Poh SB, Lee MY, Hsiao LT, Chen PM, Chiou TJ. Fatal fulminant hepatitis B after withdrawal of prophylactic lamivudine in hematopoietic stem cell transplantation patients. Int J Hematol 2005; 81: 349-51.
4. Geoffray A, Shirkhoda A, Wallace S. Abdominal and pelvic computed tomography in leukemic patients. J Comput Assist Tomogr 1984; 8: 857-60.
5. Simel DL, Weinberg JB. Leukemic ascites complicating acute myelomonoblastic leukemia. Arch Pathol Lab Med 1985; 109: 365-7.
6. Strittmatter C, Schneider J, Lüthy R, Schmid M. Stenosis of the terminal portal vein branch in acute myeloid leukemia. Schweiz Med Wochenschr 1991; 121: 1298-301.
7. Fiel I, Strauchen JA, LoValvo R, Meyer RJ, Unger PD. Acute granulocytic leukemia with ascites as the initial manifestation. Acta Cytol 1995; 39: 608-9.
8. Kojima H, Abei M, Takei N, Mukai Y, Hasegawa Y, lijima T, Nagasawa T. Fatal reactivation of hepatitis B virus following cytotoxic chemotherapy for acute myelogenous leukemia: fibrosing cholestatic hepatitis. Eur J Haematol 2002; 69: 101-4.
9. Lee HK, Yoon GS, Min KS, Jung YW, Lee Ys, Suh DJ, Yu E. Fibrosing cholestatic hepatitis: a report of three cases. J Korean Med Sci 2000; 15: 111-4.
10. Ikeda K, Shiga Y, Takahashi A, Kai T, Kimura H, Takeyama K, Noji H, Ogawa K, Nakamura A, Ohira H, Sato Y, Maruyama Y. Fatal hepatitis B virus reactivation in a chronic myeloid leukemia patient during imatinib mesylate treatment. Leuk Lymphoma 2006; 47: 155-7
11. Orbuch SJ, Findor JA. Hodgkin's disease developing in the course of a chronic liver disease with ulcerative colitis immunosuppressed with azathioprine. Acta Gastroenterol Latinoam 1979; 9: 73-80.
12. Chien RN, Yeh CT, Wang PN, Kuo MC, Hsieh SY, Shih LY, Liaw YF. Acute leukaemia in chronic hepatitis B patients with lamivudine therapy. Int J Clin Pract 2004; 58: 1088-91.