Acute liver failure as the first relapsing manifestation of very late relapsing of Hodgkin’s disease

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Abstract

Hodgkin’s disease is, in general, a lymph node-based disease. It usually starts in an area within the lymphatic system and spreads, in an orderly manner, along the lymphatic chain to contiguous lymph node areas. There have been sporadic case reports of acute liver failure caused by hematological malignancies. Generally, liver failure is a feature of stage IV end-stage disease, when it occurs in lymphoma. Thus, hepatic involvement usually occurs late in the course of Hodgkin’s disease or with advanced-stage disease, and primary presentation in the liver with acute liver failure is extremely rare. In most cases, the diagnosis was made at autopsy. We describe a patient with Hodgkin’s disease presenting with acute liver failure. This is a very unusual Hodgkin’s disease form of presentation, because the acute liver failure was the presenting feature of the disease. Furthermore, the lymphoma occurred as a very late relapse, twenty years after the first diagnosis. To the best of our knowledge, such a case has not been described to date.

Case Report

A 59-year-old woman was diagnosed in May 1986 as suffering from stage IVA nodular sclerosis Hodgkin’s disease (HD) with liver and spleen involvement. She received Mantle-like radiotherapy including submucosal, cervical, supra- and infraclavicular, axillary, hilar, and mediastinal lymph nodes. In October 1986, an exploratory laparotomy was performed, which showed retroperitoneal lymph node involvement and liver and splenic infiltration. Then, splenectomy and treatment with 12 cycles of CMOP/ABVD chemotherapy were performed. After finishing treatment, the presence of liver involvement (owing to the initial presence of infiltration of the liver) was re-evaluated.

Discussion

Hepatic involvement in HD usually occurs late in the course of the disease or with advanced-stage disease, and primary presentation in the liver is extremely rare.1,3 Acute liver failure (ALF) can result from a wide variety of causes, of which viral and toxic-induced hepatitis are the most common. ALF also has been reported in patients with malignant infiltration of the liver by malignancies such as lung, breast, melanoma, and others. Hematological malignancies are the most common underlying etiology, including Hodgkin’s lymphoma, non-Hodgkin’s lymphoma, malignant histiocytosis, and leukemia. However, it is distinctly uncommon for ALF to be the initial manifestation of a malignant process.2,4

Hepatic infiltration by hematological malignancies occurs in 15-22% of cases, but very rarely causes ALF. A review showed that only 18 of 4020 patients (i.e. 0.44%) admitted over a period of 18 years at a liver failure unit had ALF secondary to malignant infiltration. The etiology was HD in three patients. Most of the patients in this series had evidence of extra-hepatic involvement of their disease, either with peripheral or intra-abdominal lymphadenopathies, bone marrow infiltration, or splenomegaly.2 Infiltrations by lymphoma of small intrahepatic bile ducts may result in extensive cholangitis, duct necrosis, and tumor obstruction of hepatic venules. On the other hand, tumor infiltrations of hepatic parenchyma may lead to a critical mass of hepatocyte destruction and subsequent ALF. Hepatic failure can occur even if cells had infiltrated extensively into the liver, and consequently hepatic failure and jaundice were considered the result of massive liver involvement.2,4

Making a diagnosis of hepatic infiltration in patients presenting with ALF in such cases generally is difficult, and hence HD can be diag-
nosed late. However, early diagnosis is very important because it is possible that quick institution of specific chemotherapy may reverse liver disease. Clinical and laboratory findings are not helpful for differential diagnosis. All of them may be seen in a number of primary liver diseases. Ultrasonography and CT scans seem to be inadequate in diagnosing hepatic lymphoma. To diagnose hepatic involvement, the presence of mononuclear variants of RS cells in an appropriate background is sufficient if the diagnosis of HD has been established in a lymph node, but if liver tissue is the only material examined, demonstration of classical multinucleated RS cells is required.  

As the liver has limited tolerance to radiotherapy, and surgery is only feasible for solitary lesions, the choice of treatment in this case with disseminated liver involvement was combined chemotherapy. Conventional-dose chemotherapy has demonstrated very poor results in refractory and early relapsed patients after first-line chemotherapy. For late relapsed patients (<12 months), salvage chemotherapy with conventional-dose therapy shows a 35% probability of overall survival (OS) five years after therapy. The remission rate is greatest in patients with late relapse (75% vs. 55% for early relapse vs. 35% for primary refractory Hodgkin’s lymphoma). Our case demonstrates that relapsing lymphoma in the liver, even in patients without evidence of extrahepatic malignancy, should be included in the differential diagnosis of ALF and treated accordingly. In the presence of lymphadenopathy and hepatomegaly in ALF patients, hematological malignancies should be taken into account, and liver and lymph node biopsies should be performed as early as possible. This is the only way to reach the correct diagnosis and start appropriate chemotherapy, which can be life-saving.

References