Primary Hepatic Lymphoma: A Case Report and Review of the Literature

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Abstract

Primary Hepatic Lymphoma (PHL) is notably rare in the world. We report a 51-years-old Chinese adult man presented with a 30-day history of right upper-quadrant abdominal pain without weight loss, fever or night sweats. Percutaneous needle biopsy was made and immunohistochemical stains analysis showed that CD20, Bcl-2, Bcl-6, and Ki-67 (60%) were positive, while bone marrow biopsy was negative. The Diagnosis of Diffuse, Large B-Cell, Non-Hodgkin Lymphoma (DLBCL) was made. After 6 cycles of cyclophosphamide, epirubicin hydrochloride, vincristine, and prednisone combined chemotherapy, CT showed a dramatic reduction in the tumor size.

Keywords: Diagnosis; Liver Lymphoma; Treatment

Introduction

Primary Hepatic Lymphoma (PHL) is notably rare in the world [1-3]. It is a tumor confined to the liver without evidence of lymphomatous involvement of lymph nodes, spleen, bone marrow or other lymphoid structures [4, 5]. Because of nonspecific clinical symptoms or imaging pattern, it is difficult to discriminate from hepatocellular carcinoma, metastatic tumor, or liver abscess [5-8]. Most patients are treated with chemotherapy by using different combinations of drugs [9]. However, optimal therapy is still unclear and the outcomes are uncertain. Here, we present a case of primary non-Hodgkin lymphoma of the liver in a patient with a 30-day history of right upper-quadrant abdominal pain and treated with chemotherapy.

Case Presentation

A 51-years-old Chinese adult man presented with a 30-day history of right upper-quadrant abdominal pain without weight loss, fever or night sweats. He denied any history of Hepatitis A Virus (HAV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) infection and tumors. No family history of tumors. Physical examination revealed mild hepatomegaly and a large palpable, smooth, nontender mass in the right hypochondrium that extended between the costal arch and the umbilicus. The spleen was not palpable, and there were no other abdominal masses. There was no lymphadenopathy, and the remainder of examination was normal. The results of laboratory test showed a hemoglobin level of 94 g/L, a platelet count of 66 *10^9 g/L, a lactate dehydrogenase level of 554 U/L, an alkaline phosphatase level of 118 U/L, and a glutamyl transpeptidase level of 65 U/L. The tumor markers α Fetoprotein (AFP), Carcinoembryonic Antigen (CEA), CA-199 was not elevated. No positive antigens to Human Immunodeficiency Virus (HIV), Epstein-Barr Virus (EBV) or hepatitis A, B, or C (hep A, B, C) virus were observed.

Abdominal Magnetic Resonance Imaging (MRI) (Philips Achieva 3.0 T) revealed a 12.0 × 10.0 × 8.4 cm^3 mass involving the right lobe of the liver with no other abdominal masses or adenopathy (Figure A). FDG-PET scan demonstrated high glycolytic activity of a solitary mass in the right lobe of the liver without spread to the body (Figure B). Percutaneous needle biopsy was made and immunohistochemical stains analysis showed that CD20, Bcl-2, Bcl-6, and Ki-67 (60%) were positive, while bone marrow biopsy was negative (Figure C). The diagnosis of diffuse, large B-cell, Non-Hodgkin Lymphoma (NHL) was made. After 6 cycles of cyclophosphamide, epirubicin hydrochloride, vincristine, and prednisone combined chemotherapy, CT showed a dramatic reduction in the tumor size (Figure D). Now the patient is in following up.
Discussion and Review

Although rare, it is important to recognize PHL because it responds favourably to chemotherapy. This case only showed a 30-day history of right upper-quadrant abdominal pain without weight loss, fever or night sweats. However, MRI showed a large mass in the right lobe of the liver. Firstly, we thought that it may be hepatocellular carcinoma or metastatic tumor. Then PET-CT demonstrated a high glycolytic activity of a solitary mass in the right lobe of the liver without spread to the body. Therefore, we thought that it was not metastatic tumor but could be primary liver tumor (mostly PHL). Then, we performed percutaneous needle biopsy and immunohistochemical stains. Finally, the diagnosis of diffuse, large B-cell, NHL was determined according to the results of immunohistochemical stains. Here, we recommend that the biopsy is needed and important for a definitive diagnosis and identifying the immunophenotype of PHL. This type of lesion is highly chemosensitive, and chemotherapy was chosen, and the patient showed a dramatic reduction in the tumor size after 6 cycles of chemotherapy [10-12].

PHL represents 0.4% of extranodal NHLs and 0.016% of all NHLs [13]. It was firstly described by Ata et al. [14]. Osborne BM et al. reported 10 cases in his department and reviewed 19 cases that were reported in the literature [15]. Caccamo et al. defined PHL as lymphoma localized and limited to the liver without extrahepatic involvement, and the symptoms should be
the disease is confined to the liver. Liver function test can show anorexia, vomiting or nausea. Hepatomegaly is very common, and (also known as ‘B’ symptoms) [37]. Alternative symptoms include nonspecific, presented with fever, loss of weight and night sweats to onset of fulminant hepatic failure with rapid progression of discovery of hepatic abnormalities in asymptomatic patients is not well known [31-36]. Presentations vary from the incidental discovery of hepatic abnormalities in asymptomatic patients to onset of fulminant hepatic failure with rapid progression of enccephalopathy to coma and death [19]. Symptoms are usually nonspecific, presented with fever, loss of weight and night sweats (also known as ‘B’ symptoms) [37]. Alternative symptoms include the pain in the right upper quadrant or the epigastrium, fatigue, anorexia, vomiting or nausea. Hepatomegaly is very common, and jaundice may be found on physical examination [37].

Full blood count is usually within the reference range, when the disease is confined to the liver. Liver function test can show abnormal aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, total and direct bilirubin and LDH (usually lower than those with secondary liver involvement in systemic NHL) [38]. Hypercalcemia, hyperbilirubinemia and Bence Jones protein peak are rare but have been described [38-40]. CEA and AFP were within the reference ranges in all reported cases. Radiological investigation includes: (a) an ultrasound of the liver, on which hepatic lymphoma presents either as solitary (60%), multiple (35-40%) hypoechoic lesions, target lesions or extensive hypoechoic liver infiltrates (5%) [41]. (b) CT scan is also a good method in diagnosing. On tri-phasic liver CT scan PHL usually presents itself as a hypodense lesion, with possible areas of inhomogeneity. Occasionally local areas of rim enhancement or calcifications may be seen [42]. (c) MRI, because of its superior soft tissue discrimination, gives more information about the internal structure of these lesions and mode of enhancement [43, 44]. On MRI, lesions tend to be hypointense compared to healthy liver parenchyma at T1, and have slight enhanced signal intensity on T2 weighed images [44-48]. (d) Now PET-CT is a good method in diagnosing this case [49]. Positron Emission Tomography (PET) with 2-[18F]-Fluoro-2-Deoxy-D-Glucose (FDG) produces images of regional tissue glycolytic activity. Malignant tissues exhibit increased rates of glycolysis. FDG-PET has been used in a number of studies evaluating its utility in the diagnostic management of malignant lymphomas. Our case also exhibits increased rates of glycolysis. PHL can be subdivided into nodular or diffuse types according to the presence of liver infiltration. Further differentiation can be done by immunohistochemical investigation [18].

Large cell and B-cell immunophenotype are two main types of PHL, and other histologic subtypes of PHL include high-grade tumors (lymphoblastic and Burkett lymphoma, 17%), follicular lymphoma (4%), diffuse histiocytic lymphoma (5%), lymphoma of the mucosa-associated lymphoid tissue type, anaplastic large-cell lymphoma, mantle cell lymphoma, and T-cell-rich B-cell lymphoma [37]. The diagnosis of PHL still remains a challenge. Due to nonspecific clinical symptoms or imaging pattern, it is difficult to discriminate from hepatocellular carcinoma, metastatic tumor, or systemic NHL with secondary hepatic involvement [5-8] It is often made upon histopathological investigation of the resection or the biopsy specimen [50-52]. However, because of the presence of a large area of necrosis, the fine needle tumor biopsy is frequently negative. Vivian Resende et al. reported a case achieved the final diagnosis after two previous negative biopsies due to the presence of a large area of necrosis [53]. And they suggested that during the procedure one should be careful to guide the needle toward an area without necrosis in order to get a representative sample of the tumor [53].

Treatment for PHL include resection of affected lesion, chemotherapy, a combination of rituximab and chemotherapy, a combination of chemotherapy and radiotherapy, and a
combination of resection and chemotherapy [10-12, 18, 40, 50, 54-58]. The optical treatment for the patients depends on their specific condition. A Complete Remission (CR) rate of 83.3% was achieved in PHL when systemic combination chemotherapy was used as the main modality of treatment while patients don’t have chemotherapy contraindications [59]. Ma et al. reported a PHL patient whose total bilirubin was 20.87 mg/dL prior to initiation of an attenuated Rituximab Combined with Cyclophosphamide, Adriamycin, Vincristine, and Prednisone (R-CHOP) chemotherapy [60]. Though the patient’s total bilirubin improved to 1.19 mg/dL prior to the third cycle of chemotherapy, patient died from the complication of chemotherapy after fourth cycles. So, the PHL patients with jaundice are a challenge in regard to the safest and best available modality of treatment.

Venkata S et al. reported a case received radiation therapy initially to reduce his bilirubin levels and tumor size, and the patient was able to complete six cycles of R-CHOP chemotherapy and achieved a complete response [40]. They thought that hyperbilirubinemia may be a reason for delay in treatment for some of these patients. Hence, the radiation therapy prior to treatment with R-CHOP is an alternative to management for stage IV diffuse large B cell lymphoma [40]. Localized PHL could be cured by resection, sometimes the tumor burden could be reduced with neoadjuvant chemotherapy [61]. So, surgery is recommended as the first-line treatment for those patients. This disease has a better prognosis than the hepatocellular carcinoma and other primary or secondary liver cancers [58]. Massive liver infiltration, high index of proliferation, advanced stage, constitutional symptoms, bulky disease, unfavorable histologic subtype, elevated LDH levels, cirrhosis, elevated levels of beta-2 microglobulin, and comorbid conditions are poor prognostic factors [62].

Conclusion

Therefore, accurate investigation is important to reach the correct diagnosis for PHL. Generally, patients with PHL have abnormal liver function tests, partly elevation of LDH and ALP, normal AFP and CEA. If the clinical picture is suspicious for PHL, a liver biopsy or resection should be obtained and the pathological diagnosis remains the gold standard. As this disease is treatable and the development of new therapeutic drugs such as rituximab, overall survival of these patients has improved. In this case, due to financial reasons, our patient has not received rituximab treatment. But he still achieved a dramatic reduction in the tumor size after 6 cycles of CHOP chemotherapy. Now this case is in continuous chemotherapy and evaluation.

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