Case Report
Hodgkin lymphoma presenting with diffuse liver involvement: a rare case report

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Received November 28, 2015; Accepted February 15, 2016; Epub March 15, 2016; Published March 30, 2016

Abstract: Hodgkin lymphoma almost always presents with disease in nodal regions, extranodal disease can sometimes occur at lung, liver, bone marrow and so forth in about 10% of cases, and most of these cases presents with regional involvement. We report a case of Hodgkin Lymphoma in a 49-year-old female with diffuse liver involvement. She suffered from recurrent fever and compromised liver function, enhanced computed tomography and ultrasonic examination only showed enlarged liver, 18F-fluorodeoxyglucose positron emission tomography/computed tomography showed diffuse elevated standard uptake value of liver. The patient underwent percutaneous liver needle biopsies, histopathological examination revealed diffuse infiltration of inflammatory cells such as lymphocytes, histiocytes and granulocytes along with Scattered Reed-Sternberg cells, which was positive for CD15, CD30, Epstein-Barr Virus and paired box protein 5 as well as negative for CD3, CD20 and leukocyte common antigen.

Keywords: Hodgkin lymphoma, extranodal, diffuse liver involvement, PET-CT, needle biopsy

Introduction
Hodgkin lymphoma (HL) is one of the most frequent lymphomas in the world representing 10-15% of all types. Most HL patients present with disease in nodal regions, but in approximately 10% of HL cases, the disease involves extranodal regions such as lung, liver, bone marrow and so forth [1]. And most cases of HL with extranodal disease presents with regional involvement, diffuse involvement of one organ was exceptional rare. We report a rare case of Hodgkin lymphoma in a 49-year-old female with diffuse liver involvement.

Case report
A 49-year-old female presented with complaint of recurrent fever since 2 months. The patient was given anti-infection therapy over 2 weeks without any improvement; low dose prednisone (5 mg per day) effectively managed the body temperature for only one month and became useless within two weeks. On peripheral blood analysis, the patient had pancytopenia with leucocyte count of 3.5×10⁹/L and normal differentiation, hemoglobin of 100 g/L and platelet of 35×10⁹/L, the patient also had elevated erythrocyte sedimentation rate (ESR) of 84 mm/1 hour and C reactive protein (CRP) of 51.5 mg/L. With normal anti-nuclear antibody level and lumber-puncture results, careful blood culture was given several times but all came back negative. During the stay in our hospital, the patient suffered from compromised liver function with albumin of 25 g/L, alanine aminotransferase of 195 U/L and aspartate aminotransferase of 73 U/L as long as elevated bilirubin level and negative spectrum of hepatitis viruses.

While enhanced computed tomography and ultrasonic examination only showed enlarged liver, whole body 18F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) showed several lymphadenopathies in supraclavicular region, mediastinum and bilateral hilar region with elevated standard uptake value (SUV). PET/CT also revealed hepatosplenomegaly with diffuse elevated SUV of liver and mild elevated SUV of bone marrow (Figure 1).

The patient underwent percutaneous liver needle biopsies. Histopathological examination revealed highly swelling hepatocytes, dilated
hepatic sinuses, degenerated and necrotic bile duct; diffuse infiltration of inflammatory cells such as lymphocytes, histiocytes and granulocytes around portal areas along with scattered Reed-Sternberg cells, which was positive for CD15, CD30, Epstein-Barr Virus (EBV) and paired box protein 5 (PAX5) as well as negative for CD3, CD20 and leukocyte common antigen (LCA) by immune-histochemical staining (Figure 2).

Bone marrow biopsy showed active hyperplasia and scattered lymphoid cells with abnormal nucleus. Immune-histochemical staining revealed CD30 and CD3 positive for these lymphoid cells.

Because of compromised liver function, the patient refused to receive combination chemotherapy and finally died of multiple organ failure.

Discussion

Generally, extranodal involvement is less common in HL patients than in patients with non-Hodgkin lymphoma (NHL), in approximately 10% of HL cases, the disease involves extranodal regions such as lung, liver, bone marrow and so forth [1, 2]. Liver involvement, with or without nodal manifestations, is common extranodal manifestation for HL [1, 3, 4]. Ma, et al found 5 HL patients with liver involvement in all 251 patients from a retrospective analysis [1]. The most common manifestation of liver involvement is a solo lesion, which is seen in about two thirds of cases, multiple lesions are found in approximately one third of cases, Diffuse infiltration of liver is exceptional rare for HL and so far has not been reported.

The extranodal disease for HL is so rare in sites such as central nervous system and the testis, and in our case, the diffuse infiltration of liver is so rare, which should always lead the hematologist to consider the possibility of wrong pathologic diagnosis. In our case, percutaneous liver needle biopsies followed with careful immune-histochemical staining revealed Reed-Sternberg cells, which was positive for CD15, CD30, EBV and PAX5 as well as negative for CD3, CD20 and LCA. These results and the finding from bone marrow biopsy are considered to be adequate for the diagnosis of HL [5, 6].

PET/CT has become a useful and standard procedure for the assessment of HL because of its
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FDG-avid nature [7-9], and PET/CT also may identify the biopsy site for diagnosis [10, 11]. In our case, enhanced computed tomography and ultrasonic examination only showed enlarged liver, while PET/CT revealed enlarged liver with diffusely increased uptake which led to the percutaneous liver needle biopsies, and this procedure finally made the diagnosis of stage IV HL with B symptoms.

Ma, et al found no significant difference in the OS and DFS of patients with or without liver

Figure 2. (A) Pathological examination revealed highly swelling hepatocytes, dilated hepatic sinuses, degenerated and necrotic bile duct; diffuse infiltration of inflammatory cells such as lymphocytes, histiocytes and granulocytes around portal areas along with scattered Reed-Sternberg cells (hematoxylin and eosin; magnification, ×1000). Immunohistochemical staining showed that these cells were positive for (C) CD15 (magnification, ×400), (E) CD30 (magnification, ×400), and (F) PAX5 (magnification, ×400) as well as negative for (B) CD3 (magnification, ×400) and (D) CD20 (magnification, ×400).
involvement who received combination chemotherapy such as ABVD regimen (doxorubicin, bleomycin, vinblastine and dacarbazine) [1]. Diffuse infiltration usually indicates a worse prognosis than nodular infiltration in primary liver non-Hodgkin lymphoma (NHL) because of compromised liver functions and hepatomegaly [12]. In our case, this patient also suffered from elevated alanine aminotransferase, aspartate aminotransferase and bilirubin, and finally died of multiple organ failure without the chance of receiving chemotherapy.

Though it is so rare that HL can infiltrate liver with a diffuse pattern, by using PET/CT and percutaneous liver needle biopsies, those rare cases can be successfully diagnosed. The prognosis for HL with liver diffuse infiltration is extremely poor, by using targeted therapy; these patients may have a better outcome.

Acknowledgements

This study was supported by the National Natural Science Foundation of China (Grant No.81500110) and Funds of Science Technology Department of Zhejiang Province (Grant No.2014C33235).

Disclosure of conflict of interest

None.

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tium; Italian Lymphoma Foundation; European Organisation for Research; Treatment of Cancer/Dutch Hemato-Oncology Group; Grupo Español de Médula Ósea; German High-Grade Lymphoma Study Group; German Hodgkin’s Study Group; Japanese Lymphoma Study Group; Lymphoma Study Association; Nordic Lymphoma Study Group; Southwest Oncology Group; United Kingdom National Cancer Research Institute. Recommendations for initial evaluation, stag-


