

Case Report

Primary hepatic lymphoma: three case reports and a literature review

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Abstract: Primary hepatic lymphoma (PHL) is a rare malignant tumor. In this article, three cases of PHL initially misdiagnosed as benign tumors or other malignancies are reported. Clinical manifestations, laboratory examinations, and imaging all presented nonspecific findings leading to the puzzling diagnoses. Definite diagnoses were made according to immunohistochemistry of specimens acquired either through liver biopsy or hepatectomy. Two cases of diffused large B-Cell lymphoma and one little T-Cell lymphoma were found. Therefore, PHL should be taken into consideration in differential diagnoses of occupied intrahepatic lesions. Our report focuses on the imaging features of PHL in order to improve the understanding of PHL, and how restricted diffusion and enhancement patterns on MRI should be helpful to differential diagnoses.

Keywords: Magnetic resonance imaging, primary hepatic lymphoma, T-cell lymphoma, large B-cell lymphoma, solitary lesion

Introduction

Although secondary liver involvement is common in the late stage of lymphoma, primary hepatic lymphoma (PHL) is a rare and unusual type of lymphoma, with only 0.016% prevalence among all non-Hodgkin's lymphoma (NHL) [1]. It usually presents with hepatomegaly without lymphadenectasis and extrahepatic (such as the spleen, bone marrow and other lymphoid tissue) lymphoma at early stages of disease. In our case report, three patients are presented with pathologically confirmed primary hepatic lymphoma. The imaging features of these patients and a review of literature were carried out to deepen the understanding of PHL.

Case reports

Case 1

Clinical presentation: The first case is an 18-year-old man with an asymptomatic mass in the right liver lobe that was discovered accidentally using ultrasonography. There were no positive results for tumor markers. Liver function

was normal. Levels of serum alphafetoprotein (AFP) were 3.39 ng/ml (normal range 1-20 ng/ml) and carcinoembryonic antigen (CEA) was 2.21 ng/ml (normal range 1-10 ng/ml). Aspartate aminotransferase was 22 u/l (normal range 8-40 u/l), alanine aminotransferase 24 u/l (normal range 0-40 u/l), and gamma glutamyl transpeptidase 31 u/l (normal range 0-40 u/l). Serology was negative for human immunodeficiency (HIV) and hepatitis B (HBV) viruses. The patient was examined using enhanced magnetic resonance imaging (MRI). According to the features of the initial MRI, hepatic inflammatory pseudotumor was considered and a short-term follow-up was suggested by the radiologist. Five months later, due to rapid growth of the mass, a malignant tumor was suspected and a hepatic biopsy was advised by the radiologist. A complete surgical resection of the lesion was performed. The pathological diagnosis finally confirmed the presence of primary hepatic T-cell lymphoma.

Imaging findings: T1WI, T2WI, DWI and enhanced T1WI were included in the MRI protocol. On prior MRI images, the lesion was a homoge-

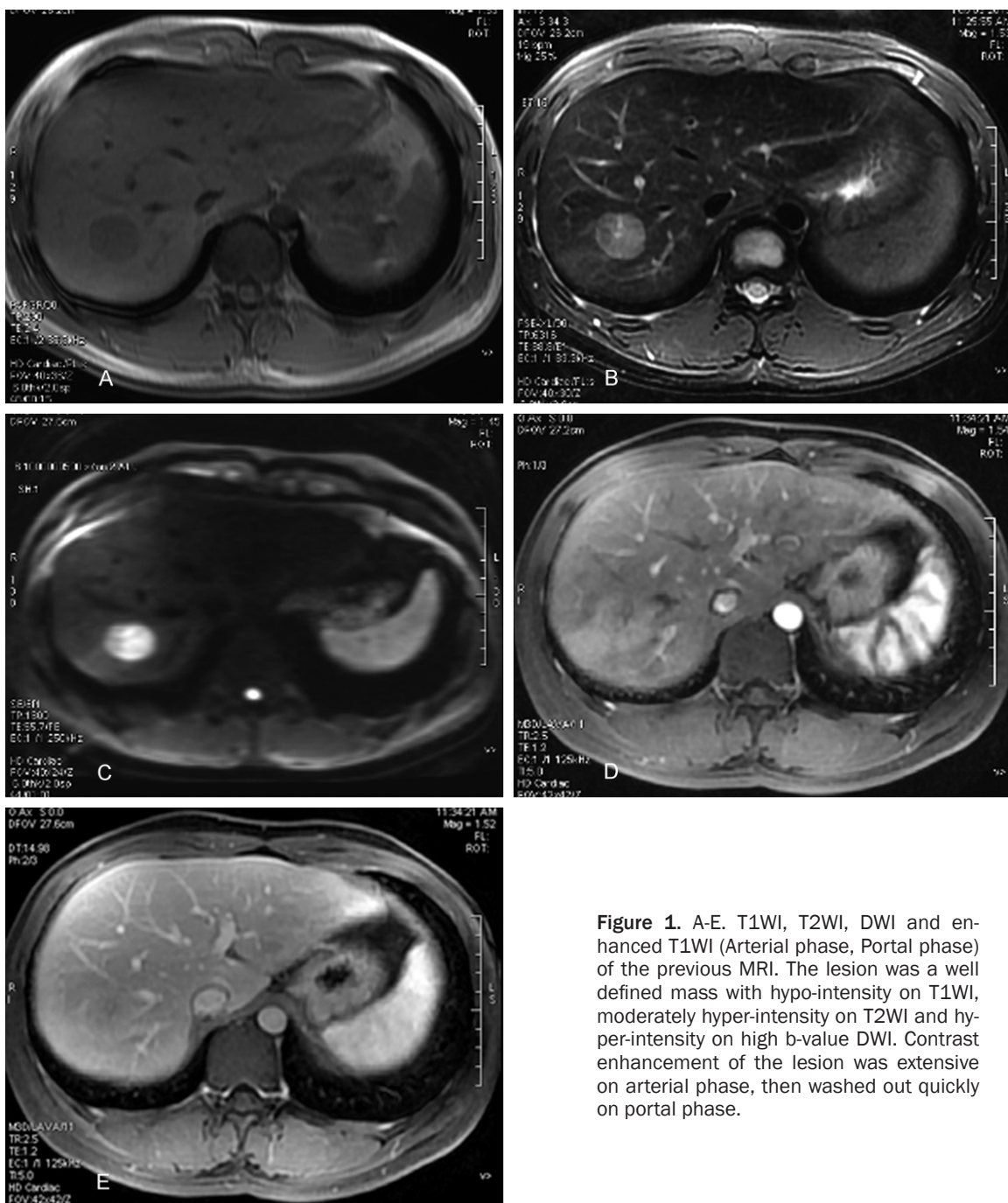


Figure 1. A-E. T1WI, T2WI, DWI and enhanced T1WI (Arterial phase, Portal phase) of the previous MRI. The lesion was a well defined mass with hypo-intensity on T1WI, moderately hyper-intensity on T2WI and hyper-intensity on high b-value DWI. Contrast enhancement of the lesion was extensive on arterial phase, then washed out quickly on portal phase.

neous and well defined mass with mild to moderate low-signal intensity relative to liver tissue on T1-weighted images, moderately high-signal intensity on T2-weighted images compared with liver tissue (**Figure 1A, 1B**). The size of the lesion was 2.5 × 2.4 × 2.1 cm. On high b-value (500 s²/mm) DWI, the signal intensity of the tumor was higher and the ADC value was lower than liver parenchyma (**Figure 1C**). Contrast enhancement of the lesion was extensive on

early post-gadolinium images and washed out quickly (**Figure 1D, 1E**). The MRI did not reveal any lymphadenopathy or other mass lesion. After a five months interval, the size of the lesion increased to 3.5 × 3.3 × 3.0 cm on later MRI images, with more extensive enhancement and inhomogeneous intensity (**Figure 2**).

Pathological findings: Destroyed hepatic structures with micro-hemorrhage were found in HE

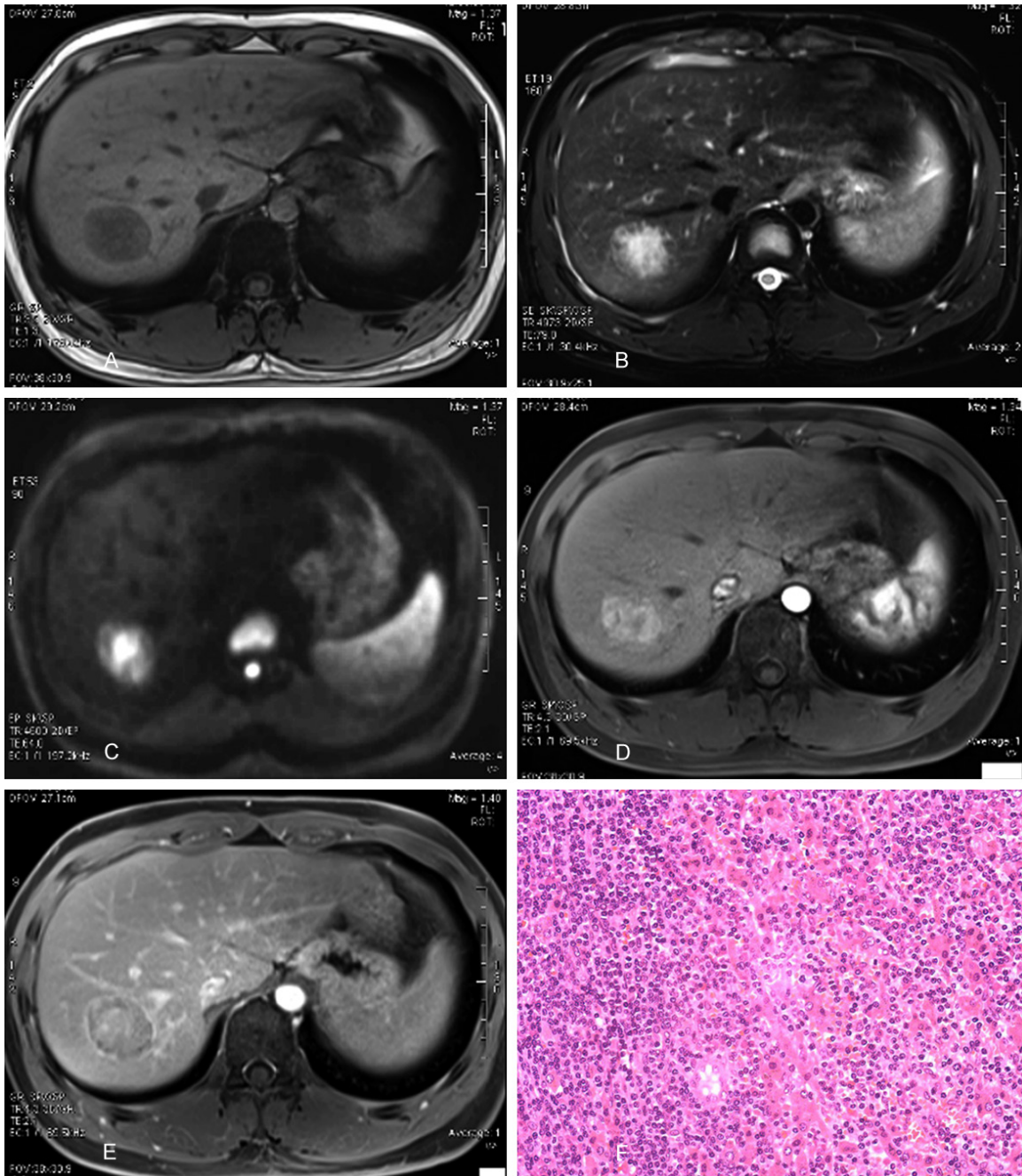


Figure 2. A-E. T1WI, T2WI, DWI and enhanced T1WI after a 5 months interval. F. HE stain. The size of lesion increased on later images with more extensive inhomogeneous enhancement on early post-gadolinium images and washed out quickly.

stains (Figure 2). A large number of lymphocytes and a few plasmacytes were observed. The size and shape of nested structures varied slightly. False alveolar structures were revealed by microscopy. The eosinophilic cell boundaries were clear with abundant cytoplasm. The results of immunohistochemistry (IHC) were as follows: CK (-), CD3 (+), CD45R0 (+), CD5 (+), Bcl

(±), CD20 (-), PAX5 (-), vimentin (-), CylinD1 (-), Ki-67 (+5%), establishing a diagnosis of primary intrahepatic little T-cell lymphoma.

Case 2

Clinical presentation: A 49-year-old man presented with nausea, yellowish discoloration of

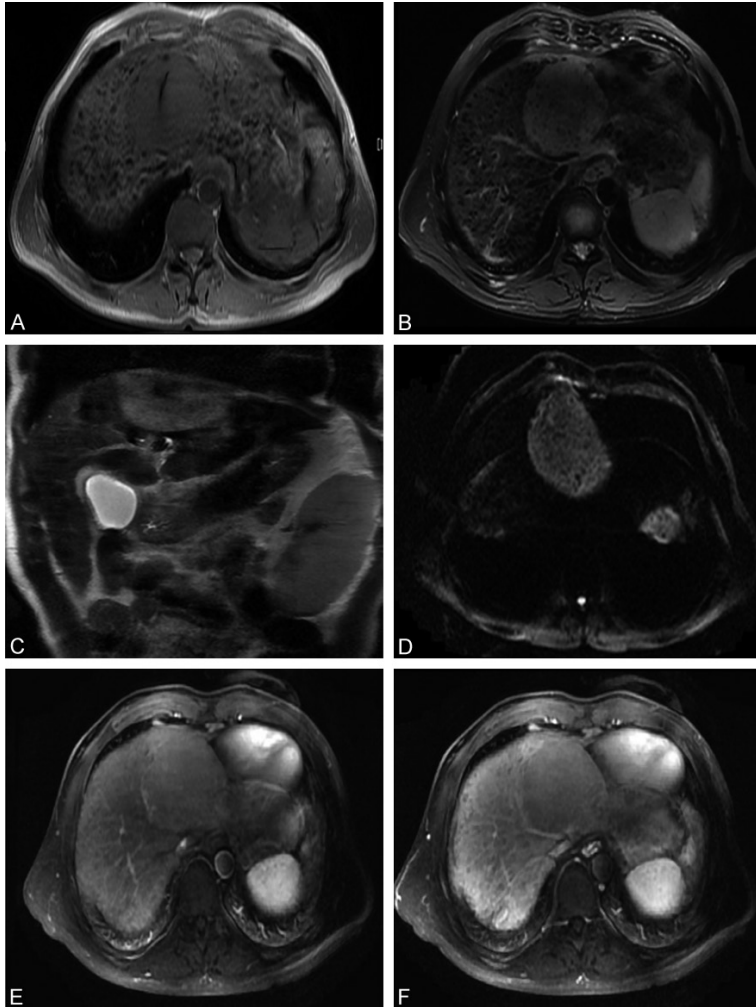


Figure 3. (A-F) Plain MRI and dynamic contrast enhancement image of a liver tumor. The lesion had a homogeneous low signal intensity on T1WI (A), high signal intensity on T2WI (B, C) and DWI (D). The lesion was slight circular enhanced on early post-gadolinium enhancement image (E), and demonstrated low signal on delayed phase (F).

the skin, and right upper quadrant abdominal pain. Primary hepatic carcinoma was suspected via radiologic investigations of a liver lesion. The symptoms were nonspecific with mild high-levels of alpha-fetoprotein (AFP) and a ten year history of hepatitis B. The patient had no complaints of fever, but significant weight loss; and no history of smoking, alcohol consumption, or drugs abuse. Laboratory results included hemoglobin, 15.3 g/dl; and a white cell count of $2.52 \times 10^9/L$, with a normal differentiation. Alanine aminotransferase was 99 u/l (normal range 0-40 u/l); gamma glutamyl transpeptidase was 127 u/l (normal range 0-40 u/l); and alkaline phosphatase (ALP) was 116 u/l (normal range 23-140 u/l). Total protein (TP) was

83.0 g/l (normal range 66-83 g/l); albumin (ALB) was 37.2 g/l (normal range 35-52 g/l); globulin (GLB) was 45.8 g/l (normal range 20-35 g/l); and ratio of albumin to globulin (A\G) was 0.81 (normal range 1.2-2.5). Levels of serum alpha-fetoprotein (AFP) were 72.92 ng/ml (normal range 1-20 ng/ml); carcinoembryonic antigen (CEA) was 1.11 (normal range 1-10 ng/ml), and carbohydrate antigen 19-9 (CA19-9) was 134.70 u/ml (0-39 u/ml). Serology was negative for human immunodeficiency (HIV) and hepatitis C (HCV) viruses, but positive for the hepatitis B (HBV) viruses.

Imaging findings: A normal chest X-ray was taken, while an abdominal MRI scan showed a large 7 cm × 6.8 cm × 4 cm sized mass in the left lobe of the liver (**Figure 3**). The lesion was homogeneous and well-defined with mild to moderate low-signal intensity relative to liver tissue on T1-weighted images; moderately high-signal intensity on T2-weighted images compared with liver tissue. On DWI (b value = 500 s²/mm), the intensity of the tumor was higher and the ADC value was lower than liver parenchyma (**Figure 3D**). The lesion

had enhanced intensity with slight circular reinforcement on early post-gadolinium dynamic contrast enhanced images, and demonstrated low signal on delayed scan in the portal phase (**Figure 3E, 3F**).

Surgical operation: Surgical treatment consisted of an enbloc resection of the tumor, anterior portion of the left liver, and gallbladder. Surgical exploration was indicated for hepatic carcinoma evolving from apparently hepatic cirrhotic nodules. During the resection procedure, an encapsulated liver tumor was found at the expanse of the left liver. The extra-tumor liver parenchyma was found with hepatic cirrhotic nodules. Hepatic segmentectomy was finally performed.

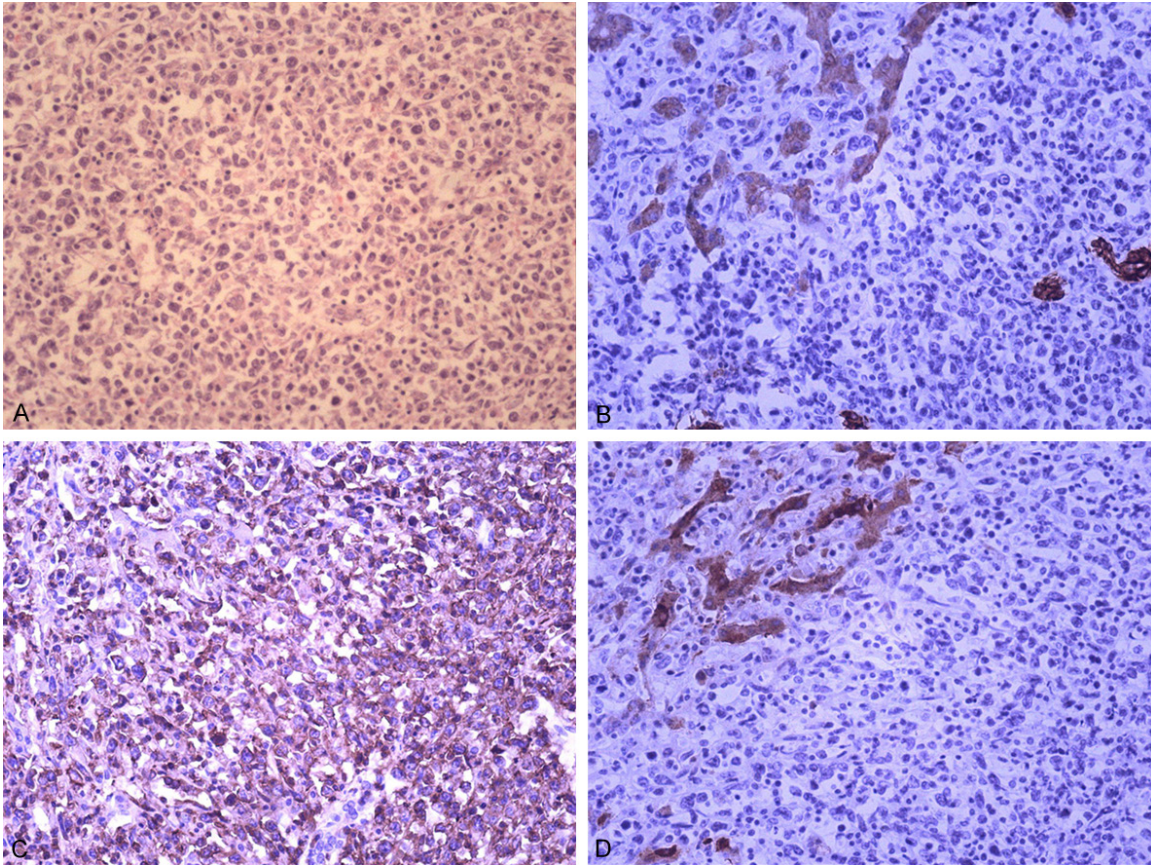


Figure 4. A-D. Histological and immunohistochemical photographs. A. Hematoxylin and eosin staining, $\times 400$; B. Anti-vimentin staining, $\times 400$; C. Anti-CD3 staining, $\times 400$; D. Anti-CK staining, $\times 400$.

Pathological findings: Macroscopic study of the piece of tumor showed a well-limited hepatic mass encapsulated with soft consistency measuring about 11.5 cm \times 8 cm \times 7 cm. The non-tumor part of the liver parenchyma was same with hepatic cirrhotic nodules. Microscopically, there was a heavy infiltration composed mainly of medium-to-large-sized lymphoid cells suggestive of lymphoma but a poorly-differentiated carcinoma could not be excluded (**Figure 4A**). Immunohistochemical study of the tumor cells showed positive for B-cell markers, CD20, CD79 α , but negative for the T-cell marker, CD3, and also negative for CK-, Vimentin-, Hepper-1, higher cell proliferation index, and Ki-67 50% (**Figure 4B-D**). A bone marrow biopsy was carried out showing normal cellularity with normal maturation in all cell lines, and no evidence of B-cell lymphoma present. Thus a diagnosis of primary hepatic large B-cell lymphoma was established, given that no additional foci of lymphoma were found anywhere else in the body.

Case 3

Clinical presentation: A 60-year-old man was found to have a space-occupying lesion in the right liver lobe on health examination, with no complaints of constitutional symptom, such as fever, night sweats, or jaundice. The patient did not mention any vomiting, abdominal pain, or significant weight loss. No positive signs were present on physical examination. Routine laboratory investigations were unremarkable. Besides normal liver function tests, AFP level (1.8 ng/ml), CA199 level (18.1 U/ml), and CEA level (1.73 ng/ml), were within normal limits. Serology was negative for the hepatitis B (HBV) viruses.

Imaging findings: Subsequent magnetic resonance imaging (MRI) revealed a well-defined and well-distributed round mass in the right liver lobe that was hypointense on T1WI and hyperintense on T2WI against normal liver parenchyma (**Figure 5A, 5B**). The solid mass

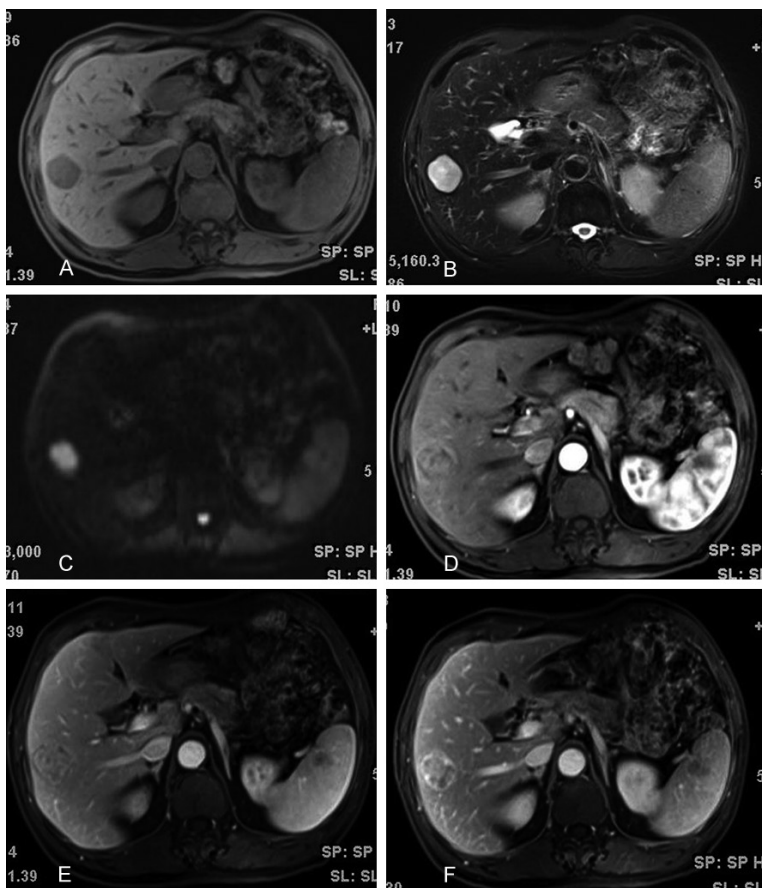


Figure 5. (A-F) Plain MRI and dynamic contrast enhancement image of a liver tumor. Note the well-defined round mass in right liver lobe that was hypointense on T1WI (A), hyperintense on T2WI (B) and showed diffusion limited on DWI (C). There was remarkable enhancement on artery phase, equal signal on portal phase and remained contrast agent on delay phase (D-F).

showed notable high-signal on DWI, which was interpreted as restricted diffusion (**Figure 5C**). Contrast-enhanced MRI scan demonstrated visible inhomogeneous enhancement. The lesion was enhanced dramatically on artery phase. Isointensity on portal phase; and obvious enhancement on delay phase were found (**Figure 5D-F**).

Pathological findings: Tissue biopsy was followed by immunohistochemistry showing that LCA, CD 20, and CD 79a were positive; while CD 5 and CD 23 were negative. Neither superior or deep lymphadenopathy nor any additional foci of lymphoma were discovered anywhere else in the body. A diagnosis of PHL, large B-cell type lymphoma was eventually confirmed.

Discussion

Hodgkin's lymphoma (HL) has a relative low incidence as mentioned in some reports. 3194

cases were classified according to the new WHO classification by pathologists to clarify the current status of malignant lymphomas in Japan. 94.71% were NHL (2189/3194) [2, 3]. PHL was first described in 1965 [4]. PHL was defined as a lymphoma localized and limited to the liver [5]. PHL was a very rare malignant tumor, which is confined to the liver with no evidence of lymphomatous involvement in other lymphoid structures, and constitutes only 0.016% of all cases of NHL previously mentioned in the introduction.

The majority of PHL cases reported are of B-cell origin. Primary T-cell lymphoma of the liver is extremely rare with only a few cases reported in the literature, and accounts for only 5-10% of all primary hepatic lymphomas [6, 7]. However, both of them are included in our article. Previous reports stated that PHL had trended towards male predominance [6, 8-11], while Yang reported that PHL in men was less frequent than in

women [12]. PHL can be found at any age, more frequently in the fifth or sixth decade of life [13]. One of our three reported male patients was just 18 years old. The etiology of PHL is unknown, although several possible factors such as hepatitis, cirrhosis, and immunosuppression have been proposed [9]. Though it is not enough to consider HCV as cause of the disease, some authors have revealed a variety of possible associations between PHL and chronic hepatitis C virus (HCV) infection [14-16]. It also seems that there is a strong association between HBV and PHL [12].

Radiological imaging of PHL is nonspecific and can present as a solitary mass or multiple lobular, hypo-attenuated masses. The most common presentation was a solitary lesion which occurred in about 77.8% of cases, followed by multiple lesions occurring in about 22.2% of patients [12]. This case report demonstrates

the appearance of PHL using current magnetic resonance techniques including DWI and DCE-MRI. In the previous studies, most conventional MRI findings of PHL were described as hypo-intense on T1WI, and hyper-intense on T2WI [6, 17]. Focal hepatic lymphomas have also been reported to be hypo-echoic on ultrasound, hypo-dense on CT, and had low and high signal intensity on T1- and T2-weighted MRI, respectively [2, 18]. In our cases, MRI images demonstrated variable-degree hypo-intense masses on T1-weighted images and hyper-intense masses on T2-weighted images, which are consistent with previous reports with respect to MRI findings. High signal intensity was noted on DWI among our three cases, indicating restricted diffusion. The reported CT scan of PHL displayed unenhanced or poorly enhanced after contrast [19]. On enhanced MRI, PHL showed as a hypovascular lesions with only moderate contrast agent uptake on the portal phase [20]. While in our cases, the enhanced pattern of lesions was remarkably different on contrast enhancement MRI, respectively showing intensification of contrast quickly in and quickly out, slightly circular enhancement and significant reinforcement among all the three phases. Liver metastases from colorectal neoplasias usually display as round focal masses with unclear edges and rim-like enhancements, and hepatocarcinoma often show hypervascularization in the arterial phase. Thus, PHL has overlapping image features with primary tumor and metastases of the liver.

Diagnosis of PHL requires a histopathological analysis of a liver biopsy or resected lesion compatible with lymphoma and the absence of lympho-proliferative disease outside the liver [21]. Afraid of the risk of tumor seeding, also known as needle-track metastases, a lot of physicians are hesitant in conducting liver biopsies, despite their low risk (only 0.005%) and accuracy of 85%, on the basis of literature [22].

Conclusion

Primary hepatic lymphoma (PHL) is a rare disease that should be considered in patient with liver masses. The rarity of the disease leads to problems of diagnosis. However, we found diffusion-weighted images and dynamic enhancement can give more helpful features for the diagnosis of PHL.

Acknowledgements

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Disclosure of conflict of interest

None.

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PHL: three case reports

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