CASE REPORT

Primary hepatic peripheral T-cell lymphoma in a patient with chronic hepatitis B infection

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We report a case of primary hepatic peripheral T-cell lymphoma in a patient with hepatitis B virus–related cirrhosis. This patient presented with a solitary hepatic lesion with computed tomography and magnetic resonance imaging features that did not resemble hepatocellular carcinoma. Subsequent biopsy of the lesion revealed that it was a peripheral T-cell lymphoma. The patient was successfully treated with multi-agent chemotherapy followed by radiofrequency ablation. Although hepatocellular carcinoma is the most frequently encountered primary hepatic tumour in patients with hepatitis B virus–related cirrhosis, primary hepatic lymphoma should also be borne in mind. Nevertheless, primary hepatic lymphoma is a rare entity, and has no proven association with chronic hepatitis B infection.

Introduction

Although secondary hepatic involvement is commonly seen in the late stages of non-Hodgkin's lymphoma, non-Hodgkin's lymphoma arising in the liver is rare. Primary hepatic lymphoma constitutes about 0.4% of cases of extranodal non-Hodgkin's lymphoma, and only about 0.016% of all cases of non-Hodgkin's lymphoma.[1] The majority of cases of primary hepatic lymphoma originate from a B-cell lineage, with diffuse large B-cell lymphoma being the most frequently reported histological subtype. Primary hepatic lymphoma arising from a T-cell lineage is less common, and described subtypes include peripheral T-cell lymphoma, anaplastic T-cell lymphoma, and hepatosplenic T-cell lymphoma.[2] To our knowledge, only 14 cases of localised primary hepatic peripheral T-cell lymphoma have been described in the literature.[3] In this article, we describe a case of primary hepatic peripheral T-cell lymphoma in a patient with pre-existing hepatitis B virus (HBV)–related cirrhosis.

Case report

A 32-year-old Chinese man had been receiving lamivudine for treatment of chronic e antigen–negative hepatitis B at United Christian Hospital since May 2001. Before commencing treatment with lamivudine, his serum alanine aminotransferase (ALT) was 324 IU/L (reference level, <41 IU/L), HBV DNA was 1.9 x 10^8 copies/mL, and a liver biopsy showed moderate hepatitic activity with bridging fibrosis. His serum ALT level decreased steadily following the commencement of lamivudine and returned to the normal range 16 weeks after starting treatment, and his HBV DNA dropped to below 200 copies/mL after 19 months of treatment. During the fourth year of treatment, there was a gradual increase in his serum ALT level. At 60 months, his serum ALT and HBV DNA levels had risen to 786 IU/L and 1.6 x 10^8 copies/mL, respectively but albumin, bilirubin, and blood coagulation parameters were within normal limits. His serum alpha-foetal protein (AFP) level was elevated to 562 ng/mL (reference level, <7 ng/mL). His full blood count was normal apart from mild thrombocytopenia (platelet count, 140 x 10^9/L; reference range, 150-400 x 10^9/L). Treatment with adefovir dipivoxil was added, after which there was a rapid decrease in his ALT and AFP levels, with both parameters returning to their normal ranges within 8 weeks of therapy. When the AFP level was elevated, a computed tomographic (CT) scan of his liver was performed to exclude hepatocellular carcinoma. This showed a 1.3-cm hypoattenuating lesion in the right liver lobe, which was non-enhancing in the arterial phase and hypoenhancing during the portal venous phase. Magnetic resonance imaging (MRI) of the liver demonstrated the same lesion with a similar enhancement pattern; the lesion appeared hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging (Fig 1). An ultrasonography (USG)-guided needle liver biopsy of the hepatic lesion was performed, revealing extensive atypical lymphohistiocytic infiltrates consisting of small and intermediate-sized lymphoid cells with variably irregular nuclear contours (Fig 2). Immunohistochemical studies showed that the abnormal lymphoid cells were positive for CD3, and negative for CD30 and CD56, establishing the diagnosis of peripheral T-

Key words
Carcinoma, hepatocellular; Hepatitis B; Liver cirrhosis; Lymphoma

Hong Kong Med J 2009;15:288-90

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cell lymphoma. A biopsy of the non-tumour liver parenchyma demonstrated cirrhosis. Staging CT scans of the thorax, abdomen and pelvis and bone marrow biopsy were negative. Serological tests for hepatitis C virus (HCV) and human immunodeficiency virus were negative. The patient was then treated with eight courses of combination chemotherapy, which consisted of cyclophosphamide, epirubicin, vincristine, and oral prednisolone. Two months after he completed chemotherapy, MRI of his liver showed a residual 0.8-cm non-enhancing lesion in the right lobe, which was hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging. As the lesion was considered too small for obtaining adequate biopsy material for confidently excluding residual malignancy, percutaneous USG-guided radiofrequency ablation was performed. The patient remained asymptomatic 6 months afterwards, and an abdominal MRI found no evidence of lymphoma recurrence.

Discussion

Hepatocellular carcinoma is the most common primary hepatic tumour, and patients with chronic HBV infection or cirrhosis are at risk of developing this malignancy. Hepatic masses larger than 1 to 2 cm in diameter in a patient with a cirrhotic liver can be treated as hepatocellular carcinoma without histological proof, if the lesions show the typical vascular pattern (arterial hypervascularity and washing out in the early or delayed venous phase) on CT scan and/or MRI.[4] This case illustrates that biopsy is necessary for lesions showing an atypical vascular pattern on dynamic imaging.

The aetiology of primary hepatic lymphoma is unknown although viruses are thought to have an important role in the pathogenesis of this disorder. The Epstein-Barr virus (EBV) is particularly important, especially in the presence of immunosuppression when reactivation of EBV may trigger the onset of primary hepatic lymphoma. A number of reports have described an increased incidence of primary hepatic lymphoma in patients with HBV or HCV infection, although the precise relationship between chronic viral hepatitis and primary hepatic lymphoma remains obscure.[2] It has been postulated that chronic antigenic stimulation by HBV may play a role in the development of primary hepatic lymphoma.[5] Aozasa et al[6] reported a 20% prevalence of hepatitis B surface antigen (HBsAg) positivity in a series of 69 patients with primary hepatic lymphoma, 52 of whom were from western countries and 17 from Japan. However, Lei et al[7] reported a series of cases of primary hepatic lymphoma in Hong Kong Chinese in which only one of seven patients was positive for HBsAg. The authors argued against a pathogenetic role for HBV in the development of primary hepatic lymphoma

一名慢性乙型肝炎患者的原發性肝周邊T細胞淋巴瘤

本文報告一名因乙型肝炎引至肝硬化患者的原發性肝周邊T細胞淋巴瘤。病發時患者肝臟出現單一病灶，電腦斷層照相術及磁共振成像術均顯示並非肝癌。後來的活檢證實是周邊T細胞淋巴瘤。病人接受多種藥劑化療，及隨後的肝腫瘤射頻消融術，成功得到醫治。雖然在乙型肝炎引至肝硬化患者中，肝癌是最普遍的原發性肝腫瘤，可是亦要緊記原發性肝細胞淋巴瘤也是其中一種可能性。縱然如此，肝細胞淋巴瘤很罕見，且並未證實與慢性乙型肝炎有關。

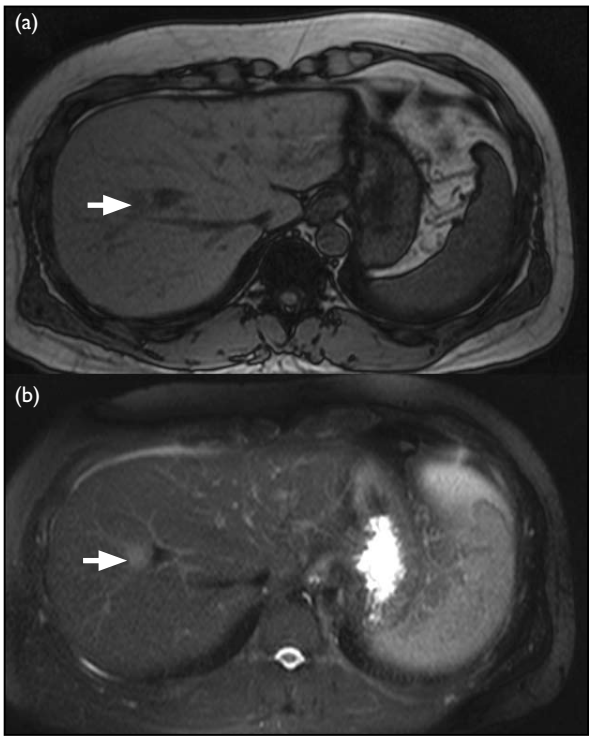

FIG 1. (a) T1-weighted magnetic resonance image of the liver showing a hypointense lesion (arrow), and (b) T2-weighted magnetic resonance image showing that the lesion appears hyperintense (arrow)

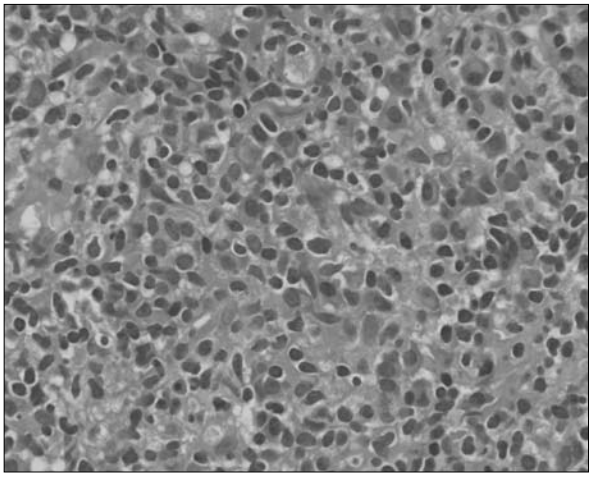

FIG 2. Photomicrograph of the liver biopsy specimen showing extensive atypical lymphohistiocytic infiltration (H&E, x 400)

due to the disproportionately low number of cases of primary hepatic lymphoma in Hong Kong, a known endemic area for chronic HBV infection. Thus far, there has not been sufficient evidence to support HBV as an important aetiological factor in primary hepatic lymphoma.

The most common presenting symptom in primary hepatic lymphoma is abdominal pain, occurring in over 40% of patients.[8] Other presenting symptoms include weight loss, fever, anorexia, nausea, night sweats, and vomiting. Our patient was asymptomatic and was diagnosed incidentally, as is the case in about 9% of patients with primary hepatic lymphoma.[8]

Primary hepatic lymphoma may appear as solitary, multifocal, or diffusely infiltrative lesions. Their appearances on CT scans and MRI are non-specific, and biopsy is needed for definitive diagnosis. Primary hepatic lymphoma lesions are positive on fluorine-18 fluorodeoxyglucose-positron emission tomography (FDG-PET), and FDG-PET may be useful for detecting extrahepatic involvement and evaluating treatment responses.[9]

The optimal treatment for primary hepatic lymphoma has not yet been defined. Treatment options include surgery, radiation therapy, chemotherapy, or a combination of these modalities. Many reports have suggested that surgical resection alone or in combination with chemotherapy can offer a good outcome.[2] Radiofrequency ablation may have a role, particularly for small (<3 cm) solitary tumours confined to the liver. Primary hepatic lymphoma has a relatively favourable prognosis when detected early. Lymphomas occurring in patients with advanced disease, with unfavourable histological subtypes, and co-existing diseases, especially cirrhosis and acquired immunodeficiency syndrome, are associated with a much poorer prognosis.[10] It has been reported that patients with primary hepatic peripheral T-cell lymphoma have a poorer prognosis, although cases of complete response to chemotherapy have been documented.[3]

In summary, primary hepatic lymphoma, though a rare disease, should be considered in patients presenting with focal hepatic lesions. Biopsy is necessary for lesions showing atypical radiological features.

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