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CASE REPORT

Multiple primary malignancies – hepatocellular carcinoma combined with splenic lymphoma: A case report

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Abstract

BACKGROUND

Primary liver cancer is one of the most common malignant tumours, while primary splenic lymphoma is a rare malignancy. Thus, cases of hepatocellular carcinoma (HCC) combined with splenic lymphoma are extremely rare.

CASE SUMMARY

We present a 62-year-old woman who was admitted to the Interventional Radiology Department with a lump in the spleen and liver as well as multiple enlarged lymph nodes visible by ultrasound. Contrast-enhanced computed of the abdomen revealed a circular, low-density, shallow mass (approximately 2.6 cm in diameter) in the left intrahepatic lobe and multiple round, low-density shadows in the spleen with clear boundaries (maximum diameter 7.6 cm). Based on the characteristic clinical symptoms and explicit radiological findings, the clinical diagnosis was HCC with metastasis to the liver portal, retroperitoneal lymph nodes, and spleen. After transcatheter arterial chemoembolization and sequential radiofrequency ablation, the -fetoprotein level returned to the normal range, and the hepatitis B cirrhosis improved. In addition, splenic tumour biopsy confirmed the diagnosis of primary malignant lymphoma, which went into remission after chemotherapy.

CONCLUSION

HCC with primary splenic non-Hodgkin lymphoma is extremely rare and easily misdiagnosed. Better understanding would facilitate early diagnosis, treatment and prognosis.

Key Words: Multiple primary malignancies; Hepatocellular carcinoma; Splenomegaly; Extra-hepatic primary malignancy; Magnetic resonance imaging; Primary non-Hodgkin's

lymphoma; Case report

Core Tip: This case of hepatocellular carcinoma with splenic primary non-Hodgkin lymphoma is extremely rare and easily misdiagnosed. A better understanding of such cases would facilitate early diagnosis, treatment and prognosis.

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INTRODUCTION

Multiple primary malignancies (MPMs) are defined as more than one synchronous or metachronous cancer in the same individual[1]. If the tumours originate from different sites and/or belong to different histological or morphological groups, they are considered MPMs. The incidence of MPMs in the cancer population varies between 2.4% and 8% but up to 17% within 20 years of follow-up[2].

Primary liver cancer is one of the most common malignant tumours. With improvements in clinical diagnosis and treatment, the diagnosis rate of hepatocellular carcinoma (HCC) complicated with extra-hepatic primary malignancy (EHPM) has increased[3,4]. In China, the stomach, colorectal, nose, pharynx, and lung are primary EHPM sites associated with hepatic malignancy, accounting for 60.7% of all EHPM cases[5]. Primary splenic lymphoma is a rare malignancy that constitutes approximately 1.1% of all cases of non-Hodgkin lymphoma (NHL)[6]. There is little evidence of HCC combined with splenic lymphoma.

This report describes a rare case of HCC combined with splenic lymphoma.

CASE PRESENTATION

Chief complaints

A 62-year-old female patient with blurred vision in the right eye for > 3 mo was admitted to the Ophthalmology Department in Lishui Hospital of Zhejiang University.

History of present illness

The patient with blurred vision in the right eye for > 3 mo was admitted to the Ophthalmology Department in Lishui Hospital of Zhejiang University.

History of past illness

This patient was a hepatitis B carrier with cirrhosis of the liver for > 2 years. She reported that she had never smoked tobacco or drunk alcohol.

Personal and family history

No specific cancer history was recorded on her pedigree.

Physical examination

Abdominal ultrasound showed intrahepatic hypoechoic nodules, multiple hypoechoic deposits in the spleen, and multiple enlarged retroperitoneal lymph nodes. The physical examination revealed that she had a palpable tender mass with a smooth surface 4 cm under the left ribcage. Contrast-enhanced computed tomography (CT) of the abdomen revealed a circular low-density shallow mass (approximately 2.6 cm diameter) on the left intrahepatic leaves; arterial phase lesions were significantly enhanced with a relatively low density in the portal phase, which is typical for liver cancer with fast forward and backward characteristics. Multiple circular low-density shadows were detected in the spleen with clear boundaries (maximum diameter 7.6 cm), and the CT value was 34 HU. The enhancement of the lesion was lightly heterogeneous and had a low density compared with the normal spleen parenchyma. Multiple enlarged lymph nodes were detected around the liver portal vein and

retroperitoneal space with partial fusion conglobation, which revealed cells suspected for HCC with possible metastasis to the liver portal, retroperitoneal lymph nodes, and spleen.

Laboratory examinations

Hepatitis B virus (HBV) markers were HBsAg+, HBeAb+, HBcAb+, serum -fetoprotein (AFP) 1394.3 ng/mL, and HBV DNA < 500 copies/mL. Immunohistochemical staining of the lesion sample was positive for CD20, PAX5, Bcl-2, Bcl-6 and CD10, and partially positive for Mum-1 and Ki67 (70% cells); CD21 staining for follicular dendritic cell network damage was positive, while CD3 and CD45RO were negative.

Imaging examinations

Positron emission tomography (PET)/CT disclosed an enlarged spleen with multiple confluent mass lesions. Radiation absorption was unusually high with a maximum standardized uptake value (SUV) of 16.2 in the spleen. Multiple enlarged lymph nodes were observed in the neck, left clavicle, axilla, right hilum, mediastinum, liver hilum and peritoneum, lower abdominal cavity, left pelvic wall, and inguinal region. There was increased radiation uptake in those regions with a maximum SUV of 15.9. In the peritoneum, lymph nodes were partly fused, with unclear boundaries and partial pressure on the surrounding (Figure 1).

FINAL DIAGNOSIS

Based on these findings, the patient was diagnosed with splenic primary NHL.

TREATMENT

The patient was recommended to be treated with hepatic arteriography and transcatheter arterial chemoembolization (TACE) (Figure 2A). Liver CT showed dense lipiodol deposition in the lesions (Figure 2B). To further consolidate treatment, CT-guided percutaneous radiofrequency ablation was performed on the hepatic lesion (Figure 2C). One month after treatment, the AFP level of the patient had returned to the normal range, and the tumour had regressed completely (Figure 2D).

Approximately 3 mo after treatment, magnetic resonance imaging of the upper abdomen showed complete necrosis of the left hepatic lobe lesions, and the hepatic portal vein, spleen and retroperitoneal lymph nodes were significantly enlarged. The largest spleen lesion reached 12.6 cm in diameter (Figure 3A). Further evaluation by splenic biopsy showed a patchy distribution of tumour cells and the disappearance of normal structures, which was considered diffuse large B-cell lymphoma (Figure 3B). Immunohistochemical staining of the lesion sample was positive for CD20, PAX5, Bcl-2, Bcl-6 and CD10 and partially positive for Mum-1 and Ki67 (70% cells). CD21 staining for FDC network damage was positive, while CD3 and CD45RO were negative. PET/CT revealed an enlarged spleen with multiple confluent masses. Radiation absorption was unusually high, with a maximum SUV of 16.2 in the spleen. Multiple enlarged lymph nodes were observed in the neck, left clavicle, axilla, right hilum, mediastinum, liver hilum and peritoneum, lower abdominal cavity, left pelvic wall, and inguinal region. There was increased radiation uptake in those regions, with a maximum SUV of 15.9. In the peritoneum, the lymph nodes were partly fused, with unclear boundaries and partial pressure on the surroundings. Based on these findings, the patient was diagnosed with splenic primary non-Hodgkin's lymphoma.

Next, the patient received R-CHOP combined chemotherapy in June 2015: Rituximab 600 mg, vindesine (VDS) 4 mg and idarubicin needle (IDA) 20 mg on d 1; cyclophosphamide IFO2.0 on d 1-3; prednisone 90 mg on d 1-5. One month after chemotherapy, abdominal enhanced CT showed that the enlarged hilar and retroperitoneal lymph nodes had disappeared, and the spleen lesions were significantly reduced. Due to financial difficulties, the patient declined further use of rituximab and underwent a CHOP regimen (IFO2.0 on d 1-3; VDS 4 mg and liposomal doxorubicin 40 mg on d 1; prednisolone 90 mg on d 1-5) on August 20, September 17, October 17, and November 22, 2015. The splenic lesion was further reduced (Figure 3C), and the patient is now on regular follow-up and in good health (Figure 3D).

OUTCOME AND FOLLOW-UP

One month after chemotherapy, abdominal enhanced CT showed that the enlarged hilar and retroperitoneal lymph nodes had disappeared, and the spleen lesions were significantly reduced.

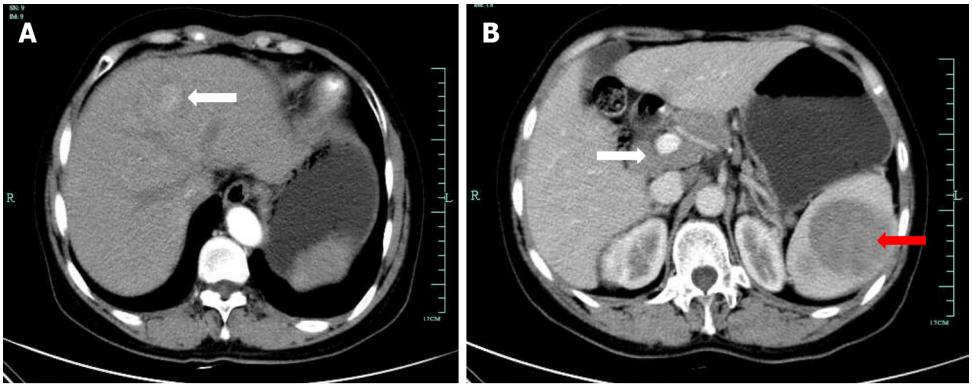

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Figure 1 Patient's enhanced computed tomography images. A: Enhanced computed tomography examination showed a mass with a diameter of approximately 2.6 cm on the left liver lobe on January 13, 2015; B: The splenic portal phase showed multiple circular low-density shadow areas with a maximum diameter of approximately 7.6 cm (red arrow); multiple enlarged lymph nodes were detected around the liver helium and retroperitoneum with partial fusion conglobation (white arrow).

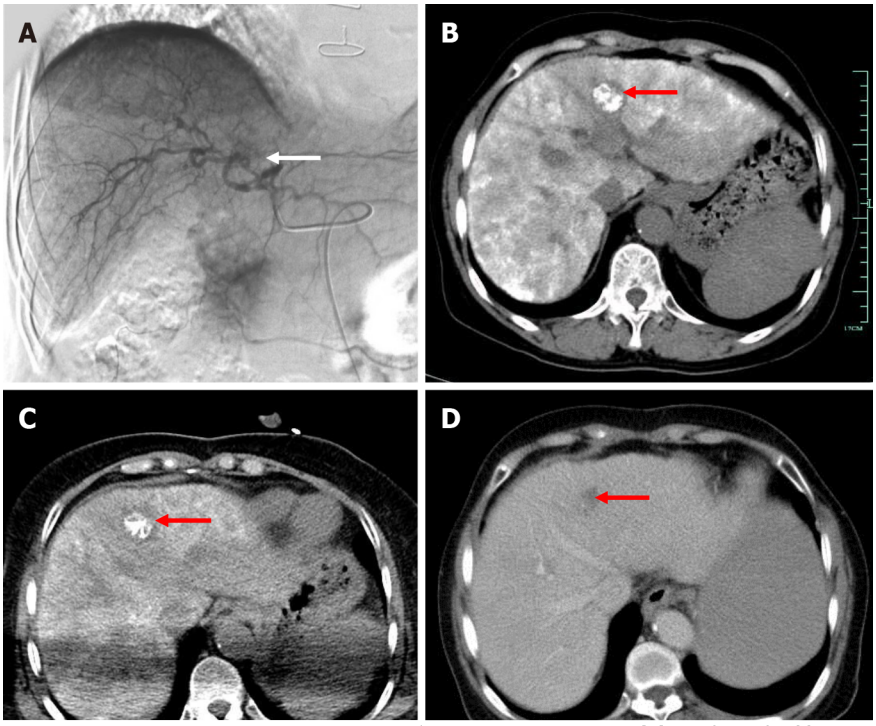

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Figure 2 Patient's digital subtraction angiography and computed tomography images. A: Hepatic arteriography, transcatheter arterial chemoembolization (TACE), and hepatic artery digital subtraction angiography imaging showed abnormal staining (white arrow) on the left hepatic artery on January 29, 2015; B: Dense lipiodol deposition in the left lobe lesions was observed two days after TACE by computed tomography (CT) scanning (red arrow); C: CT-guided percutaneous radiofrequency ablation was performed on the hepatic lesion (red arrow); D: One month after the procedure, the tumour had regressed completely (red arrow).

DISCUSSION

Multiple primary malignancies (MPMs) are defined as two or more unrelated primary malignant tumours that originate from different organs and occur in the same patient simultaneously or successively. The case reported here had a medical history of chronic hepatitis B and elevated serum AFP. Primary small hepatic carcinoma in the left lobe and primary NHL in the spleen were confirmed by enhanced CT, hepatic artery digital subtraction angiography imaging, and splenic biopsy. According to the latest National Comprehensive Cancer Network Hepatobiliary Cancers Clinical Practice Guidelines[7], these findings meet the diagnostic criteria for MPMN. Cases of primary hepatic tumour combined with splenic lymphoma are rare. Due to the lack of experience, the patient was initially misdiagnosed with primary hepatic carcinoma with metastasis to the hepatic portal, retroperitoneal

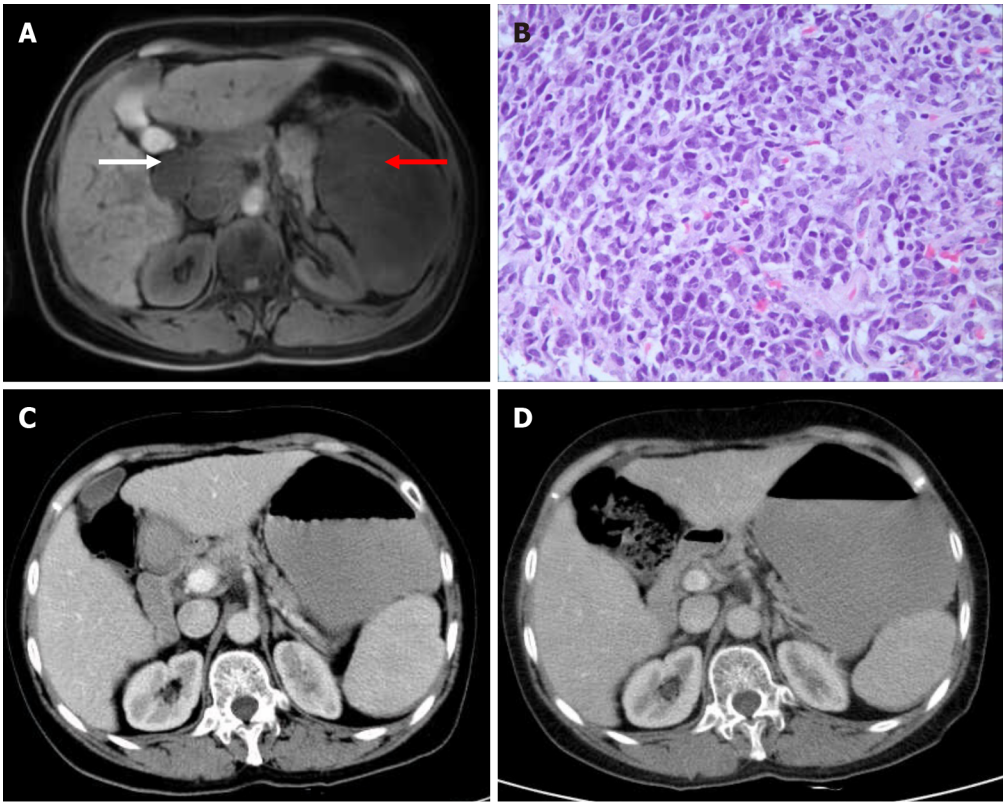

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Figure 3 Patient's magnetic resonance, pathology, and computed tomography images. A: Axial magnetic resonance imaging showed large lumps with low signals in the spleen (red arrow) on May 22, 2015. Lymph nodes were integrated into a group around the hilum and peritoneum (white arrow); B: Pathological examination of the splenic mass showed a patchy distribution of tumour cells and the disappearance of normal structures (haematoxylin–eosin staining 400 ×); C: Portal phase hepatic enhanced computed tomography (CT) examination after two rounds of R-CHOP treatment on August 19, 2015. Compared with before treatment (Figure 1), the splenic lesions and enlarged lymph nodes in the liver helium and peritoneum had shrunk, and the tumour had disappeared; D: CT scan of the patient at the last follow-up. There was no sign of tumour recurrence at follow-up.

lymph node, and spleen. Primary liver cancer transfers intrahepatically through the intrahepatic portal vein system, hepatic vein, and hilar lymph nodes. Distant metastasis commonly occurs in the lung and is extremely rare in the spleen. A large number of macrophages and lymphocytes, including cytotoxic T cells with direct killing effects, are present inside the spleen, making it unsuitable for cancer cell growth [8]. After the intrahepatic lesion was cured, the serum AFP gradually returned to normal. However, the spleen, hepatic portal vein, and retroperitoneal lymph nodes were enlarged, inconsistent with the AFP level, ruling out the possibility of liver cancer metastasis. Additionally, splenic lesion biopsy confirmed a diagnosis of NHL.

The majority of primary splenic NHL originates from B cells, characterizing splenomegaly. Compared with other imaging examinations, PET/CT has a high sensitivity for NHL lesions. It can detect not only infringed lymph nodes but also pathological changes outside the junction. Therefore, this technique is important for diagnosis, staging, treatment planning, and efficacy evaluation in malignant lymphoma [9]. Recently, researchers found that the hepatitis B rate is high in NHL patients[10], suggesting a relationship between both pathologies. The onset of most liver cancer cases is caused by hepatitis B cirrhosis in China. The diagnosis of primary liver cancer with lymph node metastasis should be concurrent, and it needs to be differentiated from NHL. Currently, imaging and pathological examination standards are lacking for the diagnosis of primary splenic NHL. Histological examination remains the gold standard for diagnosis. Therefore, timely lesion biopsy, even repeatedly, may be necessary.

TACE combined with conventional radiofrequency ablation could achieve a curative effect locally in early small hepatic carcinoma. NHL is a systemic malignant tumour. Appropriate chemotherapy should be prescribed for patients with HBV infection, minimizing liver damage with antiviral drugs. In this case, a good response was achieved after chemotherapy.

CONCLUSION

Primary hepatic carcinoma combined with primary splenic lymphoma is rare. The understanding of

EHPM should be improved to avoid misdiagnosis, and timely splenic biopsy should be performed for the accurate diagnosis of primary splenic lymphoma.

FOOTNOTES

Author contributions: Wu FZ and Chen XX contributed equally to this work; Chen WY, Mao JT and Wu QH are responsible for case analysis; Chen XX analysed the data and wrote the manuscript; Zhao ZW checks and revises the manuscript; all authors have read and approve the final manuscript.

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