

Case Report

Sarcomatous change of hepatocellular carcinoma in a patient undergoing living donor liver transplantation

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Summary

In a 53-year-old male who received a right liver graft from his son, computed tomography 1 week before living donor liver transplantation (LDLT) revealed three hepatocellular carcinoma (HCC) tumors in the liver that met the Milan criteria. Resected specimen revealed four tumors and microscopically, one of four HCC tumors in the resected whole liver comprised a glandular structure with spindle-like cells indicative of a sarcomatous change in HCC. Two hundred and sixty days after LDLT, the patient complained of left meralgia, which was diagnosed as iliac bone metastasis from HCC. Over a period of 3 months, the iliac bone metastasis rapidly enlarged. The tumor aggressively extended into the patient's bone marrow, causing severe pancytopenia. The patient died 371 days after LDLT. This tumor was detected preoperatively by computed tomography but lack of enhancement. These findings indicate that pathologic evaluation of each tumor is a key to predicting an accurate prognosis.

Keywords: Liver transplantation, sarcomatous, hepatocellular carcinoma

1. Introduction

Living donor liver transplantation (LDLT) is a therapeutic option for hepatocellular carcinoma (HCC) with end-stage liver disease. Milan criteria (1) or more expanded criteria (2) are used to select patients with HCC for liver transplantation. Tumor differentiation and pathologic features also affect the prognosis of the patients (3). Here, we report a case presenting with severe pancytopenia an early recurrence of a sarcomatous change of HCC in a patient undergoing LDLT.

2. Case report

The subject was a 53-year-old male who received a right liver graft from his son. The patient was indicated

with liver transplantation for HCC which could not be treated with partial resection due to liver dysfunction. Laboratory data on admission were as follows: hemoglobin, 14.9 g/dL; platelets, $5.4 \times 10^4/\text{mm}^3$; total bilirubin, 3.0 mg/dL; serum albumin, 2.8 g/dL; and prothrombin time international ratio, 1.46. His hepatitis C virus (HCV) RNA titer was positive (< 0.5 Meq/mL) and the genotype was 1b. The alpha-fetoprotein and des- γ -carboxy prothrombin levels before transplantation were 323 ng/mL and 64 mAu/mL, respectively. The patient's condition was complicated with hepatopulmonary syndrome. The partial pressure of oxygen in the arterial blood was 55 mmHg under room-air. The blood types of the recipient and donor were identical. There was only one HLA mismatch at the A, B, and DR loci. The T lymphocytotoxic crossmatch test was negative. The patient was diagnosed with three nodules (Segments 4, 8 and 5/6, each) in the liver based on computed tomography, compatible with HCC (Figure 1). Two of the tumors (in Segments 4 and 8, each) were 1 cm in diameter and the other (in Segment 5/6) was 2 cm.

A right liver graft was transplanted as described elsewhere (4). The weight of the graft was 684 g, which corresponded to 58% of the standard liver volume (5)

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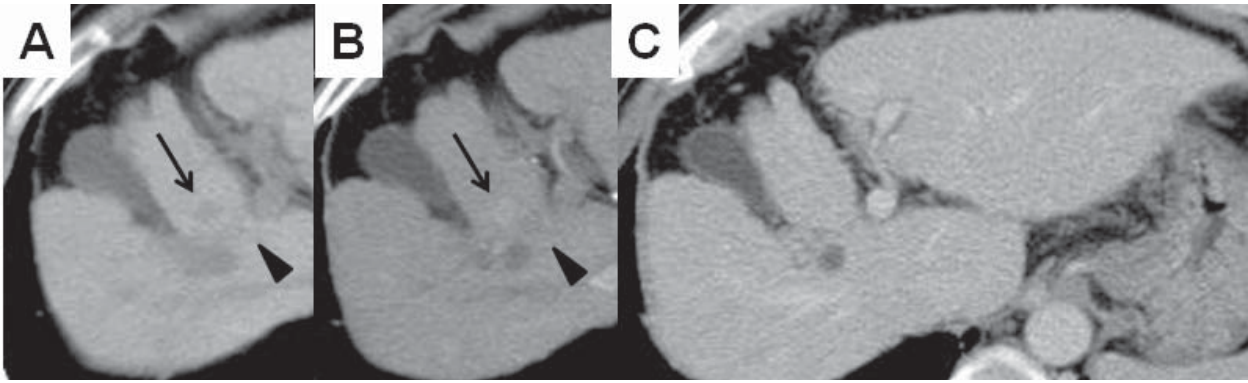


Figure 1. Computed tomography images of the tumor in segment 4. (A) non enhanced; (B) early phase; (C) late phase. The ventral part (arrows) was enhanced in the early phase and in contrast the dorsal part (arrow heads) was vague and not enhanced by contrast medium.

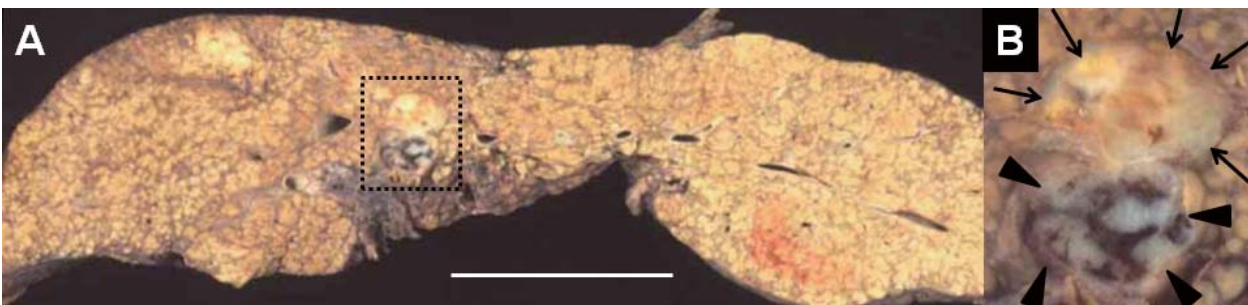


Figure 2. Resected specimen. (A) Macroscopic findings of the tumor in S4 (white line indicated 5 cm length). (B) The magnified image of (A). The ventral area of the tumor surrounded by arrows was necrotic possibly due to ethanol injection therapy. The dorsal area showed by arrow heads was a viable lesion.

of the recipient. Blood loss during surgery was 4,700 mL. Tacrolimus (Prograf, Astellas Pharmaceutical Corporation, Tokyo, Japan) and methylprednisolone (Solu-Medrol, Pharmacia Corporation, Peapack, NJ, USA) were used as immunosuppressive agents. There were no vascular or biliary complications. He was discharged from our hospital 27 days after LDLT. Two months after LDLT, interferon-alpha 2a (6 MU \times 3 per week) and ribavirin (600 mg per day) were administered for HCV infection. His HCV-RNA titer became negative 90 days after LDLT.

There were four grossly visible HCC nodules in the resected whole liver. Besides with the preoperatively diagnosed three tumors, additional tumor was found in segment 1. The size of the largest tumor (segment 5/6) was 1.7 cm in diameter. The tumor, 1.2 cm in diameter in segment 4, showed mixed white tissue and black hemorrhagic foci (Figure 2). Microscopically, it comprised an epithelial component with a pseudoglandular structure and a sarcomatous component with spindle-like tumor cells. The histologic transition between the two components suggested a sarcomatous change in HCC (Figure 3). Immunohistochemical studies supported the diagnosis, as both the sarcomatous component and epithelial component were positive for cytokeratin CAM 5.2, vimentin, and alpha-fetoprotein,

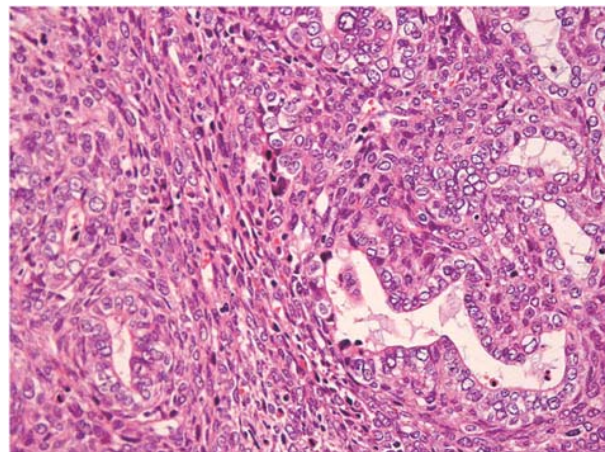


Figure 3. Microscopic findings. This tumor was consisted of glandular structure and spindle like cell.

whereas they were negative for cytokeratin 7, a marker of cholangiocellular carcinoma (Figure 4).

Two hundred and sixty days after LDLT, the patient complained of meralgia in the left leg. Computed tomography findings led to a diagnosis of bilateral iliac bone metastasis of HCC. No other metastatic lesions were detected in the liver graft, lung, brain, or spine. 18-fluoro-2-deoxyglucose positron emission

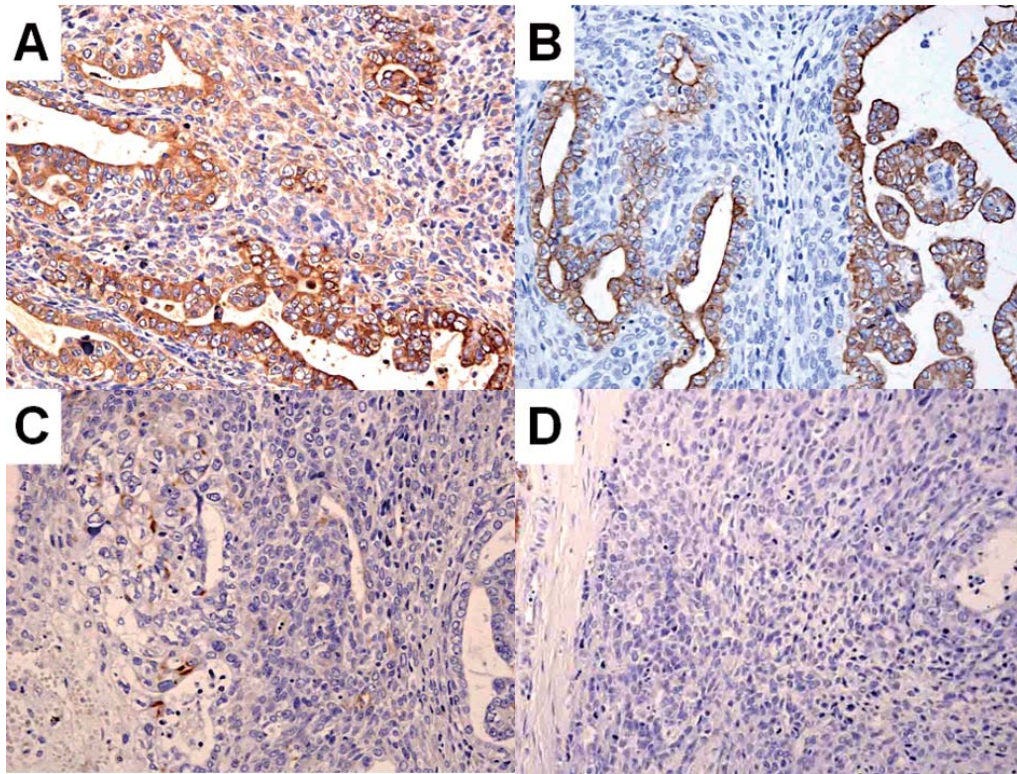


Figure 4. Immunohistochemical study of this tumor. Glandular structure was positive for alpha-fetoprotein (A) and cytokeratin CAM 5.2 (B). The spindle like cell was positive for vimentin (C) whereas cytokeratin 7 (D) was negative.

tomography images, however, showed positive signals in sternum, spine, and iliac bone. The metastatic lesion in the iliac bones rapidly enlarged from 2 cm to 20 cm in diameter over a 3-month period. The periphery of this lesion was well enhanced in the arterial phase on computed tomography. Technetium-99m hydroxymethylene diphosphonate bone scintigraphy showed no uptake in this lesion at diagnosis. He became pancytopenic (white blood cell, red blood cell, and platelet count had decreased to 1,700/ μ L, 4.8 g/dL, and 0.5×10^4 / μ L, respectively) 320 days after LDLT. Bone-marrow biopsy did not reveal hematopoietic cells, but there were several conglomerates of atypical cells with high nuclear pleomorphism and scanty cytoplasm. These immature cells could not be diagnosed as metastatic lesions. The patient died 371 days after LDLT. His alpha-fetoprotein and des- γ -carboxy prothrombin levels were 1 ng/mL and 118 mAu/mL, respectively, at that time.

3. Discussion

The coexistence of a sarcomatous component and ordinal HCC is a histologic type of HCC (6). Ishak and colleagues (7) classified spindle cell (pseudosarcomatous or sarcomatoid) -type HCC as an HCC types in a working group sponsored by the World Health Organization. Several reports indicate an incidence of sarcomatoid HCC in 1.8% of surgically resected cases (8) and 3.9% of autopsy

cases (9). Kakizoe and colleagues (9) reported that the sarcomatous component of HCC is derived from a dedifferentiation of anaplastic changes in ordinal HCC rather than collided double cancer.

Nishi and colleagues (10) reported that sarcomatoid HCC patients have a poorer prognosis than patients with ordinal type HCC. Hwang and colleagues (3) reported the prognosis in 19 patients with sarcomatoid HCC, 15 underwent liver resection and 4 received transplantation. The 3-year survival rate of the 15 patients that underwent liver resection was 18%, although they were judged to be less than stage III according to tumor-node metastasis staging system. Three of the four patients that underwent liver transplantation met the Milan criteria. Their 3-year survival rate was 38%.

Transcatheter arterial chemoembolization and/or percutaneous ethanol injection therapy might accelerate sarcomatous changes of HCC through necrosis and degeneration. Kojiro and colleagues (11) reported the results of autopsy series study indicating that 21% of patients who underwent arterial chemoembolization had sarcomatous HCC compared with 4.2% of the patients who did not undergo arterial chemoembolization. Komada and colleagues (12) reported a patient with sarcomatous HCC who received several percutaneous ethanol injections over 5 years. The present patient underwent percutaneous ethanol injection therapy 9 times in 6 years before transplantation.

Immunohistochemical studies are important for the

diagnosis of sarcomatous HCC. Kakizoe and colleagues (9) reported that 64% of sarcomatous HCC is positive for vimentin. Maeda and colleagues (8) reported that 62% of sarcomatous HCC is positive for cytokeratin CAM 5.2. Our present case was positive for both vimentin and cytokeratin CAM 5.2.

Honda and colleagues (13) reported that in the delayed enhancement phase of computed tomography sarcomatous HCC appears as an irregular intrahepatic mass, although Hwang did not describe this feature in his series (3). Koo and colleagues (14) reported that a solid component indicates variable enhancement during three-phase dynamic CT imaging. The present case, however, did not show those features. Hwang (3) reported that they diagnosed existing sarcomatous HCC by liver biopsy prior to liver resection surgery.

At our institution, 97 patients have undergone LDLT for HCC with end-stage liver disease in 12 years. This present case is the first case in our series with sarcomatous HCC. The present case indicates that pathologic evaluation of each tumor is key for predicting an accurate prognosis. Liver transplantation for sarcomatous HCC may be contraindicated due to its aggressive features.

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