Carcinosarcoma of the Liver

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Abstract

Herein we present a 73-year-old man with primary carcinosarcoma of the liver, a rare malignant tumor of the liver. The case was followed up due to HBV-related liver cirrhosis. Regular check-up by ultrasound demonstrated a hyperechoic tumor in the left lobe of the liver, and he was referred and admitted to our hospital. Dynamic CT studies revealed a mostly hypoenhancing hepatic mass with a peripheral ring enhancement. Surgical resection was performed, and the resected tumor was macroscopically a simple nodular type, 3 cm in diameter, with a dense fibrous capsule. Microscopically, undifferentiated cells were dominant in the tumor, while moderately differentiated hepatocellular carcinoma (HCC) were also observed. A transitional zone was noted between the undifferentiated tumor and HCC. Tumor tissue with adenocarcinoma, osteosarcoma and chondrosarcoma were also detected. Immunohistochemical studies demonstrated that tumor cells were HepPar 1 positive in hepatocellular carcinoma, and CK19 and partly CK7 positive in adenocarcinoma. Moreover, CD 56, chromogranin A and c-kit were occasionally positive in undifferentiated tumor cells. The diagnosis of carcinosarcoma was made based on the concomitant presence of HCC and sarcomatous components, yet it is noteworthy that various types of tumor cells were observed.

Key words: carcinosarcoma, hepatocellular carcinoma, osteosarcoma, chondrosarcoma, hepatic progenitor/stem cells

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Introduction

Primary carcinosarcoma of the liver as defined by Ishak et al is hepatocellular carcinoma (HCC) combined with differentiated sarcomatous components (1). While it has been demonstrated that carcinosarcoma could arise from a variety of tissues including the esophagus, gallbladder, pancreas and uterus, primary carcinosarcoma of the liver is very rare; as far as we could identify, only 18 case reports in the English language literature have demonstrated primary carcinosarcoma of the liver to date (2-19), yet the number of case reports has recently been increasing (11-19), probably due to the increased recognition of the tumor. The epidemiology and risk factors have not yet been determined, and apparently the prognosis is poor except for cases in whom curative resection is performed (18). In this report, we present a case with primary carcinosarcoma of the liver, which developed in the cirrhotic liver due to hepatitis B virus infection.

Case Report

A 73-year-old Japanese man was referred and admitted to our hospital for further evaluation of a hepatic tumor, which was incidentally found by ultrasound on a routine medical check-up. The patient had been diagnosed as having hepatitis B virus (HBV)-related liver cirrhosis and diabetes mellitus. He had no past history of alcohol overuse. Ultrasound
Figure 1.  Plain CT (A) showed a hypoattenuating mass in segment 4 of the liver. Arterial (B), portal (C), and parenchymal (D) phases of dynamic CT scanning demonstrated peripheral ring-like enhancement with little enhancement in the central part of the lesion.

demonstrated a hyperechoic tumor in the left lobe of the liver, 3 cm in diameter. Serum tumor markers related hepatic malignancy were all elevated; alfa-fetoprotein 120.9 ng/mL (normal range, <20 ng/mL), des-γ-carboxy prothrombin 240 mAU/mL (28<cmAU/mL), CA19-9 173.8 U/mL (<37 U/mL), carcinoembryonic antigen 8.5 ng/mL (<5 ng/mL). Dynamic study of computed tomography (CT) scanning of the abdomen revealed a mostly hypoenhancing hepatic mass in segment 4, with a peripheral ring enhancement through arterial, portal and equilibrium phases (Fig. 1A-D). On magnetic resonance imaging (MRI), the lesion appeared as heterogeneous and partial low intensity on T1-weighted images (Fig. 2A), and inhomogeneous high intensity on T2-weighted images (Fig. 2B). Portal phase images of gadolinium-enhanced dynamic MRI showed peripheral ring-like enhancement (Fig. 2C). Taken together, although a definitive diagnosis of the tumor was still undetermined, malignant characteristics were strongly suspected, and surgical resection of the segment 4 of the liver was performed. The patient was discharged with a good postoperative course, and neither local recurrence in the liver nor distant metastasis has been detected at 1 year and 7 months after the operation.

Pathological findings

The resected tumor was macroscopically a simple nodular type, 3×2.5×2 cm in diameter, with a dense fibrous capsule (Fig. 3). The central area of the tumor was necrotic. Various sizes of pseudolobules were noticed in the non-cancerous liver tissue, compatible with liver cirrhosis. Microscopically, necrotic tumor tissues were dominant in the central areas of the tumor, while viable tumor tissues were dominant in the peripheral areas. As to the histological type, undifferentiated cells that were strongly stained with chromatin were dominant in the tumor (Fig. 4A), while moderately differentiated HCC with thick trabecular formation were also observed (Fig. 4B). A transitional zone was found between the undifferentiated tumor and moderately- or poorly-differentiated HCC (Fig. 4B). Tumor tissue with glandular structures (Fig. 4C), bone (Fig. 4D) and cartilage formations (Fig. 4E) were also detectable in the tumor as well. The amount of cartilage and bone tissue components was sufficient for the diagnosis of chondrosarcoma and osteosarcoma components. Immunohistochemistry studies demonstrated that almost 30% of tumor cells at the trabecular structures were HepPar 1 positive (Fig. 5A). CK19 (Fig. 5B) and partly CK7 (Fig. 5C) were positive in glandular structures, indicating that both components of hepatocellular and cholangiocellular carcinoma were concomitantly present in the tumor. The glandular structure component was also positive for diastase digested PAS stain. Moreover, CD56 (Fig. 5D), chromogranin A (Fig. 5E) and c-kit (Fig. 5F) were occasionally positive in the tumor, suggesting that tumor cells, at least some tumor cells, possessed characteristics of neuroendocrine tumors and hepatic progenitor/stem cells as well. The sarcomatous components were positive for vimentin as well.
Figure 2. MRI showed a mass with heterogeneous and partial low-intensity on T1-weighted image (A) and heterogeneous high-intensity on T2-weighted image (B). Portal phase image of gadolinium-enhanced dynamic MRI (C) showed peripheral ring-like enhancement.

Figure 3. Macroscopic findings of the resected tumor of the liver. The tumor was a simple nodular type, 3×2.5 cm in diameter, and encapsulated by dense fibrous tissues. Non-cancerous liver tissue was definitely cirrhotic, with marked formation of regenerative nodules.

Taken together, we eventually diagnosed the tumor as carcinosarcoma of the liver because the tumor showed both definite HCC features and sarcomatous components (Fig. 4A-B). However, it is noteworthy in the present case that adenocarcinoma (Fig. 4C), various types of tumor cells (Fig. 4D-E), and even hepatic progenitor/stem cells (Fig. 5F) in addition to HCC and sarcomatous components were concomitantly observed in the same tumor.

Discussion

Carcinosarcoma of the liver, although it was thought to be extremely rare, has apparently been reported more frequently in recent years; there have been 18 case reports with 22 cases of carcinosarcoma of the liver to date, and 9 out of these 18 reports have been published in the last 5 years (11-19). The age of the patients ranged from 40 (15, 18) to 84 (9), and male or female predisposition was not observed. It is noteworthy that 17 out of the 22 reported cases, including the current report, were Asian; Japanese, Korean or Chinese. Fourteen of 22 cases (64%), including the present case, had cirrhotic liver at background, and 7 out of 14 cirrhosis were HBV positive. Only one cirrhotic liver was due to HCV infection. Therefore, liver cirrhosis as well as HBV infection, which are well known as risks for HCC, might be the etiological factors contributing to the development of carcinosarcoma, yet we should note that almost one-third of the cases developed carcinosarcoma in otherwise normal livers.

In the current case radiological findings were unique; dynamic CT study showed a mostly hypoenhancing mass, with a peripheral ring enhancement (Fig. 1A-D), which was also detected by MRI (Fig. 2C). Pathological findings suggest that this unique enhancement pattern was due to the difference in the amount of necrotic tissues (Fig. 3). Necrotic tumor tissues were dominant in the central areas of the tumor,
Figure 4. Histological findings of the tumor tissue, demonstrating a variety of tumor components (Hematoxylin and Eosin staining). A: Undifferentiated tumor tissue, strongly stained with chromatin, was dominant within the tumor. B: Moderately-differentiated HCC with a thick trabecular pattern was also observed. The transitional zone (T) was seen between HCC and undifferentiated tumor tissue (U). C: Tumor tissue of adenocarcinoma (cholangiocarcinoma) with glandular structure. D: Tumor tissue with bone formation, compatible with osteosarcoma. It also showed a transitional zone (T) between osteosarcoma (OS) and undifferentiated tumor tissue (U). E: Tumor tissue with cartilage formation, compatible with chondrosarcoma.

Although the pathogenesis of carcinosarcoma of the liver still remains unknown, previous reports have suggested two theories explaining how this rare tumor developed, i.e. the nature of carcinosarcoma as ‘combination’ tumor and ‘conversion’ tumor (11). Some authors argue that carcinosarcoma arise from a multipotent hepatic progenitor or stem cell, which may differentiate into both carcinomatous and sarcomatous neoplasms to produce a ‘combination’ tumor (7, 14). In support of this view, Thompson et al demonstrated a monoclonal origin of carcinosarcomas by two independent methods of clonality determination, supporting the single totipotential stem-cell-divergence hypothesis of carcinosarcoma (20). She and Szakacs suggested that an aberrant multipotent stem cell origin was a likely explanation of carcinosarcoma of the liver, because of the variability observed in their cases (14). By contrast, others claim ‘conversion’ tu-
tumor, which suggest that the transformation or the dedifferentiation of conventional HCC into sarcomatous components may occur (3, 4, 16, 18), based on the observation that the transitional zones were identified in the tumor (16, 18).

In the current case, we detected numerous c-kit positive anaplastic cells in the tumor (Fig. 5F) as well as a variety of tumor cells. In addition, the carcinosarcomas which were suggested to be dedifferentiated from conventional HCC in the literature were large, 5 cm or more in diameter (16, 18), while the tumor of the current case was 3 cm in diameter. These findings support the ‘combination’ hypothesis that the tumor developed from progenitor/stem cells. On the other hand, we clearly noticed the transitional zones, between distinct HCC and undifferentiated tumors (Fig. 4B), and also between undifferentiated tumors and sarcomatous components (Fig. 4D). The presence of transitional zones may support the ‘conversion’ tumor hypothesis, in that dedifferentiation of conventional HCC into undifferentiated tumors, and sarcomatous components further, resulted in carcinosarcoma. Non-cancerous liver tissue in the patient demonstrated HBV-related cirrhosis which could bear conventional HCC, and it might be probable that various tumor cells arose due to dedifferentiation of HCC. Nevertheless, while we detected the transitional zones between undifferentiated tumors and moderately-differentiated HCC, it is obvious that these observed transitions are not sufficient to explain that ‘all’ various type of tumor cells in the current case were produced by dedifferentiation of conventional HCC. Therefore, both possibilities, ‘combination’ and ‘conversion’ hypotheses, still remain in the current case for the moment.

The prognosis for carcinosarcoma of the liver is poor, and most patients died within a year, except for a few cases in which curative operation for the tumor was performed as an initial treatment (13, 18). In the present case curative operation was performed as well, and the patient is alive 1 year and 7 months after the operation without any intrahepatic or metastatic recurrence. Clearly, it appears that radical and curative surgical operation is the single treatment for the favorable prognosis of such patients.

Abbreviation: OS: osteosarcoma

References


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