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Comprehensive Treatment of Hepatic Sarcomatoid Carcinoma: A Case Report

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ABSTRACT

Hepatic Sarcomatoid Carcinoma (HSC), a rare subtype of liver cancer, contains a mixture of cancerous and sarcomatous components. The disease is prone to metastasis and has a poor prognosis. This study reports the case of a 67-year-old male patient admitted to our hospital because of a right liver mass found on a physical ultrasound examination. There was no abdominal tenderness or rebound tenderness; Laboratory tests on admission showed increased HBV and alpha-fetoprotein (AFP); Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) showed a mass in the SV segment of the liver, suggesting Hepatic Cell Carcinoma (HCC) with multiple hilar and retroperitoneal lymph node metastases, and multiple lung metastases. The patient underwent a liver tumour biopsy, and immunohistochemical detection of cytokeratin (CK) and vimentin (Vim) was positive. The pathological diagnosis was HSC. The preferred treatment for HSC is surgical resection; however, considering the presence of systemic metastases in this patient, systemic treatment (Targeted therapy + Immunotherapy + Chemotherapy) is the primary treatment supplemented by local interventional treatment. At 1-year follow-up, mRECIST evaluated as PR, and PFS was not achieved. For patients with advanced hepatic Sarcomatoid carcinoma, local treatment should be combined with systemic treatment, and individualized management should be implemented to prolong the survival period of patients as much as possible and improve the quality of life of patients.

Abbreviations

HSC: Hepatic Sarcomatoid Carcinoma, HCC: Hepatic Cell Carcinoma, ICC: Intrahepatic Cholangiocarcinoma, CT: Computed Tomography, MRI: Magnetic Resonance Imaging, PET/CT: Positron Emission Tomography/CT, WHO: World Health Organization, TACE: Transcatheter Arterial Chemoembolization, D-TACE: Drug-eluting beads-TACE, RFA: Radiofrequency Ablation, PEI: Percutaneous Ethanol Injection, PD-L1: programmed death-ligand, IDO: Indoleamine 2, 3-dioxygenase.

Keywords

Liver neoplasms, Sarcomatoid carcinoma, Embolization, Immunity, Therapy.

Introduction

HSC is a rare histological subtype of liver cancer defined by the World Health Organization (WHO) as consisting of a cancerous component ((HCC)/Intrahepatic Cholangiocarcinoma (ICC)) and a malignancy with a mixed sarcoid component, predominantly spindle cells with an epithelial phenotype [1], accounts for only 2%-5% of all liver cancer cases [2], rarely reported in the English literature. Because it is rare and there is no effective treatment, the clinical, laboratory examination, pathological and immunohistochemical observations and therapeutic efficacy of a case of hepatic sarcoma-like carcinoma admitted to our department are reported below.

Case Report

A 67-year-old male patient was admitted to the Interventional Vascular Surgery Department of our Hospital because of a one-week space occupying the right liver found in a physical examination ultrasound; the general condition of the patient was good, without abdominal pain, abdominal distension, and yellow skin and sclera, and oily skin. Past medical history of hepatitis B for 12 years. Laboratory examination: carbohydrate antigen 125 (CA125) 6.35U/ml, carbohydrate antigen 199 (CA199) 8.17U/ml, carcinoembryonic antigen (CEA) 0.72ng/ml, AFP 233.77ng/ml. Liver function Child-Pugh A grade. Contrast-enhanced CT of the chest and whole abdomen (Figure 1): An irregular isodense lesion with unclear boundaries, about 77×42mm, was seen in the SV segment of the liver. The enhanced scan showed mild heterogeneous enhancement in the arterial phase, and noticeable edge enhancement in the portal venous phase and venous phase near the portal vein and the right hepatic vein branch is not displayed, multiple enlarged lymph nodes in the hilar porta and retroperitoneum, multiple nodules in both lungs, and metastases are considered. Enhanced MRI scan: Irregular low signal on T1WI, high signal on T2WI, unclear border, high signal on IVIM, low signal on ADC in SV segment of liver, mild edge enhancement in the arterial phase of the enhanced scan, there was no noticeable enhancement in each internal phase, the specific phase of the liver and gallbladder showed low signal, and there were multiple enlarged lymph nodes in the hilum and retroperitoneum. Positron Emission Tomography/CT(PET/CT): Diagnosis of right liver mass, considering primary hepatocellular carcinoma with multiple metastases throughout the body.

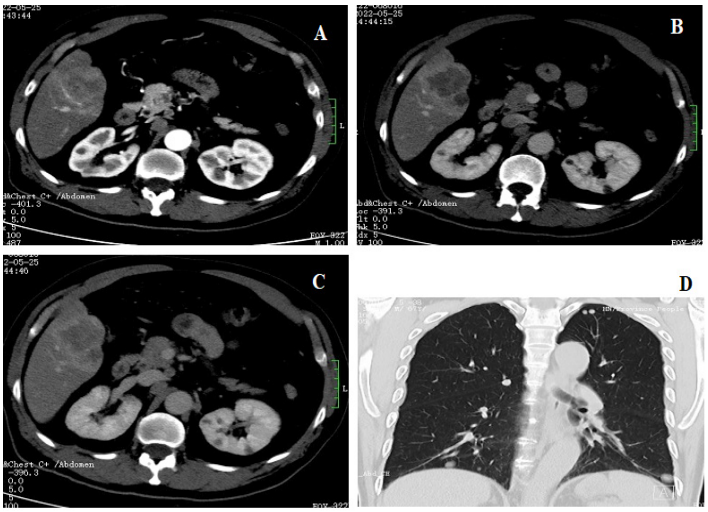


Figure 1: A: Mild heterogeneous enhancement in the SV segment of the liver in the CT arterial phase; B-C: Continuous and noticeable enhancement in the edge of the CT portal vein phase and delayed phase; D: Multiple metastases in both lungs.

According to the history of hepatitis B, elevated AFP and related imaging examination, the patient was initially diagnosed with primary liver cancer (BCLC C, CNLC IIIb). Because the patient had extrahepatic metastasis and no indication of surgical resection, Drug-eluting beads-TACE(D-TACE) (drug-loaded microspheres: Hengrui Medicine 100-300um, Idarubicin 10mg)+ plus liver tumour biopsy was performed on May 31, 2022. Immunohistochemistry: Vim (+), CK (+), Villin (partial +), Ki67 (+, 30%), CD34 (vascular +), CD117 (focal +), CK8/18 (+), EMA (partial +), E-Cadherin (+), PD-L1 (+, 70%); CK7, CK20, Hepatocyte, Arg-1, Desmin, Smur100, SMA, SOX-10, CD10, Glypican-3, DOG1 (-). Liver tumour gene detection: no mutant genes with clinical significance were found, TMB low expression (5.7Muts/Mb), microsatellite stability (MSS). The final diagnosis was HSC.

Initially, based on the patient's HBV(+), elevated AFP and imaging manifestations, the diagnosis was HCC with bilateral lung metastasis, but our department had doubts that the imaging features did not match the typical HCC manifestations. Therefore, the initial treatment plan for the patient was local interventional therapy + puncture biopsy to clarify the diagnosis and combined with systemic systemic therapy. However, the patient's family requested to wait for the pathology results to be clarified before systemic systemic therapy was performed. Subsequently, after the pathology was diagnosed as HSC, the patient's family consulted with Xiangya Hospital of Central South University and the Affiliated Cancer Hospital of Sun Yat-sen University for systemic systemic therapy, but did not obtain a clear treatment plan. Finally, the systemic treatment plan of levatinib+pembrolizumab+capecitabine was decided by the Department of Oncology of our hospital.

One month after the first D-TACE, our hospital re-examined, AFP 3357.51ng/ml increased compared with preoperative; liver function Child grade A. CT and MRI examinations showed that the right liver lesion was significantly smaller and less active than before, multiple lymph node metastases in the abdominal cavity and retroperitoneum, and multiple metastases in both lungs were more advanced than before; according to imaging findings, the liver lesion remained partially active, and the curative effect evaluation was more advanced than before. On July 12, 2022, D-TACE (drug-loaded microspheres: Hengrui Medicine 100-300um, Idarubicin 10mg) was performed again, and it was recommended to transfer to the oncology department for systemic treatment.

Reexamination in our hospital one month after the second D-TACE, CT and MRI (Figure 2). The size of the right liver lesion was 47×32mm, which was significantly smaller than before, and no biological activity was seen, but retroperitoneal lymphatic metastasis and bilateral lung metastases Increased and increased than before; and AFP 69.93ng/ml was significantly lower than before. Considering that the local interventional treatment is still progressing, it was transferred to the oncology department for systemic pembrolizumab (200mg iv qd) + lenvatinib (8mg po qd) + capecitabine (1.5g po Bid) on August 18, 2022 treat.

After receiving systemic treatment in the oncology department, the patient underwent several follow-up chest + whole abdomen enhanced CT: the original intrahepatic lesion was not biologically active, and the enlarged lymph nodes in the abdominal cavity and multiple metastases in both lungs were persistently reduced compared to the previous ones. At 1-year follow-up (Figure 3), mRECIST evaluated as PR, and PFS was not achieved.

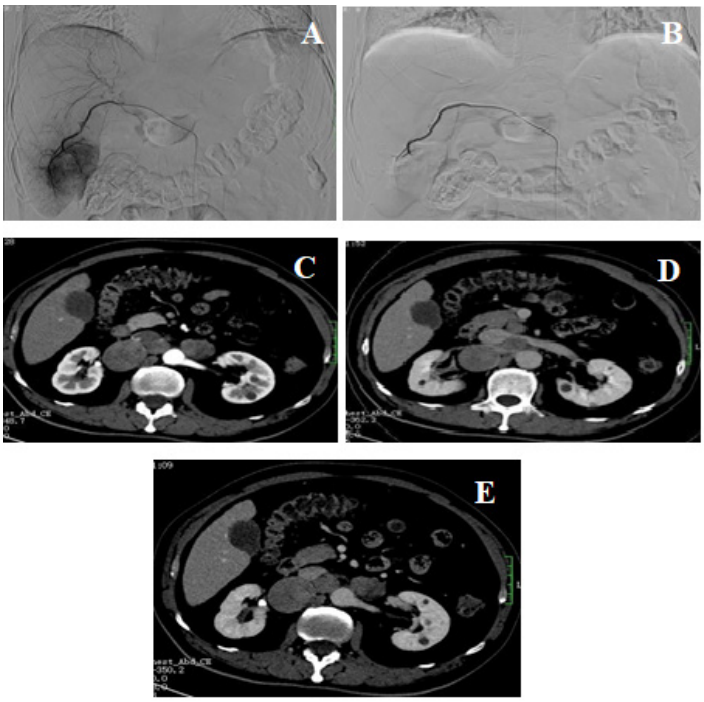


Figure 2: A: Intraoperative hepatic arteriography showed massive tumour staining in the SV segment of the liver; B: No obvious tumour staining after D-TACE embolization; C-E: SV segment lesions were significantly smaller than before, with no apparent biological activity.

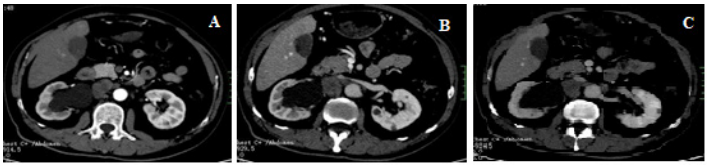
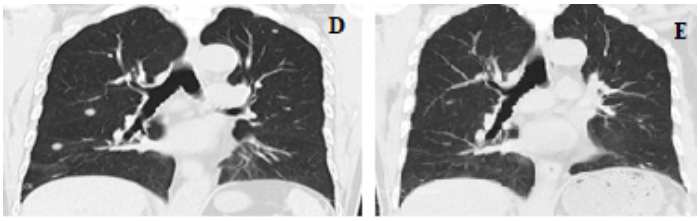


Figure 3: A-C: Liver SV lesions are similar to before, without evident biological activity.



Figures D-E: Multiple lung metastases are significantly reduced and shrunk.

Discussion

Hepatic sarcomatoid carcinoma (HSC) is a rare histological subtype of liver cancer whose pathogenesis remains unclear. Currently, two views are more recognized, and one is the sarcomatoid change of hepatocellular carcinoma. According to some studies [3], the highly infiltrated inflammatory environment of T lymphocytes in the tumour may be related to the sarcomatous changes of HCC; the other is the combination of HCC and sarcoma. There is also a small part related to preoperative anti-hepatic cancer treatment, such as transcatheter arterial chemoembolization (TACE), new anti-angiogenic drugs (Sunitinib), radiofrequency ablation (RFA) and percutaneous ethanol injection (PEI) and other treatments. However, it has also been reported that patients who have not received anticancer treatment can also have sarcomatoid changes [4-7]. In this case report, the patient had not received such anticancer treatment before diagnosis. Currently, the clinical diagnosis of HSC is difficult. The clinical presentation is nonspecific, with abdominal pain, weight loss, decreased appetite, and fatigue [8], as common complaints and symptoms. Most patients with HSC have a history of chronic viral hepatitis and cirrhosis. The imaging manifestations of HSC have dual imaging features of sarcoma and carcinoma. Unlike the typical imaging manifestations of HCC, which are "fast in and fast out", the imaging manifestations of patients with HSC are not specific. Due to tumour centre hemorrhage, necrosis and rapid growth of surviving cancer tissue at the edge, CT/MRI showed a sizeable intrahepatic mass with irregular borders, accompanied by hemorrhage, pseudo capsule, lymph node enlargement, edge enhancement in the arterial phase, portal venous phase and Peripheral sustained enhancement during the delayed phase [4,5,7,9,10]. The laboratory examination of HSC is characterized by normal or slightly elevated serum AFP, CEA, CA125 and other tumour markers. Among the 17 patients with HSC in this study [4], only about 10% of the patients had abnormally elevated AFP, which indicated that the diagnostic value of AFP for HSC was lower than that for HCC. These findings help differentiate HSC from HCC but may be confused with ICC.

Pathology and immunohistochemical staining are the gold standards for the diagnosis of HSC. The main pathological features of HSC [11] include 1. Epithelial components are mixed with heterologous mesenchymal components, and there is a transition between them; 2. Immunohistochemical staining shows epithelial tumour markers (CK, Keratin, EMA) and mesenchymal tumour markers (Vimentin) were positive. Intercellular keratin CAM5.2, CK8, CK18 and CK19 were positively expressed in HSC. In addition to the characteristic histological morphology, high expression of vimentin, programmed death-ligand(PD-L1), and increased immune cell infiltration also contribute to the pathological diagnosis of HSC [3]. According to a study [12], invasive and metastatic lesions are dominated by cancerous components, which suggests that cancerous components may dominate the highly invasive nature of HSC. However, the routine use of needle biopsy is limited due to its invasiveness and risks of bleeding, bile leakage, and tumour spread [13].

To date, there are no specific guidelines for the treatment of HSC. Radical surgery is currently recognized as the most effective treatment, which can significantly prolong the survival time of patients. Liver transplantation for patients with HSC can also achieve a similar prognosis to liver resection [6]. Compared with HCC, HSC has a lower overall survival rate even in those patients who underwent radical surgical resection because of its higher tumour invasiveness, larger tumour size, higher rate of extrahepatic metastases, and early recurrence [14]. A study [2] stated that among patients who also underwent surgical resection, only patients with stage ACJJ I benefited.

In contrast, patients with stage ACJJ II had similar OS to those of more advanced stages ACJJ III/IV and no stage II, III and IV patients survived more than two years after surgical resection. Therefore, surgical treatment can be actively considered for patients with early-stage HSC. However, for more advanced patients, the curative effect of surgical resection is limited, and effective postoperative adjuvant therapy is crucial to improve the prognosis and survival time of patients with HSC, such as Liver transplantation, TACE, ablation and radioactive seed implantation. In recent years, immunotherapy has become the direction of the treatment of HSC, and related targets for patients with HSC are often reported. CtBP1 plays a crucial role in HCC hypoxia-induced EMT and sarcomatoid transformation and can be used as a candidate target for HSC therapy [15]. Increased expression levels of PD-L1, B7-H3, and indoleamine 2,3-dioxygenase (IDO) may play an immunosuppressive role in the tumour microenvironment, suggesting combined targeting of PD -L1 and other immune checkpoints may be a potential direction for the treatment of HSC [16]. CDK4/6 inhibitors, including Abemaciclib, ribociclib, and palbociclib, are potential therapeutic targets that may help in treatment [14]. A case report [11] stated that a patient with advanced HSC with high expression of PD-L1 detected by gene sequencing had a complete response to OPDIVO (nivolumab). Therefore, future studies in patients with HSC should test targeting immune checkpoints as a breakthrough direction.

In summary, HSC is characterized by rarity, difficulty in clinical diagnosis, high invasiveness, and uncomplicated metastasis, leading to its inferior prognosis. For patients with early HSC, radical surgical resection should be actively performed, and effective adjuvant therapy should be given after surgery; for patients with advanced HSC, local treatment combined with targeted and immunotherapy should be implemented, and individualized management should be implemented to prolong the survival of patients as much as possible, improve the quality of life of patients. The patient reported in this article was initially treated with hepatic arterial chemoembolization to cause tumour ischemia and necrosis, but the tumour metastasis and progression could not be controlled. Therefore, systemic treatment was mainly used after diagnosis, supplemented by local interventional therapy as appropriate.

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