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CASE REPORT

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A case with sarcomatoid hepatocellular carcinoma and literature review

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Abstract

Sarcomatoid hepatocellular carcinoma (SHC) is a relatively rare subtype of liver cancer reported in 1.8–2.0% of surgically resected cases. Previous studies have found that SHC was more likely to occur in patients who received repeated anticancer therapies, but the underlying mechanism has not been exactly illustrated. We report a case of a 62-year-old man with SHC. With the initial implication of abscess suspected liver mass by radiological exams (enhanced Computed Tomography and liver Magnetic Resonance Imaging), the patient underwent a laparoscopic pus debridement and biopsy. The diagnosis of SHC was considered by pathologists. After a short recovery, a second radical resection of the liver tumor and hepatic hilar lymph node dissection were conducted. Postoperative pathology revealed a tumor-free incisal margin and negative lymph node. The recovery of the patient was uneventful. When confronting an occasional liver mass with previous Hepatitis B virus infection, SHC should be included for a candidate diagnosis. If diagnosis is confirmed, high biological malignancy and poor survival should be expected. Surgery is still a main option to treat SHC.

Keywords

Sarcomatoid cancer; Hepatocellular carcinoma; Sarcomatoid hepatocellular carcinoma; Hepatapostema; Hepatophyma liver abscess; Liver mass

1. Introduction

Sarcomatoid carcinoma (SC) is a rare kind of cancer that resembles spindle cell sarcoma morphologically. Sarcomatoid hepatocellular carcinoma (SHC) is an unusual SC with mainly uncovered clinical characteristics and limited treatment modalities [1]. The incidence of SHC varies from 1.8–2.0% in surgically resected cases [2, 3]. Previous studies reported that SHC was more likely to occur in patients who received repeated anticancer therapies, including transarterial embolization and radiofrequency ablation [3, 4]. Hepatitis, one of the causative factors of hepatocellular carcinoma (HCC), is also considered a risk factor for SHC [5]. Compared to nonsarcomatoid HCC, it seems to be a more advanced and aggressive subtype of HCC [6, 7]. Herein, we report a case of sarcomatoid hepatocellular carcinoma, and the literature was subsequently reviewed.

2. Case presentation

A 62-year-old man presented to our hospital with swelling pain in his right upper abdomen and nausea for 16 hours. He claimed no vomiting, diarrhea, hematochezia, jaundice or obstruction symptoms. Past medical history included hepatitis B virus (HBV) infection with discontinuous antiviral treatment, well-managed hypertension and coronary heart disease with coronary artery bypass graft postoperative status. No family or genetic history was found. The right upper abdominal tenderness and percussion tenderness over the hepatic region were the only positive signs from the physical examination. Laboratory tests showed a white blood cell (WBC) count of 13.14×10^9/L (normal range 3.5–9.5 $\times$ 10^9/L) with 75.7% neutrophils (normal range 40–75%). Liver-renal function remained normal except for a reduced albumin level of 34.5 g/L (normal range 40–55 g/L). In addition, tumor markers, including a-fetoprotein, carcinoembryonic antigen, and carbohydrate antigen 19-9, were unremarkable. The HBV deoxyribonucleic acid test displayed elevated levels of hepatitis B virus surface antibody (HBsAb) and hepatitis B virus core antibody (HBcAb) and decreased levels of hepatitis B virus E antibody (HBeAb) (Table 1).

Abdominal ultrasonography revealed an 8.2 $\times$ 6.8 cm diameter hypoechoic lesion with an irregular and shaggy margin in the right lobe of the liver. Further computed tomography (CT) scanning showed a 7.1 cm diameter analogous round mass with low density in segments V and VIII (Fig. 1A–C). Preoperative magnetic resonance imaging (MRI) indicated a margin-reinforced lesion with a 6.3 cm diameter and inhomogeneous high signal in the diffusion weighted imaging (DWI) (Fig. 2A–D), indicating the possible diagnosis of hepatic abscess.

The patient was then scheduled to undergo laparoscopic exploration. A mass containing yellow-white pus in hepatic segment VIII was observed. In the course of the operation, pus liquid and clots were cleared, and the wall of the abscess was

TABLE 1. Laboratory data.

Variable	Result	Reference Range
White Blood Cell (WBC) ($\times 10^9$/L)	13.14↑	3.50–9.50
Neutrophils ($\times 10^9$/L)	9.93↑	1.80–6.30
Ratio of Neutrophils (%)	75.70↑	40.00–75.00
Red Blood Cell (RBC) ($\times 10^{12}$/L)	3.91↓	4.30–5.80
Hemoglobin (Hgb) (g/L)	119.00↓	130.00–175.00
Total Protein (TP) (g/L)	75.00	65.00–85.00
Albumin (g/L)	34.50↓	40.00–55.00
Alanine aminotransferase (ALT) (U/L)	11.00	9.00–50.00
Aspartate aminotransferase (AST) (U/L)	19.00	15.00–40.00
Total Bilirubin (TB) (umol/L)	14.30	0.00–26.00
Direct Bilirubin (DB) (umol/L)	4.80	0.00–6.80
Lactate dehydrogenase (LDH) (U/L)	208.00	120.00–250.00
Gama glutamyl transferase (GGT) (U/L)	27.00	10.00–60.00
Alkaline phosphatase (AKP) (U/L)	112.00	45.00–125.00
Alpha fetoprotein (AFP) (ng/mL)	1.40	0.00–9.50
Carcinoembryonic Antigen (CEA) (ng/mL)	1.90	0.00–5.80
CA19-9 (U/mL)	8.00	0.00–37.00
HBsAg (IU/mL)	0.00	0.00–0.05
HBsAb (mIU/mL)	321.70↑	0.00–10.00
HBeAg (S/CO)	0.43	0.00–1.00
HBeAb (S/CO)	0.40↓	≥1.00
HBcAb (S/CO)	7.27↑	0.00–1.00

HBsAg: hepatitis B virus surface antigen; HBsAb: hepatitis B virus surface antibody; HBeAg: hepatitis B virus E antigen; HBeAb: hepatitis B virus E antibody; HBcAb: hepatitis B virus core antibody.

resected for pathological analysis. Unfortunately, the pathologist considered the diagnosis of the resected liver specimen appearance for gray red gray brown tissue size 1.7 cm × 1.2 cm × 0.7 cm as a malignant tumor with epithelioid differentiation, preferring as liver sarcomatoid carcinoma with poor differentiation. The pus culture derived from the operation demonstrated a negative bacterial result.

After one month of uneventful recovery, the patient was reevaluated with CT. With metastasis being excluded and sufficient preoperative preparation, the patient underwent radical surgery. The resected liver specimen was confirmed as an 11.0 × 7.0 × 6.7 cm sarcomatoid hepatocellular carcinoma, and all harvested hilar lymph nodes were negative. Spindle cells could be seen in the hematoxylin-eosin (HE) staining under the microscope (Fig. 3A–B). Further immunohistochemistry results demonstrated positive cytokeratin (CK) staining and a moderate Ki-67 index (Fig. 3C–D). After two weeks of recovery, the patient was discharged without severe complications. The postoperative 3-month follow-up revealed recurrence of the tumor in the remnant liver. After the multidisciplinary conference, the patient was then suggested to receive systemic therapy with the AC chemotherapy protocol (adriamycin plus cyclophosphamide). Unfortunately, the patient died after the first therapy regimen due to uncontrolled disease-related gastrointestinal bleeding.

3. Discussion

SHC is a rare histological subtype of liver cancer [2, 8]. A recent comprehensive analysis of pathologic, transcriptomic and immunologic characteristics demonstrated that SHC was distinct from traditional HCC [3]. A large-scale database analysis showed that the majority of SHC patients were male, with a one-year overall survival of 17.4% [8]. Even if SHC is highly malignant, the pathogenesis of the sarcomatoid transformation remains unknown. The potential risk factors proposed by several previous studies were transarterial embolization, radiofrequency ablation and chronic biliary inflammatory stress [4]. Nevertheless, some individuals still develop SHC even if they do not undergo anticancer therapy [9, 10]. In this case, the patient denied a history of any cancer or anticancer treatment. The past history of HBV infection may be relevant to his SHC development.

Clinically, early-stage SHC cases presented no obvious symptoms, which was similar to traditional HCC [3]. Some patients with advanced SHC usually complained of abdominal distension, abdominal pain, weight loss, fever, or jaundice. It has also been reported that some patients have high fever, accompanied by leukemia-like reactions [11, 12]. The laboratory test results were mainly nonspecific. Regarding this case, a blood test displayed an inflammatory status with

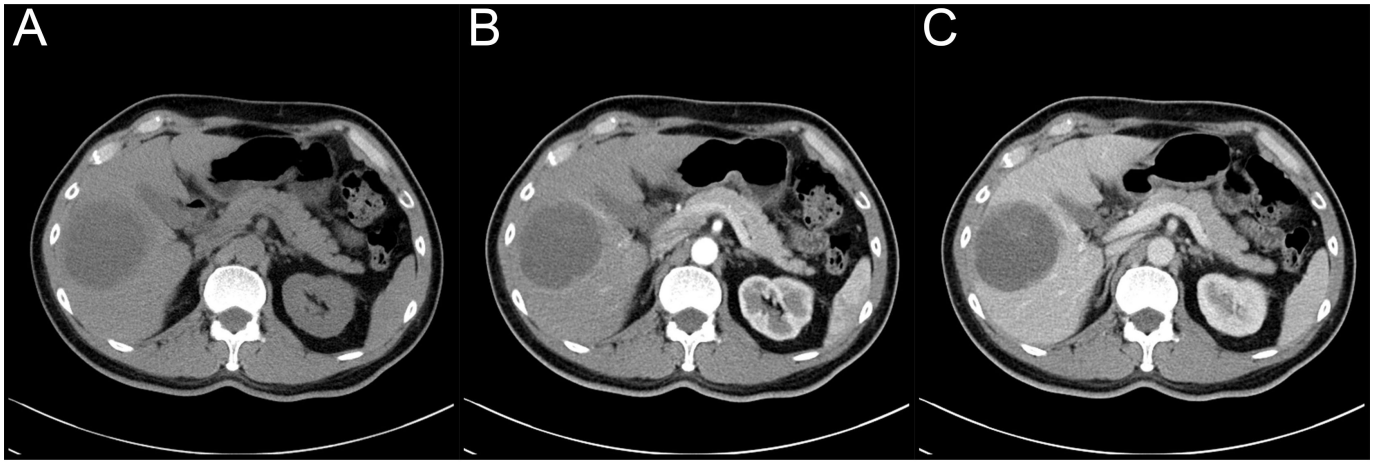

FIGURE 1. Preoperative CT evaluation (A) plain CT scanning (B) artery phase of enhanced CT scanning (C) portal vein phase of enhanced CT scanning.

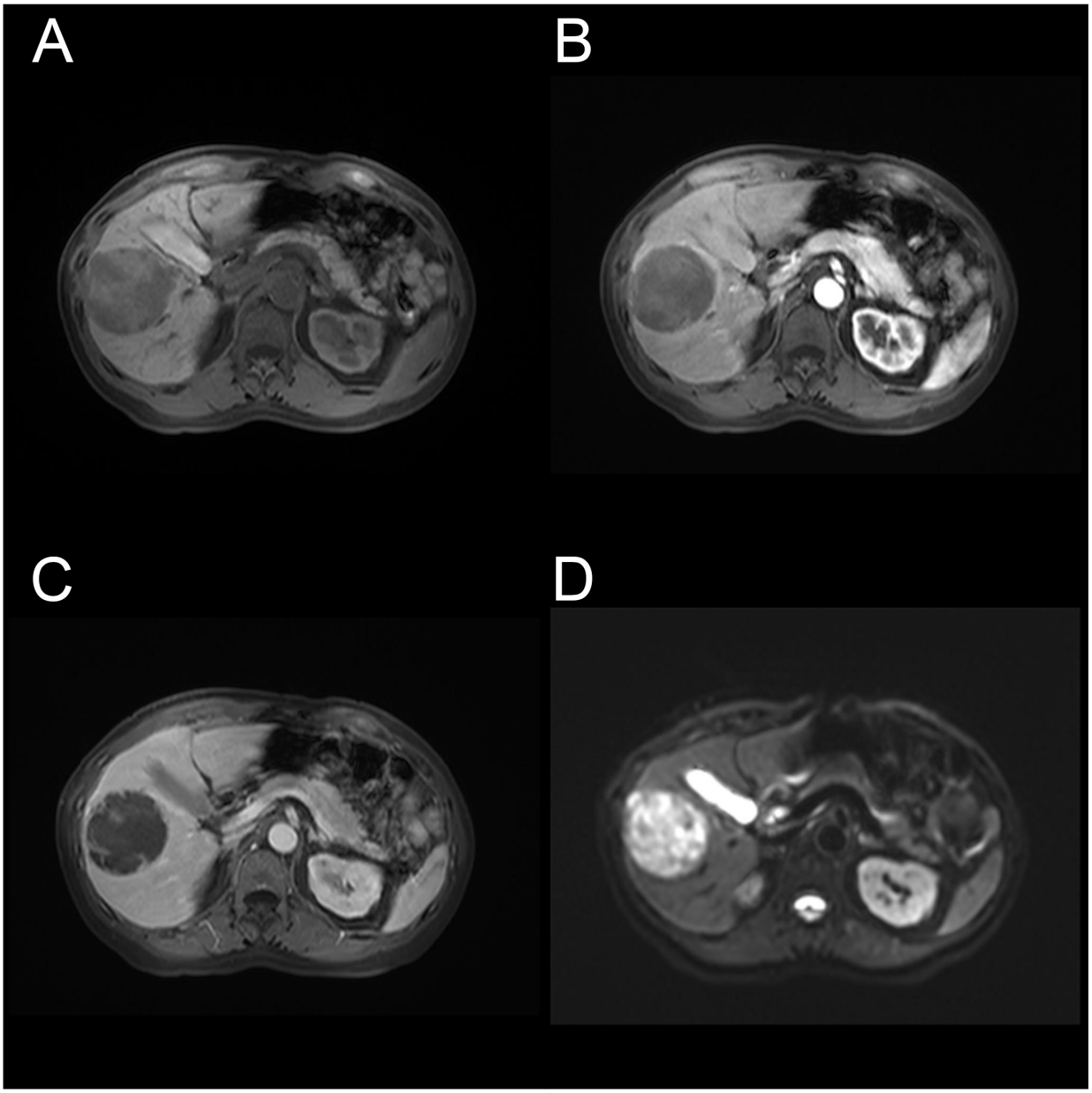

FIGURE 2. Preoperative MRI evaluation. (A) T1 weighted scanning. (B) Artery phase of enhanced MRI scanning. (C) Portal vein phase of enhanced MRI scanning. (D) DWI scanning.

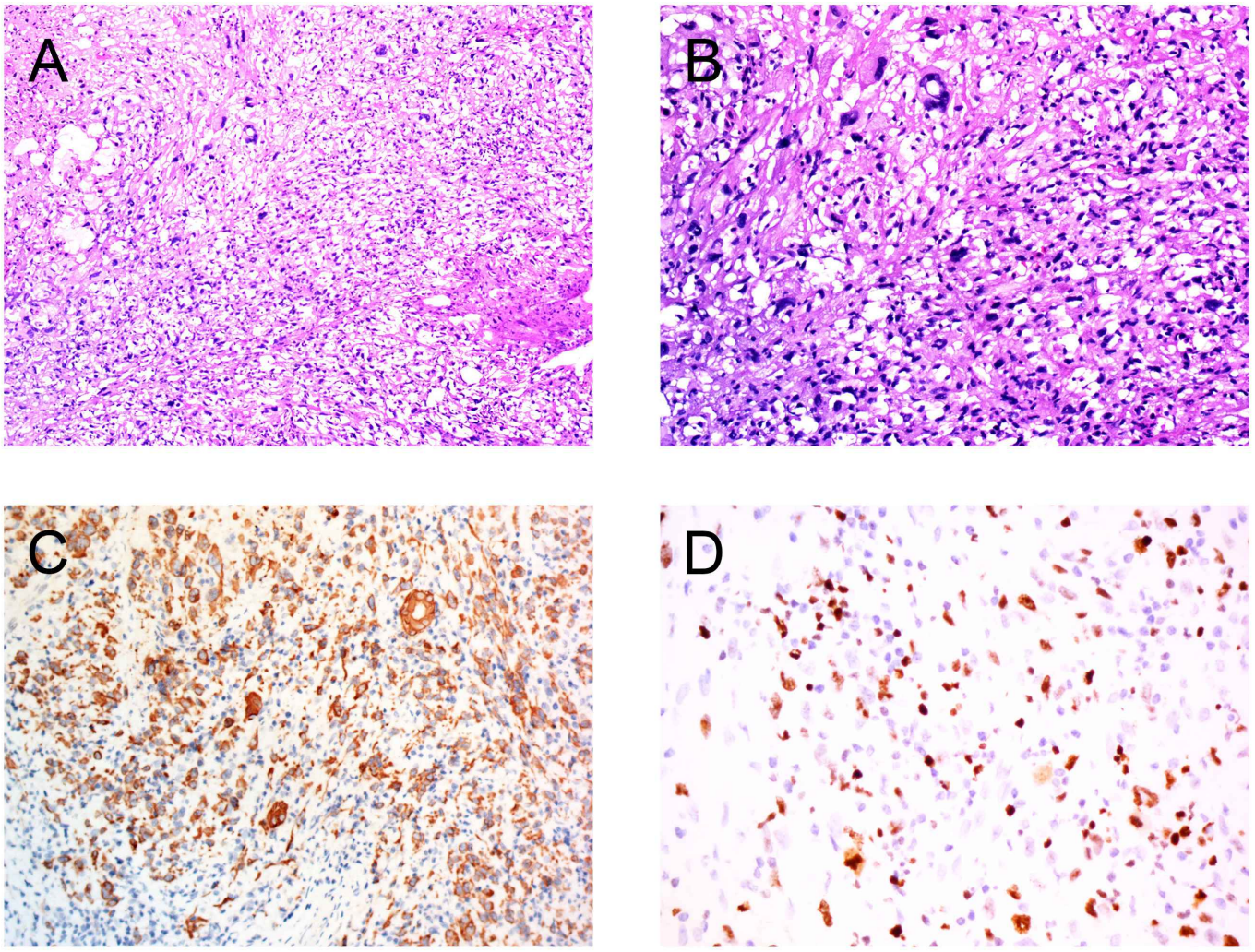

FIGURE 3. Representative pathological and immunohistochemical images of the second surgery specimen. (A) HE staining (10×). (B) HE staining (20×). (C) CK staining. (D) Ki-67 staining.

an elevated WBC count and neutrophil percentage, indicating the possibility of a hepatic inflammatory mass. Routine plasma tumor marker screening has limited significance for the diagnosis of SHC. Imaging diagnosis is one of the most important diagnostic methods for diagnosing HCC. For SHC cases, the radiological images of the initial visit usually show an occasional liver mass. Abdominal ultrasound often reveals that the tumor is a hypoechoic lesion with heterogeneous echo changes inside. CT scanning is a common tool for SHC diagnosis. Because of the dual characteristics of sarcoma and cancer in SHC, the tumor grows rapidly and is relatively large. As a result, the CT features of SHC are mostly irregular mass, with no enhancement or uneven enhancement in the central area, and annular enhancement at the edges of the arterial and portal phase tumors, which clearly differ from HCC [13]. It was reported that SHC had a hypointense signal on T1-weighted MRI. In the enhanced MRI image, irregular enhancement could be seen at the edge of the tumor in the arterial phase, and the edge signal in the venous phase was significantly reduced, showing a slight enhancement. The tumor center revealed a low signal with no delay enhancement, which was similar to this case [14, 15]. Some MRI features, such as large size, obvious heterogeneity, hemorrhage, progressive enhancement, pseudocapsule and lymph node enlargement, might contribute to the diagnosis of SHC [16]. In this case, the preoperative evaluation of radiological images could not differentiate SHC from liver abscess because the tumor grows too fast to manifest necrosis features in the center. Furthermore, ^{18}F-fluorodeoxyglucosepositron emission tomography/computed tomography (PET/CT) has also been proven to be of great significance in evaluating the preoperative evaluation of tumor aggressiveness and recurrence [17].

At present, radical resection of tumors is considered the only possible cure method [18]. The tumor should be completely removed with sufficient margins during the operation, and the hilar lymph nodes should also be clearly harvested if possible. However, due to the high malignancy and rapid progression of the tumor, patients with primary SHC are more likely to have early local recurrence and distant metastasis after surgery. Despite laboratory and radiological examinations, the gold standard of ultimate diagnosis is still pathology. The classical manifestation under the microscope is the mixture of spindle cell sarcoma-like components and cancerous epithelial components. Due to the rapid growth of the tumor, the microscopic morphology of the tumor presented part of necrosis.

After the first laparoscopy and the subsequent pathological results were confirmed, the patient finally underwent a reoperation. The pathologists arrived at the diagnosis of SHC with a negative resection margin and lymph nodes. With the development of bioinformatics and further study on the underlying molecular mechanism of SHC, clinicians have strengthened the understanding of the disease. A recent transcriptomic study indicated upregulated gene clusters associated with epithelial-to-mesenchymal transition, inflammatory responses and Programmed Death Ligand-1expression in SHC, revealing its immune infiltration status [3, 19]. Strikingly, several researchers have reported that immune check point inhibitors are useful for the treatment of advanced SHC [20].

Despite the dismal prognosis of SHC, doctors have devoted themselves to finding an accurate prediction tool. A Surveillance, Epidemiological, and End Results (SEER) analysis reported that the 8th American Joint Committee on Cancer (AJCC) TNM staging system, which is a usual tool in cancer classification and staging, is mediocre in predicting the survival of SHC patients [8]. A new four-factor-based nomogram for predicting the prognosis of SHC patients has been proposed [21]. According to the nomogram above, the patients could be scored with 10 points (size: 3 points, M-stage: 0 points, primary tumor surgery: 7.5 points and chemotherapy: 0 points). The estimated 6-month cancer-specific survival (CSS) should be more than 60%. In fact, the patients died nearly 3 months after surgery. For this case, more factors could be incorporated into the model to achieve a better predictive accuracy. More studies are needed to identify candidate factors for precise prediction.

Finally, the limitations of the study should also be mentioned. Publication bias cannot be avoided due to the low incidence of SHC. Further large-scale prospective research or cross-sectional studies are urgently required to gain in-depth knowledge of the understanding and treatment of the disease.

4. Conclusion

In general, we present a rare case of SHC. The past medical history of HBV infection may contribute to its sarcomatoid transformation. The occasional liver mass with previous HBV infection, even no anticancer therapy history, and the SHC should be included for a candidate diagnosis. If diagnosis is confirmed, high biological malignancy and poor survival should be expected. Future investigations are still needed to explore more effective treatment modalities and prognostic predictions to prolong survival and improve the quality of life of SHC patients.

AVAILABILITY OF DATA AND MATERIALS

The data are contained within this article.

AUTHOR CONTRIBUTIONS

HJD and YHB—designed the study, completed the experiment and supervised the data collection. LBW—analysed the data and interpreted the data. JFY—prepared the manuscript for publication and reviewed the draft of the manuscript. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of Shidong Hospital (Approval No: 2020-004-01). Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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