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The primary aim of *World Journal of Gastrointestinal Oncology* (*WJGO*, *World J Gastrointest Oncol*) is to provide scholars and readers from various fields of gastrointestinal oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, *etc*.

INDEXING/ABSTRACTING

The *WJGO* is now abstracted and indexed in PubMed, PubMed Central, Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 edition of Journal Citation Reports® cites the 2022 impact factor (IF) for *WJGO* as 3.0; IF without journal self cites: 2.9; 5-year IF: 3.0; Journal Citation Indicator: 0.49; Ranking: 157 among 241 journals in oncology; Quartile category: Q3; Ranking: 58 among 93 journals in gastroenterology and hepatology; and Quartile category: Q3. The *WJGO*'s CiteScore for 2022 is 4.1 and Scopus CiteScore rank 2022: Gastroenterology is 71/149; Oncology is 197/366.

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CASE REPORT

Multidisciplinary comprehensive treatment of massive hepatocellular carcinoma with hemorrhage: A case report and review of literature

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Abstract

BACKGROUND

Hepatocellular carcinoma (HCC), a major contributor to cancer-related deaths, is particularly prevalent in Asia, largely due to hepatitis B virus infection. Its prognosis is generally poor. This case report contributes to the medical literature by detailing a unique approach in treating a large HCC through multidisciplinary collaboration, particularly in patients with massive HCC complicated by ruptured bleeding, a scenario not extensively documented previously.

CASE SUMMARY

The patient presented with large HCC complicated by intratumoral bleeding. Treatment involved a multidisciplinary approach, providing individualized care. The strategy included drug-eluting bead transarterial chemoembolization, sorafenib-targeted therapy, laparoscopic partial hepatectomy, and standardized sintilimab monoclonal antibody therapy. Six months after treatment, the patient achieved complete radiological remission, with significant symptom relief. Imaging studies showed no lesions or recurrence, and clinical assessments confirmed complete remission. This report is notable as possibly the first docu-mented case of successfully treating such complex HCC conditions through integrated multidisciplinary efforts, offering new insights and a reference for future similar cases.

CONCLUSION
This study demonstrated effective multidisciplinary treatment for massive HCC with intratumoral bleeding, providing insights for future similar cases.

Key Words: Hepatocellular carcinoma; Transarterial chemoembolization; Sintilimab; Sorafenib; Translational therapy; Multidisciplinary team; Case report

Core Tip: In this study, a unique multidisciplinary approach was demonstrated for treating a patient with massive hepatocellular carcinoma (HCC) complicated by hemorrhage. Treatment included combined drug-eluting bead transarterial chemoembolization, targeted therapy, laparoscopic surgery, and monoclonal antibody therapy. This method achieved complete radiological remission and significant symptom relief, offering a novel and effective strategy for managing complex HCC patients. This report provides valuable insights for the treatment of similar conditions, paving the way for future clinical practice.

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INTRODUCTION

Hepatocellular carcinoma (HCC) is a leading cause of cancer-related death worldwide[1]. Representing 75%-85% of all primary liver cancers, it predominantly occurs in Asia, with more than 50% of cases occurring in China. The primary cause in Asia is hepatitis B virus (HBV) infection[2], while in the United States and Europe, hepatitis C virus and alcohol are common risk factors, with nonalcoholic steatohepatitis also emerging as a recognized risk[3,4]. In addition to these causes, the importance of prevention of HCC cannot be overstated[5]. The prognosis of HCC remains poor across all regions of the world, with incidence and mortality rates being roughly equivalent. From 1990 to 2019, there was a decline in mortality, incidence, and prevalence. The global health care burden caused by viral hepatitis is decreasing[6,7]. HBV, a DNA virus, can induce chronic necrotic inflammation, promote hepatocellular mutations, and lead to HCC[8]. Advances in diagnostic techniques and treatment options, including hepatic resection, liver transplantation, radiofrequency ablation (RFA), transarterial chemoembolization (TACE), external radiotherapy, and molecular targeted therapies, have improved patient prognoses[9]. Combined immunotherapy is now a standard treatment for advanced HCC[10]. However, larger HCCs remain challenging to treat, often require advanced surgical skills and are associated with increased risks of bleeding, prolonged surgery and hospital stays, and increased mortality, thus leading to poorer outcomes[9,11,12].

We report the case of a patient diagnosed with massive HCC with rupture and hemorrhage. After evaluating and discussing treatment options, the patient underwent multidisciplinary treatment, including drug-eluting bead TACE (DEB-TACE), laparoscopic partial hepatectomy, and standardized sintilimab monoclonal antibody combined with sorafenib therapy. The patient is currently in good health, without abdominal pain, discomfort, or signs of tumor recurrence, and remains under close follow-up.

CASE PRESENTATION

Chief complaints

A 40-year-old male patient was admitted to the hospital with a hepatic lesion. He experienced sudden abdominal pain, dizziness, and fatigue and was initially diagnosed with liver cancer at a local hospital, where he underwent transarterial embolization.

History of present illness

The patient improved postoperatively but was later diagnosed with massive HCC with rupture and hemorrhage at our institution.

History of past illness

He had a history of untreated hepatitis B, with tests showing positive Hepatitis B surface antigen, e antibody, and core antibody, but negative HBV DNA. Liver function was normal.

Personal and family history
The patient denied any family history of malignant tumors.

Physical examination
Physical examination revealed tenderness under the right costal margin but no palpable mass, splenomegaly, or shifting dullness.

Laboratory examinations
After admission, the patient underwent basic laboratory tests, which did not reveal any abnormal findings.

Imaging examinations
The patient's imaging findings were negative except for the liver.

FINAL DIAGNOSIS
Based on various clinical data, including patient complaints, medical history, and auxiliary examinations, the patient was ultimately diagnosed with ruptured massive HCC accompanied by bleeding.

TREATMENT
After a comprehensive assessment of the patient's condition and considering the large size of the tumor, a right hepatectomy was deemed unsuitable due to insufficient remaining liver tissue volume (< 40%), which could lead to a high probability of liver failure. Consequently, it was recommended to proceed with TACE combined with Sindilizumab monoclonal antibody and Lenvatinib treatment. The patient was also prescribed daily Entecavir capsules (0.5 mg orally) for long-term use, with no associated adverse reactions observed.

One month post-intervention, in collaboration with the interventional radiology department, drug-eluting microspheres loaded with doxorubicin were used to embolize the hepatic lesions and the main tumor artery, yielding good results. Once the condition stabilized, abdominal computed tomography (CT) and magnetic resonance imaging (MRI) were performed, locating the liver tumor in segments S6-S7 (Figure 1A-H). Three months later, after completing the second round of Sindilizumab monoclonal antibody and Lenvatinib treatment, an abdominal CT follow-up showed a reduction in tumor size (Figure 1I and J). The third round of Sindilizumab monoclonal antibody treatment was completed by the fourth month. During the fifth month post-surgery, upon hospital admission, another abdominal MRI was conducted, revealing further reduction in tumor size and compensatory hypertrophy of the left liver, indicating a postoperative residual liver volume of > 40% (Figure 1K-O). Three months postsurgery, the whole-body bone scan indicated no obvious metastatic lesions (Figure 2A).

After thorough preoperative preparation, our surgical team, in coordination with the anesthesiology and surgery team, performed a laparoscopic resection of malignant liver tumor. During the laparoscopy, a nodular lesion approximately 4 cm × 3 cm in size was observed in segment S6 of the right liver lobe, characterized by a hard texture and limited mobility. The initial step involved freeing the hepatic portal structures, intermittently obstructing hepatic portal blood flow for 15 min, and 5 min intervals. Using an ultrasonic scalpel, an incision was made 1 cm from the tumor's edge through the liver capsule and parenchyma. Local blood vessels and bile ducts were ligated and severed, followed by the complete excision of the tumor. Hemostasis and irrigation of the surgical site were performed, and after ensuring no active bleeding, the specimen was removed. An abdominal drainage tube was placed, and the abdomen was closed. The surgery lasted for 190 min with an estimated blood loss of about 800 mL. During the procedure, 1.5 units of red blood cell suspension and 275 mL of plasma were transfused.

OUTCOME AND FOLLOW-UP
Intraoperative images of the tumor and postoperative incision are shown in Figure 2B and C. Postoperative pathology results indicated a major pathologic response of the tumor, with no evidence of cancerous tissue involvement at the liver resection margins (Figure 2D-F).

Six months after admission, a follow-up abdominal CT showed fluid accumulation in the surgical area (Figure 1P), prompting treatment with Sindilizumab monoclonal antibody. In the seventh month of the treatment timeline, additional Sindilizumab treatment was administered, followed by another session in the eighth month (Figure 1Q). A follow-up abdominal MRI in the ninth month revealed a decrease in lesion size (Figure 1R-T), and Sindilizumab treatment continued. After eleven months from the start of treatment, another examination was conducted (Figure 1U). Continuous Sindilizumab treatment was maintained up to the twelfth month, with no adverse reactions noted. Fifteen months after the initial treatment, an abdominal CT scan indicated stability in the postoperative hepatic region, with no signs of recurrence (Figure 1V-X). The patient's imaging presentation was similar to that of previous studies[13].

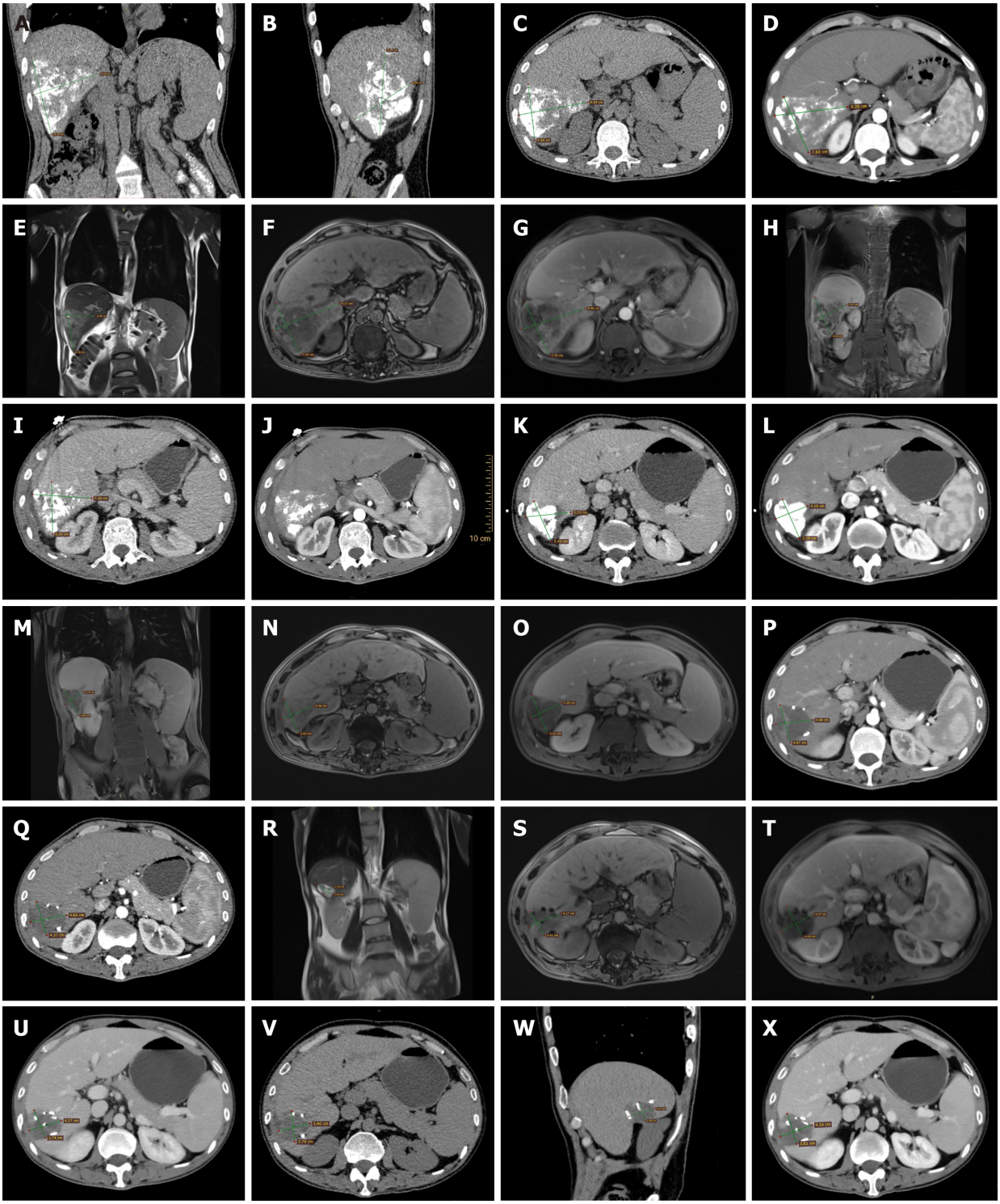

Figure 1 Images of patients after treatment. A-H: One month postintervention, abdominal computed tomography (CT) and magnetic resonance imaging (MRI) results showed that the liver tumor was located in segments S6-S7 (10.49 cm × 8.64 cm × 6.89 cm), with associated bleeding; I and J: Two months postsurgery, an abdominal CT revealed a decrease in the size of the tumor (7.28 cm × 6.33 cm × 4.5 cm); K-O: Three months postsurgery, plain plus contrast-enhanced abdominal CT and MRI scans indicated that the tumor size was 5.22 cm × 4.28 cm × 4.19 cm, and the activity of the tumor cells had essentially disappeared; P: Six months postsurgery, an enhanced abdominal CT indicated the presence of fluid accumulation in the right lobe of the liver in the surgical area (4.87 cm × 4.68 cm); Q: Eight months postsurgery, an enhanced abdominal CT showed a slight reduction in the size of the surgical area (4.66 cm × 4.37 cm); R-T: At nine months postsurgery, an abdominal MRI plain scan plus contrast enhancement indicated further reduction of the lesion and decreased subcapsular fluid accumulation (4.27 cm × 3.41 cm × 3.45 cm); U: Eleven months postsurgery, an enhanced abdominal CT showed no change in the lesion compared to the previous scan (4.27 cm × 3.74 cm); V-X: Fifteen months postsurgery, an abdominal plain plus contrast-enhanced CT scan indicated no change in the lesion compared to the previous scan (4.16 cm × 3.81 cm × 3.11 cm).

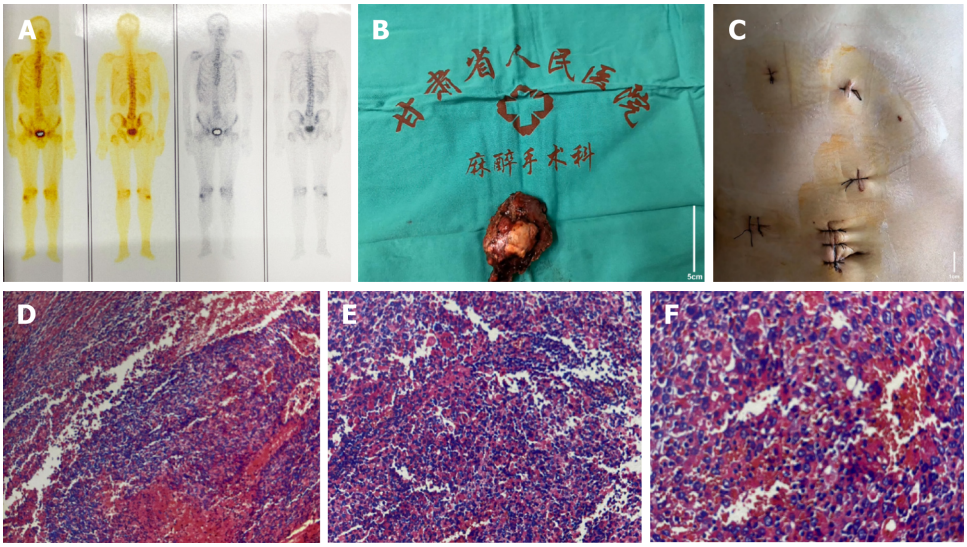

Figure 2 Surgery-related and pathological findings of the patient. A: Three months postsurgery, a whole-body bone scan indicated no obvious metastatic lesions; B: The tumor was excised during surgery; C: Photo of the incision 10 d postsurgery; D-F: Representative HE images of the tumor. The tumor tissue exhibited extensive necrosis and hemorrhage, with 5% viable tumor tissue, 80% necrotic tumor tissue, and 15% tumor stroma (fibrous tissue and inflammation). The immunohistochemical staining results were as follows: CKP (+), vimentin (-), HepPar-1 (+), GPC-3 (+), CK8/18 (+), CD68 (macrophage+), P53 (wild-type), and Ki-67 (index = 60%). (D: 10 × 10 HE; E: 20 × 10 HE; F: 40 × 10 HE).

Des-gamma-carboxy prothrombin (PIVKA-II) remains valuable in diagnosing alpha-fetoprotein (AFP)-negative HCC, as its levels correlate with certain pathological features indicative of tumor aggressiveness and poor prognosis. PIVKA-II is also useful in evaluating the effectiveness of liver cancer surgery. Serum ferritin (FER) plays a significant role in predicting the prognosis and survival of patients with advanced liver cancer and can be used in conjunction with AFP and PIVKA-II for a comprehensive assessment of treatment efficacy and prognosis. In this patient, levels of AFP, FER, and PIVKA-II showed a marked downward trend following treatment. Liver function fluctuated during the treatment period, with instances of elevation and reduction, but normalized after administration of hepatoprotective drugs such as ammonium glycyrrhizinate and acetylcysteine. On the last check-up, the aforementioned indicators were all within the normal range, suggesting effective disease control (Table 1). The patient continues to be closely monitored.

DISCUSSION

Current data indicate that although the incidence and mortality rates of liver cancer are declining annually, it is one of the cancers with high diagnostic and mortality rates in our country[14]. The primary treatment modalities for liver cancer include radical therapies such as hepatectomy, liver transplantation, ablative therapy, TACE, radiotherapy, and systemic therapy[2,15,16]. In the early stages of HCC, RFA treatment can be considered[16]. At present, there is no uniform treatment standard for large-volume liver cancer. The larger the liver cancer lesion is, the more challenging the treatment becomes[17]. HCC is commonly associated with chronic liver disease, necessitating multidisciplinary collaboration and individualized assessment to achieve maximal tumor eradication without significantly compromising liver function. Typically, the treatment approach is determined by the treating clinician's personal experience and expertise, leading to significant variation and heterogeneity in treatment protocols and long-term outcomes[18]. Conversion therapy refers to transforming unresectable liver cancer into resectable liver cancer, and one of the pathways for patients with intermediate- to advanced-stage liver cancer is to achieve curative resection and long-term survival[19]. Therefore, it is essential to emphasize the multidisciplinary team (MDT) approach in the diagnosis and treatment of liver cancer, particularly in the management of complex and challenging cases. This approach helps to overcome the limitations of single-specialty treatment, fosters interdisciplinary collaboration, and enhances the overall effectiveness of therapy.

The patient was treated by the HCC treatment team at the hospital, where an in-depth analysis and discussion were conducted on the patient with massive right liver cancer. The team also summarized the current state of liver cancer conversion therapy, aiming to provide a reference for the use of the MDT approach in the clinical management of large liver cancers.

The patient initially underwent two rounds of transformational therapy with TACE in combination with sintilimab and lenvatinib, achieving the goal of reducing the tumor size to safely perform surgical resection. If the tumor remains stable three months after downstaging treatment, treatment is considered effective[20,21]. Studies have shown that the majority of patients with BCLC-B subclassification HCC can also benefit from TACE[22]. Moreover, compared with sorafenib, lenvatinib generally has a superior overall efficacy[23]. Studies have indicated that combining TACE with lenvatinib and sintilimab for the treatment of HCC can effectively control tumor progression and prolong the survival time of patients [24]. DEB-TACE is considered to be less harmful to liver function and has a lower incidence of doxorubicin-related side effects. There was no significant difference in the indications for these two treatments compared to traditional TACE.

Table 1 Results for alpha-fetoprotein, ferritin, abnormal prothrombin assay, alanine aminotransferase, aspartate aminotransferase, γ-glutamyl transpeptidase, and alkaline phosphatase during the treatment and follow-up periods

	AFP (< 8.78 g/m)	FER (21.81-274.66 g/m)	PIVKA-II (13.62-40.38 AU/mL)	ALT (9-50 U/L)	AST (15-40 U/L)	γ-GT (10-60 U/L)	ALP (45-125 U/L)
POM 1	> 2000	417.69	80.53	40	21	52.33	95
POM 2	> 2000	450.84	73.78	58	52	76.2	139
POM 3	> 2000	237.77	453.92	30	25	53.1	116
POM 4	140.84	272.95	35.43	56	40	47.06	126
POM 4.5	8.11	285.44	10.81	26	17	41.4	87
POM 5	2.05	181.46	17.04	47	33	31.6	104
POM 6	1.22	225.3	33.28	63	47	65.88	110
POM 7	0.75	197.6	26.96	23	15	46	105
POM 12	52.12	0.84	20.73	64.29	32.34	70.97	125.61
POM 13	80.03	0.95	26.54	36.61	21.01	59.61	117.39

The values within the parentheses indicate the normal range for each indicator. AFP: Alpha-fetoprotein; FER: Ferritin; PIVKA-II: Abnormal prothrombin assay; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; γ-GT: γ-glutamyl transpeptidase; ALP: Alkaline phosphatase; POM: Postoperative month.

However, DEB-TACE is more effective at blocking tumor blood vessels. The slow release of anticancer drugs during DEB-TACE provides a continuous antitumor effect, increasing the safety of the process. DEB-TACE can significantly improve the overall survival period of HCC patients who have undergone a similar number of traditional TACE procedures[25]. Wang *et al*[26] have reported that the use of lenvatinib and sintilimab for conversion therapy in patients with initially inoperable mid- to late-stage local HCC is safe and feasible. However, the optimal duration of conversion therapy remains controversial. Some surgeons believe that surgery should be performed as soon as the criteria for operability are met to minimize the risk of disease progression and drug-induced liver damage[27]. Therefore, the most rational and individualized conversion therapy plan should be formulated based on the patient's own disease and various other conditions. The implementation of all conversion therapy plans often requires joint discussion and planning by multiple disciplines, including hepatobiliary surgery, oncology, interventional radiology, and radiology. To reduce the risk of tumor progression, patients should undergo surgery as soon as possible or when the tumor shrinks to a size that is close to a resectable range[26]. Although a future liver remnant (FLR) ≥ 20% is feasible in a healthy liver, for a liver preda-maged with fibrosis or cirrhosis, the FLR must be at least 40%[28]. Studies have shown that laparoscopic resection has survival outcomes similar to those of conventional resection, with reduced bleeding, faster postoperative recovery, and a lower incidence of postoperative complications. Additionally, laparoscopic surgery can reduce the risk of liver failure after hepatectomy[29,30]. Despite significant advances in interventional treatment techniques, the prognosis for patients with ruptured HCC remains poor, with an overall mortality rate of 24%[31,32]. During the treatment of this case, a comprehensive discussion was conducted by multiple disciplines, including hepatobiliary surgery, oncology, interventional radiology, radiology, transfusion medicine, and the anesthesia surgery room, leading to the formulation of a treatment plan with good therapeutic effects. Patients with massive liver cancer should initially undergo various forms of conversion therapy, followed by surgical resection when the tumor shrinks close to a size that is within the resectable range, potentially improving patient prognosis and survival rates and extending survival time.

CONCLUSION

In summary, our experience with a 40-year-old male patient presenting with massive HCC with rupture and hemorrhage illustrates the importance of personalized treatment plans. Despite the complexity of his case, which included no treatment for hepatitis B and the risk of liver failure, our MDT approach enabled us to carefully balance tumor factors, basic liver function, and the patient's physical condition. By combining TACE, sintilimab monoclonal antibody therapy, and lenvatinib therapy, along with antiviral treatment, we successfully managed his condition without significant adverse effects. This case study underscores the potential of personalized, MDT-based strategies for improving outcomes in patients with advanced, initially high-risk liver cancer. Such approaches can increase downstaging conversion rates and resectability, providing valuable insights for the treatment of mid- to late-stage massive liver cancer.

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FOOTNOTES

Co-first authors: Xian-Shuai Kou and Fan-Fan Li.

Co-corresponding authors: Lan Zhang and Sheng-Fen Liu .

Author contributions: Kou XS and Li FF wrote the manuscript, acquired the data, and were integral in the analysis and interpretation of the data; Meng Y also contributed to manuscript writing while overseeing the project; Zhao JM provided support in the data collection; Liu SF and Zhang L was pivotal inleading project development, managing operations, and providing additional supervision. All the authors have significantly contributed to the manuscript and have given their approval for the submitted version. The reasons for designating Kou XS and Li FF as co-first authors are threefold. First, this study was conducted as a collaborative effort, and both authors spent a lot of time and effort to complete the study and the final paper, assuming the same responsibilities and burdens. Second, the two authors from different fields with various expertise and skills improved the quality and reliability of the paper. Ultimately, Kou XS and Li FF made equal efforts to communicate and collaborate throughout the research process. Liu SF and Zhang L co-directed the writing of the paper, jointly reviewed the authenticity of the data, and supervised the writing and completion of the paper. They played a key role in developing the project, managing its operation, and providing additional oversight. In summary, we believe that the designation of Kou XS and Li FF and Fan-fanLi as co-first authors and Liu SF and Zhang L as co-corresponding authors is appropriate for our manuscript because it reflects the spirit of cooperation and equality of our team.

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