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CASE REPORT

Camrelizumab Combined with Apatinib for Portal Vein Tumor Thrombus in Advanced Hepatocellular Carcinoma: Two Case Reports

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Abstract

Aims/Background Portal vein tumor thrombus (PVTT) is a common complication of primary hepatocellular carcinoma (HCC). HCC typically infiltrates intrahepatic vessels, particularly the portal vein, leading to the formation of PVTT, marking advanced-stage HCC and correlating with poor prognosis. PVTT often complicates local treatment strategies such as surgical resection and affects the efficacy of interventions. Combination therapy, including immunotherapy and targeted therapy, shows promise in HCC treatment, but management options for HCC patients with PVTT are incompletely characterized. This study aims to investigate the efficacy and safety of camrelizumab + apatinib in treating HCC patients with PVTT.

Case Presentation Two cases of HCC with PVTT were presented. Patient 1, a 51-year-old male with a history of hepatitis B virus, was diagnosed with stage IIIA HCC and treated with camrelizumab + apatinib, achieving complete response (CR) after six cycles. Patient 2, a 50-year-old male with stage IIIA HCC, also underwent the same treatment and achieved CR after four cycles but died due to acute cardiac disease.

Results Our research found that camrelizumab + apatinib effectively shrank the size of filling defects and significantly prolonged patients' progression-free survival. In addition, no adverse effects were observed during the treatment process. However, despite the manageable safety profile demonstrated by combination therapy, further clinical research is needed to validate its long-term efficacy and safety.

Conclusion Camrelizumab + apatinib produced satisfactory efficacy and safety among the HCC patients with PVTT, providing clinical evidence for future treatment.

Key words: hepatocellular carcinoma; portal vein tumor thrombus; camrelizumab; apatinib; imaging

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Introduction

Liver cancer is the fourth leading cause of tumor-associated deaths globally (Duran and Jaquiss, 2019). Hepatocellular carcinoma (HCC) represents the majority of primary liver cancers, and accounts for 85%–90% of liver cancer (Zou et al, 2022). HCC commonly infiltrates the intrahepatic vasculature, the portal vein in particular, resulting in the development of portal vein tumor thrombus (PVTT).

PVTT, which marks the advanced stage of HCC, occurs in 44% to 62% of PVTT cases, and is prone to recurrence and metastasis (Huang et al, 2022). Moreover, rising portal pressure leads to secondary complications such as refractory ascites, and esophageal and gastric variceal bleeding (Zane and Makary, 2021), which is negative prognostic factors for HCC patients.

Currently, surgical resection remains the most effective treatment for HCC. However, due to insidious onset, rapid development, and difficulty in early diagnosis of HCC, most patients are already in the advanced stage when they are diagnosed, thus missing the opportunity for radical surgical resection to achieve long-term survival (Llovet et al, 2021).

At present, the treatment of liver cancer has entered the era of combined therapy, involving both immunotherapy and targeted therapy; this approach has been gradually introduced into the clinic, and has shown promising results. A study has verified the safety and efficacy of the combined treatment with programmed cell death protein 1/programmed cell death ligand 1 (PD-1/PD-L1) inhibitors plus antiangiogenic agents (Aoki et al, 2023). An Open-label, dose-escalation/dose-expansion study assessing anti-PD-1 antibody (SHR-1210) combined with apatinib reported manageable toxicity in patients with HCC (Xu et al, 2019). A phase 2 clinical trial reported that camrelizumab + apatinib had satisfactory efficacy and safety among patients with advanced HCC (Xia et al, 2022). However, because of the low number of studies available, the clinical evidence of treatment cannot be sufficiently assessed.

In an effort to provide a reference for clinical treatment, this study presents two cases of HCC patients who developed PVTT and displayed significant responses to atezolizumab + bevacizumab therapy.

Case Presentation

Patient 1

A 51-year-old man presented to our hospital owing to upper abdominal discomfort, with no obvious causative factors. The patient reported a history of hepatitis B virus (HBV), but had no related familial or surgery history. Whole abdominal Computed Tomography (CT) (Siemens SOMATOM Definition AS, Erlangen, Germany) revealed multiple rounds, patchy, low-density shadows on the liver, with nodules up to 2.8 cm in diameter, leading to an initial diagnosis of diffuse HCC with PVTT. Subsequent enhanced CT after one week indicated portal trunk and right branch coarsening, with filling defects and angiographic visualization of collateral vessels in the hepatic hilar area (Fig. 1A,B). Serum alpha-fetoprotein (AFP) was found to be elevated at 669.69 ng/mL using an automated biochemical analyzer (Roche Cobas 6000, Roche Diagnostics, Basel, Switzerland). Based on the abovementioned results, the patient was diagnosed with stage IIIA HCC. Thus, a combination of camrelizumab + apatinib for PVTT was introduced. Camrelizumab (SHR-1210, Jiangsu Heng Rui Medicine Co., Ltd., Jiangsu, China) at 200 mg was administrated intravenously every three weeks (q3w), and 750 mg oral apatinib vascular endothelial growth factor receptor 2 (VEGFR-2) inhibitor, Jiangsu Heng Rui Medicine Co.,

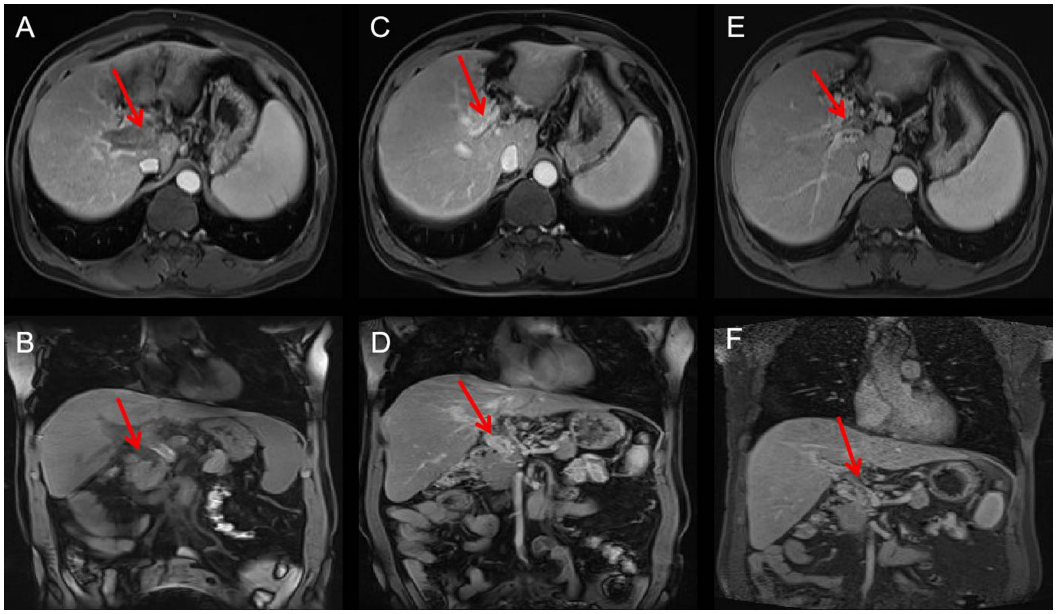

Fig. 1. Imaging findings for patient 1 with hepatocellular carcinoma (HCC) and portal vein tumor thrombus (PVTT). (A,B) Before the combination therapy. (C,D) After the six cycles of combination therapy. (E,F) After the eighteen cycles of combination therapy. Red arrows point to foci of liver.

Ltd., Jiangsu, China) was administered daily, representing one cycle of therapy. Following six rounds of treatment, the patient was reviewed using abdominal plain magnetic resonance imaging (MRI) and enhanced scanning (Philips Ingenia 3.0T, Amsterdam, Netherlands). The area of the filling defect was decreased in the left and right branches and the main trunk of the portal vein (Fig. 1C,D), and AFP levels were reduced to 36.12 ng/mL, achieving complete response (CR). The individual underwent regular clinical evaluations, and their condition remained stable despite their diagnosis. Following eighteen rounds of treatment, the patient was assessed through an abdominal plain MRI scan and enhanced scanning. The imaging results showed that the area of the filling defect had further reduced (as depicted in Fig. 1E,F), but the liver lesions were now present in both the right and left lobes of the liver, with an increasing number of lesions and larger lesion area. Moreover, the patient's serum AFP level was elevated, at 123.91 ng/mL. As a result, the patient was determined to have disease progression after a progression-free survival (PFS) exceeding 15 months. Notably, the patient did not experience any significant adverse reactions during treatment, such as fever, anemia, hypothyroidism, or hypertension.

Patient 2

A 50-year-old man presented with intermittent abdominal pain of unknown cause. The patient reported a history of hepatitis B virus and liver space-occupying lesions using color ultrasound, but had no related familial or surgery history. Serum AFP level was elevated at 28.36 ng/mL. Upper abdominal MRI enhanced scan confirmed a diagnosis of stage IIIA HCC (Fig. 2A). Treatment involved camrelizumab combined with apatinib, following the regimen of patient 1. After four

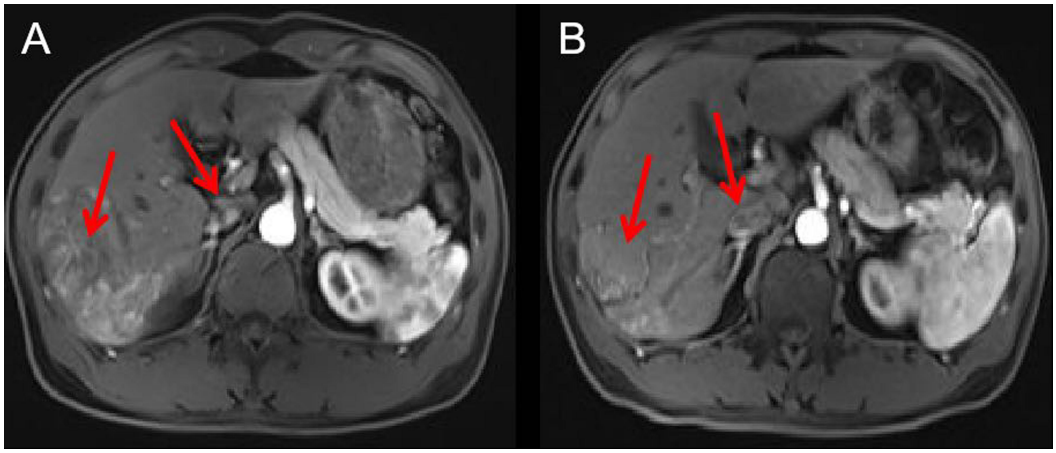

Fig. 2. Imaging findings for patient 2 with HCC and PVTT. (A) Before the combination therapy. (B) After the four cycles of combination therapy. Red arrows point to foci of liver.

cycles of treatment, MRI revealed shrinkage of clumped and nodular lesions in the right anterior lobe of the liver, and decreased PVTT of the right anterior liver lobe (Fig. 2B). The serum AFP level decreased to 4.85 ng/mL, indicating that the patient had achieved CR. Treatment continued, but the patient succumbed to acute heart disease, halting further follow-up. Baseline information of patients is detailed in Table 1.

Discussion

Monotherapy for advanced HCC, particularly with PVTT, has limited efficacy and significant adverse events. Combined therapy, like camrelizumab with apatinib, shows promise (Yuan et al, 2021). In the present study of 2 cases, this combination demonstrated potent efficacy and manageable safety. Imaging assessments supported treatment precision, offering novel therapeutic opportunities for improving patient prognosis.

HCC progression involves not only T-cell exhaustion but also hypoxia and aberrant neovasculogenesis, promoting disease advancement (Galasso et al, 2024). Combining PD-1 inhibitor camrelizumab with apatinib, a VEGFR-2 antagonist, has shown efficacy and safety in advanced HCC treatment. For example, the RESCUE trial demonstrated positive outcomes in both first-line and second-line settings (Mei et al, 2021). A multicenter retrospective study further supported the effectiveness and tolerability of this combination therapy, potentially offering improved survival rates (Yuan et al, 2021). However, it has been reported that 49.2% of patients suffered one or more adverse events, such as abdominal pain and hand-foot skin reaction (Yuan et al, 2020). Few studies have explored combination treatments for PVTT. In our study, in which 2 cases were treated with camrelizumab combined with apatinib, abdominal contrast-enhanced CT or MRI scan revealed a specific synergistic therapeutic effect with reduced portal vein filling defects. Our results align with existing findings and supplement evidence from imaging perspectives. The two patients had PFS exceeding 12 months, comparable to previous studies. Potential adverse events associated with apatinib include hand-foot syndrome,

Table 1. The base line information of the patients.

Patient	Age	Presentation	History	Imaging findings	Serum tumor markers	Diagnosis	Treatment	Response	Disease progression
1	51	Upper abdominal discomfort	HBV	Round, multiple low-density shadows on liver; PVTT; high AFP	Elevated AFP (669.69 ng/mL)	HCC with PVTT (Stage IIIA)	Camrelizumab + Apatinib	Complete response	Liver lesions multifocal, increased in number and size; elevated AFP
2	50	Discontinuous abdominal pain	HBV; liver space-occupying lesions	Clumps or nodular lesions in right anterior liver lobe; decreased vein tumor thrombus	Elevated AFP (28.36 ng/mL)	HCC (Stage IIIA)	Camrelizumab + Apatinib	Complete response	Died of acute heart disease

HBV, hepatitis B virus; PVTT, portal vein tumor thrombus; AFP, alpha-fetoprotein; HCC, hepatocellular carcinoma.

proteinuria, and hypertension (Geng et al, 2018), typically grade 1 or 2 CTCAE (Shao et al, 2020). However, no adverse effects were recorded in our study, indicating the treatment's good safety profile. Thus, our results support the concordance between imaging and clinical data. Despite limitations such as a small sample size, short follow-up time, and the need for more detailed clinical indicators, our findings support the combined application of these drugs, underscoring their safety and efficacy.

Conclusion

In this study, 2 cases of HCC with PVTT were treated with camrelizumab + apatinib, resulting in potent efficacy and manageable safety. Given the rare treatment options available against HCC with PVTT, in addition to poor survival rates, this case presentation offers clinical evidence as a basis for future treatment.

Learning Points

- Monotherapy for advanced hepatocellular carcinoma (HCC), particularly with portal vein tumor thrombosis (PVTT), often lacks efficacy. However, combined therapy, such as camrelizumab + apatinib, shows promise in improving outcomes for such patients.
- The combination of camrelizumab and apatinib demonstrated potent efficacy, as evidenced by imaging assessments and progression-free survival (PFS) outcomes in the presented cases. Importantly, this combination therapy was well-tolerated without significant adverse reactions.
- Imaging assessments, such as abdominal contrast-enhanced CT or MRI scans, play a crucial role in evaluating treatment responses. Reduction in the area of portal vein filling defects indicated a positive therapeutic effect of camrelizumab + apatinib.
- The combination therapy exhibited a specific synergistic therapeutic effect, leading to decreased filling defects in the portal vein, thereby suggesting improved vascular patency and tumor response.

Availability of Data and Materials

The original contributions presented in the study are included in the article.

Author Contributions

Conceptualization, AMG; investigation, NC and LZ; data curation, NC, LZ, XLQ, XHS and LZP; writing-original draft, NC and LZ; writing-review and editing, XLQ and XHS. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The studies involving human participants were reviewed and approved by the Ethics Committee of Affiliated Hospital of Yanbian University (2022273) and followed the statements of the most recent version of the Declaration of Helsinki. Written informed consent was obtained from recruited patients.

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Conflict of Interest

The authors declare no conflict of interest.

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