Gallbladder carcinoma (GBC) is a highly malignant tumor of the digestive system, and the 5-year survival rate of stage IVb is only 2% (1). For unresectable GBC, although the guidelines published by the National Comprehensive Cancer Network (NCCN) in 2019 recommended radiotherapy combined with chemotherapy as the first-line treatment, no promising prognosis has been reported (2). Conversion therapy refers to the achievement of long-term survival by radical surgery in some patients with advanced cancer on the premise that systemic therapy will be effective (3,4). Herein, we reported the case of a 61-year-old male patient with stage IVb GBC who was diagnosed with multiple abdominal, retroperitoneal, mediastinal, and bilateral hilar lymph nodes. The results of follow-up showed that the patient achieved a disease-free survival (DFS) of 11.3 months and overall survival (OS) of 18.1 months after conversion therapy.

The 61-year-old male patient complained of right upper abdominal discomfort for 1 month. Combined with laboratory examination, imaging examination (Figure 1A), and liver biopsy, the patient was diagnosed as stage IVb GBC with moderate-poor differentiation. After one cycle of targeted therapy (lenvatinib, 12 mg daily) combined with immunotherapy [programmed cell death-1 (PD-1) inhibitor], the patient developed progressive jaundice and the carbohydrate antigen 199 (CA199) increased to 2022.0 U/mL. Contrast-enhanced computed tomography (CT) of the abdomen showed that a partial response (PR) was achieved (Figure 1C). However, CA199 exhibited an upward trend. Two cycles of short-term chemotherapy with gemcitabine and oxaliplatin (GEMOX) were immediately administered, followed by a decreased CA199 level to 40.5 U/mL. Contrast-enhanced CT displayed gallbladder wall thickening, cholelithiasis, and choledocholithiasis (Figure 1E), and the level of CA199 was 21.2 U/mL. Cholecystectomy and partial hepatectomy were performed 2 months after discontinuation of bevacizumab. More than 100 intraperitoneal nodules of diffuse metastasis seen in the biopsy were not observed intraoperatively. Pathological complete response (pCR) was evaluated postoperatively. The combination of targeted and immunotherapy was resumed 2 weeks after surgery. In the follow-up, no clear sign of recurrence or metastasis could be observed (Figure 1F). (Note: the PD-1 inhibitor, camrelizumab, was used in the first and second cycle, followed by sintilimab).

Methods of improving the success rate of conversion therapy and enhancing the survival benefits of patients with advanced GBC are worth exploring (5). Firstly, we should administered intravenously (400 mg every 3 weeks). The patient tolerated the treatment well, and the CA199 level decreased to 58.1 U/mL. Contrast-enhanced computed tomography (CT) of the abdomen showed that a partial response (PR) was achieved (Figure 1C). However, CA199 exhibited an upward trend. Two cycles of short-term chemotherapy with gemcitabine and oxaliplatin (GEMOX) were immediately administered, followed by a decreased CA199 level to 40.5 U/mL. PET/CT showed that the abnormal 18F-FDG uptake of lesions reduced markedly (Figure 1D). At the ninth cycle of immunotherapy, contrast-enhanced CT displayed gallbladder wall thickening, cholelithiasis, and choledocholithiasis (Figure 1E), and the level of CA199 was 21.2 U/mL. Cholecystectomy and partial hepatectomy were performed 2 months after discontinuation of bevacizumab. More than 100 intraperitoneal nodules of diffuse metastasis seen in the biopsy were not observed intraoperatively. Postoperative pathology showed cholecystitis with no obvious liver tissue abnormality. Pathological complete response (pCR) was evaluated postoperatively. The combination of targeted and immunotherapy was resumed 2 weeks after surgery. In the follow-up, no clear sign of recurrence or metastasis could be observed (Figure 1F). (Note: the PD-1 inhibitor, camrelizumab, was used in the first and second cycle, followed by sintilimab).

Gallbladder carcinoma (GBC) is a highly malignant tumor of the digestive system, and the 5-year survival rate of stage IVb is only 2% (1). For unresectable GBC, although the guidelines published by the National Comprehensive Cancer Network (NCCN) in 2019 recommended radiotherapy combined with chemotherapy as the first-line treatment, no promising prognosis has been reported (2). Conversion therapy refers to the achievement of long-term survival by radical surgery in some patients with advanced cancer on the premise that systemic therapy will be effective (3,4). Herein, we reported the case of a 61-year-old male patient with stage IVb GBC who was diagnosed with multiple abdominal, retroperitoneal, mediastinal, and bilateral hilar lymph nodes. The results of follow-up showed that the patient achieved a disease-free survival (DFS) of 11.3 months and overall survival (OS) of 18.1 months after conversion therapy.
emphasize the principle of individualization to achieve rapid shrinkage of tumors and down-staging (6). PTCD and bevacizumab were provided when the CA199 increased with jaundice for the first time (Figure 1G). Jaundice was quickly improved and PR was achieved. To prevent the progression of residual lesions and perform radical surgery as soon as possible, two cycles of GEMOX (7) were added when the CA199 increased for the second time (Figure 1G). The tumor marker turned negative and the tumor shrank further.

Given the risk of recurrence of residual lesions, lesions should be promptly resected after successful systemic therapy (8). The ideal timing of the surgery is to reach the standard of imaging and serology at the same time. Among these, the imaging response is critical, and the evaluation criteria may include the time required to achieve remission, as well as the depth and duration of remission. The lesions were localized in the gallbladder after the sixth cycle of immunotherapy, and the abnormal 18F-FDG uptake of metastatic lymph nodes disappeared in the patient. PR lasted for about 3 months. Another key factor is the negative serum tumor markers. The addition of
bevacizumab and chemotherapy resulted in a rapid decrease of CA199 to normal levels, indicating the timing of surgery from another dimension. In addition, liver function (9) and systemic therapy options should be considered during the final determination of surgical time: discontinuation of small molecule targeted drugs for at least 7 days, immune checkpoint inhibitors for at least 2 weeks, and bevacizumab for at least 6 weeks (10), respectively before surgery.

In summary, we reported a successful case of conversion therapy of stage IVb GBC to demonstrate that the treatment outcomes of patients with advanced GBC can be altered. Individualized systematic therapy for R0 resection may be key to improving the success rate of conversion therapy. The dual attainment of imaging and serology may be a reference timing for R0 resection during conversion therapy.

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Footnote

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