



# Comprehensive treatment of gallbladder cancer: a case report

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**Introduction and importance:** Gallbladder cancer is an extremely aggressive digestive system tumor. It is difficult to treat as early symptoms are insidious, and patients are usually diagnosed in advanced stages. The authors' case highlights the need for effective treatment strategies and underscores the critical role of an individualized approach in the management of complicated gallbladder cancer.

**Case presentation:** The authors report a patient admitted to the hospital with back pain and discomfort who was diagnosed with advanced gallbladder cancer. The patient received two cycles of chemotherapy with gemcitabine and cisplatin (GC), but the response was unsatisfactory. The authors changed the treatment regimen to gemcitabine and oxaliplatin (GEMOX) combined with targeted therapy (lenvatinib) and immunotherapy (toripalimab), and achieved significant therapeutic effect. Subsequently, the patient underwent "extended right hemihepatectomy, cholecystectomy, lymph node dissection of the hepatoduodenal ligament" and continued to receive combined therapy after surgery, and no tumor recurrence has been observed so far.

**Clinical discussion:** The authors delve into the challenges faced during treatment, exploring the subtle impact of modified regimens and the strategic integration of surgery and combination therapy. The focus of this study is on the intricate synergy between GEMOX, lenvatinib and teraplizumab, providing a holistic view of treatment effects and new insights into the clinical decision-making process.

**Conclusions:** This case emphasizes the success of precision medicine in the treatment of advanced gallbladder cancer. The adjustment of strategy can not only improve the therapeutic effect but also promote the success of surgical intervention. This case provides a valuable lesson in the holistic management of gallbladder cancer patients and prompts further reflection on the nuances of individualized therapeutic approaches in cancer treatment.

**Keywords:** advanced gallbladder cancer, comprehensive treatment, case report

## Introduction

Gallbladder cancer (GBC) is one of the common types of biliary tract malignant tumors, accounting for about 80–90% of biliary tract malignant tumors, and it ranks the sixth among digestive tract malignant tumors<sup>[1,2]</sup>. Advanced GBC is highly aggressive and has a poor prognosis. The overall median survival time is 6 months, and the 5-year survival rate is less than 10%<sup>[3]</sup>. According to the latest data of the International Agency for Research on Cancer (IARC), there were 115 900 new patients

## HIGHLIGHTS

- This case was a patient with advanced gallbladder cancer.
- Hepatic metastasis of gallbladder cancer poses a great challenge for treatment.
- The combined treatment of chemotherapy, targeting, immunization and surgery extended the survival time of patients.

with GBC and 85 000 deaths worldwide in 2020<sup>[1]</sup>. Although the pathogenesis of GBC has not been fully elucidated, it has been confirmed that there are some risk factors related to the disease, including gallstones, polypoid lesions of the gallbladder, chronic inflammation of the gallbladder, porcelain gallbladder, and so on<sup>[4,5]</sup>. Chronic inflammation is considered to be one of the major factors in carcinogenesis, causing deoxyribonucleic acid (DNA) damage, tissue proliferation, and the release of cytokines and growth factors<sup>[6]</sup>. The clinical presentation of advanced GBC are similar to that of biliary colic or chronic cholecystitis, with the most common symptoms being pain in the right upper quadrant, nausea, vomiting, jaundice and weight loss, and a palpable mass in some patients<sup>[6]</sup>. At present, abdominal ultrasound, endoscopic ultrasonography, computed tomography (CT), MRI, positron emission tomography (PET-CT) and other methods can help with the diagnosis of GBC<sup>[7,8]</sup>. However, the gold standard for a definitive diagnosis remains pathological examination, with adenocarcinoma being the most common histological type, accounting for 98% of all gallbladder tumors<sup>[9]</sup>. The

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management of GBC is an extremely intricate task and typically involves the comprehensive implementation of various treatment modalities, including surgical resection, chemotherapy, radiation therapy, and targeted therapy, among others. Surgery stands as the most efficacious and sole potentially curative approach<sup>[10]</sup>, particularly for patients diagnosed at an early stage. However, due to the occult clinical symptoms of GBC, which is prone to regional lymph node metastasis and vascular invasion, 70–90% of patients are diagnosed in the middle and advanced stages<sup>[11,12]</sup>, and the opportunity for early surgical treatment is lost. Chemotherapy and radiotherapy are commonly used to alleviate patients' symptoms and prolong survival. In recent years, some progress has also been made in targeted therapy and immunotherapy. These new treatment modalities provide more options for patients who are unable to receive surgical intervention.

Here, we report a patient with advanced gallbladder cancer who successfully underwent surgical conversion therapy after comprehensive treatment, which prolonged the patient's survival.

This case report has been reported in line with the SCARE Criteria<sup>[13]</sup>.

### Case report

A 46-year-old woman was admitted to the hospital with the chief complaint of "back pain and discomfort for half a year". Physical examination revealed stable vital signs, deep tenderness in the right upper quadrant without rebound pain. The patient had a history of gallstones for 3 years, which was relieved after analgesic and anti-inflammatory treatment, and had not been reexamined for nearly half a year. Laboratory results from our hospital: carcinoembryonic antigen (CEA): 147.4 ng/ml, carbohydrate antigen 19-9 (CA19-9): 1411 U/ml, and liver function was child-Pugh A. MRI of the upper abdomen showed: (1) Irregular thickening of the gallbladder was considered as a malignant tumor. (2) Intrahepatic space-occupying lesions, considering metastases (Fig. 1A-D). There was no tumor metastasis in chest CT. PET/CT suggested uneven thickening of gallbladder wall and increased fluorodeoxyglucose (FDG) uptake, considering malignant tumor; focal liver lesions, FDG uptake increased, considering metastasis; no lesions were found in other parts. Ultrasound-guided liver biopsy showed adenocarcinoma. The patient received two cycles of chemotherapy with gemcitabine and cisplatin (GC, G: 1.5 g; C: 37.5 mg), and then the reexamination showed CEA: 112.9 ng/ml, CA19-9: 568.8 U/ml. Upper abdominal MRI suggests: Multiple intrahepatic occupying lesions, with some slightly larger than the previous images (Fig. 1E-H). According to the examination results, the chemotherapy regimen was changed to gemcitabine and oxaliplatin (GEMOX, G: 1.5 g; OX: 150 mg) combined with targeted therapy (lenvatinib: 8 mg) and immunotherapy (toripalimab: 240 mg). After 3 cycles of comprehensive treatment, the reexamination showed CEA: 11.53 ng/ml, CA19-9: 51.42 U/ml. MRI of the upper abdomen showed that the intrahepatic lesion had shrunk (Fig. 1I-L). The patient underwent "extended right hemihepatectomy, cholecystectomy, and lymph node dissection of the hepatoduodenal ligament", and the pathological results showed: (1) Gallbladder: adenocarcinoma. (2) Liver: suggesting adenocarcinoma of biliary origin. (3) There was no microvascular invasion, nerve invasion and lymph node involvement. One month after surgery, the patient returned to the hospital for

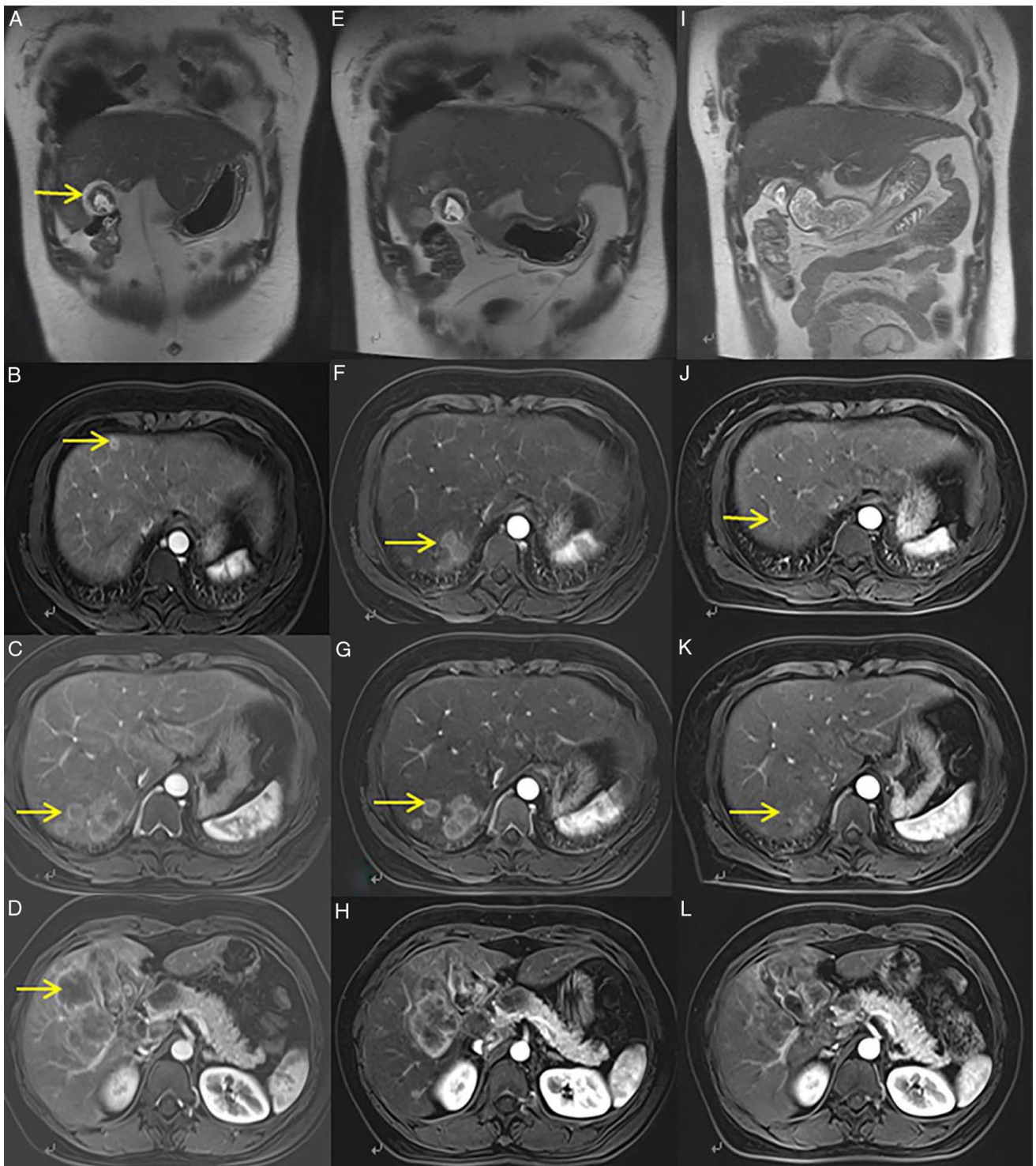
reexamination, CEA: 6.43 ng/ml, CA19-9: 29.73 U/ml. MRI of the upper abdomen suggested: (1) postoperative changes in the liver malignancy (2) postoperative changes in the gallbladder (Fig. 2A-B). The patient continued to receive combination therapy after surgery (GEMOX + lenvatinib + toripalimab). At the recent examination, CEA was 6.2 ng/ml, CA19-9: 18.75 U/ml, and upper abdominal MRI showed no tumor recurrence (Fig. 2C-D).

In summary, a case of advanced gallbladder cancer patients after receiving comprehensive treatment, self-perceived quality of life improved significantly. The survival time of the patient was more than 18 months, and no tumor recurrence was found in the postoperative follow-up of 13 months.

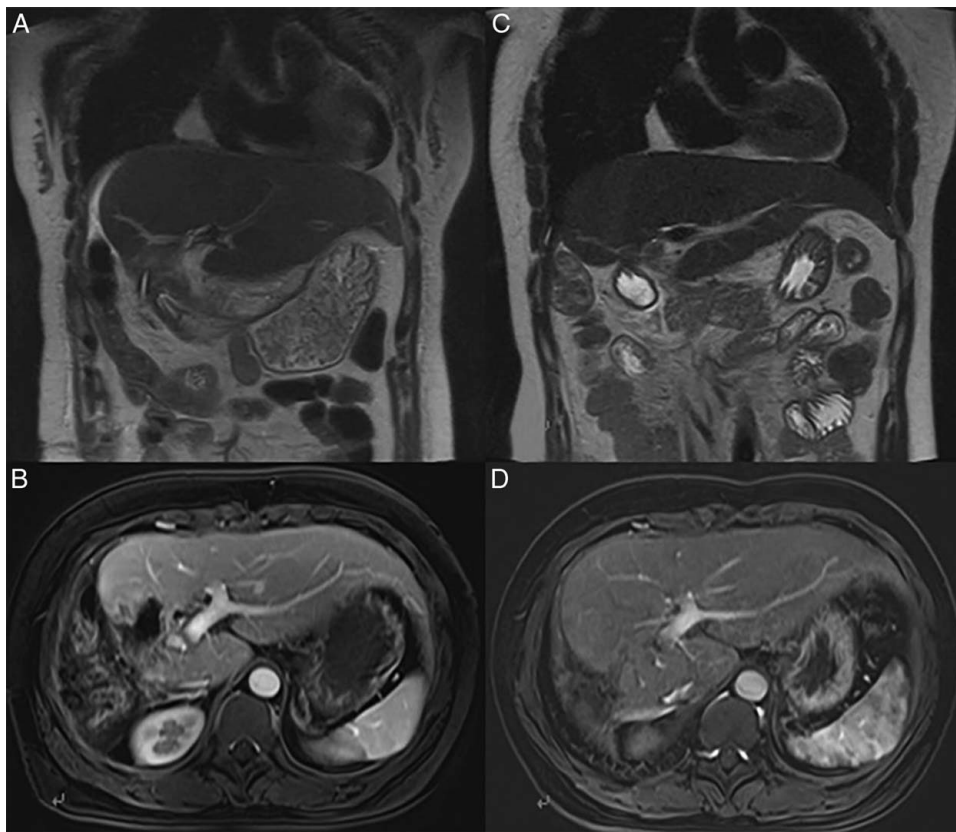
### Discussion

Gallbladder cancer is a highly aggressive tumor of the digestive system, and the treatment is challenging. This case report describes a patient with gallbladder cancer who achieved significant treatment results through comprehensive treatment, highlighting the importance of combination therapy, and the value of treatment adjustment and individualized treatment strategies, providing new treatment prospects for patients with gallbladder cancer.

First, the patient's clinical presentation was atypical, her symptoms were mainly characterized by back pain, and early symptoms of gallbladder cancer are usually relatively insidious, making early diagnosis more difficult. However, the patient's history of previous gallbladder stones and elevated blood tumor markers suggested the possibility of gallbladder cancer. This re-emphasizes the importance of early screening and diagnosis in the management of gallbladder cancer, especially for high-risk patients. Chemotherapy plays a certain role in the early treatment. For advanced GBC, gemcitabine combined with cisplatin is the standard first-line chemotherapy. The phase III ABC-02 study reported in 2010 showed that patients with advanced biliary tract cancer treated with the GC regimen of chemotherapy achieved longer median overall survival (mOS; 11.7 months VS 8.1 months,  $P < 0.001$ ) and median progression-free survival (mPFS; 8.0 months VS 5.0 months,  $P < 0.001$ ) than gemcitabine chemotherapy alone<sup>[14]</sup>. However, this patient had a limited response to the GC chemotherapy regimen. Subsequently, the treatment regimen was adjusted to GEMOX combined with targeted therapy and immunotherapy by comprehensive consideration of the treatment team. In one study, GC and GEMOX regimen were compared. GEMOX regimen had a lower incidence of hematological adverse reactions and was more suitable for patients with cardiac and renal insufficiency, and there was no significant difference in remission rate and overall survival between the two regimens<sup>[15]</sup>. For immune and targeted therapies, anti-PD-1 antibodies have been reported to enhance the efficacy of lenvatinib by altering the immune system, and lenvatinib can enhance the antitumor efficacy of anti-PD-1 immunotherapy<sup>[16]</sup>. This adjustment to the treatment regimen resulted in significant decreases in CEA and CA19-9 levels as well as tumor shrinkage, demonstrating a positive effect of the treatment. This flexibility in treatment adjustment is critical for patients, who may have variable responses to treatment. Surgical intervention also played a key role. Although the patient's condition is complex and requires a combination of multiple surgical



**Figure 1.** Patients were admitted to the hospital until preoperative MRI. The yellow arrows in (A) indicate irregular thickening of the gallbladder, the arrows in (B) and (C) indicate intrahepatic space-occupying lesions, and the arrows in (D) show nodules fused into clusters in the gallbladder bed area. Yellow arrows in (F) and (G) indicate space-occupying lesions in the liver, some of which are larger than in the previous images. (J, K) Yellow arrows indicate reduced lesions in the liver. Yellow arrows in (E) indicate irregular thickening of the gallbladder, arrows in (H) indicate massive nodules in the gallbladder bed area, (I) gallbladder lesions are better than before, and (L) intrahepatic lesions in the gallbladder bed area are better than before.



**Figure 2.** MRI of the patient after surgery and recent review. (A, B) Shows the postoperative changes. (C, D) Shows that at the most recent review, no tumor recurrence was observed.

procedures, the removal of the diseased tissue not only provides important information for determining the tumor type but also reduces the tumor burden and provides the patient with more powerful local treatment. This also highlights the synergy of surgical treatment with other treatment modalities to achieve a more comprehensive therapeutic effect.

In conclusion, this case report emphasizes the application of an integrated treatment approach and the importance of therapeutic adjustments. The development of individualized treatment plans will be an important trend in the future management of the disease to better meet the therapeutic needs of different patients. We still need further studies to validate the effectiveness of this treatment strategy to provide more treatment options. In addition, research on early diagnosis and screening methods is also an important step to reduce the late diagnosis of gallbladder cancer.

### Ethical approval statement

Ethics approval was not required for case reports under our institutional review board guidelines.

### Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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### Author contribution

S.Z. conceived and designed the study. Z.C. and Y.L. contributed to obtaining the data. H.L. and L.F. coordinated data collection. Z.C. and Y.L. compiled the data and edited the manuscript. S.Z. critically reviewed the manuscript. All authors contributed to the final submitted version.

### Conflicts of interest disclosure

The author declares no conflicts of interest.

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None.

### Guarantor

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### Data availability statement

Data sharing does not apply to this article.

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