Case Report

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Surgical management for hepatocellular carcinoma with concurrent portal vein tumour thrombus and bile duct tumour thrombus: a case report

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Introduction: Hepatocellular carcinoma (HCC) associated with concurrent portal vein tumour thrombus (PVTT) and bile duct tumour thrombus (BDTT) is sporadic and presents a puzzle to management with miserable prognostic.

Case presentation: The authors reported a case of HCC in the right liver with PVTT involving the right portal vein and BDTT developing in the common bile duct, detected in a 43-year-old man. The patient was admitted to our hospital with abdominal pain in the right hypochondrium and obstructive jaundice. Imaging studies showed a large mass in the right liver with invasion of the first branch of the portal vein and dilated intrahepatic bilateral bile ducts. A liver biopsy confirmed the diagnosis of hepatocellular carcinoma. Right hepatectomy plus thrombectomy en bloc with extrahepatic bile duct resection was performed. Subsequently, the patient received a postoperative adjuvant transarterial chemoembolization (PA-TACE) 1 month after surgery.

Discussion: In the present case, the authors were not aiming for curative treatment by aggressive management but for palliative treatment. At the time of diagnosis, the tumour had already invaded the portal bifurcation. Hepatectomy plus thrombectomy en bloc with resection of common bile duct can remove biliary obstruction caused by BDTT, optimize portal flow by eliminating PVTT, and reduce the tumour burden, consequently improving the quality of life and liver function. Then, PA-TACE takes care of microfoci left behind by the surgery, which may prolong survival time.

Conclusion: An aggressive therapeutic strategy should be considered in exceptional cases for resectable HCC with PVTT and obstructive BDTT. However, the follow-up period remains limited. A longer duration of observation is necessary to definitively assess the surgery's impact on patient's recurrence and survival time.

Keywords: bile duct tumour thrombus, case report, hepatectomy, hepatocellular carcinoma, portal vein tumour thrombus

Introduction and importance

Portal vein tumour thrombus (PVTT) is one of the most frequent complications of hepatocellular carcinoma (HCC), occurring in 10–60% of patients[1] and involving the leading truck at the time of diagnosis in 15–30% of cases[2]. Hepatocellular carcinoma with bile duct tumour thrombus (BDTT) represents a rare and unique entity of HCC in clinical practice relative to PVTT, with a prevalence from 1.2 to 12.9%[3]. BDTT results from the invasion of tumour cells in the bile ducts, forming an intra-biliary thrombus, which can obstruct the bile flow.

The presence of PVTT in conjunction with BDTT in a significant tumour HCC has a pejorative solid impact on the prognostic, with a median survival time of 12.3 months and a 5-year recurrence rate of 100%[4]. In advanced HCC with concomitant BDTT and PVTT resectable, aggressive treatment may provide benefits to improve quality of life and prolong survival time by removing the biliary obstruction, improving portal flow, reducing complications of portal hypertension and decreasing the tumour burden, which facilitates adjuvant therapy following surgery.

HIGHLIGHTS

- Hepatocellular carcinoma (HCC) associated with concurrent portal vein tumour thrombus (PVTT) and bile duct tumour thrombus (BDTT) is sporadic and presents a puzzle to management with miserable prognostic.
- We reported a case of HCC in the right liver with PVTT involving the right portal vein and BDTT developing in the common bile duct, detected in a 43-year-old man.
- Right hepatectomy plus thrombectomy en bloc with extrahepatic bile duct resection was performed. Subsequently, the patient received a postoperative adjuvant transarterial chemoembolization (PA-TACE) one month after surgery.

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In this report, we describe a case of sizeable right liver HCC with concurrent PVTT involving the first branch of portal vein and BDTT developing in the common bile duct (CBD) that was managed by a combination strategy including a major hepatectomy plus thrombectomy en bloc with extrahepatic bile duct resection followed by postoperative adjuvant transarterial chemoembolization (PA-TACE).

This case report has been reported in line with the SCARE 2023 criteria[5], Supplemental Digital Content 1, http://links.lww.com/MS9/A427.

Case presentation

Patient information

A 43-year-old male patient was admitted to our hospital with jaundice and abdominal pain in the right hypochondrium progressed for 3 weeks. Past medical history revealed a chronic hepatitis B virus (HBV) infection treated with tenofovir.

Clinical findings

The physical examination had no significant findings except jaundice. He was afebrile, and the vital signs were stable. The patient's weight was 73 kg.

Timeline

He delayed 1 month from first symtomp presentation to diagnosis due to misdiagnosing as an amoebic liver abscess.

Diagnostic assessment and interpretation

Laboratory studies demonstrated disturbed liver function tests in favour of a biliary obstruction: elevated total bilirubin (46.7 mmol/l, average value was 21 mmol/l), elevated direct bilirubin (41.8 mmol/l, average value < 8.6 mmol/l), slightly elevated transaminases (ASAT/ ALAT 100/ 107 U/l), normal serum albumin (40.2 g/l). Hemogram and test results of haemostasis were normal (prothrombin time 80.4%, platelet count 271 G/l). The serological marker of hepatitis B was positive (HBsAg positive, HBV-DNA level 932 copies/ml), and the hepatitis C virus antibody was negative. The alpha-fetoprotein (AFP) serum level was 1338 ng/ml (normal range 0–9 ng/ml).

Abdominal contrasted computed tomography (CT) scan detected a hypervascular mass in the right liver measuring $12 \times 8 \times 7$ cm, enhanced during the arterial phase with wash-out of contrast on the portal venous phase, suggesting HCC (Fig. 1). Three satellite nodules were around the primary tumour, but no lesion was observed in the left liver. The tumour invades the right portal vein with tumour thrombus extending from the division of first-order branches of the portal vein to the portal bifurcation without invasion of the left portal vein, classified in grade Vp3 according to the classification of Liver Cancer Study Group of Japan[6]. The intrahepatic bilateral bile ducts appeared dilated without intraductal calculi; the gallbladder and the CBD were not distended. Biliary thrombus in the bile duct confluence and the common hepatic duct was suspicious. The liver parenchyma appeared heterogeneous with slight surface irregularity, without portal hypertension signs. There were no oesophageal varices in the esophagogastric endoscopy. A thoracic CT scan showed no distant metastasis.

A percutaneous liver biopsy was performed, and a histological examination of the specimen confirmed an HCC. After a multidisciplinary team discussion, we retained the diagnostic of advanced HCC with PVTT in the right portal vein and suspicion of BDTT involving the primary confluence of the bile duct. The patient was informed of prognostic, risks, and different therapeutic options. A combination strategy including right hepatectomy with possible bile duct resection and PA-TACE was chosen. A remnant liver volume to body weight ratio (RLV/BW) of 0.8% with an acceptable liver function is safe for a right hepatectomy.

Intervention

The laparotomy with a J-shaped incision was performed. Upon exploration, we discovered a tumour measuring 12×10 cm in the right liver with satellite nodules (Fig. 2A-C, Video 1, Supplemental Digital Content 2, http://links.lww.com/MS9/A428) that adhered weakly to the right anterior abdominal wall by inflammation. Three nodules less than 1 cm were discovered on the surface of the left lobe, and an extemporaneous histopathological examination proved HCC (Video 2, Supplemental Digital Content 3, http://links.lww.com/MS9/A429). The liver manifests moderate fibrosis. Hepatic hilar lymph nodes were enlarged (about 1 cm) and soft. No peritoneal metastasis was detected. Firstly, the Kocher manoeuvre was carried out, mobilizing the duodenum and the head of the pancreas. Next, a regional lymphadenectomy started by dissection of the common hepatic artery and pursued toward the hilum of the liver, exposing the branches of the proper hepatic artery, main portal vein, right and left portal vein, CBD, right and left hepatic duct (Video 3, Supplemental Digital Content 4, http://links.lww.com/MS9/A430). The gallbladder was left in its bed. The right branch of the proper hepatic artery was ligated, showing a demarcated line between the right and the left livers; parenchyma transection was accomplished along this boundary, uncovering the right Glissonean pedicle (Video 4, Supplemental Digital Content 5, http://links.lww.com/MS9/A431). Then, bile duct exploration discovered a BDTT developing from the right hepatic duct to the bile duct confluence and the common bile duct without invading the left hepatic duct (Fig. 2D).

The CBD and the left hepatic duct resections were executed with a negative resection margin (Video 5, Supplemental Digital Content 6, http://links.lww.com/MS9/A432). After clamping the left portal vein and the main portal vein, the portal vein bifurcation was opened by an incision, confirming the presence of PVTT in the right portal vein reaching the portal bifurcation without extension in the left portal vein and the main portal vein (Fig. 2E). The right portal vein with PVTT was resected. Left portal vein clamping has been briefly removed for a backflow thrombectomy to eliminate eventual floating PVTT in the left portal vein (Video 6, Supplemental Digital Content 7, http://links.lww.com/MS9/A433). We carried out a reconstruction of the portal vein bifurcation using a 5-0 monofilament nylon suture. The right liver was wholly excised without significant haemorrhage (Video 7, Supplemental Digital Content 8, http://links.lww.com/MS9/A434, Video 8, Supplemental Digital Content 9, http://links.lww.com/MS9/A435). Anastomosis of the left hepatic duct to the jejunum was performed using the Roux-en-Y hepaticojejunostomy technique. Three nodules in the left lobe were removed by wedge resection.

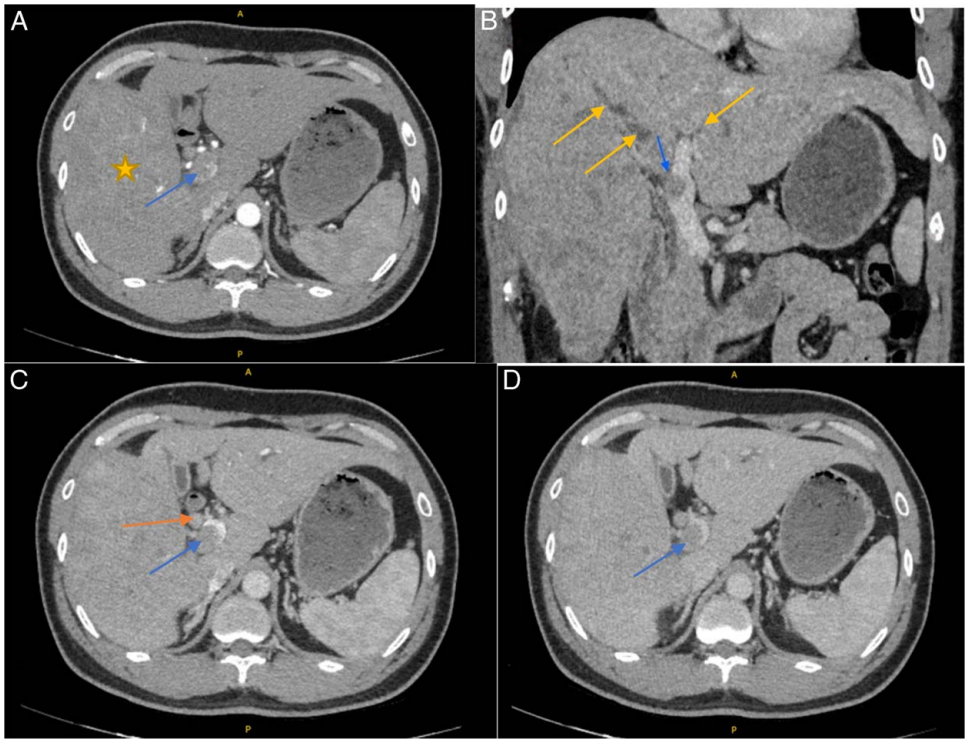

Figure 1. Abdominal computed tomography scan show a large tumour in the right liver with characteristics of hepatocellular carcinoma (HCC). [(A) Arterial phase. (B, C) Venous phase. (D) Portal phase) HCC tumour (yellow star) with portal vein tumour thrombus in the right portal vein and the portal bifurcation (blue arrow), without invasion of the left portal vein. Dilatation of the intrahepatic bilateral bile ducts (yellow arrows) due to obstruction by bile duct tumour thrombus in the bile duct confluence (orange arrow).

The histopathological examination with hematoxylin and eosin staining of the primary tumour revealed a poorly differentiated HCC (grade 3 according to the WHO) with a macrotrabecular pattern (Fig. 3A, B)[7]. The tumour invaded the right portal vein with PVTT and the intrahepatic bile duct (Fig. 3C, D). The extrahepatic bile duct specimen examination showed an endoluminal invasion of the common hepatic duct caused by carcinomatous proliferation. Lymph nodes were not involved in metastasis. The degree of hepatic fibrosis was scored F3 in the METAVIR system[8].

The postoperative course was marked by ascites that were controlled by spironolactone and albumin without post-hepatectomy liver failure or other complications. After surgery, serum bilirubin levels gradually diminished and reached normal values on postoperative day 10, and jaundice disappeared. Postoperative AFP was 57 ng/ml. The patient was discharged on postoperative day 20.

Follow-up and outcomes

One month after surgery, the patient underwent a programmatic adjuvant TACE using lipiodol and doxorubicin. The arterial angiographic catheter was inserted into the proper hepatic artery through the femoral artery using the Seldinger method, and a hepatic angiography was performed. Unfortunately, tumour recurrence had happened with three nodules of tumour stains (max 12 mm) detected in the remnant liver (Fig. 4). Lipiodol and doxorubicin were injected into the tumour-feeders with selective catheterization. The dosage of lipiodol and doxorubicin was determined by body surface area and liver function. The patient was followed up once every month in the first year after the operation with liver function assessments, AFP serum level, and abdominal ultrasounds at follow-up visits. Abdominal contrasted CT or magnetic resonance imaging was carried out once every two months or when the AFP level increased. At a 2-month postoperative follow-up visit (1-month post-TACE), AFP was 90 ng/ml. On contrasted CT, the lesions showed an accumulation of high-density material compatible with lipiodol deposition. In the arterial phase, no enhanced area appeared within the nodules. No other recurrence or metastasis was detected.

Clinical discussion

HCC is the most common type of primary liver malignancy that predominantly develops on underlying cirrhosis caused by hepatitis B, hepatitis C, non-alcoholic fatty liver disease, etc[9]. HCC tumours can invade the portal veins, the intrahepatic lymphatic system, and the bile ducts with the presence of BDTT, which is rare relative to PVTT and occurs in about 2.5–3.4% of patients with HCC[10–12]. In 1947, Mallory *et al.*[13] reported the first case of HCC presenting obstructive jaundice caused by tumour invasion of the gallbladder obstructing extrahepatic bile duct, and this type of HCC was classified as "icteric-type hepatoma" by Lin *et al.*[14] in 1975. Obstructive jaundice in HCC with macroscopic biliary invasion poses challenges to differential diagnoses from perihilar cholangiocarcinoma, choledocholithiasis, and decompensated cirrhosis. It is easily misdiagnosed in type III without apparent HCC mass in the liver[15].

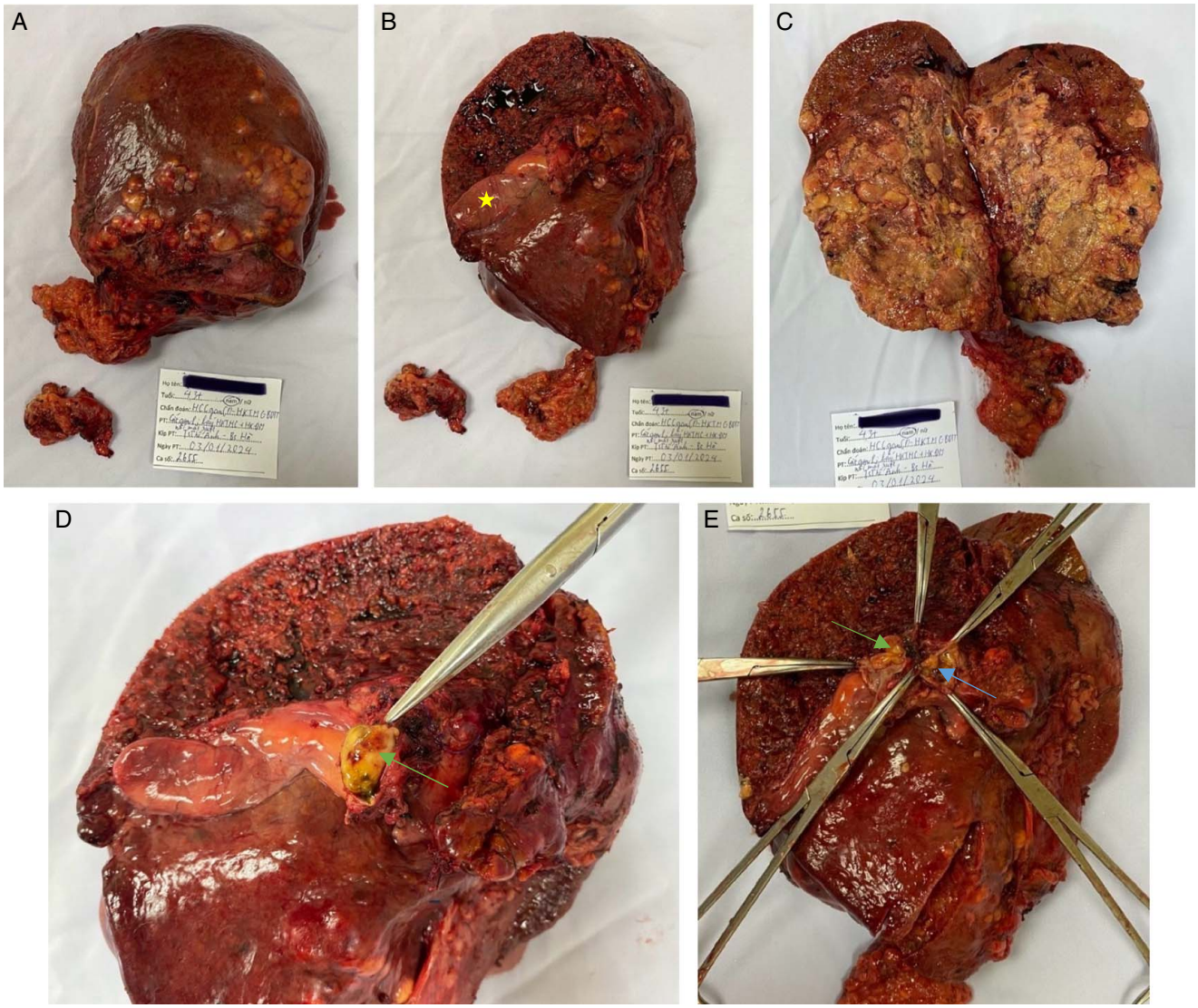

Figure 2. Surgical specimen of a large hepatocellular carcinoma (HCC) tumour in right liver. (A) Anterior view with satellite nodules. (B) Posterior view with gallbladder in place. (C) Macroscopic view of resected HCC tumour. (D) BDTT developing in common bile duct (green arrow). (E) Portal vein tumour thrombus in right portal vein (blue arrow) and bile duct tumour thrombus (BDTT) in common bile duct (green arrow).

Furthermore, biliary obstruction makes assessing the hepatic functional reserve difficult before determining treatment. It may lead to severe complications such as cholangitis, haemobilia, and hepatic failure in an underlying liver disease. Nevertheless, jaundice induced by BDTT is not necessarily a harbinger of advanced disease and a contraindication for surgery because its nature of cholestasis is different from advanced liver cirrhosis. Liver function can recover if jaundice is relieved by biliary decompression, allowing safe liver resection. Preoperative biliary drainage may be required in case of cholangitis. The data indicated that BDTT has lower malignant potential than vascular invasion in HCC, and macroscopic BDTT is not a contraindication for surgical treatment[10]. Hepatectomy in this group of patients offers similar survival at 1 and 3 years but poorer survival at five years than HCC without BDTT[16]. Several studies demonstrated that liver resection is recommended as the first-line treatment for HCC with BDTT when technically feasible and appropriately selected[11,16,17].

HCC patients with BDTT have a higher rate of macrovascular invasion, with an incidence of 40% compared to 15% in HCC patients without BDTT[3,16]. This association is explained by the juxtaposition of the bile duct and portal vein enclosed within the Glissonean sheath and the fact that the tumour can invade both structures. Although HCC with concurrent BDTT and PVTT is considered an advanced stage with dreadful prognostic, it is still unclear whether macrovascular invasion has an impact on tumour recurrence in patients with HCC and BDTT. Zeng *et al.*[3] even showed that vascular invasion is not a risk factor for tumour recurrence and poor prognostic in HCC with BDTT. In other studies, macrovascular invasion is a significantly poor prognostic factor for HCC with BDTT undergoing surgery and is associated with massive intraoperative blood loss[4,18]. Because of the high risk of recurrence in these patients after resection, adjuvant

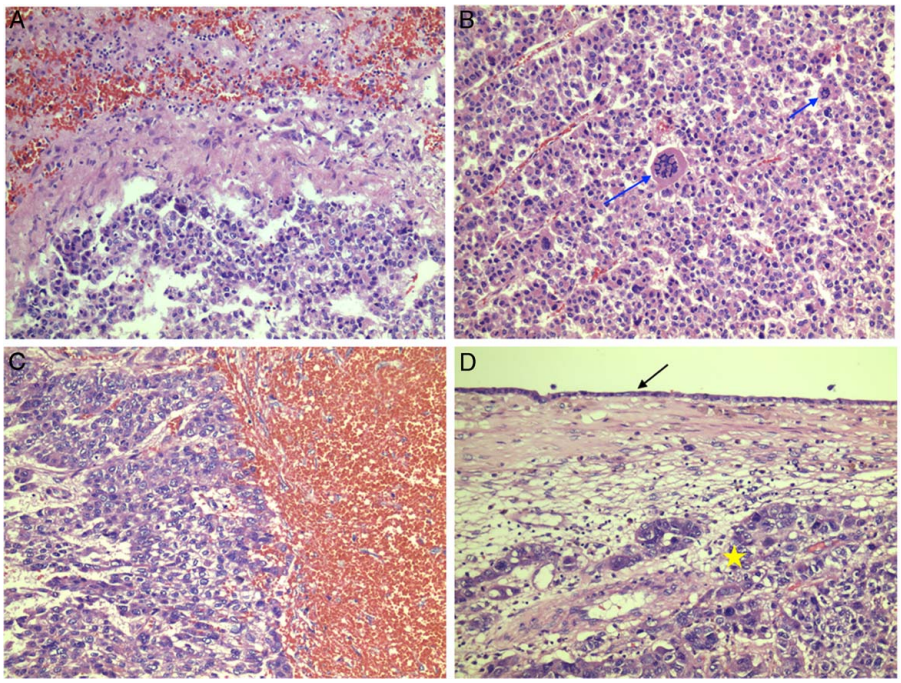

Figure 3. Histopathology of the right liver tumour stained by hematoxylin and eosin (H&E, 20×). (A, B) Poorly differentiated grade 3 hepatocellular carcinoma (HCC) with macrotrabecular pattern. Polygonal cells, prominent nucleoli, anaplastic giant cells with nuclear atypia (blue arrow). (C) Vascular invasion of HCC with portal vein tumour thrombus. (D) Bile duct invasion of HCC with bile duct tumour thrombus. Tumour tissue (yellow star) and biliary epithelium (black arrow).

therapy might be considered to target invisible residual microscopic metastasis in the remnant liver, which is usually the source of early recurrence (1 year). In contrast, late recurrence originates from de novo lesions depending on the underlying liver disease (HBV infection, cirrhosis)[19,20]. The efficacy of PA-TACE for HCC patients with concomitant BDTT and PVTT has been reported in several studies[21–23]. Huang and colleagues showed that patients could significantly benefit from PA-TACE at the time of recurrence and overall survival if they had a tumour greater than 5 cm, macrovascular invasion, poor differentiation, and AFP level greater than 400 ng/ml (the whole portrait of our patient). PA-TACE can detect and treat early postoperative

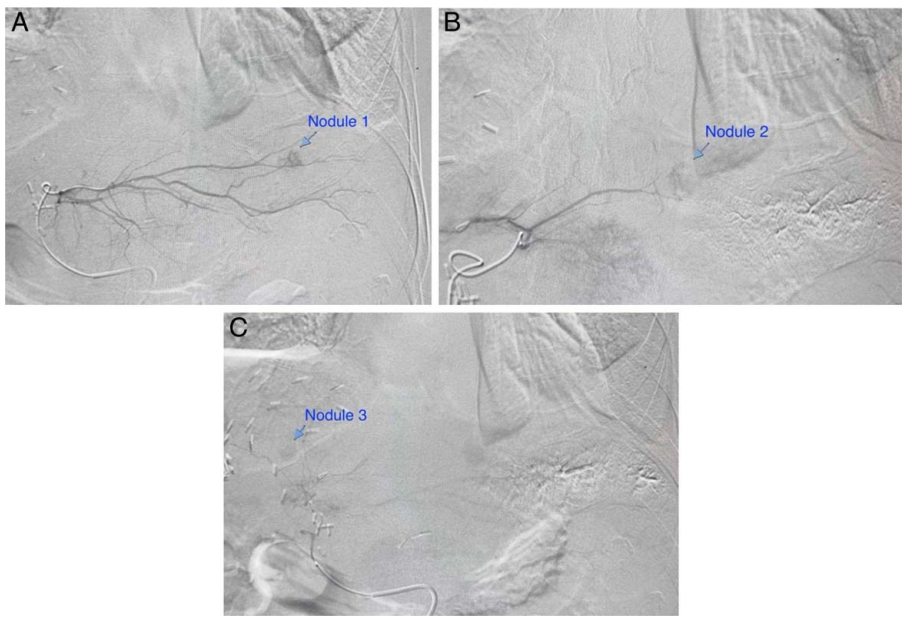

Figure 4. Hepatic angiography at 1-month postoperative detecting 3 nodules (blue arrows) located in the left liver. Adjuvant transarterial chemoembolization using lipiodol and doxorubicin was conducted.

residual cancer and early recurrent lesions. If no tumour stain is found on angiography, chemotherapeutic agents are injected into the remnant liver to prevent tumour recurrence. However, Chen *et al*.[24] found that adjuvant lipiodolized TACE may not have a preventive effect on recurrence.

On the other hand, although systemic therapy (atezolizumab-bevacizumab, sorafenib) is recommended as first-line treatment for HCC with portal invasion[25], several reports suggested the benefit of surgical treatment for HCC with PVTT if a radical resection of tumour and PVTT can be achieved[26–28]. Adjuvant TACE followed by hepatectomy may improve overall survival and disease-free survival in patients with HCC and PVTT[23,29,30]. Primarily, in the case of large tumours with concurrent PVTT classified Vp3 and BDTT in the CBD presenting obstructive jaundice, biliary drainage associated with systemic therapy would be less effective because of the necessary tumour burden and risk of complications caused by portal hypertension.

In the present case, we were not aiming for curative treatment by aggressive management but for palliative treatment. At the time of diagnosis, the tumour had already invaded the portal bifurcation. Without intervention, PVTT would have extended to the main portal vein, disturbed hepatic portal perfusion, and thus compromised liver function. Hepatectomy plus thrombectomy en bloc with resection of CBD can remove biliary obstruction caused by BDTT, optimize portal flow by eliminating PVTT, and reduce the tumour burden, consequently improving the quality of life and liver function. Then, PA-TACE takes care of microfoci left behind by the surgery, which may prolong survival time. As sorafenib and other tyrosine kinase inhibitors (TKI) agents are widely used as standard-of-care in the treatment of advanced HCC[31], the efficacy of sorafenib (the mainly focused TKI agent in published studies) as adjuvant therapy in addition to PA-TACE to prevent recurrence after surgery was remains controversial. It was demonstrated that patients could benefit more from TACE plus TKI agent if they had a tumour diameter 3.5 cm, tumour number less than 3, no BDTT, no hepatic vein tumour thrombus, ruptured tumour, and stage IIIb (American Joint Committee on Cancer 8th10 staging system)[32,33]. In selected cases, the neo-adjuvant therapies, including TACE, radiofrequency ablation (RFA), stereotactic body radiation therapy (SBRT), and hepatic artery infusion chemotherapy (HAIC), may achieve tumour downstaging facilitating radical surgery and provide beneficial effects.

Patient perspective

The patient was satisfied with the treatment and postoperative care.

Informed consent

The patient agreed to participate in the study and was periodically re-examined by appointment. Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Conclusion

HCC with concurrent PVTT and BDTT presenting jaundice is an uncommon clinical situation with a poor prognostic. The benefit of surgical management for this type of advanced HCC is still controversial. Hepatectomy with resection bile duct and portal reconstruction should only be limited in exceptional cases to improve the quality of life and need multi-disciplinary consideration. Adjuvant therapy as PA-TACE and systemic treatment can offer potential benefits and prolong survival for HCC patients after radical resection. However, the follow-up period remains limited. A longer duration of observation is necessary to definitively assess the surgery's impact on patient's recurrence and survival time.

Ethical approval

This study was conducted with the informed consent of the patient and received the requisite ethical approval from the Scientific Council of Vietnam National Cancer Hospital. The council comprises expert representatives from relevant specialties, including hepatobiliary surgeons, radiologists, oncologists, gastroenterologists, and pathologists. Their comprehensive review and endorsement ensured adherence to the highest ethical standards throughout the research process. Our procedures adhered to the Declaration of Helsinki. The authors reported no conflicts of interest.

Consent

Written informed consent was obtained from the patient for publication and any 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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None.

Author contribution

Conceptualization: A.T.P. Data curation: all authors. Methodology: all authors. Visualization: all authors. Writing—original draft: T.D.V. Writing—review and editing: C.M.T., T.V.Q.

Conflicts of interest disclosure

None.

Guarantor

Anh The Pham.

Data availability statement

None.

Provenance and peer review

None.

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