

Application of Ex Vivo Liver Resection Followed by the Autotransplantation Technique in Radical Resection of Gastric Cancer Liver Metastases: A Case Report

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Case report

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Abstract

Background Radical resection of gastric cancer liver metastases can increase the 5-year survival rate of GCLM patients. However, patients may lose the theoretical feasibility of surgery due to the critical location of liver metastasis in some cases.

Case presentation A 29-year-old female had a chief complaint of chronic abdominal pain for one year. Abdominal CT and MRI examinations suggested a mass of unknown pathological nature located between the first and second hila and the margin of the lower segment of the right lobe of the liver. The anterior wall of the gastric antrum was unevenly thickened. The diagnosis of (gastric antrum) intramucosal well-differentiated adenocarcinoma was histopathologically confirmed by puncture biopsy with gastroscopy guidance. The pathological properties of the liver mass remained unclear before surgery. She underwent radical resection (excision of both gastric tumors and ELRA simultaneously) followed by XELOX adjuvant chemotherapy. Without serious postoperative complications, the patient was successfully discharged on the 20th day after the operation. Pathological examination of the excised specimen indicated that gastrectomy with D2 lymph node dissection for primary gastric tumors and R0 resection for liver metastases were achieved. The resected mass was confirmed to be poorly differentiated gastric carcinoma (hepatoid adenocarcinoma with neuroendocrine differentiation) with liver metastases in segments 6 and 8. A Follow-up review that began one month after surgery showed no recurrence or metastasis within the liver. The mother of three children miraculously lived a happy life and went back to work as normal.

Conclusions: Application of ELRA in radical resection for GCLM can help selected patients with intrahepatic metastases located in complex sites obtain a favorable clinical outcome.

Introduction

Previous studies have reported that the incidence of GCLM ranges from 9.9% to 18.7%(1, 2), with a median survival time of 11 months and a 5-year survival rate <20%(3). Although retrospective studies in multiple centers have declared that radical resection—excision of both gastric tumors and liver metastases simultaneously—can increase the 5-year survival rate of GCLM patients—the timing and ideal surgical type still remain controversial. Based on the likelihood of a surgical treatment being successful—C-GCLM has been proposed by the Chinese consensus on the diagnosis and treatment of GCLM(4). While we acknowledge a tumor-free margin as the predictor of a better outcome, a unavoidable question may emerge—what if liver metastasis meets all the surgical qualifications judged by size and scope according to the aforementioned classification criteria, but their location is so critical that the technical risk of surgery significantly increases? It would be regretful to give up the chance of radical resection because of the limited number of eligible patients. The application of ELRA may provide an alternative solution to this problem. Here, we present a case pertaining to the treatment procedures and prognosis of a young female patient with GCLM—that showed that the application of ELRA in radical resection for GCLM can help patients with intrahepatic metastases located in complex sites obtain a favorable clinical outcome.

Case Presentation

2.1 Preoperative assessment

The patient was a 29-year-old female had a chief complaint of chronic abdominal pain for one year and she experienced continuous weight loss of 5kg over 2 months prior to her admission. According to her past medical history, she underwent ovarian cystectomy, appendectomy and subtotal hysterectomy for uncontrollable hemorrhage. No special family history was provided except that her mother was diagnosed with squamous cell carcinoma of the vulvar epithelium and the disease was cured according to her description. Other detailed basic information is displayed in Table 1. Upon physical examination, a round mass approximately 7 cm in diameter could be palpated in the right upper abdomen and the mass was smooth, pushable, hard and indistinguishable from adjacent tissue. Abdominal CT and MRI examination suggested a mass of unknown pathological nature located between the first and second hila and the margin of the lower segment of the right liver lobe (Figure 1). The anterior wall of the gastric antrum was unevenly thickened. PET/CT (whole body) examination showed two main points: 1. the anterior wall of the gastric antrum was unevenly thickened, and FDG uptake was increased, which was consistent with the manifestations of gastric cancer; and 2. a mass shadow was located at the first and second hepatic hila and the lower right lobe of the liver. As increased FDG uptake is a sign of malignancy, whether the mass was liver metastasis or primary liver cancer remained to be identified. The results of puncture biopsy with gastroscopy guidance supported the pathological diagnosis of gastric antrum intramucosal well-differentiated adenocarcinoma. ECG, chest DR and CT of the lower abdomen and pelvis showed no obvious abnormalities. Laboratory data demonstrated normal liver function and routine blood test results (Table 2). The tumor marker results showed that AFP was 9850 ng/ml and CEA was 55 ng/ml. Preoperative volumetric calculation was achieved by using 3D visualization imaging. The remnant liver-to-standard liver volume ratio was 56%. ICGR15 was 2.1%. The preoperative Child-Pugh score was 3. Due to the unknown nature and special location of the mass in the liver, it was considered to be a liver metastatic focus of gastric cancer after consultation by general and hepatobiliary surgeons. After fully understanding the risk and difficulty of the operation and after careful consideration, the patient decided to accept ELRA combined with simultaneous radical resection for gastric cancer.

2.2 Surgical procedure

A tumor protruding through the liver capsule with unclear borders and an uneven surface was found in the right liver during abdominal exploration. It was hard and pale and was tightly adhered to the surrounding omentum. Consistent with the preoperative imaging findings, the tumor extended to the junction of the left and right liver lobes and was adjacent to the vena cava. Intraoperative frozen biopsy of the liver mass was performed and the results supported a poorly differentiated malignant tumor. The presence of intrahepatic microlesions was ruled out by intraoperative ultrasound. The results of intraoperative exploration and the desire of the patient led us to perform ELRA combined with radical resection for gastric cancer as the original plan.

Hepatectomy was accomplished by using standard technique (5) with extensive lymph node dissection around the SMA and celiac trunk. The common bile duct was completely removed up to the head of the pancreas. Preservation and perfusion of the removed isolated liver was performed with ice-cold solution at 4 °C and UW solution via the intact portal vein. At the same time, temporary channel was established between the SHIVC and IHIVC with an internal diameter of 2 cm and Geo-Tex artificial vessel. The PV was also anastomosed to the vessel to construct portacaval shunt. After the intrahepatic tumor and target liver segment were completely resected, the aforementioned temporary venous channel was removed, and the remnant of the liver was implanted similar to OLT which was followed by anastomosis of the SHIVC, IHIVC, PV, HA, and bile duct. The total anhepatic period was 245 minutes: including 180 minutes of CIT for extracorporeal tumor resection and vein repair, 40 minutes of vena cava anastomosis and 25 minutes of portal vein anastomosis. Observation of the normal liver surface color after reperfusion was commonly performed, and the surgeons usually confirmed bile outflow before bile duct anastomosis. Some of intraoperative photos are presented in Figure 1. As we performed ex vivo liver resection on the back table, radical surgery for gastric cancer was accomplished simultaneously by general surgeons on the operating table.

2.3 Postoperative management and follow-up

Our medical team provided her with symptomatic treatment after surgery such as gastrointestinal decompression, abdominal drainage, anti-infection medication, nutritional support. She underwent bile leakage drainage on the fifth day after the operation. Fluid accumulated in the liver section and caused symptoms of gastric compression. The effusion was completely drained out after CT-guided puncture and catheter drainage. No other postoperative complications such as SFSS, ALF, vascular embolism, intra-abdominal infection, or hemorrhage occurred. She was successfully discharged on the 20th day after the operation. Postoperative pathological examination of the excised specimen indicated that gastrectomy with D2 lymph node dissection for primary gastric tumors and R0 resection for liver metastases were achieved. The resected mass was confirmed to be poorly differentiated gastric carcinoma (hepatoid adenocarcinoma with neuroendocrine differentiation) with liver metastases in segments of 6 and 8. The patient began her first follow-up one month after the operation, and received 6 courses of XELOX chemotherapy, during which no serious adverse reactions or treatment discontinuation occurred. No obvious signs of tumor recurrence or metastasis within the abdomen or liver were recorded during a 3.5-year follow-up. The patient had a good overall condition and did not undergo a second operation. Selected pre and post operative abdominal CT images of the patient were displayed in Figure 2. Postoperative laboratory data of the patient were displayed in Table 3.

Discussion And Conclusions

As an advanced-stage type of gastric cancer, GCLM is usually translobal, multifocal or even diffusely spread, and complicated by peritoneal, extensive lymph node and organ metastasis due to its highly malignant and rapidly invasive oncologic nature. Poor prognosis and deadly surgical complications make the resection rate so low that there is no multicenter clinical trial with large samples on the

significance of liver resection for GCLM. No well-established criteria exist except for a few retrospective studies with a limited number of cases(4). However, it is worth noting that the results of these limited studies almost indicate that patients with GCLM can benefit from radical resection (6-9). According to follow-up results, the patient we reported also obtained a good prognosis and lived with a good quality of life.

According to the C-GCLM, the definitions of both type I and II include the same criterion:“technological resectability of liver metastases judged by a hepatobiliary surgeon”. It emphasizes the principle that surgery should be performed only when R0 resection is anticipated(4). The aforementioned question arises: what if the size and scope of liver metastases comply with this standard, but the anatomical complexity puts the hepatobiliary surgeon into a dilemma? The most common situation is that the tumor is located deeply within the liver and has extensive involvement with the main hepatic veins or retrohepatic vena cava. Conventional radical resection is extremely hazardous due to the potential risk of uncontrollable hemorrhage and long ischemia time(10). These types of tumors are usually deemed unresectable because they can not be completely removed with conventional surgery(11) .

We can infer that ELRA may overcome this issue from our case report. It effectively alleviated the technical bottleneck caused by the special location of the tumor in traditional hepatectomy and allowed the hepatobiliary surgeons to perform precise liver tumor resection and effective vascular/repair by enabling them to operate with bloodless vision and access to critical structures easily since the first report of ex vivo hepatectomy by Pichlmayr et al in 1988(4, 12, 13).

The theoretical basis and detailed surgical procedures that have been reported systematically in many studies will not be repeated here(14). What we want to discuss is the subtle principle of contradiction— with greater benefit comes higher risk. From the surgical records described above, we can see that ELRA is a challenging and time-consuming surgery with cumbersome procedures and complex operations. As a satisfactory prognosis is determined by multiple factors in addition to surgery—the most valuable experience our team has summarized from this case is that accurate preoperative evaluation for specific patients based on detailed medical examination is of great importance. Strict patient selection and precise assessment of the size and quality of the remnant liver are pivotal to the decision-making process(14). Although experiences gained from previous studies have indicated that after extended hepatectomy involving 70 to 75% of the liver, the remnant liver can still function well in non-cirrhosis patients(15, 16), the strategy may need to be adjusted in the application of ELRA according to the specific situation. A major feature of ELRA is the longer CIT compared with ordinary LT(17). In addition, ELRA procedures are more complex than LT and hepatectomy so a longer operative time and more intraoperative blood loss seem inevitable(10). These are two poor prognostic indicators for LT recipients and hepatectomy patients because they may lead to graft loss due to the high incidence of postoperative biliary and arterial complications or severe hepatic dysfunction(18). Based on the above theory, the liver function, quality and estimated RLV of ELRA patients need to meet higher requirements. Livers with poor quality are less tolerant to cold ischemia-reperfusion injury. In addition, sufficient preoperative preparations, such as biliary drainage in patients with obstructive jaundice and nutritional support in

malnourished patients, are indispensable once the doctor and patient reach a consensus to perform the surgery. Without exaggeration, it can be considered that half the success will be achieved if suitable GCLM patients are screened out, but inaccurate preoperative assessments will force surgeons to discontinue the operation or will even cause fatal postoperative complications such as SFSS or ALF(19). Aji T and Dong JH et al described the largest case series of 69 patients with end-stage hepatic AE who underwent ELRA .The detailed methods and procedures applied to select patients preoperatively are explicitly described in the literature. We also adopted the same issues to evaluate the patient in this case report(14).

With greater benefit comes higher risk. Hepatobiliary surgeons must pursue more accurate and rapid surgical techniques to shorten the CIT and anhepatic phase. Under the condition of the liver in vitro, full exposure of the surgical area can help reduce the risk due to vascular or bile duct variation, which may not be detected before the operation. A longer anhepatic period can lead to circulatory and metabolic disorders. This is also a major test for the monitoring and intraoperative management of the anesthesiology department. Launching this type of major surgery can help improve the overall medical level of institutions and optimize the multidisciplinary diagnosis and treatment model. The lack of consensus and guidance on the application of ELRA drives us to accumulate more successful cases and precious experiences. For instance, Yiwen Qiu et al proposed their vascular infiltration-based classification as a tool to improve anatomic comprehension and facilitate surgical planning for ELRA(20). With the continuous accumulation of experience and the gradual improvement of technology, many so-called surgical penalty areas will also be broken through. The favorable implementation of this surgery can also enable surgeons to build confidence in dealing with more complex situations. Once successful, it will bring great significance in two aspects. For patients and their families, the painful clinical symptoms caused by the tumor will be controlled, and the quality of life will be dramatically improved. They will see improvements in mood and will achieve a better physical state that remains for the rest of their lives. From a medical point of view, an increased survival rate may provide a longer time for more postoperative treatment options and promote the progress of clinical research.

We must admit the limitation that many diseases, such as advanced cancer, still cannot be completely cured, although medical science has made rapid progress in recent years. However, it is a responsibility and obligation to create an opportunity for patients who never give up on themselves to extend their lives to fulfill their unfinished wishes. To a certain extent, this is also the meaning and motivation to encourage us to explore and push the surgical boundary. During the disease-free survival period, the female patient in our case spent irreplaceable days with her three cute children who filled her life with happiness and hope. She was deeply grateful for her brave choice and expressed her endless gratitude to our team.

In conclusion, the application of ELRA in radical resection of GCLM, as our case shows, could provide an alternative for selected patients. Surgeons' technical expertise combined with careful patient selection and perioperative management guaranteed by an experienced MDT could contribute to favorable clinical outcomes.

Declarations

Ethics approval and consent to participate

This report was carried out in accordance with the principles of the Declaration of Helsinki.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images and clinical data.

Availability of data and materials

The datasets used in the report are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Hong Wang wrote the manuscript. Chengcheng Zhang helped writing the manuscript. All authors administered the daily medical treatments in this case. Leida Zhang comprehensively supervised this study. All authors read and approved the final manuscript.

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All images were taken and post-processed by a professional photographer in our center

Abbreviations

GCLM: gastric cancer liver metastases **C-GCLM**: Chinese type for gastric cancer liver metastases **ELRA**: ex vivo liver resection followed by autotransplantation technique **SLV**: standard liver volume **RLV**: remnant liver volume **SFSS**: small-for-size syndrome **ALF**: acute liver failure **CIT**: cold ischemia time **LT**: liver transplantation **MDT**: multidisciplinary treatment **CT**: computed tomography **PET**: positron emission tomography **AFP**: alpha fetoprotein **CEA**: carcinoembryonic antigen **DR**: Digital Radiography **FDG**: β -2-[18 F]-Fluoro-2-deoxy-D-glucose **PET/CT**: positron emission tomography/ computed tomography **ICGR15**: indocyanine green retention rate at 15 min **SMA**: superior mesenteric artery **SHIVC**: Superior hepatic inferior vena cava **IHIVC**: Inferior hepatic inferior vena cava **PV**: Portal vein **HA**: hepatic artery

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Tables

Table 1 Detailed Basic Information of the Patient

item	value
Height	158CM
Weight	48KG
BMI	19.2
Obstructive Jaundice	Non
Zubrod-ECOG-WHO	1
Hypertension	Non
Diabetes	Non
Heart Disease	Non
Kidney Disease	Non
Liver Disease	Non
Breast Disease	Non
Genitourinary Diseases	Non
Infectious Disease	Non
Respiratory Function	Good
Mental State	Good
Neoadjuvant Chemotherapy	Non

Table 2 Preoperative Laboratory Data of The Patient

item	Value
WBC	6.77×10 ⁹ /L
RBC	3.62×10 ¹² /L
Hgb	111g/L
PLT	168×10 ⁹ /L
Neu	4.88×10 ⁹ /L
Neu%	(Neu%)72.1%↑
ALT	34IU/L
AST	32IU/L
ALP	37IU/L
GGT	12IU/L
ALB	38g/L
PALB	0.15g/L
TBA	16.2umol/L
DBIL	6.1umol/L
IDBIL	10.1umol/L
PT	12.50sec
INR	0.95
AFP	9850ng/ml
CEA	1.46ng/ml

Table 3 Postoperative Laboratory Data of The Patient

item	Value
WBC	5.66×10 ⁹ /L
RBC	4.07×10 ¹² /L
Hgb	121g/L
PLT	154×10 ⁹ /L
Neu	4.00×10 ⁹ /L
Neu%	(Neu%)70.6%↑
ALT	53.3IU/L↑
AST	53.5IU/L↑
ALP	113IU/L
GGT	17IU/L
ALB	42g/L
PALB	0.18g/L
TBA	17.3umol/L
DBIL	4.32umol/L
IDBIL	12.98umol/L
PT	11.40sec
PT-INR	0.85
AFP	2.8ng/ml
CEA	3.56ng/ml

Figures

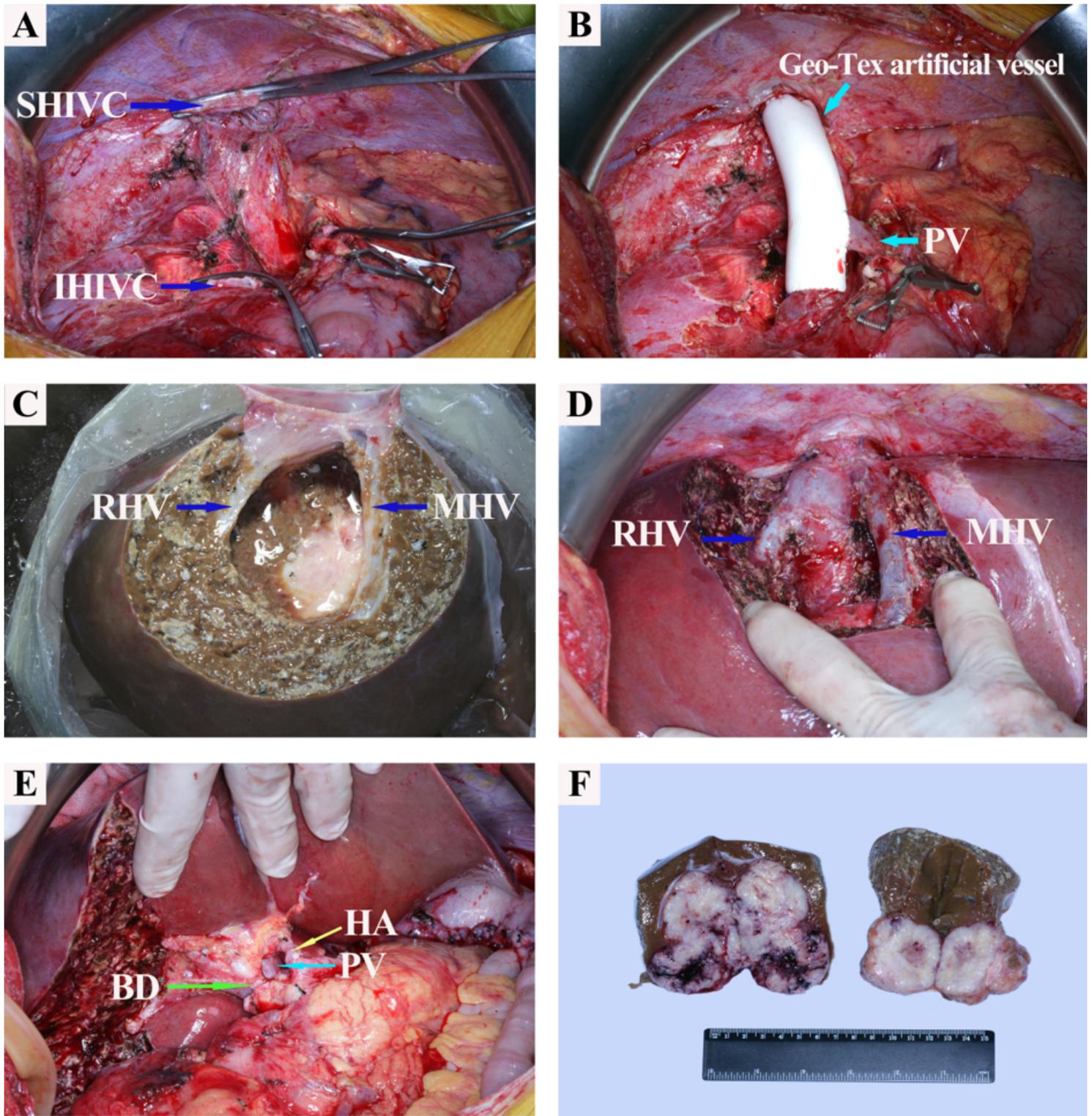


Figure 1

A. The liver was removed from the abdominal cavity; B. The PV was anastomosed to the Geo-Tex artificial vessel to construct portacaval shunt; C. The tumor has been completely resected from the isolated liver. RHV and MHV was intact; D. The remnant of the liver was implanted similar to OLT. After reconstruction, the RHV, MHV and IVC had unobstructed blood flow; E. The first hepatic hilum after reconstruction; F. The first hepatic hilum after reconstruction.

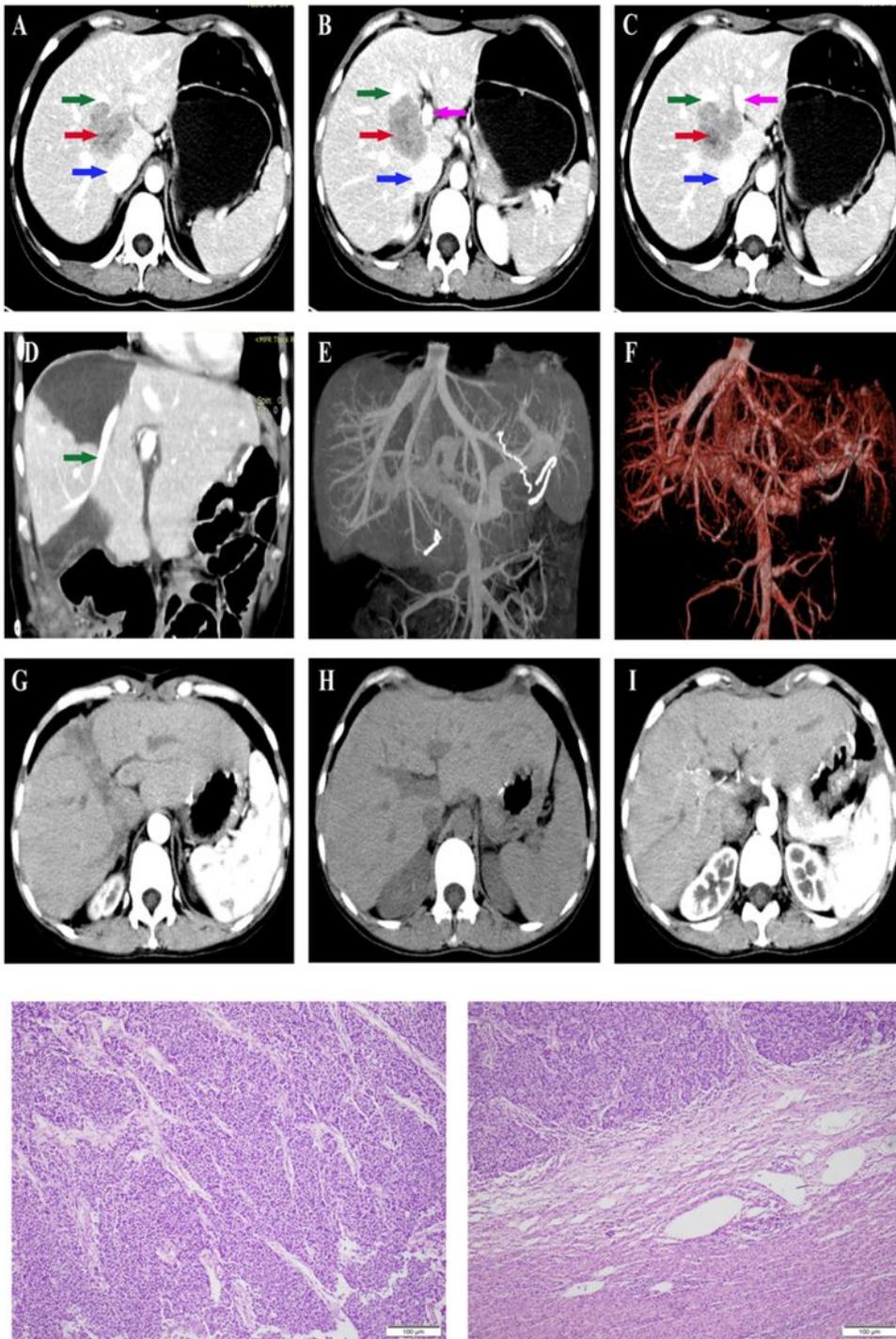


Figure 2

A-C. The tumor (pointed by the red arrow) was located between the first and second hila and it was adjacent to the MHV (pointed by the green arrow), IVC (pointed by the blue arrow) and the right branch of PV (pointed by the purple arrow); D-F. Postoperative imaging examination and upper abdominal angiography showed that the LHV, MHV, RHV, IVC, HA and PV were intact and Blood flow was unobstructed; G-I. CT results in the first, second and third year after operation showed that there were no

obvious signs of tumor recurrence. Microscopic section shows poorly differentiated gastric carcinoma (hepatoid adenocarcinoma with neuroendocrine differentiation) with liver metastases

Supplementary Files

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