

Application of ELRA in Radical Resection of GCLM : A Case Report

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Abstract Background Radical resection of gastric cancer liver metastases could increase the 5-year survival rate of GCLM patients. However, patients may lose the theoretical feasibility of surgery just due to the critical location of liver metastasis in some cases. **Case presentation** A 29-year-old female with chief complaints of chronic abdominal pain for one year. Abdominal CT and MRI examination suggested a mass of unknown pathological nature located between first and second hilars and the margin of lower segment of the right lobe of 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. Pathological property of liver mass remains unclear before surgery. She accepted 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 operation. Pathological examination of excised specimen indicated that gastrectomy with D2 lymph node dissection for primary gastric tumor 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 of 6 and 8 segments. Follow-up review showed no recurrence and metastasis within liver. The mother of three children miraculously lived a happy life and worked like normal people. **Conclusions:** Application of ELRA in radical resection of GCLM can help selected patients with intrahepatic metastases located in complex sites get a favourable clinical outcome.

Keywords: Ex-vivo Liver Resection Followed by Autotransplantation Technique;

Gastric Cancer Liver Metastases

1.Introduction

Previous studies have reported that the incidence of GCLM ranged 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 declared that radical resection (excision of both gastric tumors and liver metastases simultaneously) could increase the 5-year survival rate of GCLM patients ,timing and ideal surgical type still remain controversially debated. Based on the likelihood of a surgical treatment being successful , C-GCLM is put forward by the Chinese consensus on the diagnosis and treatment of GCLM(4). While we acknowledge tumor-free margin as the predictor of better outcome, a unavoidable question may emerge : what if the liver metastasis meets all the surgical qualification judged from size and scope according to the aforementioned classification criteria, but its location is so critical that it significantly increases the risk of surgery technically ? It would be regretful to give up the chance of radical resection because of limited eligible patients. Application of ELRA may provide alterations for this problem. Here is a case presentation about the treatment procedures and prognosis of a young female patient with GCLM , which showed application of ELRA in radical resection of GCLM can help patients with intrahepatic metastases located in complex sites get a favourable clinical outcome.

2.Case presentation

2.1 Preoperative assessment

The patient was a 29-year-old female with chief complaints of chronic

abdominal pain for one year and continuous weight loss of 5kg over 2 months prior to her admission. She recognized ovarian cystectomy, appendectomy and subtotal hysterectomy for uncontrollable hemorrhage in her past medical history . No special family history was provided except that her mother was diagnosed with squamous cell carcinoma of vulvar epithelium and the disease was cured according to her description . Other detailed basic information is displayed in Table1. On physical examination, a round mass about 7cm in diameter could be touched in the right upper abdomen which is smooth, pushable, hard and indistinguishable from adjacent tissue. Abdominal CT and MRI examination suggested a mass of unknown pathological nature located between first and second hilars and the margin of 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 manifestation of gastric cancer; 2. A mass shadow located at the first and second hepatic hilum and the lower right lobe of the liver. As increased FDG uptake is a sign of malignancy, whether it is liver metastasis or primary liver cancer remains to be identified. Result of puncture biopsy with gastroscopy guidance supported pathological diagnosis of gastric antrum intramucosal well-differentiated adenocarcinoma. ECG, chest DR and CT scan of the lower abdomen and pelvis showed no obvious abnormalities. Lab data presented a normal liver function and blood routine test (Table2). Tumor marker results showed that AFP was 9850ng/ml and CEA was 0.55ng/ml. Preoperative volumetric calculation was achieved by using 3D visualization imaging. Remnant Liver-to-Standard Liver Volume Ratio was 56%. ICGR15 was 2.1%.

Preoperative Child-pugh score was 3. Due to the unknown nature and special location of the mass in 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 operation and careful consideration, the patient decided to accept the ELRA combined with radical resection of gastric cancer simultaneously .

2.2 surgical procedure

A tumor protruded liver capsule with unclear borders and uneven surface was found in the right liver during abdominal exploration. It was hard, pale and has tight adhesion to the surrounding omentum. Consistent with preoperative imaging findings, the tumor extended to the junction of left and right liver lobe and was adjacent to the vena cava. Intraoperative frozen biopsy of liver mass was performed and the result was supportive of poorly differentiated malignant tumor. Presence of intrahepatic micro lesions was rule out by intraoperative ultrasound. Results of intraoperative exploration and wish of patient made us perform the ELRA combined with radical resection of gastric cancer as 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 done with ice-cold solution at 4 °C and UW solution via intact portal vein. At the same time, temporary channel was established between SHIVC and IHIVC with internal diameter 2cm Geo-Tex artificial vessel. PV was also anastomosed to the vessel to construct portacaval shunt. After the intrahepatic tumor and target liver segment have been 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. Observation of normal liver surface color after reperfusion was commonly done, and surgeons usually confirm the bile outflow before bile duct anastomosis. Some of intraoperative photos were presented in Figure 2. As we performed the ex vivo liver resection on the back table, the 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 symptomatic treatment after operation such as gastrointestinal decompression, abdominal drainage, anti-infection, nutritional support and so on. She underwent bile leakage at fifth day after 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, and hemorrhage occurred. She was successfully discharged on the 20th day after operation. Postoperative pathological examination of excised specimen indicated that gastrectomy with D2 lymph node dissection for primary gastric tumor 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 of 6 and 8 segments. The patient received 6 courses of XELOX chemotherapy after rehabilitation from surgery, during which no serious adverse reactions and treatment discontinuation occurred. Follow-up review showed there were no obvious signs of tumor recurrence and metastasis within abdomen and

liver to date. Selected postoperative abdominal CT images and lab data were displayed in Figure 3 and table 3.

3. Discussion and Conclusions

As an advanced stage of gastric cancer , GCLM is often translobal, multifocal or even diffusely spread, and often 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 surgical resection rate so low that there is no multicenter clinical trial with large samples on the significance of liver resection for GCLM and well-established criteria 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 patients with GCLM can benefit from radical resection(6-9). According to follow-up results, the patient we reported also obtained good prognosis and lived well-quality life.

Both the definitions of type I and II include a criterion: "Technological resectability of liver metastases judged by a hepatobiliary surgeon" according to the C-GCLM , while it emphasizes surgery should be performed only when R0 resection is anticipated(4). Here comes the aforementioned question: what if the size and scope of the liver metastasis comply with the standard, but its anatomical complexity puts the hepatobiliary surgeon into a dilemma ? The most common situation is that the tumor locates deeply in the liver and have extensive involvement with the main hepatic veins or retrohepatic vena cava. Conventional radical resection is extremely hazardous due to potential risk of uncontrollable hemorrhage and long ischemia time(10). This type of tumor are usually called unresectable tumor because it is impossible to be completely removed with

conventional surgery(11) . We can infer that ELRA may overcome this issue from our case report. It masterly broke through the technical bottleneck caused by the special location of tumor in traditional hepatectomy and allowed the hepatobiliary surgeons to perform precise liver tumor resection and effective vascular reconstruction 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 which have been reported systematically in many literatures 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 realize that ELRA is a challenging and time-consuming surgery with cumbersome procedures and complex operations. As satisfactory prognosis is determined by multiple factors besides 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 for size and quality of the remnant liver are pivotal to decision-making process(14). Although experiences gained from previous studies have indicated that after an 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 ERLA according to the specific situation. A major feature of ERAT is the longer CIT compared with ordinary LT(17). Besides, procedures of ERAT are more complex than LT and hepatectomy so that longer operative time and more intraoperative blood loss seems inevitable(10). These are

two poor prognostic indicators for LT recipients and hepatectomy patients because they may lead to graft loss for high incidence of postoperative biliary and arterial complications or severe hepatic dysfunction(18). Based on above theory, the liver function, quality and estimated RLV of ELRA patients need to meet higher requirements. Liver with poor quality is less tolerant to cold ischemia-reperfusion injury. It can be considered with no exaggeration that you get the half success if you screen out the suitable GCLM patient but inaccurate preoperative assessment will force surgeon to discontinue the operation or 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 .Detailed methods and procedures applied to select patients preoperatively are explicated in the literature. We also adopted the same issues to evaluate the patient in this case report(14).

Sufficient preoperative preparations, such as biliary drainage in patients with obstructive jaundice and nutritional support in malnourished patients, are indispensable without a doubt once the doctor and patient reach a consensus to perform the surgery. The competent physician needs to make the patients fully aware of the significance of strictly following the doctor's instructions and reviewing on time before they leave hospital. When the physical condition recovers well, patients should adhere to adjuvant chemotherapy according to the oncologist's advice to consolidate the treatment outcomes.

Launching this type of major surgery can help improve the overall medical level of institutions and optimize the multidisciplinary diagnosis and treatment model. With continuous accumulation of experience and gradual improvement of

technology, many so-called surgical penalty areas will also be broken through. The favourable implementation of such 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 are controlled and the quality of life is dramatically ameliorated. They would have a calmer mood and a better physical state to arrange for the rest of their lives. From a medical point of view, increased survival rate may provide longer time for more postoperative treatment options and promotes the progress of clinical research.

We have to admit the limitations that many diseases such as advanced cancer still cannot be completely cured although medical science has made rapid progress in recent years. But it is the 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 limits. 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. The lack of consensus and guidance on the application of ELRA drives us to accumulate more successful cases and precious experience. For instance, Yiwen Qiu et al proposed their vascular infiltration-based classification as a tool to improve the anatomic comprehension and facilitate surgical planning for ELRA(20).

In conclusion , application of ELRA in radical resection of GCLM as our case shows could provide one 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.

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

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

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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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Table 1 Detailed Basic Information

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 Lab Data

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 2 Postoperative Lab Data

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

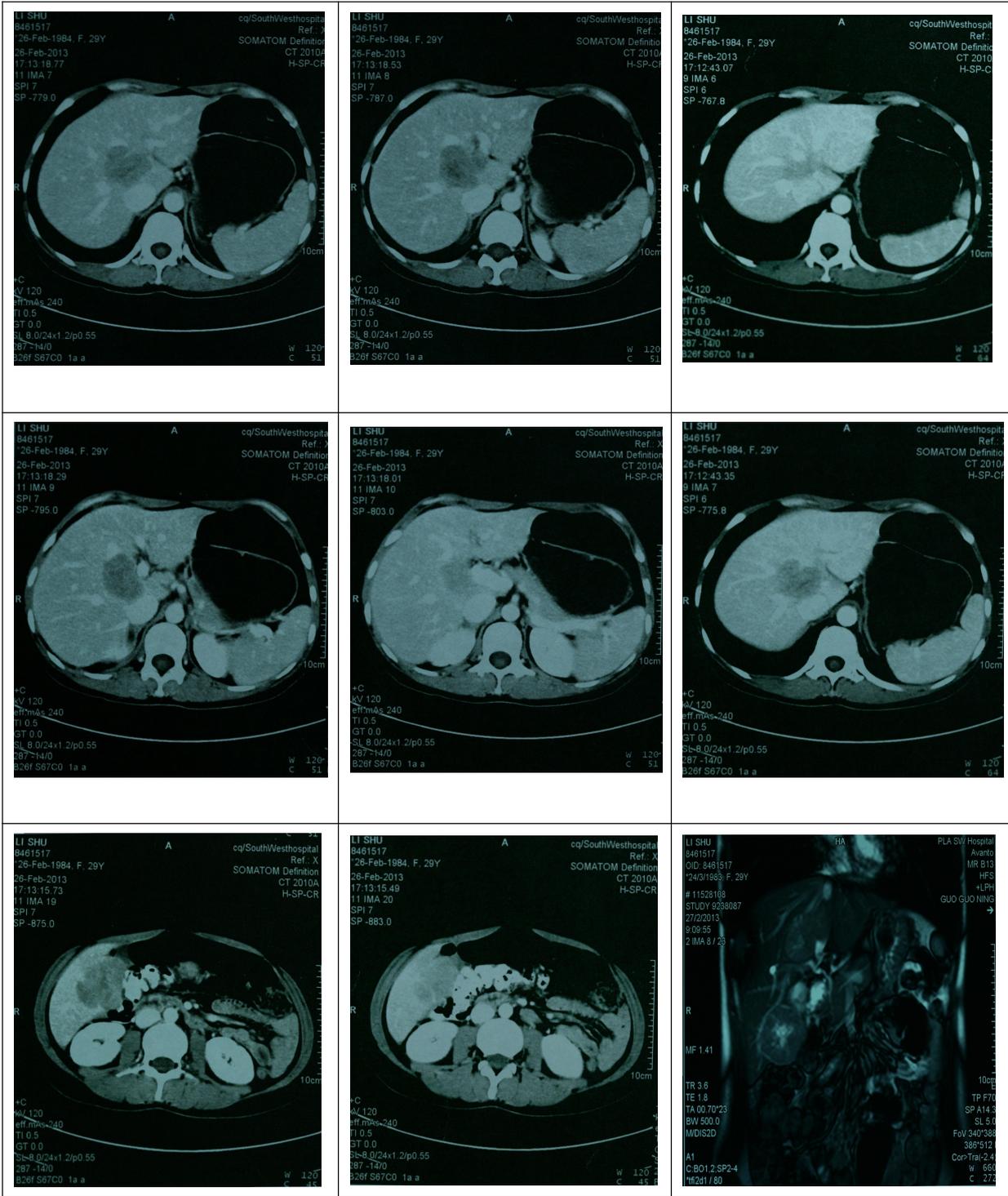


Figure 1 Selected Preoperative Abdominal CT Image

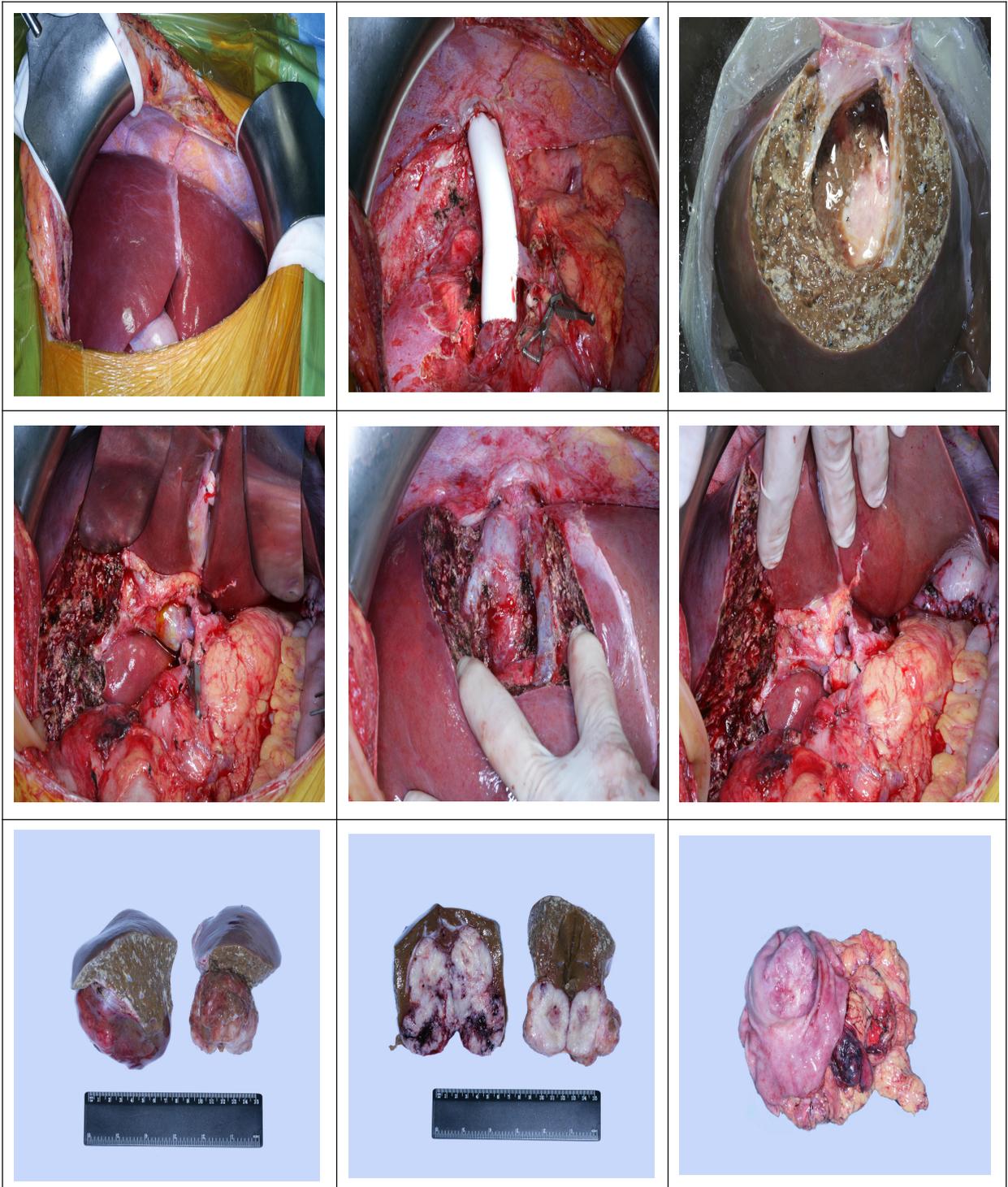


Figure 2 Selected Intraoperative Photos

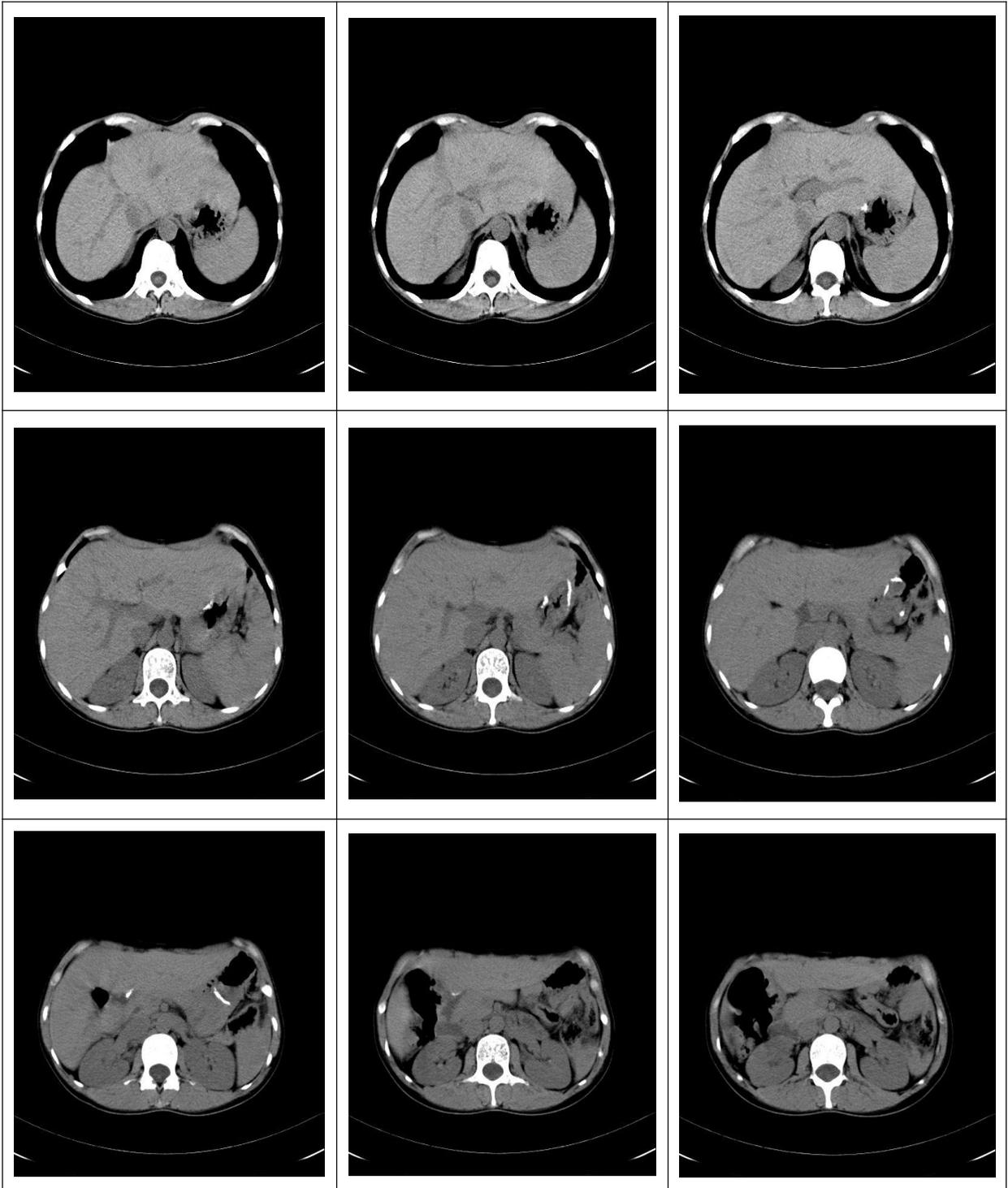


Figure 3 Selected Postoperative Abdominal CT Image

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