Resection of Giant Liver Metastasis of Gastrointestinal Stromal Tumor Using Intraoperative Ultrasound Guidance

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Abstract

We present the case of a 37-year-old woman with a history of gastrointestinal stromal tumor located in the jejunum, classified AFIP: 6a, admitted to our center for synchronous hepatic metastases. The oncological assessment performed after 12 months, in which Imatinib was administered, revealed a stable disease. The CT examination revealed a solitary hepatic metastasis, 14 cm in diameter, located in segments V and VIII, occupying partially segments IV, IV and VII, with an effect of mass on the portal bifurcation, the right hepatic vein, and the umbilical vein, which invaded the median hepatic vein. We considered it feasible to apply the vascular R1 resection concept, performing a central limited, non-anatomical, ultrasound-guided hepatectomy to allow the separation of the tumor from the right hepatic vein and the umbilical vein. Thus, we sacrificed only the portal pedicles of segments V and VIII, and we preserved partially these segments to avoid the risk of post-resectional liver insufficiency. Currently, with a follow-up of 53 months, we support the concept of ultrasound-guided hepatectomy R1 vascular in the context of systemic treatment with tyrosine kinase inhibitors, for the metastases of gastrointestinal stromal tumors.
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Cuvinte cheie: resectie hepatică, ghidaj ecografic intraoperator, tumoră stromală gastrointestinală
GIST, hepatectomie centrală

Abstract
We present the case of a 37-year-old patient with a surgical history of a gastrointestinal stromal tumor with jejunal location, AFIP classification 6a, hospitalized in our center for synchronous liver metastases. The oncological assessment performed after 12 months from surgery for primary tumor, during which Imatinib was administered, reveals stable disease. CT scan showed a single very large centrally located liver metastasis, 14 cm in diameter, involving segments V and VIII IV, IV and VII, compressing the main portal bifurcation, right hepatic vein, umbilical (scizural) vein and left hepatic vein, invading the middle hepatic vein. We considered it feasible to apply the concept of R1 vascular resection, performing a limited, non-anatomical, ultrasound-guided central hepatectomy, allowing detachment of the tumor from the right hepatic vein and from the umbilical vein. Thus, we sacrificed only the ventral portal pedicles of segments V and VIII and partially preserved these segments to avoid the risk of post-resection liver failure. Currently, the patient is disease-free after 53 months, supporting the concept of ultrasound-guided R1 vascular resection, in the context of systemic therapy with tyrosine kinase inhibitors for metastases of stromal gastrointestinal tumors.

Key words: liver resection, intraoperative ultrasound guidance, gastrointestinal stromal tumor
GIST, central hepatectomy

Introduction
Liver metastases of gastrointestinal stromal tumors (GLM) can grow to impressive dimensions, and invade vascular structures, thus the need to perform technically demanding ultrasound-guided liver resections. The present video shows a clinical case that benefitted from such type of resection.

Case Report
A 37-year-old woman (from a rural environment, no tertiary education), without relevant medical and surgical history, admitted on an emergency basis, for a syncopal episode associated with diffuse abdominal pain. Laboratory tests showed a hypochromic microcytic anemia (7 g/dl). Contrast-enhanced CT-scan revealed a hemorrhagic jejunal tumor (84 mm by 70 mm in size) with a single large synchronous liver metastasis (140 mm by 120 mm in size, occupying segments V and VIII and partially segments IV, IV and VII, with mass effect on the portal bifurcation, right hepatic vein and umbilical vein, all of which remain permeable, and invading the middle hepatic vein. A jejunal segmental enterectomy with end-to-end anastomosis (alongside the resection of invaded the mesentery and epiplooon) was performed in an emergency setting, for the primary jejunal loop tumor. We considered d’emblée resection prohibited: due to the emergency setting, the technical complexity of the prospective liver resection and the absence of any complication related to the liver metastases. Immunohistochemistry showed a GIST, prognostic group 6a (>5 mitoses/50 HPF), CD117, CD34, SMA, S100, DOG1 positive; and a Ki67 index of 20%. After debate, our institute’s multidisciplinary team decided to initiate tyrosine kinase inhibitor (TKI) therapy with Imatinib 400 mg/day, considered nowadays a standard pre-hepatectomy approach (1). The 12-month oncological follow-up showed stable disease according to the RECIST criteria (2).
Preoperative liver volumetry revealed: total liver volume: 2543 cm$^3$; tumor volume: 1010 cm$^3$; volume of segments VI and VII, and tumor-free portion of segments V and VIII: 414 cm$^3$; volume of segments II and III: 158 cm$^3$.

The resection was carried by the means of a right thoraco-phrenolaparotomy (a J-shaped incision prolonged in the 9th right intercostal space), we adopted a parenchymal sparing R1 vascular resection approach, by performing a non-anatomical limited central hepatectomy using ultrasound guidance, by detaching the tumor off the right hepatic veins, umbilical (scissural) vein, main portal pedicles and the right anterior portal pedicle. In this way, we sacrificed the ventral portion of segment V and VIII while preserving the portal pedicles dorsal branches for these segments. The transection was performed using the crush clamping technique under ultrasound guidance. Vascular control by intermittent Pringle maneuver (9 intervals of 15 minutes with breaks of 5 minutes, except every 4th break which consisted in 10 minutes) was deployed.

**Results**

The operative time was 555 min, blood losses counted for 2500 ml and the number of transfused blood units was 3 MER. There were no intraoperative incidents. The postoperative course was marked by ascites remitted spontaneously on the 18th postoperative day (POD): the patient was discharged on 23rd POD. Histology and immunohistochemistry showed GLM with positive CD 117, DOG 1, and a Ki-67 Index of 20%, with mitotic count > 5 mitoses/50 HPF; Ki67 index of 20%, high liver tumor burden. Moreover, liver transplantation for metastatic GIST has been minimally employed and has limited utility (6). Therefore, we accepted R1 vascular resection in this case as the only strategy available for surgical treatment. Although, literature states the need of R0 resection (4), and NCCN guidelines do not specify the need for extensive margins (7), the acceptance of the R1 vascular resection concept in case of GLM may be criticized, due to the current lack of investigation. However, the long-term oncological result in our case supports the feasibility of R1 vascular resection strategy for GIST liver metastases, as already proven in case of colorectal liver metastases (8), hepatocellular carcinoma (9), but not for intrahepatic cholangiocarcinoma (10).

**Discussion**

Tyrosine kinase inhibitor (TKI) therapy is currently considered a standard prehepatectomy approach (1). Although the optimal timing of GLM resection continues to be debated, waiting 3 to 9 months after the initiation of TKI therapy is recommended, since this time frame usually represents the period of greatest radiological response (3). There are multiple studies suggesting that operating during periods of responsive disease or stable disease correlates to improved outcomes compared to progressive disease (4,5). To successfully intervene at the time of greatest response, the surgeon must closely follow the radiological response (1). A central anatomic hepatectomy would not have been feasible in this case due to insufficient remnant liver volume. R0 resection would have not been feasible in this case, even considering vascular reconstruction, because the tumor involved all major vessels and portal pedicles (all hepatic veins and both main portal pedicles). Liver transplant was also considered unfeasible, due to high recurrence risk suggested by the high primary tumor prognostic group (6a: >5 mitoses/50 HPF; Ki67 index of 20%), high liver tumor burden. Moreover, liver transplantation for metastatic GIST has been minimally employed and has limited utility (6). Therefore, we accepted R1 vascular resection in this case as the only strategy available for surgical treatment. Although, literature states the need of R0 resection (4), and NCCN guidelines do not specify the need for extensive margins (7), the acceptance of the R1 vascular resection concept in case of GLM may be criticized, due to the current lack of investigation. However, the long-term oncological result in our case supports the feasibility of R1 vascular resection strategy for GIST liver metastases, as already proven in case of colorectal liver metastases (8), hepatocellular carcinoma (9), but not for intrahepatic cholangiocarcinoma (10).

**Conclusion**

We consider ultrasound-guided liver resection in the context of TKI systemic therapy, the most appropriate way in approaching the technically demanding, large and vascular invasive GLM, in order to obtain negative
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resection margins, paying special attention to the response of TKI prior to liver resection, thus establishing the proper timing of surgery. Taking into consideration the high disease-free survival in this case, we recommend R1 vascular resection in case of GLM otherwise unresectable.

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