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AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Surgery* (*WJGS*, *World J Gastrointest Surg*) is to provide scholars and readers from various fields of gastrointestinal surgery with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGS mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal surgery and covering a wide range of topics including biliary tract surgical procedures, biliopancreatic diversion, colectomy, esophagectomy, esophagostomy, pancreas transplantation, and pancreatectomy, *etc*.

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CASE REPORT

Giant hepatic extra-gastrointestinal stromal tumor treated with cytoreductive surgery and adjuvant systemic therapy: A case report and review of literature

Michel Ribeiro Fernandes, Caroline Lorenzoni Almeida Ghezzi, Tomaz JM Grezzana-Filho, Flávia Heinz Feier, Ian Leipnitz, Aljamir Duarte Chedid, Carlos Thadeu Schmidt Cerski, Marcio Fernandes Chedid, Cléber Rosito Pinto Kruel

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Author contributions: Grezzana-Filho TJM, Feier FH and Leipnitz I were the patient's surgeons and contributed to manuscript drafting; Fernandes MR reviewed the literature and contributed to manuscript drafting; Ghezzi CLA analyzed and interpreted the imaging findings; Chedid AD and Cerski CTS pathology report, analyzed and provide the pathology pictures, Chedid MF and Kruel CRP were responsible for the revision of the manuscript for important intellectual content; all authors issued final approval for the version to be submitted.

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Abstract

BACKGROUND

Primary extra-gastrointestinal stromal tumors (E-GIST) of the liver are rare. The clinical presentation may range from asymptomatic to bleeding or manifestations of mass effect. Oncologic surgery followed by adjuvant therapy with imatinib is the standard of care. However, under specific circumstances, a cytoreductive approach may represent a therapeutic option. We describe herein the case of an 84-year-old woman who presented with a tender, protruding epigastric mass. Abdominal computed tomography scan revealed a large, heterogeneous mass located across segments III, IV, V, and VIII of the liver. The initial approach was transarterial embolization of the tumor, which elicited no appreciable response. Considering the large size and central location of the tumor and the advanced age of the patient, non-anatomic complete resection was indicated. Due to substantial intraoperative bleeding and hemodynamic instability, only a near-complete resection could be achieved. Histopathology and immunohistochemical staining confirmed the diagnosis of primary E-GIST of the liver. Considering the risk/benefit ratio for therapeutic options, debulking surgery may represent a strategy to control pain and prolong survival.

CASE SUMMARY
Here, we present a case report of a patient diagnosed with E-GIST primary of the liver, which was indicated a cytoreductive surgery and adjuvant therapy with imatinib.

CONCLUSION
E-GIST primary of the liver is a rare conditional, the treatment is with systemic therapy and total resection surgery. However, a cytoreductive surgery will be necessary when a complete resection is no possible.

Key Words: Extra-gastrointestinal stromal tumor; Primary gastrointestinal stromal tumor of the liver; Cytoreductive surgery; Debulking surgery; Case report

Core Tip: Extra-gastrointestinal stromal tumor (E-GIST) of the liver is a rare condition, but the clinical presentation and treatment is similar to GIST of digestive tract. We present herein a case of giant hepatic E-GIST in an oldest person already reported and treated by cytoreductive surgery. This case highlights because it contributes to discussion of treatment approach, such as, the management of large hepatic masses, especially in GIST, and patient who would not tolerate major surgical resections.

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INTRODUCTION

Gastrointestinal (GI) stromal tumors (GISTs) arise from the interstitial cells of Cajal, located in the GI mesenchyme[1,2]. However, GISTs have also been also encountered in other sites that lack these cells, including the mesentery, omentum, and abdominal wall, suggesting that pluripotent mesenchymal stem cells are responsible for the development of GISTs outside the GI tract[3]. GISTs are currently classified according to histopathological and immunohistochemical criteria, based on expression of the tyrosine kinase KIT (CD117, c-Kit) by tumor cells[4,5]. GISTs located outside the GI tract are appropriately known as extra-GIST (E-GIST), and represent 1% of all GISTs[6,7]. Herein, we report the management of a very large symptomatic E-GIST of the liver in an older adult.

CASE PRESENTATION

Chief complaints

An 84-year-old woman, Caucasian, was admitted to our hospital with persistent upper abdominal pain.

History of present illness

An 84-year-old woman, Caucasian, was admitted to our hospital with 3-mo history right hypochondrium and epigastric pain. There was no history of fever, jaundice, coluria and acholia or unintentional weight loss.

History of past illness

The patient had no history of hepatic or GI diseases, malignancy, or previous surgeries.

Grande do Sul.

Informed consent statement: Informed written consent was obtained from the patient for publication of this report and any accompanying images.

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Physical examination

Physical examination revealed a painful, protruding epigastric mass.

Laboratory examinations

Liver function tests were within normal range, hemogram (hemoglobin 7.2 and hematocrit 24.7) and hepatitis B, hepatitis C, and human immunodeficiency virus serology were negative. Ca 19-9 levels were elevated (220 U/mL), while serum α-fetoprotein, CA-125, and carcinoembryonic antigen were within normal limits

Imaging examinations

A GI workup including endoscopy and colonoscopy did not show any significant abnormality.

Computed tomography (CT) scan of the abdomen demonstrated a large (18.0 cm × 16.1 cm × 14.7 cm), heterogeneous hepatic mass, located in segments III, IV, V and VIII, with a solid peripheral component showing intense arterial enhancement and late-phase washout (Figure 1). Magnetic resonance imaging showed evidence of blood products within the liver mass. Dilation of the intra-hepatic bile ducts around the lesion was also observed (Figure 2).

MULTIDISCIPLINARY EXPERT CONSULTATION

A percutaneous tumor biopsy was performed. Histopathological analysis suggested an undifferentiated malignancy. Immunohistochemistry revealed liver cells with low mitotic index (10%). Thus, findings on imaging exams suggesting expansive tumor, well delimited and with preservation of vascular e biliary structures, despite the inconclusive biopsy, the hypothesis of GIST was considered. Pre-operative evaluation was performed according our protocol which was adapted from ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery.

FINAL DIAGNOSIS

Histopathological analysis of the tumor showed a fusiform cell neoplasm positive for CD117, CD34 and DOG-1 and negative for spinal muscular atrophy and S-100 protein on immunohistochemical staining. The specimen presented a Ki67 index of 10%, which confirmed the diagnosis of primary E-GIST of the liver with intermediate-grade malignancy (Figure 3).

TREATMENT

As the patient presented with progressive anemia and the lesion had a hemorrhagic component, the decision was made to perform transarterial embolization (TAE) of the tumor. There was no appreciable response, as well as mass effects symptoms were present, surgery was indicated. However, for complete resection of the tumor a left trissegmentectomy would be necessary. Considering the large size and central location of the lesion and advanced age of the patient, a non-anatomic complete resection was indicated. Ligation of the left hepatic artery was carried out. During tumor enucleation, the patient developed considerable bleeding and hemodynamic instability. Thus, a near-complete resection was performed (the posterior tumor capsule close to the raw surface of the liver was not removed) (Figure 4).

OUTCOME AND FOLLOW-UP

Postoperative follow-up was uneventful. After 6 mo, she remains asymptomatic and with no evidence of recurrent disease. An abdominal CT performed 6 mo after surgery demonstrated significant debulking of the mass (Figure 5).

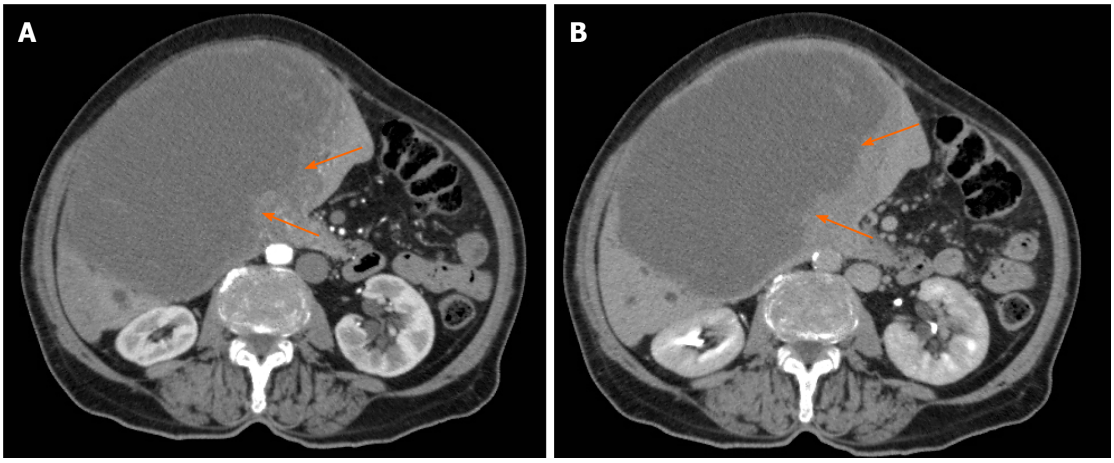

Figure 1 Abdominal computed tomography showing an expansive hepatic mass with a solid component (arrows). A: Intense arterial enhancement; B: Late-phase washout were present.

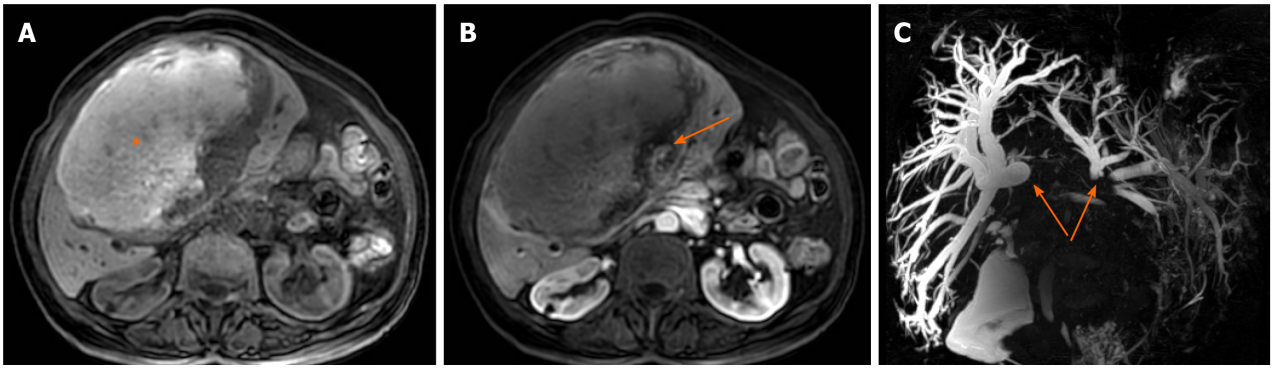

Figure 2 Magnetic resonance imaging showing a large, central, T1-hyperintense hepatic lesion. A: Blood products (asterisk); B: Arterial enhancement of the solid component (arrow); C: Magnetic resonance cholangiogram showing dilation of the intrahepatic bile ducts.

DISCUSSION

GISTs are the most common mesenchymal neoplasm of the GI tract, representing 0.1%-0.3% of all malignancies; they are typically found in the stomach (60%-70%), small intestine (20%-30%), colorectum (5%), and esophagus (< 2%)[4,8-10]. However, GISTs have been identified outside of the GI tract (E-GISTs)[6,7]. Primary hepatic E-GISTs are very unusual, with only 22 cases reported in the literature up to 2019[1,5,11-29] (Table 1). No previous reports of cytoreductive surgery for primary E-GIST of the liver were found.

GISTs presenting in the liver are usually metastatic until proven otherwise. There is no specific test able to define their primary or metastatic nature, and the diagnosis of primary hepatic E-GIST has to fulfill several conditions[15]. Endoscopic and imaging studies must show no evidence of GIST in the GI tract, absence of connection with the muscularis propria of the GI tract must be proven, and the patient must have no medical history suggesting resection of an overlooked or misdiagnosed GIST[3]. Diagnosis of a new GI tumor during the follow-up period also would preclude diagnosis of a primary GIST of the liver[15]. The patient reported in this paper has completed 6 mo of follow-up after surgery and, so far, all the aforementioned requirements for diagnosis of a primary hepatic E-GIST have been fulfilled.

The imaging picture of a primary E-GIST of the liver is a well-defined, heterogeneous, hypervascular lesion with areas of hemorrhage, necrosis, and/or cystic degeneration[30,31]. Thus, primary hepatic E-GISTs can be potentially misdiagnosed as other hepatic tumors, such as hypervascular metastasis, hepatocellular carcinoma and adenoma. Despite their rarity, primary hepatic E-GIST should be included in the differential diagnosis of primary liver lesions whenever a heterogeneous hypervascular liver mass is identified, especially in patients with no known primary neoplasia, no history of chronic liver disease, and no risk factors for adenoma[20].

Table 1 Clinical characteristics and location in selected patients with extra-gastrointestinal stromal tumor of the liver

Ref.	Year	Age/sex	Country	Presentation	Location	Size (cm)
Present	2020	84/F	Brazil	Abdominal pain + mass	Bilobar (III/IV and V/VIII)	16.2
Hu *et al*[14]	2019	79/F	China	Epigastric discomfort	RL	3.2
Joyon *et al*[15]	2018	56/M	France	Abdominal pain	Bilobar (VII/VIII and LL)	10
	2018	59/F	France	Abdominal pain + weight loss	RL	23
Carrillo *et al*[12]	2017	41/M	Spain	Abdominal pain + weight loss	RL (V/VI)	20
Lok *et al*[19]	2017	50/F	China	Abdominal pain	RL	15
Cheng *et al*[13]	2016	63/M	China	No symptoms	RL	15
Nagai *et al*[28]	2016	70/F	Japan	No symptoms	LL	6
Wang *et al*[29]	2016	61/M	China	No symptoms	Caudate lobe	7.3
Liu *et al*[18]	2016	56/F	China	No symptoms	LL + pancreas	2.2
Su *et al*[24]	2015	65/M	Taiwan	Malaise, abdominal pain, loss of appetite	LL	12
Bhoy *et al*[11]	2014	41/F	India	Abdominal pain, weight loss	RL (VI/VII)	15
Lin *et al*[17]	2015	67/F	China	No symptoms	RL	7.4
Mao *et al*[22]	2015	60/F	China	No symptoms	Bilobar (I, IV, V and VIII)	12.8
Kim *et al*[16]	2014	71/M	South Korea	No symptoms	LL	7
Louis *et al*[20]	2014	55/F	India	Abdominal pain, loss of appetite	Bilobar (II, III, VI and VIII)	14.5
Zhou *et al*[27]	2014	56/M	China	No symptoms	RL	10
Li *et al*[37]	2012	53/M	China	Abdominal discomfort	RL	20
Yamamoto *et al*[25]	2010	70/M	Japan	Loss of appetite	LL	20
Luo *et al*[21]	2009	17/M	China	No symptoms	RL	5
Ochiai *et al*[23]	2009	30/M	Japan	Abdominal fullness	Bilobar	27
De Chiara *et al*[5]	2006	37/M	Italy	No symptoms	RL (V)	18
Hu *et al*[1]	2003	79/F	United States	Shortness of breath, pleuritic chest pain	RL	15

M: Male; F: Female; RL: Right lobe; LL: Left lobe.

Complete surgical resection followed by adjuvant therapy with imatinib is the standard of care for localized GIST, but other therapeutic options have been proposed, depending on the initial presentation and clinical context. Cytoreductive surgery has been used to prolong survival and improve quality of life for patients with metastatic neuroendocrine and ovarian cancer[32,33]. However, there is a scarcity of studies analyzing the impact of alternative treatments for advanced GIST, especially those cases in which complete R0 resection cannot be achieved. Recently, it has been demonstrated that debulking surgery combined with adjuvant drug therapy prolongs overall survival of patients with metastatic primary GIST when compared with imatinib alone[34]. TAE is also recommended as an option to impair stromal tumor progression[35].

In this case, a giant hepatic GIST was observed in a very frail 84-year-old woman. TAE was indicated to reduce tumor burden, an anatomic liver resection was avoided, and a tailored therapeutic approach was recommended. Despite the hypervascular nature of the tumor, there was no significant shrinkage after TAE. It was unlikely that pain and symptomatic relief would be achieved by systemic therapy alone, which also has been associated with GI and/or intra-abdominal bleeding due to tumor degeneration in approximately 5% of giant GISTs[36]. Therefore, considering the risk/benefit ratio, tumor debulking surgery was indicated as a strategy to control pain and improve patient quality of life while avoiding the morbidity and mortality associated with a major liver resection. Six months after adjuvant therapy with imatinib, she is asymptomatic with little residual tumor, as shown in the last abdominal CT scan (Figure 5).

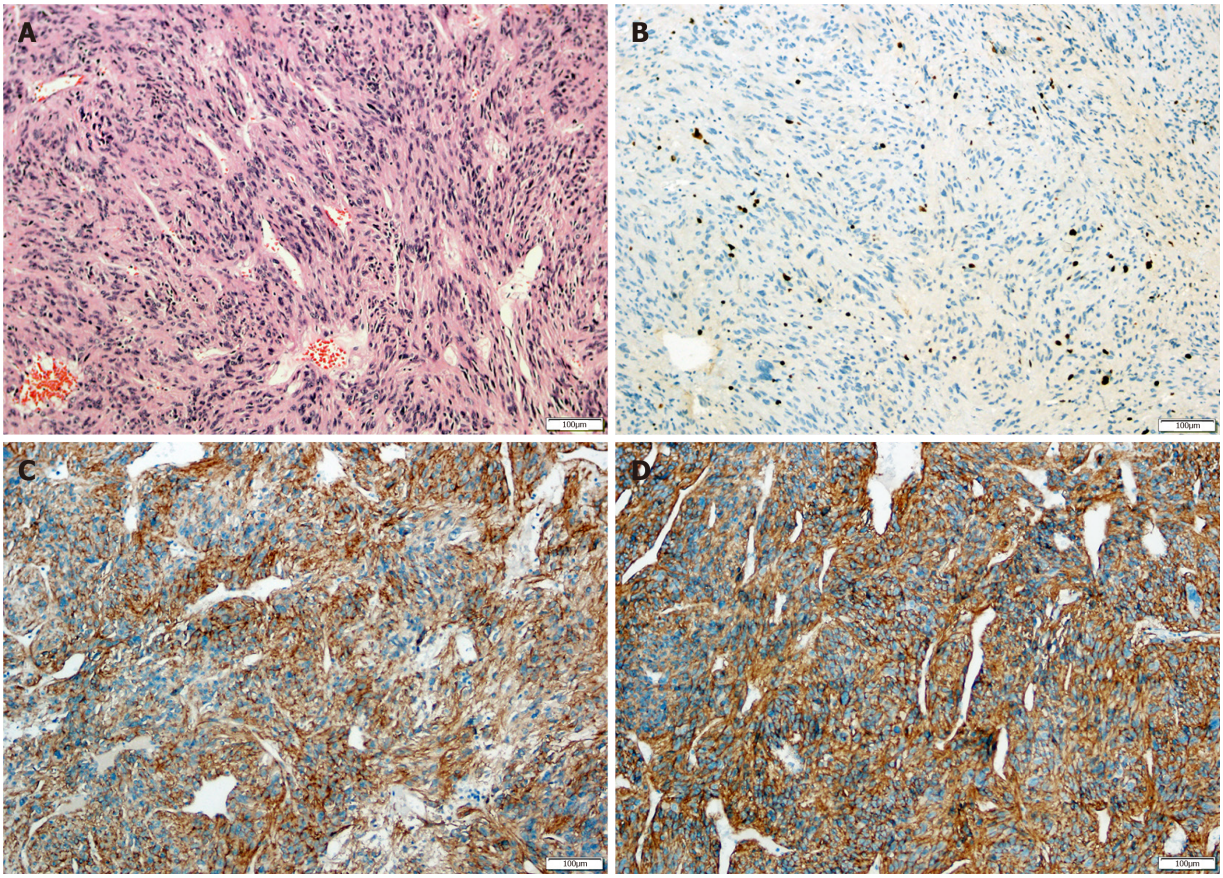

Figure 3 Histopathological examination. A: bundles of spindle-shaped cells in an irregular pattern, eosinophilic cytoplasm, with normal hepatic parenchyma in peripheral areas in hematoxylin-eosin staining (magnification, × 100); B-D: Immunohistochemical analysis showed that the tumor was positive for Ki-67 (B), CD-117 (C) and DOG1 (D) (magnification, × 100).

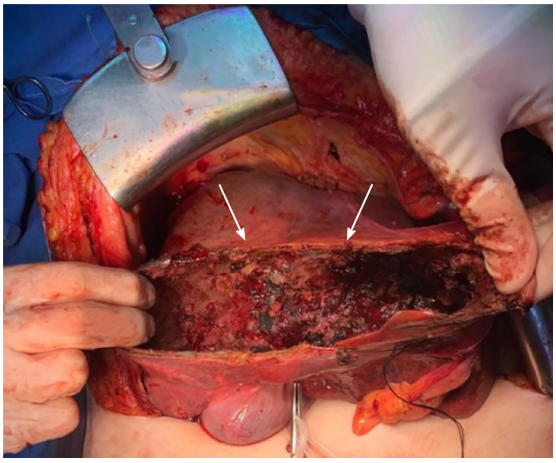

Figure 4 Area of tumor resection. Arrows show the residual tumor capsule.

CONCLUSION

E-GIST must be considered in the differential diagnosis of any large, hypervascular liver mass. Preoperative histopathological and immunohistochemical diagnosis is important to aid in therapeutic management. Aggressive strategies such as R0 surgical resection should always be the first choice, but a customized approach including a combination of TAE, cytoreductive surgery, and adjuvant or neoadjuvant systemic pharmacotherapy might be considered as an alternative, especially in high-risk patients.

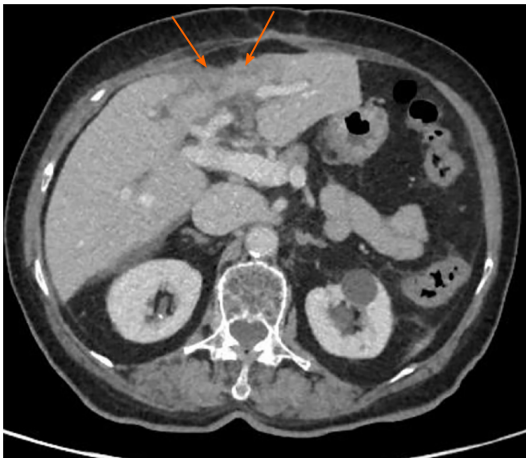

Figure 5 Follow-up abdominal computed tomography scan showing significant reduction of the hepatic mass (arrows), its solid component, and the mass effect on adjacent structures.

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