



# Palliative Pancreaticoduodenectomy for Giant Duodenal Gastrointestinal Stromal Tumor: Report of a Case

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## Abstract

Gastrointestinal stromal tumors (GISTs) represent less than 1% of all cases of abdominal neoplasms. The stomach (60%) and small intestine (35%) are the most common sites, the duodenum being affected in less than 5% of cases. A 53-year-old female patient presented to outpatient clinic with a 3-month history of diffuse abdominal pain and increased abdominal volume. CT scan revealed a giant (22.7 cm × 13.7 cm × 12.1 cm) tumor in the head and uncinate process of the pancreas and duodenum with several liver and several lung metastases. Regarding the presence of symptoms of abdominal compression, pancreaticoduodenectomy was performed. Pathology report revealed GIST with extensive necrosis and moderate nuclear atypia, without pancreatic invasion. There were four mitoses per 50 large fields, Immunohistochemical staining was positive for CD117 and CD34. Ki67 was 10%. The patient was discharged on 22<sup>nd</sup> postoperative day and is being treated with Imatinib (400 mg/daily). She is free of symptoms and has gained 2 kg of weight over the first three postoperative months. There is no consensus on the ideal treatment for patients with metastatic GISTs along with unresectable metastatic disease: palliative surgical resection versus therapy with tyrosine kinase inhibitors. The decision whether or not to resect the primary GIST in the context of metastatic disease should be performed on a case-by-case fashion, in which the severity of the symptoms or bleeding complications, tumor size and mitotic rate should be taken into account for establishing a tailored strategy.

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**Keywords:** Duodenum; Gastrointestinal stromal tumor; Metastases; Palliation; Pancreaticoduodenectomy

## Abbreviations

CT scan: Computed Tomography Scan; GIST: Gastrointestinal Stromal Tumor; PD: Pancreaticoduodenectomy

## Introduction

Gastrointestinal stromal tumors (GISTs) are rare gastrointestinal tumors, representing less than 1% of all cases of abdominal neoplasms. Each year, approximately 10 million to 20 million cases of GIST are diagnosed worldwide, with an average age of 55-60 years [1].

GISTs are supposedly originated from Interstitial Cajal cells or their precursors located throughout the muscular wall of the gastrointestinal tract. Interstitial Cajal cells are responsible for communication between the muscle layer and the mioenteric layers [1,2]. Most GISTs occur after Tyrosine Kinase receptor mutations, specially c-KIT, CD117 and Platelet-derived growth factor receptor.

When overexpressed, these proteins promote uncontrolled cell proliferation and resistance to apoptosis [3]. GISTs are found more commonly in the stomach (60%) and small intestine (35%) [3]. Duodenal GISTs represent less than 5% of cases [4]. Most cases of duodenal GISTs occur sporadically, but 5% occur in the context of familial syndromes as Neurofibromatosis type 1 [2]. Here we report the rare case of a giant duodenal GIST.

## Case Report

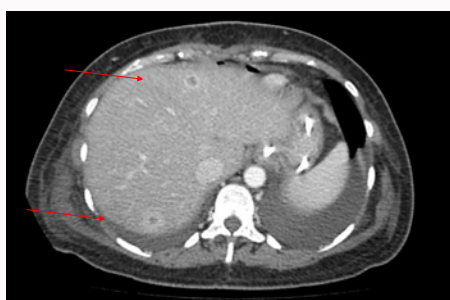
A 53-year-old female patient, with well controlled asthma, presented to our outpatient clinic with



**Figure 1:** CT scan of the abdomen (coronal view) revealing a large tumor located adjacent to portal vein with compression of adjacent structures and no cleavage plane with de head and uncinated process of the pancreas.



**Figure 2:** CT scan of the abdomen (sagittal view) showing a large tumor occupying a large extension of the abdominal cavity.



**Figure 3:** CT scan of the abdomen (axial view) showing liver metastases (red arrows).

a 3-month history of diffuse abdominal pain and increased abdominal volume. She denied weight loss or any changes in bowel habits and no jaundice was present. Abdominal CT scan revealed a giant (22.7 cm × 13.7 cm × 12.1 cm) tumor in close contact with the head and uncinate process of the pancreas and duodenum (Figure 1 and 2). The tumor was heterogeneous and lobulated, with predominantly peripheral enhancement with hypervascular areas and foci of calcification. Main pancreatic duct had 0.8 cm diameter and there was gastric distension. The head of the pancreas and uncinate process did not exhibit any cleavage plane with the tumor. CT scan of the abdomen also revealed several hepatic nodules, being the biggest a 3cm liver lesion (Figure 3). A Chest CT scan showed nodular opacities with soft tissue density



**Figure 4:** CT scan of the abdomen (axial view) displaying 50% duodenal compression by the large GIST tumor.

in the lower portions of the lungs suggestive of metastases.

Esophagogastroduodenoscopy was negative for duodenal invasion, but revealed gastric and duodenum extrinsic compression by the tumor (50% of the lumen of the lumen, as evidenced by CT scan of the abdomen) (Figure 4). Pathology report of percutaneous biopsy was positive for fusiform cell proliferation and fragments of smooth muscle GIST with a 5% Ki67 index.

Case management was discussed with medical oncology team at Hospital de Clinicas of Porto Alegre tumor board conference. Regarding the presence of evident symptoms of abdominal compression, the patient underwent surgical exploration. Local resection of the duodenal GIST was attempted. However, the tumor rupture occurred intraoperatively. Concerning the tumor rupture and also uncertainty regarding pancreas head invasion by the tumor, pancreaticoduodenectomy (PD) was performed.

Pathology report revealed a GIST with extensive necrosis and moderate nuclear atypia. There were no signals of pancreatic invasion and there were 4 mitoses per 50 high power fields. Immunohistochemical staining was positive for CD117 and CD34, being negative for S100, actin, DOG1, desmin and calponin. Ki67 was 10%.

A bile leak occurred postoperatively, being managed conservatively with success. The patient was discharged home on 22<sup>nd</sup> postoperative day. She is being treated with Imatinib (400 mg/daily) and is now free of symptoms. She also has gained 2 kg of weight over the first 3 postoperative months.

## Discussion

GIST comprises a very rare etiology for all periampullary neoplasms. Clinical manifestations of GISTs may vary widely, depending on tumor size, location, and growth rate and should be considered when choosing the best approach for palliative treatment. The most prevalent symptoms are those related to direct compression of adjacent structures such as fullness, early satiety and pain. In some cases, a palpable mass may result in bleeding, anemia, melena and hematemesis. The authors of the present study did not find any previous literature report of PD utilized as palliative treatment for metastatic GIST.

An R0 surgical resection is the only potential curative treatment for GISTs [5-7]. Local or wedge duodenal resection is the treatment of choice whenever possible as dictated by the tumor size and location [6,7]. Because GISTs rarely infiltrate at microscopic levels and rarely demonstrate lymph node dissemination, wide resection margins and regional lymphadenectomy are not necessary [8]. Large GISTs, and

tumors located in the second portion of the duodenum increase the odds for PD.

A recent meta-analysis reported on outcomes of 260 patients with duodenal GIST from eleven studies [7]. PD was performed in 98 out of the total 260 patients. As compared to local resection, PD was associated to a higher risk of postoperative morbidity, including both minor and major complications (48.3 for PD vs. 20.7 % for local resection, RR 2.34; 95% CI 1.61-3.41).

Shen et al. [2] reported on the outcomes of 74 patients presenting with duodenal GIST. Only 2 of them had liver metastasis. Fifty-seven patients were treated with either local or segmental duodenal resection. The remaining 17 patients had their GIST treated through PD. Patients who had PD were more likely to experience a higher risk of postoperative complications. 1, 3 and 5 years disease-free survival rates were 93.9%, 73.7% and 69%, respectively.

Up to 50% of all patients with GIST have metastases at presentation. The most common sites of metastasis include the peritoneum and the liver [9]. Whenever feasible, resection of the primary tumor along with resection of all metastatic disease is indicated. However, PD is only rarely performed in patients with distant metastases. For instance, only 2 out of the total 74 patients of the series reported by Shen et al. [2] had distant metastasis at the time of diagnosis. Resection of duodenal GIST along with simultaneous resection of liver metastases was accomplished in only 1 patient of these patients. Beham et al. [1] reported on the outcomes of 13 patients who received operative treatment for duodenal GIST. Only 1 patient out of the 13 patients had distant metastases.

There is no consensus over the ideal treatment for patients with metastatic GISTs with severe symptoms. There are two main possibilities to achieve this goal: palliative surgery or tyrosine kinase inhibitors, such as imatinib. Cytoreductive surgery plays an important role in relieving symptoms, especially in extreme cases such as faced by our patient. In addition to that, debulking procedures reduce the total amount of cells exposed to Imatinib therapy, which decreases the likelihood and rate of developing resistant tumor clones [10].

Since there is some evidence than neoadjuvant therapy may reduce tumor burden, Imatinib was considered as neoadjuvant therapy for this patient [11,12]. However, based on the very large tumor size, the 3 month history of compressive symptoms and the good performance status of the patient, direct surgical approach were preferred. Also, there is a potential for complications during treatment with molecular targeting agents in patients with GIST [13]. A local resection was attempted but could not be accomplished because of the very large tumor size. Intraoperative tumor rupture and also uncertainty concerning pancreas head invasion by the tumor have motivated performance of PD. Imatinib was started postoperatively. Gastrointestinal stromal tumor (GIST) has been considered radiation-resistant. Therefore, radiation therapy was accomplished to the patient

During the last three decades, improvements in operative technique, anesthesia care and intensive support have promoted progressive improvements in postoperative outcomes of PD, contributing to establish the PD as a safe and effective procedure [14-16]. PD showed to be effective as palliation for pancreatic adenocarcinoma, with an in-hospital mortality rate of 1.6% [17]. However, Palliative PD is not generally indicated, except when GIST cause significant symptoms as the case reported herein. The goals of

palliative PD are to allow better oral food intake, relief jaundice and pain and allow the patient to be discharged from the hospital, with a minimum necessity of health support for the longer period of time possible [15,17].

Although not indicated for all metastatic GIST, PD was successfully performed in the reported case. All goals of palliative PD have been achieved in the present report. Residual liver and lung tumor has been treated with Imatinib, in order to control metastatic disease. However, palliative PD should be considered in selected cases, as a rescue procedure for those patients in which systemic therapy may not be able to achieve pain control or bleeding.

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