Gastrointestinal Stromal Tumors (GISTs) of the Stomach: An Infrequent Disease with Difficult Preoperative Diagnosis

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Citation

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Abstract

Gastrointestinal stromal tumors (GISTs) are the most frequent mesenchymal tumors of the gastrointestinal tract. The stomach is the most common site of these tumors. We report a case of a 62-year-old woman with upper abdominal pain and anaemia. Preoperative gastroscopy, abdominal computed tomography and endoscopic ultrasonography showed a submucosal tumor in the gastric antrum. We performed a stapled antrectomy associated with Roux-en-Y gastrojejunostomy reconstruction. Postoperative histologic examination revealed the spindle-shape cells characteristic of GISTs. The postoperative course was uneventfull and after 12 month the patient has no recurrence. Preoperative diagnosis is difficult to establish because usually these tumors are asymptomatic and therefore, they are not suspected. Only inmunoreactivity is able to differentiate GIST from other mesenchymal tumors. Surgical resection is a safe and effective treatment. Chemotherapy with imatinib is also recommended.

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal or non-epithelial tumors of the gastrointestinal tract. The term gastrointestinal stromal tumor was first proposed by Mazur and Clark in 1983[1]. These tumors are reported to originate from interstitial Cajal cells histologically[2]. The incidence is 5-10 cases per million of population[3]. They usually present in older adults, with the median age at presentation of around 60 years as our patient. GISTs constitute between 0.1% and 1% of all gastrointestinal malignant tumors[4].

GISTs may arise anywhere in the wall of the gastrointestinal tract; however, most of them occur in the stomach. These tumors are frequently asymptomatic and when they produce symptoms they are usually not specific which hinders their early detection. For this reason many cases (50-60%) are discovered at a locally advanced stage or with distant metastasis. Sometimes, they are also detected incidentally during a workup for unrelated conditions[5].

Complete surgical excision is the treatment of choice for localized disease. Imatinib mesylate, a synthetic tyrosine kinase inhibitor is now considered as a useful adjuvant agent.

We present a case of GIST of the stomach with the aim to discuss clinical aspects, diagnosis and treatment of this entity usually asymptomatic with difficult preoperative diagnosis.

CASE REPORT

A 62-year-old woman with personal antecedents of arterial hypertension, diabetes type 2, chronic hepatopathy secondary to virus hepatitis B, chronic anaemia and vitamin B12 deficit, was remitted to our service by the gastroenterology service for surgical extirpation of a gastric tumor, found at digestive endoscopy carried out for dyspepsia, anaemia and constitutional syndrome of long evolution. Physical exploration showed a patient thin and pale. The abdomen was soft without masses and not painful.

Laboratory data showed the following: Hemoglobin 11.8 g/dl, hematocrit 35.4%, red blood count 3,700.000/µL, platelets 175.000/µL, white blood count 7.500/µL, neutrophils 82%, lymphocytes 12%, partial thromboplastin

time 32 seconds, prothrombin time 13.9 seconds, blood urea nitrogen 53 mg/dl, creatinine 1.4 mg/dl, aspartate amninotransferase 64 IU/l, alanine aminotransferase 75 IU/l, total bilirrubin 0.8 mg/dl, sodium 143 mEq/l and potassium 4.2 mEq/L. The serum carbohydrate antigen 19-9, carcinoembrionic antigen and alpha-fetoprotein antigen were normal. Breathe test was negative for Helicobacter pylori. Abdominal ultrasonography did not show any alteration. Thorax x-ray revealed arthrosis of the dorsal column and a calcified aorta. Upper endoscopy revealed cardial incompetence, a polyp in the gastric fundus and a submucosal tumor located in the gastric antrum. Endoscopic ultrasonography showed a subepithelial lesion in the gastric antrum suggestive of a stromal tumor type GIST (Fig. 1). Abdominal CT revealed a submucosal lesion in the gastric antrum and small peripancreatic adenopathies (Fig. 2).

Figure 1

Figure 1: Gastroscopy and endoscopic ultrasonography showed a subepithelial lesion in the gastric antrum.

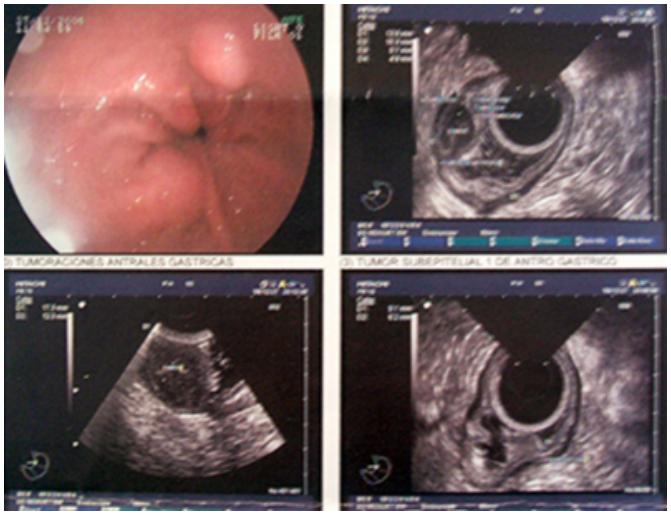
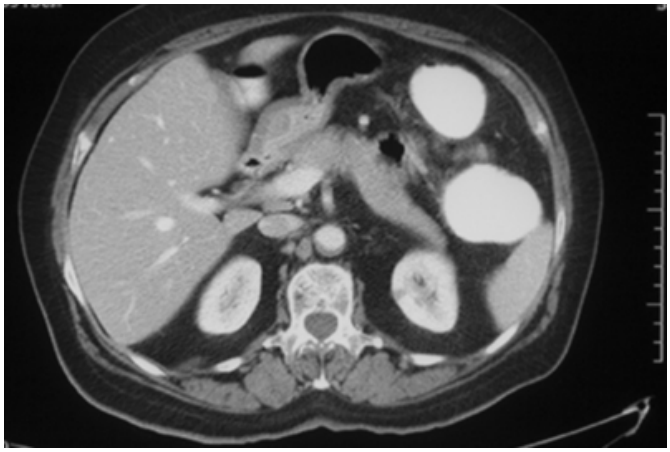


Figure 2

Figure 2: Abdominal CT revealed a submucosal lesion in the gastric wall.



Laparotomy was performed which revealed an intramural mass located in the smaller curvature of the stomach without affection of adjacent structures and neither local nor regional adenopathies. Stapled subtotal gastrectomy and Roux-en-Y gastrojejunostomy was done. Postoperatively, the patient had an uneventful recovery. Histopathology and immunohistochemistry analysis of the specimen was compatible with gastrointestinal stromal tumor. The patient was discharged with the advice of strict regular follow-up. Radiological imaging twelve months later shows no evidence of any recurrence.

DISCUSSION

GISTs are most commonly found in the stomach (60 - 70%) or small intestine (22%) and less commonly in the colon, rectum (8%) or other sites (10%)[6,7]. Extra-gastrointestinal stromal tumors (EGISTs) are reported in mesentery, omentum, retroperitoneum, liver, gallbladder, urinary bladder and vagina[8].

Most of the GISTs of the stomach are located in the gastric body (40%), followed by the gastric antrum (25%), as in our patient, and the pylorus (20%). Around 60% of them are submucosal and grow toward the light, 30% are subserosal and the remaining 10% are intramural. Occasionally, a central ulceration is observed that can penetrate in the depth of the tumoral mass[4].

Diagnosis is based on the clinical manifestations, gastroscopy and image tests. However, until in half of the cases the diagnosis constitutes a fortuitous discovery after carrying out an endoscopic or a laparotomy for another cause. Only inmunoreactivity is able to differentiate GIST

from other mesenchymal tumors[9].

The clinical manifestations depend on the size and of the localization of the tumor. The most frequent symptoms are: abdominal pain of variable duration, gastrointestinal bleeding, anaemia due to occult blood loss, abdominal mass and loss of weight. Although in 20% of the cases it is located in the pylorus, obstruction of the pylorus is very uncommon[10,11]. Our patient presented abdominal pain and anaemia.

Cases associated to HIV infection, to Recklinghausen disease and to Carney syndrome have been described[12,13].

Esophago-gastro-duodenal transit with double contrast can show a repletion defect with the gastric mucosa undamaged or ulcerated[14,15].

Upper digestive endoscopy is the first-line screening test to detect GISTs of the stomach. It may show a subepithelial lesion that occasionally may be ulcerated[16].

Abdominal CT can identify the primary tumor site in the gastric wall and any displacement or compression of adjacent organs. On contrast-enhanced CT, GISTs are usually well-defined, huge masses that contain large areas of low-attenuation necrosis and haemorrhage. Magnetic resonance is another modality that can aid in differentiating cysts from solid tumors[17].

Diagnosis of GISTs on abdominal ultrasound examination can be difficult because of their similarity in appearance with other abdominal neoplasms[18].

Endoscopic ultrasonography is a key component of the evaluation of submucosal lesions of the gastrointestinal tract, allowing determination of the wall layer of origin of the lesions including sizes larger than 4-5 cm, irregular or invasive border, cystic spaces and malignant appearing lymph nodes. Endoscopic ultrasound-guided fine needle aspiration is generally adequate for tissue acquisition[16].

Accurate preoperative characterization of the lesion is critical for treatment decisions and for an assessment of prognosis[9].

The treatment of choice for localized gastric GISTs is surgical resection. Complete surgical resection is the only curative treatment. Careful identification of the exact gastric tumor location using preoperative computed tomography and gastroscopy should allow selection of a specific operative approach. Partial resection of the stomach is recommended with the goal of obtaining negative microscopic margins. In some cases, tumor size and location may dictate more extensive surgery such as proximal or total gastrectomy for lesions near or involving the gastroesophageal junction[19].

Metastasis of GISTs to regional lymph nodes is very unusual (4%). Therefore, routine lymphadenectomy is not indicated. On the contrary, if is very important to explore the rest of the abdominal cavity due to frequent peritoneal metastasis (sarcomatosis), in up to 33% in some series[4,9].

The most common sites of metastasis are liver and lung. These metastases can develop up to 30 years after extirpation of the primary tumor; therefore, follow-up with abdominal and pelvic CT scan should be made periodically. In less than 15% of the cases, there are recurrent lesions that can be extirpated[15].

In any case of GIST the surgeon should be alert to recognize a possible coexistent tumor with different histological origin and to perform a thorough preoperative and intraoperative control. In almost 27% of the study population, this tumor coexisted with other neoplasms. The correct diagnosis before and at the time of the surgical procedure is the cornerstone that secures the patient's best prognosis[20,21].

Laparoscopic surgery with its attendant benefits lends itself to the resection of GISTs as their biological behaviour allows for curative resection without requiring large resection margins or extensive lymphadenectomy. The main criterion for performing the resection by laparoscopic approach is the size of the tumor and the valuation by preoperative cross-sectional imaging at CT scan. Patients with small GISTs can be safety resected with a laparoscopic approach, offering a quicker operation and shorter hospital stay. This pathway does not alter risk of early local or distant recurrence. Resection margins, lymph node yield, recurrence and complication rates are the same for both groups of patients with laparoscopic resection or open approach[3,22,23].

Prior to the use of the monoclonal antibody imatinib mesylate there was no effective treatment for patients with locally advanced or metastatic GIST. Imatinib in the neo-adjuvant setting prior to surgery or as adjuvant treatment after surgery may allow for complete remission and long-term survival in these patients [24,25,26].

Radiotherapy is not indicated due to possible damages it can cause in the adjacent organs[15].

In GISTs, the most important prognostic factor is mitotic count and tumor size[27]. Franquemont et al.[28] classified these tumors in low, intermediate and high risk of recurrence or metastasis according to tumor size and mitotic activity. The criterions proposed by Franquemomt et al.[28]are the following: a) low risk including tumors smaller than 5cm with less than 2 mitoses in 10 high power fields (HPF), b) intermediate risk including tumors larger than 5cm with less than 2 mitosis in 10 HPF and c) high risk including tumors larger than 5cm with more than 2 mitoses in 10 HPF. Our patient is included in the low risk group.

Wang et al.[29] pointed out that invasion of the lamina propria, haemorrhage and necrosis had also a prognostic value. Filiz et al.[4] reported that MIB-proliferative index and necrosis are important indicators of prognosis along with tumor size and mitotic index, and when used in the routine setting they will be of great help in both predicting the clinical course of small bowel GIST cases reliably and planning of postoperative therapy courses.

The global 5-year survival rates oscillate between 19 and 56%. The most important variable that affects the survival is complete resection. The second factor in importance is the histological grade that depends on the cell density and on the mitotic index[9].

CONCLUSION

The stomach is the most common site of gastrointestinal stromal tumors. Preoperative diagnosis is often difficult to make because many of these tumors are asymptomatic and therefore they are not suspected. Complete surgical resection is the only curative treatment. Application of imatinib as adjuvant therapy may contribute to the improvement of outcome.

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