Surgical options in the treatment of GIST of the upper portion of the stomach
Report of two cases

Ann. Ital. Chir., 2007; 78: 133-136

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Gastrointestinal stromal tumors are rare neoplasms arising from mesenchymal precursor cells of the gastrointestinal tract that may differentiate towards the interstitial cells of Cajal, pacemaker cells regulating autonomous motility of G.I. tract. Grading of GIST has been proven to be as difficult as their classification.
Two thirds of GISTs are located in the stomach, 20-50% in the small bowel (one third in the duodenum), and 5-15% in colon and rectum; GISTs, however, may rarely be found also in the oesophagus, omentum, mesentery or the retroperitoneum.
The distribuition of these tumors in the stomach is: pars media, 40%; antrum, 25%; pylorus, 20%; in less than 15%, GISTs location is next to the EGJ, in the cardia and in the fundus.
The upper gastric third location of GISTs is not common, so their surgical management has been not yet well investigated. Total gastrectomy is considered the therapy of choice for the GIST located next to the EGJ, but wedge resection could be considered a surgical option in selected cases.
The Authors describe 2 cases of GIST located just under the upper portion of the stomach and discuss about the different surgical options for GISTs of this region.

KEY WORDS: GIST, Gastric tumours.

Introduction

Gastrointestinal stromal tumors are rare neoplasms arising from mesenchymal cells of the gastrointestinal tract. These tumors were earlier commonly diagnosed either as leiomyoma, leiomyosarcoma or leiomyoblastoma but it is now evident that GISTs differ from all other mesenchymal neoplasms [1,2].
A characteristic feature of GISTs is that they strongly express class III receptor tyrosine kinase, called KIT, in immunohistochemistry due to some mutations in the KIT proto-oncogene [3-6].
GISTs probably originate from precursor cells that may differentiate towards the interstitial cells of Cajal, pacemaker cells regulating autonomous motility of G.I. tract [3-6].
About two thirds of GISTs are mainly composed of spindle cells (the "spindle cells" variant) and one third of epithelioid or round cells ("the epithelioid variant"), but many mixed forms exist and some GISTs have unusual morpholo gic features [4-7].
Two thirds of GISTs are found in the stomach, 20-50% in the small bowel (one third in the duodenum), and 5-15% in colon and rectum; GISTs, however, may rarely be found also in the oesophagus, omentum, mesentery or the retroperitoneum.
The distribuition of these tumors in the stomach is: pars media, 40%; antrum, 25%; pylorus, 20%. In less than 15%, GISTs location is next to the EGJ, in the cardia and in the fundus [5,8,9].
The Authors describe 2 cases of GIST located just under the upper portion of the stomach and discuss about the different surgical options for GISTs of this region.

Pervenuto in Redazione Aprile 2006. Accettato per la pubblicazione Ottobre 2006
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Case reports

CASE 1
A 72-year-old man, affected by diabetes mellitus, hyper-

tension and atherosclerotic coronaric disease, was referred to our Department for a 1-year-long history of epigastralgia and dysphagia. Laboratory data on admission showed no significant abnormalities.
Endoscopy revealed sub-cardial polypid lesion of the lesser curvature as a protruding lesion measuring about 7 cm in size. Biopsy showed proliferation of spindle-shaped cells. Abdominal CT-scan detected a well-defined lesion of approximately 7 cm in diameter, growing internal from the gastric wall, with no regional limph node enlargement or distant metastases (Fig. 1).
At laparotomy, a large tumor arising from the lesser curvature, just under the EGJ, was found. A total gastrectomy was carried out, with stapled Roux-en-Y oesophago-jejunal anastomosis.
The gross specimen appeared as a polipoid lesion 7 cm large, elastic-hard in consinstency (Fig. 2); its cut surface was brown and homogeneous, without hemorrhagic or necrotic areas.
Histologically, the tumor was composed of spindle-shaped cells, arranged in interlacing bundles, with a mitotic rate of 1/10 HPF. The lesion was extending to submucosal and muscular layer. Immunohistochemistry resulted strongly positive for CD-117 and negative for actin, desmin and S-100 protein. According to tumor diameter, mitotic activity and non infiltrating growth, the tumor was classified as a low-grade GIST.
The patient had an uneventful postoperative course and was discharged on P.O.D 10.
Follow-up was carried out by clinical examination and ultrasonography at 1 month, 3, 6 and 12 months after surgery, and endoscopy and CT scan at 12 and 24 months after surgery.
There is no evidence of recurrence at 24 month-follow-up.

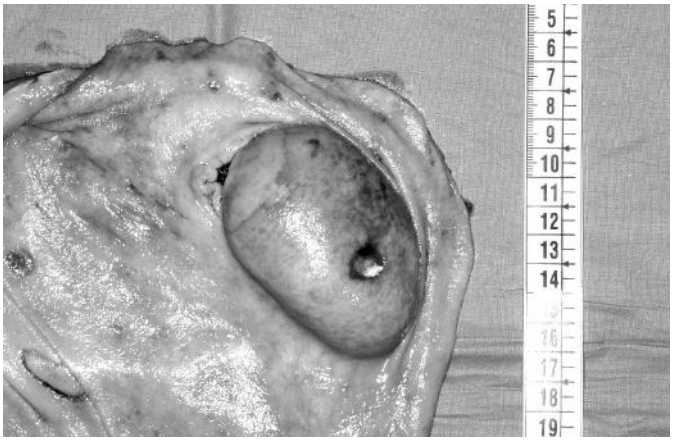

Fig. 2: Opened specimen with the tumor.

CASE 2
A 78-years-old man, affected by hypertension, atherosclerotic coronaric and cerebral disease, was admitted to our Department complaining anemia, upper abdominal pain and dysphagia. Laboratory findings revealed no significant abnormalities except for a low hemoglobin level (8.7 gr/dl).
Endoscopy (Fig. 3) showed a 5-6 cm lesion of the fundus, extending to the gastric body, on the anterior wall, and protruding into the lumen.
The biopsy results showed a proliferation of spindle-shaped cells.
Abdominal CT-scan detected a lesion of approximately

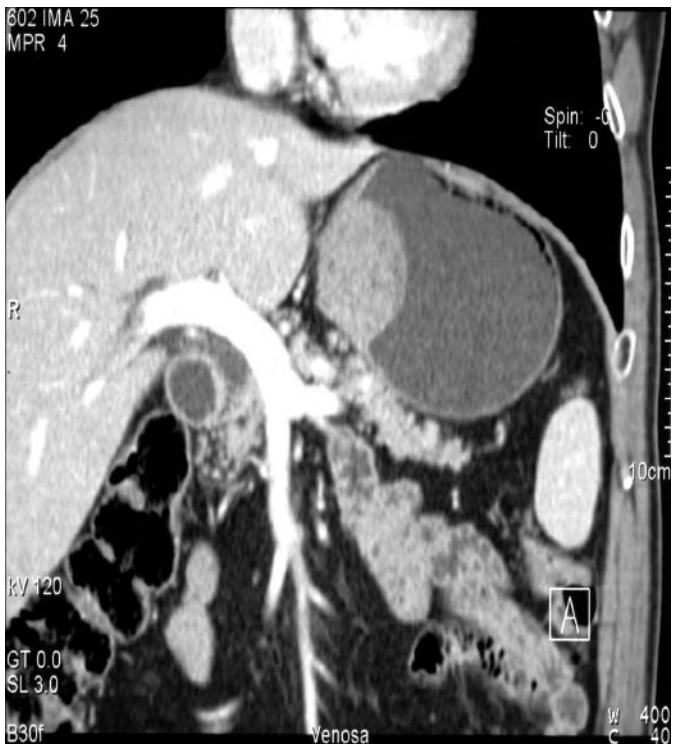

Fig. 1: CT scan reveals the presence of endogastric mass.

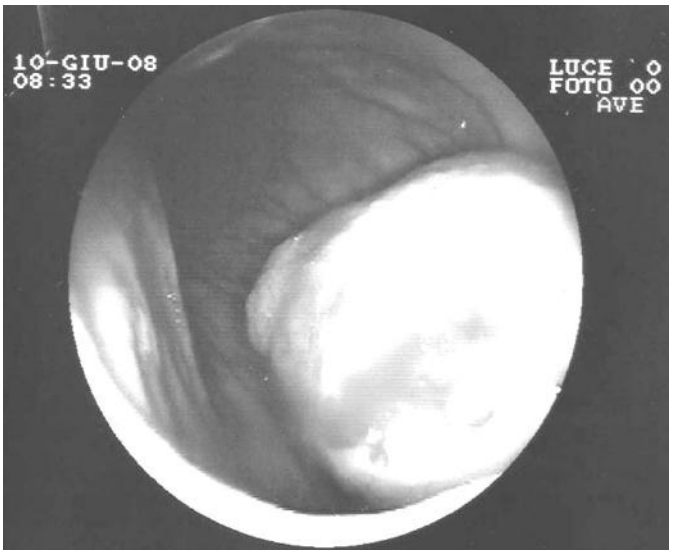

Fig. 3: Endoscopic image of the tumor.

5 cm in diameter, with hypoperfused areas, growing internal from the gastric wall, at the lumen of the stomach, with no regional limph node enlargement or distant metastases.
At surgery, since the lesion was peduncolated, arising from the anterior gastric wall, approximately 4 cm under the EGJ, a RO wedge resection was carried out, including the tumor and the surronding normal gastric mucosa approximately 1.5 cm from the tumor margin.
Grossly, the tumor had a size of 5 x 4 x 3.5 cm, elastic-hard in consinstency; its cut surface was yellow-grey with hemorragic areas and pseudocystic degeneration.
Histologically the tumor was composed of spindle-shaped cells, arranged in interlacing bundles, with a mitotic rate of 3/10 HPF. Hemorrhagic areas were found, but no necrosis. Immunohistochemistry resulted strongly positive for CD-117 and negative for actin, S-100 protein and CD-34. According to tumor diameter, mitotic activity and non-infiltrating growth, the tumor was classified as a low-grade GIST.
The patient had an uneventful postoperative course and was discharged on P.O.D 8.
Follow-up was carried out by clinical examination and ultrasonography at 1 month, 3, 6 and 12 and 18 months after surgery, and endoscopy and CT scan at 12 months after surgery.
There is no evidence of recurrence at 18 month-follow-up.

Discussion

GIST of the stomach are infrequent and accounts for approximately 1% of primary gastric neoplasms [10,11].
About 60% of GISTs are submucosal; 30% are subserosal and 10% are intramural. Submucosal GISTs grow toward the lumen, where they make a smooth projection. Several times, a central ulceration may occur,often with the clinically malignant tumors, and it may penetrate deeply into the tumor mass and results in gastrointestinal bleeding.
Grossly, they tend to be well-circumscribed and have a smooth, lobulated appearance on cut section.Gastric GISTs range from a few millimeters to 15 cm in size.
Four grades of GIST have been identified according to: number of mitoses, cellularity, atypia, necrosis, size [1,2,4,5,8,9].
For patients having complete (R0) surgical resection, histologic grade is the most important prognostic determinant: the 5-year survival rate is 18% for high grade tumors and 72% for low-grade lesions.
From a prognostic point of view, GISTs have been divided into 3 prognostic groups: benign, border-line, malignant.
Factors associated with decreased survival include: 8 cm or more in size, 3 or more mitoses/HPF, positive margins or unresectability and histopathologic grade II or higher [12-14].
The primary treatment of nonmetastatic GIST consist of excision of the tumor with a good margin of normal tissue: patients who have complete tumor resection (R0) have more favorable outcome than those with less complete surgery.
In fact, it is defined complete resection the excision of all gross disease, regardless of microscopic margins [8].
GISTs give rise to lymph node metastases only infrequently and extensive lymphadenectomy is thus not recommended.
The efficacy of radiotherapy in the treatment of GIST has not been investigated in depth; at present, it is not standard and may be reserved for palliation of symptoms.
Chemotherapy is generally considered to have only limited efficacy in the treatment of advanced disease [10,11,16].
Several reviews have reported that small tumors (5 cm or less) of the stomach can be traeted adequately by wedge gastric resection, with a generous margin of gastric wall. Larger gastric lesions may require subtotal or total gastrectomy, including omentectomy, but there is no evidence that procedures more extensive than the removal of all gross neoplasm prolong survival or delay recurrence [15].
Incomplete resection should be performed only for the palliation of symptoms due to bleeding, pain or mass effect. Non-resectable or metastatic GIST is a fatal disease that resist conventional chemotherapy or radiotherapy.
Treatment with Imatinib (selective inhibitor of protein kinases like kit) seems to be the best systemic therapy for metastatic and locally inoperable GISTs. The high rate of response to Imatinib is not only remarkable but also supports the hypothesis that dysregulated kit-kinase activity is important in human GISTs [8,15].
The high response rates with Imatinib in advanced and metastatic setting have fostered interest in its role in the adjuvant settino. There may be an improvement in surgical outcome in patients treated with Imatinib preoperatively. Currently, there are several trials to address combining surgery and Imatinib [17.]
Gastrectomy is usually performed for lesions too large for wedge resection or when the gastroesophageal junction is involved [11,12,15].
The upper gastric third location of GISTs is not common, so their surgical management has been not yet well investigated.
Total gastrectomy may be considered the therapy of choice for the GIST located next to the EGJ, but it is a long surgical procedure, with high risk for surgical and post-operative complications.
Wedge resection can be considered a surgical option in well selected cases (such as when total gastrectomy is not indicated due to patient's performance status) because it can even be defined as a complete resection of all gross disease [8].
In conclusion we can consider wedge resection, when feasible for tumor characteristics and location, an appro-

priate surgical options in the treatment of GIST located in the upper portion of the stomach.

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