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Initial presentation of a giant gastrointestinal stromal tumour of the stomach with recurrent spontaneous intra-peritoneal haemorrhage

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ABSTRACT

INTRODUCTION: Gastrointestinal stromal tumours are a rare group of tumours of the digestive tract. In the majority of cases, at the time of the diagnosis, tumours are usually small and patients are asymptomatic or have non-specific symptoms. The occurrence of digestive haemorrhage is relatively common; however, the manifestation with a spontaneous hemoperitoneum is extremely rare, specially if chronic and non-emergent.

CASE REPORT: We report an unusual case of a 65-year-old man with a history of alcohol abuse, presenting with abdominal distension due to ascites and a constitutional syndrome. He was found to have a gastrointestinal stromal tumour (GIST) of the stomach associated with a chronic hemoperitoneum, due to recurrent spontaneous haemorrhage. In an elective setting, the lesion was resected completely without rupturing the tumour pseudo-capsule and the patient had an uneventful postoperative course. The tumour was classified as a moderate-risk lesion for aggressive biological behaviour, and imatinib mesylate was initiated as an adjuvant to treatment. No evidence of disease recurrence after one year was noted.

DISCUSSION AND CONCLUSION: GISTs are uncommon and rarely present with spontaneous intra-peritoneal haemorrhage, which may be life threatening. In our understanding, this is the first reported case of the reviewed literature presenting with a chronic hemoperitoneum, due to recurrent brisk episodes of tumour haemorrhage. Tumour rupture and large tumour size are two poor independent prognostic tumour factors for recurrence. Despite this, the patient remains free of disease after surgery and instituted adjuvant imatinib mesylate.

1. Introduction

GISTs account for 1–2% of all gastrointestinal malignancies, representing the most common mesenchymal tumours of the gastrointestinal tract in adults [2]. GIST can occur anywhere along the gastrointestinal tract; however, the majority arise in the stomach (50–60%) and at the small intestine (30–35%) [1].

Although most patients have symptoms or a palpable tumour at presentation, 25% of GISTs are discovered incidentally during imaging or surgery for other disorders. The most frequent signs and symptoms are abdominal pain, digestive haemorrhage and anaemia; other less frequent signs and symptoms include dyspepsia, nausea or vomiting, constipation or diarrhea, frequent urination, and fatigue. The occurrence of spontaneous hemoperitoneum is extremely rare. Haemorrhage, tumour rupture, and bowel perforation or obstruction may require emergency surgery [1].

Surgery is the only curative treatment, however, adjuvant treatment with imatinib mesylate, a selective inhibitor of tyrosine kinase, was noted in 2001 to be highly effective in treating advanced GISTs. Currently, this inhibitor is being recommended for patients with a higher risk of recurrence and imatinib-sensitive mutation GISTs [1].

To the authors' best knowledge, this is the first report of a gastric GIST coursing with recurrent brisk episodes of intra-peritoneal haemorrhage, not accompanied with peritonitis and not requiring emergent surgery [3–9].

2. Case report

A 65-year-old male, autonomous, with cardiovascular comorbidities and a history of alcohol abuse was sent to our outpatient consult. He reported non-specific abdominal discomfort and distension, asthenia and anorexia, since he had stopped his alcohol abuse, 6 months before, when a large hematic ascites was identified. Given his history of alcohol abuse, the ascites was initially thought to be due to portal hypertension, although he had

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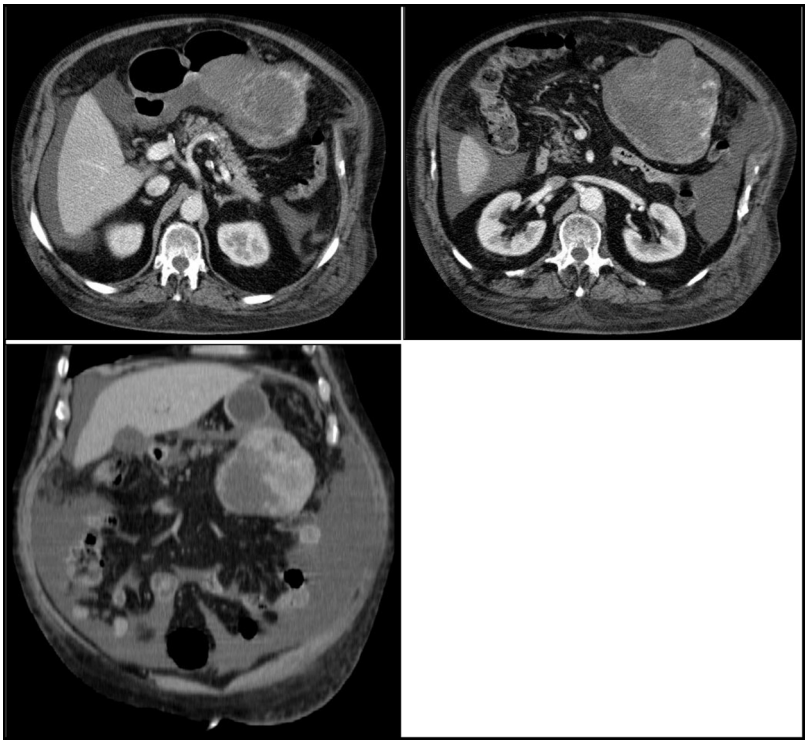

Fig. 1. Abdominal CT scan showing a giant GIST of the stomach associated with a moderate quantity of intraperitoneal fluid.

no other signs or symptoms of chronic liver disease. Cytology of the intra-peritoneal fluid was negative for malignant cells.

Laboratory testing showed progressively decreasing haemoglobin levels, with a minimum value identified of 8.6 g/dL (known baseline of 13; normal range 13–18), C-reactive protein of 191 mg/L (normal value ≤5), gamma-glutamyltransferase (GGT) of 137 U/L (normal range 12–64), aspartate amino-transferase (AST) of 68 U/L (normal range 5–34) and alanine aminotransferase (ALT) of 96 U/L (normal value ≤55). Other parameters such as electrolytes, renal function, coagulation and

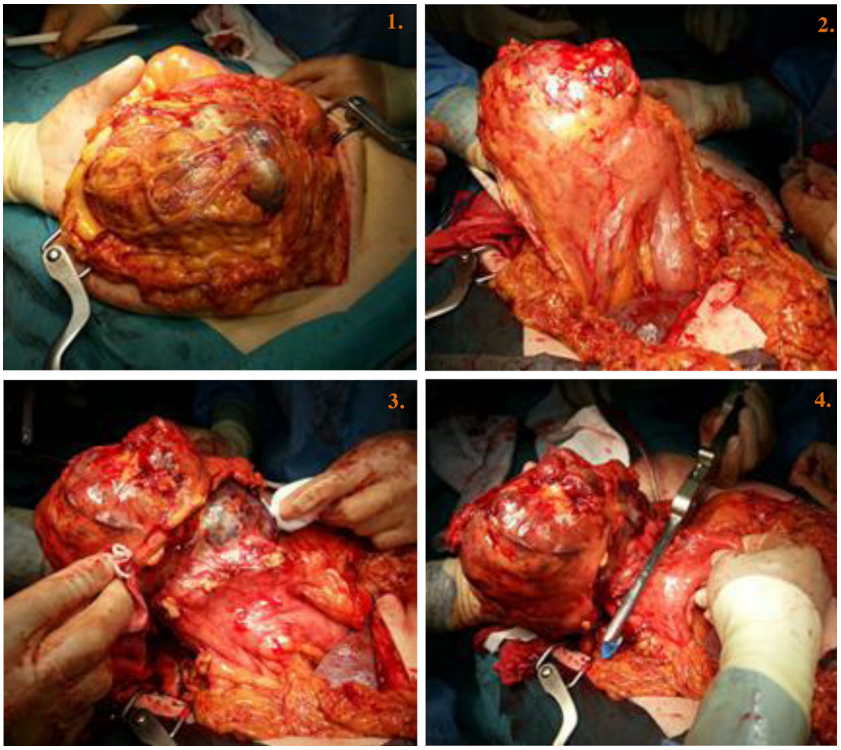

Fig. 2. Surgical steps: 1 and 2 – Laparotomy confirmed the occurrence of a giant gastric lesion, adherent to the omentum and transverse mesocolon; 3 and 4 – Laborious dissection and complete excision of the tumour was accomplished through an atypical gastrectomy.

tumour markers were normal. The patient had a good nutritional status.

Abdominal sonography and computed tomography showed a giant soft-tissue mass arising from the great gastric curvature wall, exophytic, heterogeneous, compatible with a gastric GIST; it was also identified a moderate quantity of intra-peritoneal fluid; there were no suspicious lymph nodes or metastatic lesions (Fig. 1). Upper and lower gastrointestinal endoscopies were normal, with no mention of extrinsic compression.

The patient was scheduled for a laparotomy confirming a gastric lesion originating from the posterior surface of the great gastric curvature wall, with $17 \times 12 \times 11$ cm. The lesion was adherent to the transverse mesocolon and omentum, and the presence of 500 mL hemoperitoneum was also noted. The latter presented in different phases of absorption, with some clots and hemosiderin pigment on the parietal peritoneum, which favours our hypothesis of recurrent intra-peritoneal haemorrhage.

A laborious dissection of the tumour was performed, without rupturing the tumour pseudocapsule. A complete excision of the tumour was accomplished through an atypical gastrectomy, excision of the involved omentum and superior leaflet of the transverse mesocolon (Fig. 2). The patient had an uneventful postoperative course and was discharged on the seventh postoperative day.

Histopathological evaluation of the tumour was consistent with an epitheloid cell GIST weighing 1254 g. There were extensive areas of necrosis and haemorrhage; however, the capsule did not show any identifiable breaks. The surgical excision of the tumour was adequate and there was no evidence of tumour in the fragments of excised omentum. The tumour had a low mitotic index (4 per 50 high powered field). Immunohistochemical studies revealed neoplastic cells that stained positive for c-KIT and CD34, and negative for smooth muscle actin and S-100 protein. The genetic study identified a mutation in exon 18 of the PDGFRA gene (c.2525A > T), which has previously been described in GISTs resistant to Imatinib mesylate.

The patient was started on adjuvant Imatinib mesylate. He is currently asymptomatic, with no signs of tumour recurrence on clinical and radiological follow up of one year.

3. Discussion and conclusion

GISTs are rare, accounting for only 1–2% of all gastrointestinal malignancies [2]. These tumours may occur at any age; however, more than 80% are reported in patients older than 50 years and are slightly more frequent in males. They occur mostly in the stomach (50–60%) and, especially the larger ones, can ulcerate and present with gastrointestinal bleeding. Despite this, GISTs rarely present with a spontaneous hemoperitoneum, which is life threatening [1].

We believe that the possibility of rupture of a weakened area in the wall of the tumour may be due to extensive necrosis. The normal activity of the patient or a physical blow may trigger the rupture of the weakened area.

Surgery is the mainstay of therapy for GISTs when the primary lesion is deemed resectable. All tumours should be completely resected, including the tissues macroscopically infiltrated. Lymph-node dissection is generally not indicated because nodal metastases are rare (prevalence is about 1%) [1].

The tumour must be handled with care to prevent intra-abdominal rupture and dissemination. In this case, this actually occurred before surgery, with the recurrent episodes of intra-peritoneal haemorrhage.

In terms of histopathology, approximately 20% of the lesions are epithelioid, marked by a nested architecture and more nuclear atypia, compared to the spindle type (70% of the cases where this patient is included) [1].

The most important independent prognostic factor for GIST recurrence after surgery is a high tumour mitotic rate. Also, large tumour size, tumour site, and tumour rupture, before or during surgery, have also been identified as independent prognostic factors for recurrence. Gastric GISTs have a lower risk of recurrence compared with non-gastric GISTs, nevertheless, the patient herein reported faces two poor prognostic factors for recurrence-tumour rupture (recurrent) and large tumour size. The most frequently used risk-stratification methods estimate the risk of recurrence after surgery, and the factors indicated are usually included [1].

The advent of tyrosine kinase inhibitors has changed the standard of care for GISTs and, as a direct consequence, the survival of patients has increased since its approval as an adjuvant treatment. Individuals at intermediate or high risk of recurrence can be considered for adjuvant treatment. Specific gene mutations confer insensitivity to imatinib mesylate and, therefore, must be identified. The most common mutation is a single-base substitution in PDGFRA exon 18, which is found in up to 10% of patients with high-risk GISTs. At present, a reasonable choice is to treat patients with three years of adjuvant imatinib mesylate if they are at substantial risk for recurrence and have a GIST with an imatinib-sensitive mutation. Neo-adjuvant treatment with imatinib mesylate may improve resectability by downstaging the tumour. Tyrosine kinase inhibitors substantially improve survival in advanced disease, however, secondary drug resistance is common [1].

In the patient reported, although the genetic study identified a mutation already described in imatinib-resistant GISTs, the decision to initiate adjuvant treatment with imatinib mesylate was multidisciplinary. In light of the above, it can be discussed if the decision of initiating imatinib mesylate was the most adequate, although not every patient with this mutation has been proven to be imatinib resistant. Possibly, another tyrosine kinase inhibitor might have been used, despite not being widely available and still in need of further validating studies. Despite this, the reported patient is doing well and there is no sign of tumour recurrence.

Conflicts of interest

The authors report that there are no conflicts of interests.

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None.

Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Consent

The study was approved by the Department of Surgery of Hospital Pedro Hispano. Written informed consent was obtained from the patient for publication of this case report Author Form and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author's contribution

Margarida Vinagreiro was a major contributor in data collection and writing of this manuscript. Jorge N. Valverde helped with data collection and elaboration of this manuscript. Emanuel Guer-

reiro provided important intellectual content and helped revise the manuscript. All authors read and proved the final manuscript.

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