Hemoperitoneum secondary to gastric GIST negative for c-KIT and positive for antibody anti-DOG1

Hemoperitôneo secundário a GIST gástrico c-KIT negativo e anticorpo anti-DOG1 positivo

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ABSTRACT

Although relatively rare, the gastrointestinal stromal tumors comprise most mesenchymal tumors of the digestive tract and account for 5% of all sarcomas. The most common symptoms are pain, gastrointestinal bleeding and palpable mass. This study reported the case of a young patient who developed hemoperitoneum due to gastric neoplasm rupture and required urgent surgical treatment. Pathology and immunohistochemistry analysis showed an epidemiologically rare case: epithelioid and c-KIT negative tumor.

Keywords: Gastrointestinal stromal tumors; Gastrointestinal hemorrhage/diagnosis; Gastrectomy; Gastrointestinal neoplasms; Endoscopy; Case reports

RESUMO

Os tumores estromais do trato gastrintestinal, embora relativamente raros, compreendem a maioria dos tumores mesenquimais do trato digestivo e constituem 5% de todos os sarcomas. Quanto à apresentação clínica, os sintomas mais comuns são dor, hemorragia digestiva e massa palpável. Este trabalho relatou o caso de um paciente jovem que desenvolveu hemoperitôneo por ruptura de neoplasia gástrica e necessitou de tratamento cirúrgico de urgência. A análise patológica e imunoistoquímica revelou tratar-se de um caso raro epidemiologicamente: tipo celular epitelioide e c-KIT negativo.

Descritores: Tumores do estroma gastrintestinal; Hemorragia gastrintestinal/diagnóstico; Gastrectomia; Neoplasias gastrintestinais; Endoscopia; Relatos de casos

INTRODUCTION

The gastrointestinal stromal tumors (GIST) occur mainly in individuals aged 40- 80 years, and the incidence is similar in both sexes[1]. They may originate anywhere in the gastrointestinal tract, and 50-60% of the lesions arise from the stomach, 20-30% from the small bowel, 10% from the colon, 5% from the esophagus and 5% from other sites in the abdominal cavity[2]. These tumors derive from interstitial cells of Cajal, located at the level of the myoenteric plexus, between the longitudinal and circular muscle layers of the gastrointestinal tract[3]. They have immunophenotypical and ultrastructural characteristics, both of smooth muscle and of neural differentiation, and express the KIT receptor (CD117), similar to the GIST[4].

The clinical presentation of GIST patients varies and primarily correlates with the size of the lesion[5]. The diagnosis is usually not made by endoscopic biopsies, due to its submucosal location. Computed tomography with oral and intravenous contrast is ideal to define the exophytic and intramural extension of the tumor. The recently developed anti-DOG1 antibody (DOG1 stands for discovered on GIST-1) has been reported as more sensitive and more specific for diagnosis of GIST as compared to CD117 or CD34. The standard treatment for patients with non-metastatic GIST is complete surgical resection of the lesion, since it provides greater chance of cure. The discovery of STI571 (imatinib) revolutionized treatment of this cancer for being the first therapy that specifically acted on the molecular change responsible for the etiology of the disease. This treatment is used for metastatic or unresectable disease[1].

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CASE REPORT

Male patient LGS, 28-year-old, born in the state of Ceara, was admitted to the Emergency Department of the *Hospital Municipal Dr. Moysés Deutsch* complaining of epigastralgia and hyporexia that started the day before. The patient did not report nausea, vomiting or fever. As to past history, he reported a gastric ulcer diagnosed two years before and treated with a proton pump inhibitor. Upon examination, he was in good general conditions, hemodinamically stable, normal colored mucosae and afebrile. The abdomen was flat, flacid, painful upon palpation in the epigastrium and hypogastrium, with no signs of peritoneal irritation.

He was submitted to esophagogastroduodenoscopy on the day of admission, which showed submucosal lesion in the greater curvature and on the posterior wall of the distal gastric body, with erosion in its apex, and measuring approximately 2.5cm in diameter. On the 5th day of hospitalization, the patient presented progressive drop in hemoglobin levels (from 14.0 to 8.3), with no hemodynamic repercussion. The abdomen was flacid, painful upon diffuse palpation with sudden positive decompression. Based on this clinical picture, an abdominal computed tomography was ordered, and demonstrated free fluid in the abdominal cavity and a tumor in the greater curvature of the stomach (Figure 1). The presumptive diagnosis was hemoperitoneum and exploratory laparotomy was indicated. During surgery hemoperitoneum was confirmed, with a semi-pediculated tumor lesion attached to the gastric body and fundus, measuring roughly 8cm, and signs of rupture. No other lesions or bleeding in other peritoneal structures or carcinomatosis were observed. Partial wedge gastrectomy was the surgery chosen, with resected margins of 6cm and suture of the gastric wall in two planes. The pathological examination demonstrated GIST, of epithelioid architectural pattern, mitotic index of 1 per 50 high-magnification fields and moderate cell pleomorphism. The lesion had no signs of necrosis or of gastric mucosa infiltration. The immunohistochemistry was negative for DC117 and the results are demonstrated on chart 1. Despite being a severe case, the patient progressed with no intercurrent events and was discharged from hospital on the 5th postoperative day. The patient remained on outpatient monitoring with no signs of disease relapse.

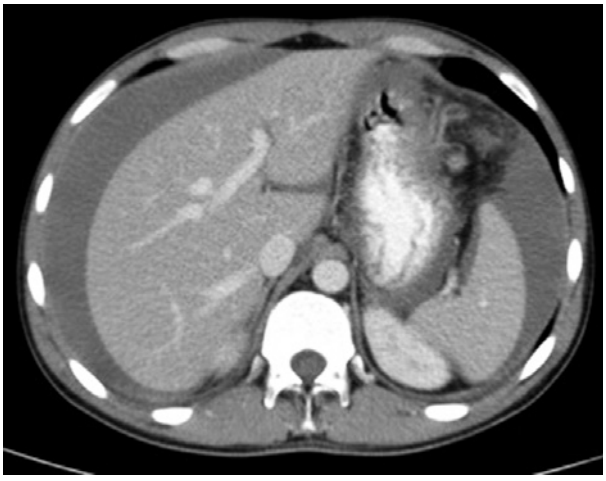

Figure 1. Computed tomography revealed a tumor in the greater curvature of the stomach, with heterogeneous contrast uptake, measuring 9.2x7.7cm

Chart 1. Immunohistochemical results of the surgical specimen

Marker	Result
CD117 (c-KIT) MTB1	Negative
Vimentin	Diffusely positive
S-100 protein	Negative
Melan-A (M27C10)	Negative
HMB-45	Negative
CD56 123C3	Negative
CD45 (LCA, leukocyte common antigen) PD7/26/16 and 2B11	Negative
CD10 56C6	Negative
SMA (smooth muscle actin) 1A4	Negative
CD34 QBEnd/10	Negative
AE1 + AE3	Negative
DOG1 SP31	Focal positivity

DISCUSSION

GIST account for only 1% of all primary gastric tumors. In immunohistochemistry they are positive for c-KIT (CD117). It is known that approximately 95% of all GIST are positive for this receptor[5]. Histologically the GIST derive from smooth muscle cells. In the 1990´s, some inconsistencies in broad classification of tumors as GIST were reported. An important discovery was the identification of CD117 receptor expression for almost all GIST, unlike leiomyomas, leiomyosarcomas and other spindle cell tumors of the tract gastrointestinal that are often CD117 negative[5,6]. As described in the literature, the first acute symptom of this patient was gastrointestinal hemorrhage. Bleeding is present in approximately 40% of cases[6,7]. DOG1 is a membrane protein discovered through analysis of the gene expression patterns of GIST, which showed to be a useful immunohistochemical marker[8]. The immunohistochemical results of the concomitant use of DOG1 and KIT in GIST demonstrated that 85% of the cases were positive for both markers (DOG+/KIT+), 6% were negative for DOG1 and KIT, 6% were DOG+/

KIT- and 3% were DOG-/KIT+. DOG1 specificity was very high for few types of non-GIST tumors that are immunoreactive for DOG1[8]. The CD117- DOG1+ patients can be treated with tyrosine kinase inhibitors like the C-KIT positive individuals. As to surgical approach, exploratory laparotomy was chosen, but some authors[9] described a case of hemoperitoneum secondary to gastric GIST treated by laparoscopy and vertical gastrectomy, with no intercurrent events, and surgeries that started by laparoscopy and were converted to laparotomy, due to intense bleeding and hemodynamic instability[10].

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