Clinical and Diagnostic Presentation of Gastrointestinal Stromal Tumour (GIST): A 5-Year Follow-Up

Apresentação clínica e diagnóstica de tumor estromal gastrointestinal (GIST): acompanhamento de 5 anos

Presentación clínica y diagnóstica de tumor estromal gastrointestinal (GIST): seguimento de 5 años

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ABSTRACT

Objective: To describe a clinical case of Stromal Gastrointestinal Tumor, highlighting the diagnostic characteristics and a 5-year follow-up of the patient after surgery. **Case report:** A 51-year-old patient presented with a tumor in the stomach region, diagnosed by the clinic, associated with imaging and immunohistochemistry, in which a partial abdominal gastrectomy was performed for total tumor removal and after a surgical procedure pharmacological treatment with GLIVEC chemotherapy for 3 years, with cure. **Final considerations:** Gastrointestinal stromal tumors are very common mesenchymal tumors in the region of the gastrointestinal tract. Its severity is known and investigated through the clinic for diagnosis, associated with imaging and immunohistochemistry analysis, in order to observe the tumor markers, mainly the c-KIT. The treatment involves several modalities seeking to improve the patients' quality of life and, generally, they present a good prognosis.

Keywords: Gastrointestinal, Gastrointestinal stromal tumours, Protein c-kit.

RESUMO

Objetivo: Descrever um caso clínico de Tumor Estromal Gastrointestinal, destacando as características diagnósticas e um seguimento de 5 anos do paciente após a cirurgia. **Relato de caso:** Paciente de 51 anos que apresentou tumor na região do estômago, diagnosticado pela clínica, associado com exames de imagem e imuno-histoquímica, no qual foi realizada uma gastrectomia parcial via abdominal para retirada total do tumor e após procedimento cirúrgico foi realizado o tratamento farmacológico, por meio da quimioterapia com GLIVEC por 3 anos, apresentando cura. **Considerações finais:** Os Tumores Estromais Gastrointestinais são tumores mesenquimais muito comuns na região do trato gastrointestinal, sendo sua gravidade conhecida e investigada, através da clínica para o diagnóstico, associado com exames de imagem e exames de análise da imuno-histoquímica buscando observar os marcadores tumorais, principalmente o c-KIT. O tratamento envolve várias modalidades buscando melhorar a qualidade de vida dos pacientes e, geralmente, apresentam bom prognóstico.

Palavras-chave: Gastrointestinal, Tumor estromal gastrointestinal, Proteína c-KIT.

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RESUMEN

Objetivo: Describir el caso clínico de Tumor Estromal Gastrointestinal, destacándose las características diagnósticas y un seguimiento de 5 años del paciente después de una cirugía. **Relato de caso:** El paciente de 51 años que se desarrolló en la región del estómago, diagnosticado por la clínica, asociado a exámenes de imagen e inmunoistoquímica, no se realizó una cirugía por vía abdominal para la retirada total del tumor y después del procedimiento quirúrgico se realizó el tratamiento . farmacológico, por medio de la quimioterapia con GLIVEC por 3 años, presentando cura. **Consideraciones finales:** Los tumores estrogénicos gastrointestinales son tumores mesenquimales muy comunes en la región del tracto gastrointestinal, siendo su conocida e investigada, a través de la clínica para el diagnóstico, asociados con el análisis de imágenes y los exámenes de inmunohistoquímica. el c-KIT. El hospital envuelve la calidad de los pacientes y los pacientes, generalmente, sentado bien pronóstico.

Palabras clave: gastrointestinal, tumor estromal gastrointestinal, Proteína c-KIT.

INTRODUCTION

Gastrointestinal stromal tumours (GISTs) were first reported in 1941 by Golden & Stout, who described a set of mesenchymal lesions appearing in the intestines and which were mistakenly identified as tumours originating from smooth muscle cells, such as leiomyoblastoma, leiomyoma and leiomyosarcoma. Although the term “GIST” has been first used by Mazur & Clark in 1983, it was only in 1998 that these lesions were distinguished from other similar tumours when Japanese researchers discovered the presence of the protein tyrosine kinase (KIT) and the possibility of mutations in this gene. Until that date, there was no reliable immunohistochemical test and GISTs were not always clearly recognised as a distinct type of sarcoma (TAN CB, et al., 2012) (LIN KT e TAN KY, 2017). They are lesions accounting for less than 1% of all gastrointestinal tumours, in which mesenchymal tumours are the most frequent in the region of the gastrointestinal tract (BANDYOPADHYAY D e BONATTI HJR, 2019) (LIN KT e TAN KY, 2017).

Histologically, GISTs seem to have a localisation similar to that of smooth muscle tumours, but they are lesions originating from Cajal’s interstitial cells (BANDYOPADHYAY D e BONATTI HJR, 2019) (LIN KT e TAN KY, 2017). Because gene mutation is involved, this protein KIT is positively expressed in 95% of the GISTs. Therefore, if a tumour is positive in the immunohistochemical test and its cells are morphologically consistent with GIST in terms of hematoxylin and eosin (H&E) staining, a positive diagnosis can be determined (SHIRAKAWA T *et al.,* 2017).

GISTs can be found in any portion of the gastrointestinal tract, but they affect the region of the stomach at a higher percentage, accounting for 60% of the cases (BANDYOPADHYAY D e BONATTI HJR, 2019) (LIN KT e TAN KY, 2017) (XIONG W, *et al.*, 2017). These tumours usually affect elderly individuals who present non-specific symptoms, such as abdominal pain, gastric plenitude, intestinal obstruction, which are in many cases accidently found out in examinations using computed tomography, magnetic resonance and endoscopy (BANDYOPADHYAY D e BONATTI HJR, 2019).

The treatment for this type of tumour has been currently performed by means of full surgical resection or laparoscopy, but in some cases, it may present recurrence (BANDYOPADHYAY D e BONATTI HJR, 2019) (LIN KT e TAN KY, 2017). Chemotherapy can be used with imatinib mesylate or sunitinib mesylate in association with surgical treatment, being quite effective against the tumour (SHIRAKAWA T, *et al.*, 2017).

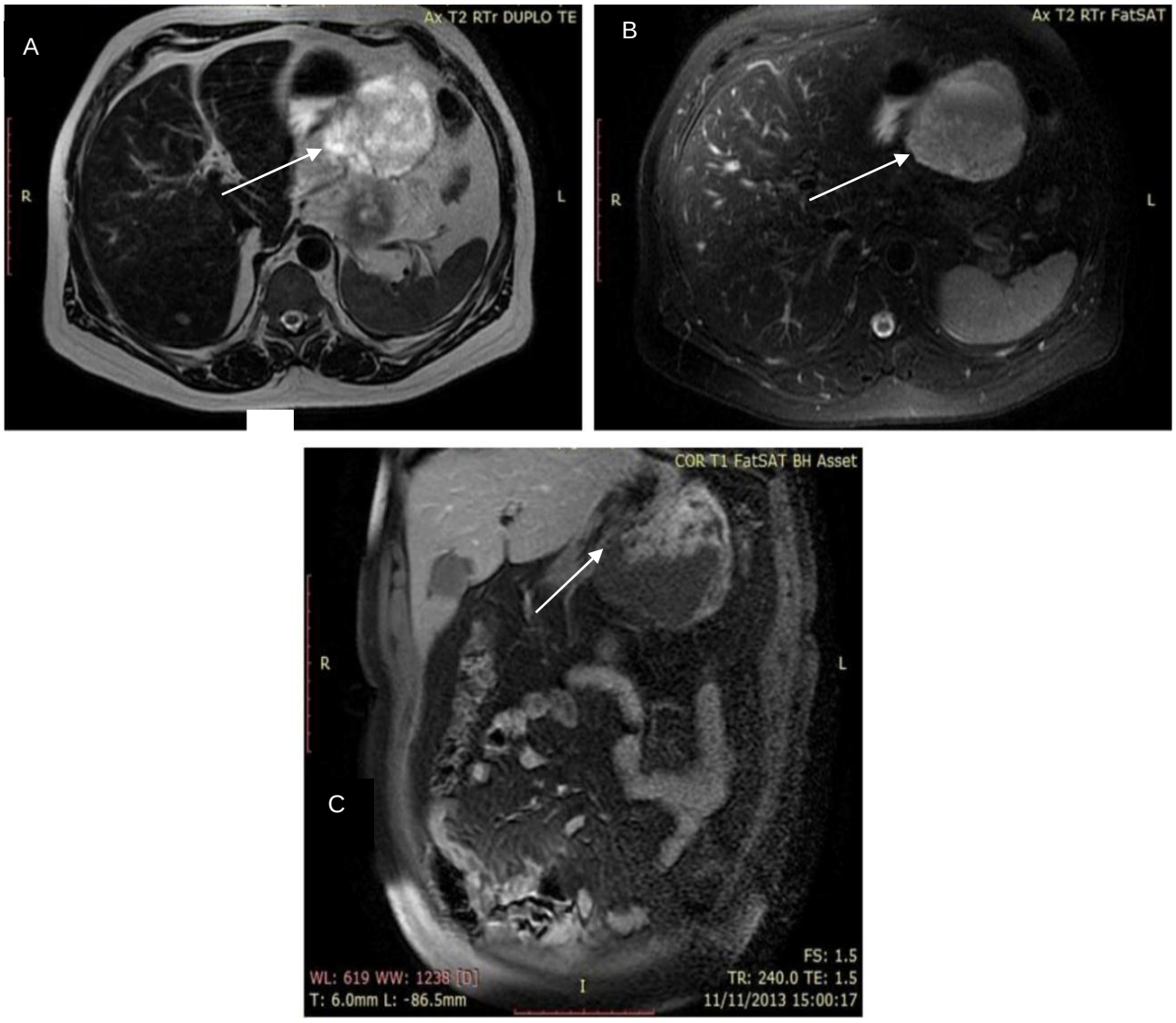
The present case report is aimed to describe a clinical case of gastrointestinal stromal tumour (GIST) by highlighting diagnostic characteristics and a 5-year follow-up of the patient after surgery.

CASE REPORT

A 51-year-old male patient with 90 kg body weight, 1.62 cm height and Body Mass Index (BMI) of 27.7 was seen for evaluation, reporting pre-diabetes (124 mg/dL), no hypertension (blood pressure of 120 x 80 mmHg),

casual drinking and no smoking. On 7th November 2013, the patient complained of sudden abdominal pain (epigastric) and intense sweating, being medicated in the emergency room and having the pain alleviated. On 8th November 2013, the patient underwent a complete abdominal ultrasound in which a complex epigastric cyst was suspected, and he was then referred to specialised treatment. Nuclear magnetic resonance (**Figure 1**) was performed on the patient, demonstrating an extensive non-stenosing exophytic growth located on the wall of the larger curvature of the stomach, with heterogeneous signal on Second Time (T2) image and diffusion restriction. A lesion of solid-cystic aspect measuring 9.7 x 7.5 x 8.4 cm (Coronal x Axial x Sagittal) was observed and central areas of necrosis and liquefaction were highlighted after injection of gadolinium contrast.

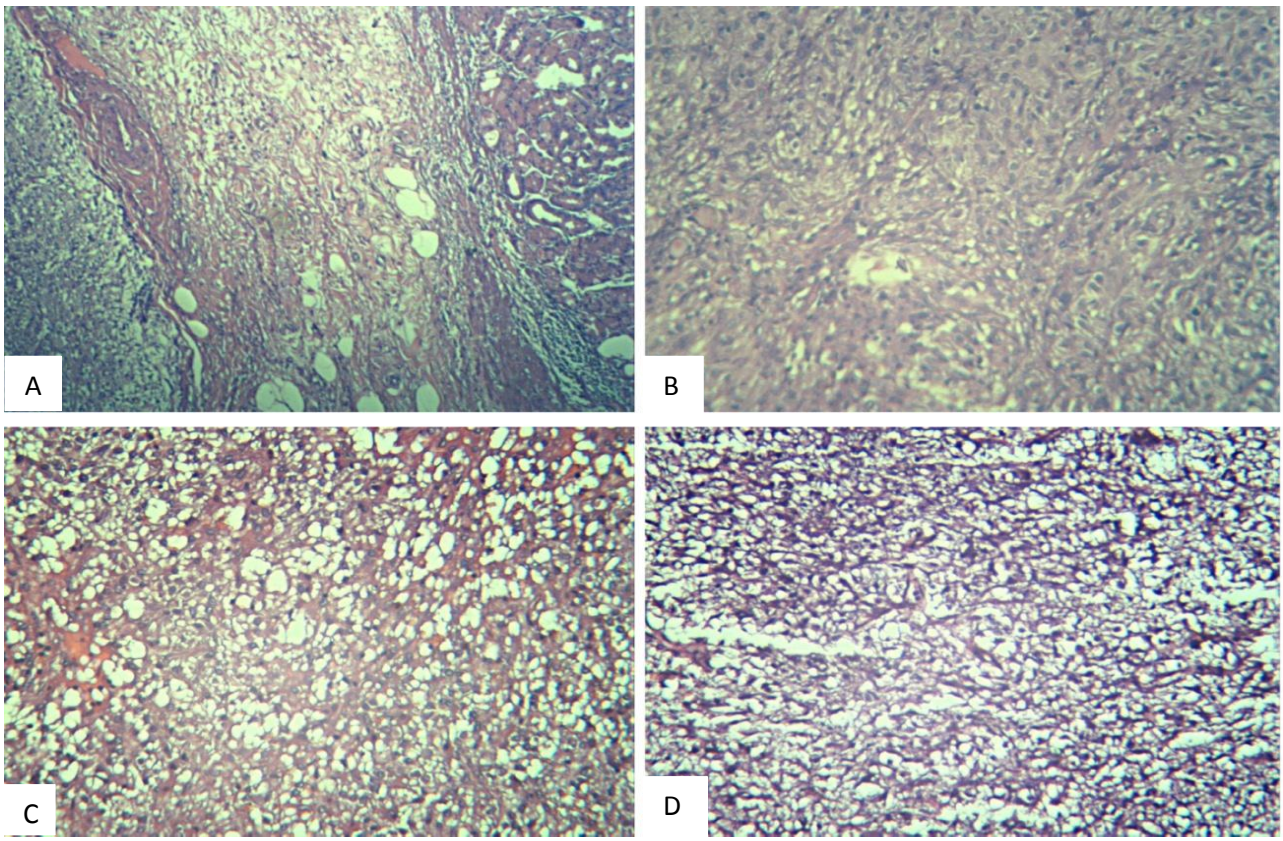
Figure 1 – A and B Axial cut. Coronal section in C. Images with different MRI parameters showing extensive parietal gastric lesion of exophytic aspect with solid-cystic component.



Fonte: Search data, 2013.

After imaging examination, the patient was submitted to upper digestive endoscopy with biopsy for histological analysis. The H&E stained histological sections revealed malignant neoplasia consisting of monotonous spindle-shaped or polygonal cells with enlarged nuclei and uniform chromatin and distinct nucleoli, being the most common type of cells. The cytoplasm is abundant, pale and eosinophilic with fibrillary appearance, including presence of light peri-nuclear vacuoles (**Figure 2**).

Figure 2 – A; B; C; D - monotonous spindle-shaped or polygonal cells with enlarged nuclei and uniform chromatin and distinct nucleoli, being the most common type of cells. The cytoplasm is abundant, pale and eosinophilic with fibrillary appearance, including presence of light peri-nuclear vacuoles.



Fonte: Search data, 2013.

Immunohistochemical study was performed by using the method of heat-mediated antigen retrieval, polymer amplification, development with diaminobenzidine and positive control assays (**Table 1**). Diagnosis of gastrointestinal stromal tumour (GIST) with fusiform and epithelioid cells was made after histopathological and immunohistochemical study.

Table 1 – Immunohistochemical results.

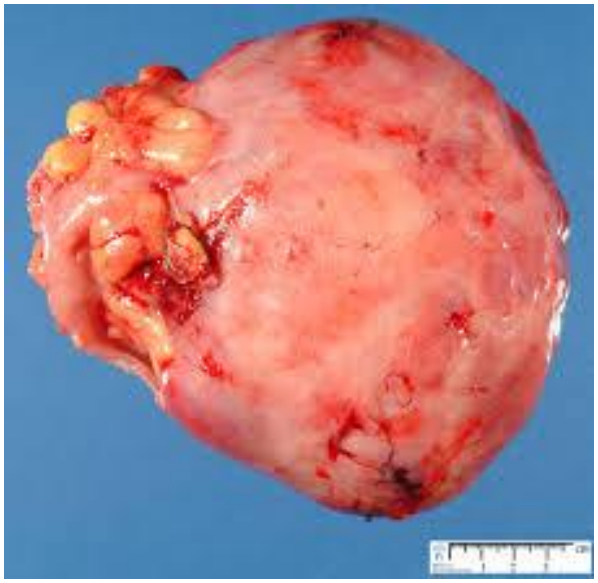
Antibodies	Clone	Result
S-100	Polyclonal	Negative
Smooth muscle actin	1A4	Focal positive
Desmin	D33	Negative
CD34	Qbend-10	Diffusely positive
CD117	Polyclonal	Positive

Fonte: Search data, 2013.

After diagnostic confirmation, the patient was referred to a general surgeon for partial gastrectomy and complete removal of the tumour to be performed via abdomen (**Figure 3**). After the surgery, histopathological and immunohistochemical study was performed again, thus confirming the diagnosis of GIST. On 30th December 2019, the patient was submitted to chemotherapy treatment with Glivec (Imatinib 400 mg daily oral) for three years (i.e. 36 months) and followed up monthly through medical appointments for laboratory examinations (blood test and creatinine levels) during the use of chemotherapeutic drugs, including imaging examinations during the first two months of treatment. The patient complained of headache, insomnia and burning feet. On 8th May 2014, the patient underwent video-endoscopy for post-operative re-evaluation of the

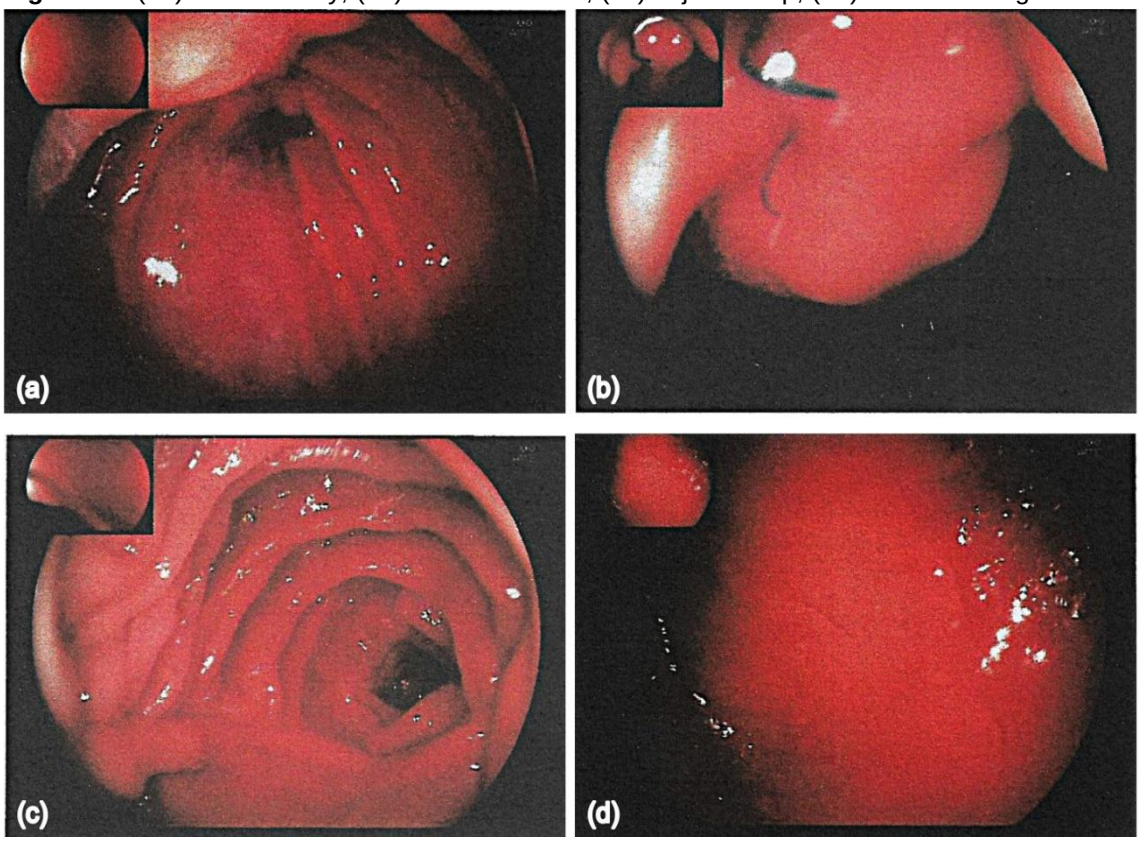
upper digestive tract, revealing reduced gastric chamber formed by part of the stomach body and macroscopically normal mucosa background, presence of suture threads at the small curvature of the residual gastric chamber, patent gastrojejunal anastomosis and free jejunal loop without obstacles (**Figure 4**) (4a) Gastric body; (4b) Suture threads; (4c) Jejunal loop; (4d) Gastric background.. The diagnosis was partial gastrectomy with Roux-en-Y gastrojejunal anastomosis.

Figure 3 – Block resection of the tumour mass.



Fonte: search data, 2013.

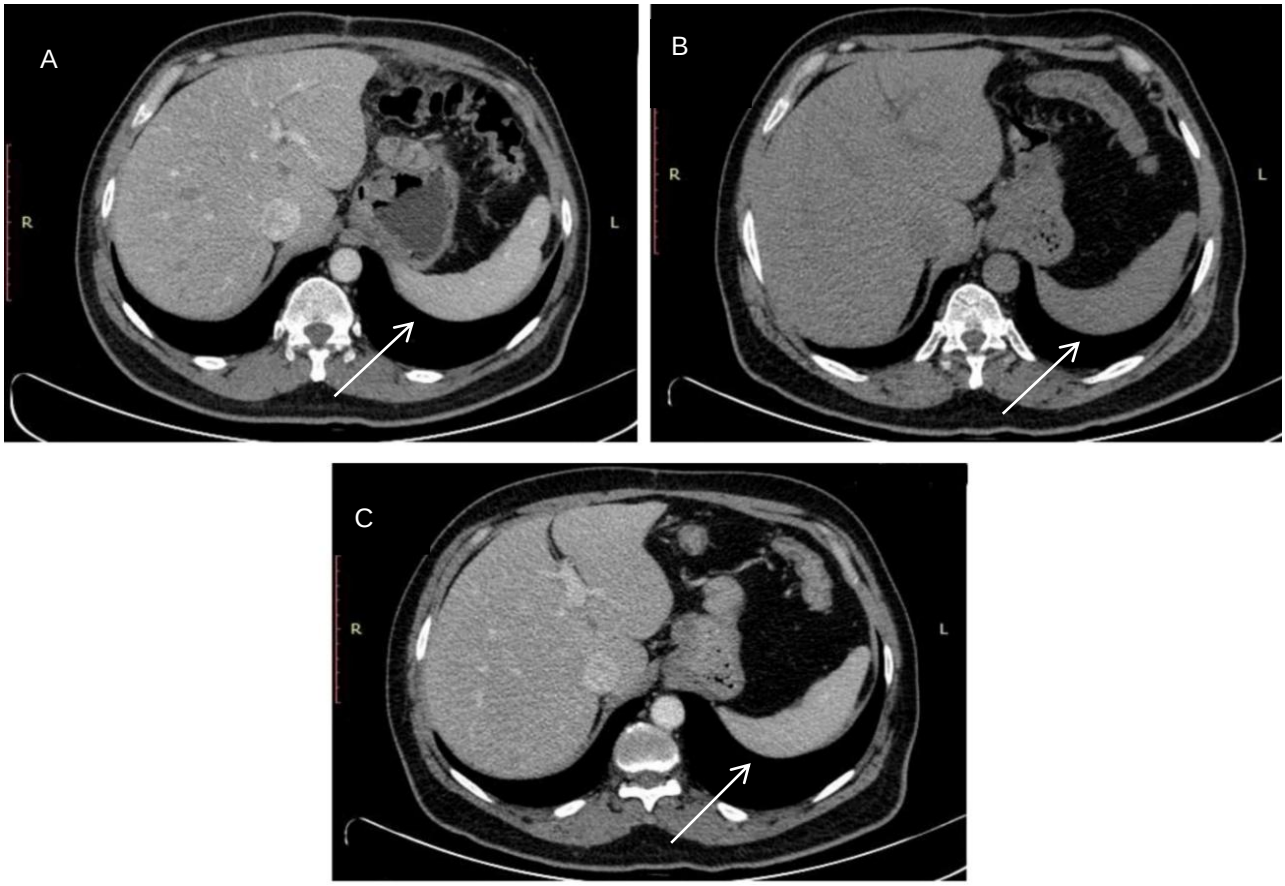
Figure 4 – (4a) Gastric body; (4b) Suture threads; (4c) Jejunal loop; (4d) Gastric background.



Fonte: Search data, 2013.

After finishing the chemotherapy with Glivec 400 orally until 30th July 2017, the patient underwent total abdominal computed tomography on 8th May 2014, 13th February 2017 and 11th December 2018 by using a multislice tomography. Helicoidal scans were acquired with soft tissue filter for multiplanar and three-dimensional re-constructions, covering from the diaphragmatic domes to the pubic synthesis before and after injection of iodinated contrast. The scans showed signs of partial gastrectomy with apparent gastrojejunal anastomosis (**Figure 5**), but without significant evolutive changes. The patient is currently under clinical follow-up.

Figure 5 – A; B e C Axial scans showing signs of subtotal gastrectomy with gastrojejunal anastomosis with no peculiarities.



Fonte: Search data, 2013.

DISCUSSION

According to Parab TM, *et al.* (2018), the clinical presentation of GISTs is non-specific and quite extensive. Symptoms like nausea, vomiting, diffuse abdominal pain, early gastric plenitude can be observed in symptomatic patients. These findings support the symptoms of the patient in our study.

Also, the radiological studies cited in the present case report demonstrate that abdominal ultrasound provides little specific results, that is, a complex cyst was observed in the epigastric region. This poor accuracy of the abdominal ultrasound as a diagnostic method is similar to that of studies by Parab TM, *et al. (2018)*. In addition, for Ninomiya S, *et al.* (2018), more accurate methods are needed for a better diagnosis. For this reason, investigative imaging methods such as upper digestive endoscopy and nuclear magnetic resonance (NMR) were ordered (NINOMYA S, *et al.*, 2019).

With regard to NMR more specifically, the lesion was shown to have an exophytic feature consisting of a solid-cystic mass measuring 9.7 x 7.5 x 8.4 cm. After injection of gadolinium contrast, it was possible to observe

a heterogeneous highlight of the lesion delimiting central areas of necrosis and liquefaction. In addition to this heterogeneous highlight, large tumours can present ulceration of mucosa, cavitations and central areas of hypodensity corresponding to previous findings (i.e. cystic degeneration, haemorrhage, and necrosis). These points of necrosis and degeneration result from the expansive growth of the tumour, presenting various dimensions which end up hampering its own blood flow. These findings were confirmed by Sandrasegaran K *et al.* (2005), who reported that they found heterogeneous neoplasms by means of intravenous contrast (SANDRASEGARAN K, *et al.*, 2005), measuring 3 to 10 cm and presenting a predominantly exophytic growth.

Although imaging examination methods are essentially important for the assessment and measurement of treatment and prognosis of GISTs, they cannot confirm such a diagnosis. This is achieved by means of biopsies and, more strictly, by immune-histochemical analysis.

In this sense, the histopathological study has demonstrated the presence of a malignant neoplasm consisting of spindle-shaped or polygonal cells with enlarged nuclei, predominantly fusiform cells. This finding is corroborated by the study by Silva SE, *et al,* (2004), who suggested the use of immunohistochemical analysis.

Therefore, this investigation showed evidence that protein S-100 (a marker of inflammatory processes) was negative, meaning that the hypothesis of lesion originating from Schwann cells or melanocytes is eliminated. For smooth muscle actin and desmin, one could observe focal positive and negative results, respectively. Two of the main immunohistochemical markers for GISTs, i.e. the glycoproteins CD34 and CD117 had positive results, with the former being the cell adhesion factor which mediates the linkage of hematopoietic stem cells to stromal cells and the latter being the growth factor receptor of mastocytes. Therefore, still according to Silva SE, *et al.,* (2004), the diagnosis of GIST could be determined.

In this way, the treatment proposed was bi-phasic as follows: partial gastrectomy for removal of the tumour and then chemotherapy with imatinib mesylate (400 mg/day PO) – an inhibitor of kinase tyrosine, for 36 months. A similar strategy was employed by Raut CP, et al., (2018) in a prospective clinical study in which 91 patients from 21 North American institutions were follow-up for six years. The resulting data are satisfactory regarding the use of imatinib. None of the patients had recurrence during the use of the drug, whereas the seven patients presenting recurrence were diagnosed two years after the treatment interruption. Nevertheless, further studies are needed for data comparisons (RAUT CP, *et al.*, 2018).

Nowadays, after chemotherapy treatment, the patient is being follow up and the examinations are demonstrating significant evolution.

CONCLUSION

The severity of GISTs should be known as they are the most common mesenchymal tumours in the gastrointestinal tract. The greatest progress in terms of diagnosis was undoubtedly the recognition of the protein c-KIT as an immunohistochemical marker, and the inhibitors of tyrosine kinase receptors represent a specific therapy. The treatment involving different modalities (i.e. surgical, clinical and endoscopic) seems to be favourable, provide a better quality of life and increase survival time for patients affected by this pathology, which even today is a challenge to medicine.

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