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Complete pathological response to Imatinib mesylate in an extraintestinal gastrointestinal stromal tumor

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ABSTRACT

INTRODUCTION: Gastrointestinal stromal tumors (GIST) are the most frequent mesenchymal tumors of the digestive tract. Extraintestinal locations (EGIST) have been described showing similar pattern of immunohistochemical markers than GIST. Inhibitors of tyrosine kinases such as Imatinib or Sunitinib are the mainstay treatment in the management of advanced or metastatic GIST. Complete pathological response to these agents is an extremely rare event, especially in the case of EGIST due to its more aggressive behavior reported.

PRESENTATION OF CASE: Here we describe the case of a 61 years old woman, with an advanced GIST, who was operated after 10 months of Imatinib mesylate. The biopsy demonstrated the extra intestinal location of the tumor and a complete pathological response was confirmed.

DISCUSSION: Complete pathological response to Imatinib is a rare event. To our knowledge, this is the first report of complete response in an EGIST. New clinical, radiological and metabolic criteria of tumoral response to neoadjuvant treatment are revised.

CONCLUSION: EGIST complete pathological response to Imatinib can be achieved. However, recommendation of systematic neoadjuvant therapy with Imatinib remains investigational and more studies are warranted in the future.

1. Background

Gastrointestinal stromal tumors (GIST) are the most frequent mesenchymal tumors of the alimentary tract, accounting for only 0.2% of all gastrointestinal tumors. Extra intestinal locations (EGIST) have been rarely described,[1] showing similar pattern of immunohistochemical markers than GIST.

Inhibitors of tyrosine kinases (TKI) such as Imatinib or Sunitinib are the mainstay treatment in the management of advanced or metastatic GIST patients.[2] Complete pathological response to these agents is an extremely rare event,[3] especially in the case of EGIST due to its more aggressive behavior reported.[4]

2. Presentation of case

We report the case of a 61 year-old woman with no relevant past medical history who was initially evaluated in a center without experience in oncological cases. She complained of abdominal distension, 12 kg weight loss and early satiety eight months before first medical evaluation. Upper gastrointestinal endoscopy and colonoscopy were normal. Contrast-enhanced abdominopelvic Computed Tomography (CT) scan showed a 20 cm highly vascular intraabdominal tumor with central necrosis and gastric compression. Also small hepatic nodules were observed, consistent with metastases. She was submitted to an exploratory laparotomy showing an unresectable giant tumor, thus only an incisional biopsy was performed and then she was derived to our center. After oncological committee evaluation, a new CT scan was performed (Fig. 1A and B). The paraffin embedded biopsy retrieved was further studied with immunohistochemical (IHC) analyses, which showed low expression of CD117, high CD34 and partial DOG-1 expression, with negative Desmin and S100 expressions (Fig. 2A and B). The morphologic and IHC analyses were compatible with a GIST. Since the high risk of dissemination after the open biopsy added to the large size of tumor and the presence of images suspicious of liver metastases, Imatinib mesylate 400 mg per day was started. The treatment was well tolerated, with no grade 3 adverse events. After 10 months of Imatinib, CT scan showed a 2 cm decrease in tumor size and diminishment of contrast enhancement

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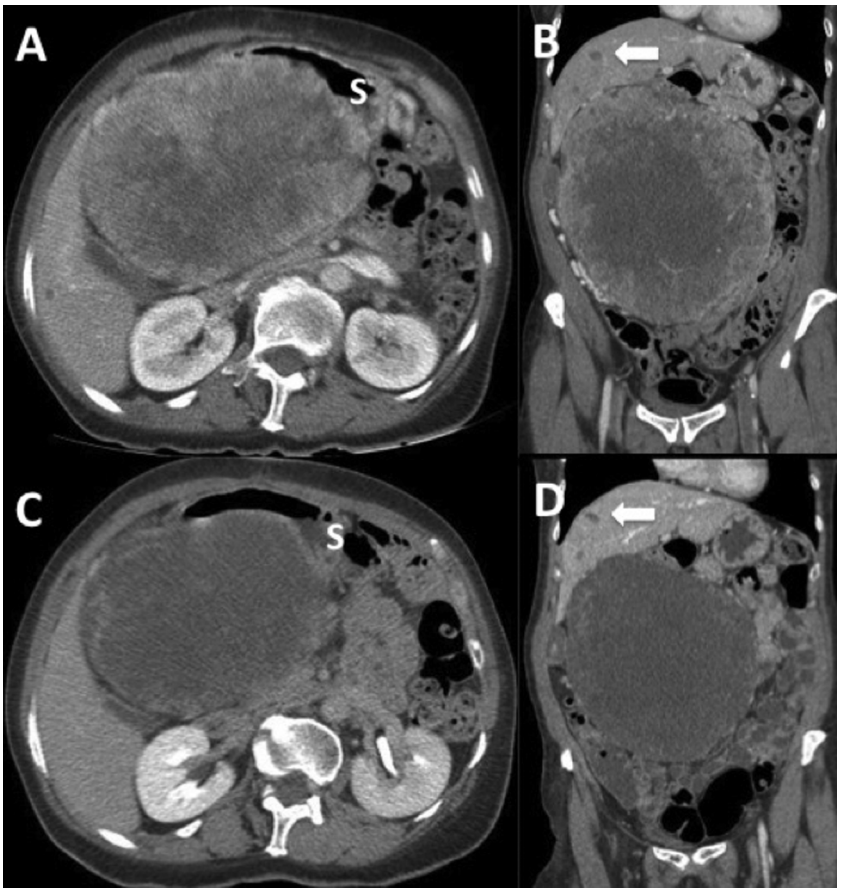

Fig. 1. Intravenous contrast-enhanced abdominopelvic CT scan. (A) and (B) Sagittal and coronal slides after open laparotomic biopsy showing a 20 cm abdominal mass with heterogeneous contrast enhancement and central necrosis. Arrow shows liver nodules suspicious of metastases; S denotes stomach. (C) and (D) Sagittal and coronal slides after 10 months of treatment with Imatinib. Note the reduction in tumoral contrast enhancement, a minor decrease in size and stability of liver lesions.

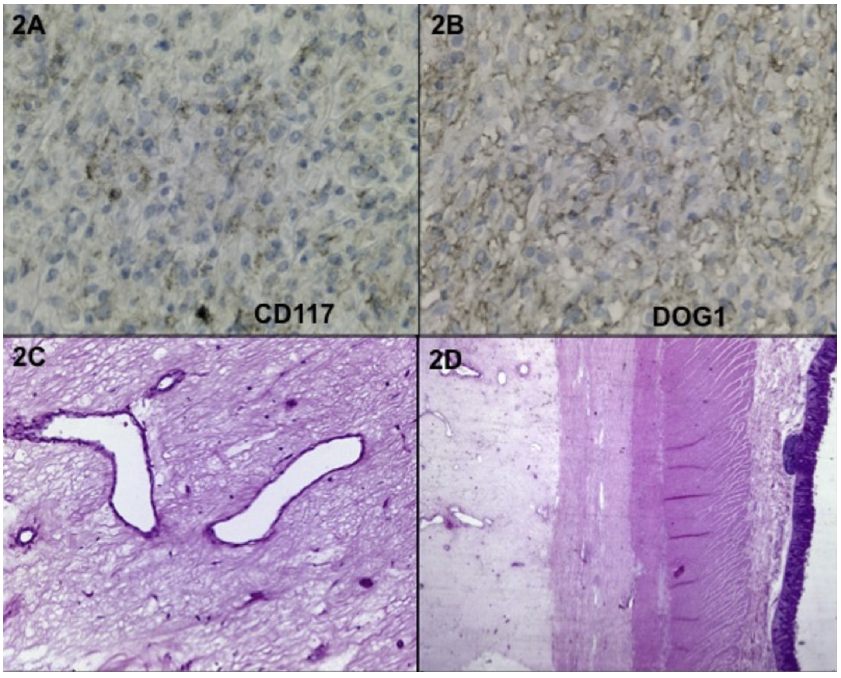

Fig. 2. Pre and postoperative biopsies. (A) Immunohistochemistry performed in the material obtained in the initial biopsy and showed low intensity CD117-positive staining and in (B) a positive DOG1 expression. Picture (C) and (D) show the postoperative biopsy of the tumor resected demonstrating hyaline fibrosis with intense connective tissue without tumoral cells. Picture (D) shows no continuity with the muscularis propia of the bowel, suggesting an EGIST.