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Gastrointestinal stromal tumor of the jejunum: A case report and review

Tumor del estroma gastrointestinal de yeyuno: reporte de un caso.

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ABSTRACT

Gastrointestinal stromal tumors are an uncommon cause of gastrointestinal bleeding. Among them those located in the jejunum represent 0,1%-3% of all gastrointestinal neoplasms. Gastrointestinal stromal tumors are potentially malignant. We report a rare cause of recurrent upper gastrointestinal bleeding in a 36-year-old male patient who presented to the emergency room with upper gastrointestinal bleeding and a palpable mass in the abdomen. Laparotomy revealed a mass in jejunum. Pathology reports a spindle cell gastrointestinal stromal tumor with potential malignant behavior. The patient is on imatinib treatment, free of recurrences. Aspects concerning morphology, immunohistochemistry and differential diagnosis of gastrointestinal stromal tumors are reviewed.

Keywords: gastrointestinal stromal tumors, GISTs, GIST spindle cell type, Kit (CD117)

RESUMEN

Los tumores del estroma gastrointestinal son una causa poco común de hemorragia gastrointestinal. Entre ellas, las localizadas en yeyuno representan el 0,1-3% de todas las neoplasias gastrointestinales. Los tumores del estroma gastrointestinal son potencialmente malignos. Reportamos una causa rara de hemorragia gastrointestinal alta recurrente en un paciente masculino de 36 años que acudió a la sala de emergencias con hemorragia digestiva y una masa palpable en el abdomen. La laparotomía reveló una masa en yeyuno. La anatomía patológica reportó un tumor del estroma gastrointestinal de células fusiformes con potencial comportamiento maligno. El paciente se encuentra en tratamiento con imatinib, libre de recurrencias. Se revisan aspectos referentes a la morfología, inmunohistoquímica y diagnóstico diferencial de los tumores del estroma gastrointestinal.

Palabras clave: tumores del estroma

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gastrointestinal, GISTs, GISTs variante fusocelular, Kit (CD117)

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are rare, constitute less than 1% of all gastrointestinal neoplasms. (1,2) GISTs arise from the interstitial cells of Cajal, a group of cells which form part of the myenteric plexus in the gastrointestinal tract. (3,4) Although the small intestine is the second-most frequent location (30%), only 10% of GISTs originate in the jejunum. (5,6) Clinical presentation can be non-specific symptoms (70%), melena, hematemesis, and anemia due to recurrent bleeding (25%); some cases are asymptomatic. (5,7)

Due to the nonspecific nature of the symptoms and limitations of diagnostic imaging studies, it is challenging to confirm the diagnosis of jejunal GIST pre-operatively. Perforations are more common for GISTs of the small bowel compared to other anatomical sites.

GISTs diagnosis is based on pathological examinations. (8) Histologically, GISTs can be divided with hematoxylin and eosin staining (H-E) into three morphologic subtypes: spindle cell type, epithelioid type and mixed type with spindle and epithelioid cells. (7) The morphology can be heterogeneous. (7)

Differential diagnosis requires immunohistochemistry study. These tumors usually express KIT, DOG1 proteins. CD34 is an additional biomarker although less specific and less frequent than previous. (7,8) GISTs are potentially malignant tumors. (9)

A 36-year-old male was admitted with recurrent upper gastrointestinal bleeding and an intraperitoneal tumor. Intra-operatively a tumor was removed from the jejunum. The morphological features with the immunohistochemical staining profile were consistent with the diagnosis of GIST of the spindle cell variant.

GISTs nowadays can be cured with a combination of surgical and medical approaches with tyrosine kinase inhibitors. (8) This report highlights the presentation of a rare cause of recurrent upper gastrointestinal bleeding, jejunal GIST. Due to GISTs broad differential diagnosis we examine their morphologic spectrum and the immunohistochemistry which are essential to establish the diagnosis, estimate the prognosis and guide adequate treatment. (10)

CASE PRESENTATION

A 36-years-old male presented to the emergency room complaining of stools like “coffee grounds” and mild abdominal pain. He described having bloody stools thirty days before for which received treatment with omeprazole. He reported no prior medical conditions or surgical procedures. He denied consumption of alcohol, aspirin, or non-steroid anti-inflammatory drugs. There was no family history of malignancy.

On physical examination he was mildly pale, his pulse was 88 per minute and his blood pressure was 110/70 mmHg. Abdomen palpation disclosed a 6 cm non-fixed hard tumor at the umbilical quadrant. Rectal

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examination did not show black stools or blood.

A complete blood count revealed hemoglobin of 10,2 g/dl, white blood cell counts of 14,3 x 10^9/L, with 86% neutrophils and 14% lymphocytes and platelet count of 250 x 10^9/L. Other laboratory tests as serum glucose, serum creatinine, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, gamma glutamyl-transferase, total protein, albumin, and urea were within normal limits.

Abdominal ultrasound demonstrated an intra-abdominal tumor of 72 mm in maximum dimensions at the left of aorta. Chest X-ray was negative.

Diagnosis of small bowel tumor was suspected. Clinical differential diagnoses encompass small bowel tumors as adenocarcinoma, GISTs, lymphomas and neuroendocrine tumors.

At laparotomy a jejunum tumor of 8 cm was resected, and it was performed a functional end-to-end anastomosis. There were no regional lymph nodes, peritoneal or liver involvement. The intraoperative and postoperative courses were uncomplicated.

Gross pathology demonstrated a part of small bowel measuring 15 cm in length and 5 cm in width, with an attached mass on the outer surface, lobulated, well circumscribed, measuring 6 x 5 cm in maximum dimensions. The mass was resected en bloc with normal proximal and distal margins (3 and 7 cm respectively). Gross appearance, the tumor was homogeneous, solid, with gray-brown surface and a hemorrhagic focus (Figure 1). Upon opening the small bowel there was a 2cm ulcer with hemorrhagic bottom at tumor level (Figure 2).

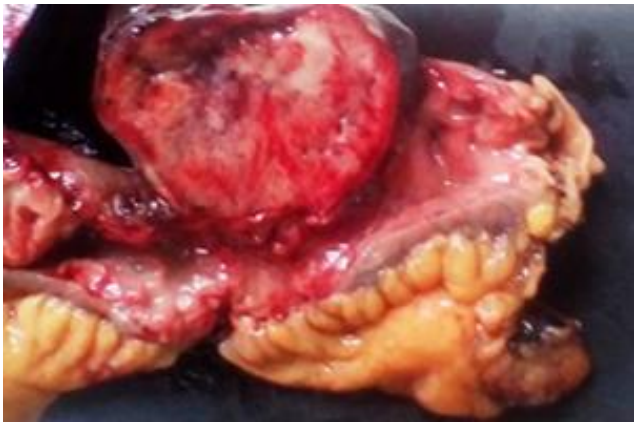

Figure 1. Gross appearance of the tumor in the jejunum. On the cut surface, the tumor has a homogeneous appearance, grayish brown in color with foci of hemorrhage.

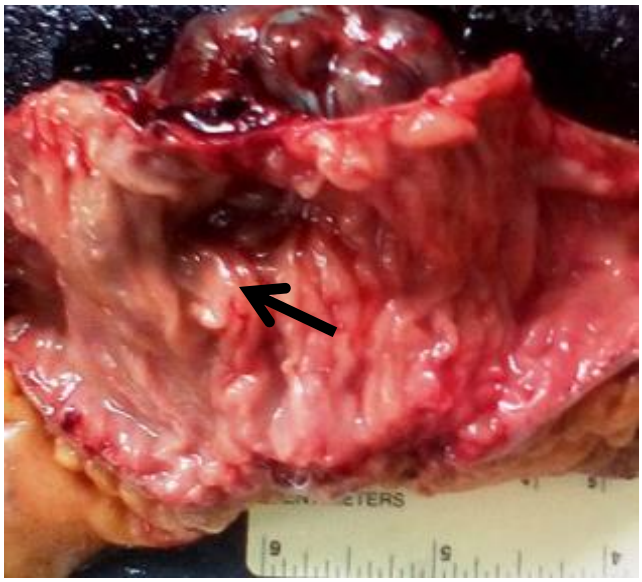

Figure 2. Opening of a jejunum segment with mucosa ulcerated at tumor level.

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Histologic study of the tumor revealed spindle tumor cells with eosinophilic cytoplasm and ovoid nuclei, arranged in fascicles or whorls, as well as extracellular deposits of collagen fibers disposed between the spindle cells (skeinoid fibers). Nuclear pleomorphism was not seen (Figure 3).

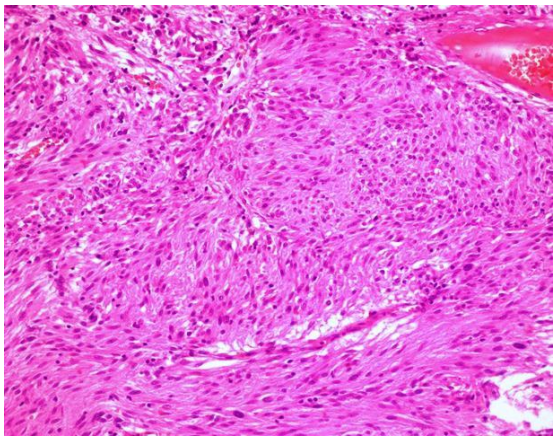

Figure 3. Jejunal GIST. Spindle cells with eosinophilic cytoplasm and extracellular collagen fibers. H&E (40X).

The immunohistochemistry staining of tumor cells revealed strong and diffuse cytoplasmic staining for Kit (CD117), focal positive staining for CD34 (Figures 4 and 5) and negative reaction for smooth muscle actin. Tumor's mitotic activity was low(1 mitosis/50 HPF) (Figure 6).

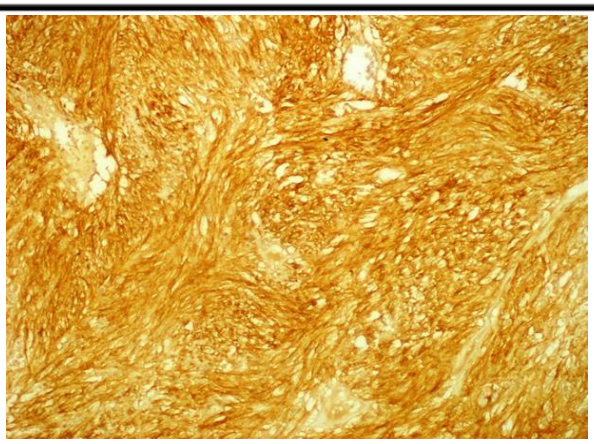

Figure 4. GIST showing strong and uniform cytoplasmic KIT (CD117) positivity. (40X).

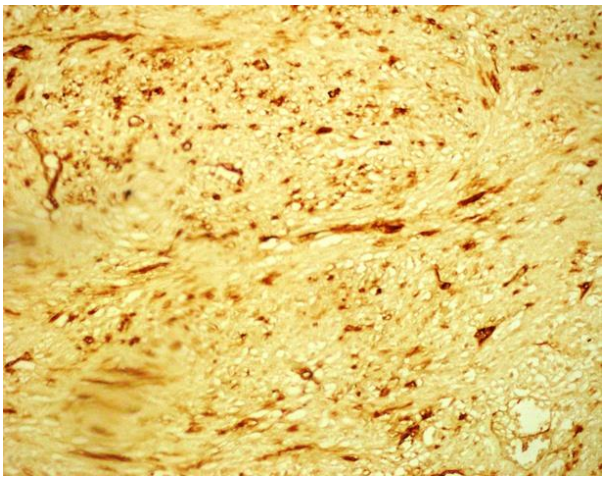

Figure 5. CD34 focal immunoreactivity. (40X).

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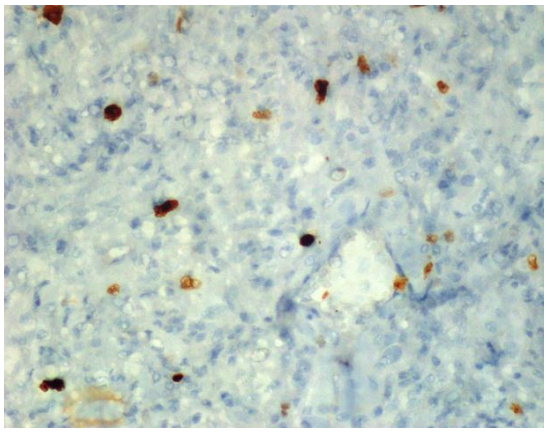

Figure 6. Ki 67 immunostain, low (2%) (40X).

A diagnosis of jejunum spindle cell GIST of low risk was made. A potential malignant behavior because of tumor size >5 cm and jejunum location, was established. Histologic differential diagnosis included other mesenchymal tumors as leiomyoma, leiomyosarcoma, desmoid fibromatosis, solitary fibrous tumor and schwannoma.
The patient has been followed-up for one year for oncologist. He is on imatinib 400 mg daily and no recurrences or toxicity has been reported. An abdominal/pelvic CT scan is performed every six months.

DISCUSSION

GISTs are rare and potentially malignant tumors which can be found in various parts of the gastrointestinal tract. (5) The most common sites are the stomach (60% to 70%) and the small intestine (25% to 35%), while colorectal (5%) and esophagus (<2%) are seldom affected. (11) Most cases are sporadic and between age of 40 and 80 years. (7) Jejunal GISTs account for only 0,1% - 3% of all gastrointestinal tumors. (5)
In presence of recurrent melena, unexplained anemia, and negative upper and lower gastrointestinal endoscopy the diagnostic hypothesis of small bowel GISTs should be considered. (5) Gastrointestinal bleeding is related to tumor invasion of the mucosa. (5,12) Histologically, GISTs are monotonous tumors with three predominant morphologic subtypes: 1). spindle cells variant (70%) composed of cells with palely eosinophilic cytoplasm and ovoid nuclei arranged in short fascicles or whorls, extracellular deposits of collagen (skeinoid fibers) and paranuclear vacuolization are also seen; 2). epithelioid cells variant (20%) with clearer cytoplasm and round nuclei and tissue architecture generally described as nested or sheet-like; and 3). a variant with mixed spindle and epithelioid cell morphology (10%) and in which the stroma can be sclerotic, collagenous or myxoid, regardless of the cytomorphology (7,13).
The presence of skeinoid fibers and nuclear palisading has been related with favorable prognosis in small intestine GISTs. (13)

Immunohistochemistry confirms GISTs diagnosis. KIT (CD117) is a very specific and sensitive marker and identifies around 95% of cases. (7) Most GISTs show strong and diffuse cytoplasmic staining. (7) The sensitivity of DOG1 to identify GISTs is estimated from 87% to 97%, and it is especially valuable in negative KIT cases (5%). (7,10) Immunoreactivity of CD34 varies from 60%-70% depending on GISTs location. This marker is also expressed in other mesenchymal tumors. (7,10,14)

Small intestinal GISTs are more frequently composed of spindle cells. A clinicopathological study of 906 GISTs located in jejunum and ileum identified this morphology in the 86% of patients. (10,14)

The main differential diagnosis for spindle cell GISTs is leiomyoma or leiomyosarcoma, desmoid fibromatoses, solitary fibrous tumors, schwannoma, inflammatory myofibroblastic tumor, inflammatory fibroid polyp, synovial sarcoma. (13) All these tumors are C-KIT negative. (13) While the spindle cell GISTs has syncytial appearance, leiomyomas and leiomyosarcomas are composed of cells with brightly eosinophilic cytoplasm and better-defined cell edges. (13) Inflammatory myofibroblastic tumor consist of myofibroblastic cells that in contrast to spindle GISTs cells have vesicular tapering nuclei and better-defined cell borders. These cells are arranged in fascicles combined with a prominent inflammatory infiltrate of plasma cells. Tumor cells are positive for smooth muscle actin and desmin. (7) In gastrointestinal schwannomas, intramural spindle cell tumors are surrounded by a distinctive peripheral cuff of lymphocytes. Immunohistochemistry reveal diffuse expression of S-100 protein and glial fibrillary acidic protein (GFAP) is commonly positive. Glial fibrillary acidic protein is not expressed in GISTs. (7,13) Solitary fibrous tumor can be positive to CD34. (7)

To predict the risk of aggressive behavior of primary GISTs some guidelines recommend classifying these tumors into risk categories: very low, low, intermediate, and high risk. This classification is based in essential prognostic parameters as tumor size, mitotic count, and anatomic site. In this case tumor size and location made predict a potential aggressive behavior. (4,13)

Radical tumor resection with clear margins is a mainstay to improve survival and reduce the risk of tumor recurrence for primary localized GIST. Imatinib has a key role as adjuvant therapy to reduce the probability of recurrence and metastasis. (4)

CONCLUSIONS

Jejunal GISTs are rare tumors that may present with recurrent upper gastrointestinal bleeding. The differential diagnosis when evaluating a mesenchymal tumor of the gastrointestinal tract is broad. The pathologist arrives to the diagnosis of GISTs through morphologic and immunohistochemical data. Immunohistochemical markers as KIT (CD117), DOG1 and CD34 allow establishing the diagnosis of GISTs.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest personal, financial, or other conflicts of interest to disclose regarding the publication of this article.

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