



## Case Report

# Primary extra-gastrointestinal stromal tumor (EGIST) of the mesentery: Case report and review of literature

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## ABSTRACT

**Introduction:** Gastrointestinal stromal tumors (GISTs) represent <1% of all gastrointestinal (GI) tumors. Extra-gastrointestinal stromal tumors (EGISTs) are mesenchymal tissue neoplasm arising outside the GI tract. This rare group comprises only 5% of all GISTs. This case demonstrates a rare entity in a patient with non-specific symptoms, a large tumor size and unremarkable past personal and family history.

**Presentation of case:** We present a 45-year old man with non-specific symptoms who was diagnosed with a primary EGIST arising in the small bowel mesentery after surgery. The tumor was not compromising the GI tract and it was completely resected. The tumor was sent for pathological examination that confirmed the diagnosis. Histological examination revealed a 15 cm in diameter mass, comprised of spindle cells and high mitotic activity. Treatment with imatinib mesylate was initiated.

**Discussion:** There have been only a few previous reports of EGISTs arising from the small bowel mesentery. It is believed that EGISTs originate from cells with similar pathological characteristics and biological behaviour as the intestinal cells of Cajal. Such tumors are associated with poorer prognosis, larger tumor size and younger presentation than their GI counterparts. The preferred treatment is complete surgical resection. The addition of specific tyrosine kinase inhibitors such as imatinib mesylate is recommended for high risk patients. Even though morphological and immunohistochemical similarities between GISTs and EGISTs are described, their pathogenesis, incidence, genetic background, complications and prognosis are not completely known because they are extremely rare.

**Conclusion:** EGISTs are very rare tumors which originate from cells outside the GI tract and are associated with a more aggressive biological behavior than their GI counterparts. These tumors may grow without any clinical implications and should be kept in mind in the differential diagnosis for patients presenting with an abdominal mass. Further studies are needed due to lack of large patient cohort studies and long-term follow-up regarding the prognosis and management of this rare pathology.

## 1. Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal (GI) tract, although they account for <1% of all GI tumors [1]. They may occur in the entire length of the GI tract, from the esophagus to the anus. Typically, they present in older patients, in whom are most common in the stomach (60–70%), small intestine (20–25%), colon and rectum (5%), and esophagus (<5%) [2,3]. Primary GISTs can rarely occur away from the GI tract, which are referred to as extra-gastrointestinal stromal tumors (EGISTs) [4]. Incidence of EGISTs is reported to be approximately

5–10% of all GISTs [4,11–13]. Both GISTs and EGISTs present the same molecular biology, as well as histological and immunohistochemical behavior [12]. By immunohistochemical test, consistent expression of CD117 (c-kit protein) and CD34 is noted [6,12]. Imaging studies of choice recommended include computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET). The standard treatment of localized, resectable and non-metastatic GISTs and EGISTs is surgery, with combination of imatinib and surgery when high-risk, recurrence or metastasis is present [7,8]. We present an interesting case of a primary EGIST arising in the mesentery in a 45-year-old man with non-specific symptoms. It is of key importance to

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recognize the rarity of this cases and emphasize the need for multi-center collaborative studies to describe the clinicopathologic parameters and clinical implications of this pathology. This work has been reported in line with the SCARE criteria [9].

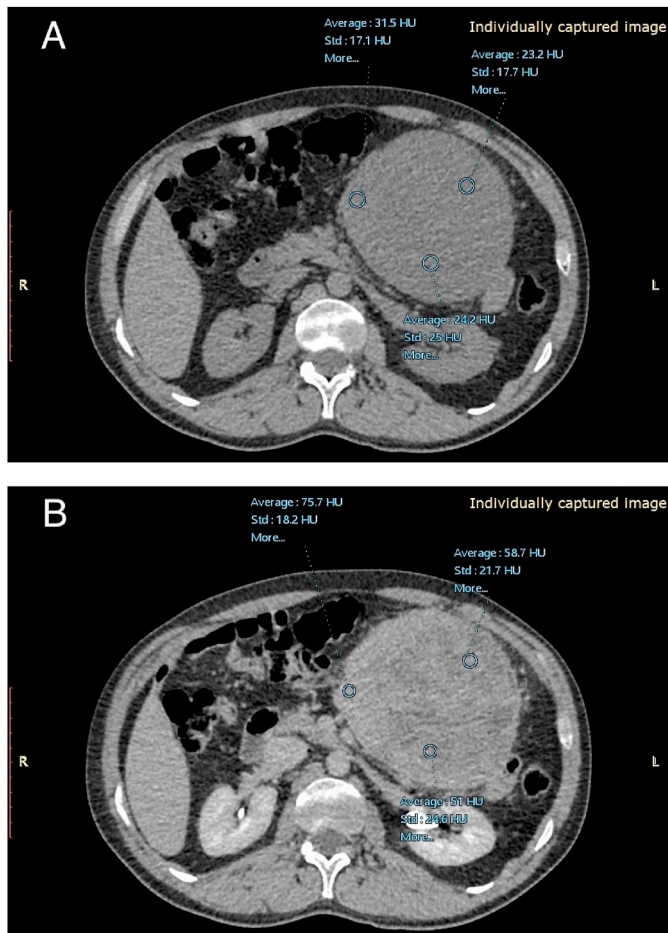
## 2. Case report

We present a 45-year-old male who sought medical care in our institution with a 2-week history of increasing abdominal distention and presence of a left sided abdominal mass. Notably absent were symptoms of nausea, vomiting, pain, anorexia, change in bowel habit or weight loss. The patient was otherwise healthy and had no past medical, surgical and family history. Additionally, tobacco, alcohol, recreation drug use or any past psychosocial history was denied. On clinical examination, vital parameters were within normal limits. Abdominal examination, exhibited a well-defined, tender, left sided abdominal mass (10–15 cm) with no pain at palpation. Blood tests including full blood count, urea and electrolytes, and liver function tests were conducted which were unremarkable and within normal limits. Workup included an abdominal ultrasonography that reported a large tumor with solid appearance, well-defined wall and with a volume of 981 cc. Contrast enhanced CT revealed a large abdominal and well-defined mass (104 × 136 × 168 mm) of undetermined origin, with heterogeneous enhancement, heterogeneous densities, areas of necrosis, high vascularity and displacing the surrounding structures (Fig. 1). Surgical approach was decided with an open laparotomy. Intraoperatively, the tumor was

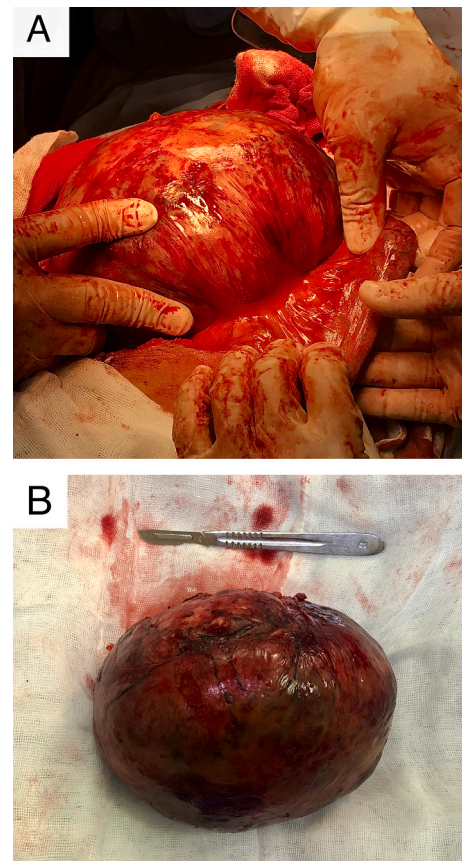
arising from the small bowel mesentery, closely related to intestinal loops and colon, without infiltration (Fig. 2). No other masses or abnormalities were present on exploration of the abdominal cavity and the tumor was found without rupture. The tumor was completely resected. Pathological examination of the specimen revealed a 15 cm in diameter mass, comprised of spindle cells. Mitotic activity was reported with mitotic index of  $<5 \times 10$  high power fields (Fig. 3) and reported a GIST with an intermediate grade of malignancy. The patient was referred to the oncology department for in-hospital visit consultation. Currently, our patient is treated with imatinib mesylate 400 mg/day. After a follow-up of 4 months from the end of surgery, the patient remains in good health and there is no local or systemic recurrence detected. The patient was grateful that he had endured his hospital stay without any complications.

## 3. Discussion

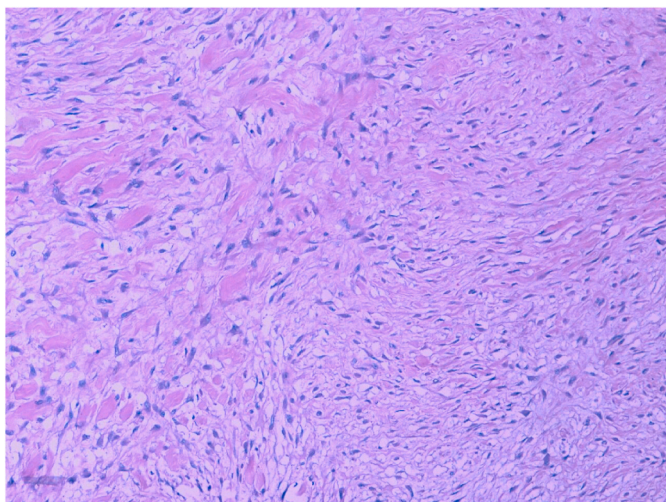
GISTs are rare mesenchymal tumors of the GI tract, and represent only  $<1\%$ . 20–30% of GISTs turn out to be of high risk or malignant [1]. The cellular origin of GISTs reside in the interstitial cell of Cajal (ICC), responsible for peristaltic contractions [5]. The annual estimated incidence of GISTs is approximately 15 cases/million. The median tumor diameter at diagnosis is 8cm, but it has been reported GISTs as large as 40 cm [10]. Median age reported is ~65 years old [25]. Clinical presentation is widely variable, and depends primarily on the location and size, these being the most useful parameters, and may cause symptoms of nausea, vomiting, GI bleeding, anemia, abdominal pain and abdominal mass. Smaller lesions may be diagnosed incidentally on imaging studies or laparotomy. EGISTs are known to be tumors not connected to the GI tract. This rare subtype accounts for 5%–10% of all GISTs [4, 11–13]. The same histological and immunohistochemical behavior is



**Fig. 1.** Abdominal CT demonstrates a large, solid, heterogeneous, well-defined mass (A). After intravenous contrast administration, a high vascular heterogeneous enhancement with areas of necrosis is visualized (B). Ranges between 23–31 HU (A) and 51–75 HU (B) are shown.



**Fig. 2.** Intraoperative (A) and excised (B) view of the EGIST arising from the mesentery. The presence of necrotic changes in the solid mass are evident.



**Fig. 3.** Tumor showing proliferation of spindle cells and few mitotic activity (mitotic index  $<5 \times 10$  high power fields).

present in both GISTs and EGISTs, as well as molecular biology with mutations in tyrosine-protein kinase (KIT) and platelet-derived growth factor receptor  $\alpha$  (PDGFRA), which encodes a receptor tyrosine kinase that is strongly expressed in ICC. The most common histological pattern is spindle-cell type in 70% (fusiform cells in intersecting whorls), followed by epithelioid type in 20% (rounded cells in a nested pattern). These rare tumors normally are characterized to have strongly presence and positivity for CD117 ( $>95\%$ ) and CD34 (70%), whereas occasional positivity for smooth muscle actin (30%), S-100 (5%), desmin (2%), and cytokeratin (2%) have also been reported [12]. EGISTs originate primarily from the mesentery, omentum or peritoneum. Isolated cases also have been reported in the pleura, pancreas, abdominal wall, mesoileum, mesoappendix, seminal vesicles, urinary bladder, rectovaginal septum, pelvic cavity and prostate gland [13–22]. Diagnostic modality includes abdominal ultrasound, CT scan, MRI, and PET [7,8]. Different classification systems have been proposed over the years and, until today, none have proved to be superior to the other [25]. Tumor size, mitotic count, location and tumor rupture are well documented prognostic factors in terms of recurrence, metastasis and consideration for adjuvant therapy. Specifically,  $>10\text{cm}$  in tumor size with any mitotic rate falls into high-risk of aggressive clinical course stratification described by the modified National Institutes of Health (NIH) consensus criteria [23,24]. Based on these criteria, our case falls into high-risk group classification. These tumors generally metastasize to the liver (28%), and the mesentery and omentum (30%). Other locations include the lung (7%), subcutaneous tissues (4.7%), lymph nodes (4.7%), or bone (2.3%) [25]. In high risk category patients is recommended follow-up with serial CT scans in addition to surgery and targeted therapy, approximately 10 years from imatinib initiation [26]. Currently, the preferred treatment for high risk patients is surgical resection in addition with adjuvant specific tyrosine kinase inhibitors like imatinib mesylate therapy. Sunitinib and ponatinib are other options for treatment when resistance or partial response to imatinib is present [12,25]. The presence of an EGIST is associated with poorer prognosis, larger tumor size and younger presentation. Despite the fact that clinicopathological, biological features and prognosis of conventional GISTs are well described, clinical implications of EGISTs have not been thoroughly investigated and have yet to be defined due to their rarity [27,28]. There have been only a few previous reports of such tumors arising in the small bowel mesentery. Our patient did not present any specific symptoms. Since distant spread of the tumor was excluded, laparotomy and complete surgical resection with clear margins was decided. No other abnormalities were found based on CT scan before surgery or during laparotomy exploration. Still, the stratification of this case falls into high-risk, so close follow-up is

required. Due to the sparsity of this cases, further investigation is necessary to study the biological characteristics of EGISTs.

#### 4. Conclusion

Primary extra-gastrointestinal stromal tumors are very rare entities. These tumors originate from cells outside the gastrointestinal tract and are associated with poorer prognosis, larger tumor size and younger presentation. They can present in patients without any specific symptoms and therefore grow without any clinical implications until an abdominal mass is evident. Clinicians must consider this pathology in the differential diagnosis of abdominal tumors outside the gastrointestinal tract. Clinicopathologic parameters and clinical implications are not yet described in literature, so multi-center collaborative studies are needed.

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None.

#### Ethical approval

This case report was conducted in compliance with ethical standards. Informed written consent has been obtained and all identifying information is omitted.

#### Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

#### Registration of research studies

Not applicable.

#### Author contribution

1. Arellano-Gutiérrez Gregorio: Concept and design, literature search, data collection, drafting, manuscript editing, manuscript review and approval of final manuscript.
2. Martínez-Aldrete Luis Francisco: Performed the procedure. Concept and design, manuscript editing, manuscript review, and approval of final manuscript.
3. Pérez-Fabián Abraham: Concept, literature search, data collection, manuscript review.
4. Maldonado-García Edwin Leopoldo: Concept and design, manuscript editing, manuscript review, and approval of final manuscript.

#### Guarantor

Dr. Gregorio Arellano-Gutiérrez.

#### Provenance and peer review

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#### Declaration of competing interest

The authors declare no conflicts of interest.

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