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Case report

Broad ligament Extraintestinal Gastrointestinal Stromal Tumor (EGIST): Case report and brief overview of EGIST

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1. Introduction

Gastrointestinal stromal tumor (GIST) represents the most common soft tissue sarcoma of the gastrointestinal (GI) tract. These tumors however are rare as they only account for 1% of all GI malignancies. The most common sites of origin are the stomach (70%) and small intestine (30%), followed by the duodenum (5%), rectum (4%), esophagus (1%), colon and appendix (1%) (Cheng et al., 2019). It is thought that GIST originates in the interstitial cells of Cajal. Miettinen in 1999 was the first to describe GIST arising outside of the GI tract, named extra intestinal gastrointestinal stromal tumor (EGIST) (Miettinen et al., 1999). The main distinction between GIST and EGIST is the primary site of tumor origin. EGIST originating from locations outside of the GI tract such as retroperitoneum, mesentery, and omentum have been reported. Limited studies to date have reported EGIST originating from mullerian structures (Cheng et al., 2019; Weppler and Gaertner, 2005).

Patients with EGIST present with many nonspecific symptoms depending on the anatomical site of the tumor. Symptoms and signs may include enlarging abdominal mass (ranging 2–32 cm, with most > 10 cm), swelling, bloating and even acute abdomen (Fletcher et al., 2002). Acute severe abdominal pain can be due to tumor rupture with subsequent bleeding, GI obstruction, or pain may mimic appendicitis (Hanayneh et al., 2018). Initial diagnosis of EGIST is challenging when based on variable presentations and imaging alone (Weppler and Gaertner, 2005). Reliable diagnosis of EGIST requires endoscopic guided fine needle aspiration (EUS-FNA) or percutaneous image guided biopsy in order to obtain tissue diagnosis when feasible (Fletcher et al., 2002).

The majority of EGISTs (> 90%) express mutations in *KIT* (CD117) and/or *PDGFRA* that alter the function of tyrosine kinase receptors causing uncontrolled cell growth. Immunohistochemical staining for DOG (99%), CD117 (97%), and CD34 (81%) are useful in suggesting mutations in *KIT* and/or *PDGFRA*. About 10–15% of EGISTs have normal expression of KIT or PDGFRA and should be evaluated for *BRAF* and/or *SDH* gene mutations (Miettinen et al., 1999).

The primary treatment of EGIST is surgery to achieve histologically negative margins. Lymphadenectomy is generally not warranted due to low incidence of nodal metastases. In SDH deficient tumors however, lymphadenetomy is recommended due to higher propensity of lymph node involvement (Li et al., 2019). Preoperative neoadjuvant imatinib (Gleevec; Novartis; Basel, Switzerland) can be considered in patients with large tumors to decrease surgical morbidity, followed by surgery. The goal, if possible, is to have complete resection of tumor with intact pseudocapsule. Multivisceral resections are not recommended but may be necessary as determined by the surgeon in order to have complete resection (De Azevedo et al., 2011).

In this report, we discuss a rare case of EGIST arising from the broad

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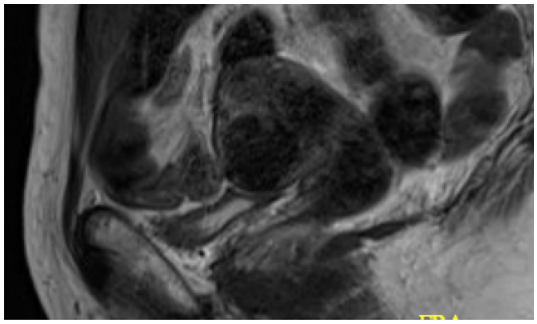

Fig. 1. Sagittal view of T2 weighted MRI of the uterus 28 months before CT imaging. Uterus: multiple calcified fibroids, largest measuring 5.0 × 3.5 cm within the right anterolateral wall. Atrophic ovaries. 3.3 cm pedunculated fibroid vs lesion in the left adnexa.

ligament, initially thought to be a leiomyosarcoma.

2. Case

Sixty-four year old woman presented to the office with acute abdominal pain, distention, and diarrhea. Computed tomography (CT) of the abdomen and pelvis revealed a large complex heterogeneous central pelvis mass, 13.7 × 13.9 cm which exerted mass effect on the adjacent bowel and bladder, findings were suspicious for uterine sarcoma. The patient had a history of suspected fibroid uterus and was previously evaluated for surgical management by magnetic resonance imaging (MRI) (Fig. 1), however was lost to follow up.

A Computed Tomography Scan (CT) showed an enlarged uterus consistent with leiomyomatous change, and a pelvic mass measuring 14.7x13 suspicious for neoplastic mass (Fig. 2A and B).

With preoperative diagnosis of pelvic mass suspicious of uterine sarcoma, laparotomy was performed revealing 1500 cc hemoperitoneum and extensive small bowel adhesions; a vascular and friable mass was found arising from the left posterior broad ligament with

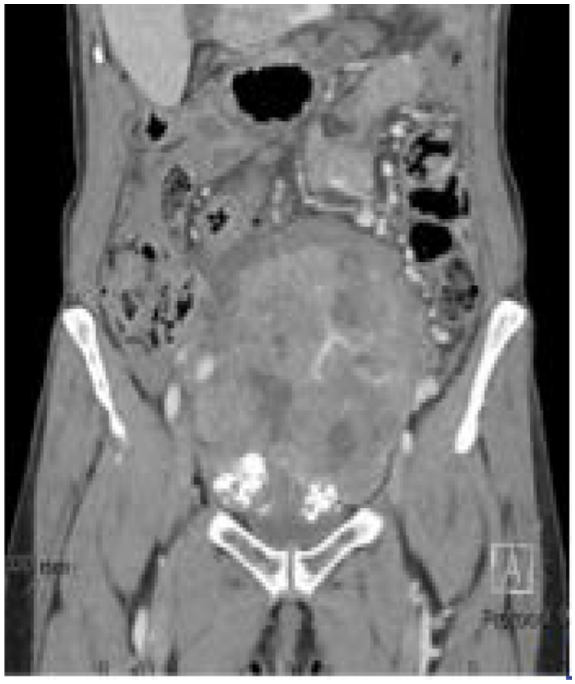

Fig. 2. A: CT Abdomen/Pelvis: Coronal view of pelvic mass when patient presented with abdominal pain and an acute abdomen. B: CT Abdomen/Pelvis: Axial view of pelvic mass when patient presented with abdominal pain and an acute abdomen.

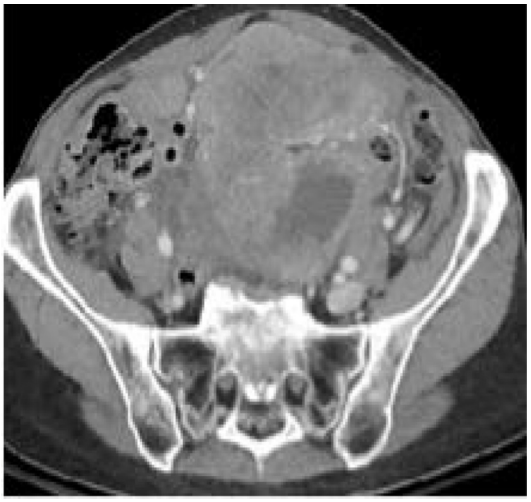

Fig. 2. (*continued*)

extension to the retroperitoneum and the left pararectal area reaching to the presacral area; the mass was severely attached to the rectosigmoid colon, the appendix and a segment of small bowel. Total abdominal hysterectomy (including tumorectomy), bilateral salpingo-oophorectomy, low anterior resection with colorectal anastomosis, small bowel resection with entero-entero anastomosis and appendectomy were performed en bloc achieving a R0 resection of the mass.

Pathology report confirmed the presence of 14 cm extra intestinal gastrointestinal stromal tumor (EGIST) with strong diffuse positivity for C-Kit and focal positivity for CD34, negative for desmin, smooth muscle actin, inhibin, S-100 and estrogen receptor (Fig. 3A and B). Tumor had no necrosis and had 3 mitoses/5 mm^2; mesoappendix showed focal extraintestinal gist. Ileum resection showed GIST involving soft tissue and muscularis propria, surgical margins negative for tumor. Rectosigmoid resection showed extraintestinal GIST involving the mesenteric fat, surgical margins negative for tumor. Uterus, cervix and bilateral tubes and ovaries showed extraintestinal GIST focally involving the left ovary and mesovarium. Final tumor stage was Stage IV (pT4, pN0, pM1, Mitotic Rate: Low). Molecular testing, (Caris Life Sciences Phoenix Arizona), determined *KIT* mutation at Exon 11, p.Y570_L576del and BRIPI mutation at Exon 7p.P210′s.

Postoperative period was without complications. Patient has

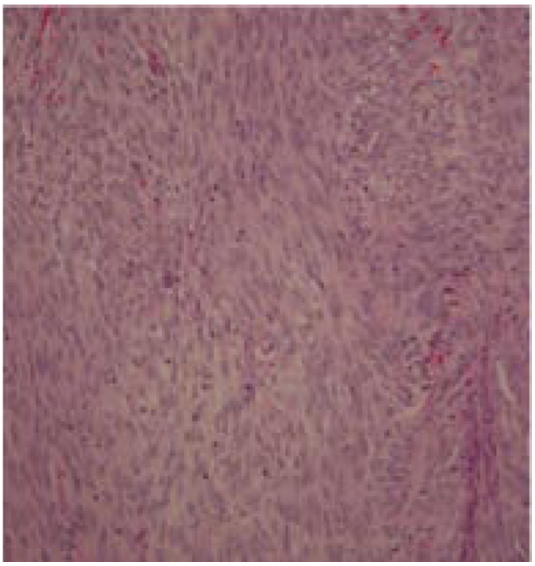

Fig. 3. A: Hematoxylin and Eosin stain.B: Immunohistochemical stain showing a positive CD117 (c-kit) stain.

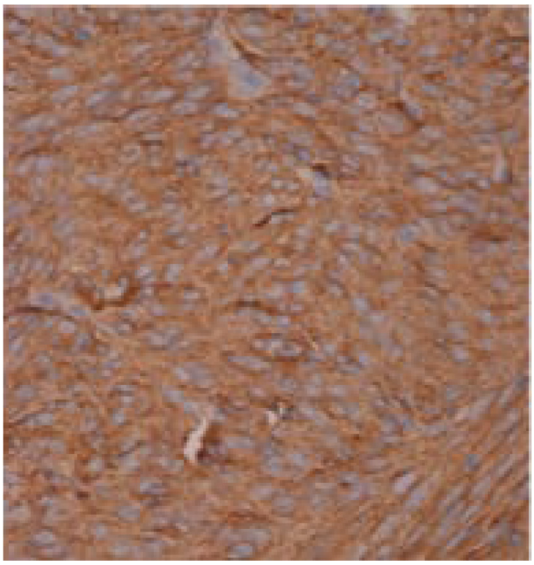

Fig. 3. (*continued*)

received adjuvant imatinib mesylate 400 mg daily which she tolerated well. Clinical and imaging results show no evidence of disease 6 months after her surgery.

3. Discussion

The extra intestinal presentation of GISTs is unusual, occurring in less than 10% of all GISTs (Cheng et al., 2019). The EGISTs presents as free pelvis masses or attached to the rectum, bladder, vagina or recto-vaginal septum, nevertheless the origin in Mullerian structures is extremely rare.

The clinical presentation of EGIST is variable, depending on tumor location, size, presence of bleeding and organs involved (Weppler and Gaertner, 2005). In this case, the patient developed an acute abdomen secondary to tumor rupture and bleeding that caused hemoperitoneum. The patient sought medical attention and surgical management was recommended. Patient history, physical, and imaging studies suspected uterine leiomyosarcoma, however intra-operative findings showed a large complex left broad ligament tumor. Multi visceral resection was necessary to achieve negative microscopic margins. It is possible that a less extensive resection may have been performed if the patient had administered imatinib preoperatively. However, it is extremely difficult to suspect this entity preoperatively and the unusual location of the tumor precluded preoperative biopsy. Despite the R0 resection (microscopically margin-negative resection) was achieved, using the Miettinen predictor of GIST biological behavior, the patient was at high risk of develop metastatic disease (34–52%). High risk tumor characteristics included tumor size of > 10 cm and pre-operative rupture. Mutational testing showed *KIT* mutation, exon 11 and adjuvant therapy with imatinib mesylate 400 mg daily was recommended for 3 years according to NCCN guidelines (Miettinen et al., 1999; Dematteo et al., 2009). Prognosis in this case is based on the location and size of the tumor, 5-year survival for this patient is 50% with a median time to recurrence of 2 years. Patient is followed clinically and with periodic CT scans to rule out recurrent disease.

CRediT authorship contribution statement

Farr R. Nezhat: Conceptualization, Writing - review & editing, Supervision. **Benjamin Zavala Retes:** Resources, Writing - original draft, Writing - review & editing. **Michael P. White:** Data curation, Writing - original draft, Writing - review & editing. **Virginia Donovan:** Writing - review & editing. **Tanja Pejovic:** Conceptualization, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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