CASE REPORT

TJG
The Turkish Journal of Gastroenterology

Extra-gastrointestinal stromal tumor presenting as a surgical emergency

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Gastrointestinal stromal tumors are the most common mesenchymal tumors of the gastrointestinal tract. These tumors are present in almost all cases of KIT-CD117 mutations. When located outside the gastrointestinal tract, they are referred to as extra-gastrointestinal stromal tumors. We present a case of a 72-year-old female with acute abdomen. Computed tomography detected intestinal obstruction and failed to determine the causative pathology. The patient underwent urgent exploratory laparotomy, which revealed pelvic extra-gastrointestinal tumor originating from the broad ligament of the uterus. This case is unique with regard to symptoms and the unusual anatomic location of the mass. Surgeons should be aware of the extra-gastrointestinal stromal tumor entity and its manifestations and management.

Key words: Acute abdomen, gastrointestinal stromal tumor, extra-(E)GIST, KIT mutation

Acil cerrahi nedeni olarak prezente olan gastrointestinal sistem dışı stromal tümör

Gastrointesitnal stromal tümörler sindirim sisteminin en sık görülen mezenkimal tümörleridir. Bu tümörlerin neredeyse tamamında KIT-CD177 mutasyonları görülür. Sindirim sisteminin dışında yerleşmeleri halinde ekstra-gastrointestinal stromal tümörler adını alırlar. Burada akut abdomen tablosunda prezente olan 72 yaşındaki kadın hasta sunulmuştur. Bilgisayarlı tomografi, intestinal obstrüksiyonu tespit edebilmiş ancak nedenini ortaya koyamamıştır. Hastaya acil ekploratif laparotomi uygulanmış ve pelvis yerleşimli, ligamantum latun uteriden köken alan ekstraintestinal stromal tümör tespit edilmiştir. Prezentasyon semptomları ve tümörün anatomik yerleşimi itibariyle literatürde bu vakanın benzeri bulunmamaktadır. Cerrahların ekstra-gastrointestinal stromal tümör antitesi, manifestasyonları ve tedavisi konusunda bilgi sahibi olmaları gerekmektedir.

Anahtar kelimeler: Akut abdomen, gastrointesitnal stromal tümör, ekstra-(E)-GIST, KIT mutasyonu

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are infrequent mesenchymal malignancies arising from the gastrointestinal tract (GIT), accounting for only 0.2% of all GI malignant neoplasms (1). Approximately 60% of GISTs arise in the stomach, 30% in the jejunum and ileum, 4-5% in the duodenum, 4% in the rectum, 1-2% in the colon and appendix, and <1% in the esophagus. Their estimated incidence, including incidental neoplasm, is 10-20 per million (2). The majority are characterized by the oncogenic mutation in either of the two related receptor tyrosine kinases: KIT-CD117 (75-80%) or PDGFRA (platelet-derived growth factor) (5-10%) (3). Recently, extra-gastrointestinal stromal tumors (EGISTs) showing features of GIST have been described at extra-gastrointestinal sites including the omentum, mesentery and retroperitoneal space (4,5). The clinical features and treatment of EGISTs are not well known since there have been only a few cases. To the best of our knowledge, there has been no report of a primary EGIST originating from the broad ligament of the uterus.

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Manuscript received: 23.06.2010 **Accepted:** 10.10.2010

Turk J Gastroenterol 2011; 22 (6): 617-620
doi: 10.4318/tjg.2011.0274

CASE REPORT

A 72-year-old female presented to the Emergency Room in 2008 with a three-day history of vomiting, diffuse abdominal pain and distention, and diarrhea and fever for one day, prior to her presentation. She was a known case of hypertension, diabetes mellitus, dyslipidemia, chronic obstructive pulmonary disease (COPD), cardiomyopathy, and chronic antral gastritis. Her vital signs included: temperature 39.8°C, pulse rate 110 bpm and blood pressure 176/83 mmHg. On physical examination, there were basal crepitations over both lung bases. The abdomen was distended with generalized tenderness. There was no guarding or rigidity and the bowel sounds were absent. Rectal examination revealed empty rectum and no masses or blood in the stool. Laboratory findings showed normal complete blood count (CBC), renal function tests (RFT), random blood glucose level of 170 mg/dl, erythrocyte sedimentation rate (ESR) of 62 mm/h, metabolic alkalosis, O2 saturation: 90.9%, and slight elevation of total bilirubin (1.4 mg/dl) and lactate dehydrogenase (LDH: 215 IU/L). The tumor markers carcinoembryonic antigen (CEA) and alpha fetoprotein (AFP) were within the normal range. Chest X-ray showed no lesion. Abdominal X-ray (erect) showed a picture of subacute intestinal obstruction. Computed tomography (CT) (abdomen and pelvis) with intravenous (IV) and oral contrast (Figure 1) was done and showed hypodense liver lesion in the left lobe with a few hypodense mesenteric lymph nodal enlargements. Small bowel loops were dilated, fluid-filled and matted in the pelvic region with no passage of oral contrast seen beyond the proximal duodenum. There was difficulty in outlining the posterior margin of the urinary bladder. Mesenteric fat stranding was seen along with multiple peritoneal nodules. She underwent exploratory laparotomy. The proximal part of the small bowel was distended with a collapsed distal part. There was a huge pelvi-abdominal mass (15x12x7 cm) originating from the broad ligament of the uterus, which was encapsulated, fragile, vascular, adherent to different areas of the small intestine, vesicoureteric pouch, uterus, and right adnexa, and extended to the left adnexa (Figure 2). There were two obstructive adhesive bands that were released. Debulking of the mass was performed along with partial hysterectomy and bilateral salpingo-oophorectomy. The pouch of Douglas was free. There we-

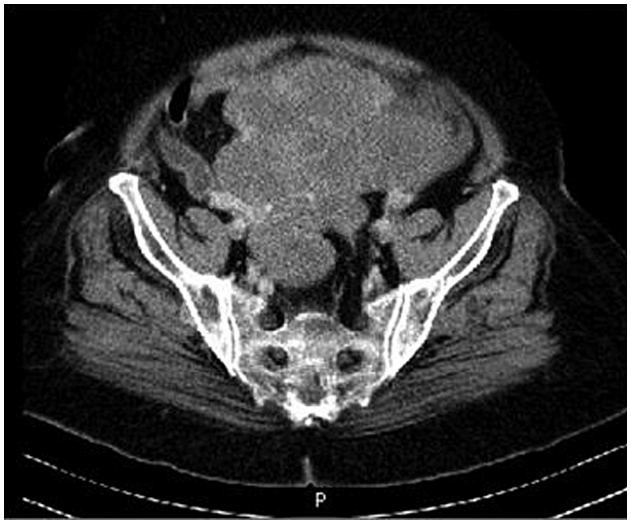

Figure 1. CT (abdomen and pelvis) with IV and oral contrast showed dilated small bowel loops with no passage of oral contrast seen beyond the proximal duodenum secondary to pelvic pathology. Multiple peritoneal nodules along with enlargement of mesenteric lymph nodes were seen in other cuts.

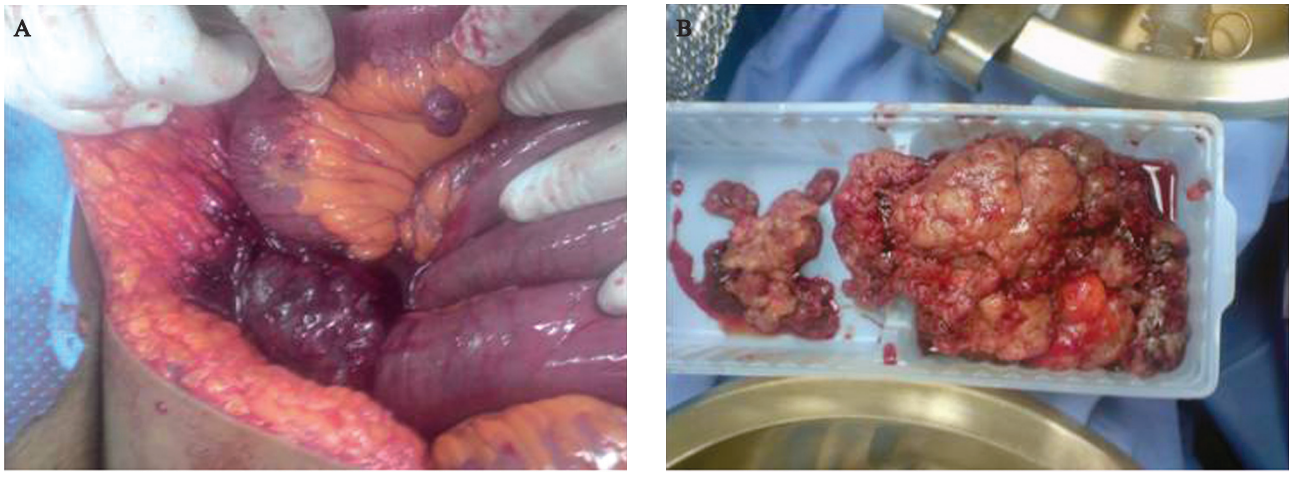

Figure 2. A. Intra-operative picture shows the huge pelvi-abdominal mass adherent to different areas of the small intestine and to the abdominal wall. Metastatic omental nodule is also seen. **B.** Gross appearance of the neoplastic mass, consisting of vascular, fragile fragments.

re multiple areas of metastasis including multiple small nodules on the anti-mesenteric side of the ileum, mesentery, dome of the bladder, right lateral pelvic wall, and omentum. The left lobe of the liver was palpated as having a parenchymal nodule of 2 x 3 cm, and a biopsy was taken. The histopathological diagnosis (Figure 3) of the mass, omentum and mesenteric implant was mesenchymal tumor consisted of spindle cells arranged in interlacing fascicles with foci of necrosis. Most of the mitotic figures were more than 5 per 50 high-power field (HPF). The neoplastic cells showed strong positive immunoreactivity for CD117 (c-kit) and vimentin and mild positive reactivity for CD34 and were negative for S100 and smooth muscle markers. Both tubes, ovaries and uterus were unremarkable. Liver biopsy was negative for malignancy. Molecular genetic analysis for KIT protein mutation was not performed due to its unavailability in our hospital. The diagnosis of EGIST was made and the patient was started on Glivec (Imatinib) 400 mg PO OD. Two weeks post-operatively, the patient developed wound dehiscence for which revision and vacuum- assisted closure (VAC) device were used. Forty-five days' postoperatively, the patient developed respiratory distress. Chest X-ray was performed and confirmed the presence of bilateral pleural effusion with partial lung collapse. The patient died shortly thereafter because of refractory pulmonary edema in addition to her poor general condition.

DISCUSSION

Extra-gastrointestinal tumor (EGIST) is a rare stromal tumor that occurs outside the GIT and comprises about 5-7% of all GISTs (6). The clinical, pathological and prognostic features of GISTs are widely known, while data about EGISTs are few. Most of the EGIST cases are located in the mesentery, omentum and retroperitoneum (4,5). There are rare cases of EGIST localization in the posterior mediastinum, liver, gallbladder, pancreas, urinary bladder, inguinal hernia sac, scrotum, uterus, fallopian tube, and rectovaginal septum, and another report of recurrent vaginal EGIST (7-17). These tumors could represent apparent GISTs that have arisen from the outermost muscle coat of the bowel, but have lost their contact to the point of origin due to an extensive extramural growth pattern (18).

Histologically, EGIST can be of spindle cell, epithelioid or mixed type. The spindle cell type, as present in our case, is the most common (6). In a large study, Reith et al. (5) noted that these EGIST expressed CD117 (100%), CD34 (50%), neuron-specific enolase (44%), smooth muscle actin (26%), desmin (4%), and S-100 protein (4%). Due to the rarity of the EGIST in the pelvic cavity, particularly adjacent to the female genital tract, and because the entity of EGIST has only recently appeared, EGIST might be excluded from the differential diagnosis of spindle-cell neoplasms and could be confused with the more common leiomyoma or leiomyosarcoma. Ortiz-Rey et al. (19) reported that when detected early, many cases of EGISTs can be accessible by a fine needle aspiration biopsy (FNAB).

The behavior of stromal tumors differs according to location, with a trend toward increasingly aggressive behavior as they proceed distally along the GIT (5). In this regard, EGISTs are similar to stromal tumors arising in the distal GIT. Reith et al.

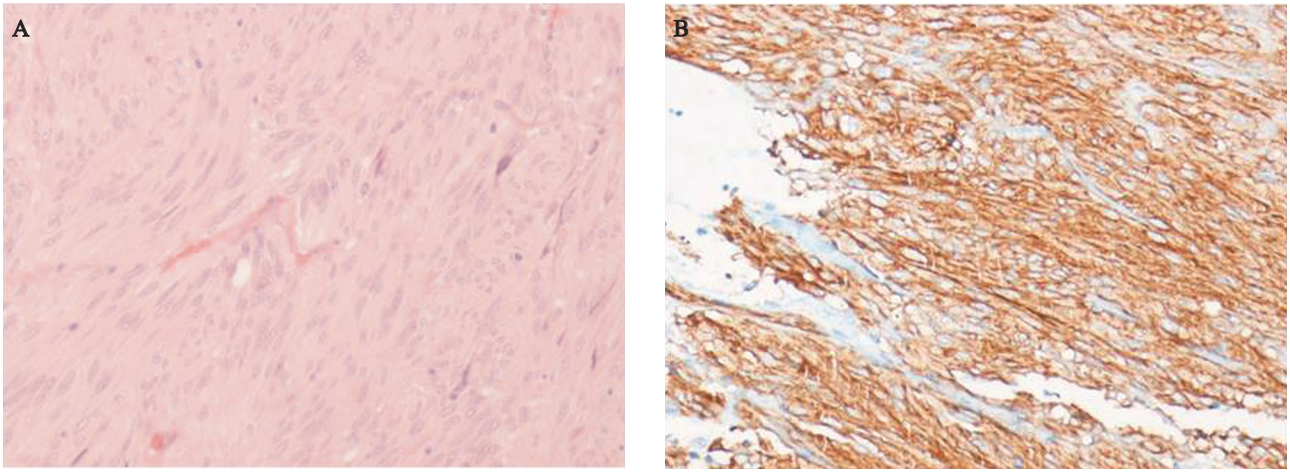

Figure 3. Histological and immunohistochemical findings of the tumor. **A.** Histology of the tumor. The tumor is composed of cellular spindle cells arranged in interlacing fascicles (hematoxylin and eosin). **B.** KIT immunostaining of the tumor: strongly positive in the tumor cells.

(5) reported that frequent mitotic activity (>2/50 HPF), high cellularity and the presence of necrosis were factors indicative of a potentially aggressive clinical course for EGIST. Only 5% of patients with less than two of the above three histologic features experienced adverse outcome (death or tumor metastasis), while 92% of patients having two or more of the features had an adverse outcome (5). Our patient displayed high-risk features (mitotic activity >5/50 HPF, presence of necrosis, moderate cellularity). In Yamamoto et al.'s (6) study, a high mitotic rate (>5/50 HPF) and a high Ki-67 labeling index (>10%) were each significantly associated with an adverse outcome. EGISTs appear to have enough space to grow. Therefore, tumor size, which is commonly used in GISTs as a prognostic factor, may not be applicable to EGISTs.

The current definitive treatment for GIST, including EGIST, is surgical resection, with postoperative recurrence seen in 50% of cases of GIST treated with surgery alone (20). Lymphadenectomy is not required, because lymph-node metastasis of GIST is rare (21). Conventional chemotherapy and radiotherapy have been reported to be ineffective in the treatment of GIST. Imatinib, a tyrosine kinase inhibitor, has been confirmed to be an effective treatment against metastatic and unresectable GIST (22). The development of imatinib resistance is a common occurrence in the clinical management of GISTs, in which case, novel tyrosine kinase inhibitor SU11248 (Sutent™) has been proven to be effective (15).

In conclusion, surgeons as well as diagnostic pathologists should be aware of the possibility that this rare tumor can manifest as a pelvic mass with acute abdomen. Recognition of microscopic patterns and the characteristic immunohistochemical phenotype is mandatory for establishing the correct diagnosis. An aggressive surgical approach is the most effective treatment. Further studies will be necessary to clarify the management and biological behavior of these rare tumors.

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