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Case report

Extragastrointestinal stromal tumors of the pelvic cavity and the vagina: Two case reports and review of the literature

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ABSTRACT

Gastrointestinal stromal tumors (GISTs) are rare tumors of gastrointestinal (GI) tract with mesenchymal cell origin. Extragastrointestinal stromal tumors (EGISTs) are unusual tumors that exhibit the same immunohistochemical and genetic abnormalities as GISTs and most commonly affect the omentum and mesentery. EGISTs of the pelvis and the female reproductive system are exceedingly rare and a frequent diagnostic pitfall. In this report, we present two cases of EGISTs along with a review of the literature.

1. Introduction

Gastrointestinal stromal tumors (GISTs), which are classified as soft tissue sarcomas due to mesenchymal origin, comprise around 1% of all primary gastrointestinal cancers (Ivkoviæ et al., 2002). They are most common in the stomach (40 to 60%), jejunum/ileum (25 to 30%), duodenum (5%) and colorectum (5 to 15%) (Ivkoviæ et al., 2002). They are postulated to arise from a precursor cell of the interstitial cells of Cajal (ICC), also known as intestinal "pacemaker" cells, due to the expression of CD117 (c-kit) on both the tumor cells and the ICC. Most GISTs harbor c-kit gene mutation (most frequently in exon 9 and 11) or platelet derived growth factor receptor alpha (PDGFRA) gene that results in activation of a c-kit receptor tyrosine kinase, and subsequent cell proliferation induction and apoptosis inhibition (Yamamoto et al., 2004; West et al., 2004). Imatinib, a tyrosine kinase inhibitor, has shown dramatic and sustained clinical benefit in GIST. Imatinib works by blocking the ATP-binding pocket required for phosphorylation and activation of the KIT and/or PDGFRA signaling pathways.

GISTs can be subserosal and extend into the abdominopelvic cavity or alternatively can arise from organs outside the luminal gastrointestinal tract and is termed extragastrointestinal stromal tumor (EGIST). Most commonly, EGISTs occur in the mesentery, omentum and retroperitoneum (Yamamoto et al., 2004; Miettinen et al., 1999). They have also been found to occur less commonly as free masses in the pelvic cavity (Peitsidis et al., 2008; Matteo et al., 2008; Angioli et al., 2009), bladder (He et al., 2014; Shin et al., 2011; KROKOWSKI et al., 2003), vagina (Weppler & Gaertner, 2005; Nagase et al., 2007; Ceballos et al., 2004; Liu et al., 2016) and the rectovaginal septum (Nasu et al., 2004; Lam et al., 2006; Melendez et al., 2014; Zhang et al., 2009; Vázquez et al., 2012; Muñoz et al., 2013). In this report, two cases of EGISTs; one occurring in the vagina and one in the pelvic cavity are discussed, along with a brief review of EGISTs occurring in the pelvic cavity and vagina. The purpose of the review is to summarize clinical presentations, typical imaging, pathological findings, and treatment modalities.

2. Case 1

A 58-year-old female with a past medical history of a Bartholin's cyst presented with postmenopausal vaginal bleeding. On pelvic exam the patient was found to have a large intravaginal tumor that was spontaneously bleeding with a necrotic component (Fig. 1).

Transabdominal ultrasonography showed an intravaginal mass that appeared to communicate with the cervix. This raised suspicion of a malignancy and further imaging was obtained to evaluate the perineal area. Magnetic resonance imaging revealed a 6.1 × 5.2 × 8.9 cm enhancing mass arising from the posterior wall of the vagina without definite involvement of the rectum, cervix, or pelvic floor musculature (Fig. 2). Proctoscopy showed that the tumor had not infiltrated into the rectum. The mass was biopsied and pathology revealed an EGIST, spindle cell type, with a mitotic rate of 4 per 50 high power fields (HPF). Immunohistochemistry was positive for CD117, DOG1, and caldesmon, but negative for desmin and smooth muscle actin. Molecular profiling of the tumor revealed an exon 11 KIT mutation. Given the size of the tumor and potential for invasion of surrounding organs the decision was made to initiate neoadjuvant treatment with imatinib for at least 6 months. After 3 months of imatinib therapy, there was favorable treatment response with shrinkage of tumor size to

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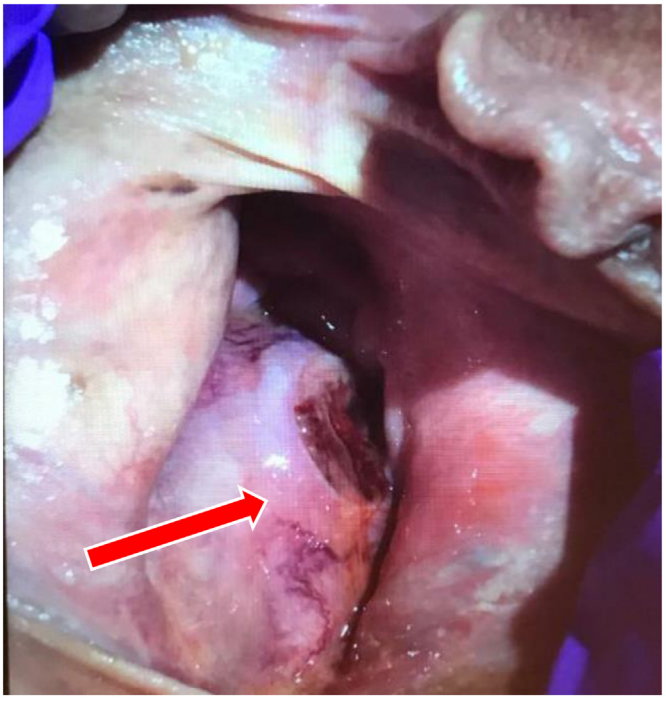

Fig. 1. Large Intravaginal mass (arrow) with necrotic component seen to be spontaneously bleeding on physical examination.

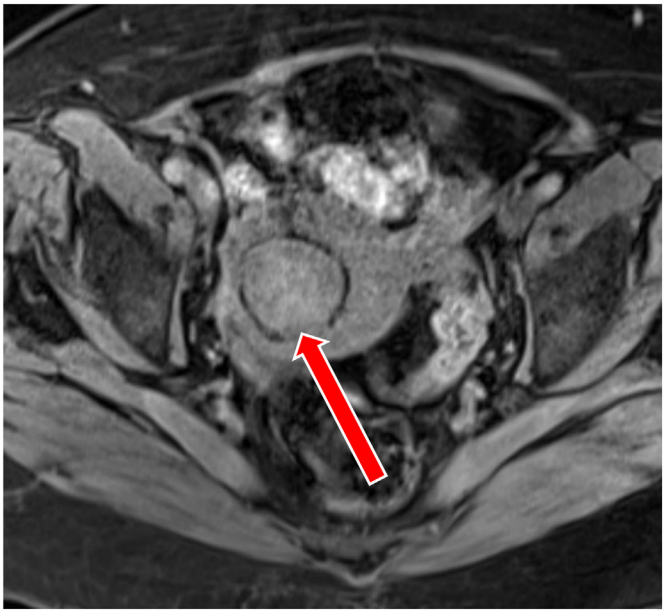

Fig. 2. Magnetic Resonance Image of the pelvis showing an 8.9 cm enhancing mass (arrow) arising from the posterior wall of the vagina without definite involvement of the rectum, cervix, or pelvic floor musculature.

3.6 × 3.6 × 5.9 cm compared with the above dimensions. The plan is to continue neoadjuvant therapy until surgery is deemed appropriate Fig. 3.

3. Case 2

A 73-year-old female with a past medical history of uterine fibroids presented to the emergency department with complaints of abdominal distension and suprapubic discomfort. Computed tomography of the abdomen and pelvis demonstrated a large well-circumscribed mass near

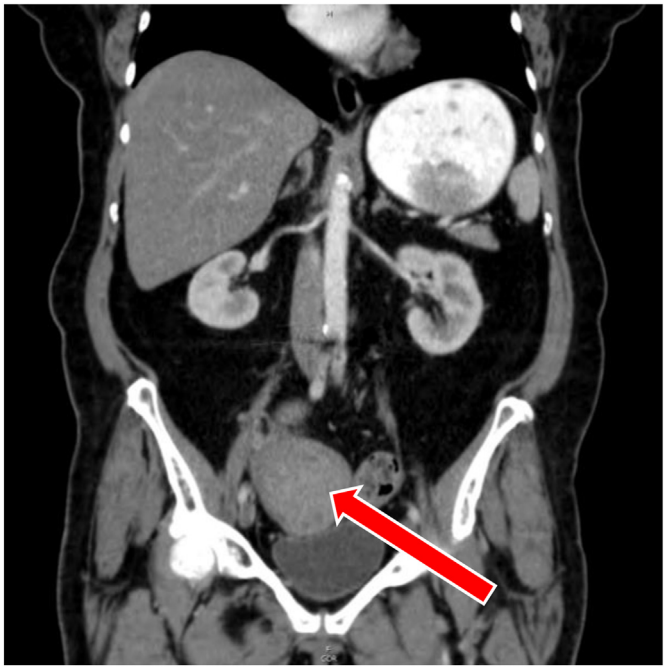

Fig. 3. Computed tomography 8 cm well-circumscribed mass (arrow) in the right adnexal region which is in close association with the uterine fundus and adjacent bowel.

the right adnexa, in close association with the uterine fundus and adjacent bowel. Transvaginal ultrasonography was suspicious for malignant degeneration of uterine leiomyoma given the findings of bridging vessels between the tumor and the uterus.

These findings prompted an exploratory laparotomy which revealed an 8 cm tumor in the anterior cul-de-sac over the surface of the bladder. The mass was firmly attached to the bladder, anterior abdominal wall and loop of small bowel. The patient underwent a total abdominal hysterectomy and bilateral salpingo-oopherectomy with partial bladder resection. The pelvic mass was ultimately diagnosed as an EGIST, spindle cell type, with 45 per 50 HPF mitotic rate (45/50HPF). Immunohistochemistry was positive for CD117, DOG1, and caldesmon, but negative for desmin and actin. Molecular profiling revealed an exon 11 KIT mutation.

The patient is currently undergoing adjuvant therapy with imatinib. After 8 months of therapy, there is no evidence of disease as seen on follow up imaging.

4. Discussion

Primary EGISTs originating from pelvic organs appear to be a diagnostic challenge and are frequently not on the clinician's differential diagnosis. Comprehensive literature review using PubMed, MEDLINE, and Google Scholar using the keywords: GIST, EGIST, vagina, and pelvis identified total of 37 cases of EGIST. After further screening to exclude EGISTs affecting the abdominal wall, seminal vesicle, omentum, liver, pancreas and prostate, 23 cases of pelvic organ EGISTs were identified. Five cases were of primary vaginal EGIST (Table 1) and 3 cases were of primary EGIST of the pelvic cavity (Table 2). Clinical, pathological and initial management features of previously published case reports (along with our cases) are summarized in the tables below in an attempt to reveal any similarities in presentation that may aid in the diagnosis of these rare tumors. (Refer to Table 1 and Table 2).

5. Vaginal EGISTs

Our literature review identified 5 cases of vaginal EGISTs. All