Extra Gastrointestinal Stromal Tumor of Uterus: A Rare Presentation

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Gastrointestinal stromal tumors (GISTs) occurring outside the gastrointestinal tract, also termed as extra GISTs (EGISTs) are rare tumors believed to arise from the peritoneum. Here, we present the case of highly aggressive EGISTs mimicking as a leiomyosarcoma of the uterus which is a very rare entity which to our knowledge has been reported once before. The diagnostic dilemma thus created was solved with the help of immunohistochemistry. These tumors are resistant to chemotherapy and radiotherapy but sensitive to targeted therapy with the tyrosine kinase inhibitor, imatinib mesylate and have a better prognosis unlike their closest differential diagnosis namely leiomyosarcoma of the uterus.

Keywords: Extra gastrointestinal stromal tumors, Imatinib mesylate, Leiomyosarcoma, Uterus

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are rare neoplasia, which are resistant to radiotherapy and conventional chemotherapy but respond well to targeted therapy with tyrosine kinase inhibitors (TKIs) after resection. They constitute <1% of all gastrointestinal neoplasms. Rarely, these tumors occur outside the gastrointestinal tract and then they are referred to as extra GISTs (EGISTs) which are more aggressive than GISTs. Here we report a case of EGIST presenting as a uterine mass, which to our knowledge has been reported once before in literature by Wingen et al., in 2005.

CASE REPORT

Mrs. RK, a 42-year-old lady presented with complaints of menorrhagia and loss of appetite for 4 months. Pap smear done as a part of the evaluation and fractional curettage cytology was found to be normal. Ultrasound abdomen and pelvis revealed the uterus to be 11.3 cm × 5.7 cm × 7.3 cm in size with an endometrial stripe of 12.5 mm. A heterogeneous, predominantly hypoechoic area measuring 5.6 cm × 4.9 cm × 5.5 cm was seen in the left lateral wall of uterus and a similar 2.3 cm × 2.3 cm × 3.6 cm area was seen extending into the lower endometrial cavity suggestive of fibroids. In view of the findings suggestive of fibroids and progressive severe menorrhagia, total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed. Intraoperatively, the left side of uterus was found to be necrotic and eaten up with omental thickening and deposits in the omentum, sigmoid colon and peritoneum giving a suspicion of leiomyosarcoma. On gross examination, a gelatinous polypoidal grayish white tumor measuring 6 cm × 4 cm was found in the endometrial cavity, infiltrating through the isthmus up to the serosal surface. Ovaries were grossly normal. Histopathological examination (HPE) showed a myxoid cellular tumor with round to ovoid to spindle cells, with mild to moderate nuclear pleomorphism and atypia with indistinct focally clear cytoplasm with no necrosis and a mitotic rate of 5/50 high power field (HPF). Immunohistochemistry (IHC) showed an immunoreactive score of 2+ for CD 117, 3+ for S-100 and 0 for smooth muscle actin (SMA), suggestive of GIST. 1 month after surgery, she presented with features of acute intestinal obstruction. Contrast enhanced computed tomography (CT) abdomen was done which showed extensive omental, mesenteric, and bowel deposits with narrowing of distal ileum and subcentimetric para-aortic, aortocaval, mesenteric, left common and external iliac lymphnodes. She underwent omentectomy with diversion loop colostomy, and multiple biopsies were taken. HPE of the omentum showed neoplastic spindle cells in diffuse sheets and focal fascicular pattern exhibiting significant atypia and pleomorphism with mitotic...
activity more than 20/10 HPF. IHC showed positivity for discovered on GIST-1, and CD 34 was negative on IHC. The mesoappendix, serosa and subserosa of the small intestine, right subdiaphragmatic peritoneum, mesentry, and large bowel biopsies showed similar tumor. Positron emission tomography - CT (PETCT) done after 2 months revealed multiple ill-defined hypermetabolic (standard uptake value, max: 7.8) soft tissue nodules scattered throughout the omentum and peritoneal cavity suggestive of diffuse omental and peritoneal metastases (Figure 1). In view of findings suggestive of extensive inoperable EGIST, the patient was started on TKIs, tablet imatinib 400 mg once daily.

DISCUSSION

GISTs are rare tumors arising from the interstitial cells of Cajal (ICC), which are responsible for peristalsis. These are the only cells in the gastrointestinal tract which stain positive for CD117, Vimentin, and CD34. Since the ICC is found only in the gastrointestinal tract, the cell of origin of EGIST is not clear. EGISTs arise from the omentum or mesentry, retroperitoneum being the common site. Rare instances of EGIST of liver, pancreas, prostate, pleura and uterus have been reported in the literature. EGISTs usually present in the 5th or 6th decade with slight female preponderance. Our patient was in the fourth decade at the time of presentation. The literature on EGIST is mainly based on individual case reports and few small series studies. The clinical presentation of EGIST depends on the site and size of the tumor. Our patient presented with menorrhagia, which is an unusual presentation of these tumors. Commonly used imaging modalities for the evaluation of GIST are CT, magnetic resonance imaging and PETCT. On imaging, these tumors are usually extraluminal or intramural. Benign lesions are small, well-defined and homogenous, whereas malignant ones are large, with well-defined or ill-defined margins, heterogenous density with a tendency to spread to adjacent structures. Tumors larger than 6 cm are reported to show necrosis.

An important differential diagnosis of a uterine body tumor, with this type of presentation is leiomyosarcoma, which is what was suspected pending HPE. On imaging, GISTs are indistinguishable from other sarcomas. Therefore, HPE and IHC are the mainstay in the diagnosis of GIST. The HPE and IHC characteristics of EGISTs are similar to GISTs; but, with a higher degree of malignancy. On gross examination, the most of these tumors are larger than 10 cm. In a series by Reith et al., 48 cases of EGISTs were evaluated pathologically and most of them were nodular or multinodular with a tan, friable surface. Some were grossly hemorrhagic or necrotic or with cystic cavities. Our patient had a 6 cm × 4 cm grayish white, mucoid, polypoidal tumor. According to histopathological cell type GISTs are classified into three types: Spindle, epitheloid, and mixed. In a series by Reith et al., the majority were of epitheloid type with CD117 positive in 100%, CD34 in 50%, neuron-specific enolase in 44%, SMA in 26%, desmin in 4% and S-100 in 4% of patients. Whereas in Patnayak et al., series of 10 cases from India, majority were of spindle cell type with IHC showing CD117 positivity in 100%, CD34 in 80%, SMA in 80%, desmin in 20% and S-100 in 20% of patients. Our case was a spindle cell type EGIST positive for S-100, Vimentin, and CD117. Leiomyosarcomas can also express CD117 positivity on IHC though the findings in various studies are varied. However, the absence of immunoreactivity to SMA and desmin ruled out the possibility of leiomyosarcoma in our patient.

Based on the histopathological findings, our patient falls in the intermediate risk category according to the scheme proposed by Fletcher et al., for prediction of risk of aggressive behavior of GISTs. This scheme divides tumors into very low, low, intermediate and high-risk categories depending on the tumor size and mitotic count. However, our patient had additional poor prognostic factors like a ruptured tumor with omental deposits at diagnosis which according to this scheme are not taken into account. Further, extra gastrointestinal location of primary GIST, even if it is not metastatic, is an independent poor prognostic factor with a higher incidence of locally advanced disease, distant metastases and poor overall survival at 5 years. These drawbacks are covered by the AJCC staging, which takes into account metastatic disease and extra gastrointestinal location of primary tumor. Our patient is staged as T3N0M1 - Stage IV and was initiated on imatinib mesylate in an out-patient setting.

CONCLUSION

In summary, we report an unusual case of a 43-year-old lady presenting with menorrhagia and loss of appetite. Fractional curettage cytology was negative for malignancy and imaging findings revealed a uterine mass suggestive
of fibroids for which she underwent surgery in the form of transabdominal hysterectomy and bilateral salpingo-oophorectomy followed by omentectomy and diversion loop colostomy. HPE and IHC confirmed the mass to be a GIST and a diagnosis of EGIST, probably peritoneal, presenting as a uterine mass was made which is an unusual presentation. Our case report suggests that EGIST should be considered as one of the differential diagnosis of women presenting with dysfunctional uterine bleeding and uterine mass on imaging with fractional curettage cytology negative for malignant cells. This needs to be differentiated from leiomyosarcoma of uterus by IHC and although it tends to have a highly aggressive behavior it has an excellent response to targeted therapy with imatinib mesylate in contrast to leiomyosarcoma.

REFERENCES


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