ADITUM Journal of Clinical Research and Clinical Case Reports

Open Access Research Article

Primary Extra Gastro-Intestinal Stromal Tumour Of Vagina- A Rare Entity with Review of Literature

Manisha Vernekar[1*], Amit Mandal[2], Puja Chatterjee[1], Rajib Bhattacharjee[3], Ranajit Mandal[4]

[1]Specialist, Department of gynecological oncology, Chittaranjan National Cancer Institute, 37, S. P. Mukherjee Road, Kolkata, W.B, India

[2]Consultant, Gynecological Oncology, Peerless Hospital, Kolkata, W.B

[3]DNB trainee, Medical Oncology, Apollo Gleneagles Hospital, Kolkata, W.B

[4]Head of the dept, Department of gynecological oncology, Chittaranjan National Cancer Institute, 37, S. P. Mukherjee Road, Kolkata, W.B, India

Article Info

Received: May 04, 2022
Accepted: May 30, 2022
Published: June 14, 2022

***Corresponding author:** Manisha Vernekar, Specialist, Department of gynecological oncology Chittaranjan National Cancer Institute, 37, S. P. Mukherjee Road, Kolkata, W.B, India.

Citation: Manisha Vernekar, Amit Mandal, Puja Chatterjee, Rajib Bhattacharjee, Ranajit Mandal (2022). "Primary Extra Gastro-intestinal stromal tumour of vagina- A rare entity with review of literature". Clinical Research and Clinical Case Reports, 3(2); DOI: http;//doi.org/05.2022/1.1053.

Abstract:

Gastro-intestinal stromal tumours (GISTs) represent 0.1–1% of all gastrointestinal malignancies. They arise mostly from the stomach and the small bowel but may also appear in the colon, rectum or esophagus. GISTs may also be found outside the gastrointestinal tract in the omentum, mesentery, retroperitoneum, uterus and bladder, where they may present as a pelvic mass. Extra-abdominal locations are very rare.

Introduction:

Gastrointestinal stromal tumors (GISTs) represent 0.1-1% of gastrointestinal malignancies. They are the most common mesenchymal tumors of the gastrointestinal tract. Generally, they are asymptomatic and found incidentally during surgical procedures or radiological studies. When symptomatic, these tumors tend to present as gastrointestinal bleeding, abdominal mass or abdominal pain. (1)
GIST may arise anywhere in the tubular gastrointestinal tract from the oesophagus to the rectum.

GISTs can be subserosal and extend into the abdominopelvic cavity or alternatively can arise from organs outside the luminal gastrointestinal tract and is termed extra gastrointestinal stromal tumour (EGIST). (2) Identical lesions may occur in extra-intestinal locations such as the mesentery, omentum and retroperitoneum, while rare sites include the gallbladder or bladder. In terms of distribution, 50-60% of lesions arise in the stomach, 20-30% in the small bowel, 10% in the large bowel, 5% in the oesophagus and 5% elsewhere in the abdominal cavity. (3)

Diagnosis is based on histopathology and immunohistochemistry. (1)

Case report

A 70 years old female, with 3 living issue, attained menopause 18 years back presented in our institute with white discharge vaginally for last 7-8 months with intravaginal mass and pain abdomen increasing in nature for 3-4 months. There was no hematemesis, malena or vomiting. She was a known case of hypertension and hypothyroidism for last 10 years and was on regular medication. There was no history of any addiction. No significant family history.

Her general and systemic examination were within normal limits. Per abdomen examination revealed a hard, fixed mass in suprapubic region.

On inspection, vulva appears to be normal. Per speculum examination was non-negotiable due to the mass filling up the introitus. Per vaginal examination revealed a hard, fixed mass arising from the posterior and left lateral vaginal wall obliterating the vaginal cavity. (Fig 1) Posterior fornix obliterated by the mass. Uterus size could not be appreciable very well due to the obliterating mass. Cervix felt and appears to be normal.

On per rectal examination anterior rectal wall was indented by the vaginal mass and rectal mucosa was free.

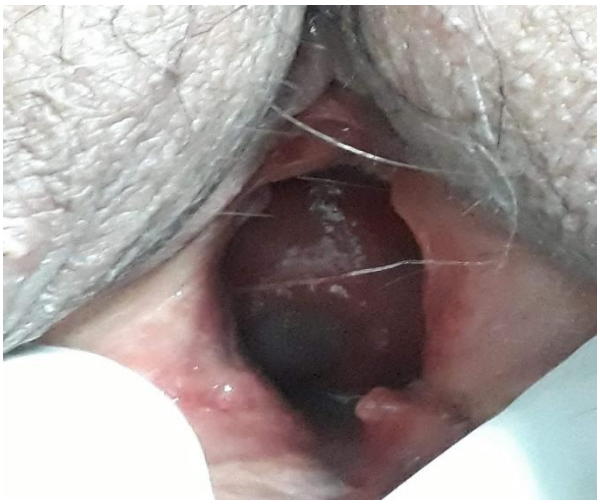

Fig 1: Per vaginal examination revealed a hard, fixed mass arising from the posterior and left lateral vaginal wall obliterating the vaginal cavity

Her complete hemogram and biochemistry investigations, chest X-ray, Electrocardiogram, Thyroid profile were within normal limit.

Ultrasound of whole abdomen revealed anteverted uterus, 6cm in size with cervix appears flattened from behind. A well defined hypoechoic SOL 12x7cm noted behind the cervix may be along the vaginal wall. There was no ascites. MRI whole abdomen showed large, lobulated, hetrogeneous SOL (11x9x9.2cm) in lower abdomen and pelvis extending into bilateral adnexal region compressing the urinary bladder, rectum and adjacent bowel.
Biopsy from the vaginal mass done outside CNCI on which was suggestive of low grade malignant spindle cell tumour.

Slide review was done in CNCI showed haphazardly arranged spindle cell with elongated clumped nuclei and opened up nuclear chromatin suggestive of leiomyosarcoma (Fig 2). Pathologist in CNCI advised Immunohistochemistry (IHC) for confirmation of the diagnosis.

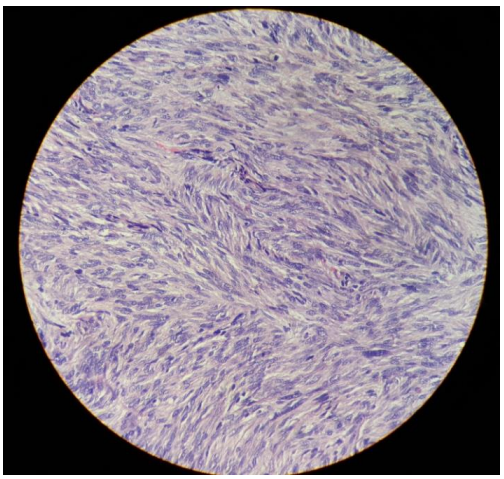

Fig 2: Haphazardly arranged spindle cell with elongated clumped nuclei and opened up nuclear chromatin

IHC expressed c-kit, CD 34, DOG 1 and are immunonegative for desmin, SMA, S 100 protein and cytokeratin. IHC confirmed as c-kit expressing Gastro intestinal stromal tumour (GIST).

Multidisciplinary board decision was taken and was advised chemotherapy as the mass was not ressectable followed by reassessment for surgery. Patient was started on neo adjuvant Tb Imatinib therapy, and currently undergoing the therapy. There is no evidence of any recurrence or disease on 3 months follow up.

Discussion

Gastrointestinal stromal tumors (GISTs), which are classified as soft tissue sarcomas due to mesenchymal origin, comprise around 1% of all primary gastrointestinal cancers. They are most common in the stomach (40 to 60%), jejunum/ileum (25 to 30%), duodenum (5%) and colorectum (5to15%). (1)

GISTs can be subserosal and extend into the abdomino pelvic 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. They have also been found to occur less commonly as free masses in the pelvic cavity, bladder, vagina and rectovaginal septum. (4)

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. (1)

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. (3)

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. (1)

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. (5)

Misdiagnoses may have significant therapeutic and prognostic implications because of the targeted imatinib-based therapy now available.

Vaginal EGISTs: Our literature review identified 6 cases of vaginal EGISTs. Most of the patients with vaginal EGISTs were postmenopausal and the tumor presented as a mass protruding from the vaginal introitus with average tumor size in largest diameter was 4.5 cm (range 2–8 cm). Most of the vaginal EGISTs presented in the posterior vaginal wall. Case reports of EGISTs arising from 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) revealed that these tumors arise from the rectovaginal septum or extended from the rectum, as opposed to arising from the vaginal wall stroma. Pathologically, tumors seen as well-circumscribed masses that may resemble leiomyomas. Spindle cell morphology (which is the most common morphology in GIST) was seen in 100% of the cases as well. CD117 was expressed on 100% of the cases. Desmin, smooth muscle actin (SMA), S100 were not expressed on any of the tumors further excluding the diagnosis of smooth muscle tumors and melanomas. Molecular profiling was performed on only 2 out of 6 cases. It revealed exon 11 KIT mutation similar to the case presented here. Vaginal EGISTs had a mitotic rate ranging between 1 and 25/ 50HPF and none were metastatic on presentation. This suggests that these tumors are indolent and have a low rate of metastatic potential. Four out of six patients were treated surgically. The unresectable tumor was treated with imatinib for an unspecified amount of time and no follow up was documented. Furthermore, out of the four cases where follow up was documented (Nagase et al., 2007; Ceballos et al., 2004; Liu et al., 2016), only one had a local recurrence which was subsequently treated with repeat surgical excision and adjuvant imatinib (Nagase et al., 2007; Ceballos et al., 2004; Liu et al., 2016). All four cases eventually went into complete remission without local or distant recurrence.

Case	Age	Presentation	Imaging	Pathology	IHC	Management	Follow up
Weppler & Gaertner, 2005	66	Post menopausal bleeding, 8 cm posterior vaginal wall mass	Poorly visualized on CT	Macroscopic: irregularly shaped Microscopic: spindle cell mitotic rate: >5/50 HPF	Positive for CD 117, Cd 34, vimentin	Unresectable mass, monotherapy with Imatinib	Not reported
Liu et al, 2016	41	Painless, 8 cm mass in the posterior vaginal wall	TVS- cervical leiomyoma MRI- elliptical mass in the cervix and posterior vaginal wall with a clear margin consistent with leiomyoma	Macrscopic: well circumscribed mass surrounded by a fibrous capsule with hemorrhage and necrosis Microscopic: spindle cell mitotic rate: 25/50 HPF	Positive for CD 117, CD 34, DOG1	Surgical resection with adjuvant imatinib	Follow up after 5 months showed no recurrence or metastasis
Ceballos et al, 2004	75	5cm posterior vaginal mass bulging into the introitus with intact mucosa	Pelvic imaging unremarkable	Macroscopic: well circumscribed, tan, lobulated mass with fleshy appearance and focal necrosis Microscopic: spindle cell, mitotic rate: 12-15/50HPF	Positive for CD 117, vimentin, CD34, h-caldesmon	Surgical excision with positive margins	Follow up at 10 months showed no recurrence
Nagase et al, 2007	66	Recurrent right vaginal wall mass, 2cm mass	CT: well circumscribed dense soft tissue mass with no evidence of distant metastasis	Macroscopic: not reported Microscopic: spindle cell mitotic rate: 1-2/50HPF	Positive for CD 117, CD 34, vimentin	Surgical excision and adjuvant imatinib	No recurrence at 6 months follow up
W Hanayneh et al 2018	58	Post-menopausal bleeding with intravaginal tumour	TVS- intravaginal mass communicating with the cervix MRI: 8.9cm enhancing mass arising from the posterior vaginal wall without definite involvement of the rectum, cervix, pelvic floor	Macroscopic: not reported Microscopic: spindle cell mitotic rate- 4/50 HPF	Positive for caldesmon, C kit, DOG-1	Neo adjuvant imatinib	8 months of follow up no recurrence
Our case	70	Vaginal discharge and abdominal pain	USG- well defined hypoechoic SOL 12x7cm noted behind the cervix may be along the vaginal wall	Macroscopic: posterior and lateral vaginal wall mass Microscopic: spindle cell	Positive for CD 117, CD34, DOG-1	Neo adjuvant Imatinib in view of unresectable mass	3 months therapy, no recurrence on follow up

Conclusion

EGISTs affecting the female reproductive tract and the pelvic cavity are rare entities. Primary EGISTs originating from pelvic organs appear to be a diagnostic challenge. Their presentation and imaging findings are nonspecific and this contributes to delay in diagnosis and treatment. Immunohistochemistry remains the most definitive method to diagnose EGISTs and differentiate them from other mesenchymal tumors. The current standard of care for EGIST is surgical resection as depicted in most of the cases. Neoadjuvant imatinib may be beneficial for locally advanced EGISTs because of the potential for shrinkage of the tumor size prior to any definitive surgery.

References

1. H. Wissam, S. Jason, T. George, H. Parekh. Extragastrointestinal stromal tumors of the pelvic cavity and the vagina: Two case reports and review of the literature. Gynecologic Oncology Reports 25 (2018) 3–7.
2. Nagase S, Mikami Y, Moriya T, Niikura H, Yoshinaga K, Takano T. Vaginal tumours with histologic and

immunocytochemical feature of gastrointestinal stromal tumour: two cases and review of the literature. Int. J. Gynecol. Cancer. 2007;17 (4):928-33.

3. Q.Y. Liu, Kan Yun-Zhen, Zhang Meng-Yang, Sun Ting-Yi, L.-F. Kong. Primary extra gastrointestinal stromal tumor arising in the vaginal wall: Significant clinicopathological characteristics of a rare aggressive soft tissue neoplasm. World J. Clin. Cases 2016;4 (4):118-124.
4. F. He, Z. Fang, P. Zhu, W. Huang, L. Li. Bladder extragastrointestinal stromal tumor in an adolescent patient: A case-based review. Mol. Clin. Oncol. [Internet] (2014), pp. 960-962
5. B.L. Eisenberg. The SSG XVIII/AIO Trial. Am. J. Clin. Oncol. [Internet]., 36 (1) (2013), pp. 89-90