International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2020): 7.803

Recurrent Gastro Intestinal Stromal Tumour in Pregnancy - A Case Report

Dr. Subha Sivagami Sengodan[1], Rashetha[2]

[1]Professor and Head, Department of Obstetrics and Gynaecology, Government Mohan kumaramangalam Medical College Hospital, Salem, Tamilnadu, India

[2]Junior Resident, Department of Obstetrics and Gynaecology, Government Mohan kumaramangalam Medical College Hospital, Salem, Tamilnadu, India

Corresponding Author E - mail: *drppsamysubha[at]gmail.com, rashethaazeem[at]gmail.com,*

Abstract: ***Purpose of study: Gastrointestinal stromal tumours found in pregnant women is such a rare entity that only a handful of cases have been cited in literature. Such an overlap has been less witnessed and the GIST recurrence during pregnancy has been least dealt with. Such a rarity makes our case a one in a million occurrence. Case: We present an antenatal women with Gastrointestinal stromal tumor of the pelvic region operated an year back who was on chemotherapy with a protein - tyrosine kinase inhibitor. Eventually the patient turned out to be a defaulter (imatinib) and had conceived when she was off the drugs. She presented to us in the early third trimester when she had already developed extensive metastatic deposits in the abdominal wall. We had her as an inpatient till the later half of third trimester, under close monitoring and we took her on an elective lscs, anterior wall tumour was resected intraoperattively with post - operative period being uneventful. GIST recurrence in this patient was confirmed histopathologically and with immuno - histo chemical analysis and 6 weeks post partum she was on chemotherapy. Conclusion: Our case has set us a classic example of how GIST can behave in an aggressive manner on withdrawal of chemotherapy and its extensive and rapid spread during pregnancy. The difficulty in the surgical management of pregnant patients presenting with GIST is deciding the optimal timing of surgery, the balance of good oncological response and minimising injury to the foetus.***

Keywords: Gastrointestinal stromal tumour, pregnancy, recurrent, imatinib, protein tyrosinase kinase inhibitor

1. Introduction

Gastrointestinal stromal tumors (GISTs) may be defined as morphologically spindle cell, epithelioid, or occasionally pleomorphic mesenchymal tumours of the gastrointestinal tract that usually express the KIT protein and harbour mutation of a gene that encodes for a type III receptor tyrosine kinase (either *KIT* or *PDGFRA*). (1) Tyrosine kinase inhibitor imatinib is the standard treatment for metastatic disease with few exceptions. A majority (80–90%) of patients with metastatic disease respond to Imatinib or achieve durable tumour growth stabilisation with continuous therapy using a daily dose of 400 mg to 600 mg. Treatment with imatinib increases survival of patients with advanced disease with a few years and is associated with only moderate toxicity. (2)

It is the most common gastrointestinal mesenchymal tumors, but their overall incidence is rare, with fewer than 10 cases per 1 million persons diagnosed every year. (3)

The mean age of patients diagnosed with GIST is 62.9 years, and men are affected 1.5 - fold more than women. Thus, the incidence of GIST in pregnancy is extremely rare, with only a handful of case reports available in the literature.

2. Case Report

28 year old G2P1L1 /married since 8 years previous normal vaginal delivery/ last child birth 7 years back / EDD 20.1.20/ known case of hypothyroid was referred here for safe confinement at 34 weeks.

3. History

She has history of GIST which was diagnosed in the year 2018 when she had complaints of scar site discharge from the laparotomy site for 7 months and she was symptomatically treated at her private hospital where she was operated for ruptured appendicitis. On CECT patient had a well - defined heterogeneously enhancing mixed mass lesion noted in the abdomino pelvic region displacing the bowel loops peripherally and laterally. Uterus found to be normal, Ovaries not seen separately, no HUN, no Ascites. CT - guided biopsy done, features consistent with Gastrointestinal stromal tumor and as neoadjuvant chemotherapy imatinib mesylate 400mg OD was given and completed for 1 year with good response to treatment.

In April 2019, tumor resection done and a size of 24 * 10* 8 cm necrotic tumour adherent to sigmoid colon mesentry, uterus, ovaries and bladder removed.

HPE revealed a neoplasm composed of spindle shaped cells with pale eosiophilic cytoplasm with elongated nuclei with coarse chromatin arranged in whorls and short intersecting fascicles. Focal areas show nuclear palisading and the nuclei exhibiting nuclear atypia. Mitotic figures – 8 to 10/HPF. The pathological grading was pT4 which showed a high grade Gastrointestinal Stromal Tumor.

A small residual enhancing mass was found in the pelvic region in the follow up with uneventful post operative period.

Patient was resumed on Imatinib mesylate with the same dosage and was tolerating well to chemotherapy. After a

period of seven months of chemotherapy, patient lost to follow up and she discontinued the drugs without medical advice.

4. Presentation

She presented now to us with nil complaints and on examination, she was found to have a cricket ball sized mass 4*4 cm in the abdomen over the previous laparotomy scar site in the midline and 5*3 cm mass in right hypochondrium.

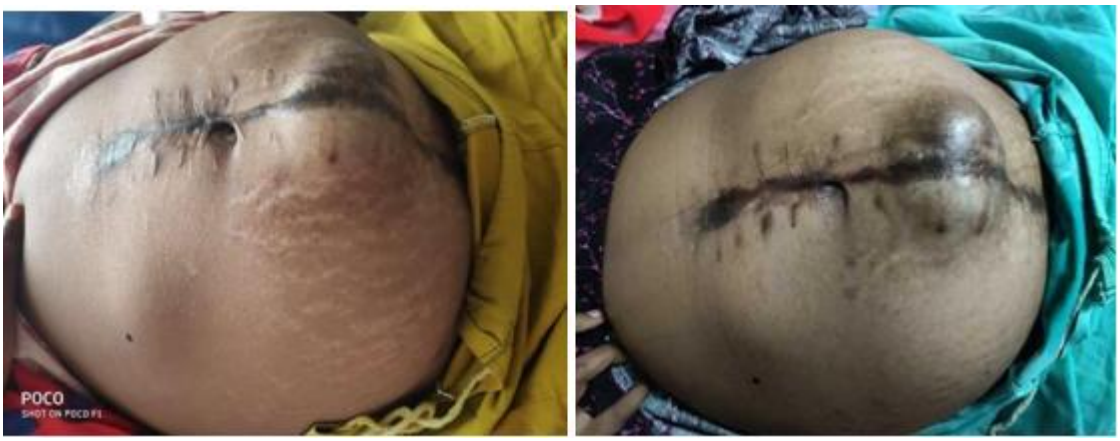
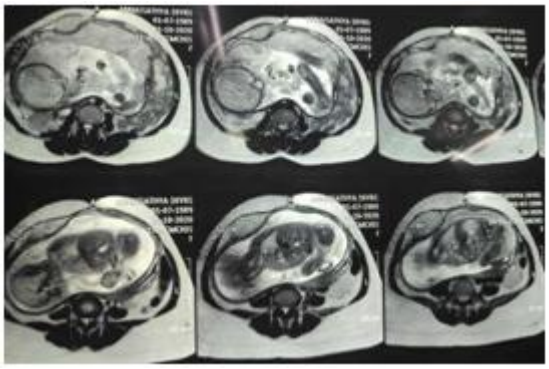
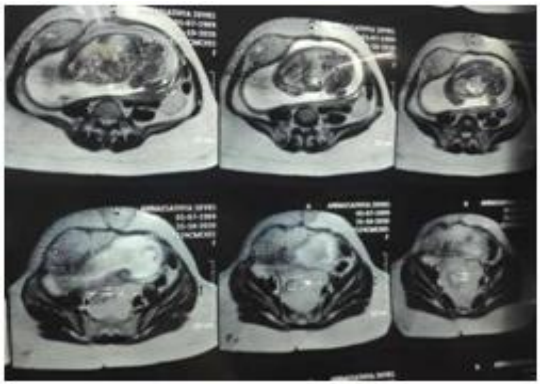


Figure 1: A & B clinical picture of the abdominal mass clearly seen present over previous scar

On evaluation with USG, multiple solid mass lesions in the abdomen and pelvis with moderate ascites. Patient was found to have multiple hemangiomas in the liver and multiple peritoneal deposits visualized.





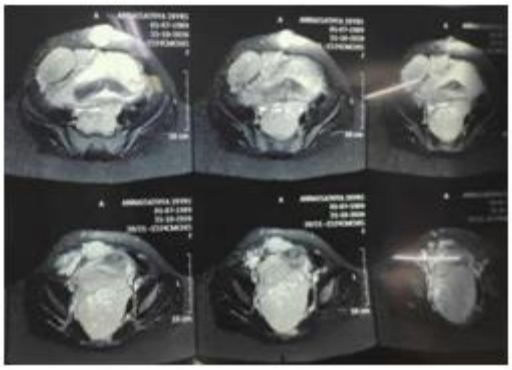


Figure 2: MRI abdomen and pelvis sowing multiple hyper intense mass lesions

MRI abdomen and pelvis taken and multiple hyperintense mass lesions of sizes 6.3X4cm, 7.6X3.7cm, 4.4X2.6cm, 3.8X3.1cm were seen anterior to the gravid uterus. A single lesion of size 10.8X7cm found in the pelvis posterior to the uterus and a single lesion of size 3.8X2.8 cm within the left iliacus muscle - all suggestive of GIST recurrence.

FNAC from anterior abdominal wall mass done and recurrent GIST was proved. Her mild anemia was corrected with two units of packed red blood cell transfusion. Elective LSCS done at 36 weeks 3 days in view of breech presentation and GIST complicating pregnancy.

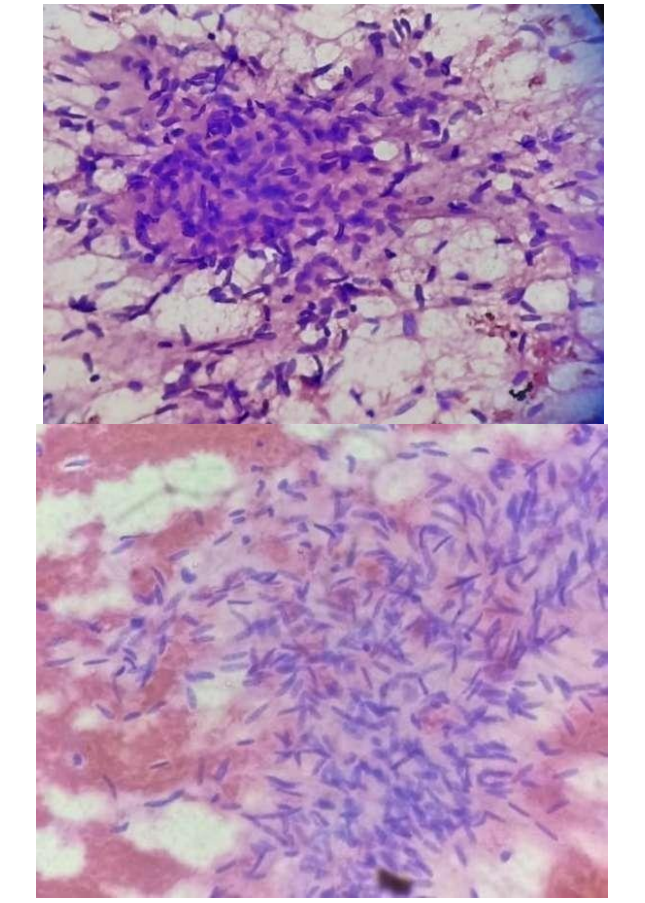


Figure 3: FNAC of the tumour showing multiple spindle shape cells

Intra Operative Findings:
Under spinal anaesthesia with surgical gasteroenterologist and oncologist assistance with supra pubic transverse incision – the metastatic deposit 8*6*5cm present in the anterior abdominal wall resected with no space for uterine incision.

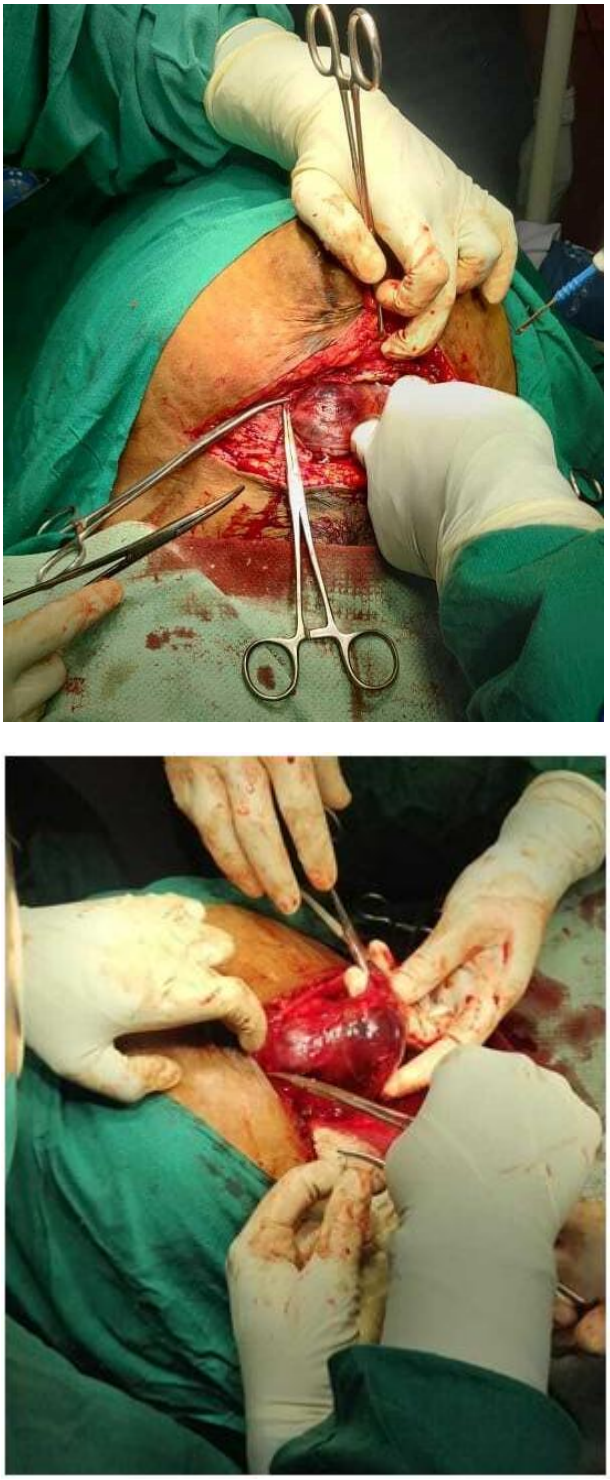
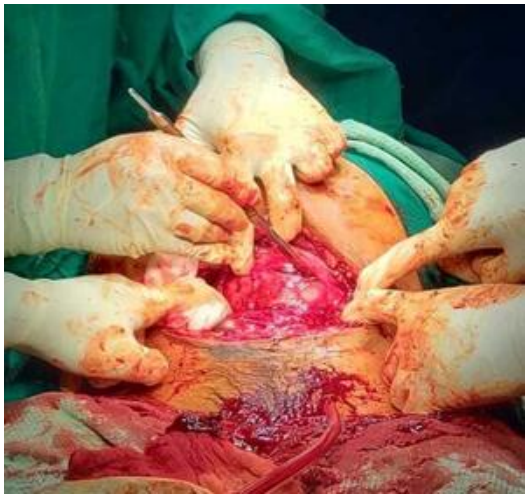


Figure 4: Resection of anterior metastatic tumour

Peritoneal deposit of tumour 6*8 cm near the lateral end of incision on right side.



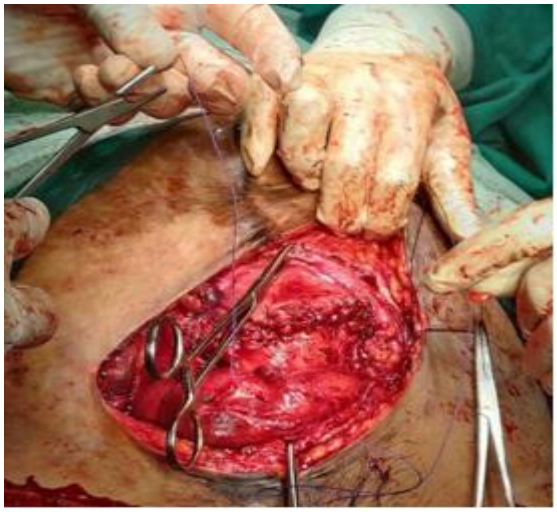


Figure 5: Uterine insicion made after tumour resection

She delivered an alive boy baby of 2.75 kg with good APGAR.3 packed cell transfused intra operatively. Patient was intensively monitored and she had uneventful postoperative period.

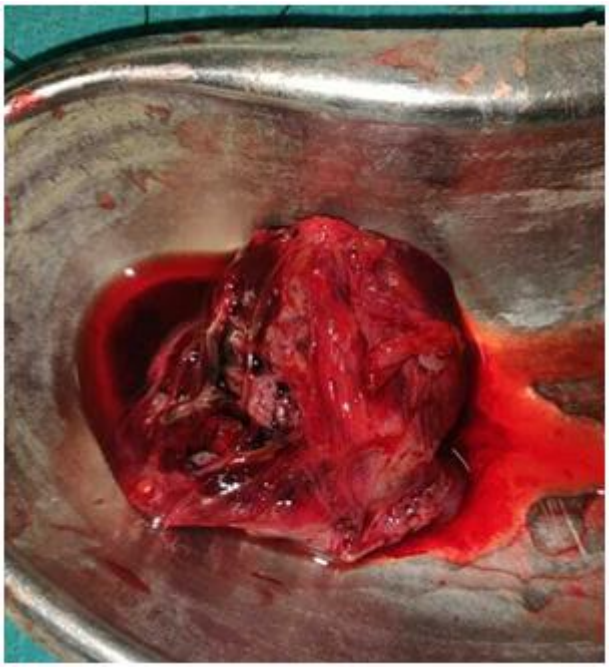


Figure 6: Resected metastatic tumour was sent for HPE

Immunohistochemistry

The Histopathology specimen was further taken up for Immuno histochemical markers analysis for a conclusive diagnosis. IHC marker analysis reported positive for CD117 and DOG 1 with a score of 4+ (Immunoreactive in 76 – 100%) in the neoplastic cells. CD 117 positivity being an absolute requirement for the definition of GIST in which the expression results from a mutation of the c - kit gene has proved beyond doubt that our case has been confirmed to be harbouring recurrent deposits of GIST in the abdomen proving it to be an extensive high grade tumor recurrence. To add a stronger validation, DOG - 1 also turned out to be positive with a 4+ score which is a highly sensitive and specific marker for diagnosing GIST.

5. Discussion

GISTs can develop in the entire gastrointestinal tract and occasionally in the omentum and mesentery. The stomach (60–75%) and the small intestine (20–30%) are the most common localizations of the tumor. (4)

Incidence of Gastrointestinal stromal tumor in pregnancy has not been clearly delineated in the literature because of the rarity in its occurrence. Only a very few cases have been reported. And GIST recurrence in pregnancy is an even more rarer entity that only a handful of patients have been reported in the literature.

In the recent years rapid progress has been made on the understanding of the oncogenesis of GISTs. The gain - of - function mutation in the c - kit proto - oncogene, which can be found in 90% of GISTs, seems to be the basis of the pathogenesis. This genetic aberration leads to an unbridled stimulation of c - kit receptor and overexpression of the tyrosine kinase protein and a subsequent growth and antiapoptotic behavior of tumor cells. The introduction of the receptor tyrosine kinase inhibitor STI - 571 (imatinib mesylate) heralds a new era in the treatment of GIST. (5)

The difficulty in the surgical management of pregnant patients presenting with GIST is deciding the optimal timing of surgery, the balance of good oncological response and minimising injury to the foetus. Thus in our case it was a multidisciplinary approach. (6)

Promising results have been reported in clinical trials on the metastatic disease. Until recently surgery was the only successful treatment of GISTs. Chemotherapy and radiotherapy had proven to be ineffective. Therefore, only localized disease could be curatively treated. (7)

The mitotic rates in combination with tumor size and tumor site seem to be the most important prognostic factors. (8) The risk of recurrence is stratified according to size and mitotic count of the tumour.

Fletcher has proposed a risk assessment dividing into four categories:

1) Very low risk (<2 cm and <5/50 HPF);
2) Low risk (2–5 cm and <5/50 HPF);

3) Intermediate risk ((a) <5 cm and 6–10/50 HPF or (b) 5–10 cm and <5/50 HPF);
4) High risk ((a) >5 cm and >5/50 HPF or (b) >10 cm and any mitotic rate or (c) any size and >10/50 HPF). (8)

In our case the mitotic rate was 8 - 10 / HPF stratifies GIST as high risk indicating the need for imatinib.

The areas of recurrence of GIST could not be completely resected in our patient and she was started on imatinib mesylate 400 mg od after 6 weeks post partum and was under regular follow up.

6. Conclusion

Our case demonstrates the complexity of managing pregnant patients presenting with GIST. The timing of delivery and the decision of tumour resection depending on the location should be a multidisciplinary approach with due consideration to patients clinical status, with surgical and oncological perspective. We succeeded in managing this patient effectively.

7. Declaration

Compliance with ethical standards

Conflict of Interest: there are no conflicts of interest for any author (financial or otherwise)

Informed consent: Written informed consent was obtained from the concerned patient

References

[1] Joensuu H. Gastrointestinal stromal tumor (GIST). Ann Oncol.2006 Sep; 17 Suppl 10: x280 - 6. doi: 10.1093/annonc/mdl274. PMID: 17018739.
[2] Croom KF, Perry CM. Imatinib mesylate: in the treatment of gastrointestinal stromal tumours. Drugs.2003; 63 (5): 513 - 22; discussion 523 - 4. doi: 10.2165/00003495 - 200363050 - 00005. PMID: 12600228.
[3] Scherjon S, Lam WF, Gelderblom H, Jansen FW. Gastrointestinal stromal tumor in pregnancy: a case report. Case Rep Med.2009; 2009: 456402. doi: 10.1155/2009/456402. Epub 2009 Sep 16. PMID: 19763238; PMCID: PMC2745024
[4] Zhao X, Yue C. Gastrointestinal stromal tumor. J Gastrointest Oncol.2012 Sep; 3 (3): 189 - 208. doi: 10.3978/j. issn.2078 - 6891.2012.031. PMID: 22943011; PMCID: PMC3418531.
[5] S. Scherjon, W. F. Lam, H. Gelderblom, F. W. Jansen, "Gastrointestinal Stromal Tumor in Pregnancy: A Case Report", Case Reports in Medicine, vol.2009, Article ID 456402, 4 pages, 2009.
[6] Zarkavelis G, Petrakis D, Pavlidis N. Gastrointestinal stromal tumors during pregnancy: a systematic review of an uncommon but treatable malignancy. Clin Transl Oncol.2015 Oct; 17 (10): 757 - 62. doi: 10.1007/s12094 - 015 - 1315 - x. Epub 2015 Jun 9. PMID: 26055339.
[7] Charo LM, Burgoyne AM, Fanta PT, Patel H, Chmielecki J, Sicklick JK, McHale MT. A Novel *PRKAR1B* - *BRAF* Fusion in Gastrointestinal Stromal Tumor Guides Adjuvant Treatment Decision - Making During Pregnancy. J Natl Compr Canc Netw.2018 Mar; 16 (3): 238 - 242. doi: 10.6004/jnccn.2017.7039. PMID: 29523662; PMCID: PMC6053908.
[8] Fletcher CD, Berman JJ, Corless C, Gorstein F, Lasota J, Longley BJ, Miettinen M, O'Leary TJ, Remotti H, Rubin BP, Shmookler B, Sobin LH, Weiss SW. Diagnosis of gastrointestinal stromal tumors: A consensus approach. Hum Pathol.2002 May; 33 (5): 459 - 65.