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Case Report

Surgery Section

Spontaneous Perforation as a First Presentation of Ileal Gastrointestinal Stromal Tumour (GIST) with Synchronous Breast Sarcoma

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ABSTRACT

Gastrointestinal Stromal Tumours (GIST's) are the most common mesenchymal neoplasms of the gastrointestinal tract. Majority of the GISTs are asymptomatic and often diagnosis is incidental. Synchronous second malignancies have been reported in patients with GIST. We report a case of 50-year-old female presenting with features of hollow viscous perforation, found to have ileal GIST with perforations along with a synchronous breast sarcoma. GIST with spontaneous perforation as its first clinical manifestation is rare. Synchronous occurrence of an ileal GIST with a breast sarcoma is unique and deserves reporting. This case report highlights the varied nature of clinical presentation of the GIST and also stresses on the importance of extensive search for the synchronous second malignancies in the extra abdominal sites as well.

Keywords: Gastrointestinal stromal tumour (GIST), Breast sarcoma, Synchronous, Ileal perforation, C-kit, Cajal cells

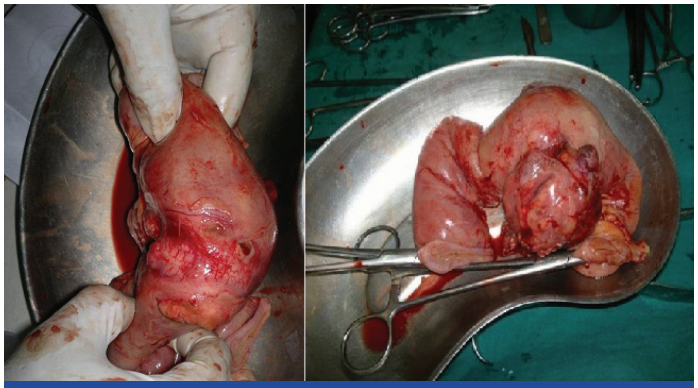
CASE REPORT

A 50-year-old female presented 36 hours after the onset of severe pain abdomen, associated with nausea and vomiting. On examination patient was conscious and of moderate built. She had mild dehydration without any pallor, cyanosis or oedema. She was normotensive (110/70 mmHg) with tachycardia (104/min) and tachypnoea (25/min). Abdominal examination revealed distension, rigidity, rebound tenderness, obliterated liver dullness and absent bowel sounds. Per rectal examination and systemic examination was normal. A lump measuring 6x5 cm was noted in the left breast. Haematological examination was within normal limits except for leucocytosis (Total count=16500/cumm). Upright abdominal X-ray showed free gas under both domes of diaphragm. A provisional diagnosis of hollow viscous perforation was made and resuscitation initiated. Exploratory laparotomy was planned and carried out on the same day of admission.

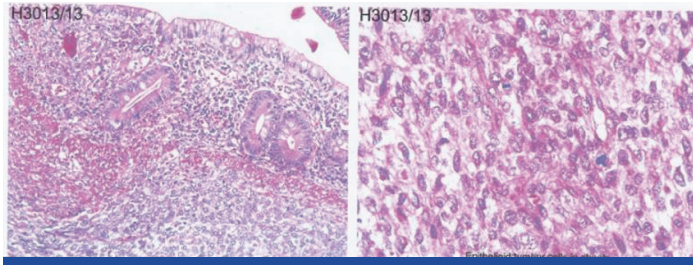
Operative findings: Laparotomy revealed feculent free fluid and a growth at the antimesenteric border of intestine measuring 10 x 8 cm, around 60 cm from the ileocaecal junction. Two perforations were noted adjacent to the mass [Table/Fig-1]. The growth was resected and end to end anastomosis was done in two layers with vicryl. All other intra-abdominal organs encountered were within normal limits. Abdomen was closed in layers after thorough peritoneal lavage; drain was placed in the right paracolic gutter. Post operative period was uneventful and the patient was discharged on tenth post-operative day. Patient was put on oral imatinib. The histopathological examination of the resected intestinal growth revealed epitheloid gastrointestinal stromal tumour (TNM staging: pT3 pN0 Mx), with free surgical lines of resection [Table/Fig-2]. Immunohistochemistry revealed CD-117/c-kit positivity.

Two subsequent fine needle aspiration cytological examination of the breast lump turned out to be inconclusive, demanding the need for histopathological examination.

An elective breast procedure was carried out 3 weeks after the initial exploratory laparotomy. Patient was admitted two days prior for assessment of fitness for surgery.

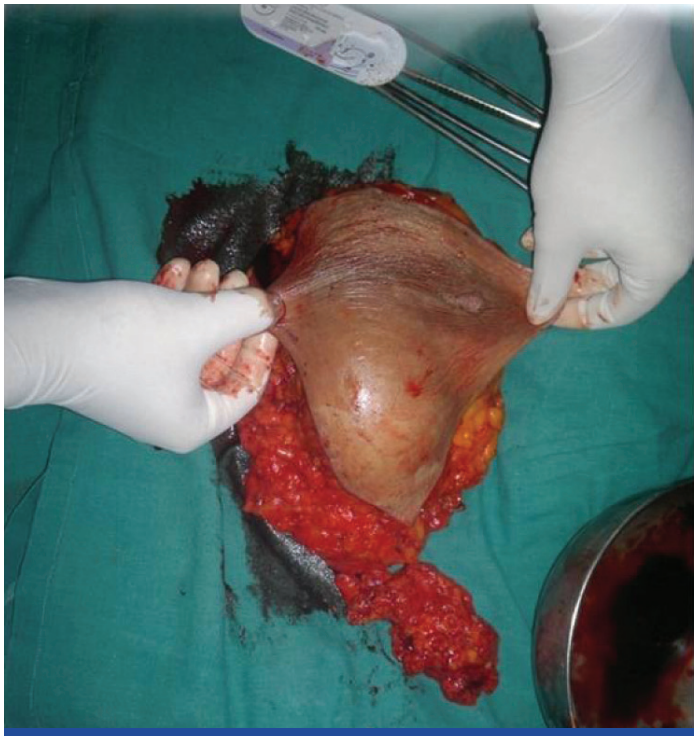


[Table/Fig-1]: Resected specimen of ileal GIST showing perforations

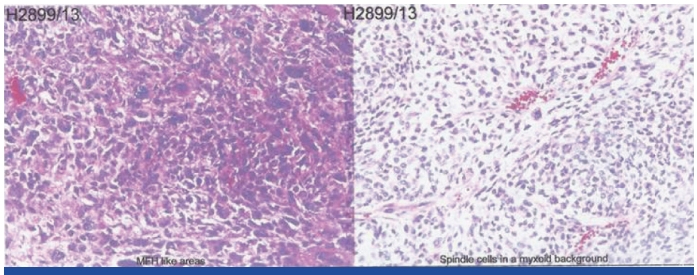


[Table/Fig-2]: HPE of resected ileal GIST suggesting epitheloid type

Clinical examination findings: A left breast lump, measuring 6 x 5 cm, with no fixity to the skin or the chest wall [Table/Fig-3]. Clinical and ultrasound examination of axilla did not reveal any enlarged lymph nodes (clinically T3N0M0). Elective simple mastectomy was planned and undertaken. The post operative period was uneventful and the patient was discharged on the seventh post-operative day and referred to radiotherapy. The histopathological examination of the mastectomy specimen revealed high grade mammary sarcoma with heterologous cartilaginous, osseous and rhabdomyoblastic differentiation [Table/Fig-4].



[Table/Fig-3]: HPE of breast, suggesting high grade sarcoma



[Table/Fig-4]: Resected breast specimen

DISCUSSION

Mazur and clark introduced the term stromal tumour in 1983 after they failed to find the ultrastructural evidence of smooth muscle or nerve sheath differentiation in several gastric tumours [1]. The origin of GISTs appears to be from the interstitial cells of Cajal, which acts as a pacemaker for the gut. GISTs always expresses CD117 (100%), a tyrosine-kinase growth factor receptor, which also serves as a target for drug therapy with imatinib (a selective tyrosine kinase inhibitor) [2]. GISTs are clinically occult, with vague pain abdomen being the most common symptom. Although the diagnostic procedure includes barium examination, computer tomography and angiography, none of them can establish the correct diagnosis with 100% certainty and sometimes patients present with complications like bleeding or perforation. There was a history of vague abdominal pain in our case which had been neglected and the severe unbearable pain of perforation peritonitis prompted her to seek the medical advice. The mechanism of bowel perforation secondary to GIST is unclear. Possible suggested mechanisms include increased intraluminal pressure due to tumor obstruction, replacement of the bowel wall by tumor cells followed by necrosis and bowel ischemia due to tumor embolization [3]. In our case necrosis of the bowel wall was suspected to be the cause of perforation.

GISTs are known to exist with synchronous second malignancies. By definition synchronous tumours are those which appear simultaneously or consecutively in several organs or systems within 4 months to one year, while those appearing at longer period are called as metachronous tumours [4]. The exact mechanism behind the occurrence of synchronous second malignancies remains elusive. Some authors have linked the role of c-kit in the development of synchronous colonic adenocarcimnomas [5]. Further studies are required to clarify the molecular and genetic mechanisms of carcinogenesis and progression associating GIST and synchronous tumors. Majority of the case reports have reported the association of epithelial tumors of the gastrointestinal tract with GISTs [5,6]. But in our case the occurrence of the tumour in an extra abdominal site; the breast, has added to its uniqueness. Breast sarcomas are thought to be rare and heterogeneous group of malignant neoplasms representing less than 1% of all primary breast malignancies and less than 5% of all sarcomas [7]. They present mainly as a lump and tumour size seems to be the most frequently reliable prognostic factor. In our case the size of the lump was 6 x 5 cm at the time of presentation. The factors like lack of health awareness, low socio-economic status and hailing from remote areas with poor health care systems and connectivity can be attributed to the delay in seeking medical advice.

Frequencies of occurrence of synchronous second malignancies have been also been studied [Table/Fig-5]. Agaimy et al., [8] reviewed a vast literature of GIST and found that the frequency of synchronous second malignancy in different series varied from 4.5% to 33% (mean 13%). In another clinical study of GIST by Adim SB et al., [9] the frequency was found to be 16.6%. Among these studies gastrointestinal carcinomas were found to be the most common second malignancies, other malignancies include hematological malignancies, melanoma, soft tissue sarcoma, cancers of the breast, kidney, prostate and female genital tract. Majority of these studies are limited to individual case reports and case series; large scale studies are required to explore the elusiveness of the disease and its associations.

Our case stands unique in two aspects. Firstly, because of the rare association of an ileal GIST with a synchronous breast sarcoma and secondly, spontaneous perforation being the first presentation of an ileal GIST.

Author of Study	Frequencies of Synchronous Malignancies in Gist
Adim SB et al., [9]	16.6%
Agaimy et al., [8]	4.5-33% (mean= 13%)
Wronski M et al., [10]	14%
Ferreira SS et al., [11]	14%

[Table/Fig-5]: Table showing frequencies of occurrence of synchronous malignancies in GIST

CONCLUSION

Treating surgeon should be aware and vigilant about the occurrences and patterns of the wide range of synchronous second malignancies in association with gastrointestinal stromal tumours. Although gastrointestinal tract is the most common site for the occurrence of synchronous second malignancies, need for thorough search of the extra-abdominal sites is prudent and its importance cannot be undermined.

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