OUR EXPERIENCE WITH RARE PRESENTATION OF GASTROINTESTINAL STROMAL TUMORS IN A RURAL MEDICAL COLLEGE HOSPITAL

Jigar Vipul Shah¹, Prarthan Nishith Joshi², Akash Agrawal³

HOW TO CITE THIS ARTICLE:

Jigar Vipul Shah, Prarthan Nishith Joshi, Akash Agrawal. "Our experience with rare presentation of gastrointestinal stromal tumors in a rural medical college hospital". Journal of Evolution of Medical and Dental Sciences 2013; Vol. 2, Issue 41, October 14; Page: 7816-7822.

ABSTRACT: Gastrointestinal stromal tumors (GIST-) are one of the most common mesenchymal tumors of the gastrointestinal tract [1-3% of all gastrointestinal malignancies]. Their behaviour is driven by mutations in the kit gene or PDGFRA gene and may or may not positively stain for kit. We report four additional cases of a GIST presenting as an abdominal mass along with a pertinent review of the literature. All four patients received surgical resection. The mean tumor size was 10.5 with an average mitotic index of 6.25 per 50 high power fields. Three patients were disease free and one patient came with recurrence. In conclusion, symptomatic patients have an increased incidence of high-risk tumors and metastases at presentation. Adjuvant therapy with imatinib improves disease-free survival in patients with large abdominal GIST tumors, but no change in overall survival was noted.

KEY WORD: Gastrointestinal stromal tumors; Imatinib; mitotic index; Meckel's Diverticulum.

INTRODUCTION: Gastrointestinal stromal tumors (GISTs) accounts for majority of mesenchymal tumours of the gastrointestinal tract. Traditionally, these tumors have been called leiomyomas, cellular leiomyomas, or leiomyosarcomas, depending on the degree of cellularity, mitotic activity, and evidence of dissemination, or leiomyoblastomas, when showing epithelioid morphology. Some families with hereditary GISTs have been described. Many GISTs show α -smooth muscle actin expression and some show desmin expression [1]. The incidence of GISTs has been historically underestimated prior to the introduction of CD117 staining. The annual worldwide incidence of GISTs since introduction of CD117 staining increased from 1.1 per 100,000 people to 2.1 per 100,000 people.

Commensurate with an increased overall incidence has been a 25-fold increase in the age-adjusted incidence of GISTs (from 0.028 per 100,000 in 1992 to 0.688 per 100,000 in 2002), with a current annual incidence of 14.5/100,000 population [2]. Most patients with GISTs are asymptomatic although patients with advanced disease may present with symptoms of a mass lesion, abdominal pain, or bleeding. At least 10 to 30% of GISTs are discovered incidentally during laparotomy, endoscopy, or other imaging studies, with 15% to 50% of GISTs presenting with metastatic disease [3]. GISTs initially presenting as an abdominal mass are exceedingly rare and only few cases have been reported in the world literature. In this paper, we discuss four additional cases of GISTs presenting as an abdominal mass admitted at a tertiary care teaching hospital in Pipariya Vadodara, India and provide a pertinent review of literature.

CASE REPORTS: Case 1: A 45-year male presented with a three-month history of an increasing lower abdominal mass with occasional pain. There was no history of nausea, vomiting, weight loss, or change in bowel habits. Physical examination revealed a mobile, mass occupying the hypogastric

and umbilical reason. Contrast-enhanced computed tomography (CECT) scan of the abdomen and pelvis identified a 15 × 10 cm large necrotic mass arising from small bowel loops mainly distal jejunal and proximal ileal loops, at the jejuno-ileal junction. The patient underwent an exploratory laparotomy and resection of the tumor and involved segment of the jejunum and ileum with resection anastomosis (Fig 1). No evidence of lymph node or peritoneal metastasis was noted. The histopathological examination of the resected tumor revealed a GIST tumor with free margins. The mitotic index was 5/50 high-power fields (HPFs). The cells showed consistent intracytoplasmic immunoreactivity for CD117 (c-Kit). The patient was treated with adjuvant imatinib therapy. The patient was disease free at 12 months follow up.

Case 2: A 30-year female presented with a three-day history of severe pain in abdomen with vomiting progressively abdominal distension associated with pain and constipation. There was no history of fever or weight loss.

Physical examination revealed a mobile mass in the periumbilical region partly extending into the right iliac region. A contrast-enhanced CT scan of the abdomen and pelvis revealed distension of jejunum and ilial loop with multiple air fluid levels and a 10 × 7 cm Rt. Tubo-ovarian mass. The patient underwent an exploratory laparotomy and was found to have a cystic mass of 8 x 8 cm arising from the 60 cm proximal to ileo-caecal junction from the anti-mesenteric border (Fig 2). There was no mesenteric node enlargement. Intra-operated finding are suggestive of Meckel's Diverticulum 8 x 8 cm tumour was found on the tip of Meckel's diverticulum.

Resection of tumor with Meckel's diverticulum and anastomosis was done. Histopathology of the resected specimen identified a malignant GIST tumor with negative surgical margins and no lymph node involvement. The histopathology shows tumour cells arranged in solid sheets. There are many spindle cells & at places also presence of epithelioid cells. The spindle cells are arranged in fascicle storiform pattern. Nuclear palisading is also seen. Mitotic count is 7/50 HPF. Immunohistochemistry was also done which showed CD 117 (c-kit) negative but few neoplastic cells were seen. The patient is disease free at 10 months follow up.

Case 3: A 50-year male presented with a 4-days history of pain in abdomen, nausea, vomiting, and not passing stool since 2 days. Physical examination revealed a fixed hard mass in the umbilical region extending to the right iliac region. X-Ray Abdomen Standing shows Multiple Air Fluid Levels are present in left side and ultrasonography of Abdomen and Pelvis shows Intestinal obstruction with free fluid in the peritoneal cavity. Emergency exploratory laparotomy was done under general anesthesia, the patient was found to have a mass of 12 x 8 cm was present 60 cm proximal to Ileocaecal junction on the anti mesenteric border with multiple adhesions by which the mass was adherent to the anterior abdominal wall with haemoperitoneum. Excision of the mass with 5 cm margin of normal tissue was resected and proximal Ileostomy was performed. Histopathology revealed a GIST tumor with Meckel's diverticulum and negative surgical margins. The mitotic index was 7/50 HPF. The patient received adjuvant imatinib therapy and was disease-free at 11-month followup.

Case 4: A 70-year female presented with an altered bowel habits and perianal swelling from 1-month. She had no history of nausea, vomiting, weight loss, or bleeding per rectum. Physical

examination revealed a mass of approximately 7 cm in diameter on the right posterior lateral wall at 7 o'clock position on lateral rectal wall at about 2 cm above the dentate line. The mass was hard in consistency with restricted mobility, with a regular surface. A provisional diagnosis of rectal tumour was made and a colonoscopy shows posterior bulging and mucosa was free. The CEA tumor marker was normal. Contrast-enhanced CT scan of the abdomen and pelvis identified a Right postero lateral wall anal canal lesion at 7 o'clock position appears normal and protruding into the right ischioanal fossa. Posterior wall lesion also found. There was no evidence of metastases. Patient was counseled for abdominoperineal resection followed by colostomy, but Patient disagreed so we went for wide excision of mass with partial anal sphincter excision. The post operative period was perfectly normal, with no complications and was discharged on POD 10. Histopathology revealed a GIST tumor with negative surgical margins. The mitotic index was 8/50 HPF. The cells showed consistent intracytoplasmic immunoreactivity for CD117 and CD34. Patient remained disease free for 2 years again came with local recurrence. Patient was kept on IMATINIB therapy for three months and the tumour regressed. Again wide excision with rest of sphincter saving surgery was done. Post operative patient had incontinence of stool later with fibrosis sphincter function regained and again kept on IMATINIB.

MATERIALS AND METHOD: Patients with tumor size >7 cm. with mitotic index ≥ 5 and presenting as palpable abdominal masses, were selected. We did not include Gastric GISTs.

RESULTS: Table 1: Reports of patients with gastrointestinal stromal tumor presenting as mass per abdomen.

All our patients (Table-1) have undergone surgical resection. 3 patients were in the age group of 40-70. CECT was done in 3 patients except one patient who presented with small bowel obstruction. None of the patients had a pre operative diagnosis of GIST. All patients presented with palpable abdominal mass. Mean tumour size is 10.75 and mitotic index average is 6.25. None of the patients had metastases. IHC was done in all patients, one patient was CD 117 negative, but few neoplastic cells are seen. 3 patients received adjuvant imatinib except one patient with CD 117 negative. All patients were disease free at 10, 11 and 12 months and one patient had local recurrence after 2 years.

5. DISCUSSION: Usually 70 % of GIST's occur in stomach, 20 – 30 % in small intestine and nearly 10 % in other parts of gastro intestinal tract, omentum or mesentery [4]. Patients present with gastro intestinal haemorrhage or metastasis, intestinal obstruction is rare due to outward pattern of growth. GIST are tumours of the connective tissue, that is sarcoma, they are non epithelial. The histopathologist identifies the characteristic of GIST (spindle cells in 70 – 80 %) and epithelioid aspect in 20 – 30 % GIST are thought to arise from interstitial cells of Cajal (ICC) that are normally part of the autonomic nervous system of the intestine [5]. Most 50 – 80 % GIST arises because of a mutation in a gene called c-kit. The c-kit product / CD 117 are expressed on ICCs and large number of other cells. The pathologist can use immunohistochemistry (specific antibodies that stain the molecule CD 117 / CKIT) 95 % of all GISTS are CD 117 positive (other possible markers include CD34, DOG-1, DESMIN, AND VIMENTIN). 35 % of GIST cells have a mutation in another gene PDGFR- α (PLATELET DERIVED GROWTH FACTOR RECEPTOR – ALPHA) which is a related tyrosine kinase.

Preferred imaging modalities in the evaluation of GIST are CT and MRI. CT advantages include its ability to demonstrate evidence of nearby organ invasion, ascites and metastasis. The ability of MRI to produce images in multiple planes is helpful in determining the bowel as the organ of origin (which is difficult when the tumour is very large), facilitating diagnosis. Malignancy is characterized by local invasion and metastasis usually to liver, omentum peritoneum.

However cases of metastasis to bone, pleura, lungs and retro peritoneum have been seen. Malignant lymphadenopathy is uncommon and imaging usually shows absence of lymph node enlargement.

Complete surgical resection is the treatment of choice and biological therapy IMATINIB is recommended as adjuvant therapy after surgery and unresectable or metastatic disease in patients with primary or recurrent disease. Radiation therapy and chemotherapy have a very limited role in the management of GIST. Results have shown that IMATINIB therapy have reduced the risk of disease recurrence (6 % recurrence on adjuvant IMATINIB versus 17% without therapy at 12 months). The 2 year survival of patients with advanced disease have risen to 75 – 80 % following imatinib treatment. Patient who develops resistance to imatinib may respond to multiple tyrosine kinase inhibitor sunitinib. Tumour size and mitotic index are the two most important prognostic factors used for risk assessment of GIST. Additional factors like anatomic location, histologic variant and type of mutation have also been associated with varying prognosis and difference in survival rate [6]. We could not find a correlation between the size of the tumour and mitotic index. And also tumour size and mitotic index did not predict the behaviour of GIST for our group of patients.

CONCLUSION: All GISTs tumours should be considered to have malignant potential and no GIST tumour can be correctly classified as benign. Tumour size mitotic rate and location can be used to predict the risk of recurrence in GIST patients. Tumour < 2 cm and mitotic index 5/50 HPF have been shown to have less recurrence and better prognosis. Symptomatic patients tend to have a higher incidence of high-risk tumors and metastases at presentation [7]. Surgery is the main modality of therapy for non metastatic GISTs. Nowadays laparoscopic surgery has shown to be effective for removal of these tumours and the decisions for laparoscopic surgery is affected by tumour size, location and growth pattern. Adjuvant therapies with imatinib for patients improve disease-free survival and significantly reduce the risk of disease recurrence. Finally, GISTs are the most common form of sarcoma, which constitutes more than 70 types of cancer and should always be considered in the differential diagnosis of an abdominal mass in adult patients.

REFERENCES:

1. Miettinen M, Sobin LH, Lasota J. Gastrointestinal stromal tumors presenting as omental masses-a clinicopathologic analysis of 95 cases. *American Journal of Surgical Pathology*. 2009;33(9):1267– 1275.
2. Samelis GF, Ekmektzoglou KA, Zografos GC. Gastrointestinal stromal tumours: clinical overview, surgery and recent advances in imatinib mesylate therapy. *European Journal of Surgical Oncology*. 2007; 33(8):942–950.
3. Roberts PJ, Eisenberg B. Clinical presentation of gastrointestinal stromal tumors and treatment of operable disease. *European Journal of Cancer*. 2002; 38:S37–S38.

4. DeMatteo RP, Lewis JJ, Leung D, Mudan SS, Woodruff JM, Brennan MF: Two hundred gastrointestinal stromal tumours: recurrence patterns and prognostic factors for survival. *Ann Surg* 2000, 231:51-58.
5. Miettinen M, Sarlomo-Rikala M, Lasota J: Gastrointestinal stromal tumors: recent advances in understanding of their biology. *Hum Pathol* 1999, 30:1213-1220.
6. Fujimoto Y, Nakanishi Y, Yoshimura K, Shimoda T. Clinicopathologic study of primary malignant gastrointestinal stromal tumor of the stomach, with special reference to prognostic factors: analysis of results in 140 surgically resected patients. *Gastric Cancer*. 2003; 6(1):39-48.
7. Mussi C, Schildhaus HU, Gronchi A, Wardelmann E, Hohenberger P. Therapeutic consequences from molecular biology for gastrointestinal stromal tumor patients affected by neurofibromatosis type 1. *Clinical Cancer Research*. 2008; 14(14):4550-4555.

Table 1: Reports of patients with gastrointestinal stromal tumor presenting as mass per abdomen.

Age, sex	Duration of symptoms	Preoperative investigations	Preoperative diagnosis	Treatment	Tumor size, cm	mitosis/50 HPF	Primary site	Metastases	Follow up
45, M	3 months	CECT	Small bowel carcinoma	S + CT ^I	15	5	Jeuno-ileal junction		DF 12 months
30, F	3days	CECT	Right Tubo-ovarian mass	S	10	5	Meckel's diverticulum		DF 10 months
50 M	4 days	US and xray	Small bowel obstruction	S + CT ^I	12	7	Meckel's diverticulum		DF, 11 months
70 F	2 years	CECT	Ca rectum	S + CT ^I	7	8	rectum		Local recurrence after 2 years

F: female, M: male, NM: not mentioned, CECT: contrast-enhanced computed tomography scan, SBO: small bowel obstruction, FNAC: fine needle aspiration cytology, S: surgery, HPF: high-power field, NM: not mentioned, MR: magnetic resonance imaging, LN: lymph node, GIST: gastrointestinal stromal tumor, US: ultrasound, CT: chemotherapy, DF: disease-free, PD: progressive disease, SD: stable disease, LOF: lost to followup.

^IAdjuvant imatinib therapy.

^{II}Two cycles of dacarbazine and doxorubicin.

^{III}Patient discontinued imatinib after few months.

Fig 1: Growth at the jejuno-ileal junction

Fig 2: Growth on the tip of Meckel's diverticulum

AUTHORS:

1. Jigar Vipul Shah
2. Prarthan Nishith Joshi
3. Akash Agrawal

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of General Surgery, SBKS MIRC, Sumandeep Vidyapeeth.
2. Assistant Professor, Department of General Surgery, SBKS MIRC, Sumandeep Vidyapeeth.
3. Resident, Department of General Surgery, SBKS MIRC, Sumandeep Vidyapeeth.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Jigar Vipul Shah,
Assistant Professor,
Department of General Surgery,
SBKSMIRC, Sumandeep Vidyapeeth,
Pipariya, Vadodara, Gujarat, India – 391760.
Email – jigarshah2225@yahoo.in

Date of Submission: 27/09/2013.

Date of Peer Review: 28/09/2013.

Date of Acceptance: 05/10/2013.

Date of Publishing: 08/10/2013