Case Report

Gastrointestinal stromal tumor of stomach – A case report

Anjali Sadanandan[1*], Jaison Jacob John[2], Shivashekar G[3]

[1] Post Graduate, [2]Professor, [3]Professor and HOD, Department of Pathology, SRM Medical College Hospital and Research Centre, Kattankulathur, TamilNadu, INDIA.
Email: dr.anjali.sadanandan@gmail.com

Abstract

Gastrointestinal stromal tumours (GISTs) are mesenchymal neoplasms that account for approximately 2% of all malignant gastric tumors. GISTs range from indolent, hardly proliferating to fast-growing, recurring and metastasizing lesions. Malignant potential and prognosis of these tumors are based on tumor size and mitotic count. The primary treatment of GIST consists of surgical excision of the tumor with a good margin of normal tissue. Specific targeted therapy (Imatinib mesylate) is effective in most cases with KIT mutations and many with PDGFRA mutations. In this case report we present a case of mixed type of GIST with high malignant potential.

Key Word: Gastrointestinal stromal.

[*]**Address for Correspondence:**
Dr. Anjali Sadanandan, Post Graduate, Department of Pathology, Arunodayam, Veliyam P O, Kollam-691540, Kerala, INDIA .
Email: dr.anjali.sadanandan@gmail.com

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INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are mesenchymal neoplasms that account for approximately 2% of all malignant gastric tumors. The incidence is between 14.4 and 11 cases per 1 million in the general population. GIST constitute majority of primary non epithelial neoplasms of stomach and can also involve small bowel, oesophagus, omentum, mesentery, retroperitoneum. GIST arises from the wall of the gastrointestinal tract and is thought to originate from the Interstitial Cells of Cajal (ICC), which regulate the motility of the gastrointestinal tract. In this case report we present a case of mixed type of GIST with high malignant potential.

CASE REPORT

51 year old female presented with complaints of dull epigastric pain and fullness for 3 weeks, fever for 2 days, 3 episodes of vomiting since one day. No significant past history. On examination, patient was moderately built. Abdominal examination revealed diffuse tenderness present more in epigastric and left hypochondrial regions. No definite mass was palpable. Other systems were normal.

USG showed a large heterogenously echogenic mass lesion measuring 14 x 13 cms in the epigastric and umbilical regions. Hypo echoic areas were noted within the lesion. Lesion appeared to be arising from the greater curvature of stomach. Liver, GB, pancreas, bilateral kidneys and spleen were normal.There was no ascities or significant lymphadenopathy.

CT scan (Figure 1) showed a large well defined lobulated exophytic heterogeneous soft tissue density lesion measuring 16.3 x 15.5 x 9.6 cms arising from the greater curvature and posterior wall of stomach. Lesion was displacing the transverse colon and bowel loops .No evidence of calcification, significant perigastric or retroperitoneal lymphadenopathy.

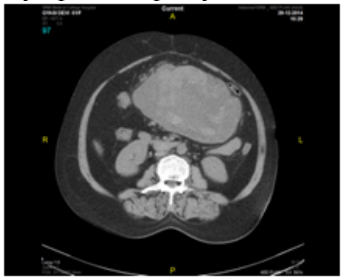

Figure 1: CT scan showing a large well defined lobulated exophytic heterogeneous soft tissue density lesion measuring 16.3 x 15.5 x 9.6 cms arising from the greater curvature and posterior wall of stomach.

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The patient underwent an enbloc resection of tumor and was sent for histopathological examination.

Gross (Figure 2): A fairly circumscribed soft tissue mass measuring 18X13X11cm with extensive areas of haemorrhage and congestion was received. Cut surface of the mass appeared grey white, fleshy in consistency with focal areas showing cysts filled with haemorrhagic fluid. Areas of haemorrhage and necrosis were also noted.

Figure 2: Enbloc resection specimen showing a fairly circumscribed fleshy soft tissue mass measuring 18X13X11cm.

Histopathological examination (Figures 3a,3b,3c) revealed predominantly interlacing fascicles of pleomorphic spindle cells which are cigar-shaped with blunt or rounded edges and dispersed chromatin with occasional small nucleoli. The cytoplasm is eosinophiic and fibrillary.Few cells exhibited cytoplasmic vacuoles at both ends of nucleus . Focal areas also showed round to polygonal cells with central nucleus and abundant acidophilic or clear cytoplasm exhibiting epitheliod morphology with areas of haemorrhage and necrosis. Occasional bizarre cells were noted. Mitotic activity was >5/50 hpf. The resected margins were free of tumor.

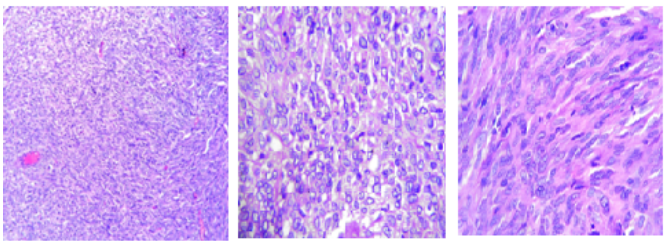

Figure 3a Figure 3b Figure 3c

Figure 3a: Photomicrograph of gastrointestinal stromal tumour exhibiting epithelioid and spindle cell morphology (H&E, 100x)
Figure 3b: Photomicrograph of gastrointestinal stromal tumour exhibiting epithelioid morphology (H&E, 400x)
Figure 3c: Photomicrograph of gastrointestinal stromal tumour exhibiting spindle cell morphology (H&E, 400x)

Immunohistochemistry (Figures 4a, 4b) showed that the tumor cells were positive for CD117, CD 34.Tumour cells were negative for S-100, SMA, and desmin and CK. The findings favoured the diagnosis of mixed type of GIST with high malignant potential.

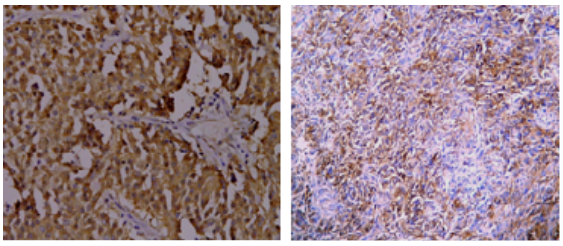

Figure 4a Figure 4b

Figure 4a: Photomicrograph of mixed type of gastrointestinal stromal tumour showing CD 117 immunoreactivity (IHC, 400x).
Figure 4b: Photomicrograph of mixed type of gastrointestinal stromal tumour showing strong CD 34 immunoreactivity (IHC, 100x).

DISCUSSION

Gastrointestinal stromal tumours (GISTs) are mesenchymal neoplasms that account for approximately 2% of all malignant gastric tumors[1].The incidence is between 14.4 to 11cases per 1 million in the general population [2]. GIST constitute majority of primary non epithelial neoplasms of stomach and can also involve small bowel, oesophagus, omentum, mesentery, retroperitoneum [1-3].The sex incidence is equal and the peak incidence is between the fifth and eighth decades of life [3,4] . GIST arises from the wall of the gastrointestinal tract and is thought to originate from the Interstitial Cells of Cajal (ICC), which regulate the motility of the gastrointestinal tract [2]. 95% GIST's have gain of function mutations of the KIT proto-oncogene, which encodes for a transmembrane tyrosine -kinase receptor (CD117).Most of the remaining 5% of GISTs have mutation of platelet derived growth factor receptor alpha (PDGFRA) .A very small number of tumours have no detectable mutation (wild type).The gain-of-function mutations in the KIT gene occurs at exon 11 most commonly, other mutations are found in exons 9, 13, and 17. This results in stimulation of numerous downstream signal transduction pathways including the RAS, JAK and SRC kinase pathways resulting in malignancy. GISTs that harbour a mutated PDGFRA induce activation of the same signal transduction pathways as gain-of-function mutations in KIT [1-3]. Clinical symptoms vary, and many tumors are discovered incidentally. The usual complaint is vague upper abdominal discomfort or pain. Anorexia, nausea, vomiting, and weight loss are uncommon. Larger tumors may ulcerate, giving rise to frank upper or lower gastrointestinal hemorrhage or anemia. Rarely, tumors may bleed into the peritoneal cavity [2]. GISTs range from indolent, hardly proliferating to fast-growing, recurring and metastasizing lesions. Around 60% of GISTs occur in stomach. Around 60% are submucosal, 30% subserosal and 10% intramural [1]. Grossly, most GISTs are solitary rounded or lobulated lesions with a clearly defined

margin. They primarily involve the muscularis propria and submucosa. Larger tumors bulge into the gastric lumen and have attenuated mucosa covering their surface. Subserosal extension may occur, and the peritoneal covering may be interrupted. The cut surface displays a flat, whorled silk appearance and may produce hourglass defect at cardia or pylorus if tumor encircles stomach. The tumour substance is usually firm with foci of necrosis or hemorrhage. Large tumors may be cystic in the middle [1]. Morphologic types include smooth muscle type, epithelioid type, neural type and mixed type. Morphologic variations include prominent myxoid matrix (PDGFRA mutations), signet ring cell features, granular cell changes, oncocytic cytoplasmic features, GANT (Gastrointestinal autonomic nerve tumor) type tumors, rhabdoid features, crystalloid formation (with schwannian differentiation), heavy inflammatory infiltrate, and tumor giant cells [1].Malignant potential and prognosis of these tumors are based on tumor size and mitotic count (Table 1).

Table 1: Guidelines for assessing malignant potential of GISTs

Tumor	Predicted biologic behaviour	Metastasis rate or tumor related mortality
≤2cm, ≤5 mitoses / 50HPFs	Benign	0
2 – 10 cms, ≤ 5 mitoses / 50 HPFs	Very low malignant potential	< 3%
> 10 cms, ≤ 5 mitoses / 50 HPFs or ≤ 5 cms, > 5 mitoses / 50 HPFs	Low to moderate malignant potential	12 – 15 %
> 5 cms, > 5 mitoses / 50 HPFs	**High malignant potential**	**49 – 86 %**

The primary treatment of GIST consists of surgical excision of the tumor with a good margin of normal tissue. Specific targeted therapy (Imatinib mesylate) is effective in most cases with KIT mutations and many with PDGFRA mutations thereby inactivating the ability of KIT to perform intracellular signalling. Mutational analysis may provide helpful data in planning therapy because different mutations of KIT and PDGFRA may affect prognosis and response to therapy. Tumours lacking KIT or PDGFRA mutations likely will not respond to therapy.

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