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SPECTRUM OF GASTRO-INTESTINAL STROMAL TUMOURS PRESENTATION WITH SPECIAL REFERENCE TO E-GIST AND ASSOCIATION WITH NF-1: A RETROSPECTIVE STUDY AT A TERTIARY REFERRAL CENTRE IN EASTERN INDIA

Gastrointestinal sistem dışında yerleşen ekstra GİST (E-GİST) vakalarının klinik spektrumu; Batı Hindistan'daki bir 3. Basamak hastane deneyimi.

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ABSTRACT

To study various modes of presentation of GISTs at a tertiary level referral centre in Eastern India.

A retrospective, single institution study was carried out on 48 patients with a histological diagnosis of GIST, who underwent treatment in Department of Surgery, Medical College, Kolkata, during the period 2010-2013.

Of the 48 cases studied, 26 were males and 22 were females. The age of patients ranged from 24 to 60 years, mean age being 44.04 years. Eight patients presented with acute small bowel obstruction and one with recurrent subacute small bowel obstruction, 9 with vague abdominal pain, 14 with abdominal lump, 12 with upper GI bleed, 2 with gastric outlet obstruction and 1 with urinary symptoms. The commonest location of lesion was stomach (45.8%) followed by small gut, colon, retroperitoneum, omentum and urinary bladder. Most (91.7%) lesions were unifocal. All patients underwent surgical resection of tumours. Histologically, 42 were of spindle cell type whereas 6 were epithelioid type. Thirteen patients received imatinib therapy post operatively.

Though rarity in incidence and diversity in presentation, GISTs should always be kept in mind while dealing with an abdominal tumour even if extraintestinal. A high index of suspicion is necessary for correct diagnosis and treatment of GISTs.

Key words: Stromal tumour, gastrointestinal, extra-gastrointestinal.

ÖZET

Bu çalışmanın amacı Batı Hindistan'daki 3. basamak bir hastanedeki GİST klinik prezentasyonlarını ortaya koymaktır. Kalkuta Tıp Merkezine gelen ve histopatolojik olarak GİST tanısı konulan 48 hastanın retrospektif olarak değerlendirilmesi yapılmıştır.

Çalışmaya alınan 48 hastanın 26'sı erkek ve 22'si kadındı. Yaşları 24-60 arasında (ortalama; 44.04) değişmektedir. Biri nüks olmak üzere 8 hasta ince barsak tıkanıklığı, 9 hasta karın ağrısı, 14 hasta distansiyon, 12 hasta kanama, 2 hasta mide çıkışı tıkanıklığı sendromu ve bir hasta üriner sistem şikayetleri ile gelmişti. Olguların en sık yerleştiği yer mide (%45.8) olup bunu sırasıyla ince barsaklar, kolon, retroperiton, omentum ve mesane kaynaklı GİST lezyonları izlemiştir. Olguların çoğunda (%91.7) lezyon tek odaklıydı. Vakaların hepsinde cerrahi tedavi uygulanmıştır. Histopatolojik olarak olguların 42'si iğsi hücreli, 6'si ise epiteloid tipte idi. 33 hastada ameliyat sonrasında imitinip tedavisi uygulandı.

Sonuç olarak, gastrointestinal sistem dışında çok nadir bulunmakla birlikte, karın içerisinde değişik yerlerde extra-GİST tümörlerin de olabileceği akılda bulundurulmalıdır.

Anahtar kelimeler: Stromal tümör, gastrointestinal sistem, gastrointestinal sistem dışı.

INTRODUCTION

Gastro-intestinal stromal tumours (GIST) are the most common mesenchymal neoplasms of GI tract. They account for 0.2% of all GI tumours. GISTs have a wide array of clinical presentations, often posing a diagnostic dilemma. Hence, a high index of suspicion is necessary for correct preoperative diagnosis.

To study various modes of presentation of GISTs at a tertiary level referral centre in Eastern India.

MATERIAL AND METHOD

A retrospective, single institution study was carried out on 48 patients with a histological diagnosis of GIST, who were treated in the Department of Surgery, Medical College, Kolkata, during the period 2010-2013. The parameters assessed included patients' demographic characteristics, mode of presentation, site, size and numbers of lesions, histological type, mitotic count, c-kit positivity, treatment rendered and follow up.

RESULTS

Of the 48 cases studied, 26 were males (54.2%) and 22 were females (45.8%). The age of patients ranged from 24 to 60 years, the youngest diagnosed patient being 24 years old while the oldest was 60 years old, mean age being 44.04 years. GISTs were more commonly found in patients aged >50 years (Table 1).

Most common mode of presentation was with an abdominal lump (29.2%) followed by upper GI bleeding (25%), small bowel obstruction (20.9%) and vague abdominal pain (18.7%). One patient presented with features of gastric outlet obstruction and one patient had obstructive urinary symptoms (Table 2).

The commonest location of lesion was stomach (45.8%) followed by small gut (31.2%) and colon (12.5%) (Table 3).

Table 1: Age and sex distribution.

Age in years	Total	Male	Female	Percentage
21-30	2	0	2	4.2
31-40	12	6	6	25
41-50	14	8	6	29.2
51-60	20	12	8	41.6

Table 2: Mode of presentation.

Mode of Presentation	Total	Percentage
Acute small bowel obstruction	8	16.7
Recurrent small bowel obstruction	2	4.2
Vague abdominal pain	9	18.7
Upper GI bleed	12	25.0
Obstructive urinary symptoms	1	2.08
Abdominal lump	14	29.2
Gastric outlet obstruction	2	4.2

E-GISTs were found in 10.4% of cases with tumours located in retroperitoneum, omentum and urinary bladder (Table 4).

All patients underwent surgical resection of tumours, 30 en-bloc resection, 12 wedge resection, 4 distal gastrectomies and 2 subtotal gastrectomies.

Most (91.7%) lesions were unifocal (Pie Diagram 1). Interestingly, two patients were known cases of Neurofibromatosis-Type 1 and both had multifocal lesions. The association of GIST with NF-1 was found to be 4.16% in this study. Lymph nodes were absent in all but 1 case of retro peritoneal GIST. Histologically, 42 were spindle cell type whereas 6 were epithelioid type (Table 5). According to tumour size and mitotic count, risk stratification was done as per NIH/NCI workshop, 2001.

Most cases (58.4%) were in the low risk group (Table 6).

Forty two out of 48 tumours were c-kit positive (87.5%). Thirteen patients received imatinib therapy post-operatively, criteria being size > 5cm, mitotic count >5/50 hpf, multifocal lesion, non resectability, recurrence and metastasis.

During follow up (average duration: 18months), none of the patients showed any evidence of recurrent disease.

Table 3: Site of involvement.

Site	Total	%
Stomach	22	45.8
Small Intestine	15	31.2
Colon	6	12.5
Retroperitoneum	3	6.25
Omentum	1	2.08
Urinary bladder	1	2.08

Table 4: Site of E-GISTs.

E-GIST	**n**
Retroperitoneum	3
Omentum	1
Bladder	1

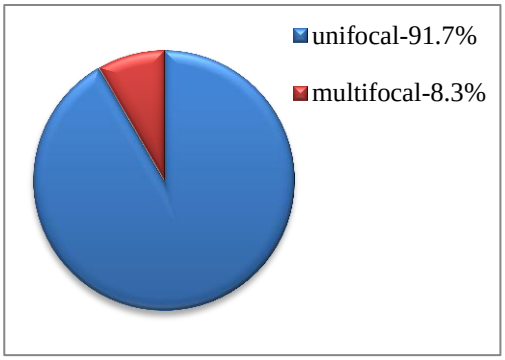

Figure 1: Pie Diagram 1.

Table 5: Histological variety.

Histology	Total	%
Spindle cell type	42	87.5
Epithelioid type	6	12.5

Table 6: Risk groups.

Risk	Total	%
Low	28	58.4
Intermediate	10	20.8
High	10	20.8

DISCUSSION

Gastrointestinal stromal tumors (GIST) are rare malignancies. Although they are the most common sarcoma of the gastrointestinal (GI) tract, they represent only 0.2% of all GI tumors, with an annual incidence in the United States of 14.5 per million persons (1,2). The term GIST was first employed in 1983 by Mazur and Clark to describe nonepithelial tumors of the GI tract that lacked the ultrastructural features of smooth muscle cells as well as the immunohistochemical characteristics of Schwann cells (3). Based upon their histologic and immunohistochemical features, GIST are thought to arise from the interstitial cells of Cajal (ICC), which are components of the intestinal autonomic nervous system that serve as pacemakers regulating intestinal peristalsis (4). GISTs are now identified by the near universal expression of the CD117 antigen (~95%), part of the KIT receptor, in the appropriate histopathological context and PDGFRA positivity in ~5%. CD117 expression is characteristic of most GIST, but not other gastrointestinal smooth muscle tumours, which are more likely to express high level of desmin and smooth muscle actin (1,6). A few GISTs show no detectable KIT or PDGFRA mutations.

Primary GIST can arise throughout tha GI tract, but are most common in the stomach (40-70%), followed by small bowel (20-40%) and colorectum (5-15%), and are rarely found in the esophagus (<5%) (7). In our study, the percentages of lesions in stomach (45.8%) and small intestine (31.2%) were comparable to those mentioned in literature. Some GISTs arise primarily in the omentum, mesentry or retroperitoneum. They are unrelated to the tubular GI tract and therefore called Extragastrointestinal Stromal Tumour (E-GISTs) (7-12). E-GISTs are identical to GISTs in histological and immunohistochemical features (11,13). The presence of ICC-like cells in the extraintestinal sites have been reported in many organs including urinary bladder, gallbladder, omentum, mesentry, urinary tract, uterus, fallopian tube, myocardium and prostate leading to formation of E-GIST in these organs (14,15). Reith et al1 reported 48 cases of E-GISTs and 6 of them originated in the retroperitoneum (3). Seventeen cases of EGSTs of the retroperitoneum have been reported by Yamamoto et al and by Barreda Bolanos et al. Sakurai et al. implicated the possible pathogenesis of primary omental GISTs from ICC-like Kit-positive cells existing in the normal omentum (11,12,16,17). Though less common, our study also had cases of E-GIST in the retroperi-

toneum, omentum and urinary bladder. E-GIST of the urinary bladder is a very rare tumour and the majority of the cases published show invasion of the serous membrane and/or of the entire bladder wall (18,19).

GIST usually present in patients from 40 to 60 years of age, as also seen in our study, although they have been diagnosed in children younger than age 10 years. They are equally common in men and women, and occur in all racial and ethnic groups. A very few GIST are familial, caused by an activating germline mutation of KIT. In our study,we found 2 cases of familial GIST associated with NF-1 (4.16%), but the reported association in the literature is 8-10%. Both the cases of GIST associated with NF-1 had multiple tumors affecting the ileum with adhesions.

Most of the GISTs are asymptomatic with vague symptoms and are discovered upon imaging or at laparotomy for other reasons. They are highly vascular and friable which often erodes causing haemorrhage. As such, upper GI bleed is the most common presenting symptom. However, in our study, abdominal lump was the most common presenting symptom, upper GI bleed being the second most common. Bleeding can sometimes be torrential and life threatening. GISTs can also present as mechanical intestinal obstruction and can lead to perforation.

Between 15-50% of GIST present as metastatic disease, the most common site of metastasis being liver and peritoneum (7,20). Pulmonary metastasis is present in less than 5% of cases. Invasion of adjacent organs may be present. Lymph node metastasis is very uncommon in GIST. Diffuse peritoneal spread with tumour-associated ascites though rare may be present. Large, necrotic tumours may form intratumoural abscess or intestinal fistula. In our study, one case, the retroperitoneal GIST presented as abscess in the perisplenic area with vague abdominal pain being the presenting complaint. Intraoperative enlarged lymph nodes were also present which came out to be metastatic in final histopathological report. Lymph node positivity in our study was 2.08%.

Surgery is the treatment of choice for all resectable nonmetastatic tumours. The reported resectability rate for localized primary GIST is 70-80% (20-22). Although endoscopic resection of small lesions has been reported, but there is potential risk of R1/R2 resection andtumour spillage (23,24). Adjuvant therapy with Imatinib mesylate, a tyrosine kinase inhibitor is given for GISTs with size > 5cm, mitotic count >5/50 hpf, multifocal lesion, recurrence and metastasis. Imatinib is also used as neoadjuvant therapy.

The most common sites of recurrence are the tumour bed, liver and peritoneum. The presentation of recurrent GIST depends on the site of recurrence. Patients may present with jaundice, ascites, lump abdomen, features of acute / chronic obstruction or bleeding. Therefore, regular follow up of patients is of prime importance.

In conclusion, though GISTs constitute only 0.2% of all GI tumours, it should always be kept in mind while dealing with cases of abdominal lesions even if extraintestinal. Its varying presentation only increases the level of challenge faced during diagnosis. A high index of clinical suspicion is essential to diagnose and treat a case of GIST.

REFERENCES

1. Fletcher CD, Berman JJ, Corless C, et al. Diagnosis of gastrointestinal stromal tumours: A consensus approach. Hum Pathol 2002;33:459-65.

2. Jemal A, Murray T, Ward E, et al. Cancer statistics. CA Cancer J Clin 2005;55:10-30.

3. Mazur MT, Clark HB. Gastric stromal tumours: Reappraisal of histogenesis. Am J Surg Path 19837:507-19.

4. Kindblom LG, Remotti HE, Aldenborg F, et al. Gastrointestinal pacemaker cell tumour (GIPACT): Gastrointestinal stromal tumours show phenotypic characteristics of the interstitial cells of Cajal. Am J Pathol 1998;152:1259-69.

5. Rubin BP, Singer S, Tsao C, et al. KIT activation is a ubiquitous feature of gastrointestinal stromal tumours. Cancer Res 2001;61:8118-21.

6. Bauer S, Corless CL, Heinrich MC, et al. Response to imatinib mesylate of a gastrointestinal stromal tumour with very low expression of KIT. Cancer Chemother Pharmacol. 2003;51:261-5.

7. Bumming P, Andersson J, Meis-Kindblom JM, et al. Neoadjuvant, adjuvant and palliative treatment of gastrointestinal stromal tumours (GIST) with imatinib: a centre-based study of 17 patients. Br J Cancer 2003;89:460-4.

8. Demetri GD, van Oosterom AT, Blackstein M, et al. Phase III multicenter, randomized, double-blind, placebo-controlled trial of SU11248 in patients following failure of imatinib for metastatic GIST. Proc Am Soc Clin Oncol 2005;23:4000.

9. Yamamoto H, Oda Y, Kawaguchi K, et al. C-kit and PDGFRA mutations in extragastrointestinal stromal tumour (gastrointestinal stromal tumour of the soft tissue). Am J Surg Pathol. 2004; 28:479-88.

10. Miettinen M, Lasota J. Gastrointestinal stromal tumours: definition, clinical, histological, immunohistochemical, and molecular genetic features and differential diagnosis. Virchows Arch. 2001;438:1-12.

11. Reith JD, Goldblum JR, Lyles RH, Weiss SW. Extra-gastrointestinal (soft tissue) stromal tumours: an analysis of 48 cases with emphasis on histologic predictors of outcome. Mod Pathol. 2000;13(5):577-85.

12. Min KW, Leabu M. Interstitial cells of Cajal (ICC) and gastrointestinal stromal tumour

(GIST): Facts, speculation, and myths. J Cell Mol Med 2006;10:995-1013.

13. Gun BD, Gun MO, Karamanoglu Z. Primary stromal tumour of the omentum: Report of a case. Surg Today 2006; 36:994-6.

14. Sakurai S, Hishima T, Takazawa Y, Sano T, Nakajima T, Saito K, Morinaga S, Fukayama M. Gastrointestinal stromal tumours and KIT-positive mesenchymal cells in the omentum. Pathol Int 2001;51:524-31.

15. Roberts PJ, Eisenberg B. Clinical presentation of gastrointestinal stromal tumours and treatment of operable disease. Eur J Cancer 2002; 38:S37-S38.

16. DeMatteo RP, Lewis JL, Leung D, et al. Two hundred gastrointestinal stromal tumours: Recurrence patterns and prognostic factors for survival. Ann Surg. 2000;231:51-8.

17. Rossi CR, Mocellin S, Mencarelli R, et al. Gastrointestinal stromal tumours: from a surgical to a molecular approach. Int J Cancer 2003; 107:171-6.

18. Joensuu H, Fletcher C, Dimitrijevic S, et al. Management of malignant gastrointestinal stromal tumours. Lancet Oncol 2002;3:655-64.

19. Davila RE, Faigelm DO. GI stromal tumours. Gastrointest Endosc. 2003;58:80-8.