Original Research Paper

Volume-8 | Issue-11 | November-2018 | PRINT ISSN No 2249-555X

General Surgery

CLINICAL PRESENTATION, MANAGEMENT AND OUTCOMES OF GASTROINTESTINAL STROMAL TUMORS

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ABSTRACT

INTRODUCTION: The present study investigated the incidence, management and outcome of Gastroin-testinal Stromal Tumors (GIST) in KAPV medical college,Tiruchirappalli.

METHODS: A retrospective review of all GIST patients admitted between 2013 and 2017 was conducted. Patients' demographics, clinical presentation, tumor characteristics, radiological, pathological and immunohistochemical findings, surgical procedures, recurrence and mortality were recorded.

RESULTS: A total of 4 GIST patients were identified. Stomach and small intestine were the most common sites of tumor. The majority of cases had tumor size >5 cm, 3 cases had primary and 1 case had locally advanced tumor. All the cases were surgically managed. Chemotherapy was initiated. During follow up 3 cases showed good response and 1 died due to liver metastasis.

CONCLUSION: the incidence of GIST in Tiruchirappalli is apparently low. Surgical resection is the preferred choice of treatment

KEYWORDS : stomach,omentum,resection,immunohistochemistry

1. INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasms, accounted for 13% of all gastrointestinal malignancies, which arise anywhere within the gastrointestinal tract . GISTs originate from the stomach are most common followed by small intestinal origin. However, in rare cases, it may be seen in intra-abdominal sites such as the omentum, mesentery and retroperitoneum. Earlier, GISTs were considered as variants of smooth muscle tumors. With the advancement of molecular technology and immunochemistry, GISTs recognized as originating from interstitial cells of Cajal or their stem cell precursors. c-KIT gene mutation occurs in vast majority of GIST cases (more than 80% of GISTs) followed by platelet derived growth factor receptor a (PDGFRA) mutations. c-KIT and PDGFRA genes are located in the fourth chromosome in humans . CD117, a protein encoded by the c-KIT gene, is an important marker in the diagnosis of GIST. Other markers used are; CD34, vimentin, keratin, smooth muscle actin (SMA) and S100. The risk of GIST is increasing in people who have inherited the mutation and in some instances GISTs can be found in several members of the same family.

GIST can be asymptomatic and incidental finding. Depending on the size and site, the symptoms of GIST vary, which include abdominal pain and bleeding. Diagnostic work up consists of endoscopy with ultrasonography and cross-sectional imaging techniques such as computed tomography (CT) and/or magnetic resonance imaging (MRI). Several criteria for risk stratification exist such as Fletcher's criteria; the first attempt in assessing the malignant potential of GIST. These criteria are based on the size of tumor and mitotic activity . GISTs greater than 2 cm in diameter are often surgically resectable, whereas less than 2 cm in diameter are closely monitored for metastasis. Surgical resection remains the established mode of effective treatment for GISTs. However, the use of oral inhibitors likes imatinib that targeting mutations are indicated in patients with inoperable or metastatic disease. Other approaches include photodynamic therapy (PDT) that utilizes reactive oxygen species to kill tumor cells .

2. PATIENTS AND METHODS

A retrospective analysis was conducted for all the patients who were admitted to the surgery department at KAPV government medical college,Tiruchirappalli, between 2013 and 2017. Patients with a confirmed diagnosis of GIST were included in the study. The collected data included patients' gender, clinical presentations, radiological investigations, laboratory findings, tumor characteristics, pathological findings, surgical procedures, intra and post-operative complications. Investigations included ultra-sonography, CT scan, MRI and endoscopy. Immuno-histochemical analysis was performed using markers such as CD117, CD34, SMA and S-100 protein. Mitotic rate was measured using high power fields (HPF). Post-operative complications, recurrence and mortality data were recorded during the follow up period.

3. RESULTS

This study included 4 GIST patients; 2 males and 2 females. Mean age of the patients at diagnosis was 51.25 years. The most presented clinical symptoms were abdominal pain,abdominal discomfort and occasionally vomiting. Most common site of tumor was stomach followed by small intestine .

Fig 1shows radiologic findings for one of our cases with large omental GIST Fig 2 shows intraoperative picture and Fig 3 shows cutsection of resected tumour

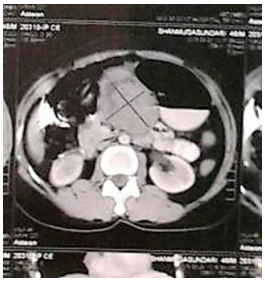

FIG 1-CT SCAN FEATURE OF OMENTAL GIST

FIG 2-INTRAOPERATIVE SPECIMEN

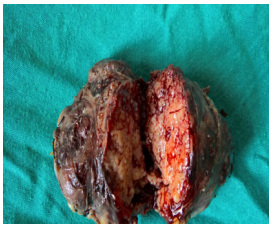

FIG 3-CUTSECTION OF TUMOUR

Tumors originated from stomach in 2 patients, from jejunum in 1 patient and in lesser omentum in 1 patient.. shows the demographics and clinical presentation of GIST patients.

Table 1- demographics And Clinical Presentation

S NO	AGE	GENDER	SITE	TUMOUR SIZE	CLINICAL FEATURES
1	55	FEMALE	STOMACH	8X8CM	ABDOMINAL PAIN AND DISCOMFORT
2	46	FEMALE	STOMACH	6X5CM	EPIGASTRIC PAIN AND OCCASIONAL VOMITING
3	56	MALE	JEJUNUM	5X5CM	LOWER ABDOMEN DISCOMFORT AND MALENA
4	48	MALE	OMENTUM	15X15CM	ABDOMINAL DISCOMFORT

All the cases were surgically managed. Chemotherapy was initiated in half of the patients.The mean hospital length of stay was 9.5 days, ranging from 8 to 45 days. Patients were followed up for 37.5 months. Complications such as bleeding were reported in 1 case and infection in 2 patients. During the follow up period, 3 patients were alive without evidence of recurrence, 1 was alive with metastatic disease. shows the management and outcome.

TABLE 2-MANAGEMENT AND OUTCOME

S NO	SITE	PROCEDURE	IHC	MITOSIS	FOLLOW UP
1	STOMACH	BILLROTH TYPE II GASTRECTOMY	CD 117+VE	<5/50HPF	NO RECURRENCE
2	STOMACH	BILLROTH TYPE II GASTRECTOMY	CD 117+VE	<5/50HPF	NO RECURRENCE
3	JEJUNUM	RESECTION AND ANASTOMOSIS	CD 117+VE	<5/50HPF	NO RECURRENCE
4	OMENTUM	RESECTION	CD 34+VE	14/50HPF	METASTASIS TO LIVER

4. DISCUSSION

The present study describes the frequency, clinical presentation, management and outcomes of GIST. We reported 4 cases over 5 years. The Taiwanese cancer registry-based study reported more than 5% increase in incidence of GIST in ten years , likely reflects the advancements in diagnosis of the disease. A 30-year study in Japan also showed similar trend of significant increase in the GIST incidence during the last decade. However, it is difficult to compare the incidence rates in different countries due to the differences in study time periods and the lack of application of KIT immunohistochemical confirmation in some studies.

GIST can be presented at any age regardless the gender. There is no good information regarding any association of GIST with geographic location, ethnicity or race. Experience from an Italian group showed the mean age was 60 years, with equal incidence in males and females . Sorour et al. reported the mean age of patients at diagnosis of GIST was nearly 50 years, whereas Miettinen et al. revealed GISTs occurs rarely below 40 years and very unusual in children. In our study mean age is 51.25%. Wang et al. reported high incidence of GIST between 50 and 59 years of age. In a Middle East population, GIST occurred in males over 40 years of age in most of the cases . A slight male predominance in GIST incidence was reported in Taiwanese study but the Chinese survey showed equal rates of incidence similar to the Italian hospital study . The Taiwanese data demonstrated younger age and female sex as in-dependent predictors of better survival.

Although most of patients are asymptomatic, GIST associated symptoms varies with the site and size of the lesion. The common site for GIST reported in almost all studies is stomach, accounted nearly 41% in a Jordanian study population , and more than half of GIST cases in Saudi Arabian and Egyptian studies . More-over, one in five GIST patients in Saudi Arabian study had tumors in the small bowel . Nearly half of the cases in the Egyptian study presented with gastrointestinal bleeding; followed by symptoms such as intestinal obstruction in nearly 30%, intraperitoneal hem-orrhage in 15%, and rupture and peritonitis in 8% . Our study is also in line with the previous studies regarding the site of tumor; 50% of patients had tumors in stomach followed by 25% of small bowel origin. Abdominal pain was present in most of the patients (85%).

Tumor size is crucial in the progression of the disease. The Chinese epidemiological study recorded mean diameter of 5.78 cm . An Egyptian study on gastric stromal tumors which included 16 GIST patients reported tumor sizes between 8.4 and 20 cm . In the present study, the median tumor size was 7 cm ranging from 5 to 15 cm. Our study also shows most of the cases are with tumor size around 5 cm.

GIST risk stratification systems are mainly based on tumor size that leads to assessment of the malignancy. The National Institutes of Health (NIH) consensus criteria, also known as Fletcher's criteria, were the first risk stratification system developed . Eight prognostic categories based on tumor size and mitotic activity with four subdivisions of risk groups was used to assess the malignant potential. The 5 cm size was the cut-off value to define low and non-low risk tumors.In our study all patients were diagnosed with tumour size more than 5cm which falls under high risk.

Surgical resection is the effective and established mode of treatment for GISTs. Neoplastic mass and gastric wall excision with sufficient surgical margins can be achieved with different surgical techniques which depend on the tumor dimension and localization . In our study, all of the GISTs were localized to the primary organ site. Small GISTs are usually dealt with wedge resection, whereas gastric resection and total gastrectomy is often conducted in cases of large GISTs localized near the cardia. The National Comprehensive Cancer Network (NCCN) suggested laparoscopic techniques should be used only in tumors less than 2 cm in size. However, there are some reports indicating laparoscopy was effective and safe in removing larger GISTs but inadequate resection margins or tumor spillage leading to disease progression, recurrence and poor survival remain as main issues.

5. CONCLUSION

The incidence of GIST in Tiruchirappalli is apparently low. Surgical resection is the preferred choice of treatment.The primary goal of the surgery was to remove the tumor completely with avoiding tumor rupture. Presence of residual tumor is associated with early recurrence and short survival. Sorour et al. reported 3 and 5 years disease free survival for all GIST patients as 73.2% and 64.5% respectively.

Tumor sizes have a significant impact on overall survival. Surgery among low and intermediate-risk patients generally produces good outcomes, whereas high-risk tumors often recur after resection. Moreover, secondary surgery results in poor outcomes.

The mean hospital length of stay in our study was 9.5 days, ranging from one to 45 days. Patient outcomes in our study were recorded during the follow up of patients. Only one among these patients was having gastric GIST and had metastasis in liver.

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