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Gastrointestinal Stromal Tumors in a Tertiary Center in Saudi Arabia

Alharbi H[1], AlGhamdi F[1], Mubarah A[1], Alhumaidan N[1] and Ali BI[2*]

[1]General surgery resident at Prince Sultan Military Medical City, Riyadh, Saudi Arabia
[2]General surgery, upper gastrointestinal and bariatric surgery consultant at Prince Sultan Military Medical City, Riyadh, Saudi Arabia

***Corresponding author:** Ali BI, General Surgery resident at Prince Sultan Military Medical City, Riyadh, Saudi Arabia; Email: biaa1003@yahoo.com

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Abstract

Background: Gastrointestinal stromal tumor (GIST) is considered a rare disease entity, accounting for less than 3% of all gastrointestinal neoplasms, but by far considered the most common primary mesenchymal tumors of the gastrointestinal system. It's sporadic more than in neoplastic syndromes and can be found anywhere along the GI system but the stomach is considered the most common site. Unless the tumor is unrespectable or metastatic, surgery is the mainstay of treatment

Method: Medical records of all patients diagnosed with GIST in Prince Sultan Military Medical City located in Riyadh the capital of Saudi Arabia in the time between January 2015 and December 2020 were collected, including patients' age, gender, clinical presentations, radiological investigations and features, histopathological findings and Immunohistochemically markers.

Results: A 39 cases found, with 19 males and 20 females. All were Saudi with majority of patients which was 23 (59%) were diagnosed between the age of 40 and 60 years. Most common location was stomach 22 (56.4%), followed by 8 (20.5%) cases in small bowl. Using NIH criteria for GIST risk assessment for malignant behaviour, we stratified our cases into high, intermediate, low, and very low risk (28.2%, 10.2%, 33.3%, and 20.5% respectively).

Conclusion: This retrospective review confirms multiple GIST features that correlate closely with other published studies. Further prospective studies needed with higher sample size and unified parameters for better understanding of GIST tumors features, management, and prognosis.

Keywords: *Gastrointestinal stromal tumor; Saudi Arabia*

Introduction

Gastrointestinal stromal tumor (GIST) is considered a rare disease entity, accounting for less than 3% of all gastrointestinal neoplasms, but by far considered the most common primary mesenchymal tumors of the gastrointestinal system and known to be derived from the interstitial cells of Cajal which functions as the pacemaker cell [1]. It's sporadic in incidence but might sometimes be seen as a part of other neoplastic syndromes. The disease process is thought to be due to mutations of proto-oncogenes c-KIT or platelet-derived growth factor receptor alpha polypeptide, which increase tyrosine kinase receptor activity leading to continues proliferation of stem cells that differentiate into the interstitial cells of cajal [2]. These tumors can be found anywhere along the GI system, but the stomach is considered the most common site (60%), followed by the small intestine, duodenum, colon/ rectum and very rarely from the esophagus, few primary cases has been reported to originate from the omentum, mesentery, and retroperitoneum [3]. They show a greater incidence among men and dark-skinned population with age range between 40-80 years with 63 being the median age [4]. GIST has a wide range of clinical presentations that vary from symptoms that requires emergency visits like bowel obstruction, upper or lower GI bleeding or idiopathic spontaneous intra-abdominal bleeding to patients being asymptomatic and discovered incidentally during radiological or endoscopic investigations for other symptoms [5]. Many imaging modalities can help diagnosing GIST like CT scans, PET, MRI, and

ultrasound. CT especially in small bowel GIST gives the highest yield among other modalities, it also provides information about metastasis and local invasion [6]. Immuno histology together with pathology results are often diagnostic, and the mainstay of diagnosis is identifying CD 117 antigen (an epitope of KIT receptor tyrosine kinase) with approximately 95 % cases positive for the antigen. The main histopathological variants that are usually found are spindle cell, epithelioid and mixed spindle, and epithelioid variants [7]. Unless the tumor is unrespectable or metastatic, surgery is the mainstay of treatment with R0 resection, and no lymph node dissection is recommended. The use of adjuvant imatinib (tyrosine kinase inhibitors) in high-risk group patients showed an improved survival and a decrease in the recurrence rates. In those who has an unrespectable or metastatic disease, imatinib has been the primary approach as a neoadjuvant treatment [8]. In this study, our aim is to study the cases of GIST in our center in regard of their prevalence, clinical and radiological and histological features, and prognosis.

Methodology

The medical records of all patients diagnosed with GIST and confirmed by histopathology, in Prince Sultan Military Medical City located in Riyadh the capital of Saudi Arabia. All cases of confirmed GIST between January 2015 and December 2020 were collected retrospectively. The collected data included patients' age, gender, clinical presentations, radiological investigations and features, histopathological findings and Immunohistochemical markers such as CD117, DOG-1, DOG-7, CD34, SMA, desmin and S-100 proteins, surgical procedures, prognosis. Inclusion criteria included all patients diagnosed with GIST that was found in imaging, endoscopy or post-operative finding in any location which was confirmed by histopathological report. Exclusion criteria used were all patients who had inconclusive histopathological report to confirm GIST. This study was approved by the ethical committee in our hospital.

Results

We included 39 cases of GIST tumors in our study. Gender wise, 19 males and 20 females included with all the cases were Saudi in nationality. Majority of patients were diagnosed between the age of 40 and 60 years, which was 23 (59%) patients out of the 39 cases followed by 14 (35.9%) patients above the age of 60 years. Most of the GIST tumors were in stomach 22 (56.4%), followed by 8 (20.5%) cases in small bowel, followed by 3 cases found in the abdomen with no clear origin identified, with few cases of GIST seen in the duodenum, rectum, retroperitoneal, liver or lower esophagus. Most of the patients presented as abdominal pain, gastrointestinal (GI) bleeding or incidentally found in imaging, endoscopy or intra-operatively, with the most common presentation was abdominal pain in 46.2% of patients followed by GI bleeding in 28.2%, where incidental GIST found in imaging in 2 cases, and found in gastric specimen post laparoscopic sleeve gastrectomy in 2 cases, and found incidentally intra-operatively in jejunum of one case during Whipple procedure for pancreatic head cancer. The median size was the highest in one single case of lower esophageal GIST tumor whish was reaching 18 cm, followed by the intra-abdominal GIST tumors with unknown origin in which their median size was 15 cm, with the gastric tumors median size was 5 cm, and small bowel tumors of 3 cm (Table 1).

Table 1: *Demographics and clinical presentation of GIST patients (n 39).*

Demographics and clinical presentation of GIST patients (n 39)		
Age	< 40 years	2 (5.1%)
	40 – 49 years	13 (33.3%)
	50-60 years	10 (25.6%)
	> 60 years	14 (35.9%)
Gender	Male	19 (48.7%)
	Female	20 (52.4%)
Tumor Location	Stomach	22 (56.4%)
	Duodenum	2 (5.1%)
	Small bowel	8 (20.5%)
	Liver	1 (2.6%)
	Intra-abdominal with unknown origin	3 (7.7%)
	Retroperitoneal	1 (2.6%)
	Lower Esophagus	1 (2.6%)
	Rectum	1 (2.6%)
Median size (cm)	Stomach	5
	Duodenum	2.5
	Small bowel	3
	Liver	1
	Intra-abdominal with unknown origin	16

	Retroperitoneal	8
	Lower Esophagus	18
	Rectum	2
Presentation	GI Bleeding	11 (28.2%)
	Abdominal pain	18 (46.2%)
	Incidental (radiology, endoscopy, post operatively)	5 (12.8%)
Type of Surgery	Elective	27 (69.2%)
	Emergency	4 (10.3%)
	Not operated	8 (20.5%)
Metastasis	Yes	8 (20.5%)
	No	31 (79.5%)
Recurrence	Yes	5 (12.8%)
	No	27 (69.2%)
Mitosis (≤5 vs >5 per 50 HPF)	Stomach	15 vs 5
	Duodenum	2 vs 0
	Small bowel	3 vs 3
	Rectum	0 vs 1
CD type positive	CD 117	39 (100%)
	DOG-1	28 (71.8%)
	CD 34	20 (51.3%)
	SMA	6 (15.3%)
	DOG-7	4 (10.2%)
	h-Caldesmin	2 (5.1%)
	Desmin	1 (2.6%)
	S 100	0 (0%)
Type of cells in histopathology	Spindle-cell	25 (64.1%)
	Epitheloid	0 (0%)
	Mixed	8 (20.5%)

Table 2: *NIH-Fletcher criteria for GIST risk assessment.*

NIH-Fletcher criteria for GIST risk assessment			
Risk Category	**Primary Tumor Size (cm)**	**Mitotic Count (per 50 HPF)**	**No. (%)**
Very Low Risk	< 2	< 5	8 (20.5%)
Low Risk	2 - 5	< 5	13 (33.3%)
Intermediate Risk	< 5	6 – 10	4 (10.3%)
	5 - 10	< 5	
High Risk	> 5	> 5	11 (28.2%)
	> 10	Any mitotic rate	
	Any size	> 10	

Using the National Institute of Health criteria (NIH-Fletcher) for GIST risk assessment for malignant behaviour, we stratified our cases into high, intermediate, low, and very low risk (28.2%, 10.2%, 33.3%, and 20.5% respectively) (Table 2).

From all cases followed, 5 (12.8%) cases had recurrence of tumor, and 8 (20.5%) cases had metastasis at diagnoses. Operative management was done electively on 69.2% of patients while emergent operation was done 10.3%. Laparoscopic resection done on 22 (56.4%) patients and open resection was done on 9 (23.1%) patients, with endoscopic removal of gastric small GIST done in 1 case. Seven cases were not managed operatively as 1 patient passed away after stroke, 2 cases passed away due to advanced disease, 1 case refused surgery, 1 case of pelvic GIST managed conservatively with palliative treatment, and 2 cases lost follow up.

Discussion

To the best of our knowledge, this is first retrospective study reviewing the gastrointestinal tumors in detail in the central region of Saudi Arabia, and the second over the country. The study was done in Prince Sultan Military Medical City located in Riyadh which is the capital city of Saudi Arabia; as a military

hospital, all the cases collected were Saudi in nationality given the strict eligibility rules [9,10]. There was no significant difference in number of cases between males and females, which was 19 and 20 respectively, although there was male predominance reported in the other study in western region of Saudi Arabia and in another neighbouring gulf country, however there was no significant gender predominance in large scale studies done in Iceland, Sweden and in a study done in Wuhan in China [1,11,12]. Most of the patients in our study were diagnosed at the age of 40-60 year, with only 2 cases below 40 and 14 cases above 60 years, like what was shown in Qatari and Egyptian studies where they had the mean age of 48, and to have the highest incidence between the age of 50-60 years in the studies done in Wuhan and Shanxi Province [13,14]. From the 39 cases we had, 22 (56.4%) had GIST located in stomach followed by 8 (20.5%) in the small bowel which was correlating with all the studies we a crossed in the literature either in the region or internationally. In the regional study in Qatar [10] 85.4% of cases presented with abdominal pain, followed by GI bleeding in 54.2% of cases, with our study in the line of these clinical behaviours. GIST can be asymptomatic and found incidentally in endoscopy, imaging or intra-operatively as in 12.8% of our cases, as the size and location and in which if it is intraluminal or extra luminal contribute to its presentation. Incidental finding reported to reach 18.7% in a systematic review published in 2015 [15]. Metastasis can be presented at diagnoses in approximately 20% of cases, in which was the case in 20.5% of our patients. For the risk assessment of potential malignant behaviour of GIST tumors, multiple criteria were found, in which the National Institute of Health criteria (NIH-Fletcher) is one of the well-recognized criteria for GIST risk stratification into very low, low, intermediate, and high risk. NIH criteria uses the tumor size and mitotic rate as prognostic factors, where it has been noticed that the malignant potential and the recurrence rate are higher in tumors that are 5-10 cm in size with mitosis of 10/50 HPF with recurrence rate being almost 80% in these high-risk groups [16]. In our study, 13 (33.3%) cases where stratified into low risk followed by 11 (28.2%) cases falling into high-risk group. Although regional studies in Western Saudi Arabia and in Qatar [9,10] showed majority of cases were stratified under high-risk group compared to non-high risk, variation was noticed with the Sweden and Iceland studies showed the non-high risk were most cases compared to the high risk [11,12].

Conclusion

This retrospective review confirms multiple GIST features including gender predominance, clinical behavior and histopathological features that correlate closely with other published studies. Diagnosis of GIST tumors need high clinical suspicion and good usage of investigations. Further prospective studies needed with higher sample size and unified parameters for better understanding of GIST tumors features, management, and prognosis.

Conflict of Interest

The authors declared no conflict of interest and no financial issues to disclose.

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