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Gastrointestinal stromal tumors in southern Iraq: clinico-pathologic patterns and risk stratification

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Abstract

There was no local or nation-wide data on the patterns of Gastrointestinal Stromal Tumors (GISTs) in Iraq. This study was undertaken to determine the clinical and pathologic characteristics and risk stratification of GISTs in Iraqi patients over a nine years' period. This is a retrospective descriptive study. Medical notes and histopathological reports of patients with confirmed diagnosis of GIST between January 2007 and August 2015 were reviewed for age, gender, tumor location, CD117 status, tumor stage, and National Institutes of Health (NIH) risk classification. Forty-seven patients were included in the study. Mean age at time of diagnosis was 57 years (range 29 to 85 years), and male to female ratio was 1:1. Most common sites of involvement of GISTs were stomach (21/47), and jejunum/ ileum (16/47). Immunohistochemistry for CD117 was positive in 33 cases. Out of the 47 cases, 4 were locally advanced and 15 were metastasized. The most common site for metastasis was liver (53%) followed by pulmonary (40%) and retroperitoneum (7%). Risk stratification was done for only 41 cases; 61% were stratified as high risks group, 12% belonged to intermediate risk category, while the rest 27% were stratified as very low and low risk groups. While the epidemiological patterns of GIST from Iraq resembles those from elsewhere, the disease was more advanced in Iraqi patients when compared to Western countries. At the time of diagnosis, majority of our cases were stratified under high-risk category.

Keywords: Gastrointestinal Stromal Tumors, CD117, Risk stratification, Epidemiology, Clinico-pathological features

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Introduction

Despite being the most common mesenchymal tumors of the gastrointestinal (GI) tract, the gastrointestinal stromal tumors (GISTs) account for only 0.2% of all GI tumors. [1] The current consensus is that the GISTs originate from the interstitial cells of Cajal, or from their precursors [2]. The annual incidence of GIST is estimated at 10-15 per million per year, and the prevalence is estimated at over 10 times that of the incidence, and several studies have concluded that GIST survivors around the world, number around 135-155 per million per year. GISTs have a fairly equal gender distribution, and predominantly affected patients are of around 60 years of age. Stomach is the most frequent site of GIST, followed by small intestine and colorectal area [3]. GIST is reported to metastasize most often to the liver and peritoneum, and rarely to lymph nodes, bone, lung and soft tissues [4]. The accurate diagnosis of GIST depends upon histopathologic morphology and immunohistochemistry (IHC) findings. It is reported that about 95% of GIST cases show oncogenic mutation in receptor of tyrosine kinase, which is detected by KIT (CD117) immunostaining. [5] Some patients with KIT-wild type GISTs are found to have another oncogenic mutation in platelet-derived growth factor receptor-alpha (PDGFRA) gene encoding another receptor of tyrosine kinase, which can also be detected by molecular analysis [6].

The standard treatment of GIST patients is surgical resection aiming for complete resection. Measurement of recurrence risk after resection (risk stratification) is important to select high-risk patients for chemotherapy. A 3-year adjuvant chemotherapy with the tyrosine kinase inhibitor (TKI) imatinib is recommended to improve prognosis in such high-risk patients [5]. Different models and nomograms are available for risk stratification in GIST; they depend on tumor size, site, and mitotic index. The National Institutes of Health (NIH) consensus is commonly used for this purpose [7].

While the epidemiological data of GIST is available in many countries and

regions in the world, there is a dearth of reliable local or nation-wide data on the patterns of GIST in Iraq. Basra Oncology Center (BOC) is a tertiary referral unit located in Basra, South Iraq, and most of the GIST cases from Iraq are referred to our center. Hence, this study was conducted to analyses the epidemiologic and clinic-pathologic characteristics of GISTs in Iraqi patients who were registered in BOC.

Methodology

The study was an observational, retrospective study describing the characteristics of GIST patients who were registered in BOC between January 2007 and August 2015. Since this was a retrospective study, a waiver of informed consent was sought and obtained from the institutional ethics committee. All the cases with confirmed diagnosis of GIST were included in the study according to histopathological results. The data collected for the purpose of this study included age, gender, characteristics of the tumor (including location, maximum tumor size, and mitotic index). The NIH consensus criteria were used to stratify the risk of recurrence of each case into very low, low, intermediate, and high risk of recurrence. The location of the tumor at the time of diagnosis (primary or secondary) as well as the results of imaging investigations were reviewed to classify the patients into localized, locally advanced and metastatic cases. The pattern and sites of metastasis were studied. The percentage of CD117 positivity was collected to assess the sensitivity of this test in diagnosis of GIST among our patients. All data was described as numbers and percentages. Microsoft excel was used to compile the data. Since this was a descriptive study, no statistical tests were applied.

Results

A total of 47 cases of GIST were registered in the BOC registry during the study period. The median age at diagnosis was 57 years (range 29 to 85 years), and the majority (72%) were diagnosed between ages of 40 to 70 years. There was no gender predominance (24 male and 23 female cases). Out of the 47 cases, only 4 were reported between 2007 and 2009, while the remaining 43 cases were reported between 2010 and 2015.

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Details pertaining to the tumor location, tumor stage, and site of metastasis in the patients in our study is described in table 1. The most frequent site of GIST was stomach (21/47, 45%), most tumors were localized (20/47, 43%), and liver metastases were found in 8 out of the 15 cases which had metastasized. Further, out of the 15 cases which had metastasized, 7 had primaries in the stomach, and 6 from the small intestine. IHC for CD117 was done only for 36 cases, and 33 cases (92%) showed strong positivity. Other IHC markers such as CD34 and DOG1 confirmed the diagnosis of GIST in the CD117-negative cases.

Table 1

Tumor Characteristics

Location of the tumor		**Stage of the tumor**		**Site of metastasis**		**Immunohistochemistry for CD117**	
Location	No (%)	Stage	No (%)	Site	No (%)	Result	No (%)
Stomach	21 (45%)	Localized	20 (43%)	Liver	8 (53%)	Positive	33 (70%)
Jejunum/ ileum	16 (34%)	Metastatic	15 (32%)	Pulmonary	6 (40%)	Negative	3 (6%)
Colorectal	5 (11%)	Locally advanced	4 (8%)	Retroperitonium	1 (7%)	Unknown	11 (23%)
Duodenum	3 (6%)	Unknown	8 (17%)				
Mesentery	2 (4%)						

Out of the 47 patients in our study, risk stratification based on NIH consensus criteria was possible for 41 patients. These results are presented in Table 2. Most (61%) of the cases were classified under ‘high risk’.

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Table 1

Tumor Characteristics

Location	Total cases	Very low risk	Low risk	Moderate risk	High risk
Stomach	17	2	5	5	5
Duodenum	3	0	2	0	1
Jejunum/ ileum	14	0	0	0	14
Colorectal	5	0	2	0	3
Mesentery	2	0	0	0	2
Total (%)	41 (100%)	2 (4.9%)	9 (21.9%)	5 (12.2%)	25 (61%)

Discussion

The present study was undertaken to analyse the epidemiological, clinic-pathological and risk stratification pattern of GIST patients registered in a tertiary care oncological centre in Basra, Southern Iraq over a period of 9 years. To the best of our knowledge, this is the first study to describe the pattern of GIST from Southern Iraq, and to compare the features of GIST from Southern Iraq with that reported from elsewhere in the World. On reviewing previously published studies, we found that the diagnosis of GIST has dramatically increased over the last two decades [8-12]. Reflecting this trend, even in our study we found that the number of new cases of GIST was significantly higher between 2010 and 2015 (43 cases) as compared to those in the preceding 3 years (4 cases). This finding could be the result of an increased awareness about the disease, improved diagnostic measures, increasing use of immunohistochemistry staining such as CD117, and an increased population.

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The age, gender and prevalence rate of GIST as reported from our study resembles those from elsewhere in the world [3]. This is in contrast to the reports from the Westren countries where the patients are slightly older (median age 64 years, most cases are aged 50 to 80 years) [13], and more often males than females [8].

The most frequent sites of GIST from our study in descending order of frequency were stomach, ileum and jejunum, colorectal region, duodenum and mesentery; this pattern is like the pattern reported from other local [14], regional [2], and global [8] studies. Curiously, we found in our study that locally advanced and metastatic GISTs were observed in over 1/3rd of our cases (19/47, 40%) at time of presentation, and this was much higher when compared with the USA data of 11.4% [13].

As reported from other studies [15, 16] liver was the most common site of metastasis in our patients. However, pulmonary metastases, which have been described as 'rare' in GISTs [17], and a sign of advanced disease [4], was the second most common site of metastases in our study. This may indicate that at presentation, a higher proportion of GIST patients from this region are already having advanced disease. Further studies are required to investigate more into this pattern of metastasis in GIST patients from this region.

In our study, 33 out of 36 (92%) were strongly positive for CD117 by immunohistochemistry. The proportion of CD117 positivity in our study was similar to that in previously reported studies, which report a CD117 positivity ranging from 86.6 to 100 % from Asian studies [14, 16, 18], and over 95% from Western studies [19, 20]. Further, studies are required to confirm the CD117 positivity in our country.

The importance of risk stratification in GIST is to predict the prognosis and to decide adjuvant treatment with the tyrosine kinase inhibitor imatinib. GIST patients classified under high-risk and intermediate groups have a poorer prognosis and survival, as compared to those classified under low risk and very low risk groups whose survival is not markedly inferior to that of general population [21]. As can be expected by the high proportion of pulmonary

metastasis in our study, 25 out of 41 (61%) of our patients were classified under 'high risk' of recurrence as per the NIH consensus criteria. Our results are comparable with other published studies from Asian countries which also showed that most of the GIST patients were stratified as high-risk and intermediate groups [18, 22]. This result in our study indicates that most of our GIST patients either presented late in their disease or are having faster tumor growth caused by higher proliferation activity [23].

Conclusion

By this study, we demonstrated that in patients from South Iraq, GIST most often affects patients aged between 40 to 70 years, affects both the genders equally, and most commonly involves stomach followed by small intestine. It was localized in about half of the cased at time of presentation, but most of the cases were stratified into high-risk group. When compared to GIST patients from other parts of the world, the disease was more advanced in Iraqi patients and a higher proportion of patients belonged to high-risk group as compared to Western countries. Further studies are required to substantiate the findings of our study, and to evaluate the reasons for these differences.

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