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Original research

Clinical presentation, management and outcomes of gastrointestinal stromal tumors

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HIGHLIGHTS

- Frequency, characteristics and management of GISTs over 18 years were reviewed.
- The prevalence of GISTs in Qatar is apparently low.
- The risk of GISTs is evident in Arabs versus Asians and young versus old patients.
- Surgical resection remains the preferred choice of treatment.
- Robotic and laparoscopic resections are feasible and safe approaches in some cases.

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ABSTRACT

Introduction: The present study investigated the incidence, management and outcome of Gastrointestinal Stromal Tumors (GIST) in Qatar. **Methods**: A retrospective review of all GIST patients admitted between 1995 and 2012 was conducted. Patients' demographics, clinical presentation, tumor characteristics, radiological, pathological and immunohistochemical findings, surgical procedures, recurrence and mortality were recorded. **Results**: A total of 48 GIST patients were identified. Stomach (56%) and small intestine (27%) were the most common sites of tumor. The majority of cases ($n = 27$) had tumor size >5 cm, 31 cases had primary and 15 cases had locally advanced tumor. Patients were stratified as high, intermediate, and low risk (43.8%, 18.8% and 37.5%, respectively). Almost all the cases were surgically managed and 94% were completely resectable. Robotic partial resection was performed in 4 cases and 5 cases underwent laparoscopic resection. Chemotherapy was initiated in half of patients. During follow up (average 37.5 months), 33 patients showed complete recovery, 7 had recurrent or metastatic disease and 2 died due to liver metastasis. **Conclusion**: The incidence of GIST in Qatar is apparently low. Surgical resection is the preferred choice of treatment; however, robotic and laparoscopic resections are feasible and safe approaches in some cases.

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1. Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasms, accounted for 1–3% of all gastrointestinal malignancies, which arise anywhere within the gastrointestinal tract [1]. 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

Abbreviations: gastrointestinal stromal tumors, GIST; platelet derived growth factor receptor α, PDGFRA; smooth muscle actin, SMA; magnetic resonance imaging, MRI; photodynamic therapy, PDT; Hamad Medical Corporation, HMC; high power fields, HPF; National Institutes of Health, NIH; Armed Forces Institute of Pathology, AFIP.

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technology and immunochemistry, GISTs recognized as originating from interstitial cells of Cajal or their stem cell precursors [2–4]. c-KIT gene mutation occurs in vast majority of GIST cases (more than 80% of GISTs) followed by platelet derived growth factor receptor α (PDGFRA) mutations. c-KIT and PDGFRA genes are located in the fourth chromosome in humans [5]. 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 [4]. 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 [6].

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 [2,7]. 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 [8]. Other approaches include photodynamic therapy (PDT) that utilizes reactive oxygen species to kill tumor cells [9].

The incidence and prevalence of GISTs in Qatar remain understudied. The present study aims at reflecting the epidemiology and management of GIST in Qatar.

2. Patients and methods

A retrospective analysis was conducted for all the patients who were admitted to the surgery department at Hamad Medical Corporation (HMC) in Qatar, between 1995 and 2012. Patients with a confirmed diagnosis of GIST were included in the study. The collected data included patients' gender, nationality, clinical presentations, radiological investigations, laboratory findings, tumor characteristics, pathological findings, surgical procedures, intra and post-operative complications. Investigations included X-ray, ultrasonography, CT scan, barium study, MRI and endoscopy. Immunohistochemical 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. This study was approved by the medical research center at HMC, Doha, Qatar (IRB# 13269/13). Data were reported as percentages, mean ± standard deviation, and median and range, when applicable. Chi Square test was used to compare the risk between (males and females), (young and old age), and (Arabs and Asians) patients. A 2-tailed p value of <0.05 was considered significant. Data analysis was carried out using the statistical package for social sciences version 18 (SPSS Inc, Illinois).

3. Results

This study included 48 GIST patients; 31 males and 17 females. Out of these, 12 patients were Qataris, 11 were non-Qatari Arabs and 23 were Asians. Mean age of the patients at diagnosis was 48.4 ± 13.7 years (ranged from 23 to 77 years). The most presented clinical symptoms were abdominal pain (85.4%), vomiting (52%) and blood in stool (54.2%). Bowel obstruction was seen in 3 patients; one of them had gastric volvulus and hiatus hernia. One patient presented with urinary retention (rectal mass invading the prostate). Two patients were found to have ruptured small bowel tumor at presentation (one had traffic-related trauma and one presented with abdominal pain and thought to have intra-abdominal abscess) Most common site of tumor was stomach (56%) followed by small intestine (27%) (Fig. 1).

Fig. 2 shows radiologic and intraoperative findings for one of our cases with large gastric GIST. Tumors originated from duodenum in 4 patients, from colon in 2 patients and in rectum in 2 patients. Maximum size of the tumor was equal to or less than 2 cm only in 5 patients whereas greater than 5 cm in 27 patients. GIST was localized to primary organ site in most of the cases ($n = 31$) and locally advanced in 15 patients. Distant metastasis at evaluation was found in 15% of the patients. Table 1 shows the demographics and clinical presentation of GIST patients.

Patients were stratified as high, intermediate, and low risk (43.8%, 18.8% and 37.5%, respectively). Fig. 3 shows the comparison between females and males, young (<40 years) and older (>40 years), and Arabs and Asians in regard to the risk stratification.

All the cases were surgically managed; 94% were completely resectable and only 3 patients found unresectable. Four patients underwent robotic partial resection for posterior wall gastric tumors. Five cases underwent laparoscopic resection; 3 of them were discovered incidentally during Sleeve gastrectomy. Chemotherapy was initiated in half of the patients and radiation therapy was indicated in one case (very early in the study). The mean hospital length of stay was 9.5 days, ranging from one to 45 days. Patients were followed up for 37.5 (1–186) months. Complications such as bleeding were reported in 3 cases and infection in 2 patients. During the follow up period, 33 patients were alive without evidence of recurrence, 7 were alive with recurrent or metastatic disease and 6 patients left country after surgery. Two patients died during the follow up period; one had 17 cm gastric mass underwent 3 surgical interventions and died due to recurrent liver metastasis, whereas the second one presented with 13 cm rectal mass with liver metastasis underwent 5 surgical interventions. Table 2 shows the management and outcome. Fig. 4 shows the study overview (site of origin, diagnosis, management and outcomes of GISTs).

4. Discussion

The present study describes for the first time in Qatar the frequency, clinical presentation, management and outcomes of GIST. We reported 48 cases over 17 years. Nearly 50% of cases were from South Asians, whereas 25% were nationals (Qataris). Qatar is an Arab Middle Eastern country with small population that increased from 501,000 in 1995 to 1,448,479 in 2008 and 1,832,903 in 2012. Fig. 5 shows the incidence of GIST in Qatar per year. The highest incidence rate was shown in 2008 (0.55 per 100,000) and 54% of cases were diagnosed in the last third of the study period. This finding may reflect the advancement of the modality of diagnosis after 2006. Various epidemiological studies showed the incidence of GIST as 5–20 per million of the population [4,10,11]. The Taiwanese cancer registry-based study reported more than 5% increase in incidence of GIST in ten years [4], 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 [12]. 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. In our study, GIST was equally diagnosed in Arabs and Asians with a mean age of 48 years and male predominance. Experience from an Italian group showed

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