ORIGINAL ARTICLE

GENERAL CHARACTERISTICS AND TREATMENT OPTIONS OF THE PATIENTS WITH GASTROINTESTINAL STROMAL TUMOR

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ABSTRACT

Background: Gastrointestinal stromal tumors (GIST) are rare mesenchimal tumors may develop in any site in the gastrointestinal system. KIT gene mutations are detected in 95% of cases. In this study, we aimed to assess treatment options and general characteristics of patients with GIST.
Methods: GIST patients admitted to Abdurrahman Yurtaslan Oncology Education and Training hospital's oncology clinic between February 2009 and May 2012 are observed retrospectively. Demographic characteristics of the patients and the treatment they received were recorded from hospital's database.

Results: Eighteen patients included to study havinng Mean age of 57.8 years (32-78). Five (28%) of the patients were female and thirteen (72%) were male. Diagnosis were made in 16 patients by pathological assessment of surgical material. Trucut biopsy and gastroscopic biopsy used for diagnosis in remaining two patients. Localizations of the tumor were as follows: small intestine in 9 patients, colon in 5 patients, stomach in 4 patients. All of the patients were KIT positive. Tumor was defined at high risk in 62%, at moderate risk in 17% and at low risk in 21% of the cases. Imatinib was administered in 5 patients with metastatic disease. Mean follow up period for the patients was 48 months. Relapse or progression developed in 4 of all patients in follow up period. Only one of the five patients with metastaic disease developed progression. Other 3 cases were relapsed.

Conclusion: Surgical resection of tumor without fragmentatin is the main treatment of localized GIST cases. Imatinib, a tyrosine kinase inhibitor, is used in metastatic/ inoperable tumors and in cases at high risk for metastasis, recently. In conclusion, after surgical resection of the tumor, we suggest Imatinib treatment in patients considered at high risk.

Key words: gastrointestinal stromal tumor, imatinib, KIT gene

INTRODUCTİON

Gastrointestinal stromal tumors (GIST) are rare mesenchimal tumors that originate from cajal cells or from their precursors and may develop in any site in the gastrointestinal system. Cajal cells are pacemaker cells regulating intestinal motility [1-3].

Mutation activity in receptor protein kinase (KIT/CD117) is noteworthy in these tumors. About 95% of the cases are KIT positive. Remaining 5% of the cases do not express KIT and they have been defined as KIT negative tumors. PDGFR alpha gene mutations are prominent in these KIT negative cases. Therefore, if there is typical morphological appearance, GIST diagnosis should not be ruled out in KIT negative patients and PDGFR alpha gene mutations should be assessed [4].

Imatinib, a drug used for gastrointestinal stromal tumors, inhibits KIT tyrosine kinase receptor and Bcr-abl and platelet derived growth factor receptor [5].

We aimed in this study to evaluate general characteristics and treatment options of cases with GIST.

MATERIAL AND METHODS

GIST patients admitted to Abdurrahman Yurtaslan Oncology Education and Training hospital's oncology clinic between February 2009 and May 2012 are observed retrospectively. We recorded, the age, gender and inital complaints of the patients, whether they are operated, diagnostic methods and localization of the tumor, whether metastasis present and localizations of metastasis (if present), risk of metastasis and treatments they have received. For stastistical analysis, SPSS for

Windows, version 15.0 software (SPSS Inc, Chicago, Illionis, USA) was used.

RESULTS

We included 18 patiets to the study. Mean age of the patients was 57.8 years (min:32-max:78). Five (28%) of the patients were female and thirteen (72%) were male.

The most common initial complaints were abdominal pain (in 10 patients) and abdominal distention (in 4 patients). Diagnosis were made by operation in 16 cases. One of the other cases diagnosed by gastroscopy and the other case diagnosed by trucut biopsy.

Tumor localizations of the cases were small intestine (in 9 patients), colon (in 5 patients), and stomach (in 4 patients). All of the cases were CD117 positive and 62% were CD34 positive.

Five of the nine patients with intestinal tumors were at high risk while 3 were at moderate and 1 were at low risk. Three of five patients with colonic tumors were at high risk and two were at low risk. Three of four patients with gastric tumors were at high risk and one was at low risk. Eleven of 18 patients in total were at high risk while 3 were at moderate and 4 were at low risk for metastasis.

Metastatic disease have been diagnosed in five cases and those patients received Imatinib treatment. Of the five metastatic patients, three were at high risk while one each was at moderate and at low risk for metastasis.

Mean follow up period for the patients was 48 months (min 13 months- max 128 months). Relapse or progression developed in 4 of all patients in follow up period. Only one of the five patients with metastaic disease developed progression. Other 3 cases were relapsed. Two of the relapsed cases were previously defined at high risk. Disease relapsed 1 year after diagnosis in one patient. Other relapses occured 2 and 3 years later in other two patients. Progression occured in one metastatic patient 1 year after diagnosis.

DİSCUSSİON

GIST usually occurs in the fifth decade. Cases at chilhood consists 1% of all cases. Childhood cases intersetingly occurs only in stomach [3]. Mean age of the patients in our study was over 50 years which was compatible with literature.

GIST are soft and quite fragile tumors. Therefore, diagnostic biopsies may lead tumor bleeding and spreading. In case of a suspicion of lymphoma, biopsy should be performed despite the risk of tumor spreading. Endoscopic biopsy should be preferred instead of percutaneous biopsy if preoperative treatment is indicated [6, 7]. In our study, 89% of our patients diagnosed in operation without prior interventions for biopsy.

Most common localizations of the GISTs are as follows: stomach (60%), jejenum and ileum (30%), duodenum (4-5%), colon (5%), appendix (1-2%), esophagus (>1%) and, rarely, primary tumor may be located in extragastrointestinal tissues around the stomach or intestines [3, 8]. But intestine was the most common site of GISTs in our study. Gastric GISTs are usually have a better diagnosis than intestinal GISTs.

Gastric tumors with a 10cm diameter or less and 5 or less mytosis in 50x area are defined as low metastasis risk. If a gastric tumor is greater than 5cm and has more mytosis than 5 in 50x area, then this tumor has high metastasis risk. In contrast to gastric tumors, all intestinal GIST tumors larger than 5 cm have moderate metastasis risk and if mytosis is more than 5 in 50x area than these tumors at high risk for metastasis. Intestinal GIST is defined at low risk if the tumor is smaller than 5 cm and have less than 5 mytosis [3].

In our study we found that 5 of 9 patients with intestinal GIST, 3 of 5 patients with colonic GIST and 3 of 4 patients with gastric GIST were at high risk. In contrast to literature, rate of high risk disease was more frequent in gastric localizations compared to intestinal localizations.

Surgery is the primary treatment option in localized GIST cases. Surgeons should be avoided of the fragmentation of the tumor because they are very fragile. The tumor should be resected without disturbing the integrity of pseudocapsule. Nearly 60% of the patients cured with surgical treatment. Surgical cure is associated with lenght of tumor, mitotic index and whether the tumor fragmented in surgery [9, 10].

Imatinib is the main treatment in metastatic or inoprable tumors, currently. Imatinib improves both overall and disease free survival [9]. One year adjuvant Imatinib treatment after surgery is safe and improves disease free survival compared to placebo in patients at high risk for metastasis [11].

In recent studies, authors stated that one year adjuvant treatment with imatinib is insufficient [12]. In another study, Imatinib administered for 3 years in patients at moderate and high risk for metastasis. They found that disease free survival improved and mortality decreased compared to the control group [13]. In another study, investigators administered adjuvant Imatinib after surgery for 12 months in a group and for 36 months in another group of patients. Mean follow up period was 54 months in that study. Overalll and disease free survival was significantly improved in the patients received imatinib for 36 months [14].

Only patients with metastatic disease received imatinib in our study. Of the five metastatic patients, three were at high risk while one each was at moderate and at low risk for metastasis. Recurrence/ progression occured in 4 patients in follow up period. Only one of the patients in this group had metastatic disease. The other 3 were relapsed after treatment. Two of the relapsed 3 patients were at high risk for metastasis.

Progression developed only in one of five patients with metastatic disease. All metastatic patients received Imatinib. Three patients of remaining 13 relapsed. They were not received Imatinib. Thus, recurrence/progression rates of patients received Imatinib treatment and not recived Imatinib treatment were 20% and 23%' respectively. Two of three patients with relapsed disease were at high risk for metastasis. The rate of relapsed disease should be lower in patients at high risk, if they received Imatinib treatment.

In conclusion, after surgical resection of the tumor, we suggest Imatinib treatment in patients considered at high risk.

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