A Case of Disseminated Intra-abdominal Gastrointestinal Stromal Tumor Managed with Low Dose Imatinib

Bo Hyun Jang, Byung-Wook Kim, Keun Joon Lim, Boo Gyoung Kim, Sung Min Park, Joon Sung Kim, Jeong-Seon Ji, and Hwang Choi
Division of Gastroenterology, Department of Internal Medicine, Incheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Incheon, Korea

Gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumor of the gastrointestinal tract. Imatinib mesylate is recommended as an adjuvant therapy for GIST after surgical resection. However, drug-related adverse events are common. A 74-year-old female with metastatic GIST who was managed with imatinib experienced severe adverse events, including skin rashes, tremor, and alopecia, etc. The imatinib dose was reduced and the size of the metastatic GIST continued to decrease and adverse events showed significant improvement. (Korean J Gastroenterol 2015;65:366-369)

Key Words: Gastrointestinal stromal tumors; Imatinib

INTRODUCTION

Gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumor of the gastrointestinal tract. Imatinib mesylate is recommended as an adjuvant therapy for GIST after surgical resection and 400 mg per day for 3 years is recommended as the adequate dose.1 However, drug-related adverse events up to 88.9% have been reported and usually develop in a dose-dependent manner.2,3 Conservative management is usually the only treatment option for adverse events. Here we report on a 74-year-old female with metastatic GIST who experienced severe adverse events of imatinib, which were managed successfully with dose reduction.

CASE REPORT

A 74-year-old female was admitted to our hospital due to diffuse abdominal pain for several days. She had been diagnosed with a ruptured gastric GIST into the intraperitoneal cavity 2 years ago and underwent wedge resection of the stomach. Because open laparotomy was performed immediately after visiting the emergency room, gastroscopy was not performed at that time. Abdominal CT scan showed a huge exophytic lesion at the cardia of the stomach, which measured 5.0×5.0 cm. The mucosal surface of the gross specimen obtained by surgical resection was intact but the serosal surface showed shallow ulcerations with hemorrhage. Histologic examination of the surgical specimen revealed rupture of the capsule and mitotic counts as 1/50 high power...
field and she was categorized as a very low risk group. She did not receive adjuvant therapy at that time and did not visit our out-patient clinic after surgery. She reported that she had been well before this event.

On physical examination, a huge mass was palpated on her left lower quadrant of the abdomen. CT scans showed multiple lobulated solid masses with central necrosis in the gastrosplenic space, gastrohepatic ligament, subpyloric space, and in both paracolic gutters (Fig. 1).

Ultrasound-guided needle biopsy showed spindle cells on hematoxylin and eosin stain (Fig. 2A). Immunohistochemical stain revealed positivity for c-KIT by CD 117 and CD 34 (Fig. 2B), suggesting that these lesions originated from dissemination of the previously ruptured GIST. Imatinib mesylate at a dose of 400 mg per day was started.

One month after initiation of imatinib mesylate, the patient developed nausea, vomiting, itching sensation with skin rashes (Fig. 3), and cough. Anti-histamine and prokinetics were administered to control the adverse events of imatinib. However, the symptoms continued and the dose of imatinib mesylate was reduced to 300 mg per day. Two weeks later, nausea and vomiting symptoms had improved. However, coughing symptoms persisted and new adverse events including headache and tongue paralysis arose. Imatinib mesylate was further reduced to 200 mg per day and finally the adverse events were tolerable.

Three months after initiation of imatinib mesylate, follow-up...
up CT scans showed a significant decrease in size of the lesions (Fig. 4A). Low dose imatinib mesylate was continued for 9 months and additional follow up CT scans showed further decrease in size of the lesions (Fig. 4B). The patient is in satisfactory condition without evidence of disease progression for 1 year.

**DISCUSSION**

Ruptured GIST is a high risk factor of recurrence regardless of histologic stratification. In a case series, all but one patient with spontaneous tumor rupture (n=16) developed disease recurrence within 19 months of surgery. Based on such findings, all patients with ruptured GIST are clear candidates for adjuvant therapy. At the time of surgery surgeons were not aware that this patient had received adjuvant therapy and the patient was lost during follow-up, and therefore received no adjuvant therapy for the ruptured GIST.

Factors influencing the spontaneous rupture of GIST have not been fully elucidated. According to one report, serosal involvement was associated with emergency surgery and in another report mean size of the ruptured GIST was 9.89±5.42 cm, suggesting a possible association of tumor size with intra-peritoneal rupture of GIST. No study to determine association of mitotic figure with spontaneous rupture of the GIST has been reported.

Tyrosine kinase inhibitors that target the key molecular drivers of GIST are effective in treatment as an adjuvant therapy. Imatinib mesylate is the drug of choice for adjuvant therapy in high risk groups and the recommended dose is 400 mg per day for at least 3 years. Although 1-year administration of imatinib mesylate is effective as an adjuvant therapy, 3-year administration of imatinib mesylate showed higher recurrence free survival in high risk GIST. High dose of imatinib or other tyrosine kinase inhibitors such as sunitinib can be tried in cases where imatinib mesylate with standard dose is ineffective.

Imatinib-related adverse events include fluid retention, gastrointestinal symptoms, fatigue, rash, and joint and muscle pain. Adverse events are the main cause for discontinuation of imatinib mesylate. Dose reduction of imatinib mesylate was reported to be effective in reducing adverse events such as skin reaction and neutropenia. In our case, dose reduction of imatinib mesylate was also effective in other adverse events, including nausea, vomiting, cough, headache, and tongue paralysis. However, there are no data regarding whether reduced dose of imatinib mesylate is still effective as an adjuvant therapy for GIST. In this case, the patient was followed for 1 year and reduced dose of imatinib mesylate was found to suppress the disseminated intra-abdominal GIST. Additional follow up to confirm the suppressive effect of low dose imatinib mesylate for disseminated intra-abdominal GIST is on-going.

The toxicity of imatinib mesylate can be monitored with blood level test. However, it is an expensive study and is not available in most centers. To obtain a maximal effect while
minimizing adverse events of imatinib mesylate, a stepwise reduction of dose is a smart option. We reduced the dose of imatinib mesylate every two weeks from 400 mg per day to 200 mg per day.

In conclusion, a reduced dose of imatinib mesylate was effective for 1 year in suppressing the disseminated intra-abdominal GIST in a 74-year-old female patient. Further studies comparing low dose and standard dose of imatinib mesylate as an adjuvant therapy are anticipated.

REFERENCES