CT Findings of Malignant Gastrointestinal Stromal Tumors with Metastases: an experience of Cytotoxic Agent and Imatinib Mesylate Treatment

Jyh-Ching Chen¹  Ming-Tsung Wang¹  Shang-Tao Chien²  Chih-Liang Chen³

Department of Radiology¹, Pathology², Surgery³, Kaohsiung Armed Forces General Hospital

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors that can occur throughout the gastrointestinal tract. We reported herein the case of a 78-year-old female patient with malignant GIST (M-GIST) with peritoneal metastases, treated in two stages: first with cytotoxic agent and second with imatinib mesylate (a tyrosine kinase inhibitor). M-GISTs are gastrointestinal tumors that differ from other mesenchymal tumors in the gastrointestinal tract in that they usually present large, well-circumscribed, heterogeneous masses, and commonly metastasize to liver, omentum, and the peritoneum. CT scan is helpful in the diagnosis of GISTs. Imatinib mesylate treatment for M-GISTs with metastases is beneficial in the majority of cases, while of limited value in our case.

Key words: Computed tomography (CT); Gastrointestinal stromal tumor

CASE REPORT

We report on a 78-year-old female patient with M-GIST who suffered from gradual enlargement of palpable masses over the peri-umbilical region of the abdomen for 6 months. She had no clinical history of malignancy. Clinical examination revealed multiple palpable nodules over the whole abdomen with two firm and fixed nodules over the peri-umbilical region. There were no significant findings on the plain X-ray of chest and abdomen. The tumor markers: CEA, Ca-125, AFP, and CA-199 were within normal range. The ultrasonography depicted scattered hypoechoic lesions in...
Findings of malignant gastrointestinal stromal tumors in the abdomen. CT scan images were obtained with the GE cytec 4000i CT scan (GE, Milwaukee, Wis, USA) at 120 KVP, 100 mA (with slide thickness: 10 mm, table feed: 10 mm, FOV: 34 cm). Oral contrast medium (100 ml) was given one hour before the examination in addition to an intravenous injection of 100 ml of contrast medium (Ultravist 300; Schering, Berline, Germany; 300 mg iodine/ml). A CT scan demonstrated multiple lesions presenting as soft-tissue attenuation masses along the wall of the small intestine (predominantly in the jejunum) (Fig. 1a). There were numerous well-defined soft-tissue attenuation masses scattered over the omentum and the peritoneum. An extraperitoneal subfascial mass, 2.5 cm over middle abdominal wall was also observed (Fig. 1b). An excisional biopsy of the abdominal wall mass was made. Histologically, the tumor revealed characteristics of M-GIST, consisting of spindle and epitheloid cells with dense eosinophilic cytoplasm and increased mitotic figures (Fig. 2a, 2b). Immunohistochemistry analysis of the tumor revealed that the tumor cells were positive for C-kit (Fig. 2c). The patient was then treated with Futraful (200mg, T.I.D.), a cytotoxic agent, for 10 months. The subsequent CT scan showed an increase in the number and size of tumors, with central necrosis of some masses (Fig. 3a). In place of Futraful, Gleevec (imatinib mesylate) (100mg, T.I.D.) was then given to the patient. The next follow-up CT scan was performed 7 months later after treatment with imatinib and showed neither decrease in tumor size nor in lesion number (Fig. 3b). The overall tumor response was determined through consensus opinion of two experienced radiologists based on their interpretation of the CT images. It was obvious that the tumor response to both stages of treatment in this case was not successful.

**DISCUSSION**

GISTs are infrequently encountered mesenchymal tumors of the GI tract. They occur in a wide range of age (19-82 years) with an average age of approximately 58 years. The clinical signs and symptoms usually depend on the size and anatomical location of the tumors [6]. GISTs may occur anywhere along the GI tract. Approximately 60-70% of GISTs occur in the stomach, 25-35% in the small intestine, and 5% in the colon and esophagus [5, 7]. GISTs are characterized by the expression of the C-kit receptor, also known as CD117, a tyrosine kinase growth factor receptor. Most GISTs also express CD34 protein and other possible markers including vimentin, actin, S-100 protein, and desmin [5, 7, 8]. These tumors differ immuno-histologically from...
Figure 2. The section of specimen of the same patient. 

a. Photomicrography (original magnification, x10; H&E stain) showed short fascicular growth pattern of tumor. 

b. Photomicrography (original magnification, x40; H&E stain) showed a picture of malignant gastrointestinal stromal tumor, which consisted of spindle and epitheloid cells with dense eosinophilic cytoplasm and increased mitotic figures. 

c. Immunohistochemically, the tumor cells were positive of C-kit (brown staining).

Figure 3. a. Subsequent axial contrast CT scan after Futrful treatment for 10 months showed increase of tumoral number and size with central necrosis of some masses (arrows). 

b. Next axial contrast CT scan after treatment of imatinib mesylate 7 months later showed neither decrease in tumor size nor in number.
leomnyomatous tumors and neurogenic tumors. The nomenclature for the cellular origin and diagnosis of GIST has been debated. Based on histology, an origination from the interstitial cells of Cajal was suggested, because GISTs have phenotypic similarities with these cells [5, 8]. GISTs usually present as an intramural lesion. Occasionally, they can have an intraluminal component or present with ulcerations and might have an exophytic extension. Most GISTs (70-80%) are benign. However, it is possible to predict the evolution from benign GISTs to M-GISTs according to the tumor size and mitotic frequency [1, 5]. M-GISTs usually present as large, well-circumscribed, heterogeneous, centrally necrotic gastrointestinal stromal tumors, ranging between 4-25 cm and are usually predominantly extraluminal [9, 10]. Small size M-GISTs are more frequently located in the stomach than in small intestine. M-GISTs with metastases are frequently noted in the liver or the peritoneum. Peritoneal lymphadenopathies are uncommon [1].

Abdominal sonography may show GISTs as multiple non-specific masses in the abdomen with displacement of the stomach. Barium studies of the GI tract can demonstrate the features of submucosal masses of GISTs [6]. On CT scans, the majority of GISTs are demonstrated as well-defined, hypodense masses with extrinsic components and with a heterogeneous central attenuation implying necrosis, hemorrhage, or cystic change. In a CT scan, liver metastases appear as low-attenuation lesions, and peritoneal metastases appear as multiple nodules over the peritoneal surface [6, 9]. Primary tumors of the mesentery and omentum are usually larger than 10 cm. GISTs on magnetic resonance imaging might be revealed as low-signal intensity lesions on T1-weighted images and high signal intensity lesions on T2-weighted images [6].

This case is a senile patient (78 years old) with M-GISTs of the small intestine with metastases. As in previous studies, the CT scan of this case demonstrated scattered masses with extrinsic components of the intestine (predominantly in the jejunum) on omentum, peritoneum, and the extra-peritoneal subfascial region of the abdominal wall. The average size of the masses over the omentum and the peritoneum was approximately 1.7 cm. There was no calcification, cystic change, necrosis, or hemorrhage of the masses at presentation. There was no ascites and no evidence of liver metastases either. GISTs are very resistant to conventional cytotoxic agents [3]. Previous studies reported that imatinib mesylate, the tyrosine kinase inhibitor STI571, was useful in treating M-GISTs with metastases [10, 11]. The authors reported that a significant reduction in tumor size could take several months and that complete cystic change in some cases could occur after targeted chemotherapy [10]. Pedro et al. postulated that imatinib mesylate could result in cystic change with peripheral calcifications of the intestinal tumor and mesenteric metastases in 5 months [11]. In the present case, two different stages of treatment with Futraful and imatinib mesylate were administered for an overall duration of 17 months (10 months of Futraful and 7 months of imatinib mesylate). After treatment with Futraful for 10 months, a subsequent CT scan showed an increase in the number and size of tumors, with central necrosis of some masses. After treatment with imatinib mesylate for 7 months, the next CT scan showed no tumor regression and no decrease in lesion number. An accurate assessment of tumor response after treatment is necessary. FDG PET might be a sensitive indicator for tumor response for imatinib mesylate [10]. Determination of the tumor response according to the criteria established by the Response Evaluation Criteria in Solid Tumors (RECIST) group might be reliable [12]. Although we did not use the criteria of RECIST to determine the tumor response, it was obvious from the CT findings that the 17-month treatment with Futraful and imatinib mesylate resulted in a poor tumor response, contrary to the results reported in previous studies. A significant reduction in tumor size might require much longer treatment time, or the imatinib mesylate might be of limited value in some cases.

The differential diagnosis of GISTs in the GI tract includes benign and malignant GI neoplasms. Adenocarcinoma is most commonly found in the small intestine, and usually manifests as circumscribed lesions. GI lymphomas may be distinguished from GISTs by their association with lymphadenopathies. Differential diagnosis of other mesentery malignancies of mesenteric origin include mesenteric fibromatosis, inflammatory pseudotumor, lymphoma, and metastatic disease [6].

In conclusion, GISTs differ from other well-known mesenchymal tumors in the GI tract. M-GISTs with metastases are frequently encountered. They usually present large, well-circumscribed, heterogeneous masses, and commonly have metastases in the liver, omentum and the peritoneum. In the diagnosis of M-GISTs, a preoperative CT scan is suggested. Imatinib mesylate treatment for M-GISTs with metas-
tases is beneficial in the majority of cases. However, the tumor response to imatinib mesylate treatment in this case was not successful. A significant reduction in tumor size might require much longer treatment time, or the imatinib mesylate might be of limited value in this case.

REFERENCE

轉移性惡性腸道基質腫瘤電腦斷層的發現：細胞毒性化療劑和Imatinib Mesylate的治療經驗

陳志程¹  王明宗¹  錢尚道²  陳智良³

國軍高雄總醫院  放射科¹  病理部²  外科部³

轉移性腸道基質腫瘤（GIST）是腸道最常見的腫瘤，可以發生於腸道各處。我們報告一個78歲女性患惡性GIST併腹腔轉移。該病患曾接受兩個階段不同的治療。第一階段使用細胞毒性化療劑；第二階段使用imatinib mesylate（tyrosine活化激酶抑制劑）治療。惡性的GIST有別於其它的腸道間質腫瘤（mesenchymal tumor）。它們通常表現為大的，界限清楚的，不均勻的腫塊，且經常轉移至肝臟，網膜和腹膜腔。CT對GIST的診斷是很有助益的，Imatinib Mesylate對於多數轉移性惡性GIST是有療效的，但對於我們這個病例並無顯著療效。

關鍵詞：電腦斷層掃描；腸道基質腫瘤