Esophageal gastrointestinal stromal tumor: report of 7 patients

A.B. Shinagare, K.A. Zukotynski, K.M. Krajewski, J.P. Jagannathan, J. Butrynski, J.L. Hornick, N.H. Ramaiya

Department of Imaging, Dana-Farber Cancer Institute, 450 Brookline Ave, Boston, MA 02115, USA; Department of Radiology, Brigham and Women’s Hospital, 75 Francis Street, Boston, MA 02115, USA; Department of Medical Oncology, Dana-Farber Cancer Institute, 430 Brookline Ave, Boston, MA 02115, USA; Department of Medicine, Brigham and Women’s Hospital, 75 Francis Street, Boston, MA 02115, USA; Department of Pathology, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA

Corresponding address: Atul B. Shinagare, MD, Department of Imaging, Dana-Farber Cancer Institute, 450 Brookline Ave, Boston, MA 02115, USA.
Email: ashinagare@partners.org

Date accepted for publication 6 February 2012

Abstract

Abstract Purpose: To evaluate imaging features of esophageal gastrointestinal stromal tumors (GIST) with clinical and histopathologic correlation and imaging follow-up. Materials and methods: In this institutional review board-approved, Health Insurance Portability and Accountability Act-compliant retrospective study, 14 patients with pathologically proven esophageal GIST seen from January 2001 to October 2011, 7 patients (4 women; mean age 70 years, range 56–87 years) who had imaging of primary tumor and follow-up imaging at our institution were included. Imaging studies were evaluated by 3 radiologists in consensus. Location, size and imaging features of primary tumor and metastases, if any, were recorded, and correlated with pathologic (histopathologic subtype, presence of necrosis, mitotic rate, immunohistochemical profile) and clinical (treatment-related changes, distant spread and outcome) parameters. Results: Of 7 tumors, 5 were located in the lower esophagus and 2 in mid-esophagus. Four were intraluminal, 2 were exophytic, and 1 was intramural. All 7 patients underwent computed tomography (CT); tumors appeared as well-circumscribed, hypoattenuating masses showing mild enhancement, with mean size of 5.7 × 4.2 cm. Necrosis and calcification were seen in 1 tumor each. Five patients underwent fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT. GISTs were FDG avid with mean standardized uptake value (SUV)\textsubscript{max} of 9.5 (4.5–12.3). All tumors were positive for KIT (7/7) and CD34 (6/6). Distant metastases to liver and pleura were seen in 1 patient. On imatinib treatment, the tumors responded with decreased attenuation values and unchanged size on CT, and decreased SUV\textsubscript{max} of primary tumor and metastases on FDG-PET/CT. Conclusion: Esophageal GISTs are well-circumscribed, FDG-avid, hypoattenuating masses that can metastasize to liver and pleura, and respond to imatinib treatment with decreased attenuation value on CT and decreased SUV\textsubscript{max} on FDG-PET/CT.

Keywords: Gastrointestinal stromal tumor; esophageal; CT; FDG-PET/CT.

Introduction

Gastrointestinal stromal tumors (GISTs), the most common mesenchymal malignancy of the gastrointestinal tract, account for up to 3% of all gastrointestinal neoplasms and 5.7% of sarcomas\textsuperscript{[1,2]}. Traditionally, GISTs were classified as smooth muscle tumors, formerly designated leiomyomas, leiomyoblastomas, and leiomyosarcomas. GISTs were identified as a distinct entity in 1983, described as cellular spindle cell or epithelioid tumors\textsuperscript{[3]}. The pathogenesis and molecular basis of GISTs were understood only recently. Approximately 80% of GISTs are associated with activating mutations of the \textit{KIT} gene, which encodes a tyrosine kinase
Histopathologic and clinical correlation

The histology was reviewed by a pathologist with expertise in GIST. The following pathologic features were recorded: morphologic subtype, presence or absence of necrosis, mitotic rate, and immunohistochemical profile. Owing to the rarity of esophageal GISTs, unlike GISTs of more common sites (e.g., stomach and small intestine), site-specific prognostic factors have not been formally established. Most reported esophageal GISTs are clinically aggressive, although a small subset of cases (particularly small tumors with a low mitotic rate) have pursued a benign course. Therefore, for the purposes of this study, the tumors were dichotomized into low risk (if $<5$ cm in size and $<5$ mitoses per 50 high power fields (HPF)) and high risk (either $\geq 5$ cm or $\geq 5$ mitoses per 50 HPF). Electronic medical records were reviewed to note the clinical features including primary presentation, treatment offered, recurrence or metastasis-free interval and outcome. These features were correlated with imaging findings to note any treatment-related changes on imaging.

Follow-up imaging

The follow-up imaging studies were evaluated for the presence of recurrent or metastatic disease. Any post-treatment changes in the imaging appearance of the primary tumor and/or metastases were noted. For FDG-PET/CT studies, the change in FDG avidity and $SUV_{\text{max}}$ between baseline and follow-up imaging was recorded.

Results



Subjects

The patient population consisted of 4 women and 3 men, with a mean age of 70 years (range 56–87 years). Three patients presented with recurrent cough. In 2 of these patients, the esophageal GIST was initially not detected on chest radiographs. All 3 patients were initially treated for upper respiratory tract infection. When symptoms persisted, further imaging of the chest was performed with CT, which identified the tumor. One patient had longstanding symptoms suggestive of gastroesophageal reflux disease and was initially treated with proton pump inhibitors. The symptoms recurred after initial response, prompting endoscopy, which revealed the tumor in the lower esophagus. Another patient had a history of colon and laryngeal cancer without evidence of metastases. His esophageal GIST was initially detected as a slowly growing esophageal mass before being confirmed by biopsy. In 1 patient, the tumor was detected incidentally on pulmonary CT angiography performed for suspected pulmonary embolism. Esophageal GIST in 1 patient was diagnosed on upper gastrointestinal
endoscopy performed for evaluation of intermittent dysphagia.

Imaging features

In total, 7 CT examinations and 4 FDG-PET/CT studies of primary untreated esophageal GISTs were reviewed. All of the patients underwent CT of the chest. Of the 7 patients, the tumors were located in the lower esophagus in 5 patients (Fig. 1) and in the mid-esophagus in 2 (Fig. 2). On imaging, the tumors were intraluminal in 4 patients (Fig. 1), exophytic in 2 (Fig. 2), and intramural in 1 patient. The mean tumor size was $5.7 \times 4.2$ cm, with size ranging from 3.1 to 7.9 cm in the long axis and from 1.8 to 6.5 cm in the short axis. All the primary tumors appeared as round to oval well-defined masses with smooth sharp outlines (Figs. 1, 2), were iso- to hypotattenuating compared with the muscle, and showed mild enhancement on contrast-enhanced CT (Fig. 1). Six of 7 tumors were homogeneous (Fig. 2), and one showed the presence of central necrosis (Fig. 1). Peripheral calcification was present in 1 tumor (Fig. 2). None of the tumors showed evidence of hemorrhage. Baseline FDG-PET/CT was performed in 5 of 7 patients. All the tumors were FDG avid (Fig. 2), with mean $SUV_{max}$ of 9.5 (4.5–12.3).

Distant metastases were present in 1 patient at presentation (Fig. 2). This patient had hypodense liver metastases that measured 3–4 cm in size. The same patient also had pleural-based metastases. All the metastatic lesions were FDG avid ($SUV_{max}$ 7.6–8.6, $SUV_{max}$ of the primary tumor, 10.3) (Fig. 2). Subcentimeter pulmonary nodules were present in 1 patient; however, these were incompletely characterized on CT, were not significantly FDG avid on FDG-PET/CT, and remained stable over the next 2 years. Therefore, the pulmonary nodules were not considered to be metastases.

Histopathologic correlation

There was good correlation between the tumor size noted on CT and gross pathology. The 3 resected tumors were grossly well circumscribed (Fig. 3A). Necrosis was present in the high-risk GIST but not in the other tumors. Histologically, 6 tumors were spindle cell GISTs, composed of fascicles of elongated cells with uniform, tapering nuclei and palely eosinophilic, fibrillar cytoplasm (Fig. 3B). One tumor (case 3) was of mixed spindle cell and epithelioid type. Mitotic rate ranged from 1 to 75 per 50 HPF. Based on tumor size and mitotic activity, 4 tumors were considered high risk, and 3 were considered low risk. By immunohistochemistry, all 7 tumors were positive for KIT (Fig. 3C). CD34 was positive in each of the 6 tested patients, and 3 tumors were also positive for DOG1. Five evaluated tumors were negative for S100, 4 were negative for SMA, and 1 each was negative for desmin and caldesmon. One tumor resected after neoadjuvant imatinib therapy showed extensive stromal hyalinization, consistent with treatment effect (Fig. 3D).

Clinical correlation

Three out of 7 patients underwent surgical resection of their primary tumors, and all 7 patients were treated with imatinib mesylate, primary imatinib treatment in 4 patients, adjuvant in 2 patients, and neoadjuvant followed by adjuvant in 1 patient (see details below). Two patients underwent primary surgical resection. One of these patients with a mid-esophageal tumor underwent enucleation. The surgical margins were positive, and he received adjuvant imatinib, which was discontinued after 9 months due to significant adverse effects. He is off treatment and disease free for the past 9 months. Another patient with a lower esophageal tumor underwent resection. Surgical margins were negative. He is now 34 months following surgery and continues on adjuvant imatinib without evidence of disease. The third patient who underwent surgery initially received 4 months of neoadjuvant imatinib followed by resection of lower esophageal tumor with negative margins, and adjuvant imatinib for 1 year. The patient has been treatment free and disease free for the past 27 months (total 39 months since surgery). One woman with a mid-esophageal GIST had biopsy-proven hepatic and pleural metastases at presentation and has been on primary imatinib treatment for 21 months with continued radiologic response. The fifth patient had multiple comorbidities and was not considered to be a surgical candidate. He has received primary imatinib treatment for 23 months with continued radiologic response. The sixth patient also had multiple comorbidities and was started on imatinib,
Figure 2  (a) A 79-year-old woman with esophageal GIST. Axial image from a contrast-enhanced CT scan demonstrates a large hypoattenuating well-circumscribed exophytic mass (arrow) arising from mid-esophagus, just below the level of carina. The mass abuts the right main bronchus (arrowhead). Note the presence of calcification within the mass (curved arrow). (b) Fused $^{[18F]}$FDG-PET/CT image in the coronal plane demonstrates the FDG-avid primary esophageal mass ($SUV_{\text{max}}$ 10.3) (arrow) and FDG-avid liver metastases ($SUV_{\text{max}}$ 7.6–8.6) (arrowheads). (c) Axial image from pretreatment contrast-enhanced CT demonstrates a biopsy-proven metastatic lesion in the left hepatic lobe (arrow). Attenuation value on this study was 59 HU. Right renal cysts are noted incidentally (arrowheads). (d) Axial image from a contrast-enhanced CT obtained after 2 months of imatinib treatment demonstrates unchanged size, however decreased attenuation of the liver metastasis (arrow). The attenuation value at this time was 14 HU. A right renal cyst is again noted (arrowhead).
however, the treatment was discontinued after 2 months due to severe adverse effects. The last patient received primary imatinib, and showed radiologic treatment response after 2 months. All the patients received oral imatinib 400 mg/day, except for 2 patients; 1 was started on 400 mg/day, which was reduced to 200 mg/day, and another patient was started on 200 mg/day and treatment was discontinued after 2 months, in both cases due to adverse effects.

The median follow-up period was 26 months (range 3–151 months). At present, all the patients are alive, without evidence of recurrent disease or progression of pre-existing metastatic disease.

**Follow-up imaging**

A total of 36 follow-up CTs and 1 FDG-PET/CT were reviewed. In the patient who had metastatic disease at presentation, the size of the primary tumor and metastases remained unchanged, and the attenuation values were significantly lower on follow-up imaging (Fig. 2). Three patients who did not undergo surgery showed a similar decrease in attenuation and minimal decrease in size on follow-up imaging. One patient who received 4 months of neoadjuvant imatinib prior to surgery also showed decreased attenuation of the tumor. One patient underwent follow-up FDG-PET/CT after 2 months of imatinib treatment, which showed a significant decrease in FDG avidity of the tumor (SUV$_{max}$ decreased from 4.5 on the baseline study to 1.2 on the follow-up examination) (Fig. 4).

**Discussion**

Although GISTs are the most common sarcoma of the gastrointestinal tract, esophageal GISTs are very rare. The radiology literature about esophageal GISTs is sparse, and to the best of our knowledge, this is the first study reporting the imaging features of esophageal GIST with clinical and histopathologic correlation. In addition, treatment-related changes in the imaging appearance of primary and metastatic lesions of esophageal GIST have not been previously reported.

GISTs were originally thought to be leiomyomas or leiomyosarcomas; however, with the discovery of KIT-activating mutations and expression of the KIT protein, distinguishing GIST from smooth muscle tumors is now relatively straightforward in most cases by demonstrating the immunohistochemical detection of KIT (CD117). GISTs arise from the interstitial cells of Cajal in the

![Figure 3](image-url)
myenteric plexus (or their precursors), which play a role in gastrointestinal motility\textsuperscript{[15]}. In the pathology literature, the mean age of patients with esophageal GIST has been reported to be 63 years (range 49–15175 years) with a slight male predilection\textsuperscript{[9]}. The patient age in our study (mean 70 years) was similar to the prior reports, however, our patient population had a higher proportion of women (4/7). Although dysphagia has been reported to be a common presenting symptom\textsuperscript{[14]}, it was noted in only 1 patient in this study. Most of the patients in this study either presented with recurrent cough or were asymptomatic.

We found a predilection for involvement of the lower esophagus (5/7), consistent with the largest available pathologic series\textsuperscript{[9]}. Esophageal GISTs can present as intraluminal, intramural or exophytic masses\textsuperscript{[9,14]}. In this study, most of the patients with esophageal GIST had intraluminal masses, in contrast with GISTs at other anatomic locations, which are predominantly extraluminal\textsuperscript{[6]}. The mean largest dimension of esophageal GISTs included in our study was 5.7 cm (range 3.1–7.9 cm), compared with the previously reported size of 8 cm (range 2.6–25 cm)\textsuperscript{[9]}. Based on these data, esophageal GISTs are probably similar in size at presentation to GISTs at other locations. The well-circumscribed nature, low attenuation and mild contrast enhancement of esophageal GIST are similar to those in other locations. Central necrosis was present in only 1 of our 7 patients, compared with 67% in a previously reported large imaging study of GISTs at other locations\textsuperscript{[6]}. Similarly, the incidence of metastatic disease at presentation was low (1/7) in our study, which is similar to that reported in the largest pathology series of esophageal GISTs (18%, 3/17)\textsuperscript{[9]}. This incidence of metastases at presentation in esophageal GIST seems to be somewhat lower than GISTs at other locations\textsuperscript{[6]}. The FDG avidity of esophageal GISTs in this study (mean SUV\textsubscript{max} 9.5, range 4.5–15112.3) was not significantly different from that previously reported for GISTs elsewhere (mean SUV\textsubscript{max} 5.8, range 1.4–15119.7)\textsuperscript{[16]}. Not surprisingly, metastatic lesions were also FDG avid.

The primary differential diagnosis of esophageal GIST on imaging is leiomyoma. Imaging features of esophageal GISTs and leiomyomas can be similar, and histopathologic diagnosis is almost always needed for confirmation\textsuperscript{[6,7]}. Esophageal squamous cell carcinoma and adenocarcinoma differ from GIST in being more circumferential and infiltrative, and by having frequent nodal involvement. Lymphomatous involvement tends also to be more circumferential, but without evidence of luminal obstruction\textsuperscript{[6]}. Metastases from esophageal GIST to the liver and pleura were seen in this study. Previous studies on esophageal GIST have also reported metastases to the liver and lung\textsuperscript{[9,14]}. Metastases to pleura, bone and brain from esophageal GISTs have been reported in isolated case reports\textsuperscript{[11–13]}. There are insufficient data to compare the metastatic pattern of esophageal GIST with that of GISTs from other locations, which usually metastasize to liver and peritoneum, although lung metastases from GISTs arising at intra-abdominal locations are extremely rare\textsuperscript{[6,7]}. The esophageal GISTs in this study were consistently positive for KIT and CD34 by immunohistochemistry, which is consistent with previous reports\textsuperscript{[9,17]}. The tumor that showed central necrosis on CT correlated with the presence of necrosis on histologic examination. This was a high-risk tumor measuring 7.5 cm in size with intense FDG uptake and showing

\textbf{Figure 4} (a) A 70-year-old man with lower esophageal GIST. Fused FDG-PET image in the axial plane before starting the treatment showing an FDG-avid mass in the lower esophagus (SUV\textsubscript{max} 4.5) (arrow). Physiologic uptake is noted in the bowel, kidneys, ureters and bladder. (b) Fused FDG-PET image in the axial plane after 2 months of imatinib treatment showing markedly decreased avidity of the mass (SUV\textsubscript{max} 1.2) (arrow). Physiologic uptake is again noted in the bowel, kidneys, ureters and bladder.
**Table 1** Clinical, imaging and pathologic features of patients with esophageal GISTs

| Characteristics                  | Case 1          | Case 2          | Case 3          | Case 4          | Case 5          | Case 6          | Case 7          |
|----------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| **Age (years)/gender**           | 64/M            | 79/F            | 71/M            | 61/F            | 70/M            | 87/F            | 56/F            |
| **Presentation**                 | Cough           | Cough           | GERD            | Cough           | None            | None            | Intermittent dysphasia |
| **Size (cm)**                    | 2.3 x 1.8       | 7.9 x 4.7       | 7.5 x 6.5       | 4.9 x 4.2       | 6.3 x 3.4       | 3.5 x 2.8       |
| **Location in esophagus**        | Mid             | Mid             | Lower           | Lower           | Lower           | Lower           | Lower           |
| **Location relative to esophageal wall** | Intraluminal | Exophytic       | Intramural      | Exophytic       | Intraluminal    | Intraluminal    | Intraluminal    |
| **Margin**                       | Well defined    | Low             | Well defined    | Low             | Well defined    | Well defined    | Well defined    |
| **CT attenuation**               | Low             | Low             | Low             | Low             | Low             | Low             | Low             |
| **Homogeneity**                  | Homogeneous     | Homogeneous     | Heterogeneous   | Homogeneous     | Homogeneous     | Homogeneous     | Homogeneous     |
| **FDG-PET/CT SUV max**           | N/A             | 10.3            | 11.7            | 12.3            | 4.5             | 8.7             |
| **Metastases**                   | None            | At presentation | None            | None            | None            | None            | None            |
| **Mitoses (50 HPF)**             | 1               | 2               | 75              | 1               | 1               | 1               |
| **Necrosis**                     | Absent          | Absent          | Present         | Absent          | Absent          | Absent          | Absent          |
| **Immunohistochemistry**         | Positive CD34, KIT; negative SMA, S-100 | Positive CD34, KIT, DOG1 | Positive CD34, KIT; negative S100, SMA, caldesmon | Positive CD34, KIT; negative S100, SMA, desmin | Positive CD34, KIT; negative S100, SMA | Positive CD34, KIT; negative S100, SMA | Positive CD34, KIT; negative S100, SMA |
| **Treatment**                    | Enucleation, adjuvant imatinib | Imatinib | Resection, adjuvant imatinib | Resection, adjuvant imatinib | Imatinib | Imatinib; stopped after 2 months due to toxicity | Imatinib |
| **Clinical outcome**             | NED             | Stable          | NED             | NED             | Stable          | Stable          | Stable          |
| **Follow-up imaging**            | No recurrence   | Stable size, decreased attenuation | No recurrence   | Decreased size, attenuation and SUV max (from 4.5 to 1.2) after 2 months of imatinib | Stable size, decreased attenuation | Stable size, decreased attenuation | Stable size, decreased attenuation |

GERD, gastroesophageal reflux disease; NED, no evidence of disease.
75 mitoses per 50 HPF (an extremely high mitotic rate for GIST).

In our study, none of the patients showed disease progression or development of metastatic disease at the end of the follow-up period (mean follow-up 26 months; range 3–54 months). In prior pathology series, 56% (9/16) of patients died of disease with a median survival range 3–154 months. However, this study was reported in 2000, and the management of GISTs has significantly changed over the past 12 years. Furthermore, in that study, most of the patients who died of GIST had tumors larger than 9 cm, whereas all the tumors in our study were smaller than 8 cm. The management of GIST has been revolutionized in the past decade with the introduction of imatinib therapy. Imatinib, which can be used as primary, adjuvant or neoadjuvant treatment, has led to a significant increase in the median survival of patients with advanced GIST, from approximately 20 to 60 months.[18–20] Adjuvant imatinib treatment is currently recommended for 2 years following surgery, particularly in patients with large primary tumors.[21]

Both the primary and metastatic GISTs responded to imatinib treatment in the form of decreased attenuation of tumor, but with minimal decrease in size on CT. This change is similar to previously reported response patterns for GISTs at other locations, and is consistent with the treatment response described by Choi et al.[16], who suggested that a decrease in tumor size of more than 10% or a decrease in tumor density of more than 15% on CT is a good predictor of favorable treatment response. On FDG-PET/CT, interval decrease in SUVmax was noted, which is also in line with previous reports,[16,21] and is considered to be good treatment response. Thus, response of esophageal GIST to imatinib therapy appears to be similar to GISTs in other locations.

The most important limitation of this study was the small sample size. However, esophageal GISTs are very rare, and there are no previous studies reporting the imaging features of GIST at this site with histopathology and clinical correlation. Due to the limited number of cases, as mentioned above, there are insufficient data to compare the clinical behavior and metastatic pattern of esophageal GIST with GISTs at other sites.

In summary, esophageal GISTs are well-circumscribed FDG-avid hypoattenuating masses that can metastasize to the liver and pleura, and respond to imatinib treatment with decreased attenuation values on CT and decreased avidity on FDG-PET/CT. Comparison with previously published data suggests that esophageal GISTs are similar in size to GISTs at other locations, but that the frequency of central necrosis and metastatic disease at presentation may be lower. Larger studies with longer follow-up will be required to determine whether the malignant potential of esophageal GISTs is different from those at other sites.

**References**

[1] Lewis JJ, Brennan MF. Soft tissue sarcomas. Curr Probl Surg 1996; 33: 817–872.
[2] DeMatteo RP, Lewis JJ, Leung D, Mudan SS, Woodruff JM, Brennan MF. Two hundred gastrointestinal stromal tumors: recurrence patterns and prognostic factors for survival. Ann Surg 2000; 231: 51–58. doi:10.1097/00000658-200001000-00008.
[3] Mazur MT, Clark HB. Gastric stromal tumors. Reappraisal of histogenesis. Am J Surg Pathol 1983; 7: 507–519. doi:10.1097/00000478-198309000-00001.
[4] DeMatteo RP. The GIST of targeted cancer therapy: a tumor (gastrointestinal stromal tumor), a mutated gene (c-kit), and a molecular inhibitor (STI571). Ann Surg Oncol 2002; 9: 831–839. doi:10.1097/01.BFO2555718.
[5] Heinrich MC, Corless CL, Duensing A, et al. PDGFRA activating mutations in gastrointestinal stromal tumors. Science 2003; 299: 708–710. doi:10.1126/science.1079666.
[6] Burkhill GJC, Badran M, Al-Muderis O, et al. Malignant gastrointestinal stromal tumor: distribution, imaging features, and pattern of metastatic spread. Radiology 2003; 226: 527–532. doi:10.1148/radiology.2262011880.
[7] Wong C-S, Chu Y-CT, Khong P-L. Unusual features of gastrointestinal stromal tumor on PET/CT and CT imaging. Clin Nucl Med 2011; 36: e1–e7. doi:10.1097/RLU.0b013e31820aa233.
[8] Demetri GD, Benjamin RS, Blanke CD, et al. NCCN Task Force report: management of patients with gastrointestinal stromal tumor (GIST)—update of the NCCN clinical practice guidelines. J Natl Compr Canc Network 2007; 5(Suppl 2): S1–S29. quiz S30.
[9] Miettinen M, Sarlomo-Rikala M, Sobin LH, Lasota J. Esophageal gastrointestinal stromal tumors: a clinicopathologic, immunohistochemical, and molecular genetic study of 17 cases and comparison with esophageal leiomyomas and leiomyosarcomas. Am J Surg Pathol 2000; 24: 211–222. doi:10.1097/00000478-200002000-00007.
[10] Dan D, Seetahal S, Persad R. Gastrointestinal stromal tumor of the esophagus. J Natl Med Assoc 2009; 101: 462–465.
[11] Imai K, Saito H, Minamiya Y, et al. Pleural dissemination of esophageal gastrointestinal stromal tumors after an eight-year interval following the primary surgery. Gen Thorac Cardiovasc Surg 2010; 58: 302–305. doi:10.1007/s11748-009-0554-6.
[12] Ozan E, Oztekin O, Alacacioglu A, Aykas A, Postaci H, Adibelli Z. Esophageal gastrointestinal stromal tumor with pulmonary and bone metastases. Diagn Interv Radiol 2010; 16: 217–220.
[13] Hamada S, Itami A, Watanabe G, et al. Intracranial metastasis from an esophageal gastrointestinal stromal tumor. Intern Med 2010; 49: 781–785. doi:10.2169/internalmedicine.49.1124.
[14] Jiang P, Jiao Z, Han B, et al. Clinical characteristics and surgical treatment of oesophageal gastrointestinal stromal tumors. Eur J Cardiothorac Surg 2010; 38: 223–227. doi:10.1016/j.ejcts.2010.01.040.
[15] Kindblom LG, Remotti HE, Aldenborg F, Meis-Kindblom JM. Gastrointestinal pacemaker cell tumor (GIPACT): gastrointestinal stromal tumors show phenotypic characteristics of the interstitial cells of Cajal. Am J Pathol 1996; 33: 1259–1269.
[16] Choi H, Charnsangavej C, Faria SC, et al. Correlation of computed tomography and positron emission tomography in patients with metastatic gastrointestinal stromal tumor treated at a single institution with imatinib mesylate: proposal of new computed tomography response criteria. J Clin Oncol 2007; 25: 1753–1759. doi:10.1200/JCO.2006.07.3049.
[17] Lopes LF, West RB, Bacchi LM, van de Rijn M, Bacchi CE. DOG1 for the diagnosis of gastrointestinal stromal tumor (GIST): comparison between 2 different antibodies. Appl Immunohistochem Mol Morphol 2010; 18: 333–337.
[18] Blanke CD, Demetri GD, von Mehren M, et al. Long-term results from a randomized phase II trial of standard- versus higher-dose...
imatinib mesylate for patients with unresectable or metastatic gastrointestinal stromal tumors expressing KIT. J Clin Oncol 2008; 26: 620–625. doi:10.1200/JCO.2007.13.4403.

[19] Essat M, Cooper K. Imatinib as adjuvant therapy for gastrointestinal stromal tumors: a systematic review. Int J Cancer 2011; 128: 2202–2214. doi:10.1002/ijc.25827.

[20] Seshadri RA, Rajendranath R. Neoadjuvant imatinib in locally advanced gastrointestinal stromal tumors. J Cancer Res Ther 2009; 5: 267–271. doi:10.4103/0973-1482.59905.

[21] McAuliffe JC, Hunt KK, Lazar AJF, et al. A randomized, phase II study of preoperative plus postoperative imatinib in GIST: evidence of rapid radiographic response and temporal induction of tumor cell apoptosis. Ann Surg Oncol 2009; 16: 910–919. doi:10.1245/s10434-008-0177-7.

[22] Holdsworth CH, Badawi RD, Manola JB, et al. CT and PET: early prognostic indicators of response to imatinib mesylate in patients with gastrointestinal stromal tumor. AJR Am J Roentgenol 2007; 189: W324–W330. doi:10.2214/AJR.07.2496.