

# Esophageal gastrointestinal stromal tumor with pulmonary and bone metastases

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## ABSTRACT

Gastrointestinal stromal tumors (GISTs) are rare neoplasms of the gastrointestinal tract. One to three percent of GISTs occur in the esophagus. GISTs have a great potential for diffuse intra-abdominal spread and liver metastasis, which are the two most common modes of dissemination. Metastases to other sites, especially the bones and lung, are relatively rare. Never has an esophageal GIST been documented to present with pulmonary and bone metastases. We present an unusual case of an esophageal GIST with pulmonary and bone lesions. We include a review of the literature.

**Key words:** • gastrointestinal stromal tumor • esophagus  
• computed tomography • magnetic resonance imaging

**G**astrointestinal stromal tumors (GISTs) are the most common nonepithelial tumors of the gastrointestinal tract (1). Their incidence by anatomic location varies in different studies: 51–70% in the stomach; 25–36% in the small intestine; 5–7% in the colon, rectum, and appendix; and 1–3% in the esophagus. Primary GIST can be found in the omentum, mesentery, or retroperitoneum, unrelated to the tubular gastrointestinal tract, but most in these sites are metastatic from gastric or intestinal primaries (2–7). The distribution of metastases is predictable, with the liver and peritoneum the most common sites (5, 8). The liver is the most common site of metastasis both at presentation and at disease relapse (5). Distant metastasis to other sites, especially the bones and lung, is relatively rare (5, 9). We present radiologic findings in an unusual case of an esophageal GIST with pulmonary and bone lesions.

## Case report

A 53-year-old man presented with intermittent odynophagia and dysphagia with both liquids and solids, weakness, and weight loss in the previous 3–4 months. Barium esophagography demonstrated a mass that distorted the esophageal lumen and showed extrinsic compression of the distal portion of the esophagus adjacent to the esophago-gastric junction (Fig. 1). An enhanced computed tomography (CT) scan showed a large hypodense soft-tissue mass in the posterior mediastinum. The mass originated from the right lateral wall of the esophagus, and protruded into the esophageal lumen (Fig. 2a). A crescent-shaped pocket of air inside the mass suggested esophageal origin of the mass which later was confirmed endoscopically. Bilateral pulmonary nodules also were detected at the same time on thoracic CT (Fig. 2b).

Thoracic magnetic resonance imaging (MRI) showed a 13 x 9 x 6 cm esophageal mass indenting the left atrium. The mass showed no involvement of the mediastinal great vessels (Fig. 3). Scintigraphic evaluation and MRI of the right humerus showed suspicious lesions (Fig. 4). These suspicious pulmonary and bone lesions suggested the possibility of metastasis.

The patient underwent a biopsy from the mediastinal mass. Immunohistochemical staining demonstrated the tumor cells to be positive for c-kit (CD117) protein and CD34 protein. The histologic features and staining pattern of the tumor cells were consistent with a GIST (Fig. 5). Because the tumor size was  $\geq 10$  cm, and 5–10 mitoses were identified per 50 high power fields (HPF), the tumor was considered to be a high-risk GIST.

After diagnosis, the patient received imatinib mesylate (Gleevec; Novartis Pharma, Basel, Switzerland) 400 mg/day for two months. The clinical response was good, and the patient's dysphagia, odynophagia, and weakness resolved. Control contrast-enhanced CT scans showed a minimal decrease in tumor size. In the esophageal lumen, the crescent-

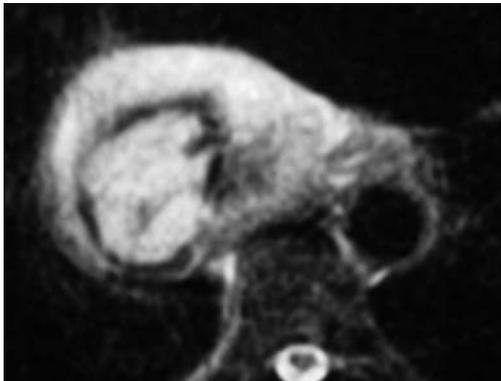
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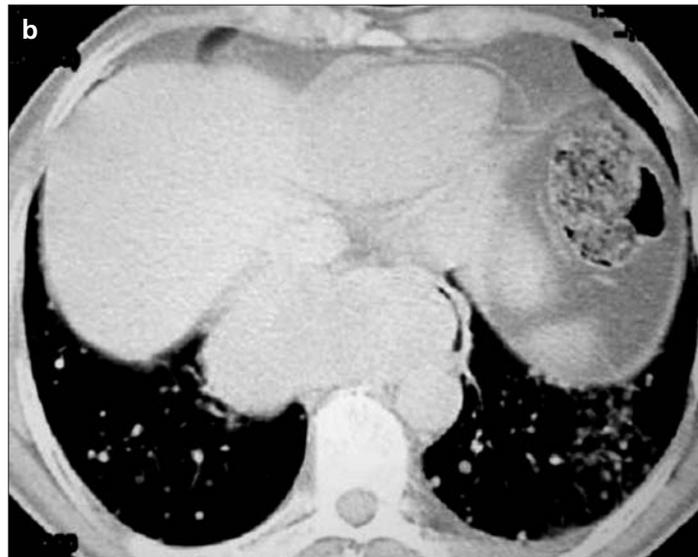
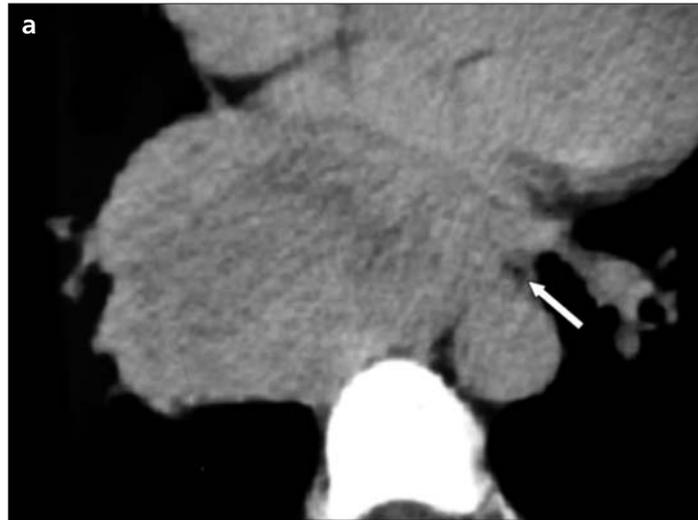
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**Figure 1.** Barium esophagography demonstrates a mass that distorts the esophageal lumen and shows extrinsic compression on the distal portion of the esophagus adjacent to the esophagogastric junction.



**Figure 3.** Axial T2-weighted thoracic MR image shows a 13 x 9 x 6 cm esophageal mass indenting the left atrium. The mass showed no involvement of the mediastinal great vessels.



**Figure 2. a, b.** An enhanced CT image in the mediastinal window setting (**a**) shows a large hypodense soft-tissue mass in the posterior mediastinum. The mass originates from the right lateral wall of the esophagus, and protrudes into the esophageal lumen. Crescent shaped air pocket (*arrow*) inside the mass confirms esophageal origin of the mass. CT image in the lung window setting (**b**) shows bilateral, scattered pulmonary nodules suspicious for metastases.

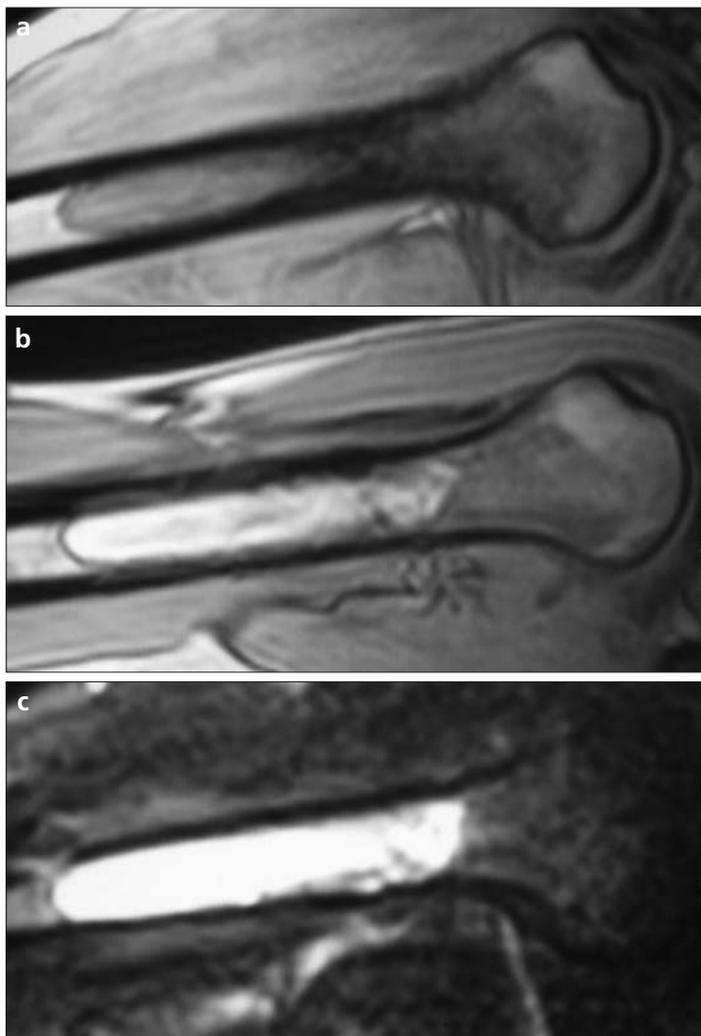
shaped air pocket was significantly increased (Fig. 6a), which was considered to represent volumetric decrease in tumor mass, consistent with clinical improvement in the patient's swallowing function. There was also significant regression of the suspicious pulmonary lesions which were believed to be metastases (Fig. 6b).

### Discussion

GISTs are rare, accounting for 0.1–3.0% of all gastrointestinal neoplasms, and 5.7% of sarcomas (10). According to a consensus on the diagnosis of GIST, the term “GIST” should ap-

ply only to neoplasms displaying c-kit (CD117) immunopositivity with very rare exceptions (11). It is important to mention that normal kit-positive cells in abdominal soft tissues include mast cells present in the wall of the gastrointestinal tract, and the interstitial cells of Cajal (intestinal pacemakers) present around the myenteric plexus (9). Although the origin of GISTs is not fully understood, their association with the Cajal cells suggests that these cell subsets could represent a multipotential stem-cell-like population, which is the logical candidate for GIST histogenesis (12).

According to the largest epidemiologic analysis to date, which included 1458 recorded cases (4), as well as studies by Miettinen and Lasota (2), GIST typically present in adults 40–50 years of age. The most common clinical manifestation for patients with esophageal GISTs is dysphagia (3). Esophageal GISTs are reported up to 25 cm in diameter, and are most commonly located in the distal third of the esophagus (3). Barium studies of the esophagus may show a smooth intramural mass or a large, ulcerative mass that extends into the esophageal lumen. Distal lesions may extend into



**Figure 4.** a–c. T1- (a), T2- (b), and fat-saturated T2-weighted (c) MR images show hypointense, hyperintense, and uniformly hyperintense signals, respectively. These signal characteristics confirm the metastatic nature of the lesion.

the proximal stomach. On CT images, these lesions may be homogeneous or heterogeneous in attenuation. They may contain central areas of low attenuation from hemorrhage, necrosis, or cystic degeneration (13).

Instead of classifying lesions as either benign or malignant, current guidelines categorize GISTs as low-, intermediate-, and high-risk based on size and mitotic index (14). In our case, because the tumor size was  $\geq 10$  cm, with 5–10 mitoses per 50 HPF, the tumor was considered to be a high-risk GIST.

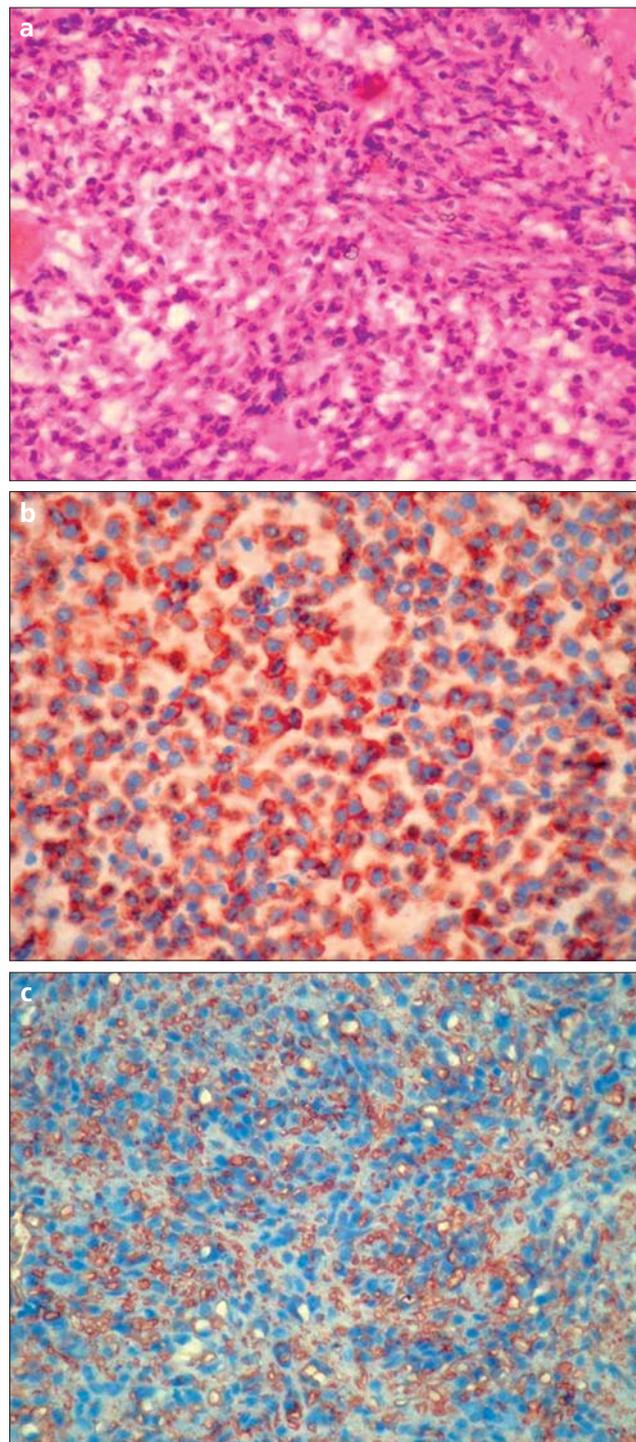
Metastasis is characteristically the malignant behavior of the GIST. Overall, approximately 10–30% of GISTs exhibit malignant behavior (9, 15). GIST rarely metastasizes to regional lymph nodes (<10%). It most often metastasizes to the liver (50–60%) and peritoneum (20–

43%). Metastasis to the lung and bones is rare (10%), although rectal GIST frequently metastasizes to lung (16).

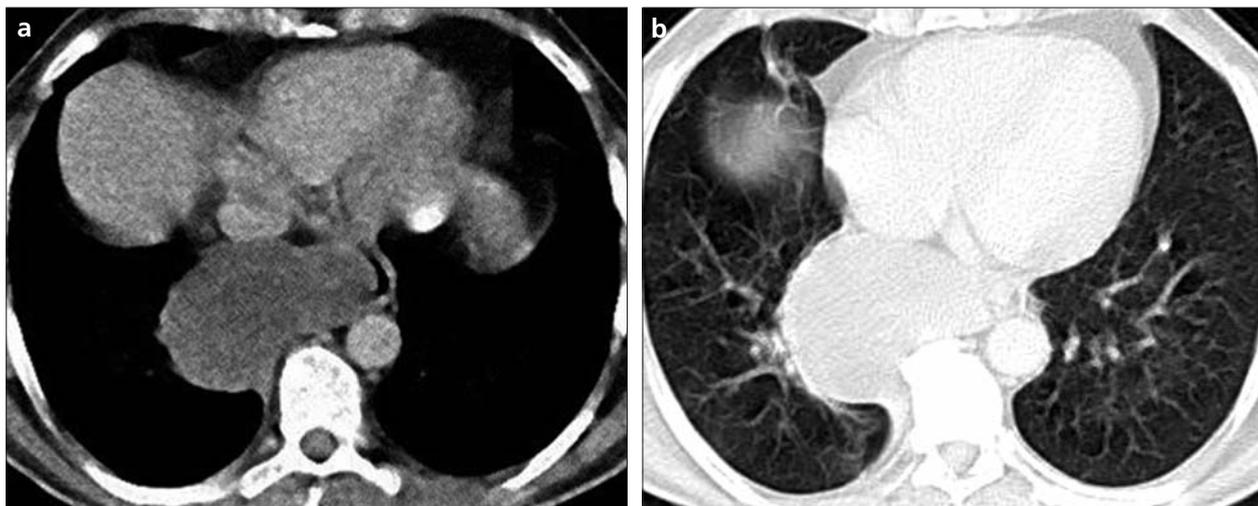
Surgical resection of a localized GIST is the mainstay of therapy (17–19). Any

patient with locally advanced or metastatic disease (“advanced” GIST) should first receive imatinib mesylate (1).

In conclusion, we presented an unusual case of an approximately 10-cm



**Figure 5.** a–c. Histopathologic views include hematoxylin and eosin stain of the gastrointestinal stromal tumor (GIST) within the esophageal wall (40x) (a), c-KIT (CD 117) stain of the GIST with diffuse positivity (40x) (b), and CD 34 stain of the GIST with diffuse positivity (40x) (c).



**Figure 6. a, b.** Control contrast-enhanced CT (**a**, mediastinal window setting; **b**, lung window setting) shows minimal decrease in the tumor size. In the esophageal lumen, crescent-shaped air pocket was significantly increased, and there was also significant regression of the suspicious pulmonary lesions.

esophageal GIST with suspicious pulmonary and bone lesions. Only a few reports of esophageal GIST have been published, and, to our knowledge, there have been no reports of the radiologic appearance of an esophageal GIST presenting with pulmonary and bone metastases. This case emphasizes that metastasis should be considered in any case of an esophageal GIST with suspicious pulmonary or bone lesions.

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