

## Case Report

# Primary malignant extra-gastrointestinal stromal tumor of the posterior mediastinum: a case report and review of the literature

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**Abstract:** Gastrointestinal stromal tumors (GISTs) are neoplasms that most arise from the common mesenchymal tissue of the gastrointestinal tract, but they have been rarely reported in the esophagus. GISTs occur anywhere along the gastrointestinal tract; they are most common located in the stomach and the small intestine and less frequent in the colon and rectum. A GIST in the posterior mediastinum usually arises from the esophagus, it is rarely found in the extragastrointestinal area. This is the case report of primary GIST arising from esophagus that had extended into the posterior mediastinum in a 74-year-old male patient, confirmed by an immunohistochemical study and a molecular analysis.

**Keywords:** Extra-gastrointestinal stromal tumor (EGIST), mediastinum, malignant, KIT

## Introduction

Gastrointestinal stromal tumors (GISTs) are neoplasms that arise either from the most common mesenchymal (non-epithelial) tissue of the gastrointestinal tract (GIT) or, rarely, from other intra-abdominal soft tissues [1]. These neoplasms are probably originated from the interstitial cells of Cajal (ICC), which is the pacemaker for the peristaltic movement of the GIT [2].

GISTs occur anywhere along the gastrointestinal tract; they are most common located in the stomach (50-60%) and the small intestine (30-35%) and less frequent in the colon and rectum (5%) and the esophagus (<1%) [3]. However, they may also be encountered in locations outside the gastrointestinal tract, such as the uterine [4], prostate [5], pancreas [6], pleura [7], pericardium [8], abdominal wall [9], omentum [10] and retroperitoneum [11], in which case they are referred to extra-GISTs (EGISTs).

Herein we present a rare primary GIST arising from esophagus that had extended into the posterior mediastinum in a 74-year-old man

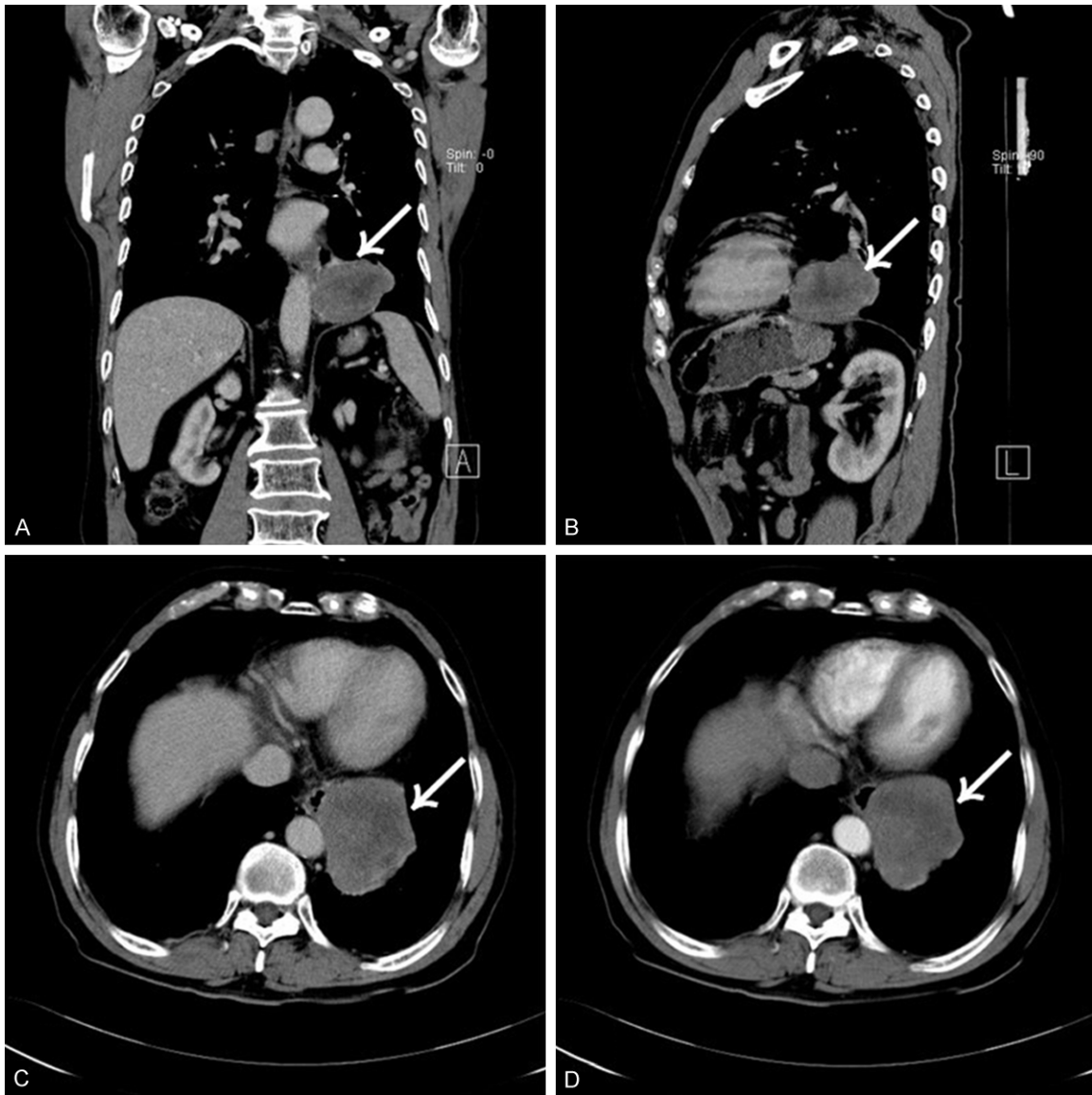
confirmed by means of an immunohistochemical study and molecular analysis.

## Case report

A 74-year-old male patient presented to the Department of Thoracic Surgery (Taizhou People's Hospital, Taizhou, China) with cough, which had endured for two months. He had no dysphagia or chest symptoms. A chest computed tomography (CT) was taken and a 6.9×7.6 cm-sized mass was noted on the left lower lung field. Endoscopic ultrasonography (EUS) examination showed an irregular margin, inhomogeneous, hypoechoic mass located in left lower lung field. Chest enhanced CT revealed that the mass abutting the mediastinum at the left lower lobe, maybe originating from mesenchymal tissue and not accompanied by lymphadenopathy (**Figure 1**). An abdominal enhanced CT showed no abnormalities. Tumor markers, including CA125, CA153, CA199, CA724, CEA, AFP, NSE and PSA, were all within the normal limit.

Given the anterolateral location of the tumor, a left lateral thoracotomy approach under general anesthesia via a double-lumen endotracheal

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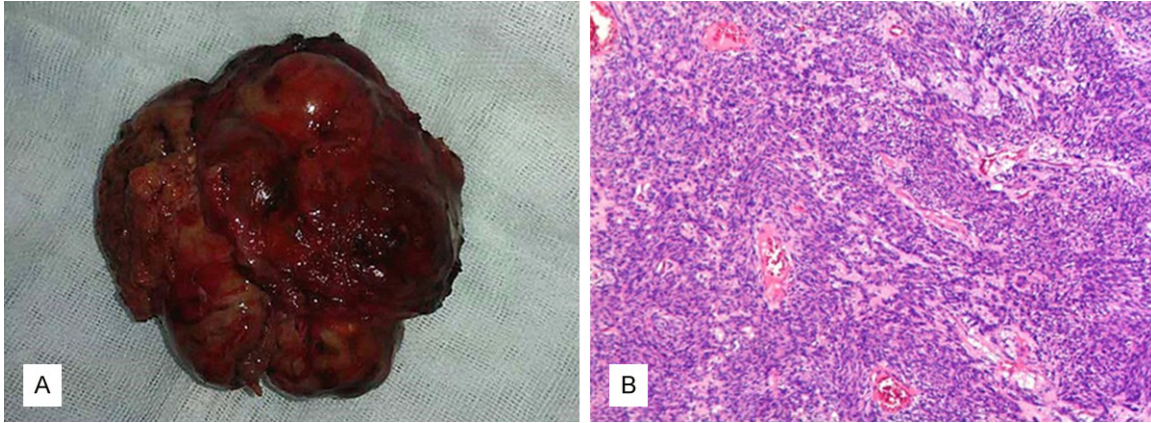
**Figure 1.** Chest CT demonstrates a 6.9×7.6 cm large-sized and well-delineated heterogeneous posterior mediastinal mass in the left lower thorax. A. Coronal view; B. Sagittal view; C, D. Transverse view.

tube with the patient in the supine position was carried out. The mediastinal pleura overlying the tumor were opened; the mass lesion was exposed after dissection of lower esophageal muscularis propria, superjacent diaphragm and adhesions of right lower lobe. The lesion appeared well vascularized and with a medium consistency. After careful dissection, the mass was enucleated. The tumor was a 8.0×7.5×6 cm, well encapsulated, firm mass involving the muscular layers of lower esophagus (Figure 2A). Microscopically, the tumor was composed of spindle cells with ill-defined cytoplasmic bor-

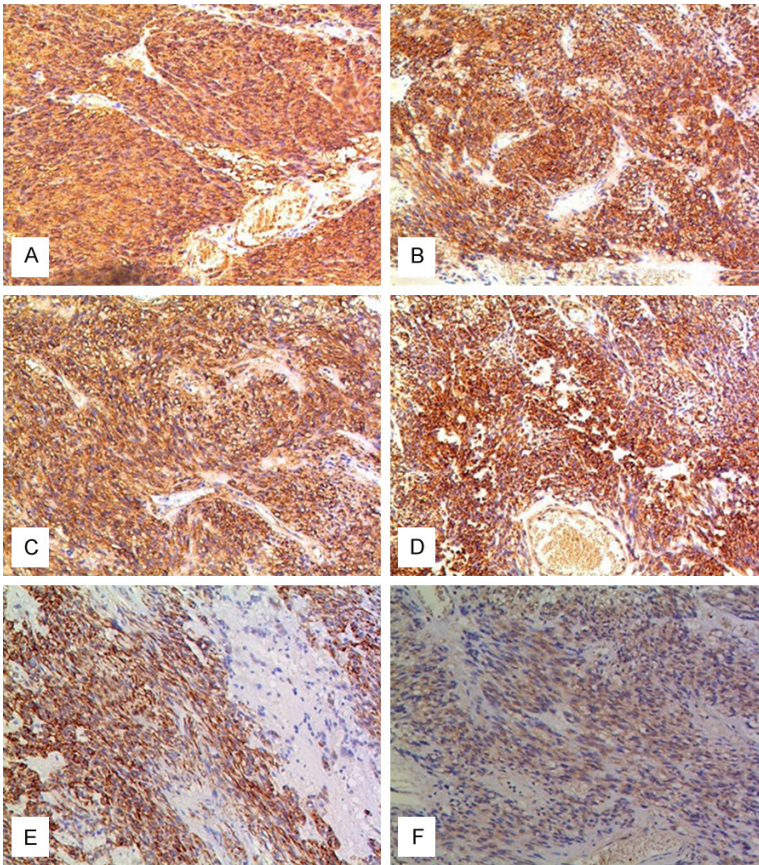
ders. The nuclei were elongated and bland-looking without prominent nucleoli (Figure 2B). The mitotic index was 6/50 in high-power field. There were hemorrhagic and necrotic foci on the cut surface of the tumor. Immunohistochemistry confirmed the histological diagnosis of GIST: the tumor cells stained diffusely for c-kit (CD 117), CD34, DOG-1, Vimentin, Desmin, Bcl-2, and CD 99 but negative for SMA or S-100 protein (Figure 3). The tumor was graded as high risk. Finally, molecular analysis was showed that the tumor harbored deletion in exon 11 of KIT (Figure 4).



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**Figure 2.** Macroscopic and microscopic findings of malignant GIST in the posterior mediastinum. A. The mass is multinodular, relatively well circumscribed and partly covered with the muscular layers of lower esophagus. B. The tumor was composed of spindle cells with eosinophilic cytoplasm (hematoxylin and eosin staining; magnification,  $\times 200$ ).



**Figure 3.** Immunohistochemical analysis of the resected tumor nodules. The tumor cells exhibited (A) strong diffuse cytoplasmic immunoreactivity for CD34; (B) Intense cytoplasmic staining for CD117; (C) Intense cytoplasmic staining for DOG-1; (D) Intense cytoplasmic staining for Vimentin; (E) Intense cytoplasmic staining for Desmin; and (F) moderate cytoplasmic staining for CD99 on gastrointestinal stromal tumor. CD, cluster of differentiation. The scale bar is 50  $\mu$ m.

### Discussion

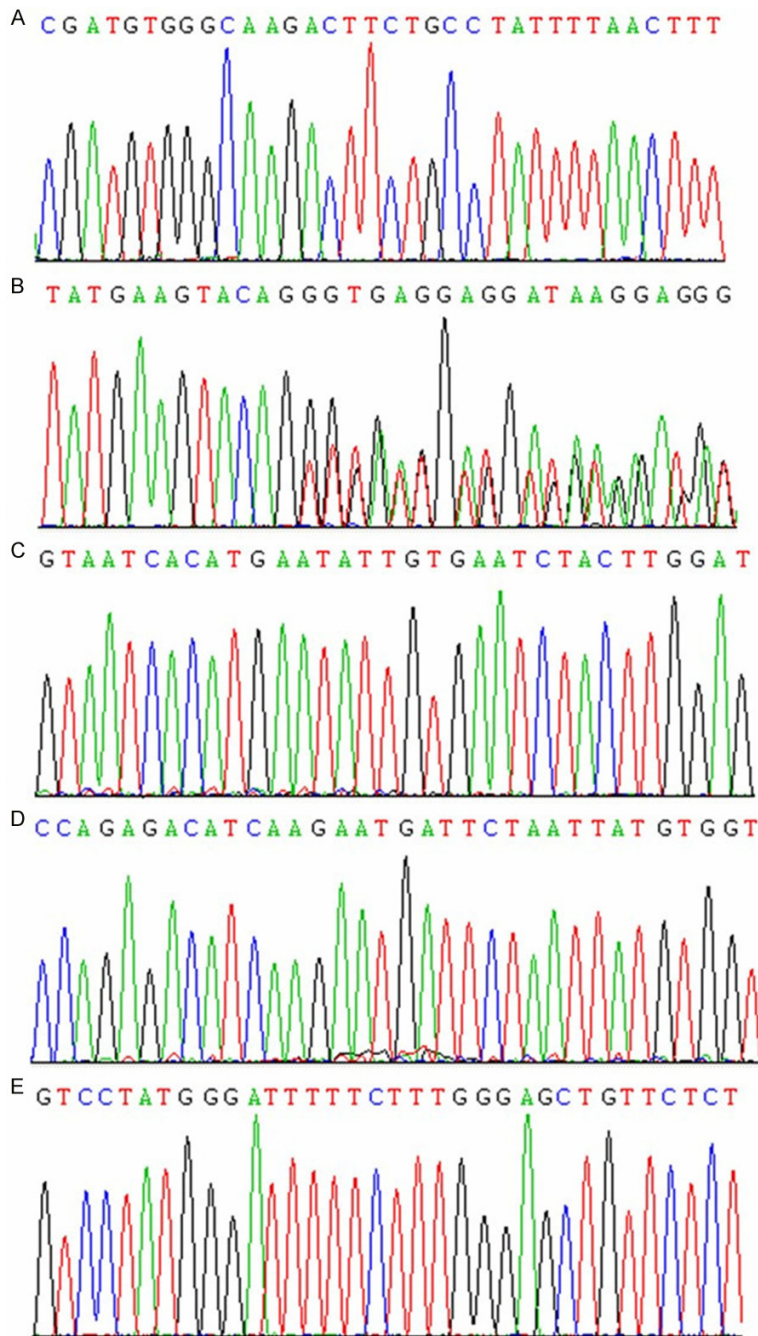
GISTs can arise at any age, but more than 80% are reported in individuals older than 50 years (median 63 years) [3]. Men and women are affected at a roughly similar frequency.

Three categories of morphology are seen in GISTs: spindle cell, epithelioid, and mixed [12]. The tumors can have substantial histological variation, which necessitates a broad differential diagnosis and immunohistochemistry stains are used to confirm a suspected diagnosis. The tumors can be positive for KIT (95%), CD34 (60-70%), ACAT2 (smooth muscle actin; 30-40%), S100 (5%), DES (desmin; 1-2%), and keratin (1-2%) [13]. KIT is the most specific and sensitive marker.

In general, GISTs with mitotic rates  $\leq 5/50$  high power fields (HPFs) have a favorable prognosis, although tumors  $>2$  cm in size in this group already have some tumor-related mortality. However, GISTs with



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**Figure 4.** Molecular analysis of the resected tumor nodules. The tumor harbored deletion in exon 11 (B) of KIT, and negative in exon 9 (A), 13 (C), 17 (D), 18 (E) of KIT.

mitotic rates >5/50 HPFs and tumor size >5 cm have a significant tumor-related mortality [14].

The majority of GISTs are benign (60-80%). Malignant GISTs are rare. The patient described herein had a tumor 8.0×7.5×6 cm in size, with hemorrhage, necrosis and high mitotic counts

warranted a diagnosis as a malignant mediastinal GIST. Kim et al [15] also described a case of malignant gastrointestinal stromal tumor in the posterior mediastinum, which had a tumor 10.0×8.0 cm in size, with infiltration of adjacent structures, including the right lower lobe of the lung field, inferior pulmonary ligament and lower esophageal muscle layer. Lee et al [16] had reported a case of a pedunculated esophageal GIST in the posterior mediastinum, but without clear-cut involvement of the gut wall, it is possible that it originated from tissues outside the alimentary tract. There is also a rare case of huge GIST of the stomach extending into the posterior mediastinum reported by Machishi et al [17]. A review of these cases is summarized in **Table 1**.

About 75-80% of GISTs have KIT mutations, typically affecting the juxtamembrane domain encoded by exon 11 [1]. Mutations also occur in the extracellular domains of KIT (exons 8 and 9; prevalence about 6%), and in the kinase I and II domains (exons 13 and 17; about 2%) [13]. Of the 20-25% GISTs do not have KIT mutations, about a third (8%) have platelet-derived growth factor receptor, alpha polypeptide (PDGFRA) mutations in domains homologous to those in KIT [18]. KIT and PDGFRA mutations are mutually exclusive.

### Disclosure of conflict of interest

None.

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**Table 1.** Case comparison of the primary EGIST of the posterior mediastinum

	Machishi et al [17]	Leea et al [16]	Kim et al [15]	The current report
Age/gender	61/Female	64/Man	71/Female	74/Man
Size (cm)	20×15×10 cm	8×9 cm	10.0×8.0 cm,	8×7.5×6 cm
Location	Posterior wall of the fornix	Right posterior mediastinal	Right lower thorax	Left lower posterior mediastinal
Pattern	Spindle	Spindle	Spindle	Spindle
Mitosis (No./10 HPF)	1	NA	NA	NA
Mitosis (No./50 HPF)	NA	NA	14	6
Immunohistochemistry				
CD117 (KIT)	Positive	Positive	Positive	Positive
CD34	Positive	NA	NA	Positive
DOG-1	NA	NA	NA	Positive
Vimentin	NA	NA	NA	Positive
Desmin	NA	NA	NA	Positive
bcl-2	NA	NA	NA	Positive
CD-99	NA	NA	NA	Positive
SMA	Negative	NA	Negative	Negative
S-100	Positive	NA	Negative	Negative
NSE	Positive	NA	NA	NA
Molecular features	NA	NA	KIT exon 9 mutation	KIT exon 11 mutation
Outcome	25 months without evidence of a recurrence.	26 months without evidence of a recurrence.	5 years without evidence of a recurrence.	No evidence of recurrence

EGIST, extragastrointestinal stromal tumor; NA, not available; DOG-1, discovered on GIST.

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