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CASE REPORT | PATHOLOGY

A Curious Case of a Posterior Mediastinal Mass

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ABSTRACT

Gastrointestinal stromal cell tumors (GISTs) are mesenchymal stromal tumors that are characteristically CD117 positive. Distinction from other spindle cell tumors such as leiomyomas and leiomyosarcomas is based on clinical, histological, and molecular features. Endoscopic ultrasonography-guided fine-needle aspiration has become a highly used means of preoperative identification of GIST, especially if immunohistochemical staining for CD117 can be performed. We present a case of a posterior mediastinal mass diagnosed as GIST after being found to be CD117 positive, later found to be a metastatic leiomyosarcoma.

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are mesenchymal tumors of the gastrointestinal (GI) tract arising from the smooth muscle pacemaker interstitial cell of Cajal.[1,2] The expression of CD117 (the transmembrane KIT receptor tyrosine kinase) is considered a hallmark of GIST. Other spindle cell tumors of the GI tract, such as leiomyomas and leiomyosarcomas (LMS), are typically CD117 negative. However, focal positivity has been found in rare cases.[3,4] We present a case of a posterior mediastinal tumor initially diagnosed as GIST based on endoscopic ultrasonography (EUS)-guided fine-needle aspiration (FNA) immunohistochemistry in a patient who was later found to have a metastatic LMS.

CASE REPORT

A 55-year-old man with a medical history of coronary artery disease status post-bypass surgery and emphysema presented with complaints of chest pain, dyspnea, cough, and night sweats. He reported a recent 20-pound unintentional weight loss. Physical examination was unremarkable. Basic laboratory work, which included complete blood count with differential and a comprehensive metabolic profile, showed no abnormalities. A computed tomography scan of the chest without contrast revealed a retrocardiac necrotic mediastinal mass, which measured 1.2 × 8.6 × 10.7 cm with a mass effect on the esophagus, the left atrium, and pulmonary veins (Figure 1).

A transbronchial needle aspiration of the right hilar mass was performed; the cytology showed benign bronchial cells. Gastroenterology was consulted for a EUS-guided FNA. Endosonograpy showed an oval, hypoechoic mass in the mediastinum, which measured 68 × 70 mm in maximal cross-sectional diameter (Figure 2). Three passes were made with the 21-gauge ultrasound core biopsy needle using a transesophageal approach. A visible core of tissue was obtained. The histopathology showed a spindle cell neoplasm, which comprised spindle cells with large nuclei and prominent nucleoli, which stained positive for CD117, DOG1 (Figures 3 and 4) Cam5.2, and AE1/AE3. GIST-specific somatic genetic analysis of *cKIT* and *PDGFRA* did not identify any mutations, and germline genetic testing was positive for NF1, suggesting wild-type GIST. The patient underwent an esophagogastroduodenoscopy and a colonoscopy; no additional lesions were identified. A positron emission tomography scan was performed which showed the enhancement of several pulmonary nodules, hilar lymph nodes, and a pleural-based lesion involving the seventh rib. The patient was initiated on therapy with imatinib while awaiting repeat pathological analysis from another hospital.

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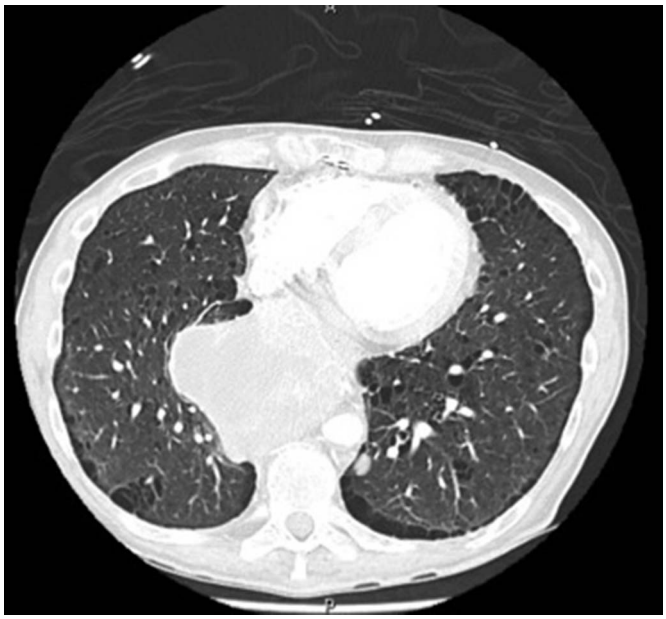

Figure 1. Thoracic computed tomography without contrast showing a retrocardiac necrotic mediastinal mass which measured 1.2 × 8.6 × 10.7 cm with a mass effect on the esophagus, the left atrium, and pulmonary veins.

Subsequently, the patient developed visual disturbances, nausea, and dizziness. He underwent magnetic resonance imaging of the brain, which showed an enhancing left frontal lesion with surrounding vasogenic edema consistent with metastasis. He underwent a left frontal craniotomy for debulking. The final pathology showed a spindle cell neoplasm, which comprised highly pleomorphic spindle cells arranged in interlacing fascicles. Abundant mitotic figures, including atypical forms, were noted. Immunohistochemical staining was diffusely positive for SMA, DOG1, and Caldesmon and scattered positivity for desmin. Tumor cells were negative for CD117, CD34, SOX-10, MDM2, CDK4, melan-A, and HMB-45. The histologic and immunohistochemical findings were consistent with a diagnosis of high-grade leiomyosarcoma (Figure 5). The patient was then started on mesna, doxorubicin, and ifosfamide.

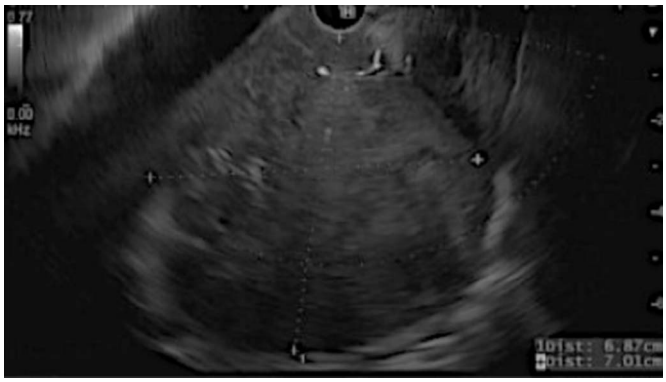

Figure 2. Endoscopic ultrasonography showing a mass in the posterior mediastinum, measuring 70 × 80 mm.

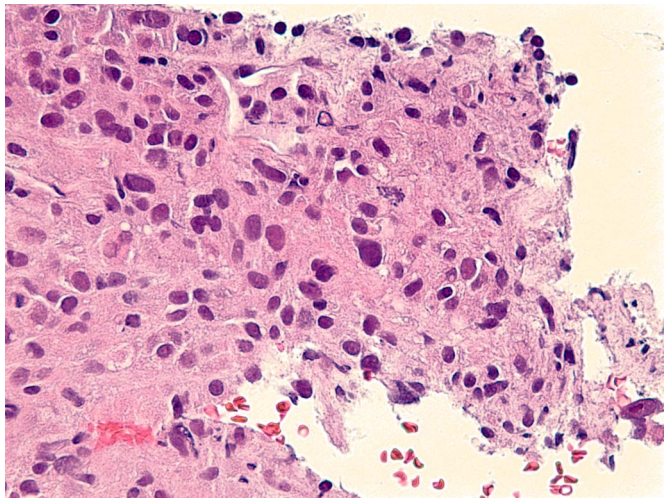

Figure 3. Spindle cell neoplasm with prominent nuclei and eosinophilic cytoplasm; the neoplastic cells have prominent nuclei and nucleoli with rare mitotic figures (hematoxylin and eosin stain, 400× magnification, endoscopic ultrasound-guided fine-needle aspiration).

DISCUSSION

GIST is the most common mesenchymal tumor with an incidence of 0.68 per 100,000 and can occur anywhere in the GI tract.[5] Smooth muscle tumors such as leiomyomas and LMS account for approximately 10% of GI mesenchymal tumors. The presentation of both GIST and LMS may be variable and nonspecific. The introduction of the immunohistochemical test for the KIT protein, CD117, made the distinction between GISTs and LMS possible because KIT staining is positive in approximately 95% of GIST cases. There is currently 1 case by M. Kafeel et al wherein a GIST was initially diagnosed as an LMS; in this case, immunohistochemical staining for KIT was not performed.[6] The distinction between LMS and GIST is important in guiding clinical decision-making; although resection is often definitive treatment in both

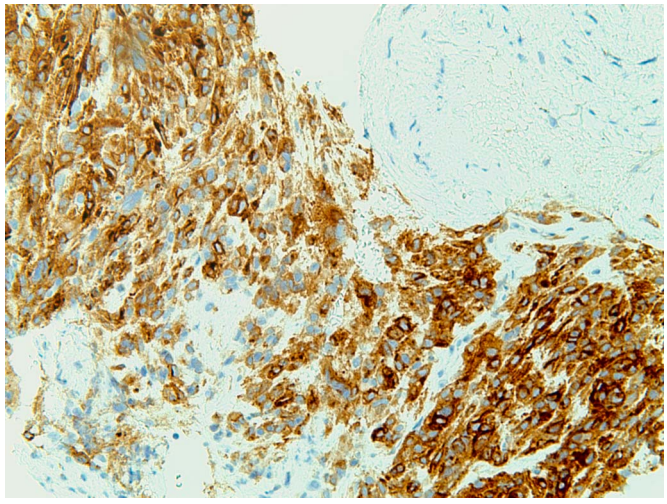

Figure 4. Diffuse staining of neoplastic cells for CD117 and DOG1 (200× magnification, endoscopic ultrasound-guided fine-needle aspiration).

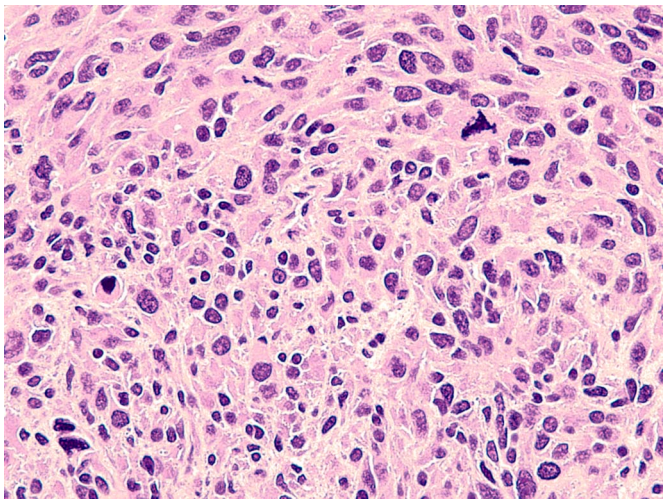

Figure 5. Spindle cell neoplasm showing highly pleomorphic cells with eosinophilic cytoplasm, large nuclei with prominent nucleoli, and mitotic figures including atypical mitoses (hematoxylin and eosin stain, 400× magnification, brain biopsy).

GIST and LMS, the first-line treatments in metastasized GIST and LMS are, respectively, the tyrosine kinase receptor inhibitor imatinib and gemcitabine-docetaxel.[7,8]

Our case is unique, given that the diagnosis of GIST was made based on positive immunohistochemical staining for CD117 and DOG1 of a EUS-guided FNA. He was started on imatinib for treatment of metastatic GIST. He developed new symptoms, including visual disturbances and dizziness, prompting a brain magnetic resonance imaging that showed metastasis. The pathology of the tumor sample, obtained through left frontal craniotomy, was highly pleomorphic with abundant mitotic figure with histomorphological similarity to the EUS-guided FNA. Unlike the EUS-guided FNA, immunohistochemistry of the brain biopsy tumor cells was negative for CD117, positive for SMA and DOG1, all features suggestive of a high-grade LMS.

There are no sonographic or radiographic characteristics to distinguish GIST from LMS.[9–12] GISTs are typically hypoechoic, homogeneous lesions with well-defined margins; however, they may appear inhomogeneous, because of liquefaction necrosis. LMS often appears heterogeneous with irregular borders and echogenic foci.[5,9–11] On light microscopy, the distinction among GIST and LMS can be difficult because both may have either a spindled or epithelioid cytomorphology.[4] Thus, the distinction between GIST and LMS is based on immunohistochemical and molecular analytic techniques, particularly staining for the KIT protein CD117. In nonresectable tumors, EUS remains the most useful method of distinguishing most of the GI mesenchymal tumors because a sample for immunohistochemistry can be obtained without the risk of tumor capsule rupture and peritoneal seeding.[13–14] Studies by TJ Wieczorek et al and Miettenen et al have shown some overlap in the molecular genetics of the different spindle cell tumors.[3,4] Both studies indicate that LMS may exhibit focal positivity for CD117, which may lead to potential diagnostic errors.[3,4] Our case highlights that although CD117 is quite specific for GIST among mesenchymal tumors of the GI tract, it is essential to recognize that limited CD117 expression may occur in other spindle cell tumors such as LMS, which could lead to possible misdiagnosis in small samples such as EUS-guided FNA, which may lead to delay inappropriate treatment.

DISCLOSURES

Author contributions: All authors contributed equally to this article. GS Kochhar is the article guarantor.

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Informed consent was obtained for this case report.

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