Int J Clin Exp Pathol 2017;10(8):8741-8745
www.ijcep.com /ISSN:1936-2625/IJCEP0057120

Case Report

A giant gastrointestinal stromal tumor of the stomach presenting as a posterior mediastinal mass

Huijiao Chen[1], Jin Yao[2], Yuan Tang[1], Hongying Zhang[1]

Departments of [1]Pathology, [2]Radiology, West China Hospital, Sichuan University, Chengdu 610041, Sichuan, China

Received May 9, 2017; Accepted June 20, 2017; Epub August 1, 2017; Published August 15, 2017

Abstract: Gastrointestinal stromal tumors (GISTs) involving thoracic region are very rare, most of which are esophageal in origin. Herein, we report a gastric GIST presenting as a posterior mediastinal mass, which provided diagnostic pitfalls due to its unusual anatomic location. The patient was a 68-year-old Chinese female, presenting with dysphagia, nausea and weight loss of 5 kg within 4 months. The contrast-enhanced thoracic computed tomography scan revealed a huge heterogeneous soft tissue mass in the posterior mediastinum. The core biopsy revealed a spindle cell tumor. The pathological features, in conjunction with the strong immunostaining pattern for CD117 and DOG-1 and the identification of *KIT* exon 11 mutation, confirmed the diagnosis of GIST. The subsequent surgery revealed the tumor located entirely in the abdominal cavity, laying beneath the diaphragm, and pushing the diaphragm upward into the posterior mediastinum. To our best, there has been only one similar case reported in the English literature. As patients with GISTs either resectable or not may get potential benefits from imatinib currently, the identification of GIST is very important even before surgery. Clinicians and pathologists should keep in mind that GISTs involving thoracic region do exist. The morphological features, immunohistochemical panel including CD117 and DOG-1 and molecular genetic test, in combination with clinicopathological correlation are helpful in confirming the correct diagnosis.

Keywords: GIST, posterior mediastinal tumor, thoracic tumor, diagnostic pitfall

Introduction

Gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumor of the gastrointestinal tract, which most often arises in the stomach or small intestine. Thoracic GISTs are very rare [1-17], most of which are esophageal in origin. However, herein we report a giant gastric GIST with extremely rare clinical and radiographic manifestations, which pushed the diaphragm upward into the posterior mediastinum and mimicked a primary thoracic tumor. This case provided diagnostic pitfalls for clinicians, radiologists and pathologists due to its unusual anatomic location. To our best, there has been only one similar case reported in the English literature [18].

Case presentation

A 68-year-old Chinese female presented with dysphagia, nausea and weight loss of 5 kg within 4 months. No significant past medical history was noted and the physical examination was unremarkable. The esophagogastroscopy showed a prominent narrowing of the esophagus in a region of 11 cm long and 25 cm away from the incisors, apparently caused by an external compression. No other lesions, such as erosion and ulcers, were found on the mucosa either of the esophagus or the stomach.

The contrast-enhanced thoracic computed tomography (CT) scan revealed a huge heterogeneous soft tissue mass in the posterior mediastinum (**Figure 1**), about 12 cm in maximum diameter, pushing the heart and the lower esophagus forward, and compressing the lower part of the left lung. Partial atelectasis was visualized. The patient was admitted to the department of thoracic surgery of our hospital for further management on April 7, 2013.

The CT guided mediastinal core biopsy revealed a spindle cell tumor with predominant hypercellular areas and foci of hypocellular hyalinization

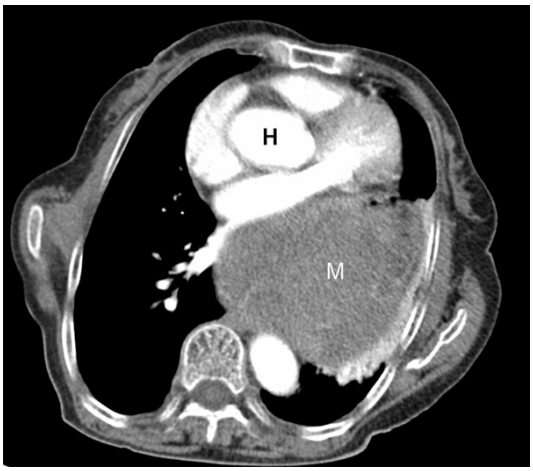

Figure 1. Contrast-enhanced CT scan demonstrated a large heterogeneous soft tissue mass in the posterior mediastinum, pushing the heart forward. H-heart, M-mass.

areas (**Figure 2A**). The tumor cells were arranged in a fascicular or whorling pattern and exhibited a syncytial appearance with elongated nuclei and pale eosinophilic cytoplasm.

Based on the clinical data and the histological features of the tumor, a diagnosis of solitary fibrous tumor (SFT) was rendered and seemed to be confirmed by the following positive immunostaining for CD34 (**Figure 2B**), and negative for smooth muscle actin, desmin and S-100 protein. However, when the case was referred to the pathologist with expertise in soft-tissue tumor (H.Z.), the diagnosis of GIST was highly suspected and confirmed by the following strong immunostaining of the tumor cells for CD117 and DOG-1 (**Figure 2C** and **2D**). The molecular genetic test demonstrated KIT exon 11 mutation (W557_K558 del).

Considering the extraordinary location of the tumor, pathologists suggested clinicians to arrange further examination to identify the anatomic relationship of the tumor and the nearby organs, especially for esophagus and stomach. The subsequent CT scan of the abdomen (**Figure 3A**) and sagittal-oblique reconstruction image (**Figure 3B**) demonstrated the mass was originated from the stomach and occupied mostly the area of posterior mediastinum.

The patient did not accept the recommendation for the preoperative imatinib therapy by the multidisciplinary team for GISTs. The following surgery revealed the tumor was locating entirely in the abdominal cavity, laying beneath the diaphragm, and pushing the diaphragm upward into the posterior mediastinum. A complete tumor resection with distal esophagectomy, gastric fundusectomy and esophagogastrostomy was performed through the abdominothoracic approach. The resected tumor was a 13×10×10 cm well-encapsulated, firm mass, which demonstrated identical morphology and immunohistochemical features to that of the biopsy (**Figure 4**). Notably, prominent perinuclear vacuoles, a common gastric GIST feature obscure in the previous biopsy specimen, were seen evidently throughout the resected tumor. The mitotic activity was up to 10/per 5 mm^2. The final diagnosis was a high-risk GIST originated from the gastric fundus.

After the surgery, the patient did not accept the adjuvant therapy of imatinib and was followed regularly at 3-month intervals. She suffered the complications of pleural effusion and persistent pyloric obstruction. At the most recent follow-up 48 months later, there was no evidence of recurrence.

Discussion

GIST is a kind of KIT positive mesenchymal tumor, which usually harbors activating mutations in *KIT* or *platelet-derived growth factor receptor* α tyrosine kinase genes. The biologic behaviors of GISTs are diverse, varying from a small, harmless tumor nodule to a metastasizing and life-threatening sarcoma [19]. Several risk criteria have been proposed for estimating the risk of tumor progression for localized GISTs [20-23].

Currently, the treatments for GISTs include surgical resection and targeted therapies. GIST is the first solid tumor target for tyrosine kinase inhibitors, which are not only the treatment of choice for metastatic and unresectable GISTs or an adjuvant therapy after surgery, but also could be used preoperatively to allow more structure-preserving operation or to reduce surgical morbidity [24]. Therefore, it's essential to identify GISTs from other non-GIST mesenchymal tumors even before surgery.

The current case represents an extremely peculiar example of subdiaphragmatic abdomen GIST, which presented as a primary thoracic

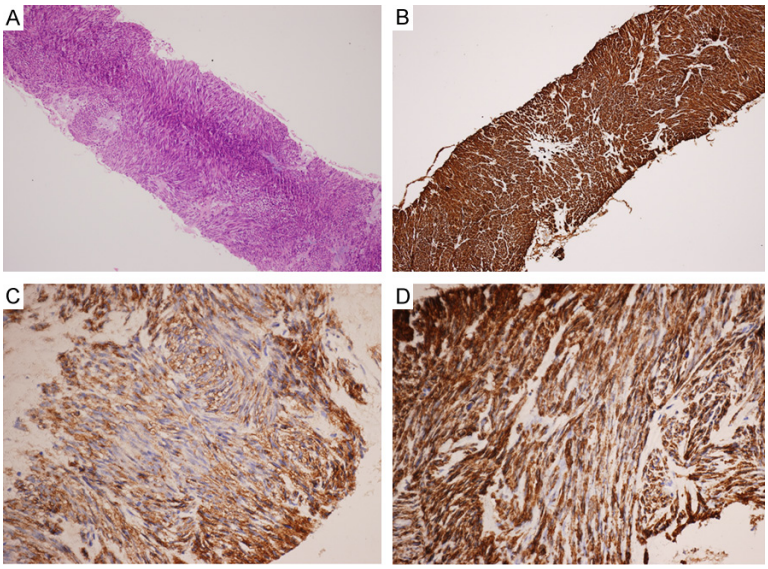

Figure 2. (A) The core biopsy revealed a spindle cell tumor with predominant hypercellular areas and foci of hypocellular hyalinization areas (×100). Immunohistochemically, the tumor cells were strongly positive for (B) CD34 (×100), (C) CD117 (×400), and (D) DOG-1 (×400).

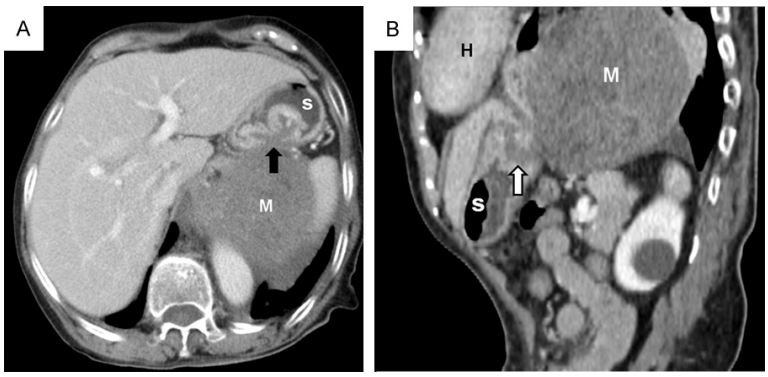

Figure 3. A: Contrast-enhanced CT scan showed an exogenous mass originated from the stomach (arrow). B: Sagittal-oblique reconstruction image showed the mass originated from the stomach (arrow) and occupied mostly the area of posterior mediastinum. H-heart, S-stomach, M-mass.

tumor and posed diagnostic pitfalls with potential therapeutic consequences. Although GIST is well known in the gastrointestinal tract, thoracic region is an uncommon anatomical location for it. Unlike the mesenchymal tumors encountered in the abdominal area, GIST is not typically considered in the usual differential diagnosis of spindle cell tumors involving the thoracic region. On the contrary, the more common spindle cell tumors of the thorax include SFT, smooth muscle tumors, neurogenic tumors and type A thymoma. GIST could simulate all of them by the spindle cell morphology. Therefore, the identification of GIST involving the thoracic area sometimes might be very challenging, especially in small biopsy samples.

Importantly, GIST can closely resemble SFT both histologically and immunohistochemically by positive staining of CD34 and lead to an erroneous diagnosis, especially when neither CD117 nor DOG-1 included in the immunohistochemical panels. Actually, besides the current case, there were thoracic GISTs once diagnosed as SFTs on biopsy tissues [6], or even postoperative specimen [7]. However, in contrast to the tumor cells in GIST, which are often arranged in sheets, fascicles or bundles, those in SFT are often randomly arranged in a "patternless" pattern with characteristic eosinophilic collagenous stroma. In addition, stromal vessels are usually small and inconspicuous in GIST, whereas SFT often exhibits a prominent hemangiopericytoma-like or staghorn vascular feature. Moreover, compared to the tumor cells of SFT with scanty cytoplasm, those of GIST usually demonstrate pale eosinophilic cytoplasm. Tumor cells of a group of GISTs, especially those arising in the stomach, may contain perinuclear vacuoles, a feature also demonstrating in the current case and a good clue for further immunohistochemical inspection.

GIST can also mimic smooth muscle tumors as both tumor types express myoid markers. There was a case reported in the English literature that a thoracic GIST was misdiagnosed as leiomyosarcoma [8] on biopsy tissues. However, smooth muscle tumor cells usually demonstrate more eosinophilic cytoplasm and cigar-shaped nuclei. Additionally, although GIST can express SMA and desmin, the staining is usu-

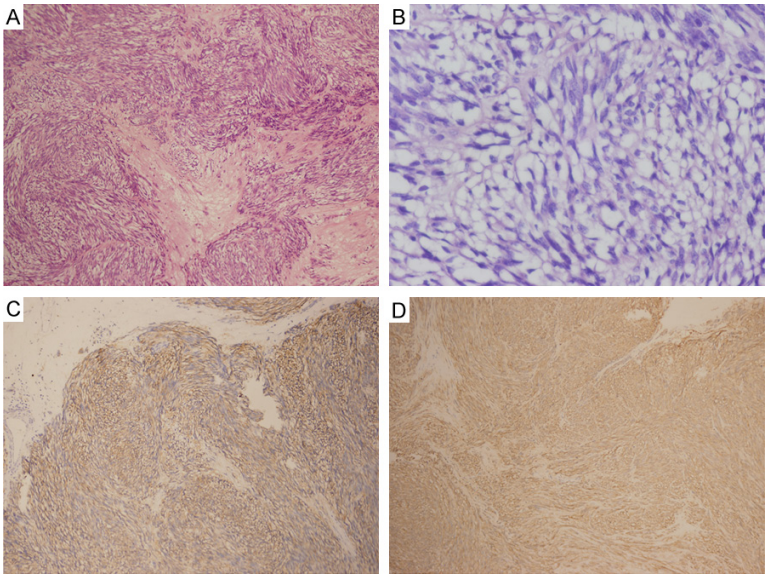

Figure 4. (A) The resected specimen demonstrated identical morphological features to that of the biopsy (×100). (B) Prominent perinuclear vacuoles were seen evidently throughout the resected tumor (×400). Immunohistochemically, the tumor cells were strongly positive for (C) CD117 (×100), and (D) DOG-1 (×100).

ally not strong, whereas the majority of smooth muscle tumors show diffuse and strong expression for both SMA and desmin. Therefore, careful inspection on both morphologic features and positive immunostaining patterns of a given tumor is the important groundwork for correct diagnosis. Once GIST cannot be excluded, CD117 and DOG-1 should be included in the immunohistochemical panel for the distinguishing purpose.

In conclusion, clinicians and pathologists should keep in mind that GISTs involving thoracic region do exist, and patients of this group may get potential benefits from imatinib particularly when surgery is not the initial treatment of choice. The identification of GIST involving thoracic region might be very challenging but significant. The presence of morphological features of GIST, immunohistochemical makers and molecular genetic test in combination with clinical-pathological correlation could help to arrival at the correct diagnosis and result in an optimal choice of therapy.

Acknowledgements

Supported by the Research Supporting Project from Science and Technology Department of Sichuan Province (no. 2014SZ0232) and National Natural Science Foundation of China (no. 814-72510, no. 81272944). The study was approved by the West China Hospital Institutional Review Board.

Disclosure of conflict of interest

None.

Authors' contribution

H.C. analysed the data and prepared the manuscript. J.Y. analysed the data of radiology. Y.T. carried out the molecular studies. H.Z. was responsible for the diagnosis and revised the manuscript.

Address correspondence to: Dr. Hongying Zhang, Department of Pathology, West China Hospital, Sichuan University, Guoxuexiang 37, Chengdu 610041, Sichuan, China. Tel: 086-28-85423847; Fax: 086-28-85422698; E-mail: hy_zhang@scu.edu.cn; hy_zh@263.net

References

[1] Miettinen M, Sarlomo-Rikala M, Sobin LH and Lasota J. Esophageal 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.

[2] Jiang P, Jiao Z, Han B, Zhang X, Sun X, Su J, Wang C and Gao B. Clinical characteristics and surgical treatment of oesophageal gastrointestinal stromal tumours. Eur J Cardiothorac Surg 2010; 38: 223-227.

[3] Zhang FB, Shi HC, Shu YS, Shi WP, Lu SC, Zhang XY and Tu SS. Diagnosis and surgical treatment of esophageal gastrointestinal stromal tumors. World J Gastroenterol 2015; 21: 5630-5634.

[4] Constantinoiu S, Gheorghe M, Popa L, Ciocea C, Iosif C, Tiutiuca R, Iordache A and Cordos I. Giant esophageal GIST: diagnostic and therapeutic challenge-case report. Chirurgia (Bucur) 2015; 110: 300-307.

[5] Zhang CQ, Lu DG, Liu QF and Xiao W. Primary extragastrointestinal stromal tumor of the pleura: a case report. Oncol Lett 2016; 11: 3135-3138.

[6] Papaspyros S and Papagiannopoulos K. Gastrointestinal stromal tumor masquerading as a lung neoplasm. A case presentation and literature review. J Cardiothorac Surg 2008; 3: 31.
[7] Long KB, Butrynski JE, Blank SD, Ebrahim KS, Dressel DM, Heinrich MC, Corless CL and Hornick JL. Primary extragastrointestinal stromal tumor of the pleura: report of a unique case with genetic confirmation. Am J Surg Pathol 2010; 34: 907-912.
[8] Kafeel M, Cheedella NK and Wang JC. Esophageal gastrointestinal stromal tumors presenting as mediastinal mass. Case Rep Oncol 2013; 6: 579-584.
[9] Lee HJ, Park SI, Kim DK and Kim YH. Surgical resection of esophageal gastrointestinal stromal tumors. Ann Thorac Surg 2009; 87: 1569-1571.
[10] Lee JR, Anstadt MP, Khwaja S and Green LK. Gastrointestinal stromal tumor of the posterior mediastinum. Eur J Cardiothorac Surg 2002; 22: 1014-1016.
[11] Iijima S, Maesawa C, Sato N, Ikeda K, Inaba T, Akiyama Y, Ishida K, Saito K and Masuda T. Gastrointestinal stromal tumour of the oesophagus: significance of immunohistochemical and genetic analyses of the c-kit gene. Eur J Gastroenterol Hepatol 2002; 14: 445-448.
[12] Ertem M, Baca B, Dogusoy G, Erguney S and Yavuz N. Thoracoscopic enucleation of a giant submucosal tumor of the esophagus. Surg Laparosc Endosc Percutan Tech 2004; 14: 87-90.
[13] Gouveia AM, Pimenta AP, Lopes JM, Capelinha AF, Ferreira SS, Valbuena C and Oliveira MC. Esophageal GIST: therapeutic implications of an uncommon presentation of a rare tumor. Dis Esophagus 2005; 18: 70-73.
[14] Basoglu A, Kaya E, Celik B and Yildiz L. Giant gastrointestinal stromal tumor of the esophagus presenting with dyspnea. J Thorac Cardiovasc Surg 2006; 131: 1198-1199.
[15] Portale G, Zaninotto G, Costantini M, Rugge M, Pennelli GM, Rampado S, Bocus P and Ancona E. Esophageal GIST: case report of surgical enucleation and update on current diagnostic and therapeutic options. Int J Surg Pathol 2007; 15: 393-396.
[16] Kim JM, Yoon YH, Lee KH and Kim JH. Malignant gastrointestinal stromal tumour in the posterior mediastinum. Interact Cardiovasc Thorac Surg 2012; 14: 497-499.
[17] Sjogren PP, Banerji N, Batts KP, Graczyk MJ and Dunn DH. Rare presentation of a gastrointestinal stromal tumor with spontaneous esophageal perforation: a case report. Int J Surg Case Rep 2013; 4: 636-639.
[18] Machishi H, Okada Y, Nagai M, Noda N, Hori T, Shimono T and Fukudome T. A rare case of huge gastrointestinal stromal tumor (GIST) of the stomach extending into the posterior mediastinum. Dig Dis Sci 2002; 47: 1492-1497.
[19] Miettinen M and Lasota J. Gastrointestinal stromal tumors. Gastroenterol Clin North Am 2013; 42: 399-415.
[20] Miettinen M and Lasota J. Gastrointestinal stromal tumors: pathology and prognosis at different sites. Semin Diagn Pathol 2006; 23: 70-83.
[21] Joensuu H. Risk stratification of patients diagnosed with gastrointestinal stromal tumor. Hum Pathol 2008; 39: 1411-1419.
[22] Agaimy A. Gastrointestinal stromal tumors (GIST) from risk stratification systems to the new TNM proposal: more questions than answers? A review emphasizing the need for a standardized GIST reporting. Int J Clin Exp Pathol 2010; 3: 461-471.
[23] Joensuu H, Vehtari A, Riihimaki J, Nishida T, Steigen SE, Brabec P, Plank L, Nilsson B, Cirilli C, Braconi C, Bordoni A, Magnusson MK, Linke Z, Sufliarsky J, Federico M, Jonasson JG, Dei Tos AP and Rutkowski P. Risk of recurrence of gastrointestinal stromal tumour after surgery: an analysis of pooled population-based cohorts. Lancet Oncol 2012; 13: 265-274.
[24] ESMO/European Sarcoma Network Working Group. Gastrointestinal stromal tumours: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2014; 25 Suppl 3: iii21-26.