Gastrointestinal stromal tumour in the posterior mediastinum

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INTRODUCTION

Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal tumours of the gastrointestinal tract. Mediastinal GISTs are rare, and nearly all mediastinal GISTs are oesophageal in origin. A single case of gastric GIST presenting as a posterior mediastinal mass has been reported [1]. Because the origin of a GIST, whether in the stomach or oesophagus, may have different prognostic implications, awareness of a gastric GIST in the posterior mediastinum and proper management of it are important. Surgical resection is the treatment of choice for GISTs which are resistant to chemotherapy [2]. We report a case of a malignant mediastinal GIST likely arising from the stomach in a patient who was treated with wide surgical excision.

CLINICAL SUMMARY

A 71-year old woman was admitted with a 1-day history of mild chest pain, epigastric discomfort and nuchal pain. She had no specific chest symptoms. Her medical history was significant only for an appendectomy. A contrast-enhanced chest computed tomography (CT) scan revealed a 9 × 8 cm posterior mediastinal tumour in the right lower thorax (Fig. 1a and b). In the supine position, general endotracheal anaesthesia was administered via a double-lumen endotracheal tube. A right lateral thoracotomy was performed. The mass lesion was exposed after dissection of lower oesophageal submucosal layer, inferior pulmonary ligament and wedge resection of right lower lobe. The mass appeared very well vascularized. After careful dissection, the mass was enucleated. The tumour was a 10.0 × 8.0-cm, well-encapsulated, firm mass involving the submucosal, muscular layers of lower oesophagus and sparing the mucosa. Grossly, the tumour was partly covered with a smooth serous membrane (Fig. 2a). The microscopic findings revealed typical features of a GIST. The tumour cells were spindle in shape, with ill-defined cytoplasmic borders. The nuclei were elongated and bland-looking without prominent nucleoli. However, the mitotic index was increased to 14/50 in high-power field. Neither epithelioid differentiation nor necrosis was present. The tumour originated from the muscle layer and was covered by peritoneum, which was supportive of gastric, rather than oesophageal, origin. The resection margin was free from tumour. The tumour cells were positive for italicize c-kit (Fig. 2b) and CD34, but negative for SMA or S-100 protein. After performing a polymerase chain reaction for a c-kit gene mutation, sequencing was completed which confirmed a deletion mutation at exon 9 of the c-kit gene. The postoperative course was uneventful. The patient was followed regularly at 6-month intervals for 5 years without evidence of a recurrence.

DISCUSSION

In 1983, the concept of a gastric stromal tumour was introduced by Mazur and Clack [3, 4]; this concept was expanded to include other mesenchymal tumours that do not demonstrate smooth muscle or Schwann cell differentiation. GISTs, derived from interstitial cells of Cajal or their precursors, are specific KIT- or PDGFRα-signalling driven mesenchymal tumours. The majority of GISTs are benign (60–80%) [5]. Malignant GISTs are rare. The patient described herein had a tumour 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 oesophageal muscle layer. Presence of tumour necrosis, high mitotic counts and infiltrative growth warranted a diagnosis as a malignant mediastinal GIST [1, 6]. The site of presentation is a prognostic factor; GISTs arising from the stomach are more indolent, whereas GISTs arising from the small intestine, colon and oesophagus are more aggressive. Gastric GISTs may extend to the posterior mediastinum, but common differential diagnoses include neurogenic tumour, oesophageal duplication cyst and oesophageal leiomyoma. In this patient, the tumour was solid and large enough to exclude these lesions, but fine needle aspiration might be helpful generally for a preoperative differential diagnosis.

GISTs have shown KIT gene mutations, commonly in exon 11 and less commonly in exon 9. KIT mutations serve as a ‘gatekeepers’ in GIST development. KIT exon mutations were deletions or deletions coexisting with single- or multiple-point mutations. Point mutations have tended to occur in tumours with benign behaviour compared with deletions. Exon 9 mutations have been associated with extragastric locations and have had a poor prognosis with larger tumour size. Sometimes, PDGFRA mutations are identified in GISTs. In general, KIT mutations have tended to occur in spindle cell tumours and PDGFRA mutations in epithelioid tumours [7]. In this case, deletion mutation at exon 9 of the c-kit gene was present. Aggressive surgical resection is the treatment of choice for GISTs with negative resection margins due to radioreistance and insensitivity to chemotherapeutic agents. Conservative surgical treatment may relegate the patient with a GIST to incurable tumour recurrence. Complete resection of a recurrent tumour has a better survival rate than incomplete resection [2, 8].

Imatinib mesylate, selectively inhibiting the mutated KIT receptor of tumour cell, has been developed as a therapeutic agent [3]. There are ongoing trials on the use of Gleevec as adjuvant therapy for selected high-risk patients with GISTs (large tumours with high mitotic indices). Patients at high risk of recurrence should undergo more frequent CT and PET scans, which are sensitive for evaluating the extent of tumour recurrence. The PET/CT scan may help follow-up tumour recurrence after complete resection, and the definitive diagnosis of these tumours depends on comprehensive immunopathologic examination of the surgical specimen [8, 9].

In conclusion, we have presented a case of a completely resected malignant mediastinal GIST, probably gastric in origin, with no recurrence for 5 years after complete resection.

**FUNDING**

This work was supported by an Inha University Research Grant.

**Conflict of interest:** none declared.

**REFERENCES**

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doi:10.1093/icvts/ivs040
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We would like to comment on the case report by Kim and colleagues concerning the surgical treatment of a gastrointestinal stromal tumour in the posterior mediastinum [1].

Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal tumours of the gastrointestinal tract (5000 new cases per year in the United States) [2]. They can be found in patients with a median age of 60 years, with frequent occurrence (70%) in the muscular wall of the stomach, followed by small bowel (10-20%), oesophagus, omentum, mesentery and retroperitoneum [2,3].

GISTs can range from small benign tumours to sarcomas at all sites of occurrence. Tumours that have metastasized at presentation have a very poor prognosis. The 5-year survival in patients with malignant GISTs is less than 40% [2]. There are three key prognostic factors: mitotic rate, tumour size, and site. Tumours that are small (<2 cm) and show mitotic activity not exceeding 5 mitoses per 50 high-power fields, have an excellent prognosis. This prognosis probably is independent of site, although this has not been shown specifically for all sites. In the stomach, most epithelioid GISTs are benign. However, we have to bear in mind that a small proportion of tumours apparently lacking mitotic activity do metastasize [2,3].

GISTs in association with paragangliomas and pulmonary chondromas constitute the Carney triad. In fact, the Carney triad is a multiple neoplasia syndrome affecting mostly females. This syndrome - or Carney complex - predisposes to a variety of tumours including adrenocortical adenomas (unilateral or bilateral) that are usually non-functioning [2,4]. Carney and Stratakis, in 2002, distinguished the inherited GISTs with paraganglioma syndrome from the Carney triad as an autosomal dominant condition in adult patients. This condition has been called Carney-Stratakis syndrome [5].

These two syndromes, even though quite rare, have entered the realm of multiple endocrine neoplasias in the last years. Carney-Stratakis syndrome is probably more frequent and may be prevalent amongst patients with GISTs that are negative for KIT/PDGFRA mutations [2].

A high index of suspicion is required by surgeons who are dealing with patients with isolated or sporadic GISTs or paragangliomas. They have to be aware of the multiple endocrine neoplasia syndromes in the last years. Carney-Stratakis syndrome is probably more frequent and may be prevalent amongst patients with GISTs that are negative for KIT/PDGFRA mutations [2].

Conflict of Interest: None declared

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