CASE REPORT

Primary omental gastrointestinal stromal tumour (GIST) presenting with a large abdominal mass and spontaneous haemoperitoneum

Isaac Seow-En,¹ Francis Seow-Choen,² Tony Kiat Hon Lim,³ Wei Qiang Leow³

¹Department of General Surgery, Singapore General Hospital, Singapore, Singapore
²Seow-Choen Colorectal Centre Pte Ltd, Singapore, Singapore
³Department of Pathology, Singapore General Hospital, Singapore, Singapore

Correspondence to

Dr Isaac Seow-En,
 prawnfret@gmail.com

Accepted 21 October 2014

SUMMARY

A 60-year-old Indonesian woman presented with a 9-day history of increasing abdominal distension, pain and tiredness. Physical examination revealed significant pallor with a palpable mass in the abdomen. CT of the abdomen reported a 22 cm complex mass in the peritoneal cavity with free intra-abdominal fluid. Laboratory results showed anaemia with a raised serum CA 125 level. At laparotomy a large haemorrhagic tumour with blood filled cystic cavities was found attached to both greater omentum and the transverse mesocolon with 2.2 L of blood in the peritoneal cavity. There was no invasion of any part of the stomach or intestines and there were no metastases seen. Histopathology of the resected specimen was consistent with that of a gastrointestinal stromal tumour arising from the omentum. Immunohistochemical studies revealed the tumour to be strongly positive for discovered on GIST-1 (DOG1) but negative for both CD117 and CD34. Platelet-derived growth factor receptor α (PDGFRA) exon 18 mutation D842V was detected.

BACKGROUND

Gastrointestinal stromal tumours (GISTs) are the most common primary mesenchymal tumours of the gastrointestinal tract, most often arising from the stomach. However, GISTs presenting with rupture and haemoperitoneum are infrequent. Furthermore, GISTs occurring as primary tumours outside the gastrointestinal tract are very unusual as well. The combination of primary omental or mesenteric GISTs presenting with haemoperitoneum has been rarely described, with only one case previously reported arising from the omentum.¹

We report a case of primary omental GIST presenting with abdominal mass and haemoperitoneum. We review the literature on GISTs with particular emphasis on its histopathological profile. Accumulating knowledge of these rare tumours may shed light on their histological origins and lead to improved pathological classification and guide subsequent treatment of patients.

CASE PRESENTATION

A 60-year-old Indonesian woman presented with a 9-day history of increasing abdominal distension, pain and tiredness. She had no nausea, vomiting or constipation. There was no change in frequency of bowel output or consistency of stools, but she reported a recent decrease in stool calibre. She did not report any noticeable loss of weight or appetite.

She was well previously without any chronic comorbidity. She did not have any family history of malignancy. On examination, she was noted to be anaemic with a distended abdomen and a large vague mass was palpable. Clinically there was definite ascites without signs of peritonitis or shock.

INVESTIGATIONS

Haemoglobin level was 6.9 g/dL. Total white cell count was $11.1 \times 10^9/L$. Serum CA 125 was raised at 93.77 U/mL (normal <35 U/mL), while CEA and CA 19-9 levels were normal at $<2.5 \mu\text{g/L}$ and 3.24 U/mL, respectively. Oesophagogastroduodenoscopy and colonoscopy were normal. Contrast-enhanced CT of the abdomen and pelvis showed a large complex solid-cystic mass measuring $22.8 \times 22.7 \times 8.8$ cm within the peritoneal cavity (figures 1 and 2). This was reported as likely arising from the right ovary, which was not visualised. Omental caking and high-density free fluid were noted in the abdomen. There were no enlarged nodes or liver nodules seen and the displaced bowel loops appeared normal. The kidneys, pancreas, spleen and biliary tree were noted to be normal in appearance.

DIFFERENTIAL DIAGNOSIS

Our initial impression was that of an ovarian carcinoma based on her raised CA 125 level and CT appearance.

Figure 1 (Axial view) Contrast-enhanced CT of the abdomen and pelvis showing a large complex solid-cystic mass measuring $22.8 \times 22.7 \times 8.8$ cm within the peritoneal cavity, with high-density free fluid in the pelvis.

CrossMark

To cite: Seow-En I, Seow-Choen F, Lim TKH, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-205528

Figure 2 (Coronal view) Contrast-enhanced CT of the abdomen and pelvis showing a large complex solid-cystic mass measuring 22.8×22.7×8.8 cm within the peritoneal cavity, with high density free fluid in the pelvis.

TREATMENT

Following blood transfusion, our patient underwent an exploratory laparotomy. We found a large, ruptured, septated haemorrhagic tumour attached to the greater omentum and the transverse mesocolon with a total of 2.2 L of blood in the abdominal cavity. The mass was adherent to but could be completely dissected off the transverse mesocolon, intestines and stomach (figures 3 and 4). The small bowel, colon, appendix, uterus and both ovaries were normal.

OUTCOME AND FOLLOW-UP

Histopathological analysis revealed a 683 g specimen comprising of a multiloculated cystic lesion measuring 20×18×5 cm with attached omentum measuring 30×9×1 cm. The cysts were thin walled containing haemorrhagic material. No solid discrete lesion or papillary excrescences were seen (figure 5). Microscopic sections showed a myxoid matrix with mixed

Figure 3 Intraoperative photographs showing a large ruptured septated haemorrhagic cyst arising from the greater omentum with a total of 2.2 L of free blood within the abdominal cavity.

Figure 4 The mass was adherent to but could be completely dissected off the transverse mesocolon and stomach, which were normal.

spindle and epithelioid cells containing mostly uniform nuclei and rare mildly atypical forms (figures 6 and 7). Mitotic rate was low at 1/50 HPF, and necrosis was not seen, despite extensive haemorrhage. Additional immunohistochemistry revealed discovered on GIST-1 (DOG1) to be strongly positive with both CD117 and CD34 negative. Platelet-derived growth factor receptor α (PDGFRA) exon 18 mutation (D842V) was detected. Additional immune stains for smooth muscle actin, desmin, MDM2 and HMB45 were negative. Overall morphology and immune profile were consistent with a GIST.

The patient recovered uneventfully and was discharged well on postoperative day 3. She declined further referral to an oncologist for counselling. On follow-up she was asymptomatic 6 months postoperatively. Repeat CT scan at 6 months did not show any evidence of recurrence.

DISCUSSION

GISTs are mesenchymal neoplasms originating from the interstitial cells of Cajal in the gastrointestinal tract wall. These tumours are found most often in the stomach, jejunum and ileum and far less commonly in the duodenum, rectum, colon and oesophagus.^{2 3} Extra-GISTs (EGISTs) occur in less than 5% of cases, and can arise from the mesentery, retroperitoneum,

Figure 5 Gross examination showing a 683 g specimen comprising of a multiloculated cystic lesion measuring 20×18×5 cm with areas of haemorrhage.

Figure 6 H&E staining was performed (40× magnification). Sections of the tumour showing a myxoid matrix with a mixture of spindle and epithelioid cells with mostly uniform nuclei and rare mildly atypical forms. Cystic and solid areas were present. Mitoses were rare with up to 1/50 HPF identified.

peritoneum or omentum. Although still the subject of ongoing study, EGISTs appear to be histopathologically identical to GISTs. EGISTs arising from the omentum are very rarely reported, with only 57 previous cases in literature.^{1 2 4}

The immunohistochemical hallmarks of GISTs are positivity for CD117 (c-kit) and CD34, with the former previously being described to be more specific.⁵ Recent studies reveal that CD117 is not specific for GISTs with the list of CD117 positive tumours growing. It is now accepted that both CD117 and CD34 positivity are not diagnostic for GIST.⁶ PDGFRA mutations can occur in the absence of CD117, of which mutations in exon 18 are the most common, occurring in 6% of all GISTs.⁷ Our case had the D842V mutation, which results in an amino acid substitution at position 842 in PDGFRA from an aspartic acid (D) to valine (V). Interestingly, although studies suggest that more than one-third of GISTs with PDGFRA mutations may respond to imatinib, the D842V substitution has instead been associated with tyrosine kinase inhibitor resistance.⁷

While detecting mutations in CD117 and PDGFRA are useful in diagnosing GIST as well as predicting response to tyrosine kinase inhibitors, DOG1 is a recently described protein marker reported to have increased sensitivity and specificity compared

Figure 7 H&E staining was performed (40× magnification). Sections of the tumour showing a myxoid matrix with a mixture of spindle and epithelioid cells with mostly uniform nuclei and rare mildly atypical forms. Cystic and solid areas were present. Mitoses were rare with up to 1/50 HPF identified.

with CD117 in the diagnosis of GISTs.⁸ As in the case of our patient, DOG1 was positive while CD117 was negative.

GISTs usually present with dyspepsia and abdominal pain or less commonly upper gastrointestinal bleeding and palpable abdominal mass. Spontaneous haemoperitoneum is a rare complication, occurring in 6% of cases.⁹ Tumour rupture and haemoperitoneum of EGIST is rare, with Murayama *et al*¹ reporting the only other case of ruptured primary omental GIST with haemoperitoneum. In that report, the resected tumour had a different genotypic profile from our patient being CD117 and CD34 positive and with a non-D842V PDGFRA exon 18 mutation detected. In view of high-risk features such as high cellularity and mitotic index, the patient was treated with adjuvant imatinib 400 mg/day for 24 months without evidence of recurrence.

Notably, tumour size may not be considered a reliable high-risk feature of EGISTs as the majority of reported cases exceeded 10 cm.² Ruptured GISTs have also been found to have a poorer outcome, but tumour rupture remains a controversial prognostic factor as single large tumours with high-risk histopathological features tend to rupture most often.⁹ In our patient, histopathological analysis did not reveal any additional high-risk features. She declined further counselling with the oncologist and was recurrence free on follow-up CT scan at 6 months. In any case, adjuvant imatinib is not recommended in tumours with the PDGFRA D842V mutation.

Learning points

- ▶ For intra-abdominal soft tissue tumours including gastrointestinal stromal tumours (GISTs), a thorough histopathological analysis is necessary to ascertain diagnosis and guide treatment.
- ▶ Diagnosis is especially important if the presentation is atypical, as in our patient with a primary omental GIST presenting with haemoperitoneum.
- ▶ Discovered on GIST-1 (DOG1) is an important marker in diagnosing GIST, especially for the uncommon subgroup of CD117 and platelet-derived growth factor receptor α (PDGFRA) negative tumours. Our case was negative for CD117 and CD34, but strongly DOG1 positive, with mutation in PDGFRA exon 18 resulting in a D842V substitution.
- ▶ Adjuvant treatment is not recommended in imatinib-insensitive PDGFRA D842V mutated GISTs.

Contributors FS-C performed the surgery, managed the patient postoperatively and is actively involved in follow-up care of the patient. IS-E assisted in the surgery and drafted the manuscript. TKHL and WQL carried out the molecular genetic studies as tumour pathologists. All authors read and approved the final manuscript.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Murayama Y, Yamamoto M, Iwasaki R, *et al*. Greater omentum gastrointestinal stromal tumor with PDGFRA-mutation and hemoperitoneum. *World J Gastrointest Oncol* 2012;4:119–24.
- 2 Fagkrezos D, Touloumis Z, Giannila M, *et al*. Extra-gastrointestinal stromal tumor of the omentum: a rare case report and review of the literature. *Rare Tumors* 2012;4:e44.
- 3 Todoroki T, Sano T, Sakurai S, *et al*. Primary omental gastrointestinal stromal tumor (GIST). *World J Surg Oncol* 2007;5:66.

- 4 Divakaran J, Chander B. Primary extra-gastrointestinal stromal tumor of the omentum. *J Cancer Res Ther* 2012;8:433–5.
- 5 Sarlomo-Rikala M, Kovatich AJ, Barusevicius A, *et al.* CD117: a sensitive marker for gastrointestinal stromal tumors that is more specific than CD34. *Mod Pathol* 1998;11:728–34.
- 6 Riddle ND, Gonzalez RJ, Bridge JA, *et al.* A CD117 and CD34 immunoreactive sarcoma masquerading as a gastrointestinal stromal tumor: diagnostic pitfalls of ancillary studies in sarcoma. *Cancer Control* 2011;18: 152–9.
- 7 Corless CL, Schroeder A, Griffith D, *et al.* PDGFRA mutations in gastrointestinal stromal tumors: frequency, spectrum and in vitro sensitivity to imatinib. *J Clin Oncol* 2005;23:5357–64.
- 8 Liegl B, Hornick JL, Corless CL, *et al.* Monoclonal antibody DOG1.1 shows higher sensitivity than KIT in the diagnosis of gastrointestinal stromal tumors, including unusual subtypes. *Am J Surg Pathol* 2009;33:437–46.
- 9 Joensuu H, Vehtari A, Riihimäki J, *et al.* Risk of recurrence of gastrointestinal stromal tumour after surgery: an analysis of pooled population-based cohorts. *Lancet Oncol* 2012;13:265–74.

Copyright 2014 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow