Unusual association of diseases/symptoms

Traumatic rupture of a gastrointestinal stromal tumour with intraperitoneal bleeding and haematoma formation

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Summary

A 40-year-old man presented with acute abdominal pain and falling haemoglobin after a history of minor abdominal trauma. Radiological imaging showed a large soft tissue mass situated between the anterior stomach wall and peritoneum. At diagnostic laparoscopy, intra-abdominal blood and an encapsulated haematoma were found. The procedure was converted to midline laparotomy and the mass was excised, including a stalk of tissue that connected the mass to the anterior prepyloric stomach wall. The patient recovered well and was discharged after 9 days. Histology confirmed a gastrointestinal stromal tumour surrounded by haematoma formation.

BACKGROUND

Gastrointestinal stromal tumours (GISTs) are rare malignant tumours of the gastrointestinal tract originating from the intestinal cells of Cajal.¹ These tumours most commonly arise in the stomach and the most common presentation is that of upper gastrointestinal bleeding. Other presenting symptoms might include nausea, vomiting, anorexia, weight loss and abdominal pain. Because acute presentation is uncommon they are not usually considered among the differential diagnosis of an acute abdomen. These tumours may remain asymptomatic for extended periods of time and delayed diagnosis is fairly common because of the extraluminal growth pattern these tumours may take.

Our aim is to report on a patient with GIST who presented with an acute abdomen due to intra-abdominal bleeding. He was treated by surgical exploration and excision of the soft tissue mass, which was histologically confirmed to be a GIST. We will review the histology, clinical presentation and management of GIST to raise awareness among surgeons and surgical trainees.

CASE PRESENTATION

A 40-year-old man attended the accident and emergency department in the early hours of the morning complaining of sudden onset of abdominal pain. This was mainly in his epigastrium and right upper quadrant areas with the pain radiating to the right shoulder. He had no history of severe trauma, but did give a history of tightly squeezing through a narrow hatch on a submarine the previous day. On examination he was tachycardic with a pulse of 126. He had low oxygen saturations (88%) and was increasingly hypoxic on lying flat. Abdominal examination showed a distended abdomen with tenderness in the epigastrium. He was referred to the on-call surgical team with a provisional diagnosis of an acute abdomen, with possible diagnoses being ruptured oesophagus, perforated gastroduodenal ulcer or acute pancreatitis. Plain erect chest radiograph showed no free subdiaphragmatic abdominal gas or any lung field

abnormality. Plain abdominal films were unremarkable with no signs of intestinal obstruction.

Urgent CT of his chest, abdomen and pelvis was performed at 05:00 on the day of admission. This showed no evidence of an aortic aneurysm, widening of the mediastinum or evidence of oesophageal perforation. There was a small amount of left pleural fluid. Within the upper abdomen there was a large soft tissue mass measuring 9 × 10 cm situated between the anterior stomach wall and peritoneum (figure 1). The CT differential diagnosis was either a GIST with recent internal haemorrhage, haematoma from trauma of the mesenteric or stomach vessels or, less likely, an old contained perforation of the upper gastrointestinal tract. The pancreas and liver were normal. There was a small amount of fluid in the left subphrenic area and upper abdomen and large amounts of fluid within the pelvis. No free gas was seen in the abdomen.

He was admitted under the care of the general surgeon on-call to high-dependency level care. He was monitored closely and a urinary catheter and arterial line were inserted.

A specialist upper gastrointestinal surgical opinion was requested. After further radiological review and discussion, it was decided to perform a dynamic ultrasound to assess the lesion and narrow the differential diagnosis. The ultrasound showed that the lesion was separate from the liver, but it was unable to differentiate a ruptured GIST from a traumatic haematoma caused by injury to the upper abdominal mesentery.

In view of the continuing diagnostic doubt the patient was consented for surgery. Diagnostic laparoscopy was performed first and showed intraperitoneal blood and a large encapsulated haematoma-like lesion anterior to the stomach. The procedure was converted to an upper midline laparotomy (figure 2). The lesion was found to have a stalk that arose from the prepyloric area of the anterior stomach wall (figure 2). The stalk was excised with a good margin and closed primarily (figure 2). The abdomen was washed out with normal saline and then closed with a mass suture.

Figure 1 (A, B) Axial CT scan of the upper abdomen showing an exophytic soft-tissue mass arising from the gastric wall. The tumour is large and heterogenous due to internal haemorrhage. (C) Scan obtained at a lower level showing extension of the tumour. (D) Axial scan of the pelvis shows free-fluid (blood) due to tumour bleeding into the peritoneum.

Histopathological analysis showed a $9.0 \times 8.0 \times 7.0$ cm lesion with a smooth surface. On slicing it was an encapsulated blood clot. At one end of the specimen there was a $4.0 \times 4.5 \times 4.0$ cm fragment of solid tissue. Microscopically the assessment was of plasmacytoid and spindle cell tumour shaped cells consistent with a GIST (figure 3). Immunohistochemistry was performed and the tumour was positive for c-KIT, CD34 and vimentin (figure 4). Ki67 proliferation marker was positive in less than 10% of tumour cells (figure 4). The tumour was negative for S100, AE1/AE3, CD138, SMA and HMB45. The overall assessment confirmed the diagnosis of a GIST at intermediate risk of recurrence.

OUTCOME AND FOLLOW-UP

The patient was discharged from hospital 9 days after admission. An outpatient gastroscopy was performed 1 month later and showed no evidence of residual intragastric GIST. The surgical scar was visualised in the anterior aspect of the antrum of the stomach and this was biopsied. Histologically, this showed fibrosis and chronic inflammatory changes with *Helicobacter gastritis* but no evidence of residual GIST involvement.

He was referred to a tertiary oncology hospital for a specialist opinion on whether adjuvant treatment should be offered. After further review of the histopathology it was agreed to withhold adjuvant treatment but to carry out a follow-up CT scan of his abdomen and pelvis 3 months after surgery. This showed no evidence of tumour recurrence or metastatic disease.

DISCUSSION

GISTs are primary mesenchymal tumours of the gastrointestinal tract previously thought to be gastric or intestinal smooth muscle tumours.¹ Recent advances in immunohistochemistry has enabled specific identification of these tumours, which were found to be c-KIT (CD117) positive. GISTs are rare benign or malignant tumours accounting for less than 1% of gastrointestinal neoplasms. Often they arise from the stomach but they can involve any part of the gastrointestinal tract and can also involve the mesentery and omentum. Distant metastases appear late and lymph nodes are not usually involved. The most common metastatic sites are the liver and peritoneum.

The presentation of these tumours depends on the pattern of growth, which may be intra- or extra-luminal. With

Figure 2 Initial view of the encapsulated haematoma/gastrointestinal stromal tumour mass after upper midline laparotomy. The surgeons hands around the mass gives a better appreciation of the tumour. This view shows the stalk of tissue, which connected the mass to the anterior wall of the stomach. A disc of anterior stomach wall was excised and primary closure performed.

extra-luminal growth it may take an extended period of time for symptoms to develop with patients often presenting with a large abdominal mass. Upper gastrointestinal bleeding is the most common presentation of intraluminal GISTs because of a tendency of ulceration of the overlying mucosa. Our patient presented with intra-abdominal bleeding. This is rare but has been reported before in GISTs of the stomach,² ileum³ or ileal mesentery.⁴ An acute surgical abdomen can also be caused by acute intratumoural bleeding without haemoperitoneum⁵ or sudden tumour perforation.^{3, 6} Presenting symptoms in the elective situation may include nausea, vomiting, anorexia, weight loss and abdominal pain. Physical examination is rarely revealing although advanced extra-luminal tumours may have a palpable mass. GISTs can also be an incidental finding in upper gastrointestinal endoscopies and postmortem examinations.

The differential diagnosis of spontaneous intra-abdominal bleeding is wide and includes unnoticed minor

trauma (in susceptible patients, such as haemophiliacs) with bleeding from the mesentery, liver or spleen; spontaneous splenic rupture (in patients with pathologically enlarged spleens); ruptured ectopic pregnancy; spontaneous rupture of liver lesions (such as a large hepatocellular carcinoma or haemangioma) or other intra-abdominal tumours; ruptured abdominal aortic aneurysm and other rarer causes.

Surgery is the only curative treatment for GIST lesions.^{7, 8} However, treatment needs to be tailored to the individual patient. Consideration should be given to the location, size and presence of distant metastases. The main treatment for localised GIST is surgical removal of the entire tumour along with the pseudocapsule without rupturing it. Removal of lymph nodes is not necessary when removing a GIST as these tumours do not spread via the lymphatic route.

Imatinib (Glivec) was the first medication approved for the treatment of GIST and represents a major breakthrough in the management of these tumours.⁹ Imatinib is an orally

Figure 3 (A) Structure of the tumour with haemorrhage ($\times 100$ magnification). (B) Low magnification roughly showing relation of the tumour (right) to the stomach wall (left) ($\times 50$ magnification).

administered selective inhibitor of ABL tyrosine kinase, platelet-derived growth factor and c-KIT. A small minority of GISTs possess mutations of these tyrosine kinase enzymes, which render the tumour resistant or poorly responsive to imatinib. Tumour mutational status predicts response to imatinib and survival. Results from the MetaGIST study of 1640 patients showed that patients with a KIT exon 11 mutation had the longest progression-free survival,

while those with KIT exon 9 mutation had the worst survival.¹⁰ Other poor prognostic factors from this study included poor performance status, high neutrophil counts, low haemoglobin level, male sex and small bowel GISTs. Imatinib is currently licensed in the UK for treatment of metastatic or locally advanced and irresectable GISTs. However, there is intense research interest in to defining its role in the neo-adjuvant and adjuvant setting.¹¹ Other drugs

Figure 4 (A) Positive reaction in tumour cells to c-KIT (CD117) ($\times 200$ magnification). (B) Positive reaction in tumour cells to CD34 ($\times 200$ magnification). (C) Positive reaction to vimentin ($\times 200$ magnification). (D) Positive reaction to Ki67 indicating that only a small percentage are mitotic correlating with a low mitotic index ($\times 100$ magnification).

with similar mechanisms of action to imatinib, such as sunitinib, are emerging as useful second-line treatment options.

Features that are associated with a poor prognosis include large tumour size, high mitotic count and the presence of metastases. GISTs should be classified into very low, low, intermediate and high risk categories to aid in treatment and follow-up strategies (table 1). Tumour rupture (either spontaneously or at surgery) has recently been shown to increase the risk of tumour recurrence and adjuvant treatment should be considered in such cases.^{12 13} There has been a suggestion that tumour site and whether the tumour ruptured should be incorporated into a prognostic classification system.¹⁴ The presence of tumour rupture or a non-gastric GIST with a size greater than 2 cm would be categorised as high risk for tumour recurrence.

Table 1 NIH consensus classification criteria for defining risk of aggressive clinical course of primary gastrointestinal stromal tumours (adapted from Fletcher¹⁵)

Prognostic group	Tumour size in largest dimensions	Mitotic count (per 50 high powered fields (HPF))
Very low risk	<2 cm	<5
Low risk	2–5 cm	<5
Intermediate risk	<5 cm	6–10
5–10 cm	<5	
High risk	>5 cm	>5

Prognostic group	Tumour size in largest dimensions	Mitotic count (per 50 high powered fields (HPF))
> 10 cm	Any mitotic rate	
Any size	>5	

It is difficult to quantify the risk of tumour recurrence in this particular case. The tumour size is less than 5 cm and it had a low mitotic rate consistent with low risk tumour. However, the precise tumour dimensions were difficult to measure due to haematoma formation. Because the tumour ruptured, there is a risk of seeding to the peritoneum and so we considered it to be a tumour at intermediate risk of recurrence. It is reassuring that the postoperative CT scan performed 3 months after surgery showed no evidence of tumour recurrence. The patient will continue to be followed up on a regular basis.

In summary, GISTs are rare gastrointestinal tumours that usually present in adult life. They most commonly present with upper gastrointestinal bleeding and some are found incidentally; rarely they can present with acute bleeding into the abdominal cavity and should be considered in the differential diagnosis of spontaneous intra-abdominal bleeding. The primary and only curative treatment is complete surgical excision. However, these tumours carry a risk of recurrence and metastases and they should be classified into very low, low, intermediate or high risk categories to determine intensity of follow-up and the place for additional treatment. Primary or adjuvant treatment with imatinib, a tyrosine kinase inhibitor, is a valuable treatment option in certain patient groups.

Learning points

- ▶ GISTs are rare causes of intra-abdominal bleeding and may present with surgical abdominal signs.
- ▶ The prognosis of GISTs is based on a classification by tumour size and number of mitoses present.
- ▶ GIST rupture may indicate an increased risk of disease recurrence and adjuvant treatment with the tyrosine kinase inhibitor, imatinib (Glivec), should be considered.

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Competing interests None.

Patient consent Obtained.

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