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CASE REPORT

Two Cases of Gastrointestinal Stromal Tumour Presenting Uncommonly as Intraperitoneal Rupture in Patients Prescribed Warfarin

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ABSTRACT

Gastrointestinal stromal tumour (GIST) is the most common mesenchymal neoplasm of the gastrointestinal tract. Common presentations of GIST include early satiety, indigestion, bloating, vague abdominal pain, and gastrointestinal bleeding. Intraperitoneal rupture is an uncommon presentation of GIST. We have encountered two patients prescribed warfarin, who presented with intraperitoneal haemorrhage as their initial presentation of gastric GIST. Computed tomography (CT) revealed a submucosal gastric mass with intralesional and intraperitoneal haemorrhage. The diagnosis of ruptured GIST was made based on CT findings. These two cases are, to the best of our knowledge, the first two cases with rupture and intraperitoneal haemorrhage as the initial presentation of gastric GIST while on warfarin.

Key Words: *Gastrointestinal stromal tumors; Hemorrhage; Rupture; Warfarin*

中文摘要

服用華法林患者出現罕見的胃腸道間質瘤腹腔內破裂後被確診為胃腸道間質瘤：兩例報告

農智行、王先民、李嘉樂、陳碧雲、李艷萍

胃腸道間質瘤（GIST）是胃腸道最常見的間質腫瘤。GIST的常見症狀包括易飽、消化不良、腹脹、腹部疼痛和消化道出血。腹腔內破裂是GIST的一種罕見的症狀。本文報告兩名服食華法林的GIST病人出現腹腔內破裂。CT顯示粘膜下胃腫塊及病變內和腹腔出血。後因CT檢查結果而被確診為GIST。據我們所知，這兩個為首個類似的病例。

INTRODUCTION

Gastrointestinal stromal tumour (GIST) is the most common mesenchymal neoplasm of the gastrointestinal (GI) tract and commonly presents after 50 years of age. It arises from the muscularis propria and expresses transmembrane receptor tyrosine kinase encoded by

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KIT gene (CD117) in 95% of cases.[1] The stomach is the most common location, accounting for 2% to 3% of gastric tumours, followed by the small bowel.[2] Common presentations of GIST include early satiety, indigestion, bloating, vague abdominal pain, and GI bleeding (from mucosal ulceration). Intraperitoneal rupture is an uncommon presentation. We report on two patients prescribed warfarin, who presented with intraperitoneal haemorrhage as the initial presentation of gastric GIST.

CASE REPORTS

Case 1

An 82-year-old man with a history of recent stroke and prescribed warfarin and aspirin presented during stroke rehabilitation with acute abdominal pain and signs of peritonism but no fever in August 2010. There was an episode of hypotension with systolic blood pressure of 70 mm Hg. Blood tests showed a normal haemoglobin level (144 g/l) but increased white cell count of 14.4 x 10^9 /l. International normalised ratio (INR) was within the therapeutic range. Computed tomographic (CT) scan was performed for suspected diagnosis of perforated peptic ulcer or ruptured appendicitis and revealed an ill-defined 5-cm heterogeneous enhancing submucosal mass arising from the posterior wall of the gastric fundus (Figure 1). No internal calcification or necrosis was evident. The mass extended through the serosa posteriorly into the peritoneal cavity, with evidence of acute intralesional haemorrhage, haemoperitoneum and active contrast extravasation within the mass and peritoneal cavity. Hyperdense blood was found adjacent to the gastric mass, compatible with sentinel clot sign. Emergency laparotomy confirmed a ruptured GIST at the gastric fundus with 1100 ml of fresh blood in the stomach and perilesional haematoma. Wedge resection was then performed. Histological examination confirmed GIST with extensive haemorrhage (Figure 2). The patient recovered uneventfully from surgery and was able to continue stroke rehabilitation.

Case 2

An 81-year-old woman prescribing warfarin and with a history of renal failure and atrial fibrillation presented with epigastric pain and signs of peritonism but no fever in November 2011. Vital signs, including blood pressure, were normal. Blood tests revealed anaemia (haemoglobin, 92 g/l) and mildly elevated white cell count of 12.2 x 10^9 /l but INR was within the therapeutic range. CT scan was performed for suspected diagnosis of perforated peptic ulcer and revealed a large well-defined hypervascular exophytic

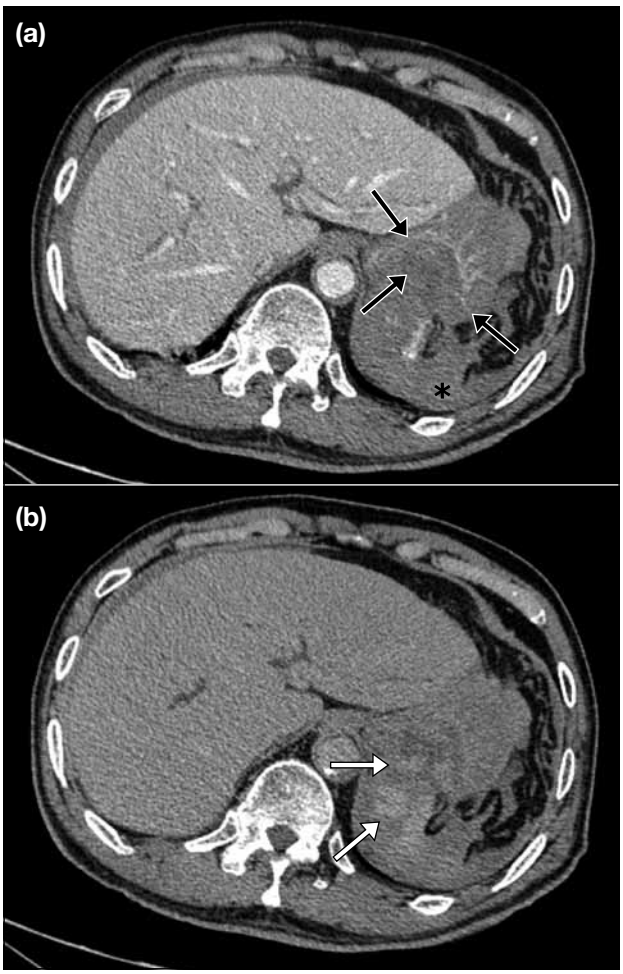

Figure 1. (a) Portovenous and (b) delayed phases of the axial images at the level of gastric fundus. Haemoperitoneum (*) is identified posterior to the gastric fundus. A heterogeneous submucosal mass (black arrows) is evident at the posterior wall of the gastric fundus, and has extended posteriorly beyond the serosa into the peritoneal cavity. A few foci of active contrast extravasation (white arrows) within and posterior to this mass are also noted.

Figure 2. Pathological specimen: the resected gastrointestinal stromal tumour is cut open revealing the internal surface of gastric mucosa.

mass in the epigastrium, arising from the lesser curve of the stomach (Figure 3a). There was evidence of internal haemorrhage and haemoperitoneum. No internal calcification was evident. Overall features were suggestive of a tumour of gastric origin and highly suspicious of GIST.

A follow up CT scan 1 month later showed resolving haemoperitoneum with no evidence of recent haemorrhage (Figure 3b). Tumour had reduced in size with cystic change of the intralesional haematoma. There was a new perforation at the left inferolateral wall of this cystic component resulting in contained cystic fluid collection adjacent to the tumour.

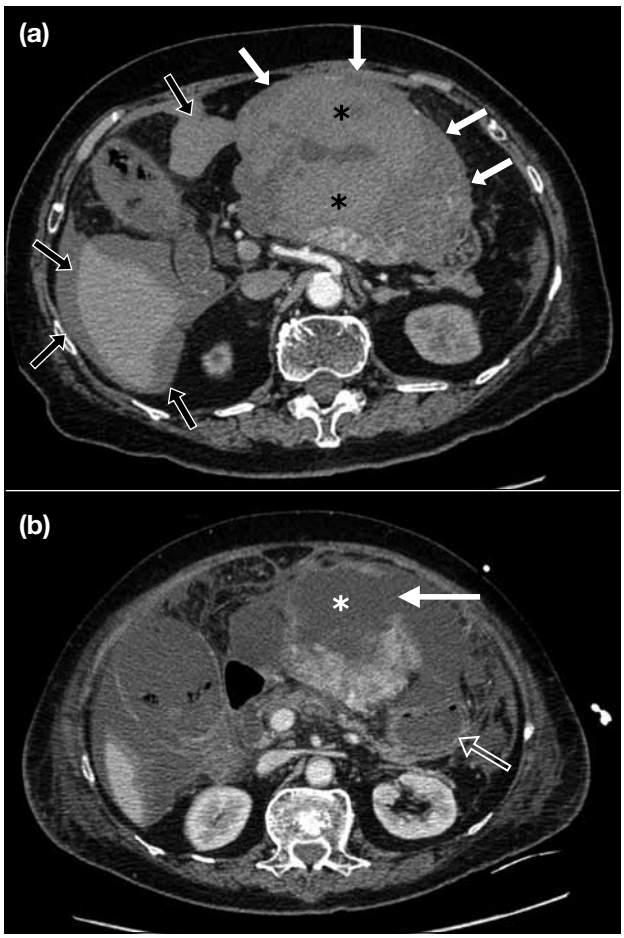

Figure 3. (a) Contrast-enhanced axial computed tomographic (CT) image reveals a large well-defined heterogeneous exophytic mass in the epigastrium arising from the lesser curve of the stomach (white arrows) without internal calcification. Evidence of internal haemorrhage and haemoperitoneum (black arrows) is shown. Higher attenuation of haemorrhage (black asterisks) in the mass suggests sentinel clot sign, i.e. the anatomic sites of bleeding. Features are suggestive of gastrointestinal stromal tumour. (b) A follow-up CT scan of the same patient 1 month later shows reduction in size of the tumour with cystic change (white asterisk) of the intralesional haematoma. A new perforation (long white arrow) is identified at the left inferolateral wall of this cystic component resulting in contained fluid collection (hollow arrow) adjacent to the tumour.

DISCUSSION

Spontaneous rupture with haemoperitoneum is an uncommon complication of gastric GIST.[3] Our search of the literature revealed fewer than 15 cases had been reported. Pera et al[4] reported the first case in 1999 in which a 83-year-old patient presented with intraperitoneal haemorrhage and hypovolemic shock. Emergency laparotomy showed haemoperitoneum caused by rupture of a large exogastric tumour attached to the greater curvature. Total gastrectomy and oesophagojejunostomy was performed and histological examination suggested a diagnosis of a GIST. Subsequently more similar cases were reported.[5-10]

Many patients with ruptured gastric GIST often present with non-specific complaints such as acute abdominal pain and progressive lowering of haemoglobin.[5-10] In our two cases, there was also anaemia and abdominal pain. Nonetheless, only the first case presented with low blood pressure. The diagnosis of ruptured gastric GIST is often not considered at presentation and only disclosed by CT findings. Furthermore, the CT findings can sometimes mimic other pathologies. Fiscon et al[11] reported a case of ruptured gastric GIST with haemoperitoneum that was initially reported as ruptured cavernous angioma of the liver on CT scan.

The major differential diagnoses of ruptured gastric GIST include bleeding from other gastric pathologies such as gastric carcinoma and perforated peptic ulcer. Gastric carcinoma tends to manifest as mucosal thickening or mass together with perigastric lymphadenopathy while in cases of perforated peptic ulcer, no mucosal or submucosal lesion will be seen. Ruptured aneurysm of the gastric artery may also mimic ruptured GIST but again no underlying mass will be identified. Bleeding from liver lesions, e.g. hepatocellulcar carcinoma, focal nodular hyperplasia, adenoma, and cavernoma may occasionally mimic ruptured GIST if the haematoma extends beyond the liver into the upper abdomen. The fact that these lesions are in continuation with the liver parenchyma usually helps differentiate them from ruptured GIST.

The radiological findings of ruptured GIST are also infrequently described in the literature. Cegarra-

Navarro et al[12] reported six cases of ruptured GIST and commented that the finding of a heterogeneous tumour of laminated or whirled appearance associated with ascites with characteristics compatible with haemoperitoneum in an appropriate context must lead to a suspicion of the existence of a ruptured GIST. In our cases, the radiological features included submucosal gastric mass with intralesional and intraperitoneal haemorrhage. Laminated hyperdensity is seen within the mass representing haemorrhage and is in keeping with the reported radiological findings. Sentinel clot signs sometimes can be found close to the tumour (case 1) and suggests more acute clotted haemorrhage and indicates the anatomic site of haemorrhage.[12] There is usually no significant pneumoperitoneum as GIST is a submucosal lesion that, when ruptured in the peritoneal cavity, will not cause direct gastric mucosal breach. One of the radiological difficulties is to differentiate spontaneous intraperitoneal haemorrhage from intraperitoneal haemorrhage due to underlying GIST, as the GIST can sometimes be small and masked within the large intraperitoneal haematoma. Follow-up imaging and endoscopic ultrasound-guided biopsy may help solve this problem. Fang et al[13] also described the angiographic appearance of GISTs that includes obviously thickened supplying arteries and early developed veins.

The two cases reported here had intraperitoneal haemorrhage as the initial presentation of gastric GIST. Interestingly, both patients were prescribed warfarin for pre-existing illness before presentation. This might have precipitated bleeding and rupture of the previously undiagnosed gastric GIST. To the best of our knowledge, these are the first case reports describing rupture and intraperitoneal haemorrhage as the initial presentation of gastric GIST related to warfarin. Patients prescribed long-term warfarin therapy are at increased risk of major bleeding, reported to be 1.1% to 8.1%.[14,15] The incidence of spontaneous intestinal intramural haemorrhage has been reported as 1 in 2500.[16] In our patients, both had a serious illness of cerebrovascular disease, cardiac disease, or renal failure and were of advanced age. This may have placed them at a higher risk of anticoagulant-related bleeding.[14] One of our patients commenced anticoagulation during stroke rehabilitation and within 1 month of stroke, which is the time at the highest risk of bleeding.[17] Major bleeding related to anticoagulant use most often affects the GI tract, soft tissues, and urinary tract. Diagnostic evaluation of GI bleeding and gross haematuria has been shown to identify previously unknown lesions in approximately one-third of cases, including malignancies in 15%.[17] These results are compatible with our cases where bleeding was the initial presentation of GIST not previously diagnosed. Although the exact mechanism for initiation of spontaneous bleeding in GIST is not completely understood, it may be related to peristalsis of the GI tract that tears the fragile tumoural vessel and initiates the bleeding that is then perpetuated by the anticoagulant effect of warfarin. This may have a similar mechanism to rectus sheath haematoma that arises as a result of trauma, anticoagulation, coughing, and intense rectus muscle contractions.[18]

CONCLUSION

Intraperitoneal rupture is an uncommon initial presentation of gastric GIST. The clinical features are often non-specific and this diagnosis is often not considered initially. A high index of suspicion is necessary during evaluation of intraperitoneal haemorrhage, especially if it is close to the perigastric region, to recognise this potential cause of acute abdominal pain, especially in patients prescribed warfarin.

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