

## Bleeding Gastrointestinal Stromal Tumour of the Stomach Complicated by Massive Deep Vein Thrombosis – a Management dilemma – a Case Report

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*Cancer is a major risk factor for venous thromboembolism (VTE). Its treatment is an added risk factor for VTE. Malignancy results in a hypercoagulable state and hence DVT requiring anticoagulation. Cancer patients are at high risk of anticoagulant associated bleeding. Bleeding complications occur more with unfractionated heparin as compared to low molecular weight heparin. Standard medical treatment based on vitamin K antagonists is less effective and is associated with increased risk of bleeding in cancer patients. Low molecular weight heparin treatment has added advantages such as less sensitivity to drug interactions, lack of need for regular monitoring and has no problem of narrow therapeutic window as opposed to warfarin. Gastrointestinal stromal tumours (GIST) are the most common mesenchymal tumours of the gastrointestinal tract. The most common presentation is of gastrointestinal bleeding, pain and/or dyspepsia. We report the case of a 67 year old hypertensive female patient who presented with a history of massive haematemesis and malaena. Upper gastrointestinal endoscopy confirmed a gastric tumour. She developed massive sudden swelling of the left lower limb whilst awaiting surgery. Doppler ultrasound scan confirmed an iliofemoral deep vein thrombosis (DVT). Inferior vena cava filter insertion was not possible due to non-availability. Coexistence of DVT needing anticoagulation and bleeding gastric GIST requiring urgent resection presented a management dilemma. Despite the risk, the patient was taken for an emergency tumor resection primarily to stop the bleeding and facilitate full anticoagulation therapy more safely. After 24 months follow up the patient had no evidence of recurrence of both the GIST and DVT.*

**Key words:** deep vein thrombosis, venous thromboembolism upper gastrointestinal bleeding, gastric tumour

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### Introduction

The risk of venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE) in cancer patients has been well recognized. Twenty percent of VTE events occur in people with cancer<sup>1</sup>. There are several factors that are known to influence the risk of VTE in cancer patients, including age, immobility, surgery and trauma<sup>2</sup>. Armand Trousseau was the first to describe the association between cancer and thrombosis when he reported cases of migratory thrombophlebitis in patients with cancer in 1867<sup>3</sup>. Although migrating superficial thrombophlebitis (Trousseau's Sign) and DVT have been described in gastric carcinoma, these are rare<sup>4</sup>.

Gastric cancers commonly present with dyspepsia, vomiting, early satiety, haematemesis and melena. When a patient with a gastric malignancy presents with significant upper gastrointestinal bleeding and develops DVT whilst awaiting surgery, a management dilemma ensues due to the conflicting issues of hemorrhage and anticoagulation in the same patient. We report the case of a patient who presented with a bleeding gastrointestinal stromal tumour of the stomach complicated by a massive DVT. Wide resection of the tumour was done despite the acute DVT. Histology confirmed C- kit positive GIST. At 24 months after surgical resection, Imatinab and anticoagulation therapy, there was no evidence of tumour recurrence or DVT.

## Case presentation

A 67 year old hypertensive female patient initially presented to the Physicians with a history of having collapsed at home following episodes of haematemesis and malaena. She admitted to having had weight loss and early satiety. There was no history of ingestion of non-steroidal inflammatory drugs (NSAIDS), alcohol or smoking. After initial resuscitation, haemodynamic stabilization and upper gastrointestinal endoscopic confirmation of a bleeding gastric tumour by physicians, our surgical firm was consulted for surgical intervention to stop the bleeding.

On examination she was pale, not jaundiced and had no significant lymphadenopathy. She had a grossly swollen left lower limb as illustrated in Figure 1. She had a blood pressure of 158/120 mmHg, pulse 102 beats per minute full volume and regular, temperature 35 degrees Celsius and a respiratory rate of 20 breaths per minute. She had epigastric tenderness, no hepatomegaly or ascites and had malaena stool on digital rectal examination. All pulses were present and of normal character. All other systems were normal.



**Figure1.** grossly swollen left lower limb

Her full blood count showed a white cell count of 9,51micromoles per litre (4- 11), hemoglobin 7.0 grams per deciliter (12 – 14), haematocrit of 23.7% (36- 44), mean corpuscular volume 75.7 femtolitres (80 – 96), platelet count  $261 \times 10^3$  (150 -450). Liver function tests as well as urea and electrolytes were normal. Total protein was 58mg/dl. International normalized ratio (INR) of 1.68, Activated partial thromboplastin time (APTT) 41.5 seconds (control 42.2 sec).

Upper GI endoscopy done showed a mass protruding into the pyloric antrum which was soft and had an ulcerated surface. Biopsies were attempted but proved difficult to take. Computed tomography showed a mass at the gastro-duodenal junction 80X40mm axially and 60mm cranio-caudally (see arrows in Figure 2). Complete thrombosis of the left iliac and femoral veins, with thrombus protruding into Inferior vena cava (IVC) was also confirmed on CT scan

A Doppler ultrasound scan of the lower limbs showed common femoral, superficial femoral, popliteal, peroneal, anterior and posterior tibial veins of the left lower limb were distended and filled with thrombi. The left common iliac and left external iliac veins were also thrombosed. The thrombus encroached into the IVC. Chest X-ray was normal. A diagnosis of massive ileo-femoral DVT in a patient with a bleeding gastric tumour was made and the patient was commenced on low molecular weight heparin, Clexane 40mg subcuticularly once daily.

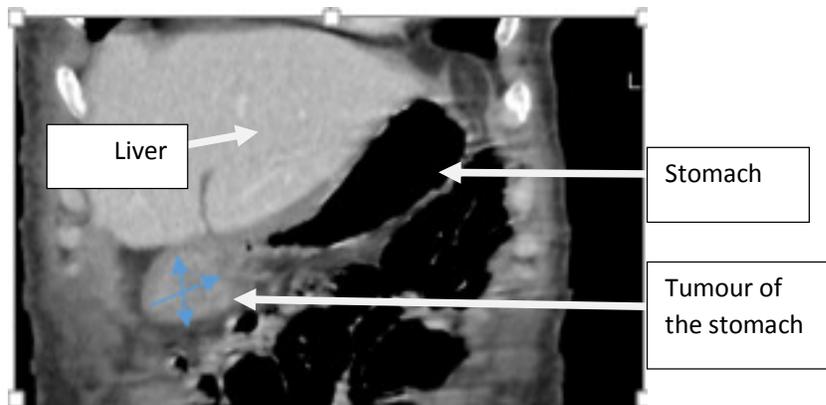
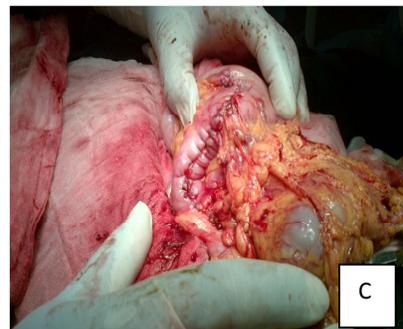
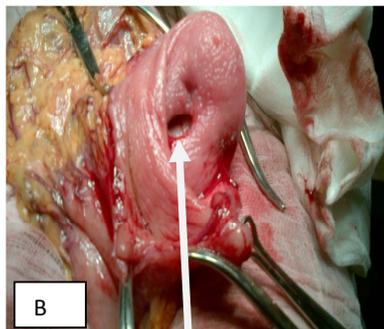


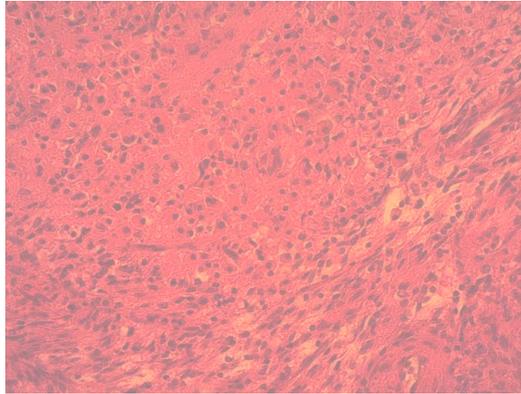
Figure 2: Computer tomography scan showing a mass at the gastric antrum.



**Figure 3a and 3b:** Gastric Tumour *insitu* (ulcer crater) **Fig 3c:** after wide local excision and closure.

The patient continued to bleed as evidenced by ongoing melena and hemodynamic instability. Anticoagulation therapy was contraindicated leaving urgent surgery as the only option to save life. In view of the massive DVT an Inferior vena cava filter was contemplated for possible deployment but was not available. Anticoagulation therapy was withheld and the patient was taken for an emergency laparotomy to stop the life threatening bleeding as the primary therapeutic goal.

At laparotomy a 90 x 40 mm ulcerated tumour with a central blood clot at the gastric antrum was noted. This is illustrated in Figure 3a, b and c. There was no evidence of intra-abdominal metastatic spread and no ascites. A wide local excision of the tumour with a 2cm margin and preservation of the pyloric sphincter was done. The specimen was submitted for histological analysis and immuno-histochemistry.



**Figure 4.** Interlacing fascicles of spindle cells and epithelioid cells with oval nuclei and abundant basophilic cytoplasm characteristic of GIST.

Postoperatively the patient had a nasogastric tube (NGT) inserted, intravenous fluids, analgesia and was continued on Clexane (*Emcure*<sup>®</sup>) 40mg twice daily. The NGT was removed on day 3 post operatively and the patient started on oral feeds. She was also commenced on warfarin 2,5mg orally daily. The histological report was received on day 5 postoperative showed “a tumour composed of interlacing fascicles of spindle cells and epithelioid cells with oval nuclei and abundant basophilic cytoplasm. The cells are imbedded in collagenous stroma. Pleomorphism is minimal and mitosis rare. The appearance was consistent with a GIST and immunohistochemistry showed C-kit positive” (Figure 4). The patient was commenced on Imatinab 400mg orally daily indefinitely. Our patient did not suffer pulmonary embolism and the left limb swelling subsided over the succeeding 4weeks. She was discharged from outpatients follow up at 24months in excellent health. The DVT resolved and no sign of tumour recurrence.

### Discussion

Our patient presented a management dilemma. She developed extensive DVT that required urgent treatment in the presence of a bleeding gastric tumour also warranting urgent surgery. The extent of the DVT made the risk of pulmonary embolism (PE) extremely high. Surgery in such circumstances would further increase the chances of a PE. Adequate anticoagulation therapy was hampered by the risk of increasing bleeding from the gastric tumour. Furthermore, the CT scan findings showed that the tumour was limited to the stomach with no evidence of metastases. Surgery would therefore potentially cure the bleeding and the tumour simultaneously. The situation was worsened by the unavailability of IVC filter that was required to prevent PE in the perioperative period.

The major determinants of the risk of VTE in cancer patients include tumour stage, tumour type, chemotherapy, hormonal therapy, surgery and presence of central venous catheters<sup>4</sup>. The reported cumulative incidence of VTE was found to be 16 per 1000 patients in the first 2 years following cancer diagnoses<sup>5</sup> and 24.6 per 1000 patients in the first year following diagnosis<sup>6</sup>. Our patient had notable risk factors for DVT; advanced age and female gender, gastric malignancy as well as immobility. There is at least 2-to 4-fold increased risk of VTE in the first 6months after cancer diagnosis in patients with metastatic cancer compared to patients with limited stage cancer<sup>6</sup>.

Treatment of venous thromboembolism (VTE) with anticoagulation, although effective in patients with cancer, is fraught with higher morbidity, from bleeding and recurrent VTE, despite anticoagulation<sup>7</sup>. Our patient had ongoing upper GI bleeding as well DVT. Compared to patients without malignancy, patients with malignancy have a higher incidence of major bleeding ranging from 6.5 to 18 percent that is not always explained by over anticoagulation<sup>8</sup>. When anticoagulation is contraindicated, one treatment option is the insertion of an inferior vena cava filter for PE prophylaxis. This does not obviate the need for anticoagulation. Although retrospective cohort studies suggest lower fatality rates in some cancer patients with IVC filters, there are no large randomized trials in any patient population that have studied the safety and efficacy of vena cava filters in the treatment and prevention of VTE<sup>9</sup>. Inferior vena cava filters were not available at our hospital. Attempts to import from Republic of South Africa were unsuccessful due to prohibitive costs and unavailability at the time of need.

Whilst there is abundant literature on DVT in cancer patients, there is paucity of literature on the occurrence and management of the contradiction of simultaneous massive DVT and massive bleeding from GIT tumours –clearly a rare phenomenon. Recommended initial treatment of DVT involves use of low molecular weight heparin eg Clezan, dalteparin. Thrombolytic therapy and vena caval filters should be reserved for patients in whom there is high risk of PE yet anticoagulation is contraindicated or insufficient<sup>9</sup>. Although the risk of PE and death was high in our patient undergoing emergency major surgery in the presence of massive DVT and upper GIT bleeding, the need to remove the cause of bleeding was compulsive. It was felt that the benefits of surgery far outweighed the risk. The outcome vindicated this tough and aggressive course of action.

### Conclusion

A high index of suspicion for VTE is vital in cancer patients. Primary prevention of VTE by pharmacological agents or where contraindicated, mechanical means, is recommended in all cancer patients hospitalized for surgical or medical reasons. Multidisciplinary management of complex problems is vital. Where DVT and the risk of VTE coexists with a life threatening bleeding tumour, curative surgery should not be withheld as this offers the only chance of survival in the absence of an IVC catheter. Whilst no major conclusions can be made on the successive management of this high risk case, we are encouraged to manage any future cases similarly and not delay lifesaving surgery under similar circumstances solely on the basis of the risk of PE. Only a clinical trial can resolve this issue conclusively, however this is unlikely given the rarity of such a clinical scenario.

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