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CASE REPORT

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C-kit-negative transmural gastrointestinal stromal tumor in the stomach: A rare case of upper GI bleeding in Ghana

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Abstract

Upper GI bleeding from GIST is rare in Africa. The C-kit-negative variant is uncommon worldwide. We report a case of a 42-year-old woman managed for upper GI bleeding secondary to stomach GIST, negative for CD117 but positive for DOG 1 and CD 34. The 1-year postsurgery review is uneventful.

KEYWORDS

bleeding, C-kit negative, gastrointestinal stromal tumor, transmural

1 | INTRODUCTION

Gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumors in the gastrointestinal tract (GIT). They account for just under 1% of GI tumors.[1] GISTs are usually found in the stomach or small intestine but can occur anywhere along the GI tract and rarely involve extra-GI sites.

These tumors were originally considered leiomyomas or leiomyosarcomas because they possessed smooth muscle features under light microscopy. They are now known to originate from a pluripotential mesenchymal stem cell programmed to differentiate into an intestinal pacemaker known as an interstitial cell of cajal.[2]

The clinical presentation of GIST varies with the tumor's location along the GI tract.[3] The most common symptom of GIST is bleeding, which may present acutely as hematemesis, melena stool, or anemia in the chronic type of bleeding. They may also present with other symptoms such as vague abdominal pain, feeling of mass, appendicitis-like pain, and obstructive symptoms.

GIST may also be diagnosed incidentally during endoscopic, radiologic, or surgical procedures. These tumors may be too small to show symptoms. Approximately,

15%–25% of gastric and small intestinal GIST are aggressive and may present with metastasis.[4,5] Investigations that can be used for diagnosis include computed tomography (CT) scan, magnetic resonance imaging (MRI), endoscopy, and endoscopic ultrasound with fine needle aspiration (FNA). The mainstay of treatment is complete surgical excision with or without adjuvant therapy, imatinib depending on the presence of CD117 (C-kit) expression.

GIST of the stomach is a rare cause of upper GI bleeding in Ghana. However, there is no report of such a presentation in the country. Two previous reports in the country described GIST presenting as intussusception; gastro-gastric, and gastroduodenal intussusception.[6,7] We report a case of C-kit-negative GIST presenting as upper GI bleeding to highlight its rarity in Ghana and Africa and the need to report such cases.

2 | CASE REPORT

A 42-year-old woman presented to the hospital with a month's history of melena stools and 2 weeks history of hematemesis. She had also noticed left-sided upper abdominal pain with no associated weight loss or jaundice.

Clinical examination showed a moderately pale woman with no jaundice, with mild left-sided upper abdominal tenderness but no guarding or rebound tenderness. There was no palpable abdominal mass. We made a clinical diagnosis of upper GI bleeding. Upper GI endoscopy revealed a bleeding protruding mass arising from the body of the stomach anteriorly with features suggestive of gastrointestinal stromal tumor, as shown in Figure 1.

A contrast-enhanced CT scan was requested, which showed an 11.4 cm × 10.6 × 8.6 cm mass arising from the body of the stomach with solid and cystic areas likely due to necrosis, as shown in Figure 2. There were no suspicious regional lymph nodes noted. There were no other abnormal intraabdominal findings, and the limited view of lung bases was normal.

Her hemoglobin level was 8.2 g/dl as shown in Table 1. She had normal renal and liver function results.

The patient was hemotransfused four units of packed red cells, prepared, and underwent surgery with a hemoglobin of 11.8 g/dl. The surgery was done 1 week after diagnosis.

The peritoneal cavity was approached through an upper midline incision. The intraabdominal finding was a mass of approximately 10 cm x 8 cm arising from the body of the stomach, as shown in Figure 3. There was no evidence of intraperitoneal metastasis.

Wide excision of the mass revealed a transmural type of tumor, as shown in Figure 3. The postoperative period was uneventful.

2.1 | Histopathology and immunohistochemistry

The macroscopic evaluation showed a tumor that measured 11 cm x 9 cm x 8 cm and weighed 500 g. The cut surface revealed areas of myxoid degeneration, hemorrhage, and necrosis. The tumor was 2 cm from the closest gastric mucosal resection margin.

Microscopic evaluation showed spindle cell tumors with vague fascicular arrangements. There were areas with myxoid matrix, and necrosis was observed. The mitotic count was 3/50 HPF, as shown in Figure 4.

Immunohistochemistry analysis showed tumor cells positive for DOG1 and CD 34 but negative for CD117 (C-kit) and SMA (Figure 5).

Mutation analysis by next-generation sequencing (TruSight 15 kit) was unsuccessful due to degraded DNA due to possible pre-analytic factors. The tumor was classified as intermediate risk.

The patient has since been followed up for 12 months following surgery with normal findings on clinical examination and endoscopy.

3 | DISCUSSION

Gastrointestinal stromal tumors are the most common and account for 80% of mesenchymal tumors of the GI tract.[8] They account for less than 1% of all GI tumors, with an estimated unadjusted incidence is 1/100000 per year. The prevalence and annual incidence of GIST are 129/million and 14.5/million, respectively.[9] The expected number of new cases in the United States is 5000 per year, but the incidence in Africa is unknown.

GIST is commonly found in the stomach and other locations, such as the ileum and colon. However, some studies have reported a few sites outside the GI tract. The

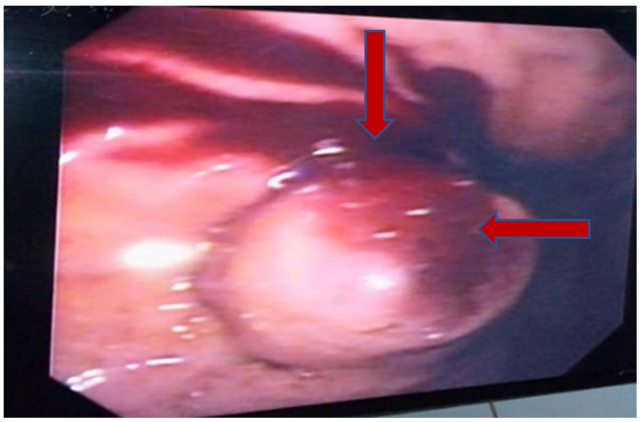

FIGURE 1 The endoscopic image of GIST shows the tumor's luminal part with some bleeding areas, as shown with the arrows.

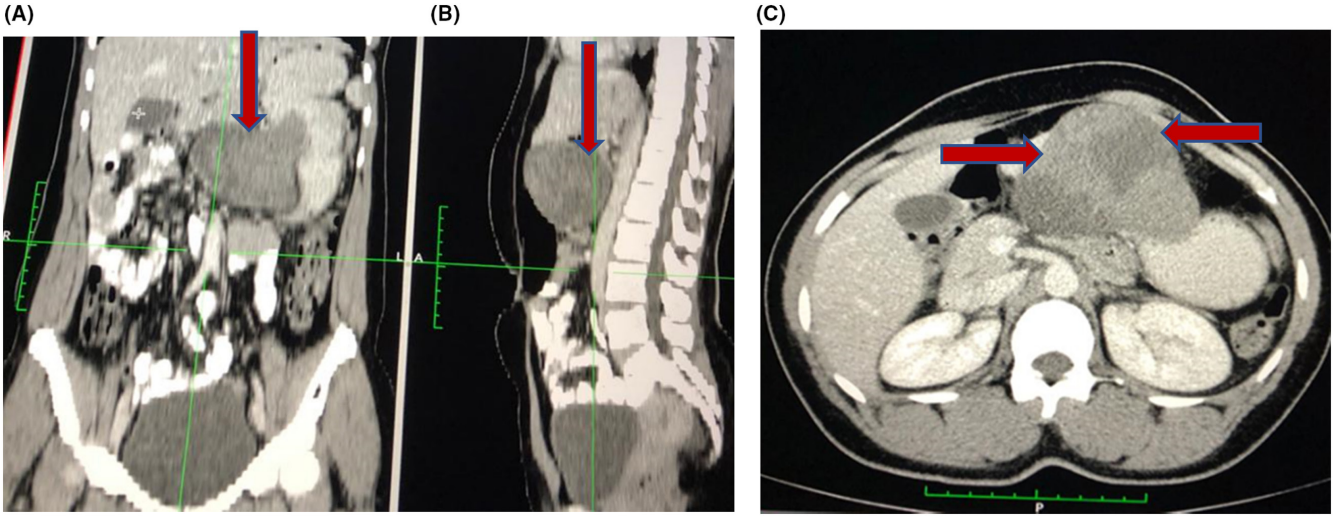

FIGURE 2 CT image of stomach GIST on coronal view (A), sagittal view (B), and axial view (C) showing the tumor arising from the body of the stomach.

TABLE 1 Results of some blood investigations and reference range.

Laboratory investigation	Results	Reference range
Hb	8.2 g/dl	12–16
WBC	7.5×10/L	4–10
CEA	1.8μg/L	0–4

Abbreviations: CEA, carcinoembryonic antigen; Hb, hemoglobin level, WBC, white cell count.

tumors can occur at any age but typically manifest in patients over 50 years, with the incidence peaking among patients between 70 and 79. The mean age is, however, lower in the African series.[10,11] There is a slight male preponderance,[12] even though some texts report equal sex distribution. Here, we report a case of a 42-year-old woman presenting with upper GI bleeding.

The clinical presentation of GIST varies with the tumor's location along the GI tract.[3] The most common symptom of GIST is bleeding, which may present acutely as hematemesis, melena stool, or anemia in the chronic type of bleeding. They may also present with other symptoms such as vague abdominal pain, feeling of mass, appendicitis-like pain, and obstructive symptoms. This patient presented with hematemesis, melena stools, and a feeling of fullness and vague abdominal pain. Even though it is a rare cause of GI bleeding in Africa, we should regard GIST as an important cause of GI bleeding.

GIST may also be diagnosed incidentally during endoscopic, radiologic, or surgical procedures. These tumors may be too small and asymptomatic. There is an early diagnosis of GIST in Japan and countries where screening for gastric cancer is standard.[13] The features of GIST at endoscopy are firm, smooth yellowish submucosal mass which displaces the overlying mucosa. Occasionally, this mass has an area of central ulceration or bleeding of the overlying mucosa from necrosis.[12] The patient presented with a similar endoscopic picture, as shown in Figure 1.

Conventional endoscopic biopsies for non-ulcerated tumors are usually unsuccessful compared to ulcerated ones, as seen in our patient. Endoscopic ultrasound with FNA biopsy increases the sensitivity of biopsy in GIST. Studies have shown that preoperative biopsy for suspicious, primary resectable GIST is unnecessary because of its attendant complications, such as intra-tumoral bleeding, tumor dissemination and rupture.[14] Biopsy, however, is required in suspected metastasis, consideration for neoadjuvant therapy in borderline resectable disease, and atypical features that put the diagnosis in doubt.

CT scan of the abdomen in our patient showed a large transmural mass in the body. Contrast-enhanced CT is essential in diagnosing and staging stomach GIST. It provides information on the tumor's location, size, relationship with adjacent structures and distant metastasis. It is also valuable for classifying GIST according to size and morphology into three categories: Small (<5 cm), Sharply demarcated, homogeneous masses, mainly exhibiting intraluminal growth patterns. Intermediate (5–10 cm): Irregular shape, heterogeneous density, an intraluminal and extraluminal growth pattern, and signs of biological aggression, sometimes including adjacent organ infiltration; and large (>10 cm): Irregular margins, heterogeneous densities, locally aggressive behavior, and distant and peritoneal metastases.[15] Furthermore, imaging

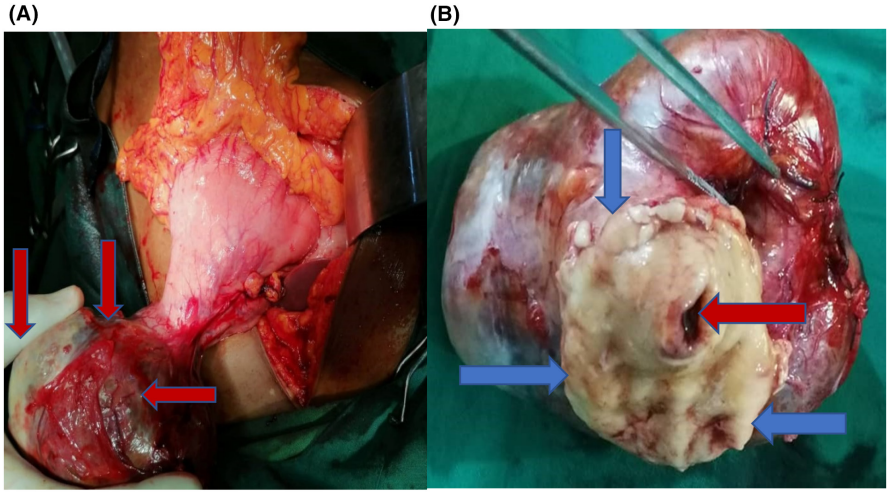

FIGURE 3 (A) shows a tumor from the body of the stomach. (B) shows a completely excised tumor with blue arrows showing the margins and red arrows showing the intraluminal part.

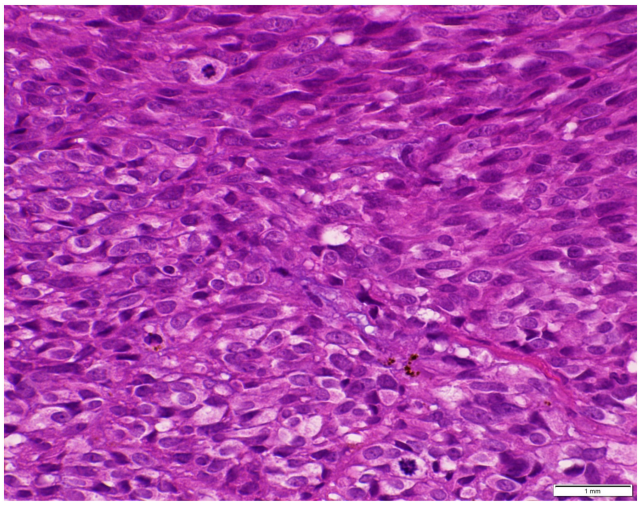

FIGURE 4 H&E stain demonstrating spindle cell tumor with two mitotic figures 900×.

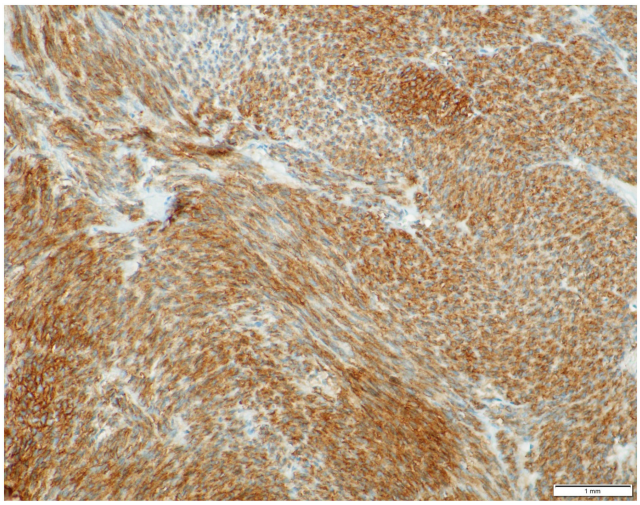

FIGURE 5 DOG1 immunohistochemistry demonstrating positive cytoplasmic staining 300×.

combined with surgical reports classifies GIST into luminal, exophytic, and transmural.[16] Other imaging modalities such as MRI, PET scan, and ultrasound are valuable alternatives. Tumors in the upper third of the stomach have a better prognosis and may not need adjuvant therapy. Tumors in the African series tend to be larger than those from other regions.[10,11]

The tumor in our patient was CD 117 negative, SMA negative, CD 34 positive, and DOG 1 positive. According to the American Society of Clinical Oncology and NCCN guidelines, the workup of GIST should consist of morphology-based diagnosis with immunohistochemical testing and ancillary molecular genetic testing.[17] GISTs usually stain for the c kit protooncogene, CD117, and overexpressed in 95% of tumors and CD 34 in up to 70% of tumors. However, C-kit-negative GISTS occur in about 5% of cases and requires other markers such as CD 34, DOG1, and PDFGR mutations to confirm GIST.[18] Per the NCCN and ASCO guidelines, molecular pathology analysis by next-generation sequencing (TruSight Tumor 15 Kit) was done. However, it was unsuccessful because the DNA was degraded and could not be sequenced, possibly due to pre-analytic factors. We, therefore, recommended buffered formalin appropriately prepared by the pathologist in preparing tissues for various analyses and avoiding over-fixation and under-fixation issues with cold ischemic time.

This patient underwent surgical resection with negative margins and followed up with normal findings on endoscopy and clinical examination. We did not give adjuvant treatment because of the negative reactivity to the C- kit. The mitotic index, location, and size determine the risk of progression of the primary tumor.[1,16] This patient had an intermediate risk of disease progression because of its location in the stomach, widest dimension, and a mitotic index of 3/50 HPF. These factors influence clinical judgment for follow-up of such patients for recurrence

and distant metastasis because there is no consensus for follow-up for recurrence and metastasis.

4 | CONCLUSION

We have managed a woman with GI bleeding secondary to stomach GIST, a rare case in Ghana and Africa. In C-kit-negative GISTs, as in this case, other markers such as DOG 1, CD 34, and genetic testing are essential in diagnosing GIST. There should be a high index of suspicion for GIST in Ghana and Africa, and the need to report GIST in these parts of the world cannot be overemphasized.

AUTHOR CONTRIBUTIONS

Samuel Mensah: Conceptualization; supervision; writing – original draft; writing – review and editing. **Ishmael Kyei:** Conceptualization; writing – original draft; writing – review and editing. **Collins Kokuro:** Writing – original draft; writing – review and editing. **Collins Afriyie:** Writing – original draft; writing – review and editing. **Michael Nortey:** Writing – review and editing. **Ernest Adjei:** Investigation; writing – review and editing.

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CONFLICT OF INTEREST

None declared.

DATA AVAILABILITY STATEMENT

Data available on request due to privacy/ethical restrictions.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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