Decreasing the burden: An unusual GIST presentation, a case report

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A B S T R A C T

INTRODUCTION: Gastrointestinal stromal tumours (GIST) are notoriously one of the most common mesenchymal tumours of the alimentary canal. Most commonly originating from the gastric stroma, they are recognized by their mass effects on the abdominal cavity. Recurrence frequently occurs with GIST and these tumours may become refractory to tyrosine kinase inhibitors (TKIs). Therefore, resection may be indicated for improved outcomes.

PRESENTATION OF CASE: We present a 52-year-old African American male with a surgical history of GIST resection with recurrence that came to the emergency room with worsening diffuse abdominal pain. The tumour was refractory to two TKIs, Imatinib and Sunitinib. Computed tomography (CT) of the abdomen and pelvis was done which showed severe metastatic disease with carcinomatosis, multiple dilated loops of small bowel in the left hemiabdomen without discrete transition point. After seventeen days on nasogastric tube, antiemetics, the patient worsened, and it was decided to go to surgery. In this report, attention is focused on the surgical approach of tumour debulking with subsequent Regorafenib therapy for decreased obstructive symptoms and improved quality of life.

CONCLUSION: This case serves as an example of the importance of surgical debulking in addition to molecular therapy for patients with severely extensive GISTS. Tumour debulking is important to decrease tumour burden, improve chemotherapeutic response and improve quality of life especially in persons refractory to pharmacological therapy.

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1. Introduction

Gastrointestinal stromal tumours (GIST), normally located in the stomach or small intestine, are known as one of the most common mesenchymal tumours found throughout the alimentary canal [1]. According to the SEER registry, the reported ten-year time horizon average annual GIST incidence in the United States was 0.32 per 100,000, fifteen-year limited duration was 1.62 per 100,00, and 3-year survival was 73% [2]. GIST main origin is from the interstitial cells of cajal, which are ultimately referred to as the pacemaker cells of the gastrointestinal tract. It is due to a gain of function mutation of the c-kit receptor tyrosine kinase that ultimately gives rise to GISTS [3]. These tumours have been identified to respond to tyrosine kinase inhibitors. However, if drug resistance develops, difficulties arise as continuous efforts are made to prevent further malignant progression [4].

Additionally, GIST with a higher mitotic index are known to have an increased risk of recurrence [5]. As surgical resection with negative margins remains to be the standard curative treatment of GIST, management of the disease may become difficult with respect to high recurrence rates [5]. Notably, about two-thirds of patients with recurrent disease have liver metastases while approximately half have peritoneal disease [6]. Here we present a case conducted at an academic institution debulking a recurrent GIST that had progressed while on TKIs with the goal of pain alleviation. The work has been reported in line with the SCARE criteria [7].

2. Case report

The patient is a 52-year-old African American male with a past medical history of gastric GIST diagnosed and resected two years prior to presentation. Primary surgical management included a partial gastrectomy, distal pancreatectomy, and splenectomy. The GIST was initially diagnosed after a ten-year prodrome of paroxysmal nausea and vomiting that further led to multiple visits to the emer-

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Emergency department at other institutions. The patient underwent a number of tests, which included computed tomography (CT) scans, esophagogastroduodenoscopy (EGD), and colonoscopies, with no untoward findings. On this presentation he walked into the emergency department complaining of worsening diffuse abdominal pain, weakness and fatigue for one week. He endorsed some nausea but denied vomiting, fever, chills or any other complaints. Flatus and bowel movements were noted. Patient stated that he was on Gleevec 800 mg a day without any response and as a result, he was changed to sunitinib, but the disease continued to progress. A proper work-up revealed a recent history of a negative colonoscopy along with a pertinent family history signifying multiple cancers in his maternal lineage, notably pancreatic, breast, and lung. Computed tomography (CT) of the abdomen and pelvis was done which showed severe metastatic disease with carcinomatosis, multiple dilated loops of small bowel in the left hemiabdomen without discrete transition point with the distal small bowel demonstrating a collapsed appearance, suggesting ileus versus early/partial small bowel obstruction (Figs. 1, 2). There was also caucercous ascites identified on the CT images. There was a mass effect on the intrahepatic vasculature, interval worsening of mesenteric and omental metastatic disease with associated mass effect on adjacent structures including substantial mass effect on the left hepatic lobe. Throughout his hospital course with the concomitant use of antiemetics and a nasogastric tube, the patient’s obstructive symptoms continued to worsen. Seventeen days after his admission to the hospital, the decision for surgical intervention was made. This decision was based on specific criteria for debulking at our institute which included prior chemotherapy with Gleevec, use of a second line therapy, a minimum of 12 cycles of chemotherapy prior, and the disease must be confined to only the abdomen. The primary focus of the operation was tumour debulking, pain alleviation, and bowel decompression.

The procedure was done by the institution’s hepatobiliary surgeon. In the operating room (OR), it was noted the tumour was adhered to multiple viscera, including the colon and the small intestine. The tumour seemed to be divided into three subregions or three lobes which included the stomach, the liver, and the duodenum as well as the centre of the abdominal cavity over the small bowel. The tumour also invaded the left paracolic gutter and colon, the right colon, and the right abdominal wall. Debulking was achieved in segments. Distal portions of the small intestine were also adhered to the mass. Multiple nodules within the root of the mesentery were also noted. With the tumour burden decreased, more visualization of the small intestine was accomplished. The terminal ileum, cecum, appendix and transverse colon were transected. The distal aspect of the left colon and rectum were unaffected; therefore, they were left in place. The terminal ileum, which was previously transected, was brought up as an endileostomy in the right lower quadrant. Two end-block resections of tumours had an additive measure of $32 \times 27 \times 15.5$ cm (Fig. 3). Within 6 days of the operation, the patient had reported that the pain was overall decreased and better managed with pain medication. The decision was made to advance to a regular diet, which the patient had tolerated well. Although the patient experienced episodes of nausea, the patient had not experienced any episodes of vomiting.

Ultimately the patient was discharged on postoperative day seventeen with complete diet tolerance and placed in the care of the oncologist to manage his response to regorafenib. After six weeks of taking regorafenib 80 mg oral daily, the patient experienced an episode of gastrointestinal bleeding, which was most likely due to
shrinking of the GIST. Nine days after the event, the patient safely resumed regorafenib 80 mg oral tablets daily. Even more important postoperatively the patient stated a significant decrease in pain and abdominal distention, with activities of daily living more easily accomplished. The patient was placed in the care of the oncologist with follow up scheduled for medical management.

3. Discussion

Gastrointestinal stromal tumours (GISTs) are known as one of the most common mesenchymal tumours found throughout the alimentary tract, arising most frequently in the stomach or small intestine [1]. The incidence of GIST ranges from 11 to 15 per million per year, although evidence may reveal that such numbers may be undervalued [8]. They were described for the first time in 1983 by Mazur and Clark, and in 1988 were broadly acknowledged by the discovery of its c-kit (CD117) mutation from Hirota [9]. The GIST’s origin is primarily from the smooth muscle layer of the alimentary tract [8]. The identifiable factors of a GIST include an activating mutation in either the c-kit, as mentioned before, or the platelet-derived growth factor receptor α (PDGFRα) gene [8].

Whilst a majority of GISTs are secondary to sporadic mutations, there have been documented cases of familial germline mutations in the KIT or PDGFRα proto-oncogenes [8].

The diagnosis of an upper abdominal mass is initially seen via a computed tomography (CT) scan, followed by an upper endoscopy. Comparatively, an upper endoscopy can characterize a submucosal tumour with or without central necrosis, while CT imaging allows for the exposure of well-defined and highly vascular tumours (Fig. 4). If necessary, a biopsy of the lesion may be utilized, but it is not customarily suggested [8].

Treatment modalities range from medical to surgical, with the latter being our main point of focus. Treatment outcomes for recurrent metastatic tumours have been improved, with respect to the recent advances in targeted molecular therapy imatinib, sunitinib, and regorafenib [1]. With considerations to the surgical treatment approach of GISTS, it is important to note the recurrence rates. Furthermore, a literature review revealed a statistically significant difference in the relapse occurrence in a GIST greater than 5 cm and in GIST with more than 5 mitosis per 50 high power field (HPF) [9].

According to Du et al., there was a significant rise in the two-year progression-free survival in patients with advanced GISTS who had residual lesions after imatinib therapy, thus requiring surgery (88.4%) compared to those who solely receiving imatinib therapy (57.7%) [10]. Our patient was considered an ultra-high-risk disease in the setting of c-kit positive, PDGFRα negative, discovered on GIST 1 positive (DOG 1+), along with a high mitotic activity with 6 mitoses per high-power field. After progressive side effects and poor response to chemotherapy agents Imatinib and Sunitinib, surgical management was ultimately considered.

A further study by Raut et al. of 69 patients with GISTS that underwent surgical debulking in addition to imatinib therapy revealed a prolonged overall survival [11]. This study highlighted, the approach of surgical debulking combined with kinase-directed therapy stemmed a median postoperative progression free survival of 7.7 months in cases with limited disease progression, thus contributing to an overall survival of 29.8 months [11]. This study concluded that the effectiveness of first-line systemic therapy with imatinib in patients with advanced GISTS may be prolonged if surgical debulking is considered [11]. This was very relevant to our case, as marginal extensions of the tumour were noted to include the liver, left colon, right colon, and abdominal wall. Debunking this large mass significantly reduced tumour burden and thus promoted to an overall increase in chemotherapeutic effectivity.

4. Conclusion

We present a case of a 52-year-old male with a Gastrointestinal stromal tumour (GIST) that was refractory to Imatinib and Sunitinib. This case serves as an example of the importance of surgical debulking in addition to molecular therapy for patients with severely extensive GISTS. In addition to the molecular therapy with Imatinib, Sunitinib, or Regorafenib, tumour debulking is also of importance to decrease tumour burden. This promotes a better chemotherapy response, decrease in pain and obstructive symptoms, increase in activity of daily living, thus overall leading to a better quality of life. It is important to keep the option of debulking available, despite gross metastatic disease, in patients with poor outcomes solely on pharmacologic therapy alone.

Declaration of Competing Interest

The authors report no declarations of interest.

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Ethical approval

This case report is exempt from ethical approval by our institution.

Consent

No identifiable factors were utilised in this case.
Author contribution

Henrik Ghantarchyan: (1) wrote the case report; (2) revised and edited the case report (3) approved the final version of the case report.

Tyrell Daniel: (1) assisted in writing the case report; (2) revised and edited the case report; (3) approved the final version of the case report.

Dr. Manrique A. Guererro: (1) participated in the patient care; (2) assisted in writing the case report; (3) revised and edited the case report; (4) approved the final version of the case report.

Dr. John Perrone: (1) revised and edited the case report; (2) approved the final version of the case report.

Dr. Paul Hanna: (1) participated in the patient care; (2) revised and edited the case report; (3) approved the final version of the case report.

Dr. Jamshed Zuberi (1) revised and edited the case report (2) approved the final version of the case report.

Dr. Derick J. Christian: (1) participated in the patient care; (2) approved the final version.

Registration of research studies

This is not a ‘first in humans’ report, so it is not in need of registration.

Guarantor

Henrik Ghantarchyan.

Provenance and peer review

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Data sharing policy

The authors declare that data supporting the findings of this study are available within the article (and its supplementary files).

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