

Recurrent Gastrointestinal Stromal Tumour (GIST) in a 35-Year-Old Patient with a History of Glioblastoma: A Rare Case Report

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ABSTRACT

Introduction: Gastrointestinal stromal tumours (GIST) are the most common mesenchymal neoplasms of the gastrointestinal tract with malignant potential. However, uncommonly, they can be associated with synchronous tumours of different histogenesis. We herein report a case of gastric GIST with synchronous tumors Glioblastoma. **Case Presentation:** A 35-year-old male patient presented with bloating and abdominal distention for the past week. The patient had experienced a weight loss of 10 kg over the past 3 months. He has a history of laparotomy for ileum tumour resection in January 2024. Immunohistochemistry study confirmed CD117-positive, referred to GIST. Previously, he also underwent craniotomy for brain tumour removal in December 2023 due to sarcomatoid glioblastoma. Abdominal CT scan indicated a recurrent mass at the previous surgical site; we performed tumour resection and functional end-to-end anastomosis. The patient was discharged 4 days after the surgery. During follow-up, he was planned to initiate imatinib for GIST and concurrent radiotherapy with temozolomide for GBM. **Conclusions:** GISTs are the commonest gastrointestinal mesenchymal tumours but are very rarely associated with Glioblastoma. There was not much literature found on this coincidence. The first treatment of both is surgery, followed by Tyrosine kinase inhibitors for ileal GIST and radiotherapy concomitant with chemotherapy in Glioblastoma.

Keywords: gastrointestinal stromal tumor (GIST); glioblastoma (GBM); surgical resection; chemotherapy

INTRODUCTION

Gastrointestinal stromal tumour (GIST) is the term applied to the group of morphologically spindle-cell or mesenchymal tumours of the gastrointestinal tract and abdomen. These tumours are the most common of the mesenchymal neoplasms in the gastrointestinal tract. This rare mesenchymal tumour accounts for only 1-3% of all gastrointestinal malignancies, and it is predominantly located in the stomach (60%). GIST in the ileum represents around 30% of all gastrointestinal stromal tumours.^{1,2}

The incidence of clinical GIST, symptomatic GIST, or GIST requiring treatment is assumed to be 6-22 cases per million per year.³ GIST occurs mainly in adults with a median age at diagnosis of 65-65 years. The incidence of GIST among young adults under 40 is exceedingly rare.^{4,5}

The presentation of GIST is nonspecific and varies from abdominal pain, gastric ulcer, gastrointestinal bleeding, palpable mass, and incidental finding from imaging studies. Malignant cases can show liver

metastases, peritoneal dissemination, and, less frequently, lung, bone, brain, pleura, and lymph node involvement. The diagnosis of GIST is based on morphology, positive immunohistochemistry (IHC) results for CD117 and DOG1, and mutation analyses of KIT and PDGFRA (platelet-derived growth factor receptor-alpha polypeptide gene).^{6,7} However, uncommonly, they can be associated with synchronous tumours of different histogenesis.

Total resection is possible in about 85% of patients, and 50% of patients experience recurrence after complete resection. The median time for recurrence following the resection of a primary GIST is two years, and the five-year survival rate is roughly 50%.⁸

In this report, we present a case of recurrent GIST originating from the ileum in a 35-year-old male patient with a history of synchronous glioblastoma. This primary tumour was discovered approximately 1 month before the diagnosis of GIST.

Case Presentation

On April 18, 2024, a 35-year-old male patient presented to the digestive surgery outpatient clinic complaining of difficulty in bowel movements for the past week. The patient also experienced abdominal distension accompanied by intermittent abdominal pain. The last bowel movement was reported a week ago, but flatus was still passable, with no complaints of urinary urgency. The patient had lost 10 kg over the past 3 months. Previously, the patient underwent Craniotomy for tumour removal on December 11, 2023, at Prof Ngoerah General Hospital, due to seizures accompanied by hemiparesis. Pathological analysis revealed sarcomatoid glioblastoma. Additionally, in January 2024, the patient underwent laparotomy for ileum tumour resection + anastomosis at a regional general hospital, with histopathology results indicating Malignant Round Cell tumor, possibly Non-Hodgkin Lymphoma and Gastrointestinal Stromal Tumor (GIST). The patient awaited results from immunohistochemistry (IHC), which were available on April 26, 2024, confirming epithelioid GIST (DOG1: positive, patchy and CD117 (C-Kit): Negative).

A contrast-enhanced CT scan of the abdomen (picture 1) revealed a lobulated cystic-solid mass with septations in the left dominant pelvic cavity, suggestive of a recurrent malignant mass suspected to have infiltrated part of the small intestine and the anterior wall of the bladder, causing partial obstruction of the small bowel up to the terminal ileum. Due to no improvement with conservative management, surgery was performed on April 20, 2024. During laparotomy exploration, a 4x4 cm mass was found at the ileum anastomosis, suspected to be a recurrent mass (picture 2), followed by ileum resection with ileo-ileal side-to-side anastomosis. Pathological examination confirmed epithelioid GIST, indicating a recurrent mass. The patient was hospitalised for 5 days postoperatively, with restored bowel movements and flatus, and was given a milk diet.

During follow-up at the digestive outpatient clinic, the patient was referred to the Hematology-Oncology department for further management. It was planned to initiate imatinib 400 mg once daily for epithelioid GIST and concurrent radiotherapy with temozolomide for sarcomatoid glioblastoma.



FIGURE 1: The CT scan indicated that the tumour was located in the ileum (red arrow).



FIGURE 2: A mass was found at the Ileum Anastomosis site, and resection was performed.

DISCUSSION

Gastrointestinal stromal tumour (GIST) is the term applied to the group of morphologically spindle-cell or mesenchymal tumours of the gastrointestinal tract and abdomen. These tumours are the result of a mutation of the gene encoding type III receptor tyrosine kinase. Most GISTs are related to activating somatic, mutually exclusive mutations of two genes, KIT and PDGFRA (platelet-derived growth factor receptor- α polypeptide gene), which are early oncogenic events during GIST development.^{4,9} Histologically, GIST is composed of the following: spindle cells (70%), epithelioid cells (20%), mixed spindle and epithelioid cells (10%).⁶

Gastrointestinal stromal tumours have been reported in all age groups, with a predominance in adults older than 50. These tumours can occur throughout the gastrointestinal tract; the most common locations are stomach (60%), jejunum and ileum (30%), colorectum (5%), and duodenum (5%).² Multiple retrospective studies have been conducted to find out prognostic factors affecting survival; however, no uniform staging system has been formulated, probably due to the rarity of the disease. The aggressiveness of GIST depends on the size, mitotic index of GIST, anatomic site of involvement, and patient's age.^{10,11}

There are no symptoms or signs specific to GIST. Clinical presentation of GIST is generally an incidental radiological finding when a patient is investigated for nonspecific symptoms such as abdominal pain, bloating, fatigue secondary to anaemia, loss of weight, obstruction, upper or lower gastrointestinal bleeding or melena. GIST can also present as an emergent idiopathic spontaneous intra-abdominal haemorrhage or, in some cases, may be present with a palpable abdominal lump.^{2,3} The size of GIST tumor is ranging from 0.6 – 25.5 cm, with a median size of 6.8 cm. Large tumours can cause mass effects and give symptoms like obstruction or compression of the gastrointestinal tract, leading to early satiety, change in bowel habits, dysphagia, and jaundice. Rupture of the tumour can lead to internal bleeding and peritonitis.^{4,12} Patients with GIST seem to have an increased risk of developing a secondary malignant neoplasm. The most common related tumours are gastrointestinal carcinoma, lymphoma/leukemia, carcinomas of prostate, breast, kidney, lung, female genital tract, soft tissue and bone sarcomas, malignant melanoma, and seminoma.⁷

Computed tomography (CT) scan usually describes GIST as a solid mass with smooth contour and bright enhancement following intravenous iodine-based contrast. Magnetic resonance imaging (MRI) is an alternative for patients unable to receive intravenous iodine contrast. Esophagogastroduodenoscopy (EGD) is typically performed in patients with gastrointestinal bleeding. Positron emission tomography (PET) scan using fluorodeoxyglucose (FDG) can help localise a GIST primary or to clarify uncertain findings on CT scan.^{3,13} Immunohistochemistry assays of GIST are usually

positive (CD117 and C-KIT). Normally, in 99% of the cases of GIST, DOG1 is expressed. These assays are specific to the GIST diagnosis and confirmation.⁴

The localised cases of GIST should be treated with surgery (surgical resection) as it is the essential and only potentially curative modality. The principles of surgery in GIST cases include macroscopic complete resection and functional preservation of resected organs, ideally by wedge resection. Tumours in the small bowel or colorectum, and especially those arising in the oesophagus or duodenum, may require more radical resection. Generally, in GIST with pathologically enlarged nodes, lymphadenectomy must be considered. En bloc resection of adjacent organs may sometimes be necessary for large tumours with direct invasion into these structures.^{3,9}

Tyrosine kinase inhibitors (TKI) are the primary choice for unresectable, advanced, metastatic or recurrent GIST. Currently, there are five TKIs, such as imatinib, sunitinib, regorafenib, ripretinib, and avapritinib. Imatinib mesylate, a small-molecule selective inhibitor of receptor tyrosine kinase, has revolutionised the therapy of advanced (inoperable and/or metastatic) GIST, and subsequently imatinib was applied in adjuvant therapy after resection of high-risk GIST. When patients have a significant risk of recurrence, imatinib adjuvant therapy is indicated after R0/R1 surgery. Recurrent GIST with conventional KIT or PDGFRA mutations are initially treated with imatinib, and when resistance or tolerance to imatinib develops, sunitinib serves as the second-line therapy.^{3,9,14} Imatinib also has already established a role in the neoadjuvant setting for downsizing the tumour size, subsequently decreasing the morbidity and increasing the chances of a negative margin. Preoperative imatinib as neoadjuvant therapy is recommended when the GIST is large, when it is more than 10 cm, and/or is considered marginally respectable on technical grounds and location. The neoadjuvant therapy period may be between 6 and 12 months and should not exceed 1 year. The five-year survival before introduction of imatinib has been reported between 28 – 35%.^{10,13}

Many studies have reported a variable effect of age and gender on the survival of GIST patients. Large cancer registry-based studies have reported better survival for younger age and female gender. Older patients had poor overall survival.¹⁰ The survival rate depends on several factors, which include risk category or stage of the GIST, the type of treatment the patient received and recurrence of GIST after treatment. Other independent factors such as tumour rupture and lymph node involvement may predict response to treatment.^{11,15}

GIST is very rarely associated with glioblastoma (GBM). There was not much literature found on this coincidence. Glioblastoma is an aggressive and fast-growing brain tumour that is classified as a high-grade glioma, grade IV astrocytoma. Affected brain tissue usually does not spread to distant organs,

although nearby brain tissue can be invaded.¹⁶ The tumour manifests itself predominantly in patients aged 55-85. Incidence rates increase with age up to 80-85 years. The incidence of GBM is 3.21 per 100,000 people. It is more common in men than women.^{16,17}

Risk factors for GBM onset are still unknown. The increased incidence of this tumour raises the issue of environmental risk factors (vinyl chloride, pesticides, smoking, petroleum refining, and synthetic rubber). Clinical presentation depends on the tumour location and size at diagnosis.^{18,19} Symptoms of GBM include recurring headache, fatigue, confusion, double vision, vomiting and drowsiness, before progressing to more neurologically distinctive ones such as seizures and motor deficits. Patients may also complain of changes in mood and attitude, in thinking and learning capabilities.^{16,17}

The classic feature of GBM is a ring-enhancing intra-axial lesion on MRI or CT scan. The diagnosis of GBM is easily made on surgical resections or biopsy samples. In immunohistochemistry, GBMs are defined by their Isocitrate dehydrogenase (IDH) status, dividing this entity into glioblastoma IDH-mutant or IDH-wild type.^{18,19}

Surgery is the first-line therapy for GBM, and gross total resection (GTR) improves survival. Postoperative radiotherapy plus concomitant chemotherapy with temozolamide (TMZ) for six weeks and adjuvant chemotherapy of six cycles with an alkylating agent has also been the standard treatment. GBM has a very poor outcome, as the estimated median survival period is 12-15 months and the 5-year survival rate is 5.6%.^{20,21}

CONCLUSIONS

Gastrointestinal stromal tumours (GIST) are rare mesenchymal tumours that originate from the gastrointestinal tract. This tumour can be asymptomatic and have a variety of clinical presentations when they are large or rapidly growing. GIST are diagnosed by imaging or post-operative studies. For primary, non-metastatic GIST, radical resection is the main treatment. The treatment of unresectable and recurrent GIST is mainly based on TKI administration. GIST is rarely associated with glioblastoma (GBM). There was not much literature found on this coincidence. Glioblastoma is the most aggressive type of brain tumour. The symptoms of GBM can vary depending on the location of the tumour in the brain. The standard treatment for GBM is a combination of surgery and chemotherapy tumour.

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