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# CASE REPORT

## Gastrointestinal stromal tumour in a jejunal diverticulum: The eighth reported case worldwide with a brief review of the literature

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*Abstract*

Jejunal diverticulosis is uncommon and so are gastrointestinal stromal tumours (GIST) arising in the jejunum. GIST arising in a jejunal diverticulum is a rarity and to date there are only 7 cases in the English literature. Our case of GIST occurring in a jejunal diverticulum of a 48-year-old lady would be the first reported in Malaysia and the 8th in the world. As in most cases, the clinical presentation and radiological findings of this patient were non-specific. With a history of acute abdominal pain, vomiting and fever, the patient was provisionally diagnosed as a case of twisted ovarian cyst and subjected to laparotomy. An intact roundish jejunal diverticulum 5.0 cm x 5.0 cm, about 50 cm distal to the duodeno-jejunal junction was found and resected with a segment of small intestine. Microscopic examination showed a tumour of the cut open diverticular wall, with epithelioid to spindled cells, demonstrating a mitotic rate of 1-2 per 5 $mm^2$, confined to, while infiltrating the wall of the diverticulum. The immunohistochemical profile of positive staining for CD117, DOG-1, smooth muscle actin and CD34, and negative expression of desmin and S100 protein, clinched the diagnosis of GIST. Based on the AFIP Criteria for risk stratification,[1] the patient was categorised as having moderate risk for disease progression, and was not offered further targeted imatinib as an immediate measure. The patient has remained well at the time of writing i.e. 8 months following excision, and continues on active surveillance by the surgical and oncological teams, with the option of imatinib, should the necessity arise. This case is presented not merely for the sake of documenting its rarity, but as a reminder to stay alert for uncommon conditions in histopathology practice.

*Keywords:* gastrointestinal stromal tumour, GIST, jejunum, diverticulum

### INTRODUCTION

Jejunal diverticulosis is an uncommon condition, with rates reported as between 0.02% to 4.6%.[2-6] Gastrointestinal stromal tumours (GIST) are rare mesenchymal tumours of the gastrointestinal tract, with an incidence of 10-15 / 1000000 worldwide.[5,6] Furthermore most patients present with masses in the stomach and definitely less frequently in the intestines. Therefore, GIST arising in a jejunal diverticulum is a rarity. To the best of our knowledge, there are only 7 cases reported to date in the English literature.[7-13] Hence, we present here a case of GIST discovered in a jejunal diverticulum, the first case recorded in Malaysia and the 8th in the worldwide literature.

### CASE REPORT

A 48-year-old woman with no history of any significant past illnesses presented at the emergency department of the University of Malaya Medical Centre with complaints of acute left lower abdominal pain for 3 days, and which was associated with episodes of fever and vomiting. The pain was intermittent and not relieved by analgesia or rest. There was no other associated symptom e.g. vaginal bleeding or tarry and bloody stools, noted. Blood investigations revealed leucocytosis with elevated serum C-reactive protein at 171 mg/$dL^3$. Computerised tomography revealed a large cyst at the left adnexa with no sign of solid enhancement or perforation. A diagnosis of twisted ovarian cyst

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was made and an emergency exploratory midline laparotomy was performed. Intra-operatively, an intact roundish jejunal diverticulum 5.0 cm x 5.0 cm with a narrow base (Figure 1) was identified. This was located about 50 cm distal to the duodeno-jejunal junction. The remaining small and large intestines, appendix, liver, peritoneum, and genital tract did not exhibit any significant abnormality. Together with the diverticulum, the small intestine was segmentally resected and this was followed by primary anastomosis. The resected small intestine revealed an intact diverticulum filled with necrotic and haemorrhagic material. The diverticulum had an irregular wall thickness of 0.2 cm to 1.0 cm, but with an absence of any obvious nodules. The wall was brownish to yellowish and soft to firm, with no clear delineated tumour seen.

Microscopically, a GIST arising in a jejunal diverticulum was confirmed and the tumour involved the diverticular wall. Most of the wall of the diverticulum demonstrated an infiltrating cellular tumour which had focally ulcerated the diverticular mucosa, but still confined within the diverticulum and had not infiltrated into the surrounding intestine. In few areas, the diverticulum still retained layers of the intestinal wall implying the tumour had indeed arisen from a true diverticulum of the jejunum. The neoplastic cells were epithelioid to spindled and exhibited moderate nuclear atypia and mitotic rate of 1-2 per 5 $mm^2$ (1-2/ 50 high power fields as per Miettinen *et al*.[1]). Focal tumour giant cells and necrosis of the tumour were also observed. Immunohistochemically, the neoplastic cells expressed strong positivity for CD117, DOG1, smooth muscle actin and CD34, but not S100 protein and desmin (Figure 2). The tumour was confined to the diverticulum and the surgical margins of the resected intestine were clear. The tumour was categorised as having moderate risk for disease progression (metastases and tumour related death) based on the widely used risk assessment criteria for GIST of United States Armed forces Institute of Pathology (AFIP).[1] The patient was not offered further targeted imatinib. The patient has remained well at the time of writing i.e. 8 months following excision, and continues on active surveillance by the surgical and oncological teams.

## DISCUSSION

Unlike the congenital Meckel diverticulum which is the most common diverticulum in this area, diverticulosis in the jejunum, as earlier stated, is rare. Like a Meckel diverticulum, most jejunal diverticula are also asymptomatic with only less than 10% of the cases developing complications such as bleeding, mucosal ulceration, inflammation, perforation, or obstruction e.g from volvulus[14], which then clinically highlight their existence. In this case, the patient gave no history of any complaint which may have been related to any of the above complications in the past, making it possible that the patient's diverticulosis had remained asymptomatic till this present event.

In comparison with the common adenocarcinomas, mesenchymal tumours are rare in the gastrointestinal tract[15], ranging from benign (e.g. leiomyoma, lipoma, haemangioma etc) to various sarcomas. Nevertheless, gastrointestinal stromal tumour (GIST), derived

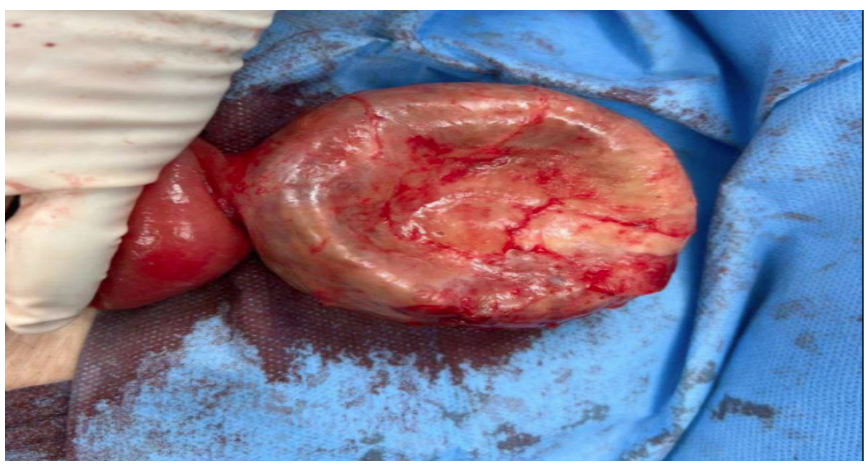

FIG. 1. Intraoperatively, a jejunal diverticulum with a narrow base, arising 50 cm distal to the duodeno-jejunal junction, was identified.

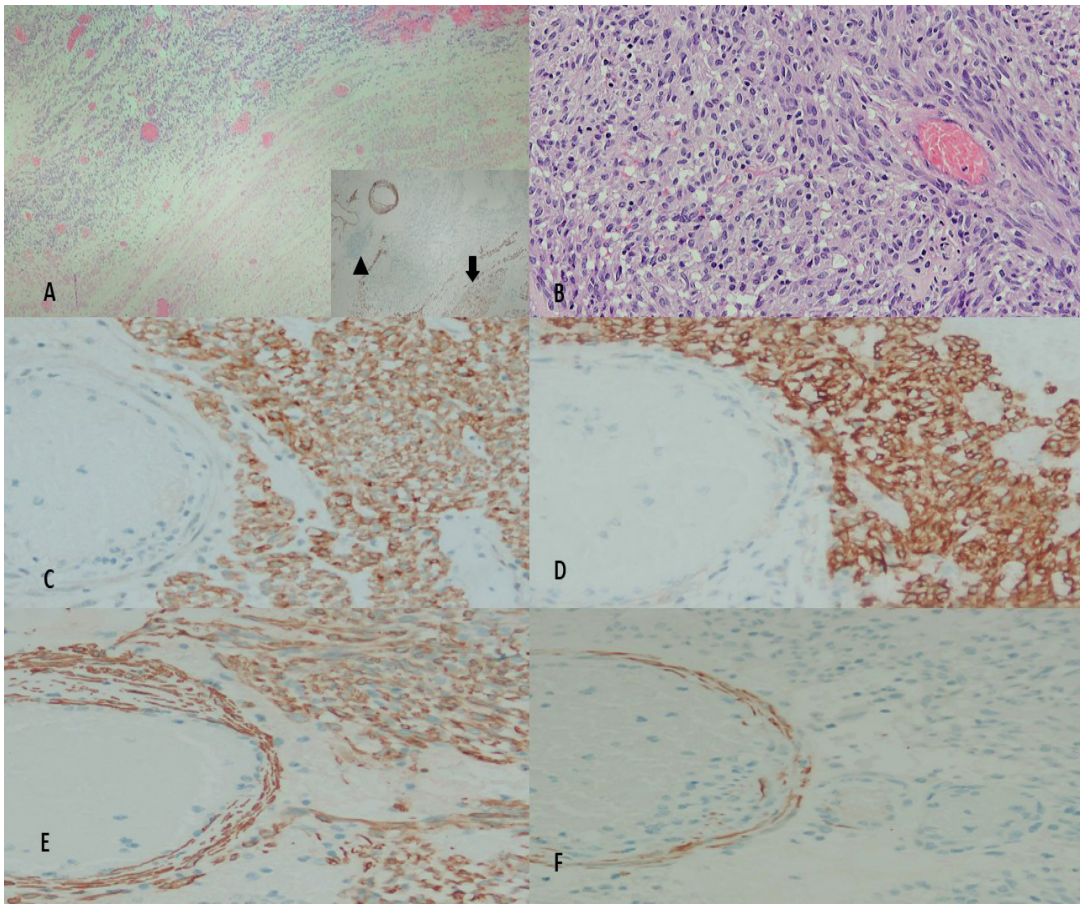


FIG. 2. Histomorphology and immunophenotype of the case: (A) the tumour infiltrating the diverticulum (H+E) with the inset showing tumour without desmin expression (arrowhead) and desmin highlighting the attenuated muscular layer of the jejunal wall (arrow); (B) the tumour at higher magnification (H+E x200) showing proliferation of spindled neoplastic cells with mild to moderate nuclear atypia; and (C) the neoplastic cells demonstrating CD117; (D) DOG-1; and (E) smooth muscle actin expression; (F) but not desmin.

from the interstitial cells of Cajal[15], is the most common primary mesenchymal tumour of the gastrointestinal tract. For GIST, the stomach is the most frequently involved site (approximately 60%), followed by 30% arising in the jejunum, 5% ileum, 4% rectum, 1-2% in the rest of the colon and appendix, and less than 1% in the oesophagus.[1] Non-specific symptoms of abdominal pain, or symptoms related to bleeding, mucosal ulceration, intestinal obstruction or perforation appear to be the common clinical presentations of GIST. The tumour frequently involves the submucosa and mucosa of the gastrointestinal tract resulting in endoluminal tumours. Invasion of the subserosa can take place with resultant exoluminal tumours and if there is invasion both luminally and extraluminally, the tumour can appear like a dumb-bell. The tumours can also completely remain intramurally.[12,16] Most GISTs are sporadic and harbour gain-of-function mutations of *KIT or PDGFRA,* which are mutually exclusive. However, 10-12% of adult GISTs are of wild-type *KIT and PDGFRA*. Instead, these latter wild-type *KIT and PDGFRA GISTs* can be associated with mutations in BRAF, NF1, RAS, NTRK3 or subunits of the succinate dehydrogenase (SDH) complex.[17]

This particular case of GIST developing in a jejunal diverticulum is thus extremely rare and interesting, and to the best of our knowledge, probably the first case recorded in Malaysia and the 8th in the worldwide English literature.[7-13] To date, an extensive review of the English-language literature has revealed only 7 documented cases of GIST in a jejunal diverticulum.[7-13] Pertinent information retrieved from the 7 documented reports is summarised in Table 1. The cases were aged between 22 to 69-years, with almost equal

**TABLE 1: Cases of reported gastrointestinal tumours in jejunal diverticula**

| | Clinical presentation | Provisional diagnosis | Operative findings | Final diagnosis and risk stratification | Imatinib treatment | Outcome |
|---|---|---|---|---|---|---|
| Chung D, 2021 [7] | 69, female, abdominal pain, vomiting, constipation low-grade fever. | Perforated gut with peritonitis | Perforated jejunal diverticulum, 5.5 cm x 4.0 cm, 30 cm from duodenojejunal flexure | GIST (*risk not stated) | No | Well 6 weeks post-surgery. |
| Arata *et al*, 2020 [12] | 46, male, abdominal pain. | Perforated gut with peritonitis | Perforated jejunal diverticulum, 7.0 cm x 6.5 cm, at antimesenteric border. | GIST (high risk) | Yes | No recurrence at follow-up (duration of follow-up unavailable). |
| Petroianu *et al*, 2016 [10] | 59, male, abdominal pain vomiting | Intestinal obstruction caused by intestinal tumour. | Perforated jejunal diverticulum, 8.0 cm x 4.5 cm, 80 cm from Treitz ligament. | GIST (risk not stated) | Yes | Jejunal and peritoneal recurrence at 1-year. Lesions resected and patient remained well 38-months after second operation. |
| Shoji *et al*, 2014[11] | 61, male, abdominal pain nausea. | Perforated gut with peritonitis | Perforated jejunal diverticulum, 5.9 cm x 5.3 cm, at antimesenteric border, 40 cm from Treitz's ligament | GIST (moderate risk, managed as "malignant" due to perforation) | Yes | Follow-up information unavailable. |
| Jaykar *et al*, 2013 [8] | 58, male, abdominal pain vomiting fever. | Perforated gut with peritonitis | Perforated jejunal diverticulum, 3.0 cm x 2.0 cm 15-20cm from duodenojejunal flexure | GIST ("benign") | Information unavailable | Follow-up information unavailable. |
| Sadaf *et al*, 2010 [13] | 22, female, melaena | Small bowel tumour in diverticulum. | Tumour in non-perforated jejunal diverticulum, 4.0 cm x 4.0 cm, at anti-mesenteric border. | GIST (low risk) | No | Well 9 months post-surgery. |
| Schepers *et al*, 2009 [9] | 56, female. Information unavailable | Information unavailable | Tumour in jejunal diverticulum. No further information available | GIST (risk not stated) | Information unavailable | Follow-up information unavailable. |

*United States of America Armed Forces Institute of Pathology Risk Stratification criteria[1]

gender distribution with 4 males and 3 females. Abdominal pain appeared to be the most common presentation, and our patient's condition was also brought to light by the severe abdominal pain she suffered. At least 5 of the cases reported so far had perforated their jejunum on presentation. Our patient was fortunate that she presented prior to any perforation occurring. Tumour perforation is known to be associated with high risk for disease relapse.[18] Surgical resection remained the mainstay of management and adjuvant imatinib was known to be offered in 3 of the cases. The size of the diverticula ranged between 3 to 8 cm in those where the size of the diverticula were documented. Information about long-term follow-up of the cases was not well documented in most instances, except for Petroianu *et al*'s case[10] in whom disease recurrence occurred after one year, for which the patient underwent en-bloc jejunal segment resection with clearance of the mesenteric tumour nodules leaving the patient well at 38-months following the second operation.

With no specific defining symptoms, the diagnosis of GIST in a diverticulum is difficult as evidenced by at least 5 of the 7 reported cases demonstrating gut perforation at the time of presentation. Imaging e.g. computerised tomography (CT) scan or endoscopy, may at best be suggestive. However, in this case, as with many others, the diagnosis was not apparent on imaging. The patient was thus provisionally diagnosed as a twisted ovarian cyst, and the definitive diagnosis of GIST arising in a diverticulum was only confirmed after post-operative examination. The diagnosis of GIST could have been missed in this case if the sampling was not detailed and thorough. Fortunately, in this case, the cellular morphology was fairly classical and the diagnosis could be confirmed via a characteristic immunoexpression profile of the tumour. There are many risk stratification systems for GIST[19], including NIH Consensus Criteria[20], American Forces Institute of Pathology (AFIP) Criteria[1], and modified NIH Criteria (Joensuu Risk Criteria).[21] The AFIP Criteria for risk stratification proposed by Miettinen *et al*[1] is widely used, and categorises risk for metastasis and tumour-related death based on mitotic activity, tumour size and anatomical site, into the categories of none, very low, low, moderate and high risk. This tumour was classified as possessing moderate risk. Notably, risk stratification based on the AFIP Criteria above applies best to *KIT*/*PDGFRA* mutants.[15] Unfortunately, due to lack of readily available resources and financial constraints, mutational analysis as per the recommendation of the recent 2021 Clinical Practice Guideline (CPG) of the European Society for Medical Oncology (ESMO)–European Reference Network for Rare Adult Solid Cancers (EURACAN)–European Reference Network for Genetic Tumour Risk Syndromes (GENTURIS)[22] was not carried out in the final workup of this case. The patient was offered the standard treatment which was surgical resection. Based on the combined surgical-pathological-oncological consensus assessment following AFIP Criteria risk stratification[1], adjuvant imatinib was immediately advocated. Instead, the patient has been placed on close follow-up with an option for adjuvant therapy, should the need arise in the future (ESMO-EURACAN-GENTURIS CPG[22]).

## CONCLUSION

In summary, this rare case documents a GIST arising in a jejunal diverticulum; the first case reported in Malaysia and the 8th documented case in the English literature so far. Although the clinical presentation of the tumour was, as expectedly non-specific, its histological features and immunohistochemical profile were nevertheless characteristic. We report this case to ensure vigilance, particularly as jejunal GISTS are generally more aggressive than its more common counterpart in the stomach, and its recognition is important.

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*Conflict of interest:* The authors declare no conflict of interest.

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