Research Article

Symptoms Contributing to the Diagnosis of Small Bowel Tumors

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Short Title: Characteristics of small bowel tumors

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Abstract

Introduction: Small bowel tumors (SBTs) are difficult to diagnose because of limited opportunities and technical difficulties in evaluating the small bowel. Asymptomatic conditions or nonspecific symptoms make SBT diagnosis more challenging. In Asia, SBTs are reported to be more frequently malignant lymphoma (ML), adenocarcinoma, and gastrointestinal stromal tumor (GIST). In this study, we examined 66 patients diagnosed with SBTs and determined their clinical characteristics.

Methods: This retrospective study was conducted from January 2013 to July 2020 at Kurume University Hospital. The modalities used to detect SBTs were computed tomography (CT), positron emission tomography, magnetic resonance imaging, and ultrasonography. Endoscopy was also performed in some cases to confirm SBT diagnosis. The study included 66 patients. The medical data collected included presenting symptoms, tumor location, underlying condition, diagnostic modalities, pathologic diagnosis, and treatment.

Results: ML and adenocarcinoma were the most common tumors (22.7%), followed by GIST (21.2%) and metastatic SBT (18.2%). Symptoms that led to SBT detection were abdominal pain (44.5%), asymptomatic conditions (28.8%), hematochezia (12.1%), and anemia (10.6%). CT was the most used modality to detect SBTs. Nineteen patients were asymptomatic, and SBTs were incidentally detected in them. GISTs and benign tumors were more often asymptomatic than other malignant tumors.

Discussion/Conclusion: Abdominal pain was the main symptom for SBTs in particular adenocarcinoma, ML, and metastatic SBT. In addition, GIST, which was highly prevalent in Asia, had fewer symptoms. An understanding of these characteristics may be helpful in the clinical practice of SBTs.

Introduction

Small bowel tumors (SBTs) are relatively rare and account for only 3%–6% of all gastrointestinal tumors and 1%–3% of all gastrointestinal malignancies [1]. SBTs include adenocarcinomas, gastrointestinal stromal tumors (GISTs), neuroendocrine tumors (NETs), and lymphomas [2]. SBT diagnosis is often delayed because symptoms are long-term asymptomatic or nonspecific with abdominal pain, abdominal distention, fecal occult blood, nausea, or vomiting [3]. More advanced stages of tumor growth present with small bowel obstruction or perforation; however, the incidence of obstruction and perforation in SBTs remains unknown.

Early diagnosis is important for managing SBTs. The diagnostic modalities used for evaluating SBTs include endoscopy and radiographic imaging, such as computed tomography (CT) and small bowel series, or enteroclysis. Although SBTs have traditionally been evaluated using small bowel series, clinically, dynamic contrast-enhanced CT is an excellent tool for detecting and diagnosing SBTs. CT enteroclysis is also a useful modality for evaluating SBTs [1,4]. In endoscopic examination, video capsule endoscopy is effective in detecting SBTs [5,6]. In addition, double-balloon endoscopy (DBE) has improved SBT diagnosis by enabling the evaluation of the entire small bowel through detailed imaging and pathology with biopsy [7-9].

Establishing early definitive diagnosis of SBTs is crucial for early treatment and improved prognosis. Therefore, it is necessary to accumulate sufficient information on SBTs. In this study, we reviewed 66 cases of detected and diagnosed SBTs and attempted to clarify the clinical characteristics of SBTs.

Materials and Methods

Patients

In this study, we retrospectively analyzed data from a medical database from January 2013 to July 2020. The study included 66 patients. SBTs were defined as tumors or polyps between the proximal jejunum and distal ileum. The medical database was used to collect information on the clinical characteristics of each disease with respect to presenting signs and symptoms, tumor location, underlying condition, diagnostic modalities, pathologic diagnosis, and treatment. The clinical features and diagnoses in the presence or absence of symptoms were evaluated. The study protocol was reviewed and approved by the Ethics Committee of the Kurume University School of Medicine (ID 22057).

Modalities

The modalities used to detect SBTs were CT, positron emission tomography (PET), magnetic resonance imaging (MRI), and ultrasonography (US). CT was performed using Revolution CT and Discovery CT 750HD (GE Healthcare Japan, Tokyo, Japan). In FDG-PET, 18-F FDG (370–555 MBq) was intravenously injected, and scanning was initiated after 60 min. Patients were scanned using a combined PET/CT scanner (Siemens Biograph 6, high-resolution PET/CT). MRI was performed using Discovery MR 750w (GE Healthcare Japan, Tokyo, Japan). US was performed using a curvilinear probe (3.5–5 MHz). Endoscopy was performed in some cases to confirm SBT diagnosis. The DBE system (Fujinon Toshiba ES Systems Co., Ltd., Tokyo, Japan) consists of a high-resolution video endoscope (EN-450P5/20), flexible overtube, and balloon controller for inflation/deflation of the latex balloons. DBE was performed via both the oral and anal approaches.

Statistical analysis

Continuous variables are presented as mean (SD) values and were compared between two groups using the Student's t test. Categorical variables are presented as

percentages and were compared between the groups using the χ^2 test. Statistical analyses were performed using the JMP® Pro 16.0 software (SAS Institute; Cary, NC, USA). Statistical significance was set at p values <0.05.

Results

Characteristics of SBTs

This study included 66 patients with histologically confirmed SBTs. Table 1 shows the characteristics of patients with SBTs. The study included 43 male (65.2%) and 23 female (34.8%) patients. The median age of the patients was 63 years (range: 13–88 years). There was no difference in the incidence of SBTs with respect to the lesion site between the jejunum and ileum. Nine different histological types of SBTs were identified. Lymphoma and adenocarcinoma were the most common tumors (22.7%), followed by GIST (21.2%), metastatic SBT (18.2%), Peutz-Jeghers syndrome (PJS) (7.6%), and NET (3.0%). The symptoms that triggered SBT detection were abdominal pain (44.5%), asymptomatic conditions (28.8%), hematochezia (12.1%), anemia (10.6%), and vomiting (3.0%). There was no small bowel obstruction; however, small bowel perforation was observed in six cases (9.1%). CT (68.2%) was the most common examination modality used to detect SBTs, followed by endoscopy (13.6%) and PET (12.1%). Nine endoscopic examinations in which SBTs could be detected included lower gastrointestinal endoscopies. There was no increase in the number of SBTs in the 3 years from 2017 to 2020 compared with that from 2013 to 2016.

Comparison of clinical characteristics of SBTs

The clinical characteristics of each SBT are presented in Table 2. There were 15, 15, 14, 12, and 5 cases of adenocarcinoma, malignant lymphoma (ML), GIST, metastatic SBT, and PJS, respectively. ML and metastatic SBTs were predominantly identified in male patients. Most tumors were detected in patients in their 60s; however, PJS was often detected at a younger age (median 16 years old, 13–47). ML was more common in the ileum (10/15,

66.7%); however, the presence of other SBTs in the jejunum and ileum was almost equal. Most SBTs were detected with patients presenting with abdominal pain; however, GISTs were asymptomatically detected in 50% of patients (7/14) (Figure 1A). Six patients presented with perforation, three had GIST, one had adenocarcinoma, one had ML, and one had metastatic SBT. GISTs may grow asymptomatically and eventually lead to perforation. Most types of SBTs were diagnosed using CT (Figure 1B).

Comparison of SBTs with and without symptoms

Table 3 compares the characteristics of the SBTs with and without symptoms. There were no differences in sex, patient age, tumor location, diagnostic modality, or the period of diagnosis. Although there was no significant difference in tumor size, patients with symptoms tended to have larger tumors than patients without symptoms ($P<0.0744$). Furthermore, there was no difference between the type of symptoms and tumor size or cancer stage (data not shown). Most cases of adenocarcinoma, ML, metastatic SBT, and PJS were symptomatic, whereas GISTs were more often asymptomatic than other malignant tumors ($P<0.049$). Benign tumors such as adenomas, myomas, and lipomas were not symptomatic. Asymptomatic cases, namely tumors detected incidentally, had a high detection rate using CT; however, the detection rate of SBTs using other modalities such as endoscopy, PET, or MRI tended to be higher than that in patients with symptoms.

Characteristics of underlying diseases and SBTs in asymptomatic patients

Table 4 shows the characteristics of 19 patients with incidentally detected asymptomatic SBTs. Eight of the 19 patients had abnormal physical examinations: six had positive fecal occult blood, one had hematuria + proteinuria, and one had anemia. Six patients with fecal occult blood underwent total colonoscopy, where one case each of lipoma and NET was detected at the terminal ileum. CT or MRI was subsequently performed in four patients, revealing that three patients had GISTs and one had ML. The patient with hematuria and proteinuria was diagnosed as having a GIST using CT, and the patient with anemia was diagnosed as having small bowel adenocarcinoma using CT. In addition, metastatic SBT was

found in one patient each during the course of hepatocellular carcinoma and ovarian carcinoma, and GIST was found in one patient each during the course of hepatocellular carcinoma, ovarian carcinoma, and prostate carcinoma. One patient each with hepatitis C, mucocutaneous pigmentation, hemorrhoids, and post-stroke sequelae was found to have an SBT during the disease course.

Treatment for SBTs

Table 5 presents the treatment options for each SBT. For adenocarcinoma, most cases (11/15, 73.3%) were treated with surgery, while two, one, and one case underwent surgical resection + chemotherapy, chemotherapy, and BCS, respectively. For ML, chemotherapy was the main treatment, with surgical resection + chemotherapy, chemotherapy alone, and surgery alone being preferred in five, five, and four cases, respectively. For GISTs, nine patients underwent surgery, two patients underwent surgical resection + chemotherapy, and one patient each underwent chemotherapy, follow-up, and endoscopic therapy. Seven patients whose primary cancer was under control underwent surgical resection for metastatic SBT, two underwent chemotherapy, two received radiation, and one received supportive care. Four patients with PJS were surgically and one was treated endoscopically. Four patients with NET required chemotherapy after resection. Adenoma was endoscopically resected in one patient, and one each of leiomyoma and lipoma were surgically resected.

Discussion/Conclusion

Early detection and diagnosis of SBTs are difficult because SBTs have few symptoms until they progress and because of few opportunities and technical difficulties in performing small bowel examinations. Therefore, diagnosis and treatment of SBTs are usually delayed, and the consequences tend to be severe [10,11]. In our study, even with the usefulness of new modalities such as video capsule endoscopy and DBE, it was observed that there was no increase in the number of detected cases of SBTs between 2013–2016 and 2017–2020 (54.5%

vs. 45.5%). Thus, even with new modalities and improved image quality, SBT detection continues to be challenging.

A previous study showed that the most common symptoms of SBTs were bleeding and abdominal pain, including obstructive symptoms [7]. Yoo et al showed that the most common symptoms were obscure bleeding (39.3%), as well as abdominal pain and weight loss (28.6%) [12]. The clinical symptoms varied depending on clinicopathologic features of SBTs. In cases of lymphoma, abdominal pain, including obstructive symptoms, was the most common (50%), whereas obscure bleeding was the most common in GIST cases (85.7%). In our study, abdominal pain, bleeding, and anemia were observed in patients with small bowel adenocarcinoma and lymphoma. In contrast, half of the patients with GIST, NET, and lipoma were asymptomatic because the tumors are submucosal, which are less likely to cause symptoms compared with other SBTs. However, 21.4% of GISTs were perforated, and this is because GISTs in the small bowel can grow to a large size before causing symptoms and GISTs cause ulceration, cavitation, and fistulation to the small bowel [13]. Hence, the number of cases of GISTs with perforation and abdominal pain and bleeding was considered to be increasing. In this study, we were able to detect small bowel tumors in 19 patients (28.8%), even if they were asymptomatic. However, most of the cases were detected incidentally, and patients without symptom have few opportunities to reach a diagnosis. Although it is difficult to diagnose small bowel tumors at an early stage, we increase chances of diagnosing them by carefully examining and treating patients with symptoms such as abdominal pain, bloody stools, anemia, and vomiting.

Lee et al showed that the most common SBTs were GIST (n=29, 25.9%), lymphoma (n=18, 16.1%), and adenocarcinoma (n=14, 12.5%) in a Korean multicenter study [14]. In a Taiwanese study, the most common type was lymphoma (n=20, 29.0%), followed by GIST (n=19, 27.5%), adenocarcinoma (n=18, 26.1%), metastatic cancer (n=10, 14.5%), and only a few cases of NET (n=2, 0.9%) [15]. In contrast, NET was the most common type of SBTs reported in Western studies. Cangemi et al. showed that the most common type was NET (19.4%), followed by GIST (7.5%) and lymphoma (7.5%) in 1,652 DBEs [7]. Hatzaras et al

also showed that NET was the most common type of SBTs (417 cases; 33.1%), followed by adenocarcinomas (379 cases; 30.1%) [16]. Conversely, GISTs were found in only 89 cases (7.1%). In this study, as in Asian studies from Korea and Taiwan, adenocarcinoma, lymphoma, and GIST were the most typical histology of SBTs, whereas NET, which is more common in Western countries, was found in only 3% (2/67) of cases. These results indicate that the characteristics of SBTs differ among racial groups.

For ML, treatment methods such as chemotherapy and surgery have been established. Diffuse large B-cell lymphoma (DLBCL), which is the most common type of non-Hodgkin lymphoma, is a potentially curable disease with an overall recovery rate of 60–70% with front-line immunochemotherapy comprising rituximab with cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) [17]. In this study, the most common ML treated with chemotherapy was DLBCL (n=6), with all cases being treated with R-CHOP. However, non-surgical treatment options for adenocarcinomas and GIST have not yet been completely established. According to international guidelines [18,19], primary surgery is indicated for resectable localized small bowel adenocarcinoma without metastasis. In some cases, preoperative treatment may be required to render the lesion resectable. According to the National Cancer Database, adjuvant chemotherapy was associated with better overall survival of patients with adenocarcinoma compared with surgery alone [20]. The National Comprehensive Cancer Network guidelines also recommend adjuvant chemotherapy after surgery [19]. In this study, 13 patients underwent surgical resection and three received chemotherapy for colorectal cancer, with folinic acid, fluorouracil, and oxaliplatin (FOLFOX) or modified FOLFOX. For GISTs, surgery is the first line of treatment [21]. Some tumors may be treated using endoscopy. However, while endoscopy may have a short-term benefit, long-term results remain unknown [21]. One patient in this study underwent endoscopic treatment and remained free of recurrence. Imatinib, which inhibits bcr-abl tyrosine kinase activity, is the first-line treatment for GISTs. Initial clinical trials with this drug indicated that 53.7% of participants achieved a partial response [22]. Sunitinib and regorafenib can inhibit cells with mutations in other CD117 exons, and platelet-derived growth factor receptor alpha is a treatment for imatinib-resistant GISTs [23,24]. In this study, nine patients were cured by

surgical resection and three received chemotherapy with imatinib. Therefore, the treatment of SBTs has not yet been completely determined, and there is a need to continue gathering information and establish early detection and treatment methods.

This study had certain limitations. First, this was a single-center, retrospective, observational study. Second, the number of SBTs examined was small. For the early detection of SBTs, future multicenter and prospective studies will need to be conducted.

In conclusion, we observed that adenocarcinoma, ML, and GIST were the most common SBTs reported in Asian countries. In addition, the types of SBTs had different clinical characteristics. Abdominal pain was the main symptom for SBTs in particular adenocarcinoma, ML, and metastatic SBT, but GIST had fewer symptoms. An understanding of these characteristics may be helpful in the clinical practice of small intestinal tumors in Asia.

Statements

Acknowledgement (optional)

Not applicable.

Statement of Ethics

The study was conducted in accordance with the Declaration of Helsinki and approved by the Human Ethics Committee of Kurume University School of Medicine (No. 22057; 15 June 2022). Written informed consent was obtained from each patient included in the study. For children under 18 years of age, written informed consent to participate in the study was obtained from the participant's parent/legal guardian/nearest relative.

Conflict of Interest Statement

Takumi Kawaguchi received honoraria from Janssen Pharmaceutical K.K., EA Pharma Co., Ltd., Otsuka Pharmaceutical Co., Ltd., and Taisho Pharmaceutical Co., Ltd. The other authors declare no conflict of interest.

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Author Contributions

K.T. (Kozo Tsuruta), H.T., and K.M. designed the study; K.T. (Kozo Tsuruta), M.Y., K.T. (Kensuke Tomiyasu), S.Y., M.M., and K.K. performed the data collection; K.T. (Kozo Tsuruta), H.T., S.Y., and M.M. performed the data analysis; K.T. (Kozo Tsuruta), and HT drafted the manuscript; and K.M., and T.K. critically reviewed the manuscript. All authors have read and agreed to the published version of the manuscript.

Data Availability Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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Figure Legends

Figure 1 Clinical characteristics of each small bowel tumor. (A) symptoms, (B) diagnostic modalities. ML: Malignant lymphoma, GIST: gastrointestinal stromal tumor, SBT: small bowel tumor, PJS: Peutz-Jeghers syndrome, NET: neuroendocrine tumors, CT: computed tomography, PET: positron emission tomography, MRI: magnetic resonance imaging, US: ultrasonography.

Table 1. Characteristics of small bowel tumors

	All patients
Sex (M/F%)	43/23
Age at diagnosis, years	63 (13–88)
Location	
Jejunum	33 (50.0%)
Ileum	33 (50.0%)
Final diagnosis	
Adenocarcinoma	15 (22.7%)
ML	15 (22.7%)
GIST	14 (21.2%)
Metastatic SBT	12 (18.2%)
PJS	5 (7.6%)
NET	2 (3.0%)
Adenoma	1 (1.5%)
Leiomyoma	1 (1.5%)
Lipoma	1 (1.5%)
Symptoms	
Abdominal pain	30 (45.5%)
None	19 (28.8%)
Hematochezia	8 (12.1%)
Anemia	7 (10.6%)
Vomiting	2 (3.0%)
Perforation	6 (9.1%)
Diagnostic modalities	
CT	45 (68.2%)
Endoscopy	9 (13.6%)
PET	8 (12.1%)
MRI	3 (4.5%)
US	1 (1.5%)
Period of diagnosis	
2013–2016	36 (54.5%)
2017–2020	30 (45.5%)

Table 2. Characteristics of various small bowel tumors

	Adenocarcinoma (n=15)	ML (n=15)	GIST (n=14)	Metastatic SBT (n=12)	PJS (n=5)	NET (n=2)	Adenoma (n=1)	Leiomyoma (n=1)	Lipoma (n=1)	P value
Sex (M/F%)	7/8	12/3	7/7	11/1	2/3	1/1	1/0	1/0	1/0	0.149
Age at diagnosis, years	65 (40–88)	65 (21–86)	63.5 (40–77)	68 (42–86)	16 (13–47)	55.5 (50–61)	60	60	34	0.018
Location										0.433
Jejunum	7 (46.7%)	5 (33.3%)	9 (64.3%)	5 (41.7%)	4 (80.0%)	1 (50.0%)	0 (0%)	1 (100%)	0 (0%)	
Ileum	8 (53.3%)	10 (66.7%)	5 (35.7%)	7 (58.3%)	1 (20.0%)	1 (50.0%)	1 (100%)	0 (0%)	1 (100%)	
Tumor size (mm)	30 (20-60)	30 (5-150)	27.5 (10-100)	32.5 (15-90)	30 (15-50)	27.5 (15-40)	15	60	20	0.395
Perforation	1 (6.7%)	1 (6.7%)	3 (21.4%)	1 (8.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	

Table 3. Comparison of symptomatic and asymptomatic patients

	Symptoms (n=47%)	No symptoms (n=19%)	P value
Sex (M/F%)	35/12	8/11	0.432
Age at diagnosis, years	63 (13–86%)	63 (16–88%)	0.612
Location			0.415
Jejunum	22 (46.8%)	11 (57.9%)	
Ileum	25 (53.2%)	8 (42.1%)	
Tumor size (mm)	30 (10-150)	18 (5-60)	0.074
Final diagnosis			0.049
Adenocarcinoma	14 (29.8%)	1 (5.3%)	
ML	11 (23.4%)	4 (21.1%)	
GIST	7 (14.9%)	7 (36.8%)	
Metastatic SBT	10 (21.3%)	2 (10.5%)	
PJS	4 (8.5%)	1 (5.3%)	
NET	1 (2.1%)	1 (5.3%)	
Adenoma	0 (0%)	1 (5.3%)	
Leiomyoma	0 (0%)	1 (5.3%)	
Lipoma	0 (0%)	1 (5.3%)	
Diagnostic modalities			0.508
CT	34 (72.3%)	11 (57.9%)	
Endoscopy	6 (12.8%)	3 (15.8%)	
PET	5 (10.6%)	3 (15.8%)	
MRI	1 (2.1%)	2 (10.5%)	
US	1 (2.1%)	0 (0%)	
Period of diagnosis			0.728
2013–2016	25 (53.2%)	11 (57.9%)	
2017–2020	22 (46.8%)	8 (42.1%)	

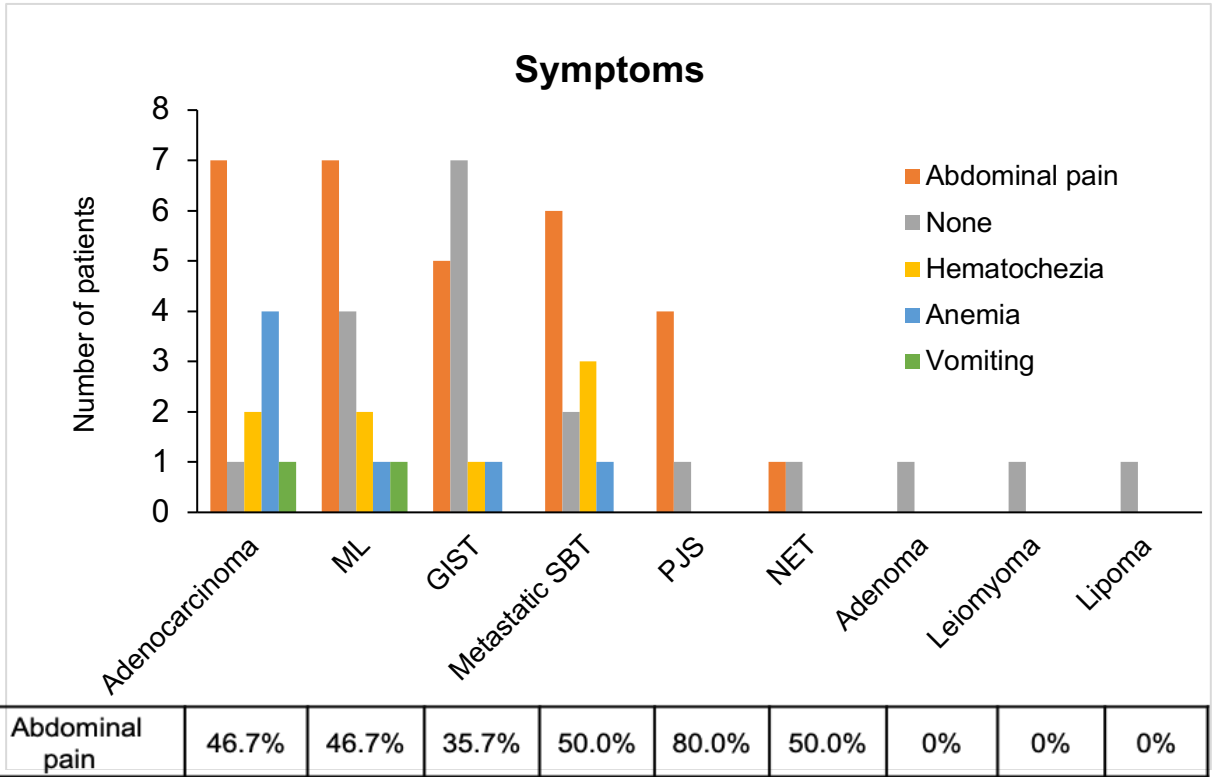
Table 4. Underlying disease and small bowel tumors in asymptomatic patients

	Abnormal medical examination (n=8%)			Cancer (n=5%)			ML (n=2)	Hepatitis C (n=1)	Mucocutaneous pigmentation (n=1)	Hemorrhoid (n=1)	Stroke (n=1)
	Fecal occult blood (n=6)	Abnormal urinalysis (n=1)	Anemia (n=1)	Hepatocellular carcinoma (n=2)	Ovarian carcinoma (n=2)	Prostatic carcinoma (n=1)					
Adenocarcinoma	0 (0%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ML	1 (16.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (100%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)
GIST	3 (50.0%)	1 (100%)	0 (0%)	1 (50.0%)	1 (50.0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Metastatic SBT	0 (0%)	0 (0%)	0 (0%)	1 (50.0%)	1 (50.0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
PJS	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)
NET	1 (16.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Adenoma	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
Leiomyoma	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (100%)
Lipoma	1 (16.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 5. Treatment for small bowel tumors

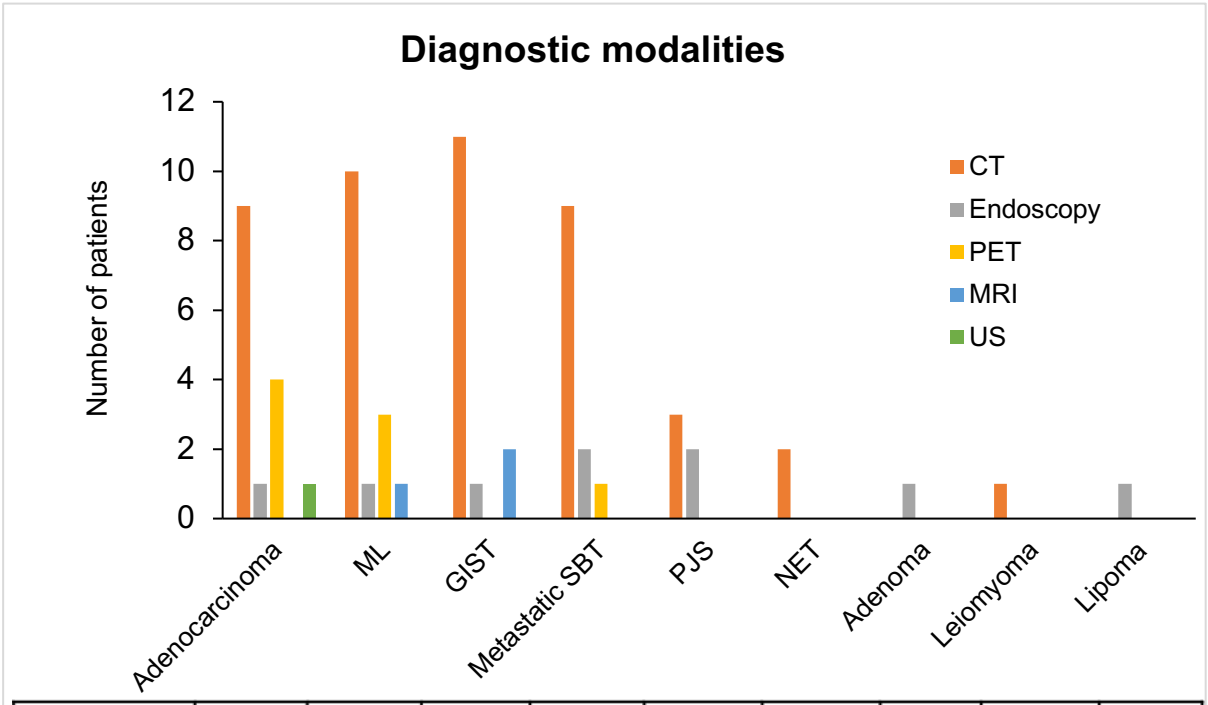
	Adenocarcinoma (n=15)	ML (n=15)	GIST (n=14)	Metastatic SBT (n=12)	PJS (n=5)	NET (n=2)	Adenoma (n=1)	Leiomyoma (n=1)	Lipoma (n=1)
Treatment									
Surgical resection	11 (73.3%)	4 (26.7%)	9 (64.3%)	7 (58.3%)	4 (80.0%)	0 (0%)	0 (0%)	1 (100%)	1 (100%)
Surgical resection + chemotherapy	2 (13.3%)	5 (33.3%)	2 (14.3%)	0 (0%)	0 (0%)	2 (100%)	0 (0%)	0 (0%)	0 (0%)
Chemotherapy	1 (6.7%)	5 (33.3%)	1 (7.1%)	2 (16.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Follow-up	0 (0%)	1 (6.7%)	1 (7.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Endoscopic therapy	0 (0%)	0 (0%)	1 (7.1%)	0 (0%)	1 (20.0%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)
Radiation therapy	0 (0%)	0 (0%)	0 (0%)	2 (16.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Best supportive care	1 (6.7%)	0 (0%)	0 (0%)	1 (8.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Figure 1A



Abdominal pain	46.7%	46.7%	35.7%	50.0%	80.0%	50.0%	0%	0%	0%
None	6.7%	26.7%	50.0%	16.7%	20.0%	50.0%	100%	100%	100%
Hematochezia	13.3%	13.3%	7.1%	25.0%	0%	0%	0%	0%	0%
Anemia	26.7%	6.7%	7.1%	8.3%	0%	0%	0%	0%	0%
Vomiting	6.7%	6.7%	0%	0%	0%	0%	0%	0%	0%

Figure 1B



CT	60.0%	66.7%	78.6%	75.0%	60.0%	100%	0%	100%	0%
Endoscopy	6.7%	6.7%	7.1%	16.7%	40.0%	0%	100%	0%	100%
PET	26.7%	20.0%	0%	8.3%	0%	0%	0%	0%	0%
MRI	0 0%	6.7%	14.3%	0%	0%	0%	0%	0%	0%
US	6.7%	0%	0%	0%	0%	0%	0%	0%	0%