



# Small bowel tumors in emergency surgery

## Acil cerrahide ince bağırsak tümörleri

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### BACKGROUND

The aim of the present study was to describe the clinical presentation, diagnostic work-up, surgical therapy, and prognosis of 13 patients with small bowel tumor admitted for surgical procedures in an emergency setting.

### METHODS

From 1996 to 2008, 13 consecutive surgical cases of small bowel tumors were treated at the Cumhuriyet University Faculty of Medicine, Department of General Surgery, and Kütahya State Hospital, Department of General Surgery. Clinical and radiological charts of these patients were reviewed retrospectively from the department database.

### RESULTS

Intestinal obstruction (7 cases) and perforation (5 cases) were the most common clinical presentations, followed by intussusception (1 case). Adenocarcinoma was the most frequent histologic type (4 cases), while small bowel sarcoma was seen in three cases and non-Hodgkin lymphoma in two cases. The remaining cases had carcinoid tumor, small bowel angioleiomyoma, Brunner's gland adenoma, and inflammatory pseudotumor of the small intestine.

### CONCLUSION

Small bowel tumors are rare, the symptoms often non-specific, and the accuracy of different diagnostic tests remains to be improved. Timing and type of the intervention to the process and biological behavior of the pathological cells predict the prognosis.

**Key Words:** Acute abdomen; adenocarcinoma; emergency surgery; small bowel tumor.

### AMAÇ

Bu çalışmanın amacı, acil cerrahi sorunları ile hastanelerimize başvuran ince bağırsak tümörü olan 13 hastanın klinik sürecini, tanı çalışmalarını, uygulanan cerrahi işlemleri ve sağkalımlarını irdelemektir.

### GEREÇ VE YÖNTEM

1996 ile 2008 tarihleri arasında Cumhuriyet Üniversitesi Tıp Fakültesi Genel Cerrahi Anabilim Dalı'nda ve Kütahya Devlet Hastanesi Genel Cerrahi Kliniği'nde ince bağırsak tümörü nedeniyle acil cerrahi girişim uygulanan 13 hastanın dosyaları retrospektif olarak değerlendirildi.

### BULGULAR

Hastaların yedisinde ince bağırsak tıkanıklığı, beşinde perforasyon ve birinde de invajinasyon vardı. Histopatolojik olarak hastaların dördünde adenokarsinom, üçünde ince bağırsak sarkomu, ikisinde Non-Hodgkin Lenfoma, birer hastada karinoid tümör, ince bağırsak anjiyoleiomyomu, Brunner bezi adenomu ve ince bağırsağın enflamatuvar psödötümörü saptandı. R0 rezeksiyon oranı %76 (10/13) iken R2 rezeksiyon üç (%23) hastada uygulanmıştır.

### SONUÇ

İnce bağırsak tümörleri çok nadir görülür. Bulguları spesifik değildir ve tanı sürecinde daha ileri tanı yöntemlerine gereksinim duyulmaktadır. Bu tümörlerin biyolojik davranış tipi ve gelişim süreçlerine yapılan girişimin zamanı ve çeşidi sağkalımı belirlemektedir.

**Anahtar Sözcükler:** Akut karın; adenokarsinom; acil cerrahi; ince bağırsak tümörü.

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## RESULTS

Although the small intestine accounts for 75% of the length and 90% of the surface area of the gastrointestinal (GI) tract, small bowel tumors (SBT) are very rare. SBTs account for only 1-1.4% of GI neoplasms. The incidence of small bowel cancer was reported in 1994 as 1.6 per 100,000 of the population.<sup>[1,2]</sup>

Several pathologic types of malignancy can arise in the small bowel including: adenocarcinoma, carcinoid tumor, stromal tumors, lymphoma, and endocrine tumors. Moreover, the small bowel is often involved secondarily by tumors that actually start from adjacent organs or by processes of peritoneal carcinomatosis, conditions that are responsible for a distinct worsening of the prognosis (up to 70% mortality).<sup>[3]</sup>

The main problem with these tumors is that they induce vague, non-specific symptoms, causing a delay in diagnosis, which is often reached in cases of acute complications such as intestinal obstruction, hemorrhage or perforation.

The aim of the present study was to describe the clinical presentation, diagnostic work-up, surgical therapy, and prognosis of 13 patients with SBT in an emergency setting.

## MATERIALS AND METHODS

From 1996 to 2008, 13 consecutive surgical cases of SBT were treated at the Cumhuriyet University Faculty of Medicine, Department of General Surgery, and Kutahya State Hospital, Department of General Surgery. Clinical and radiological charts of these patients were reviewed retrospectively.

All patients had histologically confirmed SBT and required an emergency treatment within 36 hours. Ampullary duodenal tumors were excluded from the study as they constitute a special entity. The following criteria were used for defining a GI primary lymphoma, absence of a palpable lymphadenopathy, normal peripheral blood smear and bone marrow biopsy, absence of mediastinal lymphadenopathy on chest X-ray, disease grossly confined to the affected small bowel segment, as confirmed by diagnostic imaging, endoscopy, or laparotomy, regional lymphadenopathy only initially, and absence of hepatic or splenic tumor involvement except via direct extension from primary bowel involvement.

Resection criteria were as follows: Curative resection (R0) was accepted when all macroscopic tumor tissue was extirpated with microscopically verified tissue margins and no documented metastasis; (R1) resection when all macroscopic tumor tissue was extirpated but with microscopically positive tissue margins; and (R2) resection when there was macroscopically residual disease.

There were seven male and six female patients. The ages of the patients ranged from 27 to 70 years, with a mean age at presentation of 56 years. Adenocarcinoma was the most frequent histologic type (4 cases), followed by small bowel sarcomas (3 cases; (gastrointestinal stromal tumor (GIST), leiomyosarcoma and angiosarcoma). Non-Hodgkin lymphoma was seen in two cases and carcinoid tumor, small bowel angioleiomyoma, Brunner's gland adenoma, and inflammatory pseudotumor of the small intestine in one patient each. In six cases, lesions were located in the ileum, in three cases in the jejunum and in two cases in the duodenum; in metastatic cases, lesions were in ileum+liver, and in ileum+sigmoid colon+uterus.

All patients presented as surgical emergencies, with intestinal obstruction (7 cases) and perforation (5 cases) being the most common clinical presentations; intussusception (1 case) was the other presenting clinical manifestation. Eight patients were operated immediately on the day of admission. All of them had clinically overt acute abdominal signs. Perioperatively, intestinal perforation was diagnosed in five of them. The other five patients were operated within 36 hours after the surgeon's first visit.

There were four patients with adenocarcinoma. While two of them had R0 resection, the other two had R2 resection because the lesions were in metastatic form. One of the metastatic patients died on the postoperative 7th day due to severity of her clinical condition. The other metastatic patient had peritoneal carcinomatosis. During the operation, the obstructed ileal segment and metastatic sigmoid colon were resected and primary anastomoses were performed. Total abdominal hysterectomy and bilateral salpingo-oophorectomy were also performed. This patient also had cytoreduction and hyperthermic intraperitoneal chemotherapy. Intraperitoneal chemotherapy was continued for five days in the postoperative period, through the abdominal drains. She is currently alive and no recurrence was detected six months after the operation. The other two adenocarcinoma patients who had R0 resection are alive at 10 years and 10 months follow-up, respectively.

There were three patients with small bowel sarcoma. One of them had GIST, one angiosarcoma and one leiomyosarcoma. All of them admitted with acute abdominal signs. The patient with GIST had perforated lesion in the jejunum. He is currently alive at three years. The patient with angiosarcoma was operated five years ago due to cardiac angiosarcoma. He had admitted with acute abdominal signs. In the operation, recurrent jejunal lesion was detected to have caused intestinal obstruction. He is also alive at three years. The patient with leiomyosarcoma was operated due to

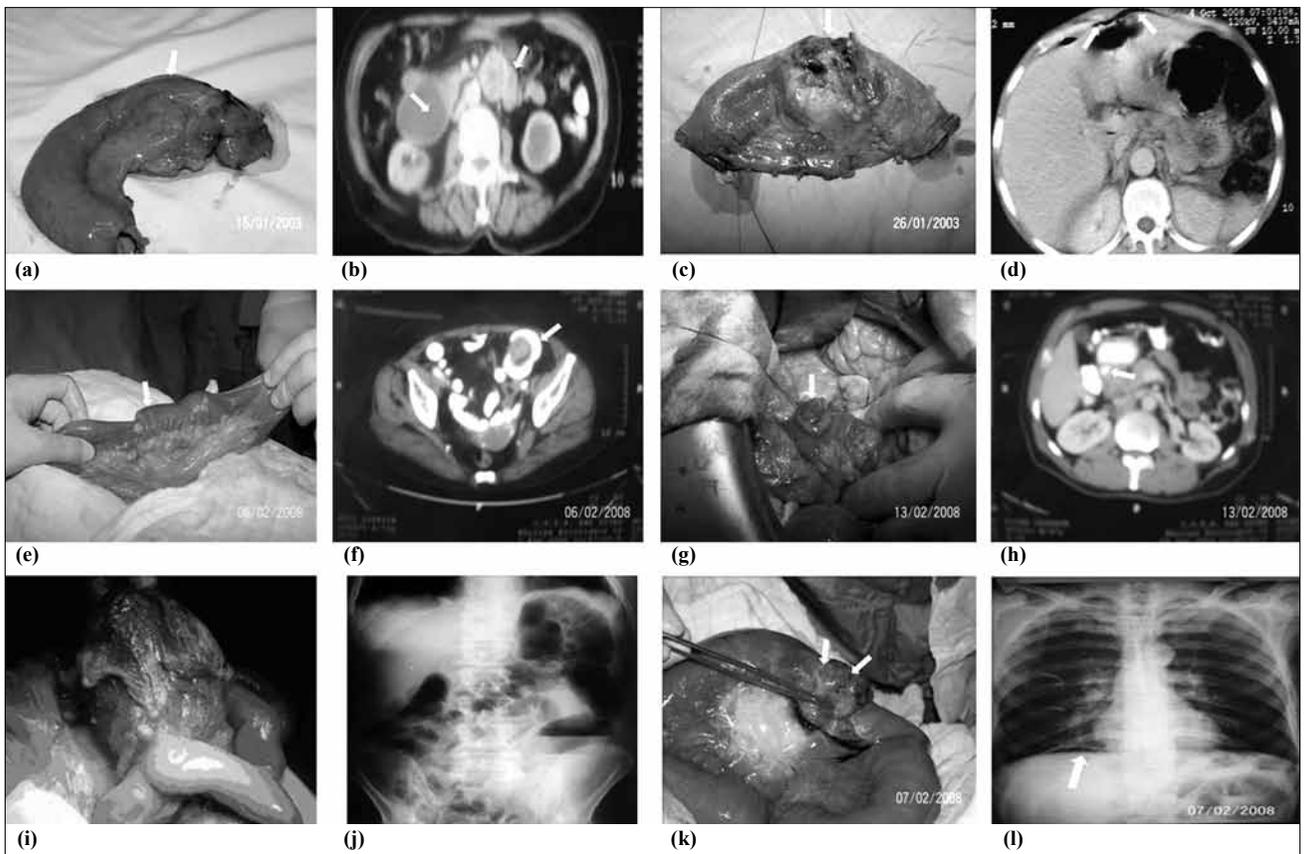
acute abdominal signs. During the operation, an ileal lesion was detected to have caused the intestinal obstruction. In these three patients, resection type was R0; however, leiomyosarcoma recurred eight months later and resection was performed. He received adjuvant chemoradiotherapy and is healthy one year after the second operation.

Two patients with non-Hodgkin lymphoma had admitted with perforation. One of them died on the postoperative 8th day due to pneumonia and sepsis. In the other patient, enteropathy-type T-cell lymphoma was determined by histopathological examination. He received adjuvant chemoradiotherapy but six months after the operation he readmitted with upper GI bleeding. Perioperatively, a recurrent bleeding lesion was detected in the stomach. After gastric resection, the oncology department plans bone marrow transplantation.

The patient with carcinoid tumor in her ileum had a bowel obstruction, but she did not have a carcinoid syndrome. Her affected segment (50 cm ileum) was radically resected and anastomosis was performed.

She is alive at four years. In the patient with Brunner's gland adenoma, the lesion was in the first part of the duodenum. Perioperatively, frozen section was performed and based on the benign results, a wedge resection was accepted as adequate treatment. The other patient with small bowel angioleiomyoma had intussusception. The affected segment (50 cm ileum) was radically resected and anastomosis was performed. She is alive at one year. The patient with an inflammatory pseudotumor of the small intestine had admitted with perforation. His affected segment (40 cm ileum) was radically resected and anastomosis was performed (Fig. 1). He has been alive for one year.

In the diagnostic period, the diagnosis was suspected preoperatively in 7 (53%) patients. Computed tomography (CT) scans, especially multidetector type, were useful in showing the lesions in five patients (Fig. 1). Magnetic resonance imaging (MRI) was also very helpful in two patients. Gastroduodenoscopy detected the duodenal tumors (n=2). Other studies including plain abdominal X-rays and ultrasound were also useful in the preoperative period.



**Fig. 1.** (a) Small bowel adenocarcinoma with perforation (arrow), (b) Duodenal dilatation (left arrow) and the lesion (right arrow) are seen in the CT. (c) Inflammatory pseudotumor of the small intestine (arrow), (d) Free air (arrow) is seen in the CT image. (e) Small bowel angioleiomyoma presented with intussusception (arrow), (f) Demonstrative CT image of the intussusception (arrow). (g) Brunner's gland adenoma in the duodenum, first part (arrow), (h) The lesion (arrow) is seen in the CT. (i) GIST with perforation, (j) Air fluid levels are seen in the abdominal X-ray image of the patient. (k) Enteropathy-type T-cell lymphoma with perforation (arrow), (l) Free air (arrow) is seen in the chest X-ray image of the patient.

Three patients (23%) had postoperative complications (2 pneumonia, 2 sepsis, 1 wound infection, 1 pulmonary embolism and 1 GI fistula). The mean hospital stay was  $9.5 \pm 2.4$  days.

Three patients (24%) had abdominal metastases. While one of them was limited to local lymph nodes, two had widespread metastases to the liver, mesentery, sigmoid colon, peritoneum, and uterus. Curative resection (R0) rate of this series was 70% (9/13). Three patients had R2 resection. Two patients with R2 resection died on the postoperative 7th and 8th days due to severity of their clinical situations. Overall mortality of this series was 15% (2/13).

## DISCUSSION

Primary SBTs are very rare. The incidence of SBT per 100,000 persons in the white population in the United States (US) is 1.2 for men and 0.8 for women.<sup>[1,4,5]</sup> Specific factors have been attributed to protecting the small intestine from the influence of potential carcinogens.<sup>[6-8]</sup> These include a rapid transit time, which reduces mucosal exposure to potential carcinogens; the greater fluidity of the liquid contents, which are mechanically less irritating; an alkaline pH and a decreased bacterial population, which reduces the production of potentially carcinogenic substances from secondary bile acids; a high concentration of the enzyme benzopyrene hydroxylase, which may detoxify potential carcinogens; a higher concentration of lymphoid tissue; and a relatively high output of immunoglobulin A, which may enhance the local immune response.<sup>[6-9]</sup>

Small bowel tumors (SBTs) present unique challenges in terms of preoperative diagnosis, operative treatment decisions and postoperative prognostication. These lesions often go untreated for prolonged periods because they are notoriously difficult to diagnose.<sup>[1,10,11]</sup> The presenting signs and symptoms of SBTs are non-specific and often poorly defined.<sup>[5,12]</sup> The most common symptoms include abdominal pain, bleeding, weight loss, and nausea and vomiting, but they often go unrecognized until severe symptoms develop, and they can create surgical emergencies. The most frequent complaints in this series were abdominal pain in 75%, anemia in 30%, weight loss in 38%, nausea and vomiting in 50%, and signs of GI bleeding in 30%. Intestinal obstruction is usually a late sign due to the liquid contents of the small bowel and occurred in 53% in this series. Intestinal perforation (38%) was the second leading pathology of this series.

The small bowel remains a difficult area to image. Many series reported a correct preoperative diagnosis in only 21-53% of patients.<sup>[5,13]</sup> Upper GI series and the use of the enteroclysis technique have been reported to be a valuable diagnostic tool.<sup>[14]</sup> However, the reported

sensitivity rate is only between 30% and 50%. In our study, three patients underwent upper GI series, and in two patients, a pathologic finding in the small bowel was determined to be causing the obstruction. The role of CT scan, especially multidetector types, and MRI are very valuable in the preoperative diagnostic period. Capsule endoscopy (CE) and double-balloon enteroscopy (DBE) are two novel methods of enteroscopy for examining the entire small bowel. The detection rate of small bowel diseases by CE is very high. DBE can serve as a good complementary approach after an initial diagnostic imaging using CE.<sup>[15]</sup>

In this study, adenocarcinoma (30%, 4/13), small bowel sarcoma (23%, 3/13), and non-Hodgkin lymphoma (15%, 2/13) were the most frequent tumoral cases found, corresponding to the results of most series.<sup>[13,16-18]</sup> The histogenesis of small bowel adenocarcinoma is probably analogous to the colonic adenoma-carcinoma sequence; therefore, the most important risk factor for small bowel adenocarcinoma is a pre-existing adenoma, either single or multiple, in association with one of the multiple polyposis syndromes.<sup>[19,20]</sup> Most small bowel carcinomas are already metastatic at the time of diagnosis.<sup>[21]</sup> Unlike large bowel mucosa, small intestinal mucosa contains lymphatics that course through the villi extending near the luminal surface, and invasion of mucosal tumor into these lymphatics may account for this tendency of early metastasis.<sup>[22]</sup>

In small bowel adenocarcinoma, surgery is the treatment of choice and is the only therapeutic modality with curative potential. Neither chemotherapy nor radiotherapy has a proven role in the treatment of small bowel adenocarcinoma.<sup>[23]</sup> The prognosis of adenocarcinoma of the small intestine may be improving. The overall five-year disease-specific survival was 30%, with a median survival of 19.7 months.<sup>[22]</sup> One of our patients with adenocarcinoma and who had cytoreduction and hyperthermic intraperitoneal chemotherapy is alive at six months after the operation, and no recurrence was detected. Cytoreductive surgery experience of our clinic encourages us to use this procedure in some suitable metastatic and peritoneal carcinomatosis cases.

Primary small bowel sarcomas occurred throughout the intestines, but were most frequently determined in the jejunum. These tended to be large, high-grade malignancies with local invasion.<sup>[24]</sup> Leiomyosarcoma originates from smooth muscle cells within the muscularis mucosa or muscularis propria. Leiomyosarcoma rarely spreads to regional lymph nodes, but this may occur in up to 14% of patients.<sup>[25]</sup> Adjuvant chemotherapy or radiation therapy after complete resection has not been shown to diminish the risk for subsequent recurrence.<sup>[24]</sup> Leiomyosarcoma with a high number of

mitoses correlates well with the presence of metastases and, thereby, poor five-year survival, but may be more sensitive to conventional chemotherapeutic agents than GIST.<sup>[26]</sup> Although we had resected the leiomyosarcoma of our patient, it recurred eight months later and with aggressive attempts, we re-resected the tumor. Postoperatively, he received chemoradiotherapy and now is healthy one year after the second operation.

Angiosarcoma is an uncommon malignant neoplasm characterized by rapidly proliferating, extensively infiltrating anaplastic cells derived from blood vessels and lining irregular blood-filled spaces.<sup>[26]</sup> They are aggressive and tend to recur locally, spread widely, and have a high rate of lymph node and systemic metastases.<sup>[26]</sup> Our patient was operated five years ago due to cardiac angiosarcoma. He had admitted with acute abdominal signs and jejunal angiosarcoma was detected as a cause of intestinal obstruction. He received adjuvant chemotherapy and is healthy three years postoperatively.

Gastrointestinal stromal tumors are the most common mesenchymal tumors of the GI tract.<sup>[24]</sup> GISTs are most often found in the stomach (60-70%), followed by small intestine (20-30%), colon and rectum (5%), and esophagus (5%).<sup>[27,28]</sup> The key to adequate local control of intestinal GIST is gross surgical resection of the primary tumor with negative microscopic margins (R0). Lymphadenectomy is generally not indicated unless the regional lymph nodes are enlarged because GIST rarely metastasizes to the lymph nodes. Tumor recurrence is common and the five-year survival after removal of primary localized GIST is approximately 50%.<sup>[29]</sup> In our patient, complete resection of the primary tumor was possible and no recurrence was seen for three years.

The pathologic criteria for differentiating malignant and benign GIST have been a source of controversy for many years. Of all the pathologic features that have been analyzed, the mitotic rate and tumor size have been the most reliable and consistent predictors of outcome.<sup>[28]</sup> These patients represent a high-risk group and are ideal candidates for novel therapies, such as tyrosine kinase inhibitors. Imatinib mesylate (Gleevec<sup>®</sup>) selectively inhibits specific tyrosine kinases, including c-KIT (KIT) proto-oncogene and platelet-derived growth factor receptor- $\alpha$ . It is apparent that up to 80% of patients with metastatic GIST achieve a partial response or stable disease while receiving imatinib.<sup>[29]</sup> Unfortunately, resistance to tyrosine kinase inhibitors is an emerging clinical problem. In patients with multiple sites of disease and focal resistance to imatinib, surgery should be considered.<sup>[30]</sup>

More than 20 different disorders can be called non-Hodgkin lymphomas.<sup>[31]</sup> Most non-Hodgkin lympho-

mas (85%) are from B cells. Less than 15% develop from T cells. Intestinal T-cell lymphoma is a very rare entity among primary GI lymphomas.<sup>[32]</sup> One of our patients had enteropathy-type intestinal T-cell lymphoma (Fig. 1). Enteropathy-type intestinal T-cell lymphoma is a complication of refractory celiac disease.<sup>[32]</sup> Removal of gluten from the diet results in a return to normal health for the majority of celiac patients. Some patients do not respond to a gluten-free diet and are considered to be refractory celiac disease.

Controversy remains regarding the role of primary surgical therapy in patients with localized lymphoma (stages I and II).<sup>[24]</sup> Much of the information on the effectiveness of surgery for early GI lymphoma is based on limited, retrospective reviews that do not specifically compare primary surgical therapy with primary medical management, be it chemotherapy, radiotherapy or radiochemotherapy.<sup>[31,33]</sup> Perhaps the most significant investigative question posed by this and other series is whether there is a need for postoperative therapies after complete surgical resection of localized lymphoma.<sup>[34]</sup> Patients with advanced lymphoma (stages III and IV) are not candidates for complete surgical resections. Because of more sophisticated treatment options (combinations of chemotherapy, monoclonal antibodies, immunotherapy, radiation, and hematopoietic stem cell transplantation) by medical oncologists, the need for surgical intervention in these patients has diminished.

Carcinoids are rare slow-growing neuroendocrine tumors, with an incidence of 2/100,000 in the United States. The bowel is the commonest site for a primary carcinoid tumor, followed by the lungs.<sup>[27]</sup> The appendix is the commonest site within the bowel, and tumors in the appendix rarely metastasize.<sup>[35]</sup> Morphologic and histologic criteria can not accurately predict the behavior of these tumors. Although the mitotic rate, multiplicity, female gender, and the presence of carcinoid syndrome have been implicated as predictors of a worse prognosis, the size, depth of invasion into the muscularis propria and evidence of lymph node involvement or metastases are the most dependable features for predicting outcome.<sup>[36-38]</sup> Carcinoid tumors can be transmurally invasive and they can create great desmoplastic reaction causing constriction and small intestine occlusion, as in our patient. Carcinoid syndrome occurs in less than 10% of patients with carcinoid tumor.<sup>[39]</sup> Clinically, this syndrome develops when vasoactive substances produced by the carcinoid tumor escape hepatic degradation and gain access into the systemic circulation.<sup>[40]</sup> This syndrome can be seen in GI carcinoid tumor patients with liver metastases.

The Brunner's gland tumor, also known as Brunner's gland adenoma, is a rare benign lesion of the duodenum. It can be incidentally discovered during an

endoscopy and sometimes is the cause of bleeding or obstruction.<sup>[41]</sup> Endoscopic biopsy result, however, is usually negative because the tumor is almost entirely covered by thick intact duodenal mucosa in the biopsy sites, and the biopsy is often not deep enough to reach the submucosal tumor tissue.<sup>[39]</sup> In our case, the endoscopic biopsy was also negative, and the condition was diagnosed as chronic gastritis, although the final pathologic diagnosis indicated that the patient suffered from Brunner's gland adenoma (Fig. 1). It is a tumor without malignant predisposition. The outcome of operation is usually excellent and there is no recurrence reported.

Angioleiomyomas are well-defined benign smooth muscle tumors with prominent abnormal thick-walled venous channels.<sup>[42]</sup> The presence of angioleiomyoma in the GI tract is extremely rare, but a few cases have been reported where they presented as volvulus, peritonitis and perforation of the intestinal tract.<sup>[43,44]</sup> One of the patients in this series had angioleiomyoma, and to the best of our knowledge, this is the first reported case in which the angioleiomyoma presented primarily with intussusception (Fig. 1). They tend to occur mostly in the jejunum (44%), followed by ileum (37%) and duodenum (19%). The operative management is usually surgical resection of the affected bowel segment with end-to-end anastomosis, as in our patient.

Inflammatory pseudotumor of the small intestine is a very rare condition.<sup>[45]</sup> It is a localized predominantly submucosal mass characterized histologically by inflamed granulation tissue with variable numbers of eosinophils.<sup>[46]</sup> They are clinically interpreted to be neoplasm and treated by segmental resection. Although these lesions generally pursue a benign clinical course, some intraabdominal and retroperitoneal lesions of this type have typically shown local recurrence and even distant metastases.<sup>[47]</sup> The etiology of these tumors is not known but they may represent an unusual inflammatory response to precipitating factors such as surgery, trauma and localized infection.<sup>[48,49]</sup> To the best of our knowledge, our case is the first to be reported in which inflammatory pseudotumor of the small intestine presented with perforation (Fig. 1).

In conclusion, SBTs are rare, the symptoms are often non-specific, and the accuracy of different diagnostic tests remains to be improved. SBTs remain a challenging problem for both GI surgeons and gastroenterologists, and we should consider these lesions when confronted with vague GI symptoms.

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