Published in final edited form as:

Am J Surg Pathol. 2008 September ; 32(9): 1412–1420. doi:10.1097/PAS.0b013e31816250ce.

Stromal, Fibrous, and Fatty Gastrointestinal Tumors Associated With A *PDGFRA* Gene Mutation

J. Aidan Carney, M.D., Ph.D., F.R.C.P.I., F.R.C.P and Constantine A. Stratakis, M.D., D. (Med). Sci

Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN (JAC emeritus member) and Section on Endocrinology and Genetics, DEB, NICHD, NIH, Bethesda, MD (CAS)

Abstract

We report the case of a woman with 3 different types of gastrointestinal tumors—stromal, fibrous, and fatty—and a germline defect of the *PDGFRA* gene (V561D). The patient, now 52 years old, presented in 1977 at age 22 years with a gastric tumor and a duodenal lipoma. Subsequently, she developed KIT-negative, CD34-positive obstructing small intestinal fibrous tumors that required three laparotomies and intestinal resections. Most recently (in 2002), more than 100 of the fibrous tumors were resected and in addition multiple small intestinal lipomas and multiple gastric KIT- and CD34-positive stromal tumors. The nosology of the fibrous tumors was not clear, although they resembled inflammatory fibrous polyps. The lesions were hypocellular and featured poorly outlined spindle, stellate, and polygonal CD34-positive and KIT-negative cells. They penetrated through the muscularis propria and expanded the subserosa and occasionally extended into the mesentery. There was no metastasis. The patient is currently asymptomatic; radiologic study in June 2007 revealed postoperative changes only. None of the patient's primary relatives have had similar tumors.

Keywords

GIST; gastrointestinal fibromas; gastrointestinal lipomas; *PDGFRA* mutation; GIST syndrome

Introduction

Stromal tumors of the stomach (GISTs) are currently attracting great interest because of 1) shared attributes with the interstitial cells of Cajal (ICC) (13), 2) expression of the receptor tyrosine kinases KIT and *PDGFRA* (platelet-derived growth factor receptor α) (10, 11, 16), 3) exhibition of mutations of the *KIT* and *PDGFRA* genes (11, 13), 4) response to certain synthetic tyrosine kinase inhibitors (7), and 5) occurrence as a component of several syndromes.

The tumors may be benign or malignant, single or multiple, sporadic or familial, syndromic or nonsyndromic. The sporadic neoplasm occurs equally in older men and women and usually behaves as a benign tumor (23); the familial neoplasm affects the sexes equally and tends to occur in younger individuals. The tumors occur alone or with other conditions, including 1) neurofibromatosis 1 (NF 1) (23, 30), 2) mast cell tumors, urticaria pigmentosa, and skin pigmentation and combinations of these conditions (20, 24), and 3) paraganglioma (the Carney-Stratakis syndrome) (4, 26). The neoplasms are also the major component of the

nonfamilial Carney triad, a disorder that includes pulmonary chondroma, extra-adrenal paraganglioma, and other tumors (3, 21).

Gain-of-function (activating) *KIT* mutations occur in 85% to 90% of gastric GISTs (29). A minority of the tumors has gain-of-function (activating) mutations of the *PDGFRA* gene (11). *PDGFRA* is a member of the same family of receptor kinases as *KIT* (29). The mutations result in constitutive ligand-independent kinase dysfunction. Succinic dehydrogenase subunit B, C, and D (*SDHB*, *SDHC* and *SDHD*) gene mutations were recently found in GISTs associated with paragangliomas (22).

Herein, we report the clinical and pathological findings in a phenotypically normal woman, now 52 years old, in whom a gastric and a duodenal neoplasm was identified at age 22 years. Subsequently, she underwent three operations for multiple gastric GISTs and small intestinal fibrous and lipomatous tumors. Molecular studies of one of the GISTs showed a germline defect of the *PDGFRA* gene (V561D) (26). The combination of tumors in the patient probably represents another syndrome involving gastric GISTs.

Case Report

In September 1977, a 22-year-old woman complained of occasional nausea. Esophagogastroduodenoscopy revealed a 5-mm nonulcerated gastric antral polyp and a rounded, sessile, 6-mm polyp just beyond the superior angle of the duodenum that was biopsied.

At age 32 (July 1987), she complained of abdominal cramping pain. A gastric barium study with follow-through showed a 3-cm gastric mass, 2 polypoid 1.5-cm masses in the descending portion of the duodenum, and 11 submucosal small intestinal lesions, one to three cm in diameter, with a smooth contour. At laparotomy, several gastric abnormalities were found: a large mass extended from the posterior wall; there was a golf-ball-sized antral mass; and the serosal surface was studded with verrucous lesions. Four segmental gastric resections were performed to excise 1) 2 firm, white nodules with a homogeneous cut surface, each 0.5 cm; 2) several firm to soft, violaceous to tan nodules, each 1 to 1.5 cm; 3) an irregularly shaped bosselated, firm but elastic mass, 2 cm in diameter; and 4) a posterior wall lesion, measuring 6 × 3 × 0.5 cm. Several tumors were not excised. There were multiple masses throughout the small bowel, one of which had become intussuscepted. The intestinal wall was very thick and leathery, and the serosa had a whitish appearance. Some tumors extended into the mesentery. The area of the intussusception including several of the neoplasms was resected. Microscopically, the examining pathologist thought the lesions were very unusual and obtained the opinions of 4 consultants. The respective diagnoses were 1) malignant schwannoma, leiomyosarcoma, and multiple hamartomas, 2) multiple leiomyoblastomas; 3) high grade round cell (lipoblastic) liposarcomas; and 4) inflammatory fibroid polyp (small intestine) and multifocal stromal tumors (stomach). The final pathological diagnosis rendered was gastric and small intestinal mesenchymal nodules of uncertain nature. An 8-month course of chemotherapy (cyclophosphamide, doxorubicin, dacarbazine, and vincristin) was administered.

At age 35 (February 1990), the patient developed acute small bowel obstruction. During the third laparotomy, the surgeon found multiple small intestinal polypoid lesions, measuring up to 5 cm in diameter; one was intussuscepted. A 23-cm segment of mid small bowel was resected. The pathological diagnosis rendered was neurofibromatosis.

At age 47 (January 2002), the patient had renewed symptoms of intestinal obstruction. Esophagogastroduodenoscopy showed a gastric submucosal prepyloric mass and a lesion partially obstructing the first part of the duodenum. Abdominal computed tomographic (CT)

examination revealed marked thickening of the entire small bowel wall and an 8-cm mass involving the gastric greater curvature. Colonoscopy showed mild diverticular disease. At laparotomy, the thickened small bowel was dilated and was, as described in the surgical report, “extensively infiltrated with a white tumor extending from 20 cm distal to the ligament of Treitz to 90 cm proximal to the ileocecal valve.” The involved small bowel was resected (estimated by the surgeon to weigh more than 15 pounds [6.8 kg]). The large tumor obstructing the first part of the duodenum was also excised. There were multiple small gastric serosal nodules and 2 large masses attached to the greater curvature: an 8-cm cystic lesion and a 6-cm stalked lesion that was adherent to the liver and diaphragm. A partial gastrectomy and local excision of the greater curvature lesions were performed; several small tumor nodules were not resected. The appendix was abnormal and was excised.

At age 52 (June 2007), the patient was well and had no complaints. Abdominal CT examination showed postoperative changes only. No member of the patient’s family has had gastric or small intestinal tumors. The patient’s parents were of Italian and English-Scottish extraction. The father died at age 54 of complications of diabetes mellitus and the mother at age 81 of hypertension and renal failure. Her only sibling, a brother, died suddenly at age 46; there was no autopsy.

Materials and Methods

The clinical, radiologic, endoscopic, and pathological reports from the patient’s duodenal biopsy and 4 subsequent surgical procedures were obtained together with the histologic slides from the 1977, 1987, 1989, and 2002 operations and the paraffin blocks and the resection specimens from the most recent (2002) laparotomy. Additional blocks from the latter resections were processed.

The specimens were fixed in 10% neutral buffered formalin and embedded in paraffin. Sections 5 μ thick were obtained for routine and immunohistochemical staining. The following stains were used: hematoxylin–eosin (H & E), periodic acid-Schiff with diastase predigestion, and Masson trichrome. In immunohistochemical studies (streptavidin-biotin peroxidase complex method), antibodies were selectively used against the following: CD117 (Dako, Carpinteria, California; polyclonal, dilution 1/100), CD34 (Beckton Dickinson and Co, San Jose, California; MY10, dilution 1/100); actin (Dako; 1A4, dilution 1/100); desmin (Dako; DER11, dilution 1/200); vimentin (Dako; VG1, dilution 1/20); S-100 (Dako; polyclonal, dilution 1/100); neurofilament (Dako; 2F11, dilution 1/800); calponin (Dako; CALP, dilution 1/500); fascin (Dako; 55K-2, dilution 1/500); CD35 (Dako; Ber-Mac-DRC, dilution 1/5); cyclin D1 (Lab Vision Corp, Fremont, California; SP4, 1/50); BCL-2 (Dako; dilution 1/20); and PKC θ (Becton, Dickinson and Co; 27, dilution 1/200).

Results

The different gastrointestinal tumor types found at the patient’s surgical procedures were generally similar. All were represented in her 2002 surgical specimens. Therefore, only the findings in this procedure are described to avoid repetition. The findings at the earlier procedures and those in 2002 are summarized in Table 1. The 2002 pathological findings included 1) gastric GISTs, 2) gastric, duodenal, jejunal and appendiceal fibrous tumors, 3) jejunal lipomas, and 4) jejunal diverticula.

Pathology

Stomach and Duodenum—Two large lesions were attached to the serosa: an 8 cm cyst containing liquid and sediment (Fig. 1 A) and a 6-cm pedunculated tumor. There was also a series of intramural and subserosal tumorlets, 1 to 3 mm in greatest dimension (Fig. 1 B);

some were calcified and gritty when cut. Microscopically, the 6 cm tumor featured a solid sheet of sharply outlined, moderate-sized epithelioid cells with clear or acidophilic cytoplasm (Fig. 1 C); there were some spindle cells. The tumorlets were composed of plump spindle cells with occasional epithelioid cells; some had varying amounts of hyaline material; others were completely hyalinized and sometimes calcified; most were circumscribed, some showed subtle infiltration among the bundles of the muscularis. A plaque-like submucosal fibrous tumor, 1 cm thick and histologically similar to the jejunal tumors to be described later, was covered by fundal-type mucosa (Fig. 2). Results of immunostaining of both lesions are presented in Table 2. The rim of duodenum was thickened by a sclerotic hypocellular submucosal fibrous tumor extending from Brunner's glands through the markedly thickened muscularis propria to the subserosa. The collagen bundles in the submucosa were arranged in parallel and vertical to the long axis of the bowel.

Jejunum and Appendix—The 120-cm length of small intestine was markedly dilated, twisted and distorted by numerous tumors; the serosa had an opaque off-white appearance. One hundred fourteen intramural spheroidal or oval, circumscribed, submucosal nodules ranging in size from 0.5 to 7.5 cm, protruded into the bowel lumen, many side-by-side. The lesions were covered by a flat mucosa, devoid of plicae (Fig. 3 A); a few, covered by intact serosa, protruded from the bowel. A wide-mouthed diverticulum, 7 cm in diameter, had a 6 mm-thick wall (Fig. 3 B). The tumors had different consistencies: the majority (80%) felt hard, some were firm, and a few were soft. The hard tumors (fibrous) had an off-white cut surface, the firm tumors an off-white and yellow appearance (combined fibrous tumor and lipomas), and the 12 soft tumors appeared yellow (lipomas) (Fig. 3 B). The appendix measured 4.5 × 2.5 × 2.5 cm; the wall was thickened and whitish, and the tip dilated. Microscopically, the tumors were of 2 types (Fig. 4), fibrous and fatty that occurred separately, side-by-side, and superficial to one another, the lipoma always being closest to the mucosa. Exceptionally, a fibrous tumor infiltrated just into a lipoma (Fig. 4 A). The fibrous tumors were circumscribed but unencapsulated with a uniform, bland appearance, interrupted by occasional large blood vessels and a few medium-sized to large, spherical to oval microcysts. The lesions were hypocellular to moderately cellular focally and composed of haphazardly arranged, small stellate, spindle, and polygonal cells with a minimal amount of acidophilic cytoplasm set in abundant collagen fibers and collagen bundles (Fig. 4 B). Vimentin staining showed that the cells had ample cytoplasm that extended into narrow tapering cell processes. The nuclei were moderately chromatic, uniform, small, round, oval, polygonal and irregular in shape with fine evenly dispersed chromatin granules and a single small nucleolus. Mitotic figures were not seen. The cells were compatible with fibroblasts but will be referred to herein as fibroid tumor type (FTT) cells for several reasons including the fact that their lineage could not be identified. There was a sprinkling of eosinophils close to the mucosa in some of the tumors but not elsewhere; mast cells were scattered throughout the tumors. Immunostaining results are presented in Table 2.

From the submucosal base of the fibrous lesions, the process extended through the muscularis propria to involve the subserosa and rarely the mesentery (Figs. 5 and 6). Tumor cells and collagen penetrated into the muscularis propria, separating and encasing groups of fibers, many of which were degenerating and anucleate. There was no ICC hyperplasia. The appendiceal lumen, submucosa and muscularis propria were replaced by a hypocellular mass of spindle and stellate collagen-producing FTT cells that extended into the mesoappendix.

The soft submucosal tumors were circumscribed but unencapsulated and composed of masses of mature fat cells.

The diverticulum (Fig. 3 B) was lined by flattened jejunal mucosa. The muscularis mucosae was hypertrophied (0.3 mm thick) and its layers were easily distinguishable. The submucosa was replaced by a hypocellular sheet of polygonal and spindle cells FTT cells and collagen, punctuated by dilated thin-walled vessels. The muscularis propria was not recognizable. (Another jejunal diverticulum measuring $4.5 \times 3.5 \times 2.5$ cm was previously found and excised when the patient was 34 years old.)

Discussion

The patient we describe had 3 types of gastrointestinal tumors: 1) gastric GISTs, 2) more than 100 fibrous tumors involving the stomach, duodenum, jejunum and appendix, and 3) duodenal and small intestinal lipomas. The gastric and duodenal lesions were first found in 1977 when the patient was 22 years old. Subsequently, she underwent 3 small bowel resections over a 15-year period for intestinal obstruction caused by the jejunal fibrous tumors. The patient is presently asymptomatic; a recent abdominal CT examination showed postoperative changes only. No member of her family is similarly affected.

The occurrence of 3 different types of tumors in any patient would be an unexpected finding, particularly if the individual was young, each of the neoplasms multifocal and multicentric, and all occurred in the same organ or system of the body. Because of these considerations, it seemed unlikely that the tumor events in our patient were random—rather it was more likely they were related and resulted from a common etiology that probably was genetic. And, in fact, molecular analysis of the patient's tumor and peripheral blood DNA showed a germline mutation in the *PDGFRA* gene (V561D mutation) (26).

Somatic *PDGFRA* mutations have been reported in sporadic GISTs (6, 12, 18). Germline mutations of the gene have been described in several families. In one, a missense mutation of the gene (2675G>T) was found (5). In another, the mutation (Y555C) occurred with small intestinal neurofibromatosis (8). In the latter, the tumors were histologically similar to the fibrous tumors in our patient and in both cases the tumors were S-100 negative. The diagnosis of neurofibromatosis was based on the histology the small intestinal tumors; the affected members did not have the NF 1 phenotype. Patients with classical NF 1 phenotype have exhibited small intestinal spindle cell GISTs associated with ICC hyperplasia that were KIT- and CD34-positive (1). The gastric and jejunal spindle cell tumors in our patient were KIT-negative.

Classification of our patient's gastric GISTs and the small intestinal lipomas was straightforward. Nosology of her gastric, small intestinal and appendiceal fibrous tumors was less certain. These tumors had the following features: they 1) were hard, white, polypoid, broad-based, nonulcerated, lesions that protruded into the gut lumen or occasionally from the serosa; 2) exhibited hypocellularity to moderate cellularity without detected mitotic activity; 3) displayed a patternless sheet of elongated CD34-positive, CD 117-negative stellate and spindle cells set in an abundant moderately to heavily collagenized stroma; 4) had a sharply defined internal border (toward the mucosa); 5) penetrated through the muscularis propria into the subserosa; and 6) did not metastasize. The patient's jejunal diverticula were likely secondary to fibrous replacement of the muscularis propria.

The patient's pathologic findings extended from the stomach to the appendix but did not involve the colon. The gastric GISTs were not ulcerated and probably did not cause symptoms despite their large size. The small intestinal fibrous lesions caused repeated episodes of intussusception—their broad-based configuration and collagen content militated against twisting and strangulation but favored intussusception. The small intestinal lipomas presumably did not cause symptoms. None of the tumors types metastasized during the long

follow-up period. The jejunal diverticula may have resulted from fibrous replacement of the muscularis propria.

These fibrous tumors shared histologic and immunohistochemical attributes with inflammatory fibrous polyps, lesions putatively of dendritic cell origin, but they also showed histologic and some immunohistochemical differences from these tumors (Tables 3 and 4)—the lesions were not identical. As mentioned earlier, CD34-positive spindle cells populate NF 1-associated small intestinal GISTs, but the latter tumors also feature CD 117-positive cells and skenoid fibers that were not present in the fibrous tumors we describe.

Each of the 3 tumor types in our patient or similar tumors has occurred multifocally in other patients, alone, or with other tumors, as part of a syndrome: cases of (1) familial small intestinal inflammatory fibroid polyps have been reported (2, 8); 2) multiple gastric GISTs, with and without other associations, have been described (3, 15, 27, 29); and 3) multiple small bowel lipomas, occasionally with associations (9, 19, 31) have been described. But, to our knowledge, no patient with intestinal GISTs, fibrous tumors and lipomas has ever been reported.

Acknowledgments

We thank Gregory J. Moses, M.D. for sharing data and pathologic material with us.

References

- Andersson J, Sihto H, Meis-Kindblom JM, et al. NF1-associated gastrointestinal stromal tumors have a unique clinical, phenotypic, and genotypic characteristics. *Am J Surg Pathol*. 2005; 29:1170–1176. [PubMed: 16096406]
- Antony PP, Morris DS, Vowles KDJ. Multiple and recurrent inflammatory fibroid polyps in three generations of a Devon family: a new syndrome. *GUT*. 1984; 25:854–862. [PubMed: 6745724]
- Carney JA. Gastric stromal sarcoma, pulmonary chondroma, and extra-adrenal paraganglioma (Carney triad): Natural history, adrenocortical component, and possible familial occurrence. *Mayo Clin Proc*. 1999; 74:543–552. [PubMed: 10377927]
- Carney JA, Stratakis CA. Familial paraganglioma and gastric stromal sarcoma: A new syndrome distinct from the Carney triad. *Am J Med Genet*. 2002; 108:132–139. [PubMed: 11857563]
- Chompret A, Kannengiesser C, Barois M, et al. *PDGFRA* germline mutation in a family with multiple cases of gastrointestinal stromal tumor. *Gastroenterology*. 2004; 126:318–321. [PubMed: 14699510]
- Corless CL, Schroeder A, Griffith D, et al. *PDGFRA* mutations in gastrointestinal stromal tumors: frequency, spectrum and in vitro sensitivity to imatinib. *J Clin Oncol*. 2005; 23:5357–5364. [PubMed: 15928335]
- Demetri GD, von Mehren M, Blanke CD. Efficacy and safety of imatinib mesylate in advanced gastrointestinal stromal tumors. *N Engl J Med*. 2002; 347:472–480. [PubMed: 12181401]
- De Raedt T, Cools J, Debiec-Rychter M, et al. Intestinal neurofibromatosis is a subtype of familial GIST and results from a dominating activating mutation of *PDGFRA*. *Gastroenterology*. 2006; 131:1907–1912. [PubMed: 17087943]
- Fenoglio-Preiser, CM.; Noffsinger, AE.; Stemmermann, GW., et al. Chapt 6 The nonneoplastic stomach. 2. Philadelphia, PA: Lippincott-Raven; 1999. *Gastrointestinal Pathology: an atlas and text*; p. 153-236.
- Fletcher CD, Berman JJ, Corless C, et al. Diagnosis of gastrointestinal stromal tumors: a consensus approach. *Hum Pathol*. 2002; 33:459–465. [PubMed: 12094370]
- Heinrich MC, Corless C, Duensing A, et al. *PDGFRA* activating mutations in gastrointestinal stromal tumors. *Science*. 2003; 299:708–710. [PubMed: 12522257]
- Hirota S, Isozaki K, Moriyama Y, et al. Gain-of-function mutations of *c-kit* in human gastrointestinal stromal tumors. *Science*. 1998; 279:577–580. [PubMed: 9438854]

13. Hirota S, Ohashi A, Nishida T, et al. Gain-of-function mutations of the platelet-derived growth factor derived receptor alpha gene in gastrointestinal stromal tumors. *Gastroenterology*. 2003; 125:660–667. [PubMed: 12949711]
14. Johnstone JM, Morson BC. Inflammatory fibroid polyp of the small intestine. *Histopathology*. 1978; 2:349–361. [PubMed: 721077]
15. Kang DY, Park CK, Choi JS, et al. Multiple gastrointestinal stromal tumors; clinicopathologic and genetic analysis of 12 patients. *Am J Surg Pathol*. 2007; 31:224–232. [PubMed: 17255767]
16. Kindblom LG, Remotti HE, Aldenborg F, et al. Gastrointestinal pacemaker cell tumor (GIPACT): gastrointestinal stromal tumors express characteristics of the interstitial cells of Cajal. *Am J Pathol*. 1998; 152:1259–1269. [PubMed: 9588894]
17. Lewin, KJ.; Appelman, HD. Tumors of the Esophagus and Stomach. (Atlas of Tumor Pathology fascic18). 3. Washington, DC: Armed Forces Institute of Pathology; 1996.
18. Lasota J, Miettinen M. KIT and PDGFRA mutations in gastrointestinal stromal tumors (GISTs). *Sem Diag Pathol*. 2006; 23:91–102.
19. Margolin FR, Lagios MD. Polypoid lipomatosis of the small bowel. *Gastrointest Radiol*. 1980; 5:59–60. [PubMed: 7358252]
20. Marshall JB, Diaz-Arias AA, Bochna GS, et al. Achalasia due to diffuse esophageal leiomyomatosis and inherited as an autosomal dominant disorder. Report of a family study. *Gastroenterology*. 1990; 98:1358–1365. [PubMed: 2323526]
21. McKusick, VA. Mendelian Inheritance in Man: A Catalogue of Human Genes and Genetic Disorders. 1. 12. Baltimore, MD: The Johns Hopkins University Press; 1998. Entry 160980
22. McWhinney SR, Pasini B, Stratakis CA. International Carney Triad and Carney-Stratakis Consortium. Familial gastrointestinal stromal tumors and germ-line mutations [Letter]. *New Engl J Med*. 2007; 357:1054–1056. [PubMed: 17804857]
23. Miettinen M, Lasota J. Gastrointestinal stromal tumors: review on morphology, molecular pathology, prognosis, and differential diagnosis. *Arch Pathol Lab Med*. 2006; 130:1466–1478. [PubMed: 17090188]
24. Nishida T, Hirota D, Taniguchi M, et al. Familial gastrointestinal stromal tumours with germline mutation of the KIT gene. *Nat Genet*. 1998; 19:323–324. [PubMed: 9697690]
25. Pantanowicz L, Antonioli DA, Pinkus GS, et al. Inflammatory fibrous polyps of the gastrointestinal tract. Evidence for a dendritic cell origin. *Am J Surg Pathol*. 2004; 28:107–114. [PubMed: 14707872]
26. Pasini B, Matyakhina L, Bei T, et al. Multiple gastrointestinal stromal tumors caused by platelet-derived growth factor receptor α gene mutations: a case associated with germline V561D defect. *J Clin Endocrinol Metab*. 2007; 92:3728–3732. [PubMed: 17566086]
27. Prakash S, Sarraan L, Socci N, et al. Gastrointestinal stromal tumors in children and young adults: a clinicopathologic, molecular, and genomic study of 15 cases and a review of the literature. *J Pediatr Hematol Oncol*. 2005; 27:179–187. [PubMed: 15838387]
28. Riddel, RH.; Petras, RE.; Williams, GT., et al. Tumors of the intestine (Atlas of tumor pathology, 3rd ser. fasc. 32). Washington, D.C: Armed Forces Institute of Pathology; 2003.
29. Rubin BP, Singer S, Tsao C, et al. KIT activation is a ubiquitous feature of gastrointestinal stromal tumors. *Cancer Res*. 2001; 61:8118–8121. [PubMed: 11719439]
30. Takazawa Y, Sakurai S, Sakuma Y, et al. Gastrointestinal stromal tumors of neurofibromatosis type 1 (von Recklinghausen's disease). *Am J Surg Pathol*. 2005; 29:755–763. [PubMed: 15897742]
31. Yakabe S, Muranaka T, Sumii T, et al. Jejunal lipomatosis with diverticulosis: Report of a case. *Surg Today*. 1998; 28:846–849. [PubMed: 9719009]

Fig. 1. Gastric stromal tumors (GISTs). **A**, An empty cyst (likely a degenerated GIST) was attached to a thickened white serosa. A small GIST was present in the muscularis propria (long arrow). The submucosa was thickened and white (short arrow). **B**, A large intramural (top right) and a series of small serosal GISTs (arrows). **C**, Sheet of sharply outlined epithelioid cells with acidophilic and clear cytoplasm. Nuclei were round, central and had inconspicuous nucleoli.

Fig. 2. Gastric fibrous tumor. A, A tumor has expanded the submucosa and elevated the mucosa. B, The cells stained for CD34 (vascular channels in the muscularis propria also [below]), and also for vimentin (C).

Fig. 3. Jejunal tumors. **A**, The normal mucosal plical pattern was effaced by a series of fibrous tumors, several juxtaposed. Two of the tumors were yellow (lipomas) (arrows). The cut surface of the wall had lost its normal layered structure and appeared uniformly white (bottom left). **B**, Dilated, partially opened intestine showed a series of closely packed, elevated lesions (fibrous tumors) covered by intact mucosa. There was also a large diverticulum (arrow). **C**, Side-by-side, broad-based polypoid tumors, two fibrous (white), one lipomatous (yellow), were covered by intact mucosa. Narrow white strands of a fibroid tumor (arrows) penetrated into the muscularis propria. The subserosa was thick and white.

Fig. 4. Jejunal tumors. **A**, The intact mucosa was elevated by two juxtaposed tumors, one fatty, the other fibrous. The subserosa was markedly thickened. **B**, Hypocellular fibrous tumor was composed of spindle and polygonal cells with little apparent cytoplasm, embedded in the collagen fibers and bundles. Some of the latter mimicked skenoid fibers (arrows) but were PAS-D negative.

Fig. 5. Jejunal fibrous tumor (Masson trichrome). **A**, Submucosal fibrous tumor that has virtually replaced the muscularis propria longitudinal layer. **B**, Narrow tongues of tumor cells (not visible at this magnification) and collagen (stained blue) penetrated into and surrounded bundles of the muscularis propria circular layer, expanded the zone between the muscularis layers, almost replaced the longitudinal muscle coat, and expanded the subserosa.

Fig 6.
Jejunal fibrous tumor. Submucosal lesion penetrated through the muscularis propria and extended into the mesentery along vascular channels.

Table 1

Summary of Gastrointestinal Pathologic Findings

Year	Stomach	Duodenum	Jejunum
1977	Intramural tumor	Lipoma	
1987	GISTs	Fibrous tumor	Fibrous tumors
1990			Fibrous tumors, diverticulum
2002	GISTs and fibrous tumors	Fibrous tumor	Fibrous tumors, lipomas, diverticulum

* Appendiceal fibrous tumor also.

Table 2

Immunostaining Results*

Immunostain	GISTs	Fibrous tumors	Lipomas
CD117	+, strong	–	–
CD34	+, strong	+	–
Vimentin	+, strong	+	–
PKCθ	+, strong to weak	–	–
Actin	–	–	–
Desmin	–	–	–
S-100	A few + cells	–	Equivocal
Neurofilament	–	–	–

*
+, positive; –, negative.

Table 3

Pathologic Features of Small Intestinal Inflammatory Fibroid Polyps and Fibrous Tumors in the Present Case

Feature	Inflammatory fibroid polyp (9, 14, 17, 28)	Fibrous tumors (present case)
Ulceration	Yes	No
Cellularity	Moderately cellular	Hypocellular to moderately cellular
Eosinophils	Abundant	Close to mucosa
Thick-walled vessels	Yes	Scattered dilated sinusoids
Perivascular stromal cell cuffing	Yes	No
Fibrogenic	No	Yes; some sclerotic
Transmural	No	Yes (mucosa not involved)
Microcysts	No	Occasional
Destruction of muscularis mucosae	Yes	No
Lymphocytic aggregates	Yes	Rare
Secondary changes in mucosa	Yes	No; thinning only
Infiltration of mucosa	Yes	No

Table 4

Immunohistochemical Reactivity of Small Intestinal Inflammatory Fibrous Polyps and Fibrous Tumors (present case) to Selected Antibodies.

Antibody	Inflammatory fibrous polyp (25)		Fibrous tumor (present case)
	Reactivity	% cases	
CD117	Negative	100	Negative
CD34	Positive	100	Positive
Calponin	Positive (strong)	88	Positive (weak)
Cyclin-D1	Positive	100	Negative
Fascin	Positive	100	Positive
CD35	Positive	100	Positive
Bcl-2	Negative	100	Negative
Actin	Positive	25	Negative