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Solitary Schwannoma of the Colon: Report of Two Cases

SATOSHI INAGAWA[1,4], MASAO HORI[1], JIRO SHIMAZAKI[1], SHIGEMI MATSUMOTO[2], HIROSHI ISHII[3], MASAYUKI ITABASHI[1], SHINYA ADACHI[4], TORU KAWAMOTO[4], and KATASHI FUKAO[4]

Departments of [1] Pathology, [2] Internal Medicine, and [3] Surgery, Ibaraki Prefectural Central Hospital and Cancer Center, 1-3-1 Amakubo, Tsukuba, Ibaraki 305-8558, Japan
[4] Department of Surgery, Institute of Clinical Medicine, University of Tsukuba, Ibaraki, Japan

Abstract Some patients with gastrointestinal schwannoma (GIS) have been previously reported in the literature. However, GIS of the colon is quite rare. In addition, it is sometimes difficult to differentiate neurogenic tumors from other soft tissue tumors. We herein describe two cases of schwannoma of the colon, while also reviewing the relevant Japanese literature. The first case, a 73-year-old woman underwent a sigmoidectomy with lymph node dissection following the diagnosis of submucosal tumor. In the second case, a submucosal tumor was located in the cecum of a 44-year-old man. An endoscopic tumor resection was performed in the second case. The resected tumors measured 3.6 and 1.0 cm in maximal diameter, respectively. Microscopically, the tumors consisted predominantly of spindle-shaped cells that proliferated in an interlaced fashion. Mitosis was rarely seen in these tumors. Immunohistochemically, the tumor cells were strongly positive for S-100 protein, weakly positive for glial fibrillary acidic protein, and negative for CD34, α-smooth-muscle actin, and cytokeratin (CAM 5.2) in both cases. The tumors in the two cases were both diagnosed to be benign schwannoma of the colon. In general, schwannoma of the gastrointestinal tract is considered to be benign and should therefore be distinguished from other spindle-cell tumors or malignancies. Once diagnosed as schwannoma, extensive surgery should be avoided. Actually, such patients tend to show a good postoperative course with no evidence of recurrence.

Key words Schwannoma · Neurilemmoma · S-100 protein · Colon

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Introduction

Schwannoma arises from Schwann cells, which cover the peripheral nerves. It commonly occurs in the peripheral nerve of the limbs or body, spinal cord, and central nervous system. Isolated gastrointestinal schwannoma (GIS) is relatively rare. Since Verocay[1] first described gastrointestinal schwannoma in 1910, there has been a relatively small number of reports. The incidence of submucosal schwannoma has been reported to range from 2% to 6% of all submucosal tumors of the intestine,[2–4] and most GIS have been found to occur in the stomach.[5,6] Indeed, Stout[7] reported only two cases of schwannoma of the colon out of 42 cases of GIS.

However, neurogenic tumors are often difficult to distinguish from other soft tissue tumors. Therefore, the exact incidence of schwannoma of the colon is not known. To our knowledge, reports of schwannoma of the colon are quite rare; in Japan only 46 patients with this disease have been described. We herein report two cases of schwannoma of the colon, and review the previous reports of benign schwannoma of the colon in the Japanese literature.

Case Reports

Case 1

A 73-year-old woman visited her local physician with a 5-day history of progressive abdominal distension and bloody stool. The following day she was referred to our hospital with a suspected diagnosis of cancer of the colon. Her medical history was otherwise unremarkable. On physical examination, all findings were unremarkable except for slight tenderness in her left lower abdomen. Laboratory tests and the serum levels of carbohydrate antigen 19-9 and carcinoembryonic antigen

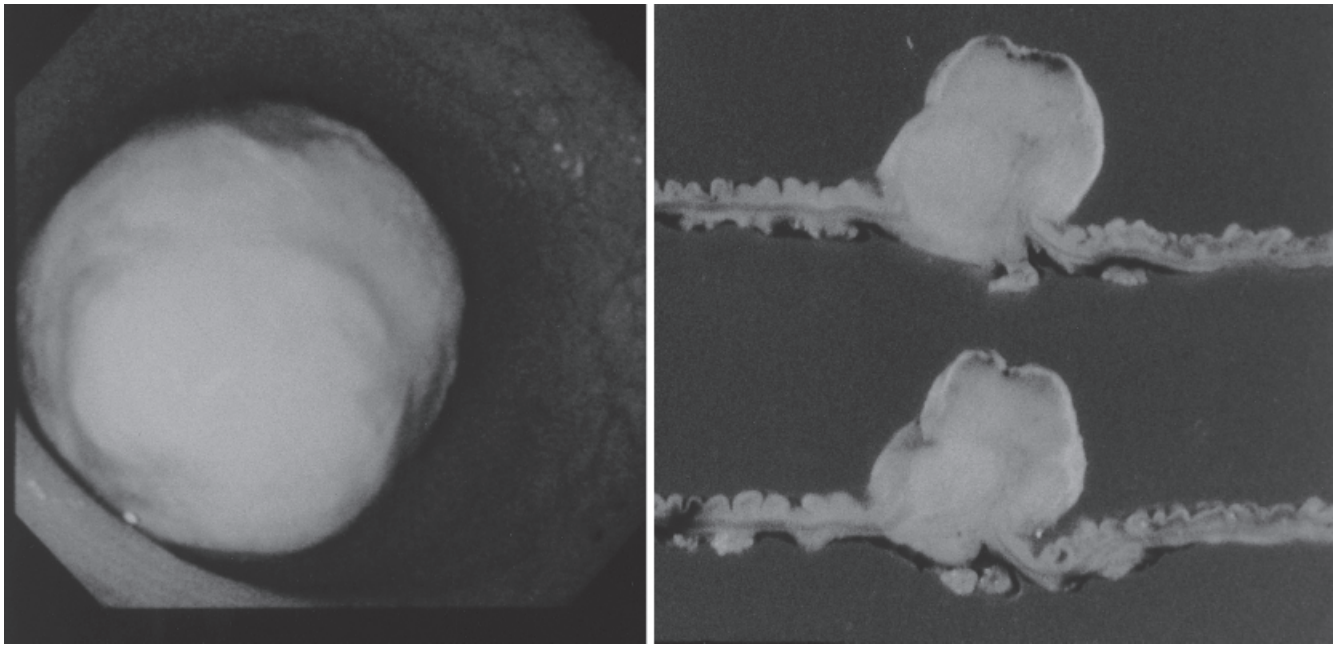

Fig. 1. a In case 1, colonoscopy revealed an intraluminal oval tumor covered with necrotic tissue, which measured approximately 3.5 cm in diameter. **b** A macroscopic examination of the sigmoid colon showed a well-circumscribed submucosal tumor covered with necrotic tissue, which measured 3.6 × 2.8 × 3.0 cm in size. The cut surface of the tumor consisted of solid and myxoid parts and was gray-yellowish in color

were all within normal limits. A barium enema revealed an oval tumor with a partly uneven surface, which caused an obstruction of two thirds of the lumen of the sigmoid colon. An abdominal computed tomography scan showed a solid, high-density mass with an irregular surface within the sigmoid colon. No infiltration of the tumor to the surrounding organs was seen. Colonoscopy revealed an intraluminal, oval, solid, and hard tumor covered with necrotic tissue, measuring approximately 3.5 cm in maximal diameter (Fig. 1a). Despite repeated tumor biopsies, only necrotic tissue was observed in the specimens. Accordingly, under a diagnosis of a submucosal tumor, a sigmoidectomy with lymph node dissection was performed. A macroscopic examination of the resected sigmoid colon showed a well-circumscribed submucosal tumor covered with necrotic tissue, which measured 3.6 × 2.8 × 3.0 cm in size and extended to the muscle layer and the subserosa. The tumor was slightly hard. The cut surface of the tumor showed solid with myxoid areas, and was gray-yellowish in color (Fig. 1b). A light microscopic examination revealed submucosal spindle-cell tumors surrounded by a fibrous capsule, composed of various sized schwann-like cells, arranged in whorls (Fig. 2a). The surface of the tumor was covered with necrobiotic tissue and fibrinous exudate (Fig. 2b). A palisading of tumor cell nuclei and high cellularity pattern were seen throughout the tumor (Fig. 2c). The spindle cells were wavy and intermixed with collagen strands. Hyperchromatic, pleomorphic, bizarre nuclei were often observed in the tumor (Fig. 2d), although mitosis was hard to detect in any part of the tumor. In the findings of immunohistochemical staining (IHC), the tumor cells were strongly positive for vimentin and S-100 protein (Fig. 3), and weakly positive for glial fibrillary acidic protein (GFAP), whereas α-smooth-muscle actin, cytokeratin, and CD34 were consistently negative. As a consequence of these pathological findings, the tumor was diagnosed to be cellular schwannoma. The patient's postoperative course has been good with no evidence of recurrence or metastasis 8 months after the operation.

Case 2

A 44-year-old man was pointed out to have occult blood in his stool during a comprehensive physical checkup. He was admitted to our hospital for further examination. His medical history and results of physical examinations were unremarkable. However, colonoscopy revealed a submucosal tumor in the cecum with a smooth and intact mucosa, measuring 1.0 cm in diameter (Fig. 4). Based on the histological findings of a biopsy sample, a benign spindle-cell tumor was diagnosed. Accordingly, an endoscopic tumor resection was performed. Macroscopically, a localized, gray, soft, and solid tumor was observed in the submucosa. In a light

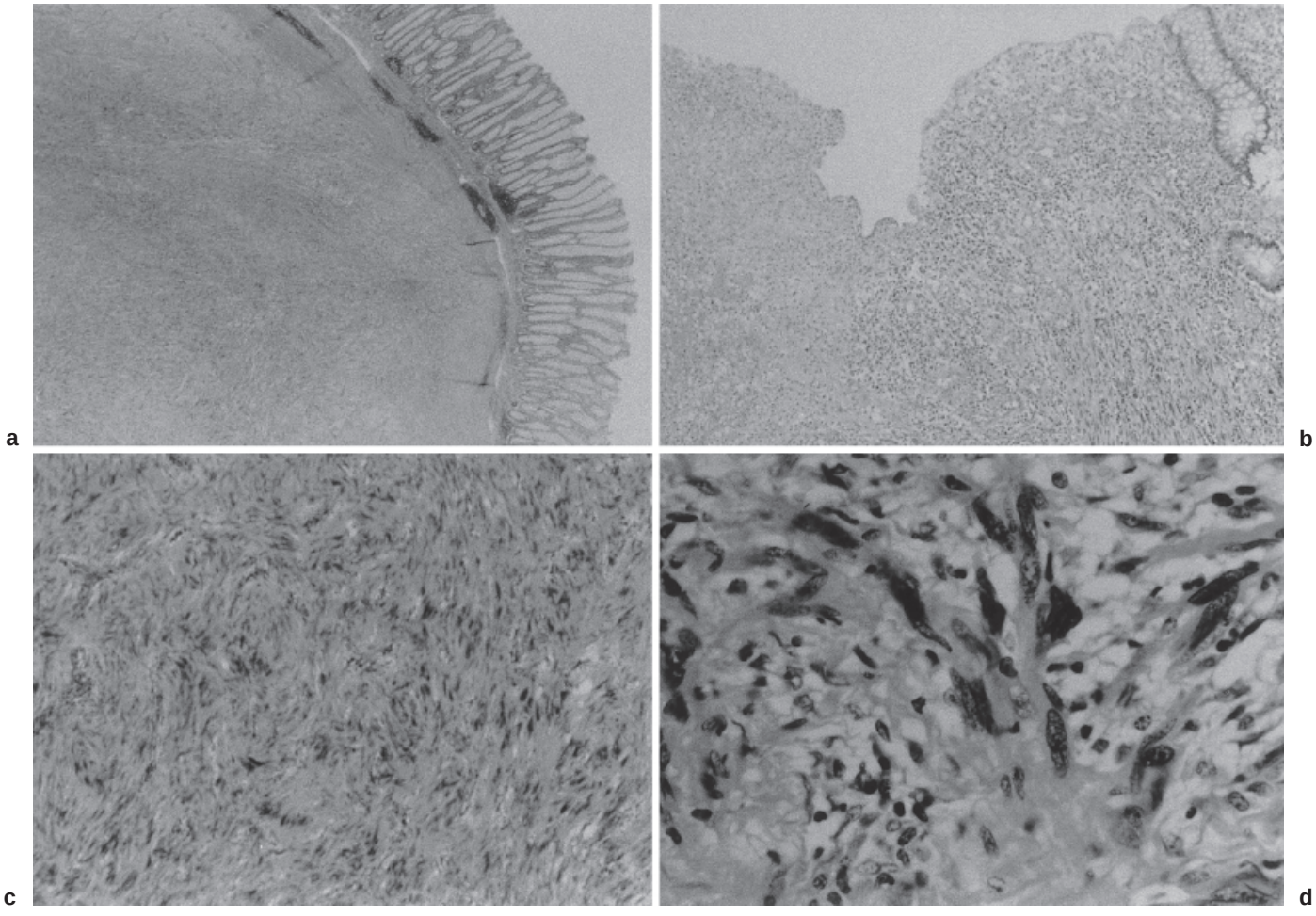

Fig. 2. **a** A low-magnification photomicrograph of a submucosal spindle-cell tumor surrounded by a fibrous capsule (H&E, ×100). **b** The surface of the tumor was covered with necrobiotic tissue and fibrinous exudate (H&E, ×100). **c** Tumor cells at a higher magnification showing the palisading of tumor cell nuclei and high cellularity (H&E, ×200). **d** Hyperchromatic and bizarre nuclei were seen at a higher magnification (H&E, ×400)

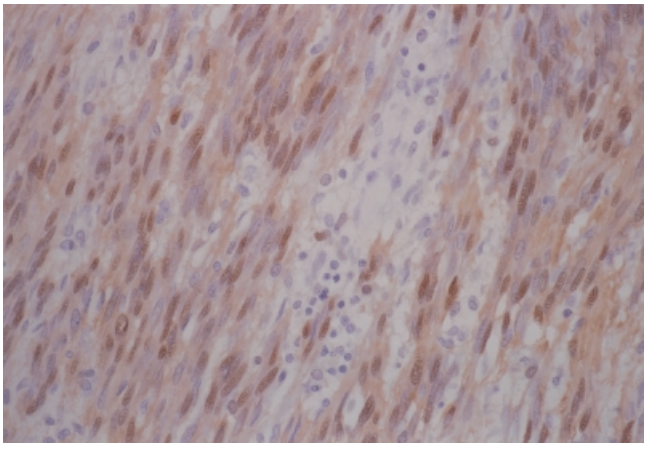

Fig. 3. Immunohistochemical staining of the neoplastic spindle cells was strongly positive for S-100 protein (×200)

microscopic examination, the tumor contained some mature Schwann-like cells of various sizes, which were arranged in whorls. No degenerative changes were particularly obvious in the tumor. In IHC, the tumor cells were strongly positive for vimentin and S-100 protein, and weakly positive for GFAP. However, α-smooth-muscle actin, cytokeratin, and CD34 were consistently negative. The tumor was diagnosed to be schwannoma. The patient is presently doing well without any evidence of recurrence 9 months after the endoscopic tumor resection.

Discussion

Schwannomas originate from the peripheral nerve sheath and occur most commonly in the peripheral nerve of body and limbs, spinal cord, and central ner-

vous system. Recently the number of reports of GIS has increased, owing to advances in IHC, which now makes it easy to distinguish GIS from other spindle-cell tumors. However, isolated intestinal Schwann-cell tumors are relatively rare. In particular, schwannomas occurring in the large intestine are extremely rare.[5,6,8,9] We herein describe two cases of solitary schwannoma of the colon.

There is often confusion surrounding the differential histological diagnosis of neurogenic tumors from other soft tissue tumors. In particular, the pathogenesis of schwannomas and neurofibromas is often confusing.[8] However, it is imperative that these two diseases be distinguished from each other because such tumors accompanied by von Recklinghausen's disease are generally neurofibroma. On the other hand, schwannoma is not so frequently accompanied by von Recklinghausen's disease.[5]

In a Japanese literature search, we identified 46 cases (including the current cases) of benign schwannoma of the colon. We reviewed these cases in order to clarify the clinicopathological features of this tumor type (Table 1). In these reports, IHC has been used since 1989, and all of the cases (21/21) which made use of IHC were positive for S-100 protein. Before then a diagnosis of schwannoma was made using microscopic examinations. The male to female ratio of patients with primary schwannoma was 21:25, and their mean age was 60.4 years (range 25–90 years). Although one case involved the entire colon,[10] in 21 cases (45.6%) the tumor was located in the rectum, and constipation as well as difficulty in defecating were the most frequently associated complaints (30.4%). A definitive diagnosis was preoperatively made in only 7 (15%) of the cases, because when this tumor occurred in the colon it was difficult to obtain a sufficiently large biopsy specimen to make a pathological diagnosis. Moreover, a correct diagnosis of schwannoma is often difficult because of the limited information available on such tumors. There-

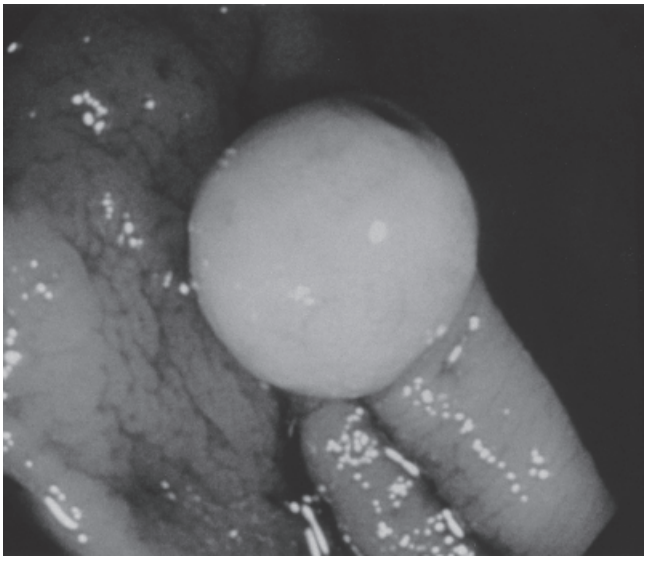

Fig. 4. In case 2, a colonoscopy revealed a spherical polyp with smooth mucosa, which measured 1.0 cm in diameter and was located in the cecum

Table 1. Summary of cases with benign schwannoma of the colon reported in Japan

Male : female	21 : 25		
Age (years)	60.4 ± 12.8 (range, 25–90 years)		
Tumor size	4.6 ± 2.5 cm (range, 0.8–10.0)		
Location		Preoperative diagnosis	
Appendix	2 (4.3%)	Acute appendicitis	2 (4.3%)
Cecum	4 (8.7%)	Carcinoma	8 (17.4%)
Ascending	5 (10.9%)	Submucosal tumor	18 (39.1%)
Transverse	6 (13.0%)	Schwannoma	7 (15.2%)
Descending	5 (10.9%)	Leiomyoma	4 (8.7%)
Sigmoid	2 (4.3%)	Others	7 (15.2%)
Rectum	21 (45.7%)		
Entire	1 (2.2%)		
Symptoms		Treatment	
Constipation, defecation difficult	14 (28.6%)	Appendectomy	1 (2.2%)
Bleeding, bloody stool	10 (20.4%)	Colectomy	24 (52.2%)
Abdominal pain	10 (20.4%)	Miles	10 (21.7%)
Discomfort	5 (10.2%)	Tumor resection	5 (10.9%)
Occult blood in stool	6 (12.2%)	Endoscopic resection	2 (4.3%)
Anal pain	4 (8.2%)	Others	4 (8.7%)
Ulceration[a]			
(+)	11 (34.4%)		
(−)	21 (65.6%)		

[a] Clearly described in 31 cases

fore, overly aggressive surgery has often been performed. We suppose that the ulceration and hardness of the tumor as revealed by colonoscopy are relatively typical features of schwannoma, since ulceration was found in 34% of cases described in the literature, and because biopsy sampling could not be performed in some cases due to the hardness of the tumor.[11]

Macroscopically, schwannoma appears as a spherical, solid, and well-encapsulated tumor which is gray in color. Secondary changes that are sometimes associated with this tumor including hemorrhaging, cystic changes, and calcification.

In most cases, schwannoma was diagnosed using microscopic examinations only. Histopathologically, schwannomas are composed of elongated bipolar spindle cells with zonally variable cellularity and a focally prominent nuclear palisading pattern. In addition, there is sometimes peripheral cuff-like lymphocyte infiltration surrounding the tumor.[5] This lymphoid cuff is sometimes useful in differentiating GIS from other spindle-cell tumors such as fibroma or leiomyoma. However, if tissue is only stained with hematoxylin and eosin (H&E), it is sometimes difficult to distinguish from the smooth-muscle tumors, gastrointestinal stromal tumors (GIST),[12] and gastrointestinal autonomic nerve tumors (GANTs). Compared with smooth-muscle tumors, schwannomas tend to have spindle cells that contain an eosinophilic cytoplasm that is devoid of coarse fibrillar material or any discernible cell walls, and their nuclei are generally thinner than smooth-muscle cell nuclei, and are also tapered.[13] In addition, GANTs often demonstrate an epithelioid appearance, and sometimes are observed predominantly in the tumor.[14–17] To make a final microscopic diagnosis, IHC is thus an invaluable tool. In many experiments, several authors[12,18–22] have reported the usefulness of S-100 IHC to distinguish schwannoma from smooth-muscle tumors. In addition, numerous studies have reported schwannoma to be distinguished from GIST using either CD34 or c-kit protein IHC,[23,24] whereas to distinguish GIS from GANTs, IHCs of S-100 and GFAP are useful[25] because these IHCs are generally positive in cases of GIS in comparison with GANTs.[14–17]

In the case of cellular schwannoma, it may sometimes be misdiagnosed as a malignant peripheral nerve sheath tumor (MPNST) because of its increased cellularity, nuclear hyperchromasia, and the presence of mitosis.[8,9,26] Woodruff et al.[26] suggested schwannomas to be benign because MPNSTs frequently affected larger nerves, and a nerve origin was more frequently recognized for MPNST than with cellular schwannomas. In addition, Hruban et al.[27] reported that MPNSTs have a greater cellularity and more mitotic nuclei than the cellular schwannomas and that the cells involved were mostly anaplastic. Nevertheless, if the final diagnosis is difficult, an electron microscopic examination is also a useful diagnostic tool.[9,14–17,28,29] In our two cases, the diagnosis of schwannoma was made without any trouble using light microscopy, because the histological findings revealed by H&E and IHC were typical of these tumors.

In general, gastrointestinal schwannomas are considered to be benign tumors. Therefore once a schwannoma is diagnosed, as in our second case, the correct treatment would be to resect the tumor locally with a sufficient surgical margin; however, overly aggressive surgery should be avoided. In addition, to our knowledge there has only been one previous report of an endoscopic resection of a schwannoma.[30] In both of our cases the postoperative course has been very good, with no evidence of recurrence or metastasis at 8 months and 9 months after performing a resection, respectively.

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