Two cases of sporadic intra-abdominal desmoid tumor with a very unusual onset

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Case report

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Abstract

Background

Intra-abdominal desmoid tumors are rare soft tissue tumors that arise mainly in the mesentery and pelvis. Causes include mutations in the *APC* gene, which is the causative gene of familial adenomatous polyposis (FAP), estrogen-associated changes after childbirth, and mechanical factors, such as history of abdominal surgery. However, there are cases of intra-abdominal desmoid tumors that develop in the absence of such causes, although they are rare, and diagnosis is often difficult from clinical findings. We encountered 2 cases of patients with sporadic intra-abdominal desmoid tumors with a very unusual onset.

Case presentation

The first patient was a 51-year-old man. He presented to the clinic with sudden onset of abdominal pain, and was referred to our department because of a giant tumor detected on abdominal ultrasonography. Imaging diagnosis displayed a 19-cm tumor with internal tumoral hemorrhage, but no definitive diagnosis was made. Resection of the tumor was performed for diagnostic and therapeutic purposes. The second patient was a 41-year-old man. Right hydronephrosis was detected on abdominal ultrasonography at a medical check-up. We diagnosed invasion of the primary mesenteric tumor into the right ureter by diagnostic imaging, and performed ileocecal resection with partial right ureteral resection for a definitive diagnosis and therapeutic purposes. The tumors of both patients had developed from the ileal mesentery. Although the tumors were substantially different in their macroscopic morphology and progression pattern, they showed similar pathological characteristics, i.e., they consisted of bundles of collagen fibrils of spindle-shaped fibroblasts with low cell atypia, and were diagnosed to be desmoid tumors by positive immunohistochemical staining for β-catenin. Both patients had no susceptibility factors for desmoid tumors.

Conclusions

To our knowledge, there have been very few reports to date of sporadic intra-abdominal desmoid tumors that were diagnosed owing to acute abdominal pain caused by tumoral hemorrhage or asymptomatic ureteral obstruction. Intra-abdominal desmoid tumors can cause various symptoms depending on the location of their occurrence and their progression pattern and are often difficult to differentiate from other mesenchymal tumors on imaging findings. Diagnosis therefore requires experience and knowledge that is not bound by preconceptions.

Background

Desmoid is a Greek word meaning “band or tendon like” derived from “desmos”, and was first used in 1838 [(1)]. The NCCN guidelines describe this type of tumor as an aggressive fibromatosis, which does not metastasize but has a very high local recurrence rate even after complete resection, and it is treated as a

borderline malignant tumor [2]. Their etiology is thought to be multifactorial. It is widely known that germline mutations in the adenomatous polyposis coli (*APC*) gene, which cause FAP, are associated with the development of desmoid tumors, and occur in 10–15% of FAP patients. The risk of onset of desmoid tumors in FAP patients is more than 800 times that in a healthy person [3]. In sporadic desmoid tumors, somatic mutations of the *APC* gene or the catenin beta 1 (*CTNNB1*) gene are involved, and it has been reported that *CTNNB1* gene mutations are found in about 50–85% of sporadic desmoid tumors [4–6]. Both of these genes are involved in important signal transduction pathways that are associated with cell proliferation and differentiation, and play roles in regulating the cellular level of β-catenin, which acts on cell-cell junctions. Therefore, when a mutation occurs in either the *APC* gene or the *CTNNB1* gene, β-catenin accumulates in cells, and cells that overgrow uncontrollably form tumors [7]. It has also been reported that estrogen is involved in the development and growth of desmoid tumors and hence often occur in women, particularly in multiparous women. In fact, estrogen receptors are highly expressed in a large number of desmoid tumors, and tamoxifen has recently been reported to be effective as a treatment [8, 9]. A history of trauma or surgery is also considered to be a factor in the development of desmoid tumors, and mutations in genes involved in the wound-healing process of tissues are considered to be a cause of desmoid tumor development [10]. Intra-abdominal desmoid tumors often occur in the abdominal cavity, when the above causative factors are present. They have no characteristic symptoms and are often found mainly as abdominal distensions or bowel obstructions associated with tumor growth or invasion [11, 12]. Furthermore, no characteristic findings are displayed on diagnostic imaging, and it is often necessary to differentiate them from other mesenchymal tumors, such as gastrointestinal stromal tumor (GIST) and sarcoma. Although complete surgical resection is the first choice in the National Comprehensive Cancer Network (NCCN) guidelines(2), even if complete resection is possible, the local recurrence rate is very high and careful follow-up is required [13]. We here report 2 cases of patients with sporadic intra-abdominal desmoid tumors who had unusual onsets and underwent surgical resection.

Case Presentation

Case 1 was a 51-year-old man who presented to the clinic because of sudden left-abdominal pain. Ultrasonography displayed an intra-abdominal tumor, and he was referred to our hospital for further examination. He had previously been healthy and had no history of hospitalization or abdominal surgery. A tender and mobile infant head-sized mass in the left abdomen was detected by palpation. Ultrasonography displayed a smooth and solid mass of 19.8 cm × 15.9 cm × 14.8 cm, which contained cystic components (Fig. 1a). On enhanced abdominal computed tomography (CT), the tumor appeared as a well-marginated mass with scattered density, which appeared to be arising from the small intestine (Fig. 1b). Abdominal magnetic resonance imaging (MRI) displayed a region with a high signal on T1-weighted images in part of the tumor, suggesting intratumoral hemorrhage (Fig. 1c). Cyst components are displayed on the T2-weighted image (T2WI) (Fig. 1d). Small intestine endoscopy demonstrated ischemic mucosal changes 20 cm from the ileocecal valve, and gastrointestinal imaging displayed slight stenosis owing to exclusion from the external intestinal wall. Based on the above, GIST was first

considered and surgery was performed for therapeutic diagnosis. The tumor was located in the mesentery, 20 cm from the terminal ileum, and had developed involving a part of the proximal ileum. Therefore, small intestinal resection was performed. The tumor was 19 × 16.5 × 9 cm with a capsule that originated from the ileum mesentery, and hematoma and sac formation were observed on the split surface (Fig. 2). Histopathological findings showed that proliferation of bland spindle-shaped cells with minimal mitotic activity formed a broad bundle of stromal fibrosis (Fig. 3a). The tumor was diagnosed as a desmoid tumor on the basis of positive immunohistochemical staining for β-catenin (Fig. 3b), and negative staining for c-kit, CD34, and DOG-1. The Ki-67 labeling index, which is an index of cell proliferation, was approximately 6% (Fig. 3c). The surgical margin was pathologically negative, indicating that the desmoid tumor was completely resected. The patient has been alive without recurrence for 3 years since the surgery.

Case 2 was a 41-year-old man who had no subjective symptoms and was diagnosed with right hydronephrosis on abdominal ultrasonography on physical examination, and was referred to our hospital for urological examination. His past medical history was free of prior abdominal trauma, surgery, or any genetic disease. No abnormalities were noted on physical examination, and no abnormalities were found on blood biochemistry analysis. The physical examinations that were performed and serum biochemistry analysis did not reveal any abnormalities. Upper and lower gastrointestinal endoscopy did not display any abnormal findings. Drip infusion pyelography displayed narrowing of the right ureter (Fig. 4a), and abdominal pelvic CT displayed a 3.5-cm tumor that had uniform contrast with the dilated ureter (Fig. 4b). MRI T2WI displayed a low signal mainly at the center of the tumor (Fig. 4c). On ^{18}F-fluorodeoxy glucose positron emission tomography (FDG-PET), mild accumulation of FDG was observed at the site of the tumor (Fig. 4d), but there was only a slight increase in overall accumulation in the late phase, from a maximum standardized uptake value (SUV) in the early 3.50 s to late 4.51 s in part of the margin. Based on the above diagnostic findings, the tumor was suspected to be a desmoid tumor because it was a low-grade but strongly invasive tumor, and surgery was performed for diagnosis and treatment. The tumor was a 4-cm hard mass located in the ileum mesentery, and had grown so as to infiltrate the surrounding tissue. Because the dorsal side of the tumor was invading the ureter and hence could not be dissected, ileocecal resection with part of the right ureter (5-cm in the major axis) was performed. Histological analysis showed that the tumor was 3.7 × 3.5 × 3.2 cm (Fig. 5) and invaded the adventitia of the ureter. Pathologically, the tumor consisted of infiltrating and proliferating spindle-shaped fibroblasts, with low cell atypia, characterized by a keloid-like eosinophilic collagen fiber bundle (Fig. 6a). Immunostaining demonstrated that the tumor cells were CD34, DOG-1 negative and strongly β-catenin positive in the cytoplasm and nucleus (Fig. 6b), and was diagnosed as a desmoid tumor. The Ki-67 labeling index was less than 1% (Fig. 6c). The lesion was completely excised with clear margins. The patient has been alive without recurrence for 3 years since the surgery.

Discussion

The incidence of desmoid tumors is 0.03% of all neoplasms, and less than 3% of soft tissue tumors, and hence is an extremely rare disease with an onset frequency of about 2–4 per 1-million people. Approximately 10–20% of all cases occur in the abdominal cavity, as in our present cases, whereas 80–90% occur in the limbs, neck, shoulders, chest, and abdominal wall [14–16].

Desmoid tumors often occur in the abdominal cavity of patients who have risk factors, such as FAP, experience of pregnancy and childbirth, and a history of abdominal surgery. However, our patients had none of the above risk factors. In patient 1, sudden left abdominal pain triggered the diagnosis. MRI displayed intratumoral hemorrhage, suggesting that the abdominal pain was owing to rapid tumor-capsule extension. To date, there has been only 1 reported case of a desmoid tumor that was discovered owing to intratumoral hemorrhage [17]. In Patient 2, right hydronephrosis was detected on abdominal ultrasonography. There are relatively many reports of desmoid tumors that cause ureteral obstruction, and most of these are found in advanced cases at the time of diagnosis [18]. In patient 2, the tumor arose near the right ureter on the proximal side of the ileum mesentery, which caused right hydronephrosis when the tumor was still relatively small.

The differences between desmoid tumors and GISTs in diagnostic imaging are characterized by their site of occurrence, shape, contrast effects, and tumor content. GISTs originate from the gastrointestinal tract and are characterized mainly as a well-defined circular or lobulated tumor with a heterogeneous contrast effect, sometimes with necrotic vessels and cysts inside. On the other hand, desmoid tumors originate from outside of the gastrointestinal tract, often have a morphologically invasive form, and have relatively uniform contrast effects and rarely have necrosis or cysts inside [19]. In the imaging analyses of patient 1, the tumor had a well-defined circular shape. The inside of the tumor was heterogeneous on imaging, accompanied by necrosis and cyst formation, which were very different from the previously reported imaging characteristics of desmoid tumors. On the other hand, in patient 2, the mesenteric tumor had a uniform contrast effect, with an irregular rim shape and invasive growth, which was consistent with the characteristics of desmoid tumors. FDG-PET of patient 2 displayed slight FDG accumulation in the main lesion, indicating negative malignancy. FDG accumulation is generally low in desmoid tumors [20] because it reflects tumor burden and cell proliferation, and is hence useful in differentiating malignancies. Based on the above findings, patient 1 was initially diagnosed as having GIST and patient 2 was suspected as having a desmoid tumor.

The NCCN Guidelines suggest that careful observation of histologically confirmed desmoid tumors is a treatment option only for slow-growing cases without functional restriction. Fiore et al. reported that half of the cases of “wait and see” were free of recurrence for 5 years. [21] However, there are no precise treatment guidelines specific to intra-abdominal desmoid tumors. Surgery may be the first choice for patients with rapidly growing tumors or those with the risk of losing organ function owing to invasion of the tumor to other organs. As in patient 2, intra-abdominal desmoids with obstructive uropathy often require ureteral resection. If desmoid tumors are suspected before surgery, a treatment strategy including ureteral resection is necessary [22].

Macroscopically, the appearance of the tumors from the 2 patients were completely different. In patient 1, the tumor showed necrosis, cysts, and hematoma, which are rare in desmoid tumors, and grew expansively. By contrast, in patient 2, the tumor was hard like a stone, and showed highly invasive growth. On the other hand, histologically, the tumors showed very similar characteristics. Desmoid tumors are characterized by much more abundant collagen fibrils compared with GISTs, which are also mesenchymal tumors, and by the orderly arrangement of spindle-shaped fibroblasts with low cell atypia and mitosis [23]. Positive immunostaining for β-catenin assists in the diagnosis of desmoid tumors [24], and negative immunostaining for c-kit, CD34, and CD117 assists in clearly distinguishing them from GISTs. The tumors from our patients had all of the above characteristics. Ki-67 is an indicator included in the diagnostic criteria as a risk factor for malignancy and recurrence in GISTs as well as other neoplastic diseases, which suggests that the tumor in patient 1 has higher malignancy than the tumor in patient 2. However, in desmoid tumors, Ki-67 is not well documented as a prognostic or risk factor for recurrence [25, 26]. This is thought to be because desmoid tumors do not have metastatic potential, even when cell proliferation is rapid. Complete resection without pathological remnants was considered important to achieve a low recurrence rate and a favorable prognosis [13, 27], and complete resection was performed in both of our patients.

The NCCN Guidelines state that if surgical resection significantly impairs function or the tumor is difficult to resect, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), hormonal therapy, and systemic therapy mainly based on chemotherapy and molecular-targeted agents should be used. In addition, radiation therapy may be indicated if remnants are suspected after resection. However, radiation therapy for intra-abdominal desmoids has the risk of radiation enteritis and is hence not recommended by the NCCN Guidelines. Even if residual tumors are suspected in our patients, systemic therapy can be selected. It should be noted, however, that treatments other than surgical resection for desmoid tumors have not been established and are still in the experimental stage.

He et al. reported that incomplete resection (marginal status R1 or close to R1), large tumor diameters, tumors in the extremities, and younger onset are risk factors for recurrence [13]. In patient 1, the tumor size was very large, which is considered to be a risk factor for recurrence, and careful follow-up is considered to be necessary.

Conclusion

We encountered 2 patients with sporadic intra-abdominal desmoid tumors with unusual onset. Intra-abdominal desmoid tumors can cause various symptoms and conditions depending on the site of occurrence, and radiographic study findings are also diverse, making diagnosis difficult. Therefore, diagnosis may require knowledge and experience that is not limited by preconceptions. In our patients, complete resection was possible by surgery, but the local recurrence rate is extremely high, and careful follow-up is required.

Abbreviations

GIST: gastrointestinal stromal tumors; CT: computed tomography; NCCN: national comprehensive cancer network; MRI: magnetic resonance imaging; FAP: familial adenomatous polyposis; T1WI: T1 weighted image; FDG PET: ^{18}F-fluorodeoxy glucose positron emission tomography; APC: adenomatous polyposis coli; HE: Hematoxylin and Eosin.

Declarations

Ethics approval and consent to participate:

This case report was approved by the Institutional Review Board at Tokyo medical university Hachioji medical center.

Consent for publication:

The patient involved in this study gave his informed consent authorizing use and disclosure of his protected health information.

Availability of data and materials:

Not applicable

Competing interests:

The authors declare that they have no competing interests.

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Authors' contributions:

HK and SK designed the report. IK, MN, ST, KK , AT and SK coordinated and helped to draft the manuscript. HK analyzed the data and wrote the manuscript. All authors read and approved the final manuscript.

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Figures

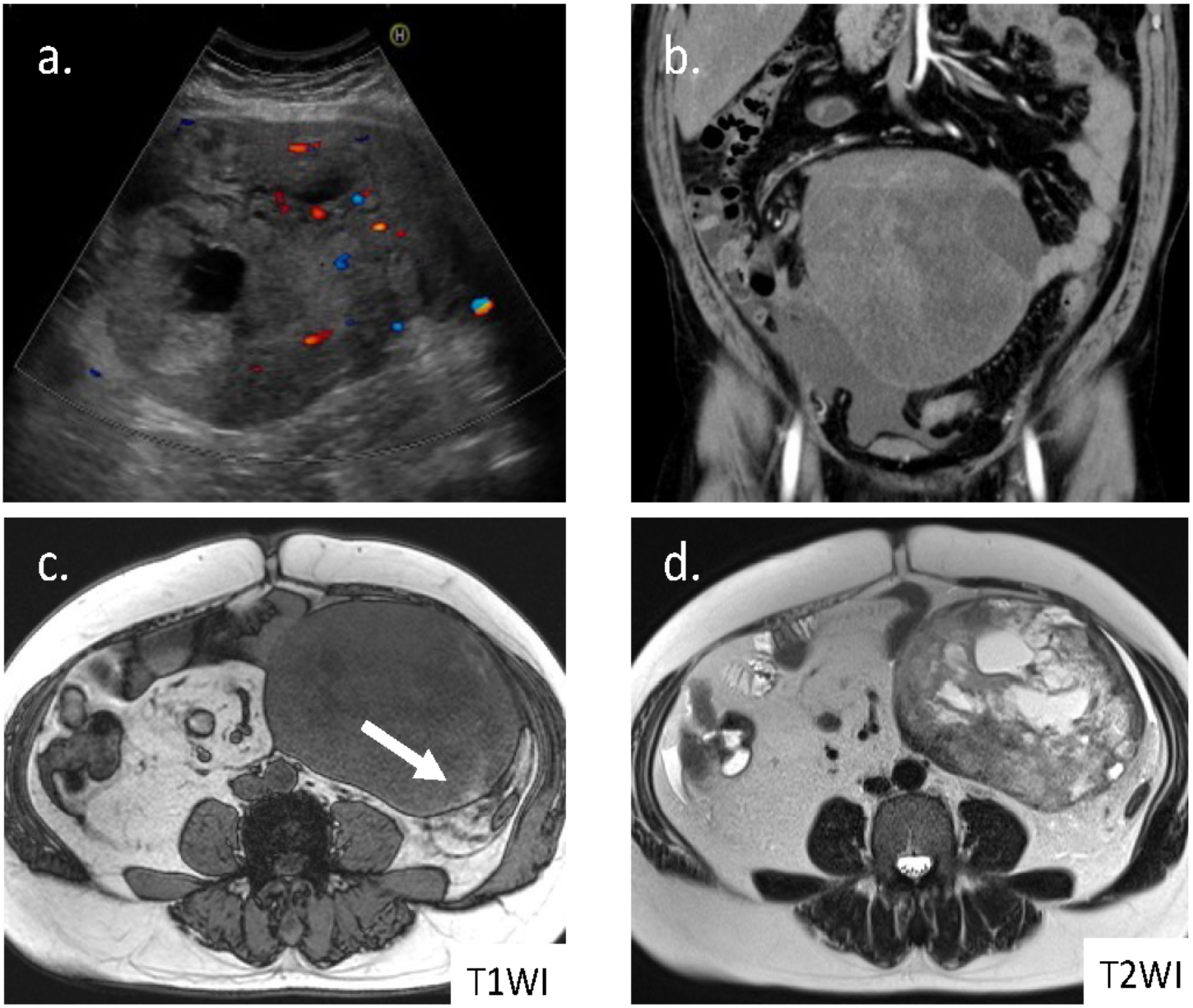

Figure 1

Diagnostic findings in Case 1 a. Abdominal ultrasonography displaying a large solid mass with cystic degeneration, and an irregular echoic pattern with vascular signals inside. b. Abdominal contrast-enhanced CT displaying a large, well-defined circular tumor with a heterogeneous interior, which appears to be partially continuous with the small intestine. c. MRI displaying some high-intensity signals (white arrow) on the T1WI. d. Cyst components are scattered on the T2WI.

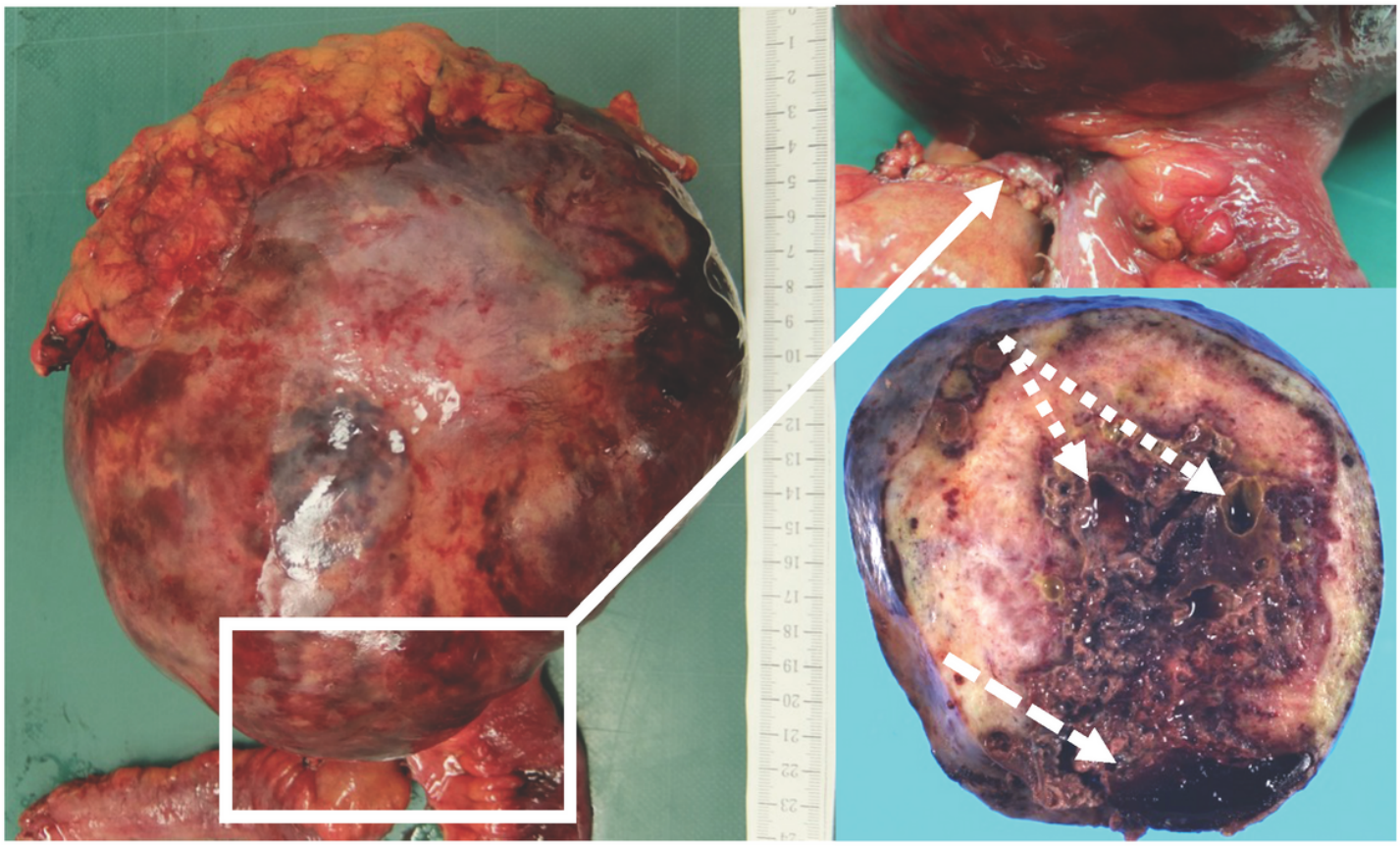

Figure 2

Macroscopic characteristics of the tumor in Case 1 The resected specimen appeared to originate from the small mesentery (white arrow). The tumor was grossly covered by a capsule, and the surface was smooth, elastic, and soft. Split surface contained hematoma (white dashed line) and cyst components (white dotted arrow).

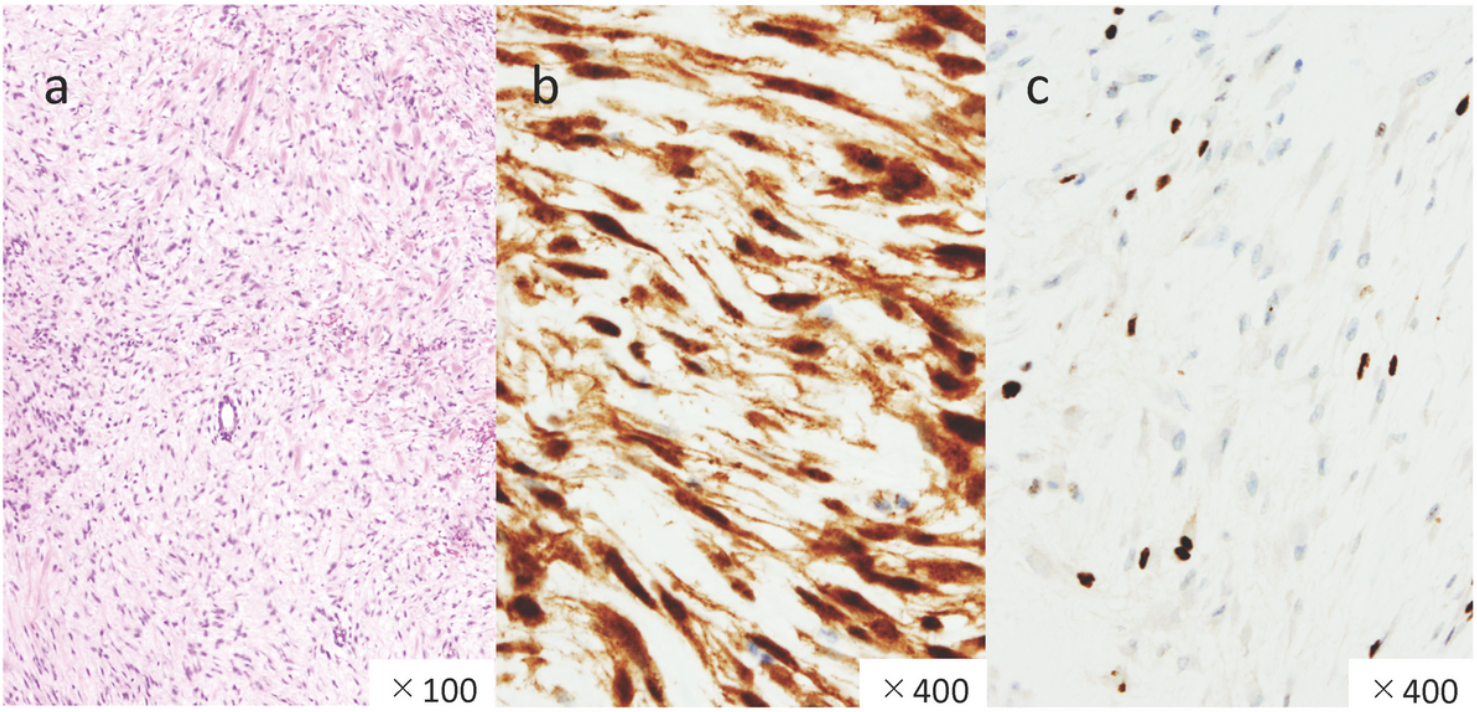

Figure 3

Histological and immunohistological features of desmoid tumors in Case 1 a. HE staining demonstrated the proliferation of low-density stromal cells forming thick collagen fibrils (low-power view). b. Strong immunostaining for -catenin was observed (high-power view). c. Expression of Ki-67 analyzed by immunostaining. The labeling index was 6% (high-power view).

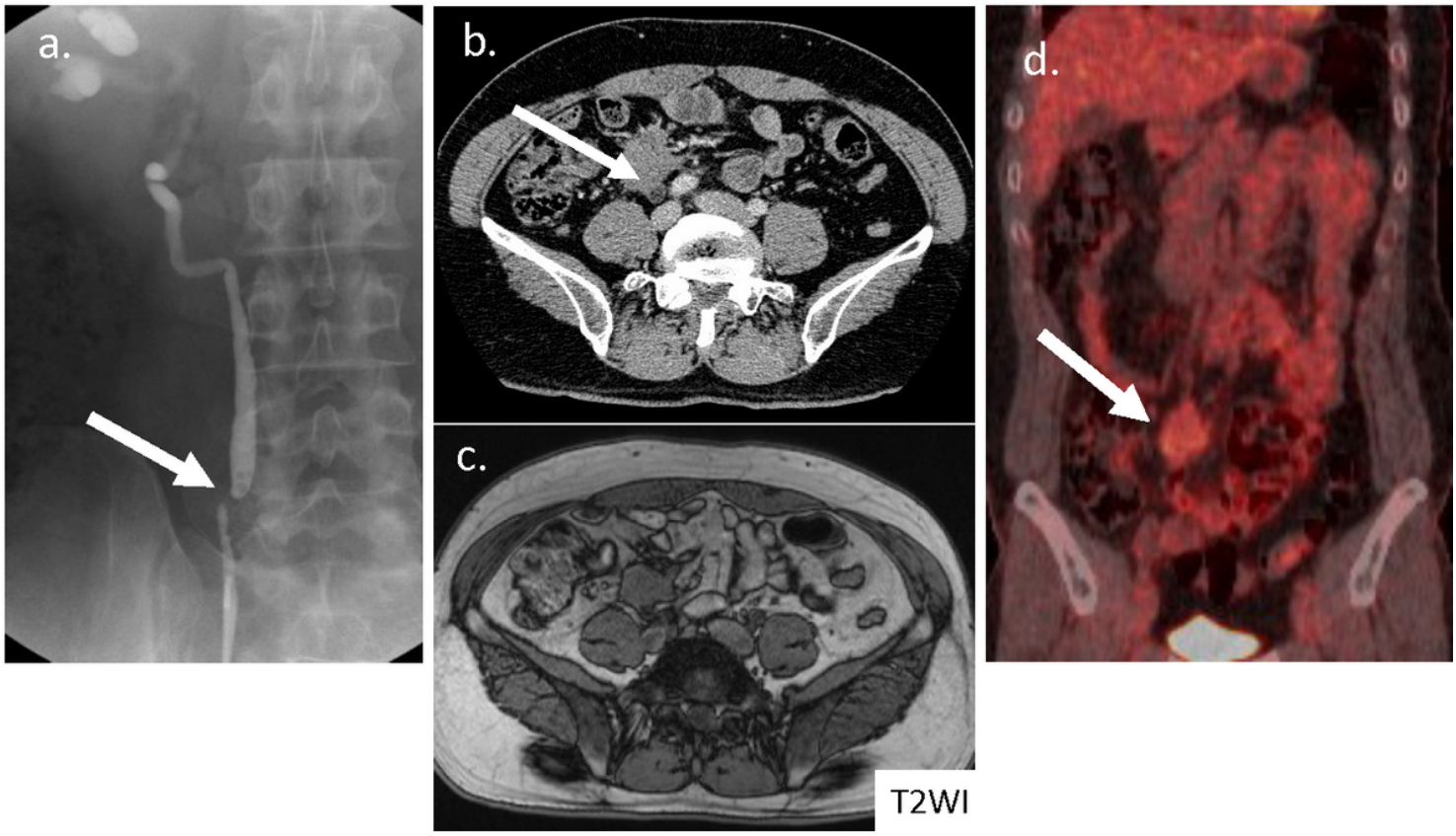

Figure 4

Diagnostic findings in Case 2 a. Drip infusion pyelography displaying right uropathy stenosis (white arrow). b. Abdominal contrast-enhanced CT displaying a homogenously enhanced 35-mm mass with an irregular, spiculated margin encasing the right dilated ureter at the level of the right common iliac artery (white arrow). c. T2WI displaying a low signal mainly at the center of the tumor. d. FDG-PET CT displaying slightly increased FDG in the mass (white arrow).

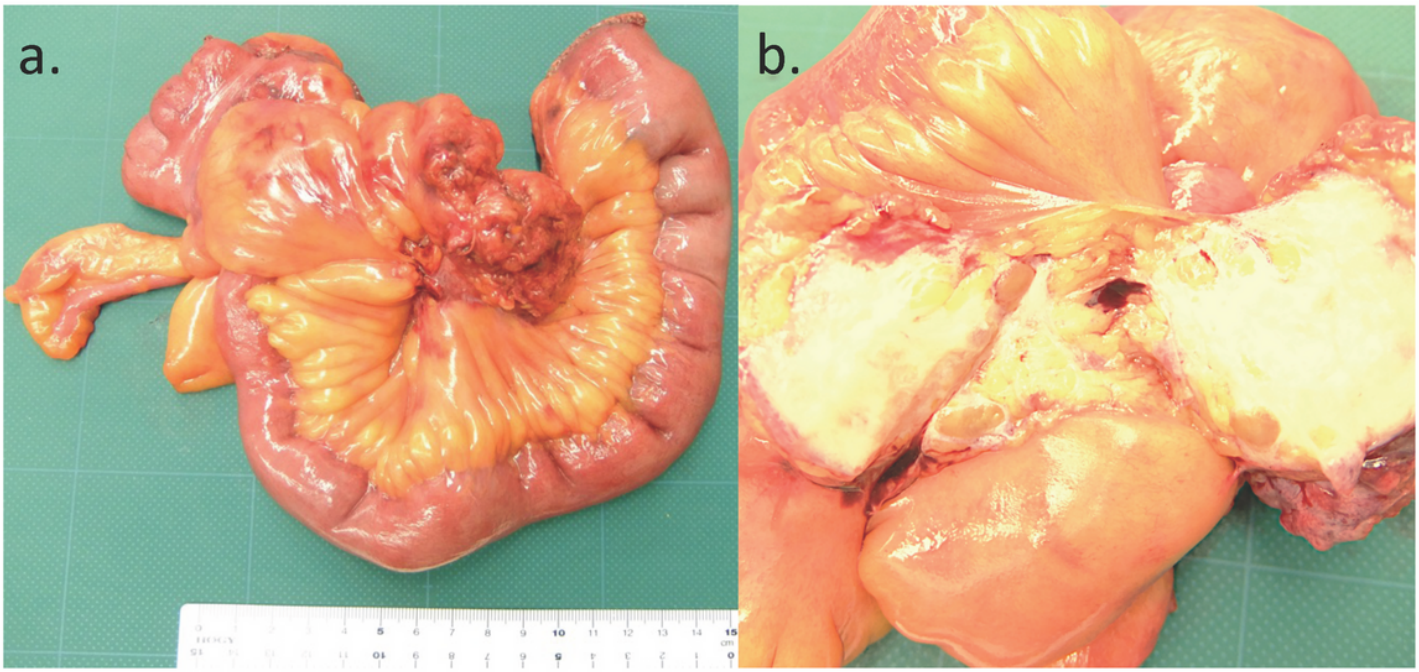

Figure 5

Macroscopic findings of the resected specimen in Case 2 a. A bulky mass with tentacle-like spiculated extensions with infiltrative growth is located at the center of ileum. b. The cut surface of the tumor is equally whitish, fibrous, and firm, partially involving the mesenteric adipose tissues.

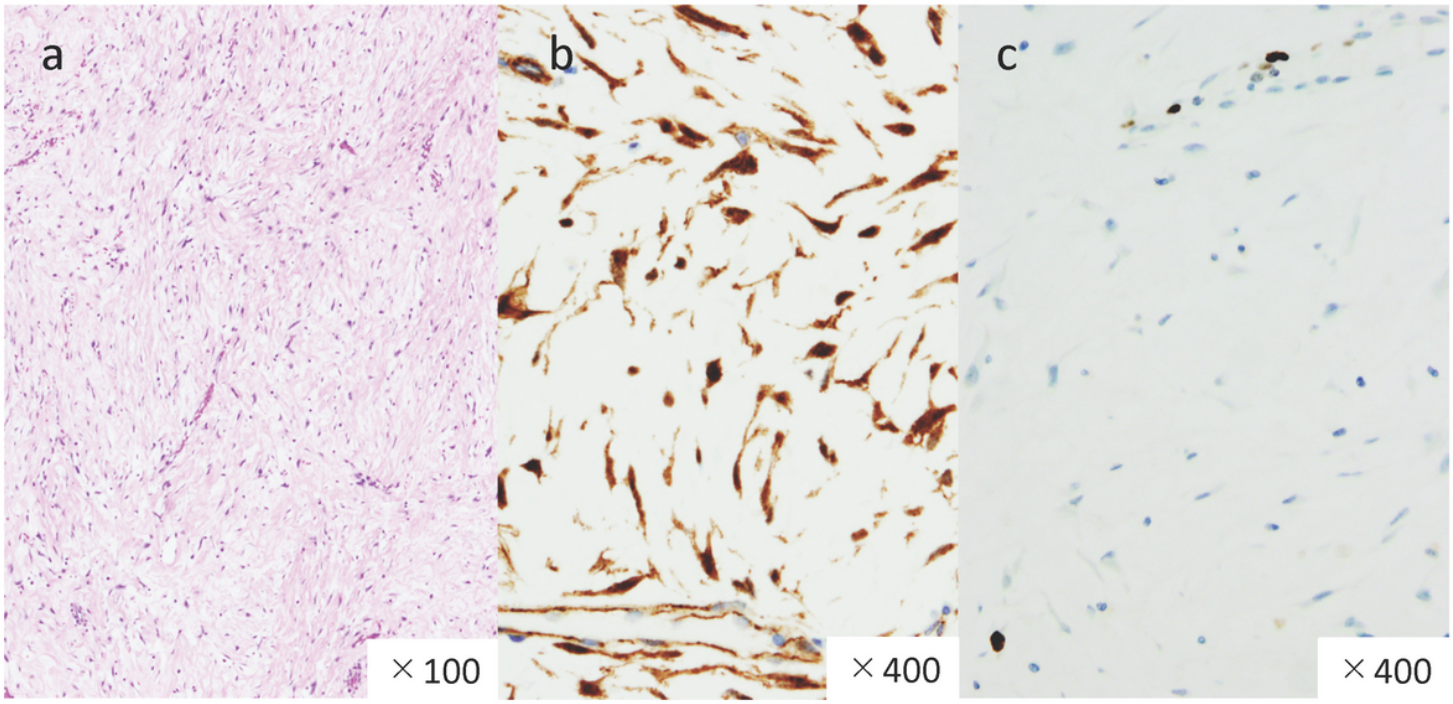

Figure 6

Histological and immunohistological features of desmoid tumors in Case 2 a. HE staining shows proliferation of spindle-shaped cells. Wavy collagenous bands of fiber lies in stroma. (low-power view). b. Immunohistological staining for β-catenin shows strongly positive staining of cell. (high power view). c. Immunohistological expression of Ki67 in tumor : Labeling index =1% (high power view).