

Case Report

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# Spontaneous Regression of Metachronous Intra-Abdominal Desmoid Tumor in a Patient with Familial Adenomatous Polyposis

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## Keywords

Spontaneous regression · Desmoid · Metachronous

## Abstract

Desmoid tumors are clonal fibroblastic neoplasms that arise in soft tissues. Patients with familial adenomatous polyposis (FAP) can develop intra-abdominal desmoid tumors. However, metachronous appearance of intra-abdominal desmoid tumor is rare, and its clinical course is not well known. Here, we report a case of spontaneous regression of metachronous intra-abdominal desmoid tumor in a 36-year-old man with FAP. The patient was diagnosed with FAP and underwent laparoscopic total colectomy. Intra-abdominal desmoid tumor appeared 2 years later and progressed despite treatment with tamoxifen and sulindac. He received four cycles of combinatory therapy with dacarbazine and adriamycin, resulting in shrinkage and stabilization of the desmoid tumor even after cessation of chemotherapy. A new intra-abdominal desmoid tumor developed 2 years later at a different site from the first lesion and progressed from 65 mm to 70 mm in diameter within a month. The size of the first lesion, however, remained unchanged. We prepared for chemotherapy because the second lesion progressed, but follow-up computed tomography showed spontaneous shrinkage of the second lesion. The patient

still has not needed additional therapy as of more than 4 years after the appearance of the second lesion. Immunohistochemical staining showed the presence of macrophages in the second lesion. Although metachronous intra-abdominal desmoid tumor is rare and management protocols have yet to be established, this case suggests that an active surveillance approach may be applicable under careful follow-up in asymptomatic patients.

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## Introduction

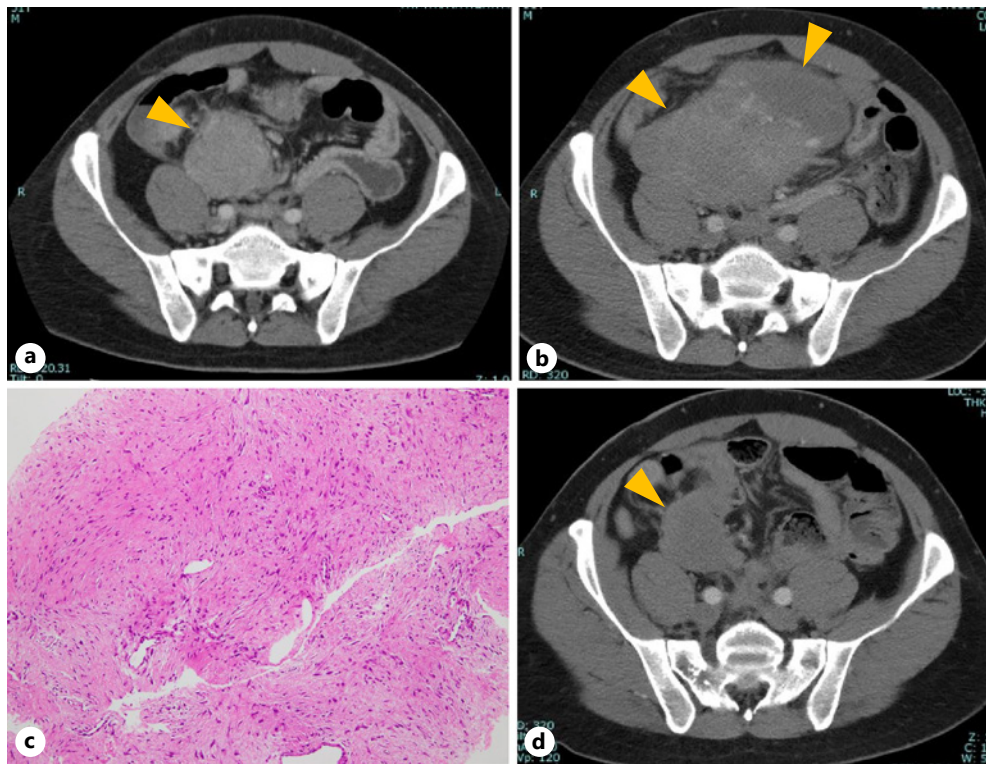
Desmoid tumors are clonal fibroblastic neoplasms arising in the deep soft tissue. Desmoid tumors grow infiltrative and have a tendency to show local recurrence [1]. The incidence of desmoid tumors is reportedly 2–4 per million. Most desmoid tumors arise sporadically and some are related to trauma, pregnancy, or hereditary cancer syndromes. Approximately, 10–25% of patients with familial adenomatous polyposis (FAP) develop desmoid tumors [2]. Most desmoid tumors in patients with FAP arise intra-abdominally, representing a main cause of death among FAP patients.

Recently, the Desmoid Tumor Working Group published consensus-based guidelines for dealing with desmoid tumors [3]. Active surveillance is proposed for asymptomatic patients under the supervision of an experienced team. Medical therapies such as surgery, radiotherapy, and/or systemic therapies are considered in patients with symptoms or progressive disease. Intra-abdominal desmoid tumors are close to the gastrointestinal tract and can readily cause intestinal obstruction, ulceration, or bowel ischemia [4]. On the other hand, surgical resection with adequate margins is anatomically impossible, and intra-abdominal desmoid tumors show a strong tendency toward relapsing. Optimal management has thus yet to be defined, particularly for patients with intra-abdominal desmoid tumors.

Desmoid tumors arising metachronously have mainly been reported from extra-abdominal sites [5]. Reports describing metachronous intra-abdominal desmoid tumors are rare, and little is known about the clinical course of this entity. Further, although spontaneous regression can be observed in desmoid tumors, whether metachronous desmoid tumors at intra-abdominal sites can regress spontaneously has not previously been reported. Here, we present a case of spontaneous regression in a FAP patient with metachronous intra-abdominal desmoid tumor.

## Case Presentation

A 36-year-old man with FAP was diagnosed with ascending colon cancer. He underwent laparoscopic total colectomy, removing an ascending colon cancer with a final stage of T1N0M0 stage I. Follow-up computed tomography (CT) 2 years later showed an intra-abdominal mass and desmoid tumor was suspected (shown in Figure 1a). The patient was started on tamoxifen and sulindac, but the intra-abdominal desmoid tumor progressed (shown in Figure 1b). The pathological diagnosis of desmoid tumor was confirmed from CT-guided biopsy (shown in Figure 1c). Bowel obstruction appeared and insertion of a long intestinal tube was performed. After bowel obstruction resolved, we started combined chemotherapy with dacarbazine and adriamycin (dacarbazine at 150 mg/m<sup>2</sup> on days 1–4 and adriamycin at 20 mg/m<sup>2</sup> on days 1–4 every 4 weeks). The desmoid tumor shrank after four cycles of this regimen. We changed the regimen to tamoxifen and sulindac and continued follow-up monitoring. The desmoid tumor stabilized for 2 years (shown in Figure 1d). Tamoxifen was stopped after the emergence of portal thrombosis. Four months later, follow-up CT showed a new intra-abdominal lesion



**Fig. 1.** **a** CT reveals an intra-abdominal desmoid tumor. **b** CT shows progression of the intra-abdominal desmoid tumor despite treatment with tamoxifen and sulindac. **c** HE staining of the intra-abdominal desmoid tumor. **d** CT shows the intra-abdominal desmoid tumor has shrunk and stabilized in size after treatment with four cycles of dacarbazine and adriamycin. HE, hematoxylin and eosin.

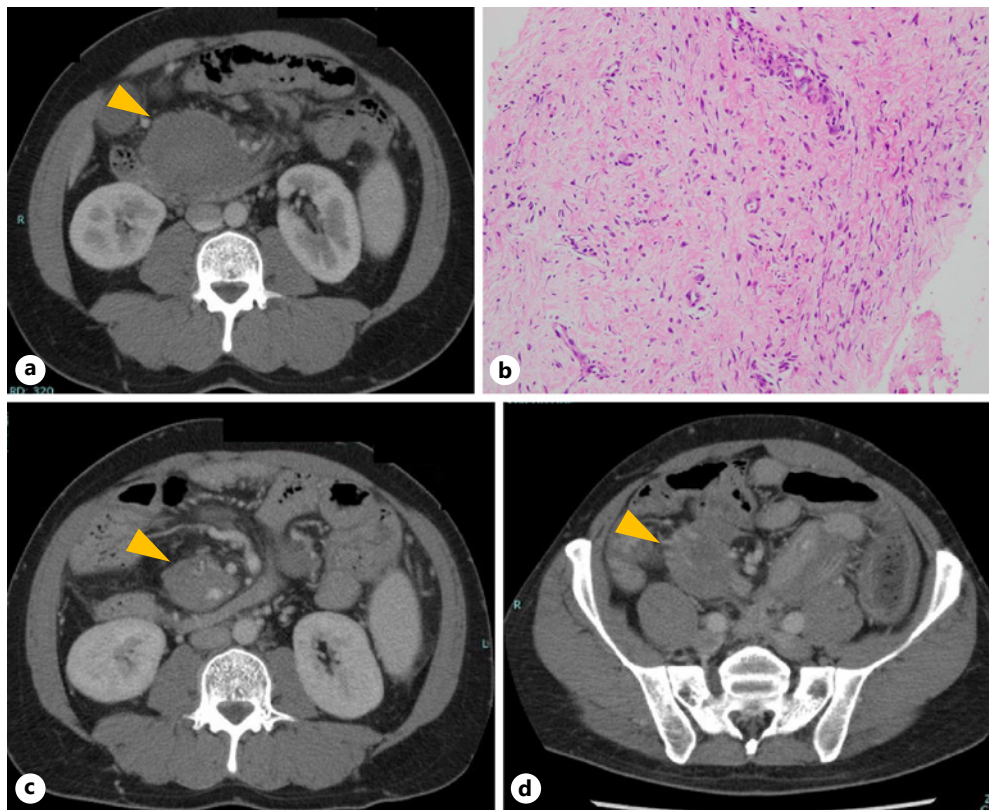
(diameter, 65 mm) in the upper abdomen (shown in Figure 2a). On the other hand, the initial lesion showed no change in size. The new lesion progressed from 65 mm to 70 mm within a month. We performed CT-guided biopsy of the new lesion and histopathological examination revealed desmoid tumor (shown in Figure 2b). We prepared to start combined chemotherapy, but the next follow-up CT revealed desmoid tumor had stopped progressing and had started to regress spontaneously. After 4 years from that spontaneous regression was first identified, the second lesion was 41 mm in diameter and the initial lesion has also remained stable (shown in Figure 2c, d). Recently, we undertook evaluation of immune cells in the desmoid tumor that had shown spontaneous regression. Immunohistochemical analysis of this second lesion showed positive staining for CD68 as the most significant finding. Clear positive staining was also seen for CD163, while CD3, CD8, and CD56 showed weak positive staining. Negative results were seen for CD4 (shown in Figure 3a–f).

## Discussion

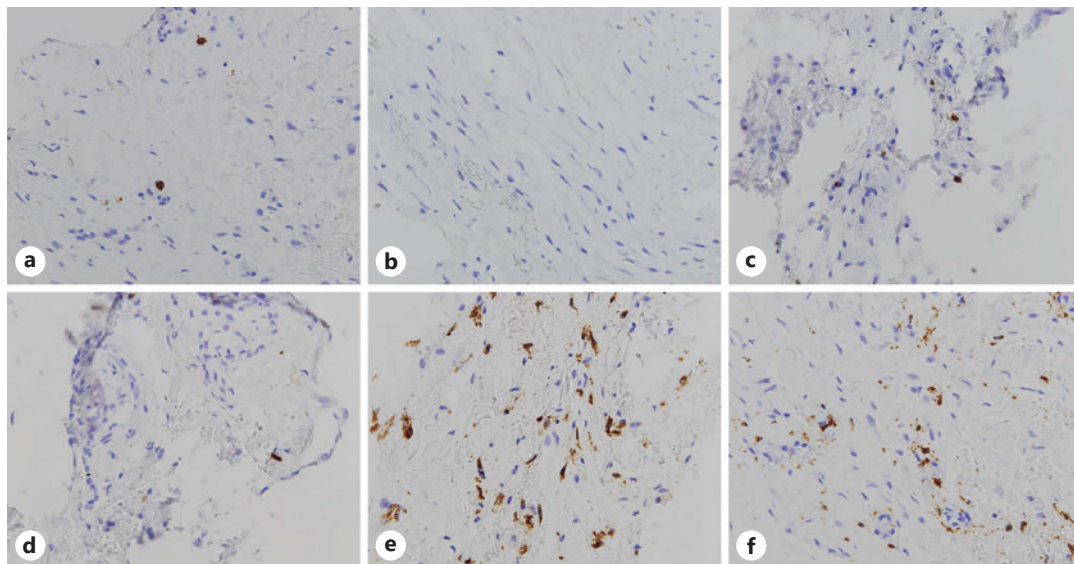
The clinical course of metachronous intra-abdominal desmoid tumors is not well understood. We encountered a patient with FAP and metachronous intra-abdominal desmoid tumors. The initial lesion required chemotherapy, but the second lesion regressed spontaneously and has been observed for 4 years.

An aberrant Wnt/APC/ $\beta$ -catenin pathway is considered to be the main pathogenesis for desmoid tumor [6]. Most desmoid tumors are sporadic and show mutations in *CTNNB1*, the





**Fig. 2.** **a** CT shows the metachronous intra-abdominal desmoid tumor. **b** HE staining of the metachronous intra-abdominal desmoid tumor. **c** CT image of the metachronous intra-abdominal desmoid tumor 4 years after initiation of regression. **d** CT shows initial intra-abdominal desmoid tumor at the same time as (**c**).



**Fig. 3.** Immunohistochemical staining of metachronous intra-abdominal desmoid tumor for CD3 (**a**), CD4 (**b**), CD8 (**c**), CD56 (**d**), CD68 (**e**), and CD163 (**f**).

gene encoding  $\beta$ -catenin. Desmoid tumors associated with FAP are often caused by germline mutation in the *APC* tumor suppressor gene. The incidence of desmoid tumors among FAP patients is 10–25% [2], an over 800-fold greater risk compared with the general population [4]. Desmoid tumors in FAP patients tend to occur in the intra-abdominal space, with 50% arising in this region [7]. A relationship between the incident site and prophylactic surgery for FAP patients has been suggested. Our patient received laparoscopic total colectomy 2 years prior to the identification of the initial intra-abdominal desmoid tumor. The second intra-abdominal desmoid tumor appeared more than 4 months after discontinuation of tamoxifen due to portal thrombosis under treatment with sulindac. The possibility that the cessation of tamoxifen contributed to the development of the second intra-abdominal desmoid tumor cannot be ruled out.

A system for the management of desmoid tumor has been proposed by the Desmoid Tumor Working Group [3]. Asymptomatic patients can be observed initially without active treatment under the supervision of an experienced team. This policy is aimed at avoiding overtreatment since desmoid tumors can stabilize and regress spontaneously. Penel et al. [8] reported that the 2-year event-free survival rate did not differ significantly between patients who underwent surgery and those managed under a wait-and-see approach. Bonvalot et al. [9] reported that 28% of sporadic desmoid tumors in the abdominal wall showed spontaneous regression. The mechanism underlying spontaneous regression of desmoid tumors is unclear, but initial size <7 cm is associated with spontaneous regression. Active treatment is considered for patients with subsequent progression or symptomatic tumor burden. Intra-abdominal desmoid tumors can readily cause intestinal obstruction, ulceration, or bowel ischemia. For this reason, the management of intra-abdominal desmoid tumors is difficult.

Metachronous desmoid tumor has mainly been reported at extra-abdominal sites [5]. Metachronous extra-abdominal desmoid tumors require surgical resection. Reports describing metachronous intra-abdominal desmoid tumors are very rare, and the clinical course is unknown. In the present case, the initial size of the second lesion was 65 mm, subsequently progressing to 70 mm. We were preparing to start combined chemotherapy, but the next follow-up CT revealed this second desmoid tumor had stopped progressing and started to regress spontaneously. Interestingly, the behaviors of the initial lesion and second lesion differed in the present case. Doyen et al. [10] reported nonidentical *CTNNB1* mutations in multiple metachronous desmoid tumors. Iwama et al. [11] also reported a recurrent desmoid tumor with a different, additional mutation in *APC* in a patient with FAP. Such findings suggest the possibility of differing biology between lesions. Although metachronous intra-abdominal desmoid tumor is rare and its management has not been established, the present case suggests that active surveillance can be applied under careful follow-up in asymptomatic patients.

Siozopoulou et al. [12] reported the status of immune infiltration in 33 desmoid tumors. Positive results for CD3 and CD8 were seen in 100% and 97%, respectively. Conversely, 27.3% of samples showed positive results for CD4, and only 9.1% and 0% of samples were positive for CD56 and CD68, respectively. The second desmoid tumor in our case was strongly positive for CD68, a marker for macrophages. Macrophages are divisible into pro-inflammatory M1 and anti-inflammatory M2 types [13]. The lesion that regressed also showed positive results for CD163, although to a lesser degree than CD68. CD163 is a marker for M2-like macrophages. On the other hand, Romero et al. [14] reported the presence of CD163 positive macrophage in desmoid-type fibromatosis and its relation to the poor prognosis. A key limitation in the present study was that our specimen is a biopsy sample so that the evaluation of desmoid tumor as a whole is difficult and we were unable to compare immune statuses between the first and second desmoid tumors due to insufficient specimens.

## Conclusion

In summary, we encountered a case in which metachronous intra-abdominal desmoid tumor showed spontaneous regression in a patient with FAP. A standard approach for treating metachronous desmoid tumors has not yet been established. Active surveillance appears applicable for metachronous desmoid tumors under careful monitoring if the lesions remain asymptomatic.

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## Statement of Ethics

Written informed consent was obtained from the patient for publication of the details of medical information including images. Case reports are granted an exemption from requiring ethical approval at Kyushu University Hospital.

## Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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## Author Contributions

K.T. and E.B. contributed the design of the report and drafted the manuscript. K.K., K.I., and Yoshinao O. interpreted the histological slides. K.Y., R.T., Yuta O., M.N., A.O., T.H., H.S., H.A., H.K., and K.A. contributed to interpretation of data and critically revised the manuscript.

## Data Availability Statement

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

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