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RESEARCH ARTICLE

Comparison of Surgical and Oncological Outcomes Between Sporadic and Familial Adenomatous Polyposis-Associated Abdominal Desmoid Tumors: A Single Center Retrospective Study

Ahmet Rencüzoğulları, Uğur Topal, Cihan Atar, İsmail Cem Eray, Orçun Yalav

Çukurova University Faculty of Medicine, Department of General Surgery, Adana, Turkey

ABSTRACT

Aim: Desmoid tumors (DT) originate in musculoaponeurotic tissues. However, there is scarce data regarding DT-related clinical and oncological outcomes. This study presents the oncological outcomes of patients who underwent surgery for abdominal DT in our clinic over a 10-year period and compares the outcomes between sporadic and familial adenomatous polyposis (FAP)-associated DTs.

Method: The records of patients who underwent surgery for DT between January 2011 and 2021 were retrospectively analyzed.

Results: The study included 18 patients, of which 15 were female, and with a median age of 43 (range: 21-59) years. Of the 18 cases, four developed DT following surgery for FAP coli syndrome. The mean age was lower in patients with FAP-associated DTs than in those with non-FAP-associated tumors (28 vs. 46.5 years, p=0.574). After a follow-up period of 68.1 months (95% confidence interval: 12,799-123,519), four patients developed recurrence, and the recurrence rate was higher (50% vs. 14.28%, p=0.130). Additionally, the time to recurrence was shorter in patients with FAP-associated DTs than in those without FAP (31.3 vs. 120.9 months, p=0.028). The tumor board decided that adjuvant tyrosine kinase inhibitor therapy would be administered to four patients and adjuvant 50.4 Gy radiotherapy to three patients.

Conclusion: DT are more common in women. As recurrence is more common and the time from index surgery to recurrence is shorter in patients with FAP-associated DTs, more intensive follow-up protocols would be necessary in this group.

Keywords: Desmoid, familial adenomatous polyposis, surgery

Introduction

Desmoid tumor (DT), known also as desmoid-type fibromatosis, is a monoclonal, non-metastatic, locally aggressive, sometimes multifocal, and fibroblastic proliferative disease that originates from connective tissues.[1] The incidence of DT is very low, with only 2-4 new cases per million each year. Approximately 85-90% of DT cases are sporadic and harbor mutations in the β-catenin-encoding *CTNNB1* gene, while the remaining 10-15% of cases are associated with familial adenomatous polyposis (FAP) and harbor germline APC mutations.[2,3]

The biology of DT that can point to a standard therapeutic approach is poorly understood. Several treatment options are available for DTs, including antiestrogen therapy, non-steroidal anti-inflammatory drugs, radiotherapy, chemotherapy, and surgical resection. Due to its local aggressiveness and non-metastatic nature, complete macroscopic surgery has been the standard approach for many years. However, many questions remain unanswered regarding early diagnosis, the role of surgery (indication, role, timing, and scope), and the place of conservative therapy. Despite radical local treatment, local recurrence or regional spread in many patients has led to difficulties in the management of patients with DT.[3-5]

There are several differences between sporadic and FAP-associated DTs in terms of the demographic characteristics, clinical behaviors, and mutational statuses.[6,7] Sporadic DTs

Address for Correspondence: Uğur Topal, MD,
Çukurova University Faculty of Medicine, Department of General Surgery, Adana, Turkey
E-mail: sutopal2005@hotmail.com **ORCID ID:** orcid.org/0000-0003-1305-2056
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can occur in any part of the body but are often located in the abdominal wall and limbs, whereas FAP-associated DTs are more commonly located intra-abdominally.[4,8]

There are limited studies in the literature comparing the clinical characteristics and management of sporadic and FAP-related DTs, and the question of how the emerging characteristics of this rare tumor affect its clinical management has not yet been fully addressed.[6,7] The present study compares the clinical characteristics of sporadic and FAP-associated DTs as well as their surgical outcomes.

Materials and Methods

The Çukurova University Local Ethics Committee's approval was gained for the study (approval number: 114/31, date: 10.09.2021), which included patients who underwent surgical therapy for DT between January 2011 and 2021. The patients' medical records were reviewed retrospectively for the collection of clinical data. In our institution, all patients diagnosed with DTs were treated following the clinical management guidelines for FAP,[9] in which an intraoperative diagnosis or clinical diagnosis during follow-up with computed tomography (CT) or magnetic resonance imaging (MRI) is considered sufficient. For patients with sporadic DTs, the histopathological confirmation of the diagnosis was mandatory, especially for differential diagnoses such as malignant mesenchymal tumors.

The patients were divided into the following two groups: group 1 included patients with sporadic DTs, and group 2 featured those with FAP-associated DTs. The two groups' demographic and clinical characteristics, presenting symptoms, medical history, applied surgical therapy, tumor size, surgical margin positivity, need for reoperation, need for chemotherapy/radiotherapy during the follow-up, presence of recurrence, time to recurrence, and size of recurrence masses were compared.

The extent of surgical resection aimed to obtain a negative surgical margin. Adjuvant treatments were decided by considering tumor-related and patient-based factors in the multidisciplinary tumor council, accompanied by the guidelines shown in Figure 1.[2,3] Patients with DT were routinely followed up in the clinic with a CT or MRI every 4-6 months for the first 2 years of treatment and then every 12 months until the disease was documented as sustained and stable.

Statistical Analysis

A statistical analysis of the study data was carried out with IBM SPSS Statistics (version 23.0. Armonk, NY: IBM Corp.). Descriptive statistics were presented as the mean, standard deviation, median, frequency, ratio, and minimum/maximum. A Shapiro-Wilk test was used to assess the normality of the continuous variables; a Mann-Whitney U test was used to compare non-normally distributed data; and Pearson's chi-square, Fisher-Freeman-Halton, and Fisher's exact tests were used for the comparison of categorical variables. A Kaplan-Meier analysis and log-rank test were used for the survival analyses. The level of statistical significance was set at 0.05 for all tests.

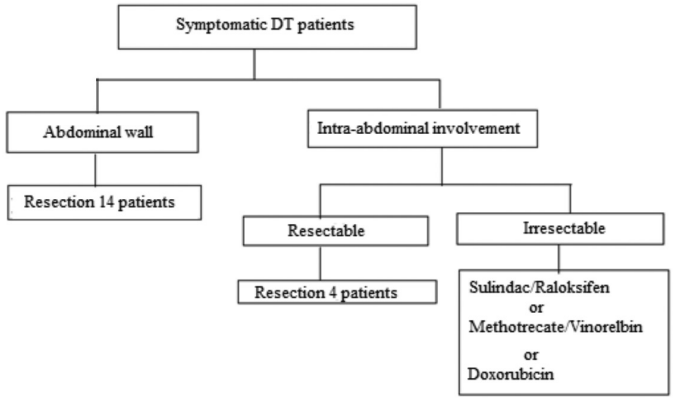

Figure 1. Treatment algorithm
DT: Desmoid tumors

Results

Of the 18 patients included in the study, four developed FAP-associated DTs. There was a female predominance in both groups (78.6% vs. 100% p=0.574), and comorbidities were more common in group 1 (57.1% vs. 0%, p=0.43). The demographic and clinical characteristics are presented in Table 1.

The development of tumors in the location of previous surgical incisions was common in both groups (50% vs. 75%, p=0.375), and the tumor size was similar in the two groups (6.6 cm vs. 11.5 cm, p=0.192). Surgical treatment was applied to one patient in group 2 due to recurrence, and local excision with intestinal resection was performed in this patient. Local excision was performed in two patients with recurrence in group 2. The conducted surgical procedures are presented in Table 2.

Oncologic follow-up data are presented in Table 3. Although the difference was statistically insignificant, recurrence was more frequent in group 2 patients (14.3% vs. 50%, p=0.13) (Figure 2). The time to recurrence was shorter in group 2 than in group 1 (31.3 vs. 120.9 months, p=0.028) (Table 3). In line with the tumor board's decision, adjuvant tyrosine kinase inhibitor therapy was applied to four patients after the first surgery, and adjuvant 50.4 Gy radiotherapy was applied to three patients after the second surgery.

Table 1. Patient demographics

	Sporadic DT, (n=14)	FAP-associated DT, (n=4)	Total, (n=18)	
	n (%)	n (%)	n (%)	
Gender				
Male	3 (21.4)	0 (0)	3 (16.7)	0.310
Female	11 (78.6)	4 (100)	15 (83.3)	
Age	46.5 (26-59)	28 (21-33)	43 (21-59)	0.574
Comorbidities				
No	6 (42.9)	4 (100)	10 (55.6)	0.043
Yes	8 (57.1)	0 (0)	8 (444)	
Previous surgery				
No	4 (28.6)	0 (0)	4 (22.2)	0.225
Yes	10 (71.4)	4 (100)	14 (77.8)	
Symptoms				
Palpable mass	6 (42.9)	2 (50)	8 (44.4)	0.800
Abdominal pain	8 (57.1)	2 (50)	10 (55.6)	
Localization				
Intra-abdominal	1 (7.1)	0	1 (5.6)	
Anterior abdominal wall	13 (92.9)	1 (25)	14 (77.8)	0.002
Intra-abdominal + anterior abdominal wall	0	3 (75)	3 (16.7)	

DT: Desmoid tumors, FAP: Familial adenomatous polyposis

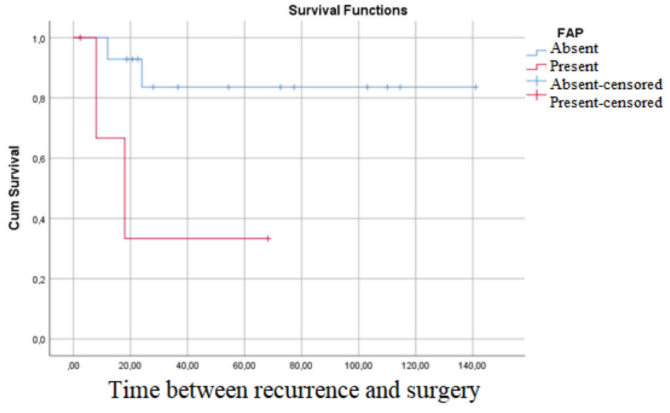

Figure 2. Kaplan-Meier curves for local recurrence rates in group 1 and group 2

FAP: Familial adenomatous polyposis

Discussion

By comparing sporadic and FAP-associated DTs, the present study has revealed that FAP-associated DTs recurred faster and more often. There is evidence that FAP-associated DTs represent a challenging disease. Compared with sporadic tumors, FAP-associated DTs have been reported to originate more often from more critical anatomical regions, have a higher risk of complications, and have a higher chance of being intra-abdominal.[3] In this study, DTs in FAP patients also tended to be located in a complicated intra-abdominal region. Contrary to previous findings, there was no size difference between the sporadic tumors and FAP-associated tumors.[6]

A study of the literature comparing the characteristics of sporadic and FAP-associated desmoid-type fibromatoses revealed FAP in 70 (16%) out of 447 DT patients,[10] which is a lower rate than reported in the present study (22%).[6,7] Some patients who present with sporadic desmoid-type fibromatoses may have undiagnosed FAP, and these patients may benefit from screening colonoscopy.

The female predominance reported in DTs in earlier studies[7,11] is supported by the present study, and although this is associated with DT expressing estrogen receptors, and thus being exposed to the proliferative effect of estrogen, the exact mechanism is unknown. While some studies failed to establish a significant age difference between DT development in FAP and non-FAP settings,[10] other have

Table 2. Surgical outcomes

		Sporadic DT, (n=14) n (%)	FAP-associated DT, (n=4) n (%)	Total, (n=18)	
Location of desmoid tumor previous surgical incision					
No		7 (50)	1 (25)	8 (44.4)	0.375
Yes		7 (50)	3 (75)	10 (55.6)	
Surgery					
Debulking + right oophorectomy		0 (0)	1 (25)	1 (5.6)	
Local excision		13 (92.5)	2 (50)	14 (77.8)	0.158
Local excision + segmental small bowel resection		1 (7.5)	1 (25)	2 (11.1)	
Surgical margin positivity					
No		12 (85.7)	3 (75)	15 (83.3)	0.612
Yes		2 (14.3)	1 (25)	3 (16.7)	
Size		6.5 (3-23)	11.5 (4-23)	7 (3-23)	0.192
Secondary surgery					
No		10 (71.4)	3 (75)	13 (72.2)	0.888
Yes		4 (28.6)	1 (25)	5 (27.8)	
Reason for secondary surgery	Metachronous recurrence	2 (50)	1 (100)	3 (60)	N/A
	Positive surgical margins	2 (50)		2 (40)	
Secondary surgical procedure	Local excision	2 (50)	0	2 (40)	291
	Local excision + intestinal resection	0	1 (100)	1 (20)	
	Re-excision for positive surgical margin	2 (50)	0	2 (40)	

DT: Desmoid tumors, FAP: Familial adenomatous polyposis, N/A: Not applicable

Table 3. Oncological follow-up data

	Sporadic DT, (n=14) n (%)	FAP-associated DT (n=4) n (%)	Total, (n=18) n (%)	
Chemotherapy				
No	11 (78.6)	2 (50)	13 (72.2)	0.261
Yes	3 (21.4)	2 (50)	5 (27.8)	
Radiotherapy				
No	12 (85.7)	3 (75)	15 (83.3)	0.612
Yes	2 (14.3)	1 (25)	3 (16.7)	
Recurrence				
No	12 (85.7)	2 (50)	14 (77.8)	0.130
Yes	2 (14.3)	2 (50)	4 (22.2)	
Size of recurrence mass	9 (3-15)	7.25 (4.5-10)	7.25 (3-15)	N/A
Time to recurrence in groups (months)	120,904±13.09 95% CI (95,247-146,561)	31,386±15.196 95% CI (1,602-61,171)	**0.028**	

DT: Desmoid tumors, FAP: Familial adenomatous polyposis, N/A: Not applicable

reported DT development at an earlier mean age in FAP patients than in those without FAP.[6,7] In the present study, the age distribution was similar in patients with FAP-associated and non-FAP-associated DTs, which the authors believe makes it unreliable for individual patients as a distinguishing factor for the identification of FAP.

The most important predisposing factor for the development of DTs in FAP patients is previous surgical trauma. Previous studies have reported that prophylactic colectomy-related surgical trauma increases the risk of tumor formation in FAP patients.[12] Clark et al.[13] reported that 82% of patients with FAP-associated DTs in their study had previous predisposing surgery. It has further been shown that sporadic DTs occur in 3% of the first laparotomy but are responsible for up to 30% in subsequent laparotomy procedures.[14] Since patients with FAP are up to 100% more likely to develop colorectal cancer, prophylactic surgery is unavoidable for these patients. In their study, Church et al.[15] compared the incidence of DT at follow-ups between FAP patients undergoing ileal pouch-anal anastomosis (IPAA) and those treated with total abdominal colectomy-ileorectal anastomosis and reported a higher DT incidence in patients who underwent IPAA. This may be attributed to the increased surgical trauma associated with pelvic dissection.[15] This study also provided evidence that previous surgical trauma increases the development of DT, which supports earlier studies. All FAP patients in this study had undergone proctocolectomy and IPAA, which supports this finding.

The reported rate of recurrence is 23-31%, and the 5-year recurrence-free survival is 69% in sporadic desmoid fibromatoses, while the recurrence rate in FAP-associated tumors has been reported to be at the same level as in their sporadic counterparts. A positive resection margin, young age, large tumor size, and tumor location in the extremities have been shown to predict recurrence.[7,16-19] In their 35-year series, Koskenvuo et al.[6] reported a recurrence rate of 26% when FAP patients were included, a 5-year recurrence-free survival of 50% in the FAP group, and 74% in the sporadic group. In the study, the median time to recurrence was 29 months in the sporadic group and 26 months in the FAP group.[6] This rate is supported by the literature, where studies reported as short a time as 14-22 months.[20-22] In the present series, the recurrence rate was 22% when all patients were included, which is relatively lower compared with the literature. In this respect, the authors believe that close follow-up protocols for DTs would be appropriate, especially in cases of FAP treated with a total proctocolectomy.

Various treatment options are available for the induction of tumor remission or the management of symptoms. Surgical resection, radiotherapy, and pharmacological therapies have all been used, although there is no treatment yet that currently considers optimum.[23] The present series included patients who underwent surgical treatment. Due to the decision of the tumor board, adjuvant tyrosine kinase inhibitor therapy was administered to four patients and adjuvant 50.4 Gy radiotherapy to three patients, suggesting that a multidisciplinary approach should be adopted in the management of DT.

Study Limitations

The limitations of the present study include its retrospective nature and the limited patient population. The small sample size has created a concern that false positive results may occur in statistical analyzes. That said, considering the rarity of this tumor group, the authors believe that this study makes valid contributions to the literature.

Conclusion

Recurrence is more common and the time from index surgery to recurrence is shorter in patients with FAP-associated DTs; therefore, more intensive follow-up protocols would be necessary in this group.

Ethics

Ethics Committee Approval: This study was approved by the Çukurova University Local Ethics Committee (approval number: 114/31, date: 10.09.2021).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.R., İ.C.E., O.Y., Concept: A.R., U.T., C.A., İ.C.E., O.Y., Design: A.R., U.T., C.A., İ.C.E., O.Y., Data Collection or Processing: A.R., C.A., Analysis or Interpretation: A.R., İ.C.E., O.Y., Literature Search: A.R., U.T., C.A., Writing: A.R., U.T.

Conflict of Interest: No conflict of interest was declared by the authors.

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