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Research Article

Desmoid Tumours: A single-centre Experience

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Abstract

Objectives: To reveal the main patient and disease characteristics, treatment management and clinical course of desmoid tumours.

Methods: Patients with a diagnosis of desmoid tumour were evaluated retrospectively.

Results: Of the 11 patients with a median age of 33.0 (12.1-63.1), 7 (63.6%) were female, and 4 (36.4%) were male. Locations were intraabdominal region, abdominal wall, thoracic wall and lower extremity in 5 (45.5%), 4 (36.4%), 1 (9.1%) and 1 (9.1%) patients, respectively. Two patients (18.2%) had a diagnosis of Familial Adenomatous Polyposis (FAP). Pregnancy and cesarean section in 1 (9.1%) and surgical trauma in 2 (18.2%) patients were the etiological factors. The primary treatment of 10 (90.9%) patients was surgery, and 1 (9.1%) patient was radiotherapy (RT). A second surgical intervention was performed in four patients (36.4%) due to recurrence or progression. Three (27.3%) and 5 (45.5%) patients had received RT and systemic treatments, respectively. Mean overall survival was 130.2 ± 25.0 (95% CI, 81.1-179.2) months, and 3 (27.3%) patients died in follow-up.

Conclusion: Desmoid tumours can present with very different clinical behaviours among patients. Large-scale studies are needed to determine the biological characteristics of this extremely rare disease, the optimization of treatment options, and the determination of prognostic factors.

Keywords: Desmoid tumor, aggressive fibromatosis, FAP

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Desmoid tumours (aggressive fibromatosis) are characterized by clonal fibroblastic proliferation, can be widespread in all body parts and may have an aggressive local course.[1] Clinical behaviour can vary; sometimes, it is quite aggressive and sometimes spontaneous regressions can be seen. Desmoid tumours with an annual incidence of 2-5/1000000 constitute approximately 0.03% of all neoplasms and less than 3% of all soft tissue tumours.[2] It is observed two to three times more frequently in the female gender, and the most common age range of the disease is 15-60.[3,4] Desmoid tumours are usually seen sporadically, although 10-15% of the disease has been reported to be associated with Familial Adenomatous Polyposis (FAP).[5] Although recurrent trauma is mostly mentioned in the aetiology, scar tissue due to surgical procedures, pregnancy, oral contraceptives, FAP, Gardner syndrome are the main etiological factors.[6] Surgical excision is the first method to be chosen in the treatment, and radiotherapy (RT) and systemic treatments can also be used for this purpose.[6] Systemic therapy encompasses many different drug groups such as chemotherapeutics, nonsteroidal anti-inflammatory drugs (NSAID), hormonal therapeutics and tyrosine kinase inhibitors.[6] The fact that it is an extremely rare disease makes it difficult to conduct large-scale prospective

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Table 1. Main patient and primary treatment characteristics

Patient no	Age of diagnosis	Gender	Disease area	Surgery type	RT	Recurrence or progression	Death	OS (months)
1	37.04	Female	Abdominal wall	R0	No	No	No	16.30
2	32.96	Female	Abdominal wall	R1	N/A	No	No	22.60
3	38.72	Female	Abdominal wall	R0	No	No	No	26.32
4	23.28	Female	Abdominal wall	R1	N/A	No	No	38.57
5	34.62	Male	Intraabdominal	R2	After surgery	Yes	No	72.80
6	17.04	Male	Intraabdominal	R0	No	Yes	No	61.24
7	33.71	Female	Intraabdominal	R2	N/A	Yes	Yes	21.78
8	63.07	Female	Thoracic wall	R0	No	Yes	Yes	115.58
9	30.75	Female	Intraabdominal	R1	N/A	Yes	No	38.34
10*	17.21	Male	Intraabdominal	No	Primary treatment	No	Yes	126.55
11**	11.24	Male	Limb	R1	In progression	Yes	No	184.08

RT: Radiotherapy; OS: Overall survival; N/A: Not appropriate; *: The patient received tamoxifen for one year after radiotherapy and was followed up without medication; **: Up to the age of eighteen, he was followed up in the pediatric oncology department.

studies. Therefore, we planned to conduct a retrospective descriptive study to reveal the main patient and disease characteristics, treatment management and clinical course in desmoid tumours, a sporadic disease.

Methods

Between January 2010 and December 2019, patients aged eighteen years and older admitted to the Medical Oncology Clinic of Health Sciences University Dr Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital with a diagnosis of a desmoid tumour within a ten-year period were included in the study. Medical records were scanned retrospectively through the hospital data processing system and patient files. Patients with sufficient medical records were included in the study. Main patient and tumour characteristics such as age, gender, and disease location were recorded. Surgical trauma, other traumas, family history of FAP or colon cancer, pregnancy, cesarean section and oral contraceptive use were recorded. It was also evaluated whether colonoscopy was performed on the patients. If performed, date of surgery and type of surgical resection (R0/R1/R2), whether RT was applied, timing and nature of radiotherapy, systemic treatments and duration of systemic treatment were recorded. The last day is known to be alive, or if dead, the patient's death dates were recorded. The study was conducted after the local ethics committee's approval (Health Sciences University Dr Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital ethics committee, Decision No: 2021-03/1058).

Descriptive statistics were used to show the distribution of main characteristics of the population. Survival rates were estimated using the Kaplan-Meier method. Statistical analysis was performed using SPSS software (SPSS for Windows, version 24.0, SPSS Inc., Chicago, USA).

Results

Eleven patients with a median age of 33.0 (12.1-63.1) were evaluated in terms of main disease and treatment characteristics. Seven (63.6%) of the patients were female, and 4 (36.4%) were male. Locations were intraabdominal region, abdominal wall, thoracic wall and lower extremity in 5 (45.5%), 4 (36.4%), 1 (9.1%) and 1 (9.1%) patient, respectively. Two patients (18.2%) had a family history of FAP and colon carcinoma. Pregnancy and cesarean sections were the etiological factors in 1 (9.1%) and surgical trauma in 2 (18.2%) patients. Other traumas or use of oral contraceptives were not among etiological factors for any patient. In the records, only 3 (27.3%) patients had knowledge of colonoscopy. The primary treatment of 10 (90.9%) patients was surgery, and 1 (9.1%) patient was RT. The patient, who received RT as the primary treatment, received tamoxifen treatment for one year and was followed up without medication. RT was applied to 1 (9.1%) patient who underwent R2 resection after surgery. However, although RT was considered after surgery for 4 (36.4%) patients who could not undergo R0 resection, it was not considered appropriate due to the large RT area and the high risk of intestinal toxicity due to RT. The main patient and primary treatment characteristics are shown in Table 1.

Recurrence or progression was observed in 6 (54.5%) of the patients, and 2 (33.3%) of them underwent R0 surgical resection. Mean recurrence-free survival of patients who underwent R0 tumor resection (n=4) was 20.5±3.0 (95% CI, 14.7-26.3) months. Systemic treatments were given to 4 (66.7%) patients who could not undergo R0 resection. Median time to progression in patients in whom complete tumor resection could not be performed (R1/R2) (n=6) was 29.9 (95% CI, 0.0-75.5) months. Among the systemic treat-

Table 2. Secondary treatments in patients with recurrence or progression

Patient no	2. surgery	First line therapy	Second line therapy	Third line therapy
5	R1	Etodolac		
6	No	Doxorubicin+Dacarbazine	Imatinib	
7	No	Indomethacin	Doxorubicin+Dacarbazine	Tamoxifen+Sulindac
8	R0			
9	R1	Tamoxifen+Sulindac		
11*	R0			

*: After the patient's progression, radiotherapy was given first and then R0 resection was performed.

ments, the combination of doxorubicin and dacarbazine was used in 2 (33.3%) and tamoxifen and sulindac combination in 2 (33.3%) patients. Secondary treatments of patients with relapse or progression are shown in Table 2.

In patients with relapse or progression, PFS was 45, 35, 2, 32 and 13 months, respectively, for patients receiving etodolac, doxorubicin-dacarbazine combination chemotherapy, indomethacin, tamoxifen-sulindac combination, and tamoxifen for first-line systemic treatments. For patients receiving imatinib and doxorubicin-dacarbazine combination chemotherapy in the second line therapy, the PFS was 9 months and 5 months, respectively. The PFS for the patient who received third-line tamoxifen was 12 months. The mean overall survival was 130.2±25.0 (95% CI, 81.1-179.2) months, and 3 (27.3%) patients died due to desmoid tumour.

Discussion

Desmoid tumours are usually diagnosed in the 15-60 age range and more often in women.[7] The patients in our study are similar to the literature in terms of age and gender distribution. In terms of etiological reasons, FAP, surgical trauma, pregnancy and cesarean were the most prominent reasons. Although FAP has a significant place in desmoid tumour aetiology, a colonoscopic evaluation was not performed in the majority of patients. The colonoscopic evaluation may be beneficial in cases with a desmoid tumour or at least intraabdominal or retroperitoneally located cases (due to the high frequency of abdominal region in cases with FAP).[8,9]

Since the desmoid tumour is a disease that is difficult to conduct a randomized prospective study, treatment standardization has not been achieved. For a long time, the primary treatment of the disease has been accepted as surgical resection. The current approach includes radiotherapy and systemic therapy in addition to surgery. Despite surgical resection, a 20-45% risk of recurrence has been reported in this benign tumour.[10] Local recurrences constitute the main challenge in disease management. Although local recurrences are sometimes observed in patients with complete resection, sometimes spontaneous regression may be encountered in patients who cannot be fully resected. In our study, we observed local recurrence in two (50%) of four patients who underwent R0 resection. In one of the patients with local recurrence, death was observed due to the progression of the desmoid tumour and related complications (intestinal obstruction and renal failure). On the other hand, we did not observe any disease progression in the follow-up of two (50%) of the four patients who underwent R1 resection. It has been reported that a wait-and-see strategy can be an option in the management of the disease due to this unpredictable nature of the disease and the inability to achieve treatment optimization. However, the results regarding the wait-and-see strategy's clinical benefits are conflicting.[11,12]

Another treatment option that can be used in desmoid tumour management is RT. Radiotherapy can be considered an adjuvant strategy after surgery in patients who are not fully resected or as a definitive treatment for patients who are not suitable for surgical treatment (location, prevalence, advanced age and comorbidities, Etc.).[12,13] However, RT may not always be an easily applicable method for tumours located in the abdominal region, especially large-sized tumours. In our study, only two of the six patients (33%) with tumours that could not be fully resected could undergo RT, and RT was avoided because it was predicted that intestinal toxicity would be high in other patients. However, for more than ten years, disease-free survival was achieved in a patient who received RT as definitive therapy.

Systemic therapies can be used as neoadjuvant in patients who are not suitable for surgical treatment or palliative treatment in patients who progress after local treatments. Chemotherapeutics, antihormonal drugs, nonsteroidal anti-inflammatory drugs and targeted agents (tyrosine kinase inhibitors) constitute systemic treatment options.[14] Considering systemic treatment options, doxorubicin/pegylated liposomal doxorubicin-dacarbazine and methotrexate-vinblastine/vinorelbine chemotherapy combinations, tamoxifen-NSAID combinations, imatinib, sorafenib, pazopanib are the prominent options.[14]

Five patients in our study were treated with systemic treatment agents. In the treatment of these patients, doxorubicin-dacarbazine and tamoxifen-sulindac combinations are the main treatment options we use. We could not perform analyzes regarding response characteristics and survival rates of systemic treatments since the number of patients in our study would be far from generalizing, and the statistical power would be insufficient.

The clinical course of the desmoid tumour can vary considerably between patients. For example, a patient with an R1 resected tumour can be followed without recurrence and progression without additional treatment, while another patient with R0 resected tumour can be followed up despite various treatments for relapse and recurrence. The small number of patients in our study and our study's retrospective nature are the main limitations. However, it should be kept in mind that conducting large-scale prospective studies on desmoid tumours will not be accessible in practical terms. Large-scale and multi-centre studies are needed to determine both the biological characteristics of this rare disease, the optimization of treatment options, and the determination of prognostic factors.

Disclosures

Ethics Committee Approval: Health Sciences University Dr Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital ethics committee, Decision No: 2021-03 / 1058.

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