Desmoid tumour, a rare tumour in oncology practice: A case series and literature review

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Abstract

Aim: Desmoid tumors (DTs) are very rare tumors that grow gradually anywhere in the body they are locally aggressive, but with a low potential for metastasis. Very good results can be obtained with different combinations of treatments, such as surgery, chemotherapy, hormonal therapy, tyrosine kinase inhibitor therapy and radiotherapy. Case series even with a small number of patients are of considerable importance as experience with DTs limited. Therefore, in this study, we aimed to discuss the management of DTs with our case series.

Materials and Methods: In our study, 15 patients with DT, who were treated and followed up between January 2005 and January 2020 in two hospital medical oncology departments in Turkey, were evaluated.

Results: The median age of diagnosis of the patients was 34 (range 18-48) years. Seven (46.6%) of the patients were female and eight (53.4%) were male. Seven (46.6%) of the tumors were located in the abdominal wall, four (26.7%) were in the limbs three (20%) were in the intra-abdominal area, and one (6.7%) was in the chest wall. In terms of resectability, 14 (93.3%) were resectable, and one (6.7%) was unresectable. The five-year overall survival rate was 73.85%, and the average disease-free survival time until relapse was 35 (range 15-83) months in patients who relapsed. The two- and five-year relapse-free survival rates were 90.9% and 66.5%, respectively. The median progression-free survival (PFS) for first-line treatment was 25 (range 8.6-89.8) months. The median PFS for second-line treatment was seven (range 4.3-38.0) months. In the one patient who received third-line treatment, PFS was 8.3 months.

Conclusion: Frequent relapses in DTs are still the biggest problem in treating this disease. Although surgery treatment is the main treatment method used in desmoid tumors, controversy about adjuvant therapy after surgery continues, and new treatment modalities are required.

Keywords: Desmoid tumors; recurrence; sulindac; survival; tamoxifen

INTRODUCTION

Desmoid tumors (DTs) are extremely rare. With an annual incidence rate of 2–5 per 1,000,000, DTs account for approximately 3% of all soft tissue sarcomas and 0.03% of all malignancies (1). DTs are locally aggressive but with a low potential for metastasis; they occur with clonal fibroblastic tissue proliferation and can develop anywhere in the body. These tumors can regress spontaneously, or they can cause massive damage to tissues and organs with an aggressive course (2,3). The female/male ratio is approximately 2:1, and patients are usually between 15 and 60 years old. There is no ethnic trend (4).

Clinicopathologically, DTs are divided into two groups. The first group is sporadic and constitutes 85-90% of cases. The second group, which constitutes 10-15% of DTs, includes tumors related to familial adenomatous polyposis (FAP). The incidence of DTs in patients with FAP is about 13% (5). It is most common in the limbs and in the shoulder girdle, hip region, surgical scar areas, abdomen and thorax wall, head, neck and intra-abdominal areas. Although sporadic cases can be seen in any part of the body, FAP-related DTs are most commonly located in intra-abdominal areas (6).

The etiopathogenesis of DTs is unclear but is considered to be multifactorial. FAP, Gardner's syndrome, pregnancy and the use of oral contraceptives are contributory factors, although recurrent traumas are considered to be the most common cause of development (7-9).

The literature on DTs consists mostly of case series and retrospective evaluations. We aimed to share the clinical, follow-up and treatment results of 15 retrospective cases related to this rare tumour.
MATERIALS and METHODS
This study is based on the medical records of 15 patients with a diagnosis of DT, who were treated in two medical centers and followed up between January 2005 and January 2020. The patients were categorized on the basis of their surgical status, tumor location, treatments, recurrence and death status. Demographic characteristics and survival-related parameters were specified. Overall survival (OS) was defined as the time from diagnosis to death. Disease-free survival (DFS) was defined as the time from diagnosis to recurrence.

Statistical Analysis
Statistical package for the social sciences (SPSS) 18.0 software was used to estimate survival rate, and descriptive data were analysed using the same program. Kaplan-Meier curves and a log-rank test were used to analyse the survival data, and p-values of <0.05 were considered statistically significant.

RESULTS
Data on the 15 patients are summarized in Table 1. The median age of diagnosis was 34 (range 18–48) years. Seven (46.6%) of the patients were female, and eight (53.4%) were male; the male/female ratio was nearly 1:1.1. Seven tumors (46.6%) were located in the abdominal wall, four (26.7%) were in the limbs, three (20%) were in the intra-abdominal area and one (6.7%) in the chest wall.

At the time of diagnosis, 14 (93.3%) of the 15 patients were symptomatic, and the masses in the limbs and abdominal wall were the main reason for hospital admission, whereas abdominal pain was the reason for admission for patients with a tumor in the intra-abdominal area. In one patient with an intra-abdominal tumor, the mass was detected during routine tests.

In terms of resectability, 14 tumors (93.3%) were resectable, and one (6.7%) was unresectable. Seven (50%) R0, four (28.6%) R1, and three (21.4%) R2 resections were carried out. Postoperative radiotherapy was administered to three (21.4%) patients without R0 resection. Recurrence was observed in nine (14.2%) of the 14 patients who underwent surgery as an initial treatment. Surgical operations were performed again in four (44.4%) of the recurrent patients. While one (25%) of the patients who underwent recurrence surgery had surgery only, one (25%) patient received postsurgical radiotherapy and still continues to be followed up without relapse. The median DFS was 35 (range 15–83) months.

Five (55.6%) patients were given tamoxifen–sulindac, three (33.3%) were given dacarbazine–adriamycin and one (11.1%) was given methotrexate–vinorelbine as the first-line treatments in nine patients with relapse and unresectable treatment. The median PFS for first-line treatment was 25 (range 8.6–89.8) months. Of the six patients who received second-line treatment, three (50%) received imatinib, two (33.3%) received tamoxifen–sulindac and one (16.7%) received dacarbazine–adriamycin. The median PFS for second-line treatment was seven (range 4.3–38.0) months. One patient received imatinib as a third-line treatment; PFS was 8.3 months for this.

The median follow-up time was 52.6 (range 2.6–170.7) months. During the evaluation, five patients (33.3%) died, one (20%) of whom died owing to non-DT-related reasons. When all the patients were evaluated, the five-year survival rate was 73.85%. The two- and five-year relapse-free survival rates were 90.9% and 66.5%, respectively.

DISCUSSION
Although multimodal approaches such as surgical treatment, radiotherapy and pharmacological treatment can be used to treat DTs, discussion about the optimal management of DT continues, and no gold standard treatment method has been identified yet (10,11). The main difficulty in the treatment of these histologically benign tumors is that the probability of local recurrence is as high as 20-45% (12). The probability of recurrence increases with young age, extremity location, large tumor and positive surgical margins (13). Unpredictable clinical conditions, such as a high probability of local recurrence despite surgical treatment, an aggressive course that may develop despite surgery and radiotherapy and spontaneous regression without treatment suggest a watchful waiting strategy, but there is no standard on this subject yet (14). In a study of 426 cases by Salas et al., a watchful-waiting strategy was selected in 27 patients, and progressive disease was observed in only 20% of the patients during follow-up (15). In a study of 142 cases by Bonvalot et al., a watchful-waiting strategy was used in 83 patients. Surgical operations were performed in 59 patients. In the follow-up of these patients, five years of PFS was observed in 49% of patients who did not undergo surgery and 58% of patients who underwent surgery; no statistical difference was detected (16). In a study by Ballow et al., 70% of patients achieved disease-free survival for five years (17).

In our study, 14 (93.3%) of the 15 patients received surgery as an initial treatment. The two- and five-year relapse-free survival rates were 90.9% and 66.5%, respectively.

Radiotherapy is another local control method used in the treatment of DTs. This is a good local control option except for DTs located in the abdominal area. It can be used in initial therapy, especially in elderly patients who cannot tolerate surgery owing to additional comorbidity, in patients who refuse surgery, and in patients for whom surgery carries a high risk. Surgical R1 or R2 can be used as an adjuvant therapy in resected patients and as a neoadjuvant in unresectable disease as well as an alternative to high-risk surgery in relapsed patients. Radiotherapy is not an option for R0 resected tumors (19,20). In our study, radiotherapy was given to three patients who underwent surgery and could not achieve R0 resection and to one patient who developed recurrence and could not achieve R0 with relapse surgery. Of these
Systemic therapies are an option in cases of progression after adequate local treatment, in recurrences that are not suitable for local treatments, in the initial treatment of a growing or symptomatic intra-abdominal/mesenteric DT, and in symptomatic cases where the risk of surgical morbidity is high. Systemic treatment agents indicated by small case series and information from retrospective studies include hormonal treatments, nonsteroidal anti-inflammatory drugs (NSAIDs), chemotherapy agents and targeted therapies (21). Chemotherapy agents are especially used in inoperable, symptomatic and fast-growing tumors that are close to critical structures, in tumors that cannot be fully resected, and in tumors that are considered to have high morbidity. Doxorubicin/pegylated liposomal doxorubicin, dacarbazine and methotrexate-vinblastine/vinorelbine are the most common combinations. Some centres recommend the use of single-agent methotrexate and single-agent pegylated liposomal doxorubicin (22,23). Three of our patients with recurrent and non-resectable disease received dacarbazine plus adriamycin therapy as a first-line therapy. In these patients, the PFS achieved with chemotherapy was 25.7 (range 15.1-37.3) months. In second-line treatment, one patient received dacarbazine plus adriamycin; PFS in this patient was 7.03 months.

In the retrospective case series of 75 cases by Palassini et al., 80% of the patients had symptomatic improvement after 12 months of treatment, and 75 months of PFS was achieved in the patients with a combination of methotrexate plus vinblastine or vinorelbine. PFS was reported to be 136 months in the patients with an objective response (complete response and partial response) (24,25). One of our patients with recurrent and non-resectable disease received methotrexate plus vinorelbine treatment as the first-line treatment, and the PFS achieved with chemotherapy in this patient was 8.63 months.

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