



Aggressive fibromatosis: evaluation of prognostic factors and outcomes of surgical treatment

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Objective: The aim of this study was to evaluate the results of surgical treatment of aggressive fibromatosis and the effects of prognostic factors on recurrence.

Methods: Forty patients (24 female, 16 male; average age: 31.2 years) diagnosed with aggressive fibromatosis were evaluated retrospectively. Nine patients with tumor-positive surgical margins macroscopically were excluded. Prognostic factors such as age, gender, localization, admission status, compartment status, surgical margin, tumor size and adjuvant radiotherapy were evaluated.

Results: Recurrence rate was 29%. Average disease free survival was 46 ± 4 months. There was no statistically significant relation between prognostic factors and recurrence. Clinical results of the patients receiving adjuvant radiotherapy were more satisfactory.

Conclusion: Adjuvant radiotherapy administration appears to be a rational treatment method instead of sacrificing function to achieve wide surgical margins.

Key words: Adjuvant radiotherapy; limb salvage; recurrence; survival.

Aggressive fibromatosis (extra-abdominal desmoid tumors) are tumors fundamentally originating from connective tissue of the muscle, fascia and aponeurotic structures. Its clinical behavioral character varies, from benign fibrous lesions to fibrosarcoma.^[1] Despite exhibiting infiltrative growth characteristics such as fibrosarcoma, the tumor never metastasizes. Treatment management is difficult due to such clinical diversity.

Aggressive fibromatosis is a seldom-encountered, benign tumor. In a study executed in the Aegean Region of Turkey, 92 (1.6%) of 5658 patients with musculoskeletal system tumors were found to have aggressive fibromatosis.^[2] Annual incidence is approximately 2 to 4 cases among one million individuals.^[3-5]

Management of aggressive fibromatosis must be planned based on a multidisciplinary approach. Surgical management is considered the preferred treatment method.^[1,6-10] Recently, some authors have recommended clinical follow-up only.^[11] Surgical treatment should be in the form of wide excision with healthy tissue surrounding the tumor. However, the borders of the excision are mostly determined by tumor localization.^[12]

Radiotherapy (RT) is usually applied as an adjuvant for surgical treatment. It has also been suggested that RT implementation decelerates and terminates tumor growth. Frequently applied treatment protocol is based on a total dose of 36 to 65 Gray (Gy) allocated over 25 to 30 sessions, with five sessions weekly. The vast majority

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of the authors propose a total RT dose in the range of 50 to 60 Gy.^[3,13-17]

Our study aimed to present the outcomes of a single center and to evaluate the factors which affect prognosis.

Patients and methods

Forty-nine patients diagnosed with and surgically treated for aggressive fibromatosis between 1979 and 2009 were retrospectively evaluated. Of these, 40 patients (24 females and 16 males; mean age: 31.2 years; range: 4 to 74 years) completed final examination. Nine patients with tumor-positive surgical margins macroscopically were excluded in order to properly evaluate recurrence rates. All diagnoses of aggressive fibromatosis were confirmed histopathologically. Twenty-two patients (55%) had not undergone previous surgery and 18 (45%) had undergone previous surgery at a different clinic (Table 1). At the time of initial application, magnetic resonance imaging (MRI) revealed that 28 tumors (70%) were located inside the anatomic compartment and 12 (30%) expanded out of the compartment.

Average postoperative follow-up of 31 patients evaluated for recurrence was 70.1 (range: 13 to 276) months. Masses located in the operated area detected with physi-

cal examination or MRI in follow-up were defined as recurrences.

The aim of the surgical treatment is to reach wide excision borders without causing damage to extremity functions. In that respect, some patients were left with residual tumor to preserve extremity functions. Our algorithm scheme for aggressive fibromatosis management is depicted in Table 2.

Adjuvant RT was applied to appropriate patients (12 cases) at doses between 44 and 54 Gy over 25 to 30 sessions, with 5 sessions per week. Residue mass existence along with patient's age, tumor localization and growth rate were taken into account in the decision for RT application. Tamoxifen therapy was also administered to 4 estrogen receptor positive patients.

Statistical analyses were performed using SPSS software v.18 (SPSS Inc., Chicago, IL, USA). The effects of encountered prognostic factors over disease-free survival were analyzed using a log-rank test. Disease-free survival rates were calculated with the Kaplan-Meier survival analysis. P values of less than 0.05 were considered statistically significant.

Results

Nine patients (29%) developed recurrences within 2 years of excision. Average disease-free survival was 46 ± 4 (range: 38.1 to 53.8) months (95% CI). Disease-free survival rate for two years was $71 \pm 8.2\%$.

Table 3 shows the correlation of prognostic factors with recurrence rates. The recurrence rate was 33% in patients under the age of 31 and 25% in those aged 31 years or older ($p=0.671$). The recurrence rate of the 10 patients younger than 20 years of age, the age at which recurrences are most commonly encountered, was 40% ($p=0.363$).

A total of 12 patients received adjuvant RT and recurrence was observed in one. In the 19 patients that did not receive adjuvant RT, there were 8 recurrences ($p=0.069$) (Fig. 1).

There were 3 (23%) recurrences in the 13 patients operated originally at a different clinic and admitted with residual masses. Eight patients in this group had received adjuvant RT and no recurrences occurred in these patients ($p=0.024$). Of the 18 patients primarily admitted to our center, adjuvant RT was not administered to 14, and 5 (36%) of these patients experienced recurrence. Only one recurrence occurred the remaining 4 patients receiving RT ($p=0.730$) (Table 4).

According to pathological assessments, 13 patients had tumor-free post-resection surgical margins. Twelve

Table 1. Demographic data of 40 patients in the study.

	Number of patients	%
Gender		
Female	24	60
Male	16	40
Age		
1. Decade	6	15
2. Decade	7	17.5
3. Decade	9	22.5
4. Decade	6	15
5. Decade	5	12.5
6. Decade	4	10
7. Decade	2	5
8. Decade	1	2.5
Localization		
Foot and leg	8	20
Thigh and hip	15	37.5
Forearm	3	7.5
Arm and shoulder	12	30
Trunk	2	5
Compartment status		
Intracompartmental	28	70
Extracompartmental	12	30
Previous surgery		
No surgery before	22	55
Previously operated	18	45

Table 2. Our algorithm in the management of aggressive fibromatosis.

Characteristic of the tumor	Estimated morbidity after excision	Management
Small	No prominent morbidity	Wide excision +/- RT
Big	Minimal morbidity	Wide excision + RT Marginal excision + RT Intralesional excision + RT
Progressive	High probability of morbidity	Intralesional excision + RT +/- CT
Progressive	Prominent morbidity	Follow-up or CT
Small, no progression		Follow-up
Big, no progression		Follow-up

KT: Chemotherapy; RT: Radiotherapy.

Table 3. Correlation of prognostic factors with recurrence rates.

	Recurrence (+)		Recurrence (-)	
	n	%	n	%
Age (p=0.671)				
<31	5	33	10	67
≥31	4	25	12	75
Gender (p=0.724)				
Male	4	33	8	67
Female	5	26	14	74
Localization (p=0.346)				
Foot-leg	0	0	8	100
Thigh-hip	4	40	6	60
Forearm	1	50	1	50
Arm-shoulder	3	33	6	67
Trunk	1	50	1	50
Compartment status (p=0.287)				
Intracompartmental	6	25	18	75
Extracompartmental	3	43	4	57
Previous surgery (p=0.577)				
No previous surgery	6	33	12	67
Previously operated	3	23	10	77
Surgical margin status (p=0.417)				
Surgical margin (-)	5	38	8	62
Microscopically (+)	4	22	14	78
Tumor length (p=0.465)				
Tumor ≤9 cm	4	24	13	76
Tumor >9 cm	5	36	9	64
Radiotherapy (p=0.063)				
Radiotherapy (+)	1	8	11	92
Radiotherapy (-)	8	42	11	58

of these patients did not receive adjuvant RT and there were 5 (42%) cases of recurrence. The only patient receiving adjuvant RT did not relapse (p=0.475). There were 18 patients with residual tumors microscopically at the surgical margins according to pathological assessments. Of these, 11 received adjuvant RT with one (9%)

recurrence and three (43%) recurrences in the 7 patients not receiving adjuvant RT (p=0.107) (Table 4).

All of the nine patients, who were excluded from recurrence assessment due to macroscopically positive surgical margins, received adjuvant RT. Two of these 9 patients also received tamoxifen therapy due to positive

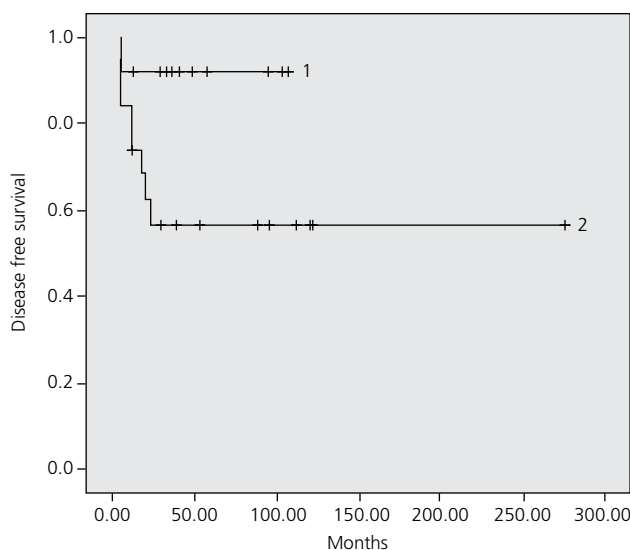


Fig. 1. Disease-free survival rates for adjuvant RT and non-adjuvant RT groups, calculated by Kaplan-Meier survival analysis. 1: Adjuvant RT group, 2: Non-adjuvant RT group.

hormonal receptors. All 9 patients were alive with disease and the masses were stable in their last control.

Recurrence occurred in 9 (29%) of the 31 patients evaluated for recurrence. Recurrences were treated with surgery alone in four patients and surgery with adjuvant RT in one, and all five were disease-free at the final follow-up. The remaining 4 recurrence cases had stable masses; one was treated with RT alone, two with RT and tamoxifen and one received no additional therapy.

Discussion

Treatment of aggressive fibromatosis is challenging due to wide variety of clinical findings and locations of the tumor, difficulty in estimating its progression and prognosis and alternative management methods. Many studies have been performed to investigate the prognostic factors of aggressive fibromatosis. The major difficulties encountered in such studies are the rarity of the tumor and lack of large patient series.^[2]

In our study, we determined patient age, tumor ex-

istence in the surgical margins, RT administration and history of previous excision to be factors affecting recurrence. We concluded that RT alone prevents recurrence formation, especially in patients with microscopically residual tumors.

Studies reporting higher recurrence rates in younger patients have been published in the literature.^[7,13] In the present study, while recurrence rate was not statistically different between patients younger than 31 years of and those 31 years or older, recurrence ratio was higher in the younger patients ($p=0.671$). Recurrence rates reached 40% in patients under the age of 20 years ($p=0.363$).

Post-resection tumor-positive surgical margin was shown to be an important negative prognostic factor.^[7,18-23] That is an expected result when anticipated under the constraints of musculoskeletal tumor surgery principals. Eleven (61%) of the 18 patients with tumor-positive surgical margins also received adjuvant RT and possible recurrence rates were diminished to one (9%). Recurrence was encountered in 3 of the 7 patients with postoperative tumor-positive margins who did not receive adjuvant RT. Therefore, we believe that adjuvant RT has a greater effect on preventing recurrences than tumor-free surgical margins.

One important factor affecting recurrence rate is history of previous surgeries. Wide excisions can be more difficult to perform in patients who underwent previous surgery due to undetermined extensions of the tumor.^[5,19] Adjuvant RT significantly reduced the recurrence rate in this patient group ($p=0.024$). On the other hand, only 4 patients of the 18 patients who applied to our clinic primarily received adjuvant RT. Recurrence rate in this group was 35%. We, therefore, think that patients undergoing their first surgery should also receive adjuvant RT.

The vast majority of previous studies stated that RT is an important method for providing satisfactory results.^[17,21,24-27] However, adjuvant RT may exhibit several complications like pathologic fracture, joint movement limitation, pain, and secondary malignancy. None of our

Table 4. Distribution of recurrences in RT and no RT groups among surgical margin and administration status.

	Radiotherapy (+)		Radiotherapy (-)	
	Recurrence (+)	Recurrence (-)	Recurrence (+)	Recurrence (-)
Surgical margin (-)	0 (0%)	1	5 (42%)	7
Surgical margin (+)	1 (9%)	10	3 (43%)	4
No previous surgery	1 (25%)	3	5 (36%)	9
Previously operated in a different hospital*	0 (0%)	8	3 (60%)	2

*Statistically significant result ($p=0.024$).

patients revealed such complications. These complications are most frequent in doses of over 50 Gy.^[17] In our series, the recurrence rate of patients receiving RT (8%) was considerably lower than those that did not (42%) ($p=0.063$).

Radiotherapy also shows efficiency in patients with macroscopically positive surgical margins. Such patients usually have tumors located in the axillary or inguinal regions which invade the adjacent vessel and nerve structures. In some patients, we performed a marginal resection with positive surgical margins in order to preserve extremity functions. All of these patients received RT and a stable disease status was achieved.

In conclusion, adjuvant RT appears to be a rational approach for aggressive fibromatosis management instead of sacrificing function to reach tumor-free margins. Providing the best possible functional and cosmetic outcome and achieving tumor-free surgical margins are the main aims of surgical management in aggressive fibromatosis.

Conflicts of Interest: No conflicts declared.

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