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Surgical treatment for local control of extremity and trunk desmoid tumors

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Abstract
Introduction Surgical treatment has been the mainstay for extremity and trunk desmoid tumors with a negative surgical margin. However, even when resection with a wide surgical margin is achieved, the local recurrence rate remains high. The purpose of this study was to analyze the clinical outcome of patients with extremity and trunk desmoid tumors after surgical treatment and to determine the factors influencing local recurrence.
Materials and methods Between January 1991 and December 2003, 30 of 58 patients with desmoid tumors referred to our institutions and surgically treated and followed up for more than 2 years were selected for this study. Patient age, gender, tumor size, location, status of disease (primary or recurrent), and surgical margins were analyzed as possible risk factors for recurrence.
Results Sixteen (53%) of the 30 patients had a local recurrence. Eight of the 19 patients (42.1%) with a negative surgical margin experienced a recurrence. Younger age (<30 years) was a significant risk factor for local recurrence ($P < 0.05$). Tumor size, surgical margin and previous surgical history were not associated with local recurrence. Younger age and female gender had a propensity for local recurrence, suggesting that the biological behavior of desmoid tumor may depend on the status of the disease at presentation.
Conclusions These results suggest that radical surgical treatment causing severe functional impairment should be avoided in selected cases on the basis of patient characteristics, and that other novel therapeutic tools may be necessary for patients in whom a higher risk of local recurrence is assumed or severe complications after surgical treatment are predicted.

Keywords Extra-abdominal desmoid · Surgery · Wide resection · Recurrence · Risk factor

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Introduction

Extra-abdominal desmoid tumors are pathologically benign, but local control is difficult to achieve because of their infiltrative nature [5]. Desmoids do not metastasize and do not influence mortality if they are not located adjacent to vital organs. However, they may occasionally cause functional impairment like joint contracture after surgical treatment or/and radiotherapy. Desmoid tumors can arise anywhere in the body, including intra-abdominal, abdominal wall, and extra-abdominal regions. Given that

intra-abdominal desmoid tumors, which are primarily associated with familial adenomatous polyposis (FAP) [9], exhibit a behavior distinct from that of extra-abdominal desmoid tumors, treatment modalities should be considered separately in extra-abdominal desmoid tumors.

The mainstay of treatment for desmoid tumors has been surgery especially with a wide surgical margin [9, 13–15, 17]. However, local recurrence rates after wide resection are not acceptable ranging from 23 to 77%. Surgical treatment with a wide surgical margin and local failure occasionally lead to severe functional impairment despite the benignity of these tumors. Recently, the possibility of conservative therapy has been reported using hormonal agents [10, 21], NSAID [18, 20], and chemotherapy [1, 8]. The treatment modality should be selected based on the characteristics of individual tumors.

In the current study, we retrospectively analyzed risk factors associated with local recurrence in patients with desmoids tumors undergoing surgical treatment.

Materials and methods

Between January 1991 and December 2003, 58 patients with desmoid tumors were referred to our institutions. All diagnoses were confirmed by pathologists based on examination of biopsy specimens. In cases in which the initial diagnosis had been made elsewhere, the pathology was reviewed and confirmed by our reference pathologists. Thirty of these patients, who were treated by surgery and followed up post-operatively for more than 2 years, were focused on in this study. Intra-abdominal desmoid and FAP patients were excluded from this analysis. Patients with insufficient data recorded were also excluded. Data were obtained through review of the patient's medical records and follow-up clinical documents. Their median age was 37.9 years (range 7–65 years). Eighteen (60.0%) were female and 12 (40.0%) were male. The anatomic distribution of the tumors was nine in the trunk (chest wall, back, neck, and abdominal wall) and four in the upper extremity including shoulder girdle, and 17 in the lower extremity including buttock. Median follow-up period was 7.4 years (range 2–15.3 years).

The resection margins of the tumor were assessed post-operatively by microscopic pathological evaluation and classified as positive or negative. The surgical procedure was planned to obtain a negative margin unless the tumor was adjacent to a neurovascular bundle. For the cases in which it was difficult to obtain a negative margin due to the presence of adjacent critical structures or assumption of severe complications after wide resection, an intra-lesional procedure was selected. Neurovascular bundle was not sacrificed to obtain a wide margin. In four patients in whom the tumor was localized in one muscle compartment, total muscle resection was performed by resection of the muscle from its origin to insertion as a radical resection. Tumor size was determined by measurement of the greatest dimension by MRI.

Patient gender, age, status of disease (primary or recurrent), tumor site, size, and surgical margins were analyzed as possible risk factors for recurrence. Local recurrence was defined as positive by either pathological determination with biopsy or MRI examination. Recurrence-free survival was estimated using the method of Kaplan–Meier from the first surgical procedure to the latest examination at our institutions. The effect of surgical margin on the recurrence rate was analyzed using the log-rank test. Difference in the recurrence rate was compared between two groups with Chi-square test. Continuous variables of age and tumor size were compared between the two groups using the Mann–Whitney U test. A P value of <0.05 was considered statistically significant. All analyses were performed using Statview software.

Results

Sixteen (53%) of the 30 patients had a local recurrence. Local recurrence free survival is shown in Fig. 1. Thirteen of 16 recurrent cases relapsed within 2 years (average 17.0 months). Local recurrence-free survival between margin negative and margin positive is shown in Fig. 2. There was no significant difference in the surgical margin status using log-rank test. Correlation of patient demographics with local recurrence was summarized in Table 1. Younger age was a significant risk factor for local recurrence with both a continuous variable analysis ($P < 0.05$) and 2×2 Chi-square analysis (<30 years, $P < 0.05$). Tumors tended to recur more frequently in females than in males, but this

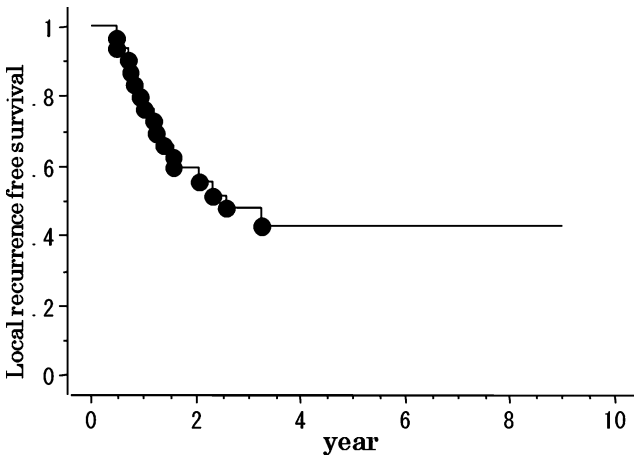

Fig. 1 Local recurrence free survival for trunk and extremity desmoids tumor after surgical treatment

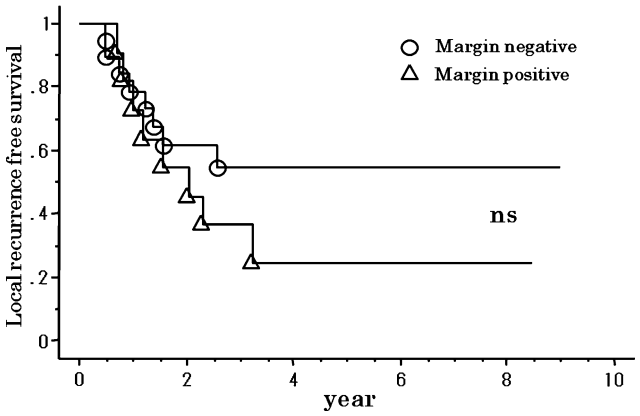

Fig. 2 Local recurrence free survival; comparison between cases with microscopic positive and negative margin

Table 1 Demographics of the 30 patients versus local recurrence

	Recurrence	No recurrence	*P* value
Gender			
Male	4	8	NS (=0.073)
Female	12	6	
Age (mean)			
Recurrence (29.8 years)			
No recurrence (47.0 years)			<0.05
Overall (37.9 years)			
Less than 30 years	8	2	<0.05
30 years or greater	8	12	
Size			
Recurrence (8.6 cm)			NS
No recurrence (7.8 cm)			
History of surgical treatment			
Recurrent	4	2	NS
Primary	12	12	
Margin (pathology)			
Positive	8	3	NS
Negative	8	11	

difference was not significant ($P = 0.073$). Tumor size and status (primary or recurrent) were not significant risk factors for recurrence. Table 2 shows the correlation between planned surgical procedure and surgical margin. Unplanned margin positive status was observed in three of the 22 (13.6%) cases with planned wide surgical procedure, in contrast to two of the two (100%) cases with planned marginal procedure. A representative case is shown in Fig. 3. The tumor was located in the vastus lateralis muscle, and pre-operative MRI evaluation revealed that a wide surgical margin could be obtained with total muscle resection. Resected specimen showed the tumor infiltration distally, and pathological examination determined the surgical margin as negative, despite which local recurrence occurred 1 year after surgery.

Table 2 Planned surgical procedure and surgical margin

Surgery	Total	Margin positive	
Total muscle procedure	4	1	25.0%
Wide procedure	18	2	11.1%
Marginal procedure	2	2	100.0%
Intra-lesional procedure	6	6	100.0%
Overall	30	11	36.7%

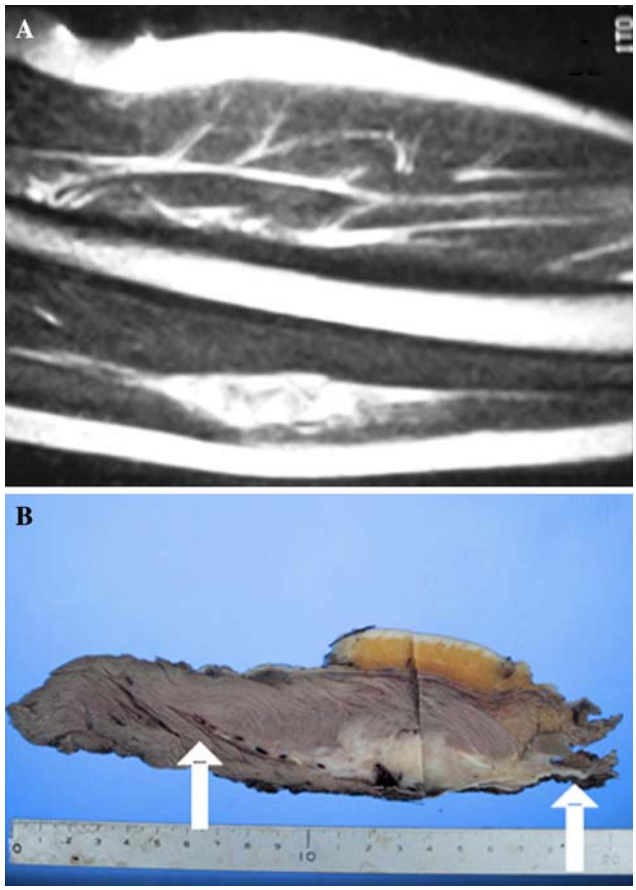

Fig. 3 Case presentation; 20 years old, female, desmoid occurred in vastus lateralis muscle. MRI revealed high intensity lesion with T2-weighed image (**a**). Specimen after total muscle resection indicated tumor infiltration into muscle bundle longitudinally (*arrows*)

Discussion

Desmoid tumor is a histologically benign tumor. But its clinical behavior is not benign, and local failure often occurs after surgical treatment. Although malignant tumors such as soft tissue sarcomas rarely recur locally if a negative surgical margin is obtained, desmoid tumors often recur after wide resection. Many authors have reported the

clinical outcome after surgical treatment with wide resection, demonstrating that the local recurrence rate ranging from 23 to 77% could not be reduced with wide resection [9, 13–15, 17].

There are two explanations for the high recurrence rate after resection of desmoids tumors. One is that desmoids tumors lack a pseudo capsule [14], form a non-palpable mass, and infiltrate along muscle bundles and fascia, impending clinical estimation of the tumor's extent. In the current study, there were three unplanned margin positive cases (14%) among 22 cases of pre-operative planned margin negative cases. However, this possibility will be overcome by the evaluation of the actual status of the microscopic margin. In fact, Posner et al. [14] identified positive margin as the most important predictive factor of local recurrence in their multivariate analysis of 138 patients in spite of the fact that their series included 19 patients with intra-abdominal disease and 11 of the 138 patients died of locally uncontrolled tumor. Ballo et al. [2] indicated that a positive margin was a significant risk factor for recurrence in their 122 patients treated with surgery alone. And they found that recurrence rates were decreased when radiation therapy was used after margin-positive resection. In their series, seven of the 122 had intra-abdominal desmoids, 58 of whom were recurrent cases. These studies indicated that a microscopic negative surgical margin is the most important factor to reduce the recurrent rate.

However, whether a negative surgical margin truly reduces the recurrence rate is still controversial. Gronchi et al. [7] analyzed a series of 128 primary desmoid patients and noted no significant association between margin status and recurrence. Merchant et al. [12] analyzed a series of 105 primary desmoid patients and concluded that margin positive was not predictive of recurrence. In our series of 30 desmoid patients, the local recurrence rate with negative margin was 42.1%, and margin positive status was not predictive of local recurrence. Moreover, of the four cases of total muscle resection based on the consideration of longitudinal infiltration of desmoids tumor, a negative margin was obtained in three cases. However, two of the four cases (50%) developed recurrences, suggesting that surgical treatment with a negative surgical margin alone may not be sufficient to eradicate a desmoid tumor.

Another possible explanation for the high local recurrence in desmoid tumors is that the recurrence rate may be largely dependent on the inherent characteristics of the disease, which when more aggressive might recur despite the quality of any surgery. In the current study, females tended to develop recurrences more frequently than males ($P = 0.073$), and younger age was a significant risk factor for local recurrence ($P < 0.05$). Some other authors [14, 17] have demonstrated similar results. The tumor biological status at the time of resection might affect the likelihood of local recurrence. Trauma has been suggested to stimulate desmoid growth. Pritchard et al. [15] reported that 12 of their 50 (24%) cases had had an episode of trauma or operation at the site of the desmoid. Pignatti et al. [6] reported that twenty of 103 (19.4%) patients had trauma at the desmoids site. In our series, two of the 30 cases (6.6%) had an obvious episode of trauma or operation. Reitamo et al. [16] reported that 13 of 40 abdominal desmoids in their series had a history of surgical trauma in the region of the subsequent tumor. And several other reports [3, 5, 19] also suggest that trauma promotes desmoid growth. On the other hand, the natural history of desmoid tumors is unknown. They usually grow slowly, but may sometimes enlarge rapidly. Some of these tumors may stop growing and may even regress naturally. For this reason desmoid has been referred to as an enigmatic tumor [2, 11]. These features also highlight the role of the inherent characteristics of desmoid tumors in influencing recurrence.

Long-term results of treatment for desmoids have rarely been reported. Dalen et al. [4] reported the treatment outcome of 30 desmoid patients with more than 20 years' follow-up. They suggested that patients with multiple tumors had severe disabling symptoms, with the number of symptoms seeming to increase with the number of operations. In the current series, six of 30 cases (20%) were left with severe dysfunction after surgical treatment. Functional impairment after surgical treatment should be considered over the long-term on the basis of age, tumor location, and extent of resection.

The efficacy of conservative therapy for desmoid tumors continues to be controversial. Several agents have been used, including NSAIDS, anti-estrogen therapy, chemotherapy, and tranilast for patients in whom surgical resection has failed. Systemic therapies for desmoid including hormonal agents [10, 21], NSAIDS [18, 20], and chemotherapy [1, 8] have been described. But these treatments lack clinical evidence of efficacy because of the uncertain natural history of desmoids. And because of their rarity, there are no randomized studies proving that they respond to systemic therapy.

Because desmoids are benign, preservation of function is particularly important. The results of the present study indicated that wide resection including total muscle resection did not improve the outcome, whereas age and gender were associated with an increased rate of recurrence. These results suggest that biological features may affect the outcome rather than surgical margins. Although surgical treatment with a wide surgical margin is the mainstay for desmoid tumors, preservation of the affected structures and their function with conservative follow-up might be an appropriate modality in selected patients with desmoid tumors.

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