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The management of extra-abdominal desmoid tumours

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Abstract We performed a retrospective analysis of 35 cases of desmoid tumours (aggressive fibromatoses) that underwent treatment at our institutions between 1987 and 2002. The purpose was to evaluate the rate of local recurrence of desmoid tumours treated with surgical excision, to assess the impact of surgical margins on local recurrence and to define the role of radiotherapy in the treatment. Nine patients experienced a recurrence at an average of 16 months after initial treatment. Seven of the 15 patients with a less-than-wide margin had a local recurrence. Comparatively, only two of the 20 patients with a wide margin had a local recurrence. Thirty-three of the 35 patients were disease free at the last follow-up. We recommend wide excision with clear margins whenever possible. Marginal resections are appropriate when wide excision would severely compromise the function of the limb. Surgical resections and selective supplementation of adjuvant radiotherapy give excellent control rates.

Résumé Nous avons exécuté une analyse rétrospective de 35 cas de tumeurs desmoides (fibromatose agressive) traitées dans notre institution entre 1987 et 2002. Le but était d'évaluer le taux de récurrence locale après traitement par excision chirurgicale, d'étudier le rôle des marges chirurgicales sur la récurrence et de définir le rôle de la radiothérapie dans le traitement. Neuf malades ont eu une récurrence à une moyenne de 16 mois après le traitement initial. Sept des 15 malades opérés avec une marge qui n'était pas large, avait une récurrence locale. Comparativement, seulement 2 des 20 malades avec une marge large

avaient une récurrence locale. Trente trois des 35 malades étaient sans maladie au dernier suivi. Nous recommandons l'excision large avec des marges claires toutes les fois que possible. Les résections marginales sont appropriées quand l'excision large compromettrait sévèrement la fonction du membre. Les résections chirurgicales avec, sélectivement, un traitement adjuvant par radiothérapie donnent d'excellents taux de contrôle de la maladie.

Introduction

Desmoid tumours, or aggressive fibromatoses, are rare, slow growing benign tumours originating from deep musculo-aponeurotic structures. These tumours are non-encapsulated, infiltrative and locally aggressive [13, 22]. However, they lack the cytological features of malignancy and have essentially no metastatic potential [5, 9, 11, 16]. Depending on the site and type of resection, the reported local recurrence rates range from 15 to 77% [4, 12, 17, 19, 20, 22]. Traditionally, desmoid tumours have been managed with surgery with wide local excision being the preferred treatment [3, 10, 16, 19]. Over the past 10 years, adjuvant therapy, employing radiation therapy, chemotherapy, anti-estrogenic agents such as tamoxifen and even NSAIDs have been used in an attempt to reduce the risk of local recurrence [1, 11, 14]. Despite various studies, the natural history of these tumours remains enigmatic, with paucity of information on the optimal treatment protocol.

Many reports have emphasized that the margin status is the single most significant determinant of recurrence in patients treated with surgery [2, 11, 16, 19]. However, some authors disagree that margin status is an important factor in outcome [18]. There are conflicting recommendations regarding surgery and a poorly defined role of radiotherapy in the management of these tumours. Whereas some reports suggest little or no benefit from radiation therapy for aggressive fibromatoses [18, 19], many studies have found external radiotherapy to be helpful in the management of this disease [2, 3, 6, 7, 10, 13, 23, 24]. The aim of this study was to evaluate the rate

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of local recurrence of desmoid tumours treated with surgical excision, to assess the impact of surgical margins on local recurrence and to define the role of radiotherapy in the treatment of these tumours.

Materials and methods

This is a retrospective study of 35 patients (Table 1) who presented with an extra-abdominal desmoid tumour between 1987 and 2002 either at The Wesley Medical Centre or the Princess Alexandra Hospital, Brisbane, Australia. Patient age at diagnosis ranged from 9 to 84 years with a mean of 32 years. There were 19 male and 16 female patients. Distribution of anatomic tumour site was forearm, three; arm, nine; chest and abdominal wall, five; back, seven; buttock, four; thigh, three; popliteal fossa, two; calf, one; and foot, one. Tumour sizes were documented in all cases and ranged from 2 to 25 cm in maximum linear dimension with a mean of 8 cm. Eighteen tumours were more than 5 cm and 17 less than or equal to

5 cm. Twelve tumours exceeded 10 cm in the largest dimension (Fig. 1).

Of the patients, ten presented after one (six patients) or more (four patients) local recurrences after initial attempts at definitive treatment outside our institution. Twenty-five patients presented with previously untreated disease. All patients were initially treated with surgical excision with the aim of a wide margin. Twenty of the 35 patients had a wide local excision. Of the remaining 15, ten had a marginal excision whereas five had positive margins at surgery. Eight patients received post-operative adjuvant radiation therapy. In addition, five patients received radiation therapy after recurrence (including one who also received radiotherapy after initial excision). The majority of patients were treated with a radiation dose between 50 and 60 Gy. One patient received low-dose chemotherapy for recurrence following surgical excision and radiotherapy. Another patient, following recurrence, was treated with adjuvant drugs alone including tamoxifen, NSAIDs and low-dose chemotherapy. The mean follow-up time was 68 (9–150) months. No case was lost to follow-up.

Table 1 Data on all patients. RT Radiotherapy, CT chemotherapy, R1 treatment at first recurrence, R2 treatment at second recurrence, AKA above-knee amputation, NED no evidence of disease, AWD alive with disease

Case number	Age/gender	Site	Recurrence	Adjuvant treatment	Last known status
1	23/M	Back	None	None	NED; 31 months
2	38/M	Buttock	None	None	NED; 150 months
3	84/M	Chest wall	None	RT 10 Gy	NED; 22 months
4	40/M	Buttock	1 (27 months)	RT 50 Gy; CT (R1)	AWD; 39 months
5	34/F	Abdo. wall	None	None	NED; 113 months
6	17/M	Arm	None	None	NED; 80 months
7	35/M	Arm	None	None	NED; 118 months
8	37/M	Arm	None	None	NED; 11 months
9	50/M	Arm	None	None	NED; 52 months
10	19/F	Forearm	None	RT 60 Gy	NED; 114 months
11	28/M	Chest wall	None	None	NED; 9 months
12	32/F	Arm	1 (12 months)	RT 64 Gy (R1)	NED; 62 months
13	33/M	Arm	1 (8 months)	RT 55 Gy (R1)	NED; 49 months
14	9/F	Foot	None	None	NED; 37 months
15	19/F	Chest wall	None	None	NED; 145 months
16	53/M	Back	None	None	NED; 10 months
17	47/F	Back	None	None	NED; 46 months
18	41/F	Arm	None	RT 50 Gy	NED; 80 months
19	21/F	Arm	None	None	NED; 53 months
20	38/F	Back	1 (18 months)	None	NED; 38 months
21	24/F	Buttock	1 (19 months)	Tamoxifen (R1)	AWD; 141 months
22	40/M	Thigh	None	None	NED; 11 months
23	10/M	Forearm	None	None	NED; 129 months
24	23/M	Forearm	None	RT 50 Gy	NED; 97 months
25	25/F	Pop. fossa	1 (8 months)	RT 63 Gy (R1)	NED; 24 months
26	61/M	Arm	None	RT 60 Gy	NED; 45 months
27	28/M	Buttock	1 (23 months)	RT 50 Gy; 60 Gy (R1)	NED; 35 months
28	22/F	Back	None	None	NED; 37 months
29	36/M	Back	None	None	NED; 110 months
30	16/F	Calf	None	None	NED; 145 months
31	12/M	Pop. fossa	2 (12, 24 months)	None (AKA) (R2)	NED; 68 months
32	22/F	Thigh	None	None	NED; 128 months
33	52/M	Back	None	RT 60 Gy	NED; 11 months
34	38/F	Chest	None	None	NED; 57 months
35	29/F	Thigh	2(24, 27 months)	RT (R1 60 Gy)	NED; 100 months

Fig. 1 Magnetic resonance image showing a desmoid tumour in the buttock

Results

Nine patients had a local recurrence including two with multiple recurrences. First local recurrences occurred after mean of 16 (8–27) months after initial excision. Seven of the 15 patients with a less-than-wide margin had a local recurrence. Comparatively, of the 20 patients with a wide margin, only two had a local recurrence. Of the eight patients who received adjuvant radiotherapy after the primary surgery, six received it for positive surgical margin whereas two had a negative margin. These two patients were given radiotherapy for their extremely large tumour masses, and it was felt that the recurrence and its subsequent operative treatment would lead to a severe functional loss. Of these eight patients treated with post-operative radiotherapy following the primary surgery (excluding those who were treated with radiotherapy after a local recurrence), two developed a local recurrence.

Of the nine patients with recurrence (Table 2), eight underwent a further surgical excision and one received

chemotherapy. Five patients received adjuvant radiotherapy whereas one received chemotherapy and tamoxifen. Two patients developed a further recurrence. One patient underwent an above-knee amputation, and the other underwent a repeat surgical excision. Thirty-three of the 35 patients were disease free at the last follow-up.

Discussion

Desmoid tumours are locally aggressive, non-metastasising tumours [9, 13, 15, 22]. Not only are they rare, they also have an unpredictable clinical course, which makes their treatment difficult. Surgery and radiotherapy have been used with varying results. Hormone antagonists like tamoxifen, chemotherapy with standard cytotoxic drugs and NSAIDs have also been reported to show clinical responses [1–3, 11, 12, 14]. Desmoid tumours are most common between puberty and 40 years of age with a peak incidence between the ages of 25–35 years. Women are more commonly affected than men [11, 19, 21, 24]. In our study, the mean age at diagnosis was 32 years, and men outnumbered the women. These lesions are reported to be most common in the shoulder musculature followed by the chest wall, back, thigh and head and neck [5]. In our study, most lesions were in the arm followed by the back.

The propensity of these tumours to recur has been widely reported. Recurrence rates have varied between 15 and 77% [4, 12, 17, 19]. In our series, 25% of the patients had a recurrence with the majority of the recurrences occurring within the first 2 years following surgery. Numerous studies have found the margin status as the most important determinant of recurrence in patients treated with surgery [2, 3, 11, 16, 19]. In a study of 194 patients with an average duration of follow-up of 12.3 years, Rock et al. [19] reported a local recurrence of 68%. Only 50% of tumours recurred after wide local excision when compared to a recurrence rate of 90% after incomplete excision. Mehrotra et al. [11] evaluated 36 patients of extremity fibromatoses with an average follow-up of 83 months. They reported a 56% recurrence rate. Seventy-one percent of patients with a positive surgical margin had a local recurrence compared to 31% with a negative margin. Ballo et al. [3], in their series of 189

Table 2 Patients with recurrences. RT Radiotherapy, CT chemotherapy, AKA above-knee amputation, NED no evidence of disease, AWD alive with disease

Case number	Primary treatment	Recurrence (months)	Treatment of recurrence	Status
4	Excision + RT	27	Chemotherapy	AWD; 39 months
12	Excision	12	Excision + RT	NED; 62 months
13	Excision	8	Excision + RT	NED; 49 months
20	Excision	18	Excision	NED; 38 months
21	Excision	19	Excision + tamoxifen + CT	AWD; 141 months
25	Excision	8	Excision + RT	NED; 24 months
27	Excision + RT	23	Excision + RT	NED; 35 months
31	Excision	12	Excision	NED; 68 months
		24	AKA	
35	Excision	24	Excision + RT	NED; 100 months
		27	Excision	

cases, reported a recurrence rate of 27% in patients with negative surgical margins. Margin-positive patients, on the other hand, had a relapse rate of 54%. In our study, 47% of patients with a positive surgical margin had a recurrence as compared to only 10% of patients with a negative surgical margin. Merchant et al. [12] evaluated 189 patients with an average follow-up of 49 months and reported a local recurrence of 23%. However, they did not find positive surgical margin as a predictive of recurrence.

Radiation therapy either alone or in conjunction with surgery has been reported to have varying success in the treatment of desmoid tumours. Various series have shown that adjuvant radiation therapy is effective in tumour control [2, 3, 10, 23]. However, some authors have reported uncertain benefits using this treatment [18, 19]. In our series, 12 patients received adjuvant radiotherapy at some stage of treatment. Eight patients received post-operative adjuvant radiotherapy after the first operation, and of these, two developed a local recurrence. Five patients (including one who also received radiotherapy after initial excision) received radiotherapy along with a repeat excision after the first local recurrence. Of these, only one developed a local recurrence. Twenty-two patients received no adjuvant therapy, and of these, two developed a local recurrence. One patient received tamoxifen and chemotherapy as adjuvant treatment for recurrence and was alive with disease at the last follow-up.

Eight patients, including the patients who received radiotherapy after the first local recurrence, received it for positive margins at surgery. Of these, only two developed a local recurrence. Therefore, radiotherapy gave a local control of 75%, which is consistent with other reports on radiotherapy. McCollough et al. [10] reported local control rates of 79% in patients treated with radiation post-operatively for known or presumed microscopic residual disease and in 88% of patients treated for known grossly apparent residual disease. Karakousis et al. [8] evaluated 26 patients with desmoid tumours of the extremities. They reported a 96% local control rate in patients treated with surgical resection and supplemented selectively by adjuvant radiation therapy.

Desmoid tumours are benign, non-metastasising in nature and, on a cellular level, lack the nuclear and cytoplasmic features of malignancy. However, despite their bland histological appearance, their clinical behaviour is frequently aggressive with wide local infiltration. The natural history of these tumours remains poorly understood, and their management still remains an enigma. Margin status seems to be the most important predictor of local recurrence. From the experience of the present series, we feel surgery is the first-line treatment for these tumours. Wide excision with clear margins should always be the goal, though negative margins do not necessarily correlate with lower recurrence rates. If the resection margins are negative, we do not ordinarily recommend post-operative radiation. We recommend adjuvant post-operative radiotherapy with total dose ranging from 50 to 60 Gy for primary cases only if the margins are positive and/or it is anticipated that the recurrence and its operative

treatment would lead to a severe functional loss. Recurrent or residual tumours should be considered for treatment only if there is actual regrowth of the tumour. It remains unclear why some tumours continue to grow while others can be safely followed for long periods. Protocol for recurrent tumour remains the same as for primary occurrences. Resection, if surgically appropriate, should be the first choice of treatment. However, unlike the treatment of primary tumours, there is a significant increase in the possibility of the use of post-operative adjuvant radiotherapy. Patients with gross residual disease following surgery or where the tumour has been peeled off major neurovascular bundles should be considered for adjuvant radiotherapy and/or chemotherapy. Mutilating procedures should only be used as a palliative measure if the tumour recurs repeatedly and compromises viability of the extremity.

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