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Radiation therapy in the treatment of desmoid tumours reduces surgical indications

H.A. Rüdiger [a,b,*], S.Y.K. Ngan [c], M. Ng [c], G.J. Powell [a], P.F.M. Choong [a]

[a] Department of Orthpaedics, St. Vincent's Hospital, Melbourne, Australia
[b] Department of Orthopaedics, University of Zürich, Balgrist, Switzerland
[c] Department of Radiation Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia

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Abstract

Background: While several modalities have been proposed for the treatment of desmoid tumour/aggressive fibromatosis, high local recurrence rates have been reported. We present a retrospective study of including patients treated with radiation therapy, some of them in combination with surgical resection.
Patients and methods: Thirty-four consecutive patients were included (mean age 40 ± 16 years, 9 male). Complete follow-up was available in 31 patients (51 ± 36 months). Seventeen patients (50%) were treated with radiation therapy alone, 17 patients with radiation therapy and surgery. Radiation therapy (external beam) was applied in most cases to a total dose of 50.4 Gy in 28 fractions. The lesion was located in the upper extremity in 11 patients, in the lower extremity in 14 cases and on the trunk in 9 cases.
Results: Overall recurrence/progression free survival was 88.5% at 5 years and 77.5% at 10 years. Recurrence free survival of the subset of patients undergoing combined treatment with radiation therapy and surgical resection was 83.6% at 5 years and 10 years. In patients who did not receive surgery but only radiation therapy, MRI showed a complete response in 20%, a partial response in 20%, and stable disease in 53% of cases. In this subset, two-third of patient had a metabolic response to radiotherapy (i.e. decrease uptake on the thallium-210 scan after radiotherapy compared to pre-therapy levels).
Conclusion: Low recurrence rates can be achieved with the use of radiation therapy alone in selected cases. Patients with a metabolic response (decrease) to radiotherapy may be treated with a non-surgical approach. Surgery might be considered in patients with a poor metabolic response to radiotherapy.

Keywords: Desmoids; Aggressive fibromatosis; Radiation therapy; Resection; Sarcoma

Introduction

Desmoid tumours, also called aggressive fibromatosis, are fibrous proliferations, whose biologic behavior is between that of a benign fibrous lesion and fibrosarcoma.[1] They arise from connective tissue of muscle and the overlying fascial sheaths or aponeurosis. Despite the histologically mostly bland appearance, the lesions frequently behave in a locally aggressive manner. Unlike sarcomas, desmoids are characterized by an infiltrative growth pattern that follows fascial planes, and may encase neurovascular structures and bone.

Combined surgery and radiotherapy remain the mainstay of curative therapy in most cases, of unilocular and small-volume disease.[2] More recently, endocrine[3,4] and chemotherapy[5,6] regimens have also been proposed. However, the disease is associated with a high recurrence rate ranging from 20% to 59%,[7–9] and its natural history is unpredictable.[10]

In 1928, Ewing[11] first proposed radiation therapy for this entity and reported a slow but ''satisfactory'' response. Nuyttens and colleagues[9] recently reported in a meta-analysis that recurrence rate in patients undergoing surgery alone was significantly lower compared to radiation therapy alone. Lowest recurrence rates were found in patients who underwent combined resection and radiation therapy. However, there are certain reservations to treating benign lesions with irradiation. In their review, Nuyttens et al.[9] also reported a radiation-related complication rate of

* Corresponding author. Department of Orthopaedics, University of Zürich, Balgrist, Forchstrasse 340, 8008 Zürich, Switzerland.
E-mail address: ortho@mm.st (H.A. Rüdiger).

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23%, including secondary malignancy (1%), skin ulcers (2%), pathological fractures (2%) and others.

The purpose of this study was to review our institutional experience in the treatment of desmoid tumours. Our aims were to (1) determine the outcome of the treatment of extra-abdominal desmoids with radiation therapy alone or in combination with surgical resection and (2) describe the characteristic of this lesion in our patient population.

Patient and methods

All 47 patients, who were admitted to our institution between 1992 and 2003 with the diagnosis of desmoid tumour/aggressive fibromatosis, were retrospectively analyzed. Patients' records and imaging studies, which were available in all cases, were assessed. Out of these 47 patients, we selected the 34 patients (9 males), who were subjected to radiotherapy (with or without additional surgical resection). Mean age at presentation was 40 ± 16 year. While 20 patients had primary disease, 14 patients were referred for the treatment of recurrent disease. Of these 14 patients, 5 presented with a first, 5 with a second and 4 with a third recurrence.

Tumour sites are depicted in Table 1. Twenty-one patients reported pain, and in 29 patients a palpable mass was found. Mean duration of symptoms was 21 ± 39 months.

Preoperatively, lesions were assessed using MRI, CT scans and functional scans (^{210}thallium or FDG-PET scans). Definitive diagnosis was made using tissue biopsies, which were performed as core needle biopsy under CT guidance in the majority of cases.

Therapy

All patients were subjected to megavoltage external beam radiation therapy. Median dose was 50 Gy (range: 24–60 Gy) with a median fractionation over 28 sessions (range: 6–30). Clinical target volume (CTV) was defined as 3–4 cm from gross tumour volume or from surgical bed in postoperative cases. Planning target volume was 1 cm plus CTV. Surgical resection was performed in 17 patients, while 17 patients were subjected to radiotherapy alone. In 13 cases, radiotherapy followed surgery by 5 ± 8 months. In 5 cases, surgery followed radiation therapy by 3 ± 3 months (from the start of radiotherapy). The decision to subject the patient to surgery was made on a case-by-case basis rather than a rigid treatment algorithm. Hormonal therapy (tamoxifen) was used in 4 patients as additional treatment.[12]

Follow-up

Patients were clinically and radiographically followed in our outpatient department. Follow-up data were retrospectively collected based on notes in patients' records and all imaging studies have been reviewed. Patients are in general followed with a local MRI every 3 months for 1 year, then every 6 months. Functional scans are performed on a yearly basis. Follow-up data was complete in 31 patients (91%), 3 patients were lost to follow-up and could not be contacted.

Statistics

Values are expressed as mean ± standard deviation unless otherwise specified. A p-value ≤ 0.05 was considered significant. Comparisons of continuous parameters were calculated using Student's t test (parametric)[13] or Wilcoxon's test (non-parametric).[14] Differences of multiple groups were calculated using analysis of variance followed by multiple pair wise comparisons using Bonferroni's post hoc procedures.[15] Survival was estimated using the method for non-parametric estimation from incomplete observations as described by Kaplan and Meier.[16] Time of follow-up was calculated from the beginning of radiation therapy to the last appointment in our outpatient clinic. All calculations were performed using SPSS software (version 15.0.0, Chicago, IL).

Results

Follow-up

Mean follow-up after RT was 51 ± 36 months (range: 8–172 months, Table 2). At the time of the last follow-up,

Table 1
Anatomic distribution of the lesions did not differ significantly between upper and lower extremities or trunk.

Tumour site	Overall	RT alone	RT + surgery
Upper extremity	11	6	5
Arm/forearm/hand	2	1	1
Shoulder	9	5	4
Lower extremity	14	8	6
Foot/calf	4	4	
Thigh	4	3	1
Pelvis/buttocks	6	1	5
Trunk	9	3	6
Total	34	17	17

Table 2
Patient with a combination treatment of surgery and RT did not significantly differ from patients with RT alone in terms of age, sex, follow-up and preoperative size of the lesion.

	Overall	Surgery + RT	RT alone	Significance[a]
N	34	17	17	n.s.
Age [years]	40 ± 16	37 ± 11	37 ± 20	n.s.
Sex (male/female)	9/25	5/12	4/13	n.s.
Follow-up	51 ± 36	59 ± 49	44 ± 22	n.s.
Preop size of lesion [mm][b]	65 ± 33	70 ± 38	57 ± 25	n.s.

n.s.: not significant.
[a] Surgery + RT vs. RT alone.
[b] Preoperative largest diameter of the lesion based on MR and CT.