Yonsei Medical Journal
Vol. 40, No. 5, pp. 439-443, 1999

The Role of Radiotherapy in the Treatment of Aggressive Fibromatosis

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Abstract

Aggressive fibromatosis is a rare benign soft tissue tumor that is difficult to cure because of its infiltrative nature and high tendency to recur locally. The authors retrospectively analyzed 20 patients with histologically-confirmed fibromatosis. All patients underwent surgery with a wide or marginal margin. Five (25%) cases with histologically-negative margins had recurred. External beam radiotherapy was administered to patients whose margins were positive or who had local recurrence. However, out of concern for safety, radiotherapy was not given to two babies and a reproductive-aged woman. The average dose was 5,020 cGy. During the follow-up (mean 32.6 months), all the patients undergoing radiotherapy showed no evidence of local recurrence. A wide local excision has traditionally been the treatment of choice. However, postoperative radiotherapy could be an effective measure for preventing local recurrence in patients with a histologically-positive surgical margin and recurrence independent of any signs of relapse.

Key Words: Aggressive fibromatosis, surgery, radiatiotherapy, recurrence

INTRODUCTION

Aggressive fibromatosis is a rare and slow-growing tumor which arises from fascial sheaths and musculoaponeurotic structures. While histologically benign in appearance, these tumors are non-encapsulated and tend to extend along fascial planes, infiltrate adjacent muscles, and engulf blood vessels and nerves. Since aggressive fibromatosis can become attached to and erode bone, as well as having a high incidence of local recurrence, some authors have classified this neoplasm as a low grade fibrosarcoma.[1-3] The optimal treatment is controversial. A wide excision of the tumor has been recommended as the treatment of choice. However, achieving a wide margin of normal tissue is difficult when the tumor size is large, when it is lying close to important neurovascular structures, or when the margin is mixed with scar tissue in recurred cases. Many adjuvant therapies, including radiotherapy, chemotherapy and hormonal therapy have been suggested as methods to control unresectable lesions and decrease local recurrence. The authors reviewed the clinical course of 20 patients who received surgery alone or surgery with adjuvant radiotherapy to determine the efficiency of adjuvant radiotherapy.

Received June 9, 1999
Accepted August 21, 1999
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MATERIALS AND METHODS

Twenty patients with histologically-confirmed aggressive fibromatosis were treated between January 1994 and December 1997. Of these, seven patients were referred to us because of recurrences and 13 patients for primary treatment. Nine patients were males and 11 were females. The average age at the time of diagnosis was 29.6 years (range 2 to 69 years) and they most commonly presented in the second decade (30%). The follow-up period from the last operation was a mean 32.6 months (range from 15 to 63 months). Of the seven patients with recurrences, four were males and three were females. The mean age of the recurred cases was 35.5 years. Among the patients with recurred tumor, two patients underwent previous surgical procedures again. The elapsed time from the last operation to their being referred to us averaged 12.6 months.

Medical records, radiographs and histological specimens were retrospectively analyzed regarding patient characteristics, size and location of the lesion, margin

Table 1. Patients Data

Case	Age(yr)/Sex	Site	Size(cm)	Referred time(mo)	Planned margin	Resection margin*	Recur	Reccured time(mo)	Radiation dose (cGy)	F/U (mo)
1	22/M	Arm	5×5		Marginal	+	No		5,400	15
2	40/F	Sole	1×1		Wide	−	Yes	23		53
3	65/M	Sole	1×1		Wide	−	No			27
4	33/F	Back	6×4		Marginal	+	No		5.040	19
5	20/M	G. toe	1×2		Amputation	−	No			41
6	2.6/M	Forearm	3×3		Marginal	+	No			25
7	15/F	Thigh	7×7		Marginal	+	No			26
8	16/M	Popliteal	5×4		Wide	−	Yes	21, 20		31, 30
9	2.3/F	Buttock	5×3		Marginal	−	Yes	9		46
10	12/F	Arm	4×4		Wide	−	Yes	13	4,500	23
11	56/F	Shoulder	4×4		Wide	−	Yes	22	4,500	29
12	23/F	Axilla	6×5		Intralesional	+	No		5,400	47
13	37/F	Back	4×4		Wide	−	No			20
14	30/F	Thigh	6×3	7, 24	Wide	−	No		4,500	44
15	20/M	Shoulder	10×12	6	Marginal	+	No		5,400	31
16	53/M	Thigh	6×6	6	Wide	−	No		5,000	47
17	45/F	Popliteal	5×4	3	Marginal	+	No		5,040	22
18	22/F	Arm	5×5	25	Marginal	−	No		5,040	63
19	10/M	Buttock	6×5	17, 19	Marginal	+	No		5,400	22
20	69/M	Sole	1×1	6	Wide	−	No			21

* Resection Margin: +, tumor positive; −, tumor free.

of resection and prior recurrence (Table 1). Histologic specimens were examined, noting the presence of interlacing bundles of uniform spindle-shaped fibroblasts in an infiltrative growth pattern with characteristic finger-like extensions, the presence of a relatively large amount of collagen in the extracellular matrix and the absence of cytologic features of malignancy and mitotic figures. All patients underwent staging investigations prior to treatment. Magnetic resonance imaging was used for evaluation of the local extent of disease, as well as the relationship of the lesions to nerves, vessels and bone. All 20 patients received operative procedures by one of the authors (K. H. Shin). Complete resection with negative histologic margins was the intent in management of all cases. If the margin appeared inadequate for local control by surgery, postoperative adjuvant radiotherapy was performed. Also, tumors which recurred after previous treatment also received postoperative radiotherapy. Radiation was administered with a 4MV linear accelerator X-ray via a parallel-opposed pair of oblique fields with or without boost radiation to the primary tumor bed. The radiation field was designed with a generous enough margin to cover the origin and insertion of the involved muscle or muscles compartment. The total irradiation dose for patients with complete excision was 4500 cGy. For 6 patients, boost irradiation of 540−900 cGy was given with shrunken fields because the tumor was not excised with a wide margin. The shrunken irradiation fields included the presurgical enhancing mass with a 4-cm margin. The total dose for the primary tumor bed ranged from 4500 to 5400 cGy (average 5,020 cGy) with 180 cGy per fraction, five days a week. The mean follow-up duration was 32.9 months from the last radiation. All patients were alive at the time of analysis and no patient was lost to follow-up.

RESULTS

The most common sites were the arm, thigh and sole. The size of the resected tumors varied from 1.0 ×1.0 cm to 10.0×12.0 cm (average 4.6×4.2 cm). Nine patients underwent wide excision, 10 patients underwent marginal or intralesional excision and one patient underwent radical amputation of an extremity. Wide margins could not be obtained because

the tumors were either located too close to neurovascular structures or had infiltrated through the bone. The patient who underwent curative amputation was diagnosed provisionally with fibrosarcoma on the biopsy, but subsequently as aggressive fibromatosis on the final pathologic report. The margins were microscopically-positive in eight patients, and three of these patients were referred cases.

Local recurrence developed in five patients (25%) at an average 18 months (range 9 to 23 months) after index treatment, and all of these cases were treated at our hospital. All cases had wide surgical margins, except one marginal resection that was finally found to have microscopically-negative margins. Two recurrent lesions were treated with re-excision and postoperative radiotherapy, while radiotherapy was not performed in three cases. A two-year-old girl underwent no further treatment because she was too young for either reoperation or irradiation (case 9). Another patient underwent amputation due to vascular disturbances with necrotic changes of the sole (case 2). A third patient refused adjuvant therapy against recommendation (case 8).

The authors planned to attempt postoperative radiotherapy for all recurred cases except one with a small-sized tumor (case 20). Another indication for postoperative radiotherapy was margin-positive cases. Among the margin positive-cases, two patients were excluded from the administration of radiation. One was a 30-month-old boy for fear of epiphyseal injuries and growth disturbances (case 6), and the other was a 15-year-old girl whose reproductive organ had been included in the radiation area (case 7). No patient experienced acute toxicity during the radiotherapy. Up to the last follow-up, all the patients were free of local recurrence.

DISCUSSION

Aggressive fibromatosis is a histologically-benign lesion, but it is difficult to cure because of its infiltrative nature and a tendency to recur. Its locally invasive and destructive behavior is similar to that of low-grade fibrosarcomas. Three treatment modalities have been reported to be of value in the management of fibromatosis: surgery, irradiation, and drug treatment. Traditionally, aggressive fibromatosis has been treated by surgery alone, but the results have frequently been disappointing. Many authors have reported that the correct initial treatment is vital and that a resected margin is the most important predictor of local recurrence.[4-6] Enneking recommended wide excision as the initial procedure and a radical excision after recurrence.[7] Hunt et al. reported that excision in the longitudinal axis should be at least twice the width so as to safely surround the irregular margins infiltrating the muscle proximally and distally.[8] Radical resection and occasional amputation is recommended for large recurrent tumors, as well as for tumors of the iliac fossa, gluteal fossa, or shoulder.

Reported recurrence rates have shown a wide range according to the surgical margin. Dahn et al. reported recurrence rates of 70% with marginal excision and 8% with radical operation.[6] However, Reitamo et al. found little difference in the recurrence rate after complete and incomplete resections.[9] Others have reported that positive margins were not always necessary for recurrence.[3] The present results were that five patients with negative margin showed recurrence. It is of interest that clean surgical margins do not necessarily guarantee a lower risk of recurrence. Aggressive fibromatosis tends to infiltrate adjacent muscles microscopically, which cannot be determined grossly at the operation field. Rock et al. reported that a higher tendency for recurrence was evident in females over 30 years of age and located in the lower extremity with intralesional or marginal resection.[10] In our cases, being female and at a young age were correlated with recurrence. No relation could be found among recurrent history, anatomical location, size of tumor at the time of treatment, and recurrence rate, as can be seen from our data.

Recurrent tumors may have a more aggressive nature and it can also be difficult to distinguish between scar tissue and tumors, which may result in inadequate safety margins for excision. Among those patients referred to us after recurrence, it was very difficult to establish a safety margin. Recurrent tumors must be excised as widely as possible, but treatment of aggressive fibromatosis is a complex problem based on factors such as age, size and anatomical location of the lesion. As well, amputation and/or major muscle group excisions are considered to be too aggressive in certain cases because these tumors grow slowly and do not metastasize. Attempted wide excision often results in less benefit than adequate margins with preservation of the neurovascular

bundle or adjacent bone.

There are many adjuvant therapies including radiation, chemotherapeutic agents, estrogen blockade and prostaglandin manipulation. These have been advocated as effective alternative treatments to radical resection to avoid or minimize serious complications and decrease the risk of recurrence. However, the effect of chemotherapy has not been tested adequately because of the indolent and non-metastasizing nature of the disease. Hormonal therapy is based on the assumption that estrogen may be a growth factor for fibroblastic tumor and that a substantial number of these tumors occur in women during their childbearing years. In none of these reports do the complete response rates approach those of conventional surgery or radiotherapy.[5,11] Brachytherapy has been used to permit the delivery of higher radiation doses to tumors and a reduction in the duration.[12] But Pisters et al. reported that brachytherapy had no impact on local control in patients with low-grade soft tissue sarcoma.[13] Although there is no standard width of coverage that is recommended to avoid recurrence after radiation, the entire involved muscle including its aponeurotic structures should be included in the radiation portals.

Aggressive fibromatosis is a radioresponsive tumor. There are numerous reports in the literature that local control has been achieved with irradiation. Greenberg et al. reported an 89% rate of relapse free survival of radiotherapy combined with surgery.[14] Goy et al. reported that patients with positive margins who underwent adjuvant radiotherapy and surgery improved local control to 78%, in contrast to 32% with surgery alone.[15] In our series, the indication of postoperative radiotherapy included recurred cases and positive surgical margins. Lack of standardization in radiation technique and variations in dose in many studies have led to confusion. Many authors have reported that doses in the range of 50−60 Gy would be adequate to control microscopic disease without causing excessive morbidity.[1,16,17] Relapse is more likely with doses of less than 50 Gy and more complications develop with doses of more than 60 Gy. This study showed good results with doses averaging 5,020 cGy. Response to radiotherapy can be extremely slow and complete resolution required 8 months to 2 years.[2,5] Therefore, the presence of persistent disease immediately following radiotherapy should not be misconstrued as a treatment failure. Radiotherapy after resection of primary or recurrent disease in a young patient requires caution, especially irradiation near the epiphysis, which may lead to growth retardation and subsequent deformation. Post-irradiation fibrosis, joint contracture, neuropathy and post-irradiation sarcoma may also occur after high-dose radiotherapy.

In conclusion, aggressive fibromatosis tends to be locally infiltrative and careful treatment planning is required. The results presented here confirm the benefit of additional external beam radiotherapy when applied in selected cases. Adjuvant radiotherapy is indicated in the treatment of patients with positive surgical margins and with recurrent disease.

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