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Post-irradiation Soft Tissue Sarcoma

C. Bloechle, M. Peiper, R. Schwarz, S. Schroeder and C. Zornig

From 1975 to 1993, 11 of 375 patients treated for soft tissue sarcoma presented with post-irradiation sarcoma. The mean time interval between irradiation therapy and onset of the second neoplasm was 15.8 years (4–31 years). The total radiation dosage ranged from 12 to 60 Gy with a mean of 40 Gy. All patients had complete staging including CT or MRI of the tumour site, and CT of the lung. Surgical resection was the treatment of choice. Wide margins could be achieved in 10 patients. One had a marginal resection. Tumours included malignant fibrous histiocytoma, haemangiosarcoma, rhabdomyosarcoma, malignant schwannoma, fibrosarcoma and undifferentiated sarcoma. All patients were reassessed in our outpatient clinic. After a mean follow-up of 4.7 years (1.0–11.5 years), only 1 patient had died because of the tumour. Although post-irradiation sarcomas are rather infrequently observed, these tumours must be suspected when alterations or symptoms occur in a previously irradiated region. Early detection provides the chance of curative, wide margin resection.

Key words: soft tissue sarcoma, irradiation, surgical treatment
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INTRODUCTION

KNOWLEDGE OF the aetiology of soft tissue sarcoma is poor. Malignant transformation of a benign mesenchymal tumour to soft tissue sarcoma is accepted in Von Recklinghausen's disease [1, 2], while it has been doubted as a general process in the pathogenesis of sarcoma [3]. Chronic lymph oedema, induced by radiotherapy, may lead to lymphangiosarcoma, known as Stewart-Treves-Syndrome [2]. Post-irradiation soft tissue sarcoma comprise another rare but well recognised entity [4–6]. This long-term complication of radiotherapy is poorly character-

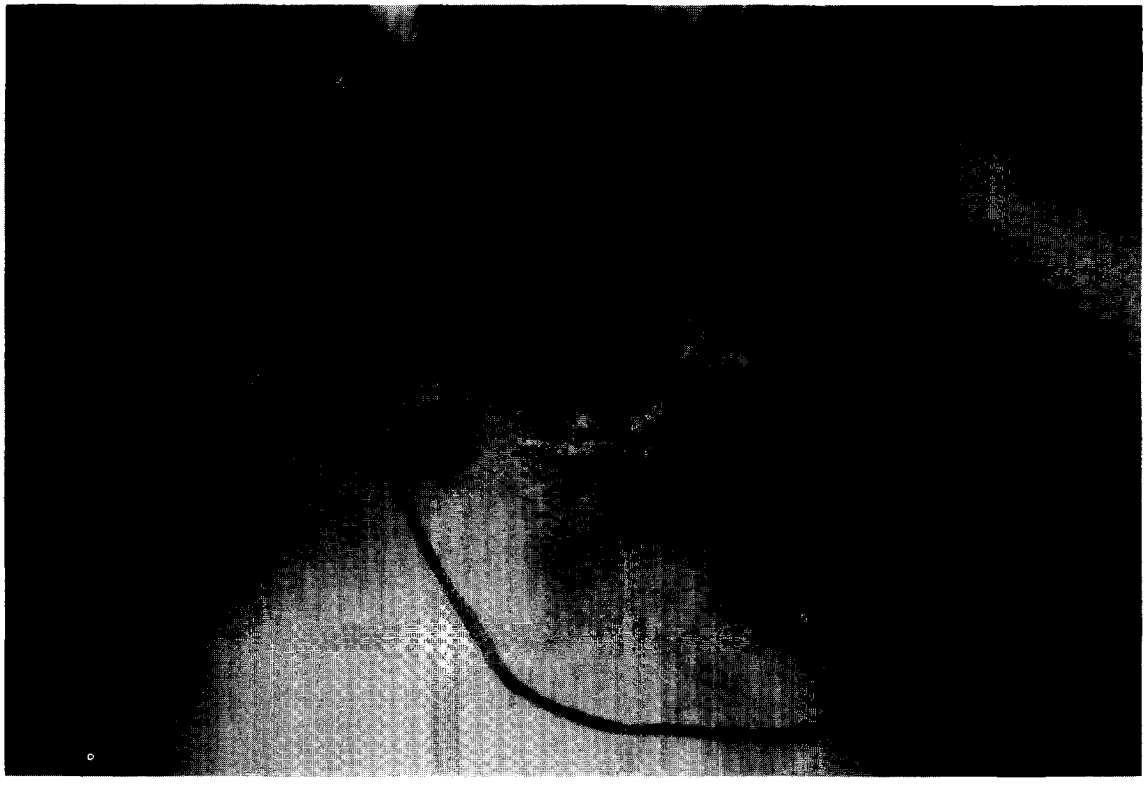

Figure 1. Multifocal recurrence of malignant fibrous histiocytoma having developed at the site of previously irradiated breast cancer (patient no. 9).

ised due to the difficulties in obtaining reliable data after latencies of up to 30 years [5]. To analyse the clinical presentation, surgical approach and outcome of patients with post-irradiation soft tissue sarcoma, we conducted a retrospective study. To our knowledge, this is the largest series of post-irradiation soft tissue sarcoma treated in a single institution.

PATIENTS AND METHODS

Of 375 patients with soft tissue sarcoma treated in our department since 1970, 11 patients presented with a sarcoma localised at the irradiation site of previously treated benign or malignant tumour disease. These patients, who all met the criteria of post-irradiation soft tissue sarcoma described by Cahan and colleagues [1], comprise the population of this study. All patients had complete staging including CT scan or MRI of the tumour site, and CT of the lung, and were reassessed in our out-patient clinic.

History, clinical presentation, surgical approach, histological characterisation of the tumour, and outcome were evaluated. All histopathological slides were reviewed by one pathologist (S.S.) and additional immunohistological studies were employed to reclassify the diagnosis according to Enzinger and Weiss [1]. The quality of resection was determined according to the R-classification of the UICC [7].

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RESULTS

The mean age of the 10 female and 1 male patients was 51.5 years (range 18–82 years). Presenting symptoms were tumour mass with a mean diameter of 6.2 cm and localised tension in all patients. Duration of symptoms averaged 6.8 months (range 1–18 months). Patient 9 presented to our department with a fourth local recurrence (Figure 1), while the other patients were treated for primary soft tissue sarcoma. The diseases, which were previously treated by irradiation, were breast cancer in 4 patients, cervix carcinoma in 3, and haemangioma, benign haemangiopericytoma, Hodgkin's lymphoma, and fibrosarcoma each in 1 patient. The mean total dosage of radiation therapy was 40 Gy, ranging from 12 Gy for haemangioma to 60 Gy for breast cancer. The mean latency between radiotherapy and clinical evidence of soft tissue sarcoma was 15.8 years (4–31 years; Table 1).

The sarcomas were resected within their anatomical unit with the surrounding fascial or bony layer. As the sarcomas were always located in the previously operated and irradiated area, large resections (including several costae) or amputations were necessary. In all but 1 patient (91%), complete tumour resection with wide margins (R0) could be achieved. The histological diagnoses and tumour grading are shown in Table 2. Synchronous lymph node metastases and distant metastases were not present in any of the patients.

After a mean follow-up of 4.7 years (1.0–11.5 years), 8 patients are alive without evidence of disease. 2 patients died of other causes without evidence of disease (patient 9 from myocardial infarction, and patient 10 from pneumonia). 1 patient (number 8) with a rhabdomyosarcoma on the left shoulder developed lung metastases after 17 months and died (Table 3).

Table 1. Clinical characteristics of 11 patients with post-irradiation soft tissue sarcoma

Patient Number	Sex	Age (years)	Initial tumour	Irradiation therapy total and single dose, f/w*, source	Latency (years)	Sarcoma site
1†	F	67	Breast cancer	21 Gy/—/— orthovoltage	26	Thoracic wall
2†	M	29	Haemangioma	12 Gy/—/—/ orthovoltage	25	Thoracic wall
3	F	29	Haemangiopericytoma	16 Gy/0.8 Gy/5/neutrons	5	Thigh
4	F	74	Cervix cancer	50 Gy/1.8 Gy/5 cobalt	19	Thigh
5	F	18	Hodgkin's lymphoma	35 Gy/2 Gy/5/6-16 MV photons	4	Neck
6†	F	71	Cervix cancer	60 Gy/—/—/orthovoltage	31	Abdominal wall
7	F	46	Breast cancer	40 Gy/2 Gy/5/cobalt	11	Thoracic wall
8	F	82	Breast cancer	50 Gy/3 Gy/5/cobalt	16	Shoulder
9	F	41	Breast cancer	50 Gy/2 Gy/5/photons	4	Thoracic wall
10	F	59	Cervix cancer	50 Gy/3.6 Gy/5/cobalt	10	Hip
11	F	50	Fibrosarcoma	50 Gy/2 Gy/5/cobalt	23	Foot

*fractions per week; †data on single dosage and fractions per week were not available for patients who underwent radiotherapy 25–31 years ago.

Table 2. Tumour characteristics of 11 patients with post-irradiation soft tissue sarcoma

Patient	Histology	Tumour size (cm)	Grading
1	Malignant fibrous histocytoma	7	3
2	Haemangiosarcoma	5	1
3	Haemangiosarcoma	5	1
4	Malignant schwannoma	11	3
5	Malignant fibrous histiocytoma	3	2
6	Undifferentiated sarcoma	4	3
7	Fibrosarcoma	8	2
8	Rhabdomyosarcoma	7	3
9	Malignant fibrous histiocytoma	Multifocal	2
10	Malignant fibrous histiocytoma	8	2
11	Undifferentiated sarcoma	4	3

Table 3. Surgical therapy and outcome of 11 patients with post-irradiation soft tissue sarcoma

Patient Number	Surgical procedure	R-stage	Outcome	Survival (months)
1	Wide margin resection	0	NED	15
2	Wide margin resection	0	NED	15
3	Wide margin resection	0	NED	15
4	Wide margin resection	0	NED	15
5	Wide margin resection	0	NED	12
6	Wide margin resection	0	NED	144
7	Interthoracoscapular amputation	0	NED	132
8	Marginal resection	1	SRD	21
9	Wide margin resection	0	DOC	47
10	Hemipelvectomy	0	DOC	108
11	Wide margin resection	0	NED	95

NED, no evidence of disease; DOC, death of other causes; SRD, sarcoma related death.

DISCUSSION

Cahan and associates have defined the following criteria for the diagnosis of post-irradiation soft tissue sarcoma: tumour site within the radiation field, latency of more than 1 year, histological determination of soft tissue sarcoma, definitive histological differentiation from the irradiated primary tumour. All sarcomas presented in this study met these criteria. In most cases the causes for radiotherapy are malignant tumours, such as malignant lymphoma, breast cancer, and cervix cancer [5]. The incidence of post-irradiation soft tissue sarcoma has been

estimated to be 0.03% [6]. The most frequently observed histological type has been reported to be malignant fibrous histiocytoma with a poor degree of differentiation [5]. The time interval between previous radiotherapy and onset of post-irradiation soft tissue sarcoma ranges from 2 to 40 years [2, 4–6] and is neither correlated to the type of primary lesion that has been treated by radiation nor to the histological type of post-irradiation soft tissue sarcoma [6]. Latency has been reported to be the longest in brachytherapy, followed by orthovoltage and megavoltage. However, differences between patients treated by brachytherapy, ortho- or megavoltage, with regard to the histological type of sarcoma and survival, have not been shown [5, 6]. Due to the fact that the diagnosis of post-irradiation soft tissue sarcoma is frequently established only in advanced stages of the disease, curative surgical treatment has been reported to be limited to approximately 50% of patients [6].

Clinical presentation in post-irradiation soft tissue sarcoma is not different from primary soft tissue sarcoma of any other aetiology [9], affecting patients of either sex and at any age. Presenting symptoms are local tension and pain in combination with mass formation. The mean symptom interval averages nearly 7 months until diagnosis is confirmed. This does not differ from soft tissue sarcoma of other origins [10, 11].

The treatment of choice for post-irradiation soft tissue sarcoma is surgical resection with wide margins. This approach does not differ from the operative strategy in soft tissue sarcomas of other origin. The clinical examination of the tumour site is often difficult due to the presence of tissue alterations in the radiated region. Hence, the preoperative imaging of tumour size, and localisation determined by CT scan or MRI is mandatory. According to this imaging, the operative strategies are determined before surgery, with the aim of tumour resection without actually seeing the sarcoma during the operation. Thus, the tumour must, three-dimensionally, be covered by uninvolved tissue. In patients in which R0 resection has been realised, survival is significantly improved compared to patients with microscopic (R1) or macroscopic (R2) residual tumour. This finding is equally relevant in all soft tissue sarcoma independent of the underlying aetiology [11].

In the present study, 10 patients remained free of tumour during follow-up, which was less than 2 years for 6 patients, but more than 7 years in 4 patients. The survival data are rather high compared with data from the literature [4–6] but the fact that none of the patients had distant lymph nodes or distant metastases at surgery probably contributed to this. The presence of lymph nodes and/or distant metastases, however, is one of the most important prognostic factors in soft tissue sarcoma [11]. Apart from the quality of resection (R0/R1/R2) and eventual metastasis, the most important prognostic factors for soft tissue sarcomas are tumour grade, size and histological type [11]. In our series, five of the post-irradiation soft tissue sarcomas were poorly (G3) and four were moderately (G2) differentiated.

Sarcomas induced by irradiation are rare. Whenever alterations or symptoms occur in previously irradiated areas, the development of post-irradiation soft tissue sarcoma must be suspected. Early detection of post-irradiation soft tissue sarcoma provides the chance of curative resection with wide margins, even though unfavourable prognostic factors such as poor differentiation or advanced tumour size may be present.

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