SUBCUTANEOUS SARCOMA
A POPULATION-BASED STUDY OF 129 PATIENTS

ANDERS RYDHOLM, PELLE GUSTAFSON, BO RÖÖSER, HELENA WILLÉN, NILS OSKAR BERG

From University Hospital in Lund, Sweden

We reviewed 129 patients with subcutaneous sarcoma diagnosed from 1964 to the end of 1985 in a population-based series of sarcoma cases from southern Sweden. The annual incidence was 0.4 per 100 000, comprising 32% of all soft-tissue sarcomas of the extremities or the trunk wall. Compared to deep-seated sarcomas, subcutaneous tumours were half the size at diagnosis, more common in the lower leg and foot, more often malignant fibrous histiocytoma, and of a lower grade of malignancy.

None of the low-grade and only 7% of the high-grade tumours recurred locally after wide local excision without radiotherapy. The cumulative five-year survival for all 129 patients was 80%. Multivariate analysis identified only high grade of malignancy and the size of the tumour (> 5 cm) as independent prognostic factors. We conclude that systemic or local adjuvant therapy is not generally indicated for subcutaneous sarcoma because of the good prognosis and low local recurrence rate after wide excision.

Most reports on soft-tissue sarcoma do not separate subcutaneous tumours from those which are deep-seated. When this has been done, widely different frequencies for subcutaneous sarcoma have been reported, ranging from less than 10% to over 50% of all soft-tissue sarcomas of the extremities and trunk wall (Markhede, Angervall and Stener 1982; Rydhom et al 1984; Collin et al 1987; Rydhom and Rööser 1987; Alvegård et al 1989). The prognosis for subcutaneous tumours has not been separately analysed. Our studies of the earlier cases in the present series (1964 to 1978), showed that subcutaneous sarcomas represent about one-third of all soft-tissue sarcomas, and that local recurrence is rare after wide excision (Rydholm et al 1984; Rydhom and Rööser 1987).

We have now extended our analysis and report the epidemiology, local recurrence rate, and survival in a consecutive, population-based, 22-year series of 129 patients with subcutaneous sarcoma. Follow-up was complete for a minimum of three years or until death.

PATIENTS AND METHODS
The database at our regional tumour centre includes all patients with a soft-tissue sarcoma of the extremity or trunk diagnosed since 1964 in the 1.5 million population of the southern health care region of Sweden. Patients who had not been treated at our centre, which started in 1970, were collected from the population-based Regional Cancer Registry, so the database includes all patients in the region, whether treated at our centre or at other hospitals. We excluded patients with strictly dermal tumours, Kaposi's sarcoma, desmoids, dermatofibrosarcoma protubersans, Stewart-Treves' tumours, and sarcomas in previously irradiated areas.

Full medical records were available for all cases, and for those diagnosed at other hospitals, histological material was sent for and re-examined. When appropriate, old material was reprocessed for histochemical staining, electron microscopy and immunohistochemical investigations. The review started in 1981 when all cases were re-examined by NOB and HW.

During the first years we used the Histological Definition and Classification of soft-tissue tumours, of the WHO International Reference Centre, defining malignant fibrous histiocytoma according to Weiss and Enzinger (1978). Since 1983 we have used the system of histological classification and nomenclature of Enzinger and Weiss (1983). The histological grading of malignancy was on a four-grade scale (Angervall et al 1986), grades I and II being termed low grade and grades III and IV, high grade.

In patients not referred to our tumour centre, the
classification of tumour depth was based on the preoperative, operative, and histopathological findings documented in the medical records. This applied to 54 of 129 patients in the present series of subcutaneous sarcoma. In most of these patients (48) the first surgical procedure had been a marginal excision; our definition was based on the surgeon’s report that a superficial tumour had been shelled out without dissection through fascia or muscle tissue, and that no muscle tissue was mentioned in the histopathological report, or found at our re-examination of the material.

In 49 patients referred after surgery (two after incisional biopsy, 39 after marginal excision, and eight after local recurrence), the classification of the subcutaneous location was also based on our findings at re-operation. Finally, in the 26 patients referred to us before surgery, the classification was based on our finding of a subcutaneous tumour that did not grow through the deep fascia. All tumours that failed to meet the above-mentioned criteria were classified as deep seated and excluded from the present series.

From 1964 through 1985, a subcutaneous sarcoma was diagnosed in 129 patients and a deep seated one in 275. The percentage of subcutaneous tumours was the same throughout the period: 32% from 1964 to 1971, 31% from 1972 to 1979, and 31% from 1980 to 1985.

The surgical margins of excision were classified according to the surgical staging system of Enneking, Spanier and Goodman (1980), cases treated earlier being classified retrospectively. The classification of margins in patients not referred (n = 54), referred after local recurrence (n = 8), or referred but not re-operated on (n = 5) was usually easy; 46 of the 67 tumours had been shelled out and the margin was classified as marginal. In the other 21 cases of these groups, the margin was classified as wide; a decision was based on the operation notes and the histopathological reports, both of which described a cuff of subcutaneous tissue around the tumour and of deep fascia beneath the tumour. If the primary tumour had been re-excised soon after to increase the surgical margin, the last margin was the one recorded.

The median follow-up time for the 68 patients who survived was nine years (range 3 to 24). For the 28 patients who had died because of tumour it was two years (range 0.25 to 11), and for the 33 patients who died of other causes, 4.3 years (range 0.6 to 19). No patient was lost to follow-up.

Statistics. In the analysis of prognostic factors, the five patients who had metastases at presentation were excluded. Epidemiological data were analysed using the Mann-Whitney U-test and the chi-squared test. Clinico-pathological and treatment factors were analysed univariately for influence on survival using Kaplan-Maier methods and the generalised Wilcoxon test. A Cox multivariate analysis of prognostic factors was performed, and the Wald statistic was used for assessment of significant factors. Associations between the factors were tested by the Mann-Whitney U-test and the Pearson Correlation Coefficient. A p value of < 0.05 was considered significant. The analyses were performed by Jonas Ranstam, MA, of the Department of Community Health Sciences, Malmö General Hospital, Sweden.

RESULTS

Epidemiology. Of the total of 404 patients with a soft-tissue sarcoma of the extremities or trunk wall diagnosed from 1964 to 1985, 129 (32%) had subcutaneous tumours. The annual incidence was 0.39/100 000, with a ratio of men to women of 1.3. The median age of the patients was 59 years (range 18 to 87) and the median size of the tumour was 4.3 cm (range 1 to 16). The most common location was the lower extremity (Table I). Malignant fibrous histiocytoma was the most common histotype, and grade III the most common grade of malignancy (Table II).

Compared to deep-seated tumours, subcutaneous tumours were half the size, more common in the lower leg and foot, more often a malignant fibrous histiocytoma, and less often of grade IV (Table III).

Treatment of primary tumour. All 129 patients were treated by surgery, three by amputation. The surgical margin was marginal in 54 and wide in 75 patients. In the 72 cases where a wide margin was obtained by local surgery, the skin was primarily closed in 41, a split skin graft was used in 27, and a rotation plasty in four. Eleven
patients had postoperative radiotherapy. Ten patients had chemotherapy, most of them according to non-standardised protocols, and were not separately analysed. Local recurrence. The local recurrence rate after surgery with a marginal margin, without radiotherapy was 0.6 (26 of 45) and after operations with a wide margin, or with a marginal margin and adjuvant radiotherapy was 0.1 (6 of 84). The local recurrence rate was twice as high for high-grade tumours than for low-grade tumours (Table IV).

Metastases and tumour-related deaths. Of the 129 patients, five with grade IV tumours already had metastases at presentation and 29 patients subsequently developed metastases. Twenty-eight of these 34 patients had died from tumour at the latest follow-up, 21 by three years and 25 by five years. Two had died from other causes, both after one year. Four patients are alive after a mean of 15 years follow-up without signs of disease. Two had soft-tissue metastases, and one had lung metastases treated by surgery. One had regional lymph node metastases, treated with radiotherapy.

The cumulative five-year survival rate for all 129 patients was 0.80. The 34 patients with metastases more often had large, high-grade tumours, which frequently had been treated by marginal surgery than had the 95 patients without metastases (Table V).

Univariate analysis of survival. After exclusion of the five patients with metastases at presentation, 124 patients remained for analysis. Tumour size > 5 cm, high malignancy grade (Figs 1 and 2), marginal excision and local recurrence all impaired survival, whereas gender, tumour localisation and histotype did not.

Multivariate analysis of survival. Gender, localisation, tumour size (1 to 5 cm, 6 cm and larger), histotype, malignancy grade (low, high), margin of excision and local recurrence were multivariately analysed for influence on survival. High grade of malignancy (RR = 8) and large size (RR = 3) were the only factors that independently impaired survival. The five-year survival rate for patients with none of these risk factors was 1.0, for patients with one of the factors 0.9, and for patients with both factors 0.7 (Fig. 3). Two-thirds of the patients (83 of 129) had less than two risk factors.

Covariations between prognostic factors. Marginal surgery was associated with a higher rate of local recurrence (p = 0.0001). There was a nonsignificant (p = 0.06) association between large tumour size and marginal excision.

DISCUSSION

Data regarding the depth of the tumour are often missing in reports on sarcoma treatment. In recent major reports, we have found only four papers which separate subcutaneous from deep-seated tumours, (Markhede et al 1982; Collin et al 1987; Rydhholm and Rööser 1987; Alvegård et al 1989) while seven fail to do so (Lindberg et al 1981; Brennan et al 1985; Enneking and McAuliffe 1985; Lindberg 1985; Suit et al 1985; Karakousis et al 1986; Potter et al 1986). In total, these papers report more than 3000 patients. Collin et al (1987), in a series which included patients presenting after a local recurrence (one-third), reported 50% superficial tumours, but included
Survival in 124 patients with subcutaneous sarcoma and without metastases at presentation related to size of tumour and grade of malignancy. Figure 1a - A = tumour 1 to 5 cm (n = 75); B = 6 to 10 cm (n = 42); C = 11 cm or larger (n = 7); (p = 0.006). Figure 1b - Malignancy: grade I (n = 7), grade II (n = 19), grade III (n = 56), and grade IV (n = 42); (p = 0.003).

Survival rates in 124 patients with subcutaneous sarcoma and without metastases at presentation. A = grades I-II, ≤ 5 cm (n = 18). B = grades I-II, > 5 cm (n = 8). C = grades III-IV, ≤ 5 cm (n = 57). D = grades III-IV, > 5 cm (n = 41).

A 74-year-old man had a painless swelling of the right upper arm for 18 months. This grew considerably over two months and became painful. Figure 3a - CT showed a subcutaneous tumour bulging into the muscles and close to the skin. Fine-needle aspiration cytology diagnosed a high-grade pleomorphic sarcoma. The 8 cm tumour was removed by wide excision, including the deep fascia and the overlying skin. Closure used a split-skin graft. Figure 3b - Histology showed a grade IV malignant fibrous histiocytoma of the myxoid subtype. The tumour was close to, but not in the deep fascia (arrowheads). At latest follow-up, four years after the operation, there were no signs of local or distant disease.
also tumours located “predominantly above” the deep fascia: this figure does not refer to only primary, strictly subcutaneous sarcoma. Alvegård et al (1989) reported one-quarter of subcutaneous tumours, and Markhede et al (1982) found less than 10%. These two series are centre-based: the lower fractions of subcutaneous tumours may be due to referral bias; patients with small subcutaneous tumours are less often referred to a tumour centre than those with large deep-seated tumours. In our population-based study we found that subcutaneous sarcomas comprise one-third of all soft-tissue sarcomas of the extremities or trunk wall.

Almost half (54/129) of the patients in our series were not referred to our centre, so the classification of tumour depth was retrospective and based on the medical records. However, from 1964 to 1971 no patients were referred before surgery, while from 1980 to 1985 half of the cases had surgery at our centre. The ratio of subcutaneous to deep-seated tumours was the same in both groups, confirming that our retrospective classification was valid. In general, subcutaneous tumours were half the size of deep-seated tumours, more common in the lower leg and foot, more often a malignant fibrous histiocytoma, and of a lower grade of malignancy. Subcutaneous tumours are more easily detected at a smaller size, but we have no explanation for the other differences.

‘Conservative surgery’ combined with pre-, per-, or postoperative radiotherapy is the routine treatment for soft-tissue sarcoma at several centres (Lindberg et al 1981; Shiu et al 1984; Enneking and McAuliffe 1985; Lindberg 1985; Suit et al 1985), with a local recurrence rate of around 20%. One-third of our patients were treated by marginal excision alone, most of them at other hospitals during the earlier years: there was local recurrence in 60% of these. Enneking (1983) reported a local recurrence rate close to 100% after marginal excision, but this difference may be partly explained by referral bias; patients treated primarly by marginal excision outside tumour centres may be referred only when there is a local recurrence.

In the cases where the margin in retrospect was classified as wide, we cannot exclude that a more careful examination of the surgical specimen in some cases had revealed a marginal margin. However, such false classifications do not change the conclusion that the recurrence rate is low after wide excision of subcutaneous sarcoma. In our experience (Rydholm, Rööser and Persson 1986) and that of others (Stener 1978), a primary soft-tissue sarcoma, whether its origin is superficial or deep, seldom grows through fascia, and this even applies to large tumours. Of the seven tumours larger than 10 cm in our series, four were treated by wide excision including the deep fascia beneath the tumour. None had radiotherapy, and none recurred locally.

In the surgical staging system of Enneking et al (1980), subcutaneous tumours are not separately classi-

fied, and it has been suggested that surgery with a wide margin for high-grade, malignant tumours is followed by local recurrence in 50% to 70% of cases (Enneking 1983). This figure is, however, based on series which were probably dominated by deep-seated and extracompartmental sarcomas. In our series, the local recurrence rate for high-grade tumours after wide excision was 7% (Table IV): the routine combination of surgery and radiotherapy is not indicated for subcutaneous sarcoma.

The well-known association between local recurrence and metastasis in cases of soft-tissue sarcoma was observed also in our series (Rööser, Gustafson and Rydhholm 1990). Patients with metastases had more often been treated by marginal excision; this could be interpreted as showing a causal relationship between inadequate surgical treatment and long-term prognosis. However, multivariate analysis failed to show that either the type of surgical margin, or local recurrence influenced survival, provided that account was also taken of tumour size and grade of malignancy. Patients who developed metastases had larger tumours, which were more often high grade, than patients without metastases. These findings show that the prognosis in subcutaneous sarcoma is governed more by host-related and tumour-related factors than by type of treatment.

Conclusions. One-third of soft-tissue sarcomas of the extremities or trunk wall are subcutaneous. These are smaller than deep-seated tumours at diagnosis, and fewer have the highest grade of malignancy. They have a better prognosis: the five-year survival is 80% and local recurrence after surgery with a wide margin is seen in less than 10%.

For these reasons the routine use of systemic or local adjuvant therapy is not indicated. In addition, we recommend that subcutaneous sarcoma should be classified separately in reports on the treatment of soft-tissue sarcoma.

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REFERENCES


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