Superficial Extremity Soft Tissue Sarcoma: An Analysis of Prognostic Factors

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Background: Experience with soft tissue sarcoma has suggested that superficial tumors have a favorable prognosis. We evaluated the prognostic features of this subset of sarcoma.

Methods: Prospective data on 215 patients presenting to Memorial Sloan-Kettering Cancer Center with primary extremity superficial soft tissue sarcomas between July 1, 1982 and July 1, 1996 were analyzed. Superficial sarcomas were defined as subcutaneous tumors not invading the investing fascia of the muscle. Analysis was by univariate and multivariate tests for local recurrence, metastasis, and tumor mortality.

Results: Ninety (42%) patients were over 50 years of age, 115 (53%) had high-grade tumors, 53 (25%) had tumors ≥5 cm, and 18 (8%) had positive margins following definitive resection. Median follow-up was 45 months (range 2 days to 151 months), 31 (14%) patients had local recurrences, 20 (9%) had distant metastases, and 15 (7%) died of disease. Five- and 10-year actuarial disease-specific survivals were 91% and 85%, respectively. On multivariate analysis, age >50 years predicted local recurrence (RR 5.7; 95% CI, 2.4-13.3; p < 0.0001). High grade (RR 4.2; 95% CI, 1.4-12.7; p < 0.006), and size ≥5 cm (RR 4.4; 95% CI, 1.8-11; p < 0.002) predicted distant metastases. High grade (RR 7; 95% CI, 1.5-31.4; p < 0.003), size ≥5 cm (RR 6.9; 95% CI, 2.3-20.8; p < 0.0006), and positive margins (RR 3.8; 95% CI, 1.2-12.4; p < 0.006) predicted tumor mortality.

Conclusion: Primary superficial extremity soft tissue sarcomas have a favorable prognosis. Size and grade of superficial tumors are the strongest factors in predicting survival.

Key Words: Soft tissue sarcoma—Prognosis—Superficial sarcoma—Extremity sarcoma—Staging.
on the outcome of small (<5 cm) sarcomas (13), finding that cohort patients with high-grade tumors had a 5-year survival of 91%. These same tumors would be considered AJCC stage III, with a projected 5-year survival of 30% (14). We predicted similar improved results for superficial tumors regardless of grade.

The purpose of this study was to evaluate the superficial extremity sarcomas in a well-characterized cohort of patients treated and prospectively followed at a single institution. In addition, we sought to evaluate this subset of tumors to determine which patient and tumor variables predict local recurrence, distant metastasis, and decreased disease-specific survival.

METHODS

Patients
We have prospectively followed all adult (>16 years of age) patients with soft tissue sarcoma admitted to Memorial Sloan-Kettering Cancer Center (MSKCC) since July of 1982. Between July 1, 1982 and July 1, 1996, 1011 patients with a diagnosis of primary extremity soft tissue sarcoma were entered. Within this group, 215 patients with primary superficial soft tissue sarcomas of the extremity were identified. Within this group, 215 patients with primary superficial soft tissue sarcomas of the extremity were identified.

Definitions
All patients presenting to MSKCC for definitive therapy (after no biopsy, or incisional or inadequate excisional biopsy of superficial tumors) were defined as having primary lesions. Event-free survival time was calculated from the date of first admission to MSKCC to the date of first diagnosis of local recurrence, distant metastasis, and death. A local recurrence was defined as the diagnosis of tumor within or contiguous with the previously resected field more than 3 months after primary therapy. Distant metastases were defined as tumor deposits located within distant organs or noncontiguous structures. Confirmed death from disease was used as the endpoint in survival statistics. Deaths from other or unknown causes were considered censored in the analyses.

A superficial sarcoma was defined as a subcutaneous tumor that did not invade the investing fascia of the muscle. Tumor grade (high or low) was determined based on cellularity, differentiation, mitoses per high power field, stromal necrosis, and vascularity (15). Tumor size was determined by greatest diameter on pathologic examination (large is defined as ≥5 cm). Positive margin status was based on pathologic examination revealing gross or microscopic involvement of resection margins with tumor. Stage was reported using the MSKCC staging system proposed by Hajdu (16). In this system, high grade, large size, and deep location are poor prognostic signs, and the patient’s stage is equal to the number of poor prognostic signs (0–3).

Data
Clinical variables analyzed included gender and age at presentation (≤50 or >50 years). Tumor variables analyzed included size (<5 or ≥5 cm), site (upper or lower extremity), location (proximal or distal), grade (low or high), microscopic margins (negative or positive), and histologic subtype of the resected specimen. Treatment variables, including surgery, chemotherapy, brachytherapy, and external beam radiation therapy, were recorded. Because multimodality treatment was administered in a nonrandomized way to a variety of patients within the cohort, we sought to avoid confounding effects on other prognostic variables, and, although these data are reported, we did not include these variables in the survival analyses. Results of an analysis of patients selected for adjuvant therapy can be misleading, because these are often the patients in the poor prognostic groups. In addition, histologic subtype was not included in the analysis of survival because there were insufficient numbers in 10 of the 14 histologic subtypes in this cohort.

Statistics
Univariate analysis was performed using the log rank test. Actuarial survival was calculated using life table method. The χ² test was used for studying categorical associations. Multivariate analysis used the stepwise Cox proportional hazards model. The likelihood ratio χ² test was used to evaluate the significance of the prognostic factors in the final Cox model. Variables representing less than 5% of the total cases were not included in the survival analyses. All estimates of relative risk (RR) were presented with a 95% confidence interval (CI). In all statistical analyses, a p-value <0.05 was considered significant.

RESULTS

Patients
Two hundred fifteen patients with primary extremity superficial soft tissue sarcoma were evaluated. Median follow-up time was 45 months (range 2 days to 151 months). One hundred thirteen (53%) patients were male, with a median age of 46 years (range 16 to 92 years).

Tumor Characteristics
The pathologic characteristics of the 215 superficial sarcomas and their respective univariate and multivariate