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Clinical outcome of deep-seated atypical lipomatous tumor of the extremities with median-term follow-up study

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Abstract

Aims: There is no consensus on the best surgical treatment for deep-seated atypical lipomatous tumor (ALT) of the extremities; furthermore, the appropriate duration for follow-up observation remains unclear. We investigated clinical and functional median-term outcomes in the primary operations for ALT of the extremities in order to find its best treatment methods and observation periods.

Methods: From 1996 to 2009, we diagnosed 41 patients with deep-seated ALT of the extremities. Wide resection was performed on 11 patients and marginal resection was performed on 30 patients. The minimum follow-up was 5 years (median, 8.5; range, 5–17.4). Patients were evaluated for their local recurrence, dedifferentiation, and post-operative function using the ISOLS/MSTS scoring system.

Results: Recurrence and dedifferentiation rates were both 0% for the wide resection group, while the rates were 23% (7/30) and 3% (1/30) for the marginal resection group, respectively. Median duration before recurrence was 7.2 years (range, 4.0–14.2). Local recurrence-free survival rate was significantly higher in the wide resection group ($P = 0.013$). In the marginal resection group, 10% (3/30) of the cases showed residual tumor. The localization of these tumors was all intermuscular. The ISOLS/MSTS scores were 98% (range, 90–100) for wide resection and 99% (range, 93–100) for marginal resection, with no statistical difference ($P = 0.694$). No ALT-related deaths occurred during the observation period.

Conclusions: In addition to long-term (at least 8 years) of continuous observation, a wide resection is necessary in order to prevent recurrence, dedifferentiation, and residual tumor.

Keywords: Atypical lipomatous tumor; Extremities; Surgical method

Introduction

Atypical lipomatous tumor (ALT) is a locally aggressive tumor with low malignant potential that constitutes 40–45%[1] of liposarcoma. Middle-aged patients are most susceptible to ALT, and the tumors do not metastasize without dedifferentiation. However, because ALT usually develops slowly and occurs in deep soft tissue, the tumors can be relatively large by the time they are discovered. Depending on its site of involvement, the prognostic implication of ALT can differ; for example, a total removal in the retroperitoneum and mediastinum is difficult, often resulting in a poor prognosis with multiple relapses that ultimately implicate important internal organs or dedifferentiation.[2–5] Nevertheless, the mortality rate for tumors originating in the extremities is near 0%.

There is no consensus on the best surgical treatment for deep-seated ALT of the extremities, as some recommend a wide resection to place emphasis on definitive therapy,[3,5,6] while others believe marginal resection is sufficient for low-potential malignancy.[7–9] The purpose of this research

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is to evaluate the median-term results of patients with deep-seated ALT of the extremities, provide a comparative study of wide resection and marginal resection, and investigate (1) the best surgical method; and (2) the appropriate duration of follow up observation for deep-seated ALT of the extremities.

Patients and methods

From 1996 to 2009, we diagnosed and treated 59 patients with ALT. The diagnosis included patients with atypical lipoma, well-differentiated liposarcoma (WDLS), and WDLS/ALT using previous classifications. The inclusion criteria were as follows: 1) the site of involvement for the tumor is the extremities and deep-seated; 2) the initial tumor resection was conducted at our institution; and 3) the follow-up period is more than 5 years. For patients with discontinuous observation periods, we contacted patients via phone to ask them for a return visit and consultation. Excluded from this study were six patients with tumors that had originated subcutaneously, seven patients that recurred after resection conducted at other hospitals, and five patients that we were unable to follow-up more than five years. The remaining 41 patients were included in our research. Patients included in our study were examined for their local recurrence rate, dedifferentiation rate, and post-operative functional evaluation, according to the different surgical treatment they received. All patients were examined using magnetic resonance imaging (MRI), and we confirmed the tumor size, site of involvement, and localization. In terms of the final diagnosis of ALT, resected specimens were diagnosed by an experienced pathologist (K.S.). Pathological findings of ALT are derived from mature adipocytes, but difference in size can be conspicuous compared to benign lipomas, in addition to atypia and hyperchromatic nuclei. Furthermore, hyperchromatic nuclei and polynuclear stromal cells are often found in the fibrous septa. A varying number (from many to none) of monovacuolated or multivacuolated lipoblasts can be found.[2] In this study, prepared specimens diagnosed as atypical lipoma, WDLS, and WDLS/ALT were reevaluated to confirm ALT under our criteria.

The surgical methodology was categorized under a wide resection group and marginal resection group. We used the resection margin as defined by Enneking et al.[10] Wide resection was defined as resection able to obtain a wide margin, and marginal resection was defined as resection able to obtain a marginal margin. Surgical methodology differed according to the time period to which the resection took place; wide resection was chosen for a large number of cases from 1996 to 2004, whereas marginal resection was performed for most cases after 2005. Because ALT is an intermediate tumor, reports recommending a more conservative approach began to surface in the literature during the 2000s.[8,9] As a result, after 2005, our institution began to increasingly perform marginal resections. Evaluation of the surgical margin was conducted using resected specimens by two or more experienced orthopedic oncologists and pathologists at the time of surgery. The least margin of the resected specimen was defined as the margin that was obtained by the surgery. Furthermore, in cases that were able to attain a wide resection, we measured the degree to which the normal tissue was attached to the periphery of the tumor.

MRI or CT imaging was conducted 3 months post-operatively. When tumors were confirmed at this point, patients were diagnosed with residual tumor. As a general rule, MRI or CT imaging was conducted once a year after initial imaging examination. Patients were diagnosed with recurrence when a recurrent tumor was confirmed by routine imaging, conducted once a year. In cases that had interruptions during the follow-up period, the period of recurrence was defined as the time patients became self-aware of their tumor before the follow-up examination. We calculated the time to recurrence from the date of operation. Post-operative functional evaluation was performed during the final observation period using the ISOLS/MSTS scoring system described by Enneking.[11] Preoperative scores were used for cases that underwent surgery for recurrence. This score is based on six parameters: pain, function, and emotional acceptance in upper and lower extremities; supports, walking and gait in the lower extremity; and hand position, dexterity and lifting ability in the upper extremity. Each parameter is rated from 0 to 5. All scores were added to obtain the overall function score and expressed as a percentage of a maximum total score of 30. There were no patients who perioperatively received chemotherapy or radiation therapy. This study had ethical approval and all patients gave written informed consent.

For statistical analysis, the correlation between clinical characteristics and surgical methodology were analyzed by Mann–Whitney's U test that evaluated the difference in median and Fisher's exact test that evaluated the difference in ratio. Local recurrence-free survival probabilities were estimated using the Kaplan–Meier method, comparing their results with a log-rank test. The difference in the mean ISOLS/MSTS scores were analyzed using Welch's t-test. Statistical significance was defined as $P < 0.05$. The data analysis software used was IBM SPSS Statistics version 21.

Results

The median age of the 41 patients included in our study was 65 years (range, 32–79), consisting of 20 male patients and 21 female patients. The site of involvement consisted of 36 cases in the lower extremities (thigh, 29; buttock, 5; lower leg, 2) and 5 cases in the upper extremities (upper arm, 2; shoulder, 2; forearm, 1). Localization was intramuscular in 20 cases and intermuscular in 21 cases. The median size of the tumors, measured by their maximum diameter, was 15 cm (range, 6.5–25). Median intraoperative blood