The Impact of Margin Status on the Oncologic Outcomes of Surgically Treated Dedifferentiated Liposarcoma of the Extremities

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INTRODUCTION: Dedifferentiated liposarcoma (DDLPS) is an aggressive variant of liposarcoma that can arise within an atypical lipomatous tumor (ALT). The primary goal of treatment for DDLPS is wide margin resection, but it remains unclear if the low-grade portion surrounding DDLPS also necessitates wide margin resection for optimal local control. We aimed to investigate the importance of surgical marginal location with respect to DDLPS and ALT tumor portions. The peripheral behavior of ALT/DDLPS is rather unique to other sarcomas in its ability to insinuate itself between tissue planes, making the achievement of a truly "wide" margin a difficult if not impossible endeavor in limb salvage surgery.

METHODS: This retrospective institutional cohort study included all patients treated surgically for histologically confirmed DDLPS from 2007 to 2019. Patient and tumor demographics and oncologic outcomes were collected. Exclusion criteria included patients with less than two years of follow up, intraperitoneal / retroperitoneal or head/neck liposarcomas, or age younger than 18 years. Pathology slides were rereviewed by a surgical pathologist specializing in soft-tissue sarcoma. Margin status was categorized into one of the following categories as described by Enneking in the surgical staging system: wide, marginal, and intralesional. These descriptors were applied to both the DDLPS and the ALT portions of the tumor. All patients were determined as either "wide throughout" or "wide on DDLPS, marginal on ALT." Statistical analysis for patient outcome and margin status was carried out using chi-square tests for each patient outcome.

RESULTS: Twenty-two patients underwent oncologic resection for extremity DDLPS. Fourteen (63.6%) patients had surgical margins that were defined as *wide on DDLPS/marginal on ALT*, and 6 (27.3%) patients had surgical margins *wide throughout,* and 2 were unable to be determined (Table 1). The overall rate of local control was 90.9% (20 of 22). Two patients with surgical margins wide on DDLPS/marginal on ALT developed local recurrence compared with no patients with margins wide throughout (p = .53)(Table 2). Six patients with surgical margins wide on DDLPS/marginal on ALT developed metastases compared to 1 patient with margins wide throughout (p = .31).

DISCUSSION AND CONCLUSION: The surgical goal in DDLPS resection, as with other sarcomas, is a wide surgical resection. In this study, wide compared with marginal resection of the surrounding low-grade portion did not appear to influence local recurrence, development of metastatic disease, or death from disease. However, due to this cohort's small size, further investigation and discussion of margin importance is necessary. This study lays the foundation for future larger scale collaborative investigations to further determine the importance of margins in the resection of DDLPS.

Table 1: Patient Demographics and Baseline Characteristics Stratified by Presence or Absence of New Metastasis

	No Metastasis (N=16)	Metastasis (N=6)	Total (N=22)	p value
Age at diagnosis (Mean (SD))	68.12 (12.07)	60.33 (14.69)	66.00 (12.97)	0.217
Sex				0.254
Female	3 (18.8%)	0 (0.0%)	3 (13.6%)	
Male	13 (81.2%)	6 (100.0%)	19 (86.4%)	
Race				0.736
Black/African American	1 (6.2%)	1 (16.7%)	2 (9.1%)	
Multiracial/Multicultural	1 (6.2%)	0 (0.0%)	1 (4.5%)	
Unknown	1 (6.2%)	0 (0.0%)	1 (4.5%)	
White/Caucasian	13 (81.2%)	5 (83.3%)	18 (81.8%)	
BMI (Mean (SD))	28.27 (5.49)	29.43 (10.07)	28.59 (6.78)	0.73
Smoking status				0.146
Current	3 (18.8%)	2 (33.3%)	5 (22.7%)	
No	6 (37.5%)	4 (66.7%)	10 (45.5%)	
Previous Smoker	7 (43.8%)	0 (0.0%)	7 (31.8%)	
Location				0.375
Antecubital Fossa	1 (6.2%)	0 (0.0%)	1 (4.5%)	
Chest Wall	0 (0.0%)	1 (16.7%)	1 (4.5%)	
Femur/Thigh	10 (62.5%)	4 (66.7%)	14 (63.6%)	
Leg (tibia, fibula)	2 (12.5%)	1 (16.7%)	3 (13.6%)	
Shoulder Girdle (scapula, clavicle)	3 (18.8%)	0 (0.0%)	3 (13.6%)	
Extremity				0.122
Lower Extremity	12 (75.0%)	5 (83.3%)	17 (77.3%)	
Trunk/Thoracic/Abdominal Cavity	0 (0.0%)	1 (16.7%)	1 (4.5%)	
Upper Extremity	4 (25.0%)	0 (0.0%)	4 (18.2%)	
Grade				0.41
G1	1 (6.2%)	0 (0.0%)	1 (4.5%)	
G2	7 (43.8%)	1 (16.7%)	8 (36.4%)	
G3	7 (43.8%)	5 (83.3%)	12 (54.5%)	
Unknown	1 (6.2%)	0 (0.0%)	1 (4.5%)	
AJCC stage				0.725
I	2 (12.5%)	0 (0.0%)	2 (9.1%)	
II	4 (25.0%)	2 (33.3%)	6 (27.3%)	
III	9 (56.2%)	4 (66.7%)	13 (59.1%)	
Unknown	1 (6.2%)	0 (0.0%)	1 (4.5%)	
Surgical Margin Description				0.451
Unknown	2 (12.5%)	0 (0.0%)	2 (9.1%)	
Wide on dedifferentiated; marginal on ALT	9 (56.2%)	5 (83.3%)	14 (63.6%)	
Wide throughout	5 (31.2%)	1 (16.7%)	6 (27.3%)	
Local Recurrence	0 (0.0%)	2 (33.3%)	2 (9.1%)	**0.015**
Died of Disease	0 (0.0%)	4 (66.7%)	4 (18.2%)	**< 0.001**
No evidence of disease	15 (93.8%)	0 (0.0%)	15 (68.2%)	**< 0.001**
Alive with Disease	1 (6.2%)	2 (33.3%)	3 (13.6%)	0.099

Table 2: Patient Outcomes Stratified by Surgical Margin

	Wide on dedifferentiated; marginal on ALT (N=14)	Wide throughout (N=6)	Unknown (N=2)	Total (N=22)	p value
Local Recurrence	2 (14.3%)	0 (0.0%)	0 (0.0%)	2 (9.1%)	0.533
Died of Disease	3 (21.4%)	1 (16.7%)	0 (0.0%)	4 (18.2%)	0.758
No Evidence of Disease	8 (57.1%)	5 (83.3%)	2 (100.0%)	15 (68.2%)	0.308
Alive with Disease	3 (21.4%)	0 (0.0%)	0 (0.0%)	3 (13.6%)	0.371
New Metastasis	6 (42.9%)	1 (16.7%)	0 (0.0%)	7 (31.8%)	0.308