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Acral Lentiginous Histologic Subtype and Sentinel Lymph Node Positivity in Thin Melanoma

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Recent analysis of mortality from melanoma has shown that thin melanomas account for 20% and 25% of melanoma deaths in Australia and the United States, respectively, despite an overall survival rate of approximately 95% for patients with these cancers.[1,2] Sentinel lymph node (SLN) biopsy is routinely recommended in patients with intermediate-thickness melanomas, but its role in thin melanomas (≤1 mm) is less well defined[3,4]; moreover, factors predictive of SLN positivity in this latter group have been variably reported. To specifically examine the prognostic significance of histologic subtype of thin melanomas for SLN metastasis, we reanalyzed these lesions in a cohort of patients originally created for a previous study of thin melanomas.[5]

Methods

The cohort for the previous study and the present reanalysis included 781 patients with thin primary cutaneous melanomas who underwent SLN biopsy from February 22, 1995, to June 27, 2011, at our institution. The SLN biopsy was performed for patients with thin melanomas on the basis of an individual patient's melanoma risk factors and comorbidities, discussion of the risks and benefits of the biopsy procedure, and patient preferences.

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Author Contributions: Dr Chu and Mr Marek had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Bartlett, Karakousis, Chu.
Acquisition, analysis, or interpretation of data: All authors.
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Predictors of SLN positivity in the previous study were found through multivariable logistic regression to be mitotic rate (odds ratio [OR], 7.01) and Clark level IV or V (OR, 3.45).[5]

Patient variables analyzed in the previous study were age and sex. Primary tumor characteristics included anatomic site, tumor thickness, Clark level, mitoses, tumor-infiltrating lymphocytes, regression, ulceration, lymphovascular invasion evident in hematoxylin-eosin–stained sections, and microsatellitosis. The following binary variables were used in the analyses: Clark level (II-III and unknown or IV-V), thickness (≤0.75 mm or 0.76–1 mm), tumor-infiltrating lymphocytes (present or absent), and mitoses (present or absent). For lesions in which an individual characteristic was not reported, the characteristic was recorded as unknown. Only patients with known mitotic rate data were included in the regression analyses (n = 698).[5] Histologic subtype was not included in the previous analysis, thus providing the basis for this reanalysis.

This study was approved, with a waiver for patient informed consent, by the Institutional Review Board of the University of Pennsylvania.

Results

In our new prognostic model inclusive of histologic subtype, univariable analysis identified nodular melanoma (OR, 3.80) and acral lentiginous melanoma (ALM) (OR, 8.17) ($P = .01$ for both) as factors significantly associated with SLN positivity. By multivariable logistic regression analysis, ALM remained a factor significantly associated with SLN positivity (OR, 16.02; $P = .004$), as did increased Clark level (OR, 3.04; $P = .02$) and mitotic rate of $1mm^2$ or more (OR, 6.04; $P = .01$). Sentinel lymph node positivity was found in 2 of 10patients (20%)with ALM, 5 of 48 patients (10%)with nodular melanoma, 14 of 534 patients (3%) with superficial spreading melanoma, and none of 37 patients with lentigo maligna melanoma. Of the patients in the group with ALM, 9 of 10(90%)were non-Hispanic white and 1 of 10 (10%) was Hispanic white. Nine of the 10 ALM lesions were found on the foot and 1 ALM lesion was found on the hand. Thickness (OR, 2.22; $P = .09$) and nodular melanoma (OR, 2.48; $P = .09$) showed a trend toward, but did not reach, statistical significance in our model (Table).

Discussion

The reanalysis found that the histologic subtype of ALM as well as mitoses and Clark level IV-V were independent predictors of SLN positivity. This finding is limited, however, by the relatively small number of patients (n = 10) with ALM in the cohort on which the reanalysis was done. The finding of ALM as a predictor of SLN metastasis should be further confirmed in other studies. Although the rate of SLN positivity was low for the study cohort of patients with thin melanomas (3.7%), a subset of patients can be identified with appreciable rates of nodal metastasis, who can be stratified for risk by the Clark level, mitotic rate, and histologic subtype of their melanoma. Further study of these factors can help guide clinical decision-making in patients with thin melanomas.

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Table

Factors Associated With SLN Positivity: Logistic Regression Analysis[a]

	No. (%)		Univariable		Reduced Multivariable	
Characteristic	**Frequency**	**SLN Positivity**	**OR (95% CI)**	***P* Value**	**OR (95% CI)**	***P* Value**
Sex						
Male	389 (55.7)	16 (4.1)	1.28 (0.57–2.87)	.54		
Female	309 (44.3)	10 (3.2)	1 [Reference]			
Anatomic site						
Axial	403 (57.7)	13 (3.2)	0.73 (0.33–1.58)	.42		
Extremity	295 (42.3)	13 (4.4)	1 [Reference]			
Clark level						
II–III and unknown	374 (53.6)	6 (1.6)	1 [Reference]		1 [Reference]	
IV–V	324 (46.4)	20 (6.2)	4.04 (1.60–10.17)	.003	3.04 (1.17–7.84)	.02
Thickness, mm						
0.01–0.75	375 (53.7)	7 (1.9)	1 [Reference]		1 [Reference]	
0.76–1.00	323 (46.3)	19 (5.9)	3.33 (1.40–8.16)	.01	2.22 (0.87–5.65)	.09
Mitoses						
Absent	273 (39.1)	2 (0.7)	1 [Reference]		1 [Reference]	
Present	425 (60.9)	24 (5.6)	8.11 (1.90–34.60)	.005	6.04 (1.34–27.32)	.01
TIL						
Absent	191 (27.4)	7 (3.7)	0.98 (0.40–2.36)	.59		
Present or unknown	507 (72.6)	19 (3.7)	1 [Reference]			

Characteristic	No. (%)		Univariable		Reduced Multivariable	
	Frequency	SLN Positivity	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Regression						
Present	146 (20.9)	4 (2.7)	0.68 (0.23–2.00)	.48		
Absent or unknown	552 (79.1)	22 (4.0)	1 [Reference]			
Ulceration[b]						
Present	27 (3.9)	0				
Absent or unknown	671 (96.1)	26 (3.9)				
NM, ALM, neither NM nor ALM[c]						
ALM	10 (1.4)	2 (20.0)	8.17 (1.62–41.09)	.01	16.02 (2.46–104.15)	.004
NM	48 (6.9)	5 (10.4)	3.80 (1.35–10.67)	.01	2.48 (0.85–7.20)	.09
Neither	640 (91.7)	19 (3.0)	1 [Reference]		1 [Reference]	

Abbreviations: ALM, acral lentiginous melanoma; NM, nodular melanoma; OR, odds ratio; SLN, sentinel lymph node; TIL, tumor-infiltrating lymphocytes.

[a] N = 698. Analysis included only patients for whom the mitotic rate was known.

[b] Ulceration was not present in the tumor of any patient with a positive finding on SLN biopsy and therefore could not be included.

[c] Histologic status was coded as ALM/NM/neither because ALM and NM were significant predictors of SLN positivity in univariable analysis.

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