Acral lentiginous melanoma: Who benefits from sentinel lymph node biopsy?

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Background: There are significant clinicopathological, genetic, and biological differences between acral lentiginous melanoma (ALM) and other types of melanoma.

Objective: We sought to investigate the use of sentinel lymph node (SLN) biopsy for patients with ALM.

Methods: This was a retrospective review of 116 patients with primary ALM. Melanoma-specific and disease-free survival were estimated using the Kaplan-Meier method, together with multivariate analyses using the Cox proportional hazards regression model.

Results: All patients were Japanese (48 male and 68 female). Metastases in SLN were noted in 13 of 84 patients who underwent SLN biopsy. No patients with thin ALM (≤1 mm) and only 2 patients with nonulcerated ALM had tumor-positive SLN. Patients with positive SLN had significantly shorter melanoma-specific survival (5-year survival rate, 37.5% vs 84.3%; $P < .0001$) and disease-free survival (5-year survival, 37.5% vs 77.9%; $P = .0024$). Among patients with thick (>1 mm) ALM, the influence of SLN positivity on melanoma-specific survival was increased (5-year survival, 22.7% vs 80.8%; $P = .0005$).

Limitations: This was a retrospective study and had a small sample size.

Conclusions: SLN biopsy should be considered for patients with thick or ulcerated ALM. For patients with thin or nonulcerated ones, it may be of limited importance. (J Am Acad Dermatol 2015;72:71-7.)

Key words: acral lentiginous melanoma; foot; hand; melanoma; nail; prognosis; sentinel lymph node biopsy.

Since the first introduction by Reed[1] in 1976, acral lentiginous melanoma (ALM) has become recognized as a distinctive histopathological subtype of melanoma. It typically occurs on the palms, soles, and nail beds and is diagnosed by histopathological examination, namely, the presence of atypical melanocytes that proliferate along the dermoepidermal junction in a diffuse lentiginous fashion. Occasional junctional nests and a frequently

Abbreviations used:

AJCC:	American Joint Committee on Cancer
ALM:	acral lentiginous melanoma
CI:	confidence interval
DFS:	disease-free survival
HR:	hazard ratio
MSS:	melanoma-specific survival
SLN:	sentinel lymph node

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hyperplastic epidermis are also observed.[2-4] Among white-skinned populations, ALM is the fourth most common histopathological subtype, accounting for less than 10% of all melanomas,[3,4] but this proportion is markedly increased in darker-skinned populations.[5-7]

Acral melanoma[8] and hand and foot melanoma[9] are specific melanomas named from their anatomical sites without considering the histopathological subtype, and are distinguished from ALM, even though most melanomas at these sites are ALM. ALM has many characteristics that differ from other subtypes: more commonly occurs in older patients, more often presents with a greater Breslow thickness, is less commonly associated with nevi, may be linked to a predisposing genetic defect, more often presents with ulceration, and is not associated with prior sunburns.[10]

CAPSULE SUMMARY

- The use of sentinel lymph node biopsy for acral lentiginous melanoma (ALM) has not been fully elucidated.
- We show that metastasis in sentinel lymph node is an independent prognostic factor for ALM.
- The merit of sentinel lymph node biopsy for thin or nonulcerated ALM may be limited, whereas patients with thick or ulcerated ALM should be considered for it.

Since the first report by Morton et al[11] in 1992, a large number of studies have proven the prognostic value of sentinel lymph node (SLN) biopsy,[12-18] and the American Joint Committee on Cancer (AJCC) has recommended the procedure for patients with certain types of melanoma such as thick (>1 mm) or ulcerated.[19] In contrast, only 1 published study examines the prognostic value of SLN biopsy for patients with ALM.[2] This study, however, only indicates the prognostic value and does not focus on the issue of who should be considered for SLN biopsy. Because there are significant genetic differences between ALM and other types of melanoma,[20,21] the biology of ALM is likely to differ from that of non-ALM, leading to differences in SLN behavior. The aim of this study is thus to investigate the use of SLN biopsy for ALM and elucidate the clinicopathological characteristics of patients with ALM who might benefit from it.

METHODS

Patients

This study is a retrospective review of our patients and was approved by the Institutional Ethics Committee of Kyushu University, Fukuoka, Japan. A total of 116 patients with primary ALM at the Department of Dermatology, Kyushu University, between May 2001 and March 2014, were identified. All lesions were ALM on the hands or feet that fulfilled the above-mentioned criteria by Reed[1] and others.[2-4] Mucosal melanomas having a histopathological lentiginous pattern were excluded. Clinical and demographic data on all patients were retrieved from our prospectively maintained data bank and analyzed. There were 48 male and 68 female patients, with a mean age of 64.5 (range: 16-89) years. We found 33 patients with in situ melanoma, 20 of whom underwent SLN biopsy based on a clinical suspicion of dermal invasion. Melanoma-specific survival (MSS) and disease-free survival (DFS) were calculated from the date of the first histopathological examination to the date of death as a result of melanoma or the date of recurrence. Data on patients without death or recurrence were censored on the date of the last follow-up before March 31, 2014, and data on patients who died of other causes were censored at the time of death. The median follow-up periods were 38 months for MSS and 31 months for DFS. At the last follow-up, 87 patients were alive, 24 had died of melanoma, and 5 had died of other causes. Patients with histopathologically tumor-positive SLN underwent subsequent complete lymph node dissection.

SLN biopsy

SLN biopsy was performed in accordance with the standard procedure described by Cochran et al.[22] Of the 116 patients, SLN biopsy was performed on 84 patients and SLN were successfully identified in all of these. All SLN were stained using hematoxylin-eosin staining and immunohistochemical staining for HMB-45 (Dako, Tokyo, Japan), tyrosinase, MART-1, MITF (Novocastra, Newcastle, United Kingdom), and S-100 protein (Nichirei, Tokyo, Japan). A tumor-positive SLN was defined as one having evidence of metastatic melanoma cells on hematoxylin-eosin staining or immunohistochemistry (the cells having malignant morphological features and positivity for at least 1 melanoma-associated marker), in accordance with the latest classification of the AJCC.[19]

Statistical analysis

All statistical analyses were performed using the SPSS statistical software package (Version 11.0, IBM Corp, Armonk, NY) and the GraphPad Prism statistical software package (Version 5, GraphPad