Table I. Comparison of clinical and flow cytometric features of CTCL cases with the same or different top circulating clone

Features	Same top clone	Different top clone	*P* value	High frequency in skin*	Low frequency in skin*	*P* value
Flow cytometric features						
CD4:CD8 ratio	4.91	2.94	.094	3.76	2.74	.71
$CD4^+CD7^-$, %	**31.6**	**6.37**	**.0066**	15.3	9.6	.39
$CD4^+CD26^-$, %	**43.7**	**7.5**	**.0004**	20.3	12	.60
Clinical features						
Men	4/7 (57)	12/16 (75)	.63	11/18 (61)	5/5 (100)	.272
Age, y	67.86	58.25	.20	60.83	62.4	.94
Stage III/IV, late stage	**6/7**	**3/16**	**.005**	6/18 (33)	3/5 (60)	.343
LDH, U/L	**275**	**188**	**.0091**	223.1	190.6	.13
LDH, >200 U/L	**6/7**	**3/15**	**.007**	8/17 (47)	1/5 (20)	.36
Systemic therapy	6/7	6/16	.069	9/18 (50)	3/5 (60)	1.0
Phototherapy	6/7	10/16	.37	12/18 (67)	4/5 (80)	1.00
Total skin electron beam therapy	0/7	3/16	.53	2/18 (11)	1/5 (20)	.54

Cases are grouped by the presence of the same top clone in both blood and skin and by frequency of the top clone in skin. Values are n/total (%) unless stated otherwise. Statistically significant differences are bolded. Statistical analysis was performed using the rank-sum test and Fisher's exact test (see Supplementary Appendix; available at http://www.jaad.org). Having the same top clone in blood and skin correlates with adverse risk features, whereas increased frequency of the top clone in the skin does not.
CTCL, Cutaneous T-cell lymphoma; *LDH*, lactate dehydrogenase.
*The clone frequency of those in the top 25th percentile was 5%; low frequency was considered <5%.

REFERENCES

1. Scarisbrick JJ, Hodak E, Bagot M, et al. Blood classification and blood response criteria in mycosis fungoides and Sézary syndrome using flow cytometry: recommendations from the EORTC cutaneous lymphoma task force. *Eur J Cancer*. 2018;93:47-56.
2. Agar NS, Wedgeworth E, Crichton S, et al. Survival outcomes and prognostic factors in mycosis fungoides/Sézary syndrome: validation of the revised International Society for Cutaneous Lymphomas/European Organisation for Research and Treatment of Cancer staging proposal. *J Clin Oncol*. 2010;28(31):4730-4739.
3. Beylot-Barry M, Sibaud V, Thiebaut R, et al. Evidence that an identical T cell clone in skin and peripheral blood lymphocytes is an independent prognostic factor in primary cutaneous T cell lymphomas. *J Invest Dermatol*. 2001;117(4):920-926.
4. Masson A De, Malley JTO, Elco CP, et al. High-throughput sequencing of the T cell receptor β gene identifies aggressive early-stage mycosis fungoides. *Sci Transl Med*. 2018;5894(May):1-14.
5. Campbell JJ, Clark RA, Watanabe R, et al. Sézary syndrome and mycosis fungoides arise from distinct T-cell subsets: a biologic rationale for their distinct clinical behaviors. *Blood*. 2012;116(5):767-771.

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Histologic predictors of invasion in partially biopsied lentigo maligna melanoma

To the Editor: Because of its location and frequent large size, the initial diagnosis of LM (lentigo maligna) or LMM (lentigo maligna melanoma) is usually made by an initial partial biopsy rather than excisional biopsy, which, in LMM cases, could be performed in an area without an invasive component. In this study, we aimed to determine the frequency of patients with a final diagnosis of LMM undetected on the partial biopsy and find out pathologic predictors of invasion in LM biopsies.

We selected 118 consecutive cases from 115 patients with a biopsy-proven LM or LMM treated with Mohs or slow Mohs surgery during October 1999-May 2013. The partial biopsy slides of LM cases were compared by 2 dermatopathologists blinded to the final diagnosis (LM or LMM).

Of 100 cases with an initial diagnosis of LM after analysis of partial biopsy, 20% were upstaged to LMM after analysis of debulking specimens. LMM cases diagnosed after partial biopsy specimen analysis had a similar mean Breslow Index to those not diagnosed after partial biopsy (0.53 ± 0.37 mm vs 0.47 ± 0.34 mm, $P = .60$). The sensitivity of the partial biopsy in detecting LMM was 47% (95% confidence interval 31%-64%) and the negative likelihood ratio 0.53 (95% confidence interval 0.39-0.71).

Clinical criteria (age, sex, size, type [primary or recurrent]) were not significantly different between cases of LM and LMM initially diagnosed as LM. However, the multivariate logistic regression analysis revealed that a pagetoid spread of tumor cells and moderate-to-strong dermal inflammation on partial biopsy were significantly and independently associated with the final diagnosis of LMM (Table I).

Table I. Comparison of pathological criteria among cases of LM diagnosed on the partial biopsy specimen according to a final diagnosis of either LM or lentigo maligna melanoma LMM on the debulking specimen

	LM diagnosis on partial biopsy, n = 72*		*P* value			Test quality, value (95% CI)		
Category	LM, n = 53†	LMM, n = 19†	Univariate	Multivariate	OR (95% CI)	Sensitivity	Specificity	Negative-likelihood ratio
Pagetoid spread	14 (26.4)	17 (89.5)	<.001	.046	6.6 (1.1-54.9)	0.89 (0.67-0.99)	0.74 (0.60-0.85)	0.14 (0.04-0.54)
Palisades formation‡	49 (92.5)	19 (100)	.57					
Cytologic atypia	38 (71.7)	19 (100)	.007					
Nuclear pleomorphism	40 (75.5)	18 (94.7)	.09	.59				
Mitosis	14 (26.4)	1 (5.3)	.10					
Multinucleated melanocytes	16 (30.2)	8 (42.1)	.50					
Nests	40 (75.5)	19 (100)	.01	.57				
Confluence	15 (33.3)	14 (73.7)	.007					
Size of largest, mm, mean ± SD	0.2 ± 0.1	0.3 ± 0.2	.90					
Inflammation								
0 (none)	18 (34)	0 (0)						
1 (weak)	31 (58.5)	4 (21.1)						
2 (moderate)	3 (5.7)	10 (52.6)						
3 (strong)	1 (1.9)	5 (26.3)						
0-1 vs 2-3			<.0001	.0013	15.3 (3.2-96.5)	0.79 (0.54-0.94)	0.92 (0.82-0.98)	0.23 (0.10-0.55)

Statistical analysis was performed using R software version 3.2.3 (www.r-project.org, Vienna, Austria).
CI, Confidence interval; *LM*, lentigo maligna; *LMM*, lentigo maligna melanoma; *OR*, odds ratio; *SD*, standard deviation.
*Suitable pathologic material could be recovered from 72 of 100 partial biopsies with an initial diagnosis of LM.
†Diagnosis after debulking specimen analysis; 53 of 80 specimens were diagnosed as LM and 19 of 20 with LMM. Values are n (%) except where indicated.
‡Palisades formation was defined as proliferation of melanocytes along the basal layer in a single-cell lentiginous growth pattern.

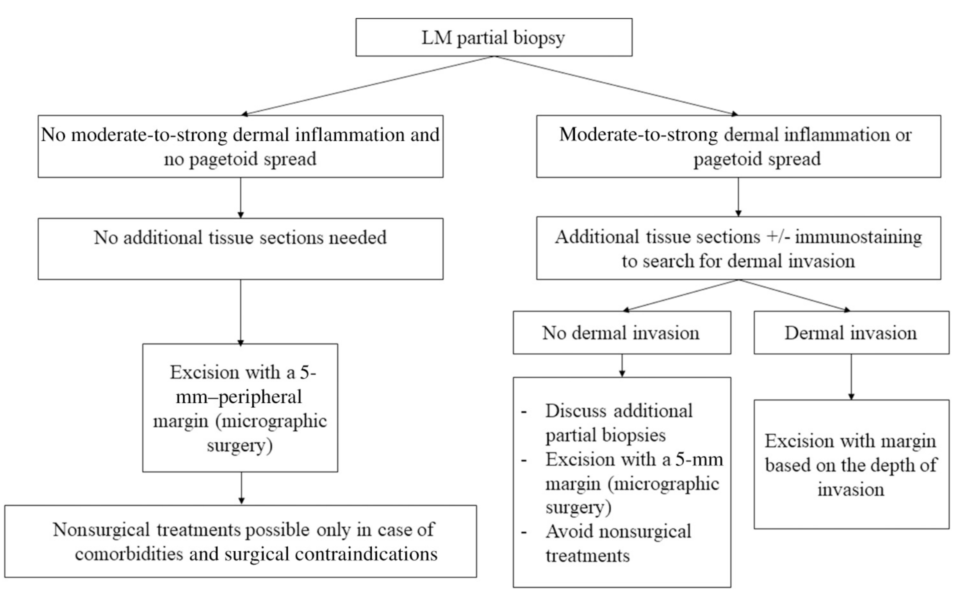

Fig 1. Algorithm for management of LM by presence or absence of histologic predictors of dermal invasion on partial biopsy: moderate-to-strong dermal inflammation and pagetoid spread. *LM*, Lentigo maligna.

In the literature, 3%-22%[1,2] of invasive melanomas were initially considered in situ on partial biopsy specimens. In our study, 90.7% (107/118) of partial biopsies were 3—4-mm punch biopsies, which reduced the surface area analyzed in comparison with the remaining 11 incisional biopsies and increased the risk of missing an invasive component.[3]

Missing an invasion could lead to additional surgical procedures (ie, enlargement of the peripheral margin up to 1-2 cm according to Breslow thickness), resulting in the destruction of the prior wound closure and compromising the implementation of sentinel lymph node biopsy. Moreover, this might also lead to inadvertently treating occult invasive LMM nonsurgically. Alternative treatments to surgery, such as imiquimod (4.2%-50%), radiotherapy, or laser therapy, can represent interesting options for nonoperable patients.[4] But, these techniques are not indicated in cases of LMM and not recommended as first-line therapy for LM in guidelines.

Our study identified 2 independent pathologic predictors of dermal invasion on biopsy specimens of LM: pagetoid spread of tumor cells and presence of moderate-to-strong dermal inflammation. The presence of 1 of these criteria should lead to the performance of an additional hematoxylin-eosin stain or immunostain to search for an invasion[5] or additional biopsies. Of note, we did not take into account regression, which is conceptually defined as an indirect sign of a previous invasion and thus LMM. We propose an algorithm (Fig 1) to optimize LM and LMM management according to the presence of these 2 predictors of invasion.

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REFERENCES

1. Somach SC, Taira JW, Pitha JV, Everett MA. Pigmented lesions in actinically damaged skin. Histopathologic comparison of biopsy and excisional specimens. *Arch Dermatol*. 1996;132(11):1297-1302.
2. Moyer JS, Rudy S, Boonstra PS, et al. Efficacy of staged excision with permanent section margin control for cutaneous head and neck melanoma. *JAMA Dermatol*. 2017;153(3):282-288.
3. Al-Niaimi F, Jury CS, McLaughlin S, Herd RM. Review of management and outcome in 65 patients with lentigo maligna. *Br J Dermatol*. 2009;160(1):211-213.
4. Read T, Noonan C, David M, et al. A systematic review of non-surgical treatments for lentigo maligna. *J Eur Acad Dermatol Venereol*. 2016;30:748-753.
5. Mahoney MH, Joseph M, Temple CL. The perimeter technique for lentigo maligna: an alternative to Mohs micrographic surgery. *J Surg Oncol*. 2005;91(2):120-125.

https://doi.org/10.1016/j.jaad.2018.10.036

Noncultured epidermal suspension grafting using suction blisters as donor tissue for vitiligo

To the Editor: Noncultured epidermal suspension (NCES) transplantation has been performed since 1992 to treat vitiligo, a chronic, autoimmune skin disorder characterized by depigmented macules and patches.[1] A new NCES technique was proposed, which involves forming suction blisters to obtain donor cells, because of the disadvantages of the standard grafting technique, such as the considerable amount of operator training required to harvest viable cells and potential scarring associated with using split-thickness grafts as donor tissue.[2]

We performed a retrospective review of all patients undergoing NCES in the Pigmentary Disorders Clinic at the University of Texas Southwestern Medical Center. Patients were required to have at least 4—6 months of follow-up