SKIN

RESEARCH LETTER

Laterality and Site-Specific Distribution Patterns of Lentigo Maligna and Lentigo Maligna Melanoma

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ABSTRACT

Background: Melanoma has been described to have preferential left-sided laterality on the human body. The distribution and invasion patterns of lentigo maligna (LM) and lentigo maligna melanoma (LMM) have not been well described.

Methods: This was a cross-sectional, retrospective study at a single, academic center. LM and LMM cases from 2008-2018 in the dermatopathology registry were analyzed.

Results: A total of 392 cases were included (241 LM and 151 LMM). There was no laterality preference overall. The only exception were neoplasms located on the head/neck, which showed a left-sided laterality. LM and LMM had the highest incidence on the head/neck, followed by upper extremities, trunk, then lower extremities. Men had a higher incidence on the head/neck and trunk, while women had a higher incidence on the extremities. Interestingly, the upper extremities and the right side of the female body had a higher propensity for invasive lesions.

Conclusion: While melanomas demonstrate preferential left-sided laterality, LM and LMM only share this pattern in respect to the head/neck region. Our results complement previous study findings which characterize LM and LMM as a head/neck and upper extremity pathology. Finally, our study suggests that certain body sites and laterality have an increased propensity for invasion.

Melanoma is known to have left-sided laterality and truncal predominance on the human body.[1] The literature, however, has largely neglected to evaluate separate melanoma subtypes. Specifically, the distribution and invasion patterns of lentigo maligna (LM) and lentigo maligna melanoma (LMM) have not been well described. This retrospective study aims to determine trends in the laterality and anatomical distribution of both LM and LMM. Additionally, given the lack of invasion pattern analysis in previous studies, this trend in LM and LMM will be investigated to determine if certain sites demonstrate increased propensity for malignant invasion.

According to 2016 data produced by the Center for Disease Control and Prevention and the National Cancer Institute, California is the leading state in both new melanoma cases and melanoma-related deaths

nationwide.[2] We chose to focus our study on this high impact patient population.

Table 1. Clinical Characteristics of Histologic Cases of Lentigo Maligna and Lentigo Maligna Melanoma (%, n)

	Men	Women	Total
	63.5%, n=249	36.5%, n=143	n=392
Laterality			
Left	47.8%, 119	51.8%, 74	49.2%, 193
Right	41.0%, 102	41.3%, 59	41.1%, 161
Midline	8.0%, 20	4.2%, 6	6.6%, 26
Not Specified	3.2%, 8	2.8%, 4	3.1%, 12
Biopsy Site			
Head/Neck	58.2%, 145	35.0%, 50	49.7%, 195
Scalp	9.6%, 24	2.8%, 4	7.1%, 28
Face	33.7%, 84	28.7%, 41	31.9%, 125
Ears	5.6%, 14	0.7%, 1	3.8%, 15
Neck	9.2%, 23	2.8%, 4	6.9%, 27
Upper Extremities	20.5%, 51	33.6%, 48	25.3%, 99
Upper Extremities	20.5%, 51	32.2%, 46	24.7%, 97
Hands	0.0%, 0	1.4%, 2	0.5%, 2
Lower Extremities	2.4%, 6	18.2%, 26	8.2%, 32
Lower Extremities	2.4%, 6	18.2%, 26	8.2%, 32
Feet	0.0%, 0	0.0%, 0	0.0%, 0
Buttocks	0.0%, 0	0.0%, 0	0.0%, 0
Trunk	18.9%, 47	13.3%, 19	16.8%, 66
Back of trunk	10.4%, 26	4.2%, 6	8.2%, 32
Front of trunk	8.4%, 21	9.1%, 13	8.7%, 34
Genitalia	0.0%, 0	0.0%, 0	0.0%, 0
Invasion			
LM	63.9%, 159	57.3%, 82	61.5%, 242
LMM	36.1%, 90	42.7%, 61	38.5%, 151

LM = Lentigo Maligna, LMM = Lentigo Maligna Melanoma

For this retrospective, cross-sectional study, the University of California, Irvine Medical Center dermatopathology database was utilized to investigate patterns of lesion distribution of LM and LMM cases from 2008-2018. LM and LMM had an anatomical distribution of 49.7% head/neck, 25.3% upper extremities, 16.8% trunk, and 8.2% lower extremities (Table 1). Men demonstrated a higher incidence on the head/neck and trunk, while women showed a higher incidence on the upper and lower extremities. Interestingly, the upper extremities of women were found to have a higher proportion of invasive cases to superficial cases compared to other body sites (LMM:LM ratio: 1.40 upper extremities vs 0.39 head/neck vs 0.63 lower extremities vs 0.90 trunk, p=0.0226). Men did not share this relationship (p=0.1318).

Similar to previous studies, our study observed a significant left-sided laterality for the head/neck region (59.1% left, p=0.0178) (Table 2).[3] The leading theory for the apparent left-sided distribution of melanoma is attributed to driving. A driver positioned in the left seat is exposed to 20 times the UV radiation on the left side of the face compared to the right.[4] However, this same left sided laterally has been reported in locations such as the UK, where drivers are positioned on the right side of the vehicle.[5] Given this discrepancy, the etiology behind this left-sided laterality is likely more complex than behavioral patterns, and possibly involve complex intrinsic factors. Numerous aspects of embryogenesis are known to occur in an asymmetric fashion.[6] Perhaps asymmetry in neural crest cell migration and distribution may play a role in the sidedness of melanoma. Finally, neither side of the body showed a higher proportion of invasive cases (LMM) (p=0.1115). When analyzing women separately, however, there were significantly more invasive cases on

the right side of the body (LMM:LM ratio 1.36 right vs 0.48 left vs 0.50 midline, p=0.0257).

The observed sex differences in the distribution pattern of LM and LMM support previous studies with similar findings in superficial spreading and nodular melanomas specifically, as well as studies that did not distinguish between subclassifications.[7] This strengthens the evidence that LM and LMM share the same sex-specific site-dependent preferences

Table 2. Distribution of LM and LMM as dependent on site and laterality (%, n)

	Left	Right	Midline	Not Specified
Head and Neck	51.8%, 101	35.9%, 70	7.7%, 15	4.6%, 9
Upper Extremities	45.5%, 45	54.6%, 54	0.0%, 0	0.0%, 0
Lower Extremities	59.4%, 19	40.6%, 13	0.0%, 0	0.0%, 0
Trunk	42.4%, 28	36.4%, 24	16.7%, 11	4.6%, 3

found in other forms of melanoma. The main limitation of this study is that it was a single-institution study, thus limiting the sample size and demographic population. This research would benefit from future multi-institution studies to further confirm the generalizability of these results across demographic populations.

These findings update the current understanding of the anatomical distribution and invasion patterns of LM and LMM and should help increase suspicion of left-sided lesions on the head/neck of the general population, trunk of men, and extremities of women.

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