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REVIEW

Sentinel node studies in truncal melanoma: does an increased number of draining basins correlate with an increased risk of lymph metastasis?

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Abstract

Objectives: To assess whether an association exists between drainage to multiple basins and lymphatic metastasis in patients with truncal melanoma. **Methods:** We retrospectively reviewed 227 patients with primary malignant melanoma between January 2006 and December 2009. All patients received an intradermal injection of ^{99m}Tc-nanocolloid and lymphoscintigraphy followed by sentinel node biopsy. Pre-staging histology with Breslow thickness from excision biopsy was also obtained. **Results:** 82/227 (36%) patients with primary truncal melanoma were identified. Nodal histology was positive for metastatic disease in 27/82 (32.9%) patients. Of these 27, 15 had 1 basin of drainage, 7 had 2 basins of drainage and 5 had 3 basins of drainage. Of the 55 node-negative patients, 35 had 1 basin, 18 had 2 basins and 2 had 3 basins of drainage. We found no significant correlation with sentinel node positivity and those that had $\geq$2 drainage basins. Breslow thickness was available in 65/82(79.2%) patients. Sentinel node biopsy was positive in 6/28 patients who had $<$1.5 mm thickness, 8/14 who had a 1.5–3.9 mm thickness and 9/23 who had $\geq$4 mm thickness. There was a significant correlation between Breslow thickness of $\geq$4 mm and nodal positivity ($P = 0.03$). **Conclusion:** This study demonstrates no association between multiple drainage basins and sentinel node histology. Sentinel lymph node status did correlate with Breslow thickness.

Keywords: *Sentinel node; lymphoscintigraphy; melanoma.*

Introduction

Sentinel node biopsy has become the standard of care for patients with malignant melanoma and is now routine practice in the staging of early melanoma. The pivotal study by Morton et al.[1] showed that the sentinel node study provides significant prognostic information, and is able to identify those patients who should proceed to immediate lymphadenectomy.

The 3 most important prognosticators in all melanoma patients have been shown to be the Breslow tumour thickness, lymph node status and the presence or absence of tumour ulceration[2]. In addition, metastasis to regional lymph nodes has been shown to be the most important prognostic factor for recurrence in early stage melanoma (i.e. in patients with no clinical evidence of lymph node metastases whose regional lymph nodes were staged with a sentinel node study/elective lymphadenectomy)[3].

It is also accepted that patients with truncal melanoma have a worse prognosis[4,5]. Although the reason for this is not clear, it has been postulated that this is due to greater cancer cell mobilization caused by multiple lymphatic tracts[6]. The local observation that patients with truncal melanoma and lymph drainage to multiple basins (MLBD) appeared to have greater risk of lymph node metastasis prompted this retrospective review. The aim of this study thus was to establish whether an association exists between multiple basins and lymphatic metastases in patients with truncal melanoma.

Methods

We retrospectively reviewed all patients with histologically proven malignant melanoma and no palpable lymphadenopathy (i.e. clinically negative lymph nodes) who

underwent a sentinel node study between January 2006 and December 2009.

Lymphatic mapping protocol

All patients received 4×10 MBq intradermal injections of ^{99m}Tc-nanocolloid administered around the biopsy site scar. Dynamic images were acquired and viewed on the p scope for at least 20 min or until visualization of the sentinel node(s). Static images were thereafter captured. Further flood source transmission shadowgram images were obtained. The report and images were available for the surgeon prior to the sentinel lymph node (SLN) biopsy.

Following lymphoscintigraphy, further intraoperative blue dye lymphatic mapping was performed. All patients had a wide local excision of the lesion followed by a sentinel node biopsy. Histopathological examination of the biopsy specimens included analysis by routine haematoxylin and eosin staining, with immunohistochemical staining reserved for those patients with inconclusive results.

Analysis

The number of draining basins identified on the examination was counted and these were correlated with sentinel node histology. Sentinel node histology was also correlated with the staging Breslow thickness. Univariate analysis of MLBD, Breslow thickness, age, sex and site against sentinel node histology was performed using the Fischer exact test.

A multivariate analysis of MLBD, Breslow thickness, age, sex and site was performed on the subset for which complete data were available using a binary logistic regression model. Variables were coded into categories, and a binary multiple logistic regression model was computed using SPSS 17.0 (SPSS Inc.).

Results

82/227 (36%) patients with primary truncal melanoma were identified. The primary site of disease was as follows: abdomen (7), back (59), and chest (16). The mean age of patients was 50 years (range 16–78 years). There were more male (49) than female patients (33).

Number of basins

Sentinel node histology was positive for metastatic disease in 27/82 (32.9%) patients. In these patients, 15/27 had 1 basin of drainage, 7/27 had 2 basins of drainage and 5/27 had 3 basins of drainage. Of the 55 patients with negative SLNs, 35 had 1 basin, 18 had 2 basins and 2 had 3 basins of drainage (Table 1). Overall, 15/50 (30%) patients with single lymphatic basin of drainage (SLBD) and 12/32 (38%) with MLBD had a positive SLN (Fig. 1). An example of a patient with MLBD is shown in Figs. 2 and 3.

Table 1 **Site of the primary melanoma and number of drainage basins on sentinel node study**

	1 basin negative	1 basin positive	2 basins negative	2 basins positive	≥3 basins negative	≥3 basins positive
Abdomen	1	4	1	1	0	0
Back	22	9	16	6	2	4
Chest	12	2	1	0	0	1
Total	35	15	18	7	2	5

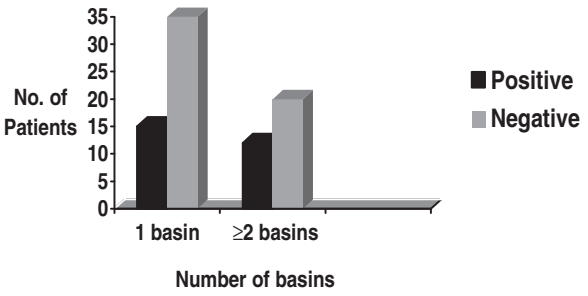

Figure 1 **Number of drainage basins versus sentinel node histology.**

Breslow thickness

Breslow thickness from excision biopsy was available in 65/82 (79.2%) patients. The distribution of Breslow thickness and sentinel node histology is outlined in Table 2. Of those with a positive SLN, 15/51 (29%) had a Breslow thickness of <4 mm and 8/14 (57%) had a Breslow thickness of ≥4 mm.

Factors significantly increasing the risk of SLN metastases

Univariate (Table 3) and multiple logistic regression (Table 4) analyses were performed to determine the risk factors for SLN metastasis. By univariate analysis, the only significant association between SLN metastasis was found in those with tumours with a Breslow thickness ≥4.0 mm ($P = 0.03$; Fisher exact test). This did not quite reach significance on the logistic regression analysis ($P = 0.06$).

Patients with 2 basins of lymphatic drainage did not have an increased risk of lymphatic metastases. In patients with 3 or more basins of drainage, although there was an increased incidence of SLN positivity versus 1 basin of drainage (i.e. 71% vs 30%), this failed to reach statistical significance on either univariate ($P = 0.08$) or regression (odds ratio 7.1; $P = 0.12$) analysis.

There was also no association between the sex, age or site of disease with SLN positivity.

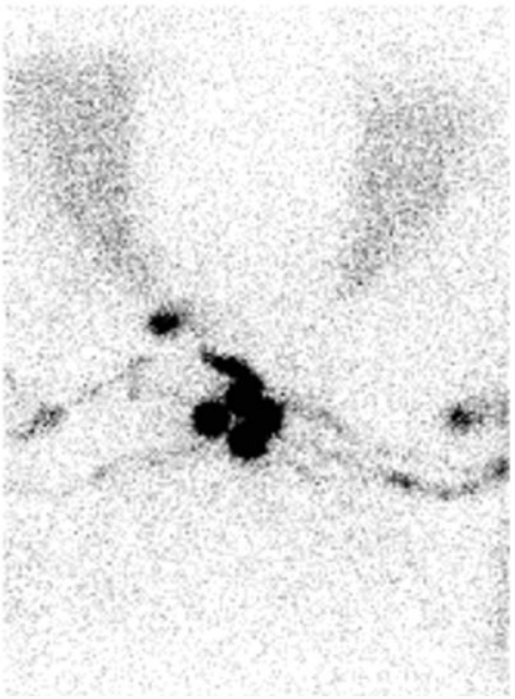

Figure 2 **Posterior dynamic images following injection around the scar of a melanoma on the upper back shows lymphatic channels to both axillae and to the left neck.**

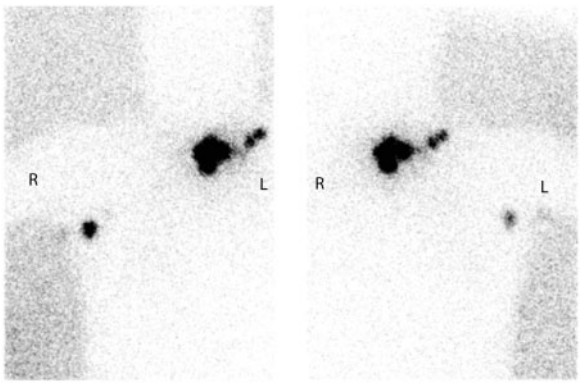

Figure 3 **Anterior delayed images confirmed sentinel nodes in the right and left axillae and in the supraclavicular fossa of the left neck.**

Discussion

It is well established that lymphatic drainage in truncal melanoma is often unpredictable, with the presence of both multiple lymphatic basins as well as interval nodes[7]. Hence lymphoscintigraphic studies are crucial to precisely and confidently map the lymphatic pathway/s in truncal melanoma. The incidence of multiple drainage basins found in our study (39%) is not dissimilar from that reported in the literature (23–36%)[8–11].

Table 2 **Breslow thickness versus sentinel node histology**

Breslow thickness	Positive sentinel node (%)
<1.5 mm	6/28 (21)
1.5–3.9 mm	9/23 (39)
≥4 mm	8/14 (57)

Table 3 **Univariate analysis of associations with positive sentinel node histology**

Factor	Positive SLN (%; $n=82$)	*P*
Age		
≤39 years	24	ns
40–59 years	29	0.77
≥60 years	48	0.12
Sex		
Female	27	ns
Male	37	0.47
Basins involved		
1	30	ns
2	28	1.00
3	71	0.08
Site		
Posterior	32	ns
Anterior	35	1.00
Breslow thickness; incomplete data: $n=65$		
<4.0 mm	29	0.03
≥4.0 mm	57	

ns, not significant.

Table 4 **Multiple logistic regression analysis of association with positive sentinel node histology in a subset of 65 patients for whom Breslow thickness was available**

Factor	Positive SLN (%; $n=65$)	Odds ratio	95% CI	*P*
Age				
≤39 years	24	1	–	ns
40–59 years	29	0.94	0.22–4.03	0.94
≥60 years	48	2.31	0.54–9.95	0.26
Sex				
Female	27	1	–	ns
Male	36	0.93	0.29–2.91	0.90
Basins involved				
1	30	1	–	ns
2	28	0.89	0.24–3.30	0.86
3	71	7.10	0.58–86.21	0.12
Site				
Posterior	32	1	–	ns
Anterior	35	0.98	0.25–3.77	0.97
Breslow thickness				
<4.0 mm	29	1	–	ns
≥4.0 mm	57	3.41	0.95–12.31	0.06

ns, not significant.

A recent study attempting to map lymphatic drainage patterns in melanoma into discrete groups found that truncal melanoma has the highest incidence of drainage to multiple lymphatic basins[11]. Whether this relates to

increased SLN metastases has been debated in the literature.

Only one study[6] has shown an association between MLBD and SLN positivity (30% positive with MLBD vs 16% positive with SLBD; $P = 0.03$). However, several studies have not replicated these results, finding no association between SLN metastasis and MLBD[9,10,12].

It has been postulated that there is a risk of increased SLN positivity in MLBD due to tumour blocking existing lymph channels and collateral lymphatics may then form[13]. Indeed at our institute we have observed on occasion that the lymphatic drainage to a contralateral node may be negative, but that the ipsilateral less active lymph node may be positive. This anecdotal finding prompted this retrospective review.

Retrospective multivariate analysis of our results did show a non-significant trend between MLBD and SLN positivity, with an odds ratio of 7 (95% confidence interval (CI) 0.95–12.31) for SLN positivity between 3 basins and 1 basin. Although not significant, this may reflect the small number of cases that had 3 draining basins, and further studies may be needed to clarify this association.

In addition to increased SLN positivity, it has been suggested (although not conclusively proven) that MLBD may lead to a worse prognosis, both in terms of locoregional recurrence and overall survival. The Sunbelt melanoma trial[12] found that no increased risk of locoregional recurrence or in overall mortality in patients with MLBD. In contrast, Jiminez et al.[8] found that patients with MLBD had a worse prognosis, independent of SLN status. Dale et al.[14] also showed that overall survival was reduced in patients with dual basin involvement versus single basin involvement (median overall survival of 33 vs 56 months). A further interesting study by Wall et al.[15] found that multiple lymphatic channels to a single basin were an independent risk factor for locoregional recurrence as well as increased mortality.

Thus, it is probably prudent in patients with MLBD or multiple lymphatic channels to institute a close follow-up regime to monitor for disease recurrence, even if the initial sentinel node histology is negative.

Conclusion

The presence of MLBD is not unusual in truncal melanoma. In our experience, drainage to multiple drains was not associated with an increased risk of sentinel node metastases. Long-term follow-up of these patients may be useful to determine the prognostic significance of multiple drainage basins.

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