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The Role of Sentinel Lymph Node Biopsy in Thin Melanoma (Breslow Thickness ≤ 0.75 mm and 0.76 mm - 1.0 mm Respectively): Our Results and Review of the Literature

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Abstract

Introduction: The Sentinel Lymph Node Biopsy (SLNB) in melanoma is an important tool of staging. The impact on overall survival still remains unclear. The guidelines in regard to depth, taking in mind where SLNB staging benefits do not outweigh the risks of the procedure, are constantly reviewed and modified. Patients and Methods: From 2010 to 2015, 104 patients with thin melanoma Stage IA with presence of adverse or high risk features and from IB only TIb, N0, M0 (American Joint Committee on Cancer, AJCC Melanoma Staging and Classification 7th Edition 2009) were included and divided into 2 groups: Group A: 68 patients with Breslow ≤ 0.75 mm and Group B: 36 patients with Breslow 0.76 - 1.0 mm. Initially all patients underwent excision of the primary site and subsequently wide local excision and SLNB. We analyzed the histopathology reports of SLNB procedures in both groups. Results: There was no positive SLN in group A (0%). 4 patients from group B had positive SLN (11.1%) and underwent Completion Lymph Node Dissection (CLND). The total percentage of positive SLNs from both groups was 3.8%. Conclusions: Our findings justify the SLNB procedure in thin melanomas of 0.76 - 1.0 mm. In melanomas ≤ 0.75 mm, SLNB should be considered on an individual basis when "high-risk features" are present. More comparable studies should be evaluated in order to accurately define the threshold value of Breslow thickness where SLNB is safely deemed unnecessary.

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Keywords

Thin Melanoma, SLN, SLNB

1. Introduction

The Sentinel Lymph Node Biopsy (SLNB) in melanoma is an important tool of staging. AJCC [1] and National Comprehensive Cancer Network (NCCN) [2]-[4] guidelines describe the factors that affect staging. However these are constantly reviewed and modified. Ulceration and mitotic rate are considered as factors that affect the staging of thin melanoma (AJCC T1a to T1b). Until 2013, the NCCN 2011 [2] guidelines recommended the following factors as "adverse features": Breslow ≥ 0.75 mm, positive deep margins, Lymphovascular Invasion (LVI), and Clark level IV. From 2013, the NCCN 2013 [3] and NCCN 2016 [4] guidelines for SLNB with Breslow up to 1 mm take into account the "high-risk features": Ulceration, High mitotic rate and Lymphovascular Invasion (LVI). The purpose of this study is to evaluate the role of SLNB in thin melanomas, with Breslow thickness ≤ 0.75 mm and 0.76 - 1.0 mm respectively.

2. Patients and Methods

From 2010 to 2015, 104 patients with thin melanoma Stage IA with presence of "adverse" or "high-risk features" and from Stage IB only TIb, N0, M0 (AJCC) were included and divided in 2 groups:

- Group A: 68 patients with Breslow ≤ 0.75 mm.
- Group B: 36 patients with Breslow 0.76 - 1.0 mm.

All patients had signed the appropriate consent form and assured that the ethical and moral issues were respected. Initially all patients underwent excision of the primary site and the histopathology report confirmed the presence of melanoma as well as the important associated histopathologic features. Subsequently the patients underwent wide local excision and SLNB under general anesthesia preferably, or even local anesthesia in some cases, if the SLNB concerned the groin or axillary area. At the day of surgery all patients underwent lymphoscintigraphy and the position of SLN was found with the γ-camera and marked at the skin. At the operating room we injected the patent blue at the pre-existing scar intradermally for lymphatic mapping. Intraoperatively we used the gamma probe in order to find the SLN, which was dyed blue in most of the cases. Then we excised the SLN and sent it to histopathology department.

We retrospectively reviewed and analyzed the histopathology reports of SLNB procedures in both groups. Demographic characteristics (Gender and Age) are shown in **Table 1**.

3. Results

In Group A, there was no positive SLN (0/68 patients with positive SLN 0%).

In Group B, 4 out of 36 (4/36) patients were found with positive SLN (11.1%) and underwent completion lymph node dissection (CLND).

In both Groups, 4 out of 104 (4/104) patients had positive SLN (3.8%) (**Table 2**).

The accuracy and the true positive rate of SLNB in the detection of thin melanomas were estimated by measuring the Sensitivity and the Positive Predictive Value. All of our positive cases (100%) were true positives (TP) and therefore we had no false positive (FP) results (0%).

The sensitivity was measured using the formula:

Table 1. Demographic characteristics of 104 patients.

	Male		Female		Total	
Gender	47 (45.2%)		57 (54.8%)		104	
	≤30	31 - 49	41 - 50	51 - 60	61 - 70	>70
Age	5 (4.8%)	19 (18.3%)	22 (21.2%)	21 (20.2%)	20 (19.2%)	17 (16.3%)

Table 2. Positive sentinel lymph nodes results in relation to depth of primary thin melanoma in our department.

	Group A	Group B	Total
Breslow Thickness	≤0.75 mm	0.76 - 1.0 mm	<1.0 mm
No of Patients	68	36	104
Positive SLN	0	4	4
Percentage	0%	11.1%	3.8%

$$\text{Sensitivity} = \text{TP}/(\text{TP}+\text{FN})\times 100 \quad \text{(FN: False Negative)}$$

Therefore the Sensitivity was 100%.

The Positive Predicting Value (PPV) was measured using the formula:

$$\text{PPV} = \text{TP}/(\text{TP}+\text{FP})\times 100$$

Therefore the PPV was also 100%.

As such in our study the true positive rate of SLNB was 100%.

The demographic and clinical data as well as the histopathologic features of the patients with thin melanoma and positive SLNs are described in **Table 3**. Furthermore the CLND histopathology report of the patient 2 revealed 1 positive lymph node.

4. Discussion

Sentinel Lymph Node Biopsy (SLNB) in melanoma is an important tool of staging. The impact on overall survival still remains unclear. The guidelines in regard to Breslow thickness, taking in mind where SLNB staging benefits do not outweigh the risks of the procedure, are constantly reviewed and modified. Factors associated with increased incidence of positive SLNs in melanoma patients have been thoroughly studied and reported in the literature and include tumor thickness [5]-[24], ulceration [16]-[22], mitotic rate [7] [16] [19] [23] [24], lymphovascular invasion [16] [20], Clark level [18] [21], microsatellites [16], presence of vertical growth phase [5], anatomical location [22] and age [6] [17] [21]-[24].

Currently the NCCN recommendations for SLNB in melanomas with Breslow thickness ≤ 1 mm, apart from the primary tumour thickness take into account the "high-risk features": Ulceration, High Mitotic Rate and Lymphovascular Invasion. Microsatellitosis when present in the initial biopsy or wide excision specimen defines at least N2c and at least Stage IIIB disease [3] [4]. From 2013 the NCCN guidelines divide further the Stage IA and Stage IB in to two more subcategories considering as threshold value the Breslow thickness of 0.75 mm and recommend that melanoma patients with Breslow thickness ≤ 0.75 mm with any features should be considered for wide excision. This recommendation is followed by the footnote: "*In general, SLNB is not recommended for primary melanomas* ≤ 0.75 *mm thick, unless there is significant uncertainty about the adequacy of microstaging. For melanomas* 0.76 *to* 1.0 *mm thick, SLNB may be considered in the appropriate clinical context. In patients with thin melanomas* (≤1.0 *mm*), *apart from primary tumor thickness, there is little consensus as to what should be considered* '*high-risk features*' *for a positive SLN. Conventional risk factors for a positive SLN, such as ulceration, high mitotic rate, and lymphovascular invasion* (*LVI*), *are very uncommon in melanomas* ≤ 0.75 *mm thick. When present, SLNB may be considered on an individual basis*" [3] [4].

In our study (**Table 1**) there was no positive SLN in any patient of the ≤0.75 mm group (group A). Same results in the ≤0.75 mm group (group A) were also reported in the literature by Wong *et al.* 2006 [8], Vermeeren *et al.* 2009 [11] and Hinz *et al.* 2012 [13] (**Table 4**). However other studies by Bedrosian *et al.* 2000 [5], Bleicher *et al.* 2003 [6], Kesmodel *et al.* 2005 [7], Ranieri *et al.* 2006 [9], Wright *et al.* 2008 [10], Murali *et al.* 2012 [12] and Han *et al.* 2012 [14] reported positive SLN in the ≤0.75 mm group (group A), ranging from 1.7% to 6% (**Table 4**). In our study (**Table 1**) in the 0.76 - 1.00 mm group (group B) the percentage of positive SLNs was 11.1%, whereas in the above-mentioned studies [5]-[14] it was ranging from 3.9% to 12.8%. Because of the existence of the above studies with positive SLNs in the Breslow thickness ≤ 0.75 mm group (group A), the SLNB procedure in melanoma patients with Breslow thickness ≤ 0.75 mm should be considered on an individual basis when "high-risk features" are present.

Table 3. Demographic and clinical data and features of histopathology results of the patients with primary thin melanoma and positive sentinel lymph node.

	Patient 1	Patient 2	Patient 3	Patient 4
Breslow Thickness	1.0 mm	0.9 mm	0.85 mm	0.99 mm
Gender	Female	Female	Male	Male
Age	33	22	67	52
Tumour Site	Left Thigh	Right Thigh	Back	Back
Histological Type	SSM	NM	SSM	SSM
Level of Invasion (Clark Level)	III	IV	III	III
Growth Phase	Vertical/Radial	Vertical	Vertical/Radial	Vertical/Radial
Mitotic Rate	<6/mm^2	10/mm^2	4/mm^2	1/mm^2
Tumor Infiltrating Lymphocytes	Yes (Brisk)	Yes (Brisk)	Yes (Non Brisk)	Yes (Brisk)
Regression	No	No	No	(Yes 15%)
Ulceration	Yes (M.D 2 mm)	No	No	No
Satellite Lesions	No	Non-evaluable	No	No
Vascular Invasion	No	No	No	No
Neural Invasion	No	No	No	No
Margin	Free	Free	Free	Free

[a]SSM: Superficial Spreading Melanoma; [b]NM: Nodular Melanoma; [c]M.D: Maximum Diameter.

Table 4. Studies with positive SLN in patients with thin melanoma.

Authors	Year	Positive SLN ≤ 0.75 mm		Positive SLN 0.76 - 1.0 mm	
Bedrosian *et al.* [5]	2000	1/40	2.5%	3/31	9.7%
Bleicher *et al.* [6]	2003	2/118	1.7%	6/154	3.9%
Kesmodel *et al.* [7]	2005	1/91	1.1%	8/90	8.9%
Wong *et al.* [8]	2006	0/109	0%	8/114	7.0%
Ranieri *et al.* [9]	2006	2/86	2.3%	10/98	10.2%
Wright *et al.* [10]	2008	16/372	4.3%	15/259	5.8%
Vermeeren *et al.* [11]	2010	0/39	0%	5/39	12.8%
Murali *et al.* [12]	2012	3/113	2.7%	26/290	9.0%
Hinz *et al.* [13]	2012	0/12	0%	5/109	4.6%
Han *et al.* [14]	2012	2/33	6.0%	20/238	8.4%
Total		27/1013	2.7%	106/1422	7.7%

5. Conclusion

Our findings justify the SLNB procedure in thin melanomas of 0.76 - 1.0 mm. In melanomas ≤ 0.75 mm, SLNB should be considered on an individual basis when “high-risk features” are present. More comparable studies should be evaluated in order to accurately define the threshold value of Breslow thickness where SLNB is safely deemed unnecessary.

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