Mitotic rate as predictive factor for positive sentinel lymph node in pT1 and pT2 melanomas

Cristian FIDANZI[1], Matteo BEVILACQUA[1], Angelo Massimiliano D'ERME[2], Flavia MANZO MARGIOTTA[1], Riccardo MORGANTI[3], Paolo VIACAVA[4], Giovanni BAGNONI[2], Agata JANOWSKA[1].

[1] *Unit of Dermatology, University of Pisa, Pisa, Italy.*
[2] *Melanoma and Skin Cancer Unit AVNO (Area Vasta Nord Ovest) and Unit of Dermatology, Livorno Hospital, Livorno, Italy.*
[3] *Statistical Support to Clinical Trials Department, University of Pisa, Pisa, Italy.*
[4] *Unit of Pathology, Hospital of Livorno, Livorno, Italy.*

Corresponding author: Cristian Fidanzi, MD, cri.fidanzi@outlook.it

Introduction

Sentinel lymph node biopsy is a crucial step in the management of patients affected by melanoma. The decision whether to perform it or not is based on different histological parameters but the mitotic rate is no more considered a prognostic variable after the release of the 8th edition of the American Joint Committee on Cancer (AJCC) guidelines[1].

Our objective was to investigate the risk factors that augment the chance for sentinel lymph node positivity in melanomas with a Breslow thickness less than 2,00 mm including the mitotic count. A retrospective monocentric study was performed on a homogenous cohort of 408 patients treated for cutaneous melanoma. Histological and clinical features were gathered and correlated with the increased risk for sentinel lymph node positivity by means of univariate and multivariate analyses.

A statistically significant correlation between high mitotic index and positive sentinel lymph node was found in pT1 and pT2 patients suggesting that in the case of pT1a melanoma with high number of mitoses a discussion whether a sentinel lymph node biopsy is required should be done.

Materials and Methods

We carried out a retrospective monocentric study on a homogenous cohort of patients affected by cutaneous melanoma that were diagnosed between the years 2006 and 2016 in Livorno, a city with an high incidence of melanoma[2]. All pathology reports that included the word melanoma were identified through a pathology database of the hospital of Livorno. A total of 408 cases were identified taking into account the histological and clinical features of these melanomas and SLN positivity. Univariate and multivariate analyses by logistical regression on the correlation between SLN positivity and high-risk features such as Breslow thickness, Clark level, ulceration, regression, lymphovascular invasion, infiltrating lymphocytes, perineural invasion and mitotic rate were performed. The following data were extracted as well: age, gender, site, staging, cell type and presence of pigmented cells.

Multivariate analyses stratifying for the lesion thickness were also performed in order to see if the high-risk features could impact the SLN positivity based on the melanoma stage. The primary outcome of the study was to evaluate if the number of mitoses increased the risk of a positive SLNB in pT1 and pT2 melanomas. Secondary outcomes included whether other high-risk features were strongly associated with SLN positivity in all types melanomas.

Results

Univariate and multivariate analyses for the different variables registered were performed for significant predictors of SLN positivity both in all cases and only in pT1 and pT2 patients. Results in Table IV shows that multivariate study for all melanomas showed a statistically significant correlation between Breslow depth, T stage, perineural invasion, regression areas and a positive sentinel lymph node as expected. When analyzing the presence of mitoses per mm^2 though, it was a positive predictive factor for SLN only in pT1 and pT2 cases. Interesting enough, ulceration did not show a statistically significant correlation with SLN positivity when we considered every melanoma case and when we considered only melanomas with a thickness lower than 2mm.

Table IV. Multivariate analysis of the "N+ sentinel node" predictive factors. RC: regression coefficient

Dependent variable: N+ sentinel node [(0) N0, (1) N+]	RC	OR	95% CI		p-value
Factor			Lower	Upper	
Ulceration: (0) absence, (1) presence	-0.153	0.858	0.410	1.798	0.686
Regression: (0) absence, (1) presence	-0.933	0.394	0.111	1.391	0.148
Perilesional lymphoid infiltrates: (0) absence, (1) presence	-0.233	0.792	0.382	1.642	0.531
Perineural vascular invasion: (0) absence, (1) presence	0.795	2.215	0.765	6.411	0.143
T Stage (continuous)	0.683	1.981	1.341	2.925	0.001
Breslow thickness	0.175	1.192	0.999	1.421	0.051
Clark level	-0.206	0.814	0.480	1.382	0.446
Mitoses per mm2	-0.038	0.963	0.875	1.060	0.440
Constant	-3.566	0.028			0.001

Table V. Multivariate analysis* of the "N+ sentinel node" predictive factors (only pT1/pT2 patients). RC: regression coefficient

Dependent variable: N+ sentinel node [(0) N0, (1) N+]	RC	OR	95% CI		p-value
Factor			Lower	Upper	
perineural vascular invasion: (0) absence, (1) presence	4.016	55.481	5.359	>100	0.001
Mitoses per mm2	0.166	1.181	1.015	1.374	0.031
Constant	-3.080	0.046			<0,001
Ulceration					0.227
Breslow thickness					0.105
**Step-wise method was used*					

Discussion

Our study shows how the mitotic count is a relevant prognostic factor for SLN positivity in patients with pT1 and pT2 melanoma which brings about some controversy regarding the latest AJCC guidelines which no longer divides patients in pT1a and pT1b according to the mitotic index[1]. This is a crucial point for the management of these patients since a pT1b stage is an indication for SLNB and the probability of its positivity ranges from 5% to 10%[3]. Furthermore, a positive sentinel lymph node is associated with a worse prognosis and these patients may benefit from adjuvant therapy and/or vigilant follow-up. The present study corroborates the relevance of Breslow depth, T stage, regression, perineural and vascular invasion as positive predictive factors for SLN positivity. It also shows the higher chances of a positive SLN in patients with thin melanomas and a mitotic index > 2 mitosis/mm^2 even though there are some controversial data regarding this matter in the current literature[4].

References

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