CASE REPORT

The importance of mitosis as a factor for predicting sentinel lymph node biopsy for thin melanoma *

Mitose como fator prognóstico para biópsia de linfonodo sentinela em melanoma fino

Renato Santos de Oliveira Filho[1]
Daniel Arcuschin de Oliveira[3]
Maria do Carmo Assunção Queiroz[5]
Mayra Calil Jorge[2]
Renato Leão de Oliveira[4]
Fábio Xerfan Nahas[6]

Abstract: 23-year-old female patient, with superficial spreading melanoma (SSM) on the back, Breslow 0.35 mm, Clark II, without ulceration and with 2 mitosis/mm². Patient was submitted to margin enlargement and sentinel biopsy of 2 lymph nodes (left armpit). Histopathology revealed micrometastasis in the subcapsular sinus of both. Following the recommendation of the 2009 *American Joint Committee on Cancer Melanoma Staging* (AJCC), the patient underwent complete axillary lymphadenectomy. No other lymph nodes were metastatic. The clinical application of dermoscopy has enabled more accurate diagnosis of cutaneous melanoma, probably contributing to a greater proportion of thin melanomas at diagnosis. The mitotic rate was included as an important prognostic factor for thin melanomas by the AJCC, suggesting biopsy for these patients.
Keywords: Lymphatic metastasis; Melanoma; Mitosis; Neoplasms; Sentinel lymph node biopsy.

Resumo: Paciente, sexo feminino, 23 anos, com melanoma extensivo superficial em dorso, Breslow 0,35 mm, Clark II, sem ulcerações e com 2 mitoses / mm². Foi submetida à ampliação de margem e biópsia de dois linfonodos sentinela (axila esquerda). O exame anatomopatológico mostrou micrometástases, no seio subcapsular de ambos. Seguindo a recomendação do "*American Joint Commitee on Cancer*" 2009, a paciente foi submetida à linfadenectomia axilar total, sem outros linfonodos metastáticos. A aplicação da dermatoscopia vem permitindo maior precisão diagnóstica de melanoma cutâneo, contribuindo para maior proporção de melanoma fino ao diagnóstico. A taxa mitótica foi incluída como um importante fator prognóstico para melanomas finos pelo "*American Joint Commitee on Cancer*" 2009, sugerindo biópsia para esses pacientes.
Palavras-chave: Biópsia de linfonodo sentinela; Melanoma; Metástase linfática; Mitose; Neoplasias

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[1] Ph.D. in Medicine awarded by the University of São Paulo Faculty of Medicine (FMUSP); Oncology Surgeon, Hospital Israelita Albert Einstein, São Paulo, Brazil.
[2] Medical Student, Botucatu Faculty of Medicine, Universidade Estadual Paulista "Julio de Mesquita Filho" (UNESP), São Paulo, Brazil.
[3] Medical Student at Anhembi Morumbi University, São Paulo, Brazil.
[4] Surgery Resident-MEC-Santa Casa de Misericordia de Votuporanga, São Paulo, Brazil.
[5] Ph.D. in Medicine awarded by the University of São Paulo Faculty of Medicine (FMUSP); Pathologist in the Pathology Anatomy Laboratory, LOCUS Laboratory, São Paulo, Brazil.
[6] Plastic Surgeon, Senior Professor at the Federal University of São Paulo (UNIFESP), São Paulo, Brazil.

INTRODUCTION

The incidence of melanoma is increasing worldwide and the proportion of thin melanoma (Breslow thickness ≤ 1 mm) at diagnosis is significant. [1,2] Sentinel lymph node biopsy has proved to be an accurate approach for regional lymph node staging with minimal morbidity, and has been adopted by the 2009 *American Joint Committee on Cancer Melanoma Staging (AJCCMS)*. The lymph node status is the most important prognostic factor for melanoma. [3,4] The sentinel lymph node biopsy was developed to identify the 20% of patients with primary intermediate thickness melanoma (0.76mm - 4 mm) who have lymph node metastases. [3] It is known that a small proportion (less than 10%) of melanoma patients with thin melanoma at diagnosis, develop lymph node metastases. [1,5,6,7] Given the increasing number of patients with thin melanoma diagnosis, there is substantial interest in detecting high risk prognostic factors for lymph node metastases. It follows that it will be of great interest to select a subgroup in which sentinel lymph node biopsy may be helpful. According to the 2009 AJCCMS, the presence of mitosis greater than or equal to 1/mm^2 in the primary tumor T1 classifies melanomas as T1b. These patients should undergo sentinel node biopsy. In a recent meta-analysis, three studies analyzed melanomas with a mitotic rate greater than or equal to 1/mm^2. In this study 588 cases were analyzed, of which 350 cases had a mitotic rate of ≥ 1/ mm^2. Of the latter, 24 had a positive sentinel lymph node. 238 cases revealed no mitoses and five had a positive sentinel lymph node (OR: 2.91, CI: 95% [1.12 to 7.55]; 68% I2). [1,8,9] The present clinical case report draws attention to the importance of mitotic rate as a prognostic factor for patients with melanoma.

CASE REPORT

23-year-old female patient presented with superficial spreading melanoma on the back at the radial growth phase, Breslow 0.35 mm, Clark II, no ulcerations, no regression areas and 2 mitoses/mm ^{2} (Figure 1). The anatopathological examination revealed moderate intratumoral and peritumoral lymphocytic infiltration, without angiolymphatic or perineural invasion or satellitosis and with tumor-free surgical margins (Figure 2). Immunohistochemistry of the primary tumor was not done. Physical examination revealed several dysplastic nevi on the trunk and a scar on the back where an excisional biopsy of the melanoma had been made. The patient´s mother had had melanoma. The patient was being monitored (with regular dermoscopy) by a dermatologist in view of the presence of multiple dysplastic nevi. Patient was asymptomatic.

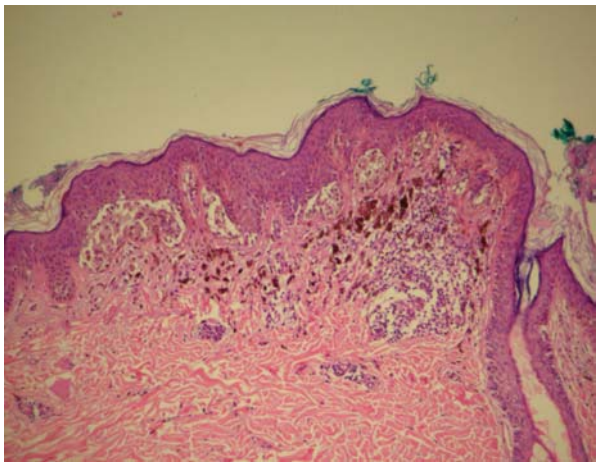

Figure 1: Nest of melanocytic cells and asymmetrical lymphocytic infiltrate

Given that abdominal ultrasound, chest radiography and serum LDH were normal, she was classified as pT1bNxMo. The patient was submitted to amplification of the margins and sentinel node biopsy. The preoperative lymphoscintigraphy showed two lymph nodes in the left axillary region, both of which were removed. Although the conventional anatopathological examination with HE showed no presence of cancer, the immunohistochemical survey however revealed micrometastases in both sentinel lymph nodes for antigens Melan A and S100 Protein. The micrometastases were found within the subcortical sinus, measuring 1.0 mm and 0.2 mm in the lymph nodes (Figure 3). The patient then underwent total axillary dissection, with no involvement of any other node among the 18 removed. PET-SCAN was normal and the patient is now on interferon immunotherapy.

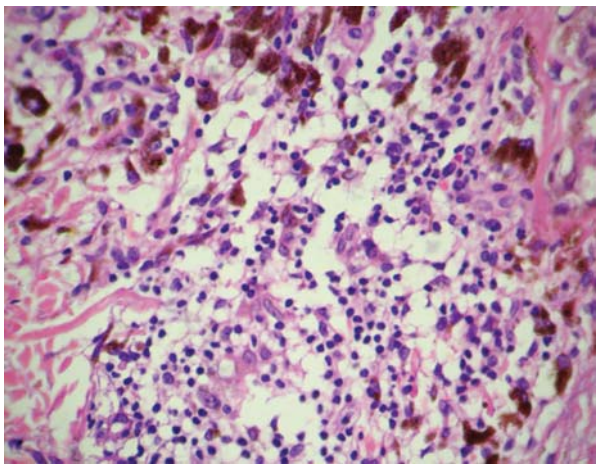

Figure 2: Invasion of melanocytic cells with lymphocytic infiltrate

Figure 3: Micrometastasis in subcortical sinus of sentinel lymph node

DISCUSSION

The incidence of melanoma is increasing worldwide. [2,10] Thin melanomas represent a significant proportion of new cases of melanoma. The clinical application of dermoscopy has enabled greater diagnostic accuracy for cutaneous melanoma, probably contributing to a greater proportion of thin melanomas detected at diagnosis. Although it has not yet been definitively established which patients should undergo sentinel lymph node biopsy, the 2009 American Joint Commitee on Cancer Melanoma Staging includes mitosis as an important prognostic risk factor for thin melanomas, suggesting sentinel node biopsy for patients in this condition. [11,12] Positive biopsy moves these patients up to stage III. Published data suggest that a biopsy combined with immediate lymphadenectomy may improve overall disease-free survival rates. [13] Mitosis in primary melanoma identifies patients with a high risk of recurrence, as can be clearly observed in the case described above. ❑

REFERENCES

1. Silva FB, Oliveira Filho RS, Iared W, Atallah AN, Santos IDAO, Ferreira LM. Indications of sentinel node biopsy in thin melanoma. Einstein. 2010;8:235-40.
2. Nasser N. UVB: suscetibilidade no melanoma maligno. An Bras Dermatol. 2010;85:843-8.
3. Morton DL, Thompson JF, Cochran AJ, Mozzillo N, Elashoff R, Essner R, et al. Sentinel-node biopsy or nodal observation in melanoma. N Engl J Med. 2006;355:1307-17.
4. Oliveira Filho RS, Ferreira LM, Biasi LJ, Enokihara MM, Paiva GR, Wagner J. Vertical growth phase and positive in thin melanoma. Braz J Med Biol Res. 2003;36:347-50.
5. Ranieri JM, Wagner JD, Wenck S, Johnson CS, Coleman JJ 3rd. The prognostic importance of sentinel lymph node biopsy in thin melanoma. Ann Surg Oncol. 2006;13:927-32.
6. Guitart J, Lowe L, Piepkorn M, Prieto VG, Rabkin MS, Ronan SG, et al. Histological characteristics of metastasizing thin melanomas: a case-control study of 43 cases. Arch Dermatol. 2002;138:603-8.
7. Thompson JF, Shaw HM. Is sentinel lymph node biopsy appropriate in patients with thin melanomas: too early to tell? Ann Surg Oncol. 2006;13:279-81.
8. Kesmodel SB, Karakousis GC, Botbyl JD, Canter RJ, Lewis RT, Wahl PM, et al. Mitotic rate as a predictor of sentinel lymph node positivity in patients with thin melanomas. Ann Surg Oncol. 2005;12:449-58.
9. Wong SL, Morton DL, Thompson JF, Gershenwald JE, Leong SP, Reintgen DS, et al. Melanoma patients with positive s who did not undergo completion lymphadenectomy: a multi-institutional study. Ann Surg Oncol. 2006;13:809-16.
10. Curado MP, Edwards B, Shin HR, Storn H, Ferlay J, Heanue M, Boyle P, editors. Cancer incidence in five continents. Lyon: IARC Scientific Publication; 2008. (n. 160, vol. 9).
11. Puleo CA, Messina JL, Riker AI, Glass LF, Nelson C, Cruse CW, et al. Sentinel node biopsy for thin melanomas: which patients should be considered? Cancer Control. 2005;12:230-5.
12. Balch CM, Gershenwald JE, Soong SJ, Thompson JF, Atkins MB, Byrd DR, et al. Final version of 2009 AJCC melanoma staging and classification. J Clin Oncol. 2009;27:6199-206.
13. Faries MB, Thompson JF, Cochran A, Elashoff R, Glass EC, Mozzillo N, et al. The impact on morbidity and length of stay of early versus delayed complete lymphadenectomy in melanoma: results of the Multicenter Selective Lymphadenectomy Trial (I). Ann Surg Oncol. 2010;17:3324-9.

Mailing Address / Endereço para correspondência:
Renato Santos de Oliveira Filho
Av. Rebouças, 2849
CEP 05401-350 - São Paulo - SP, Brazil
E-mail: mayracalil@hotmail.com

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