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
Daniel Arcuschin de Oliveira
Maria do Carmo Assunção Queiroz
Mayra Calil Jorge
Renato Leão de Oliveira
Fábio Xerfan Nahas

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 mitoses/mm². Patient was submitted to margin enlargement and sentinel biopsy of 2 lymph nodes (left axilla). 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 sentinelas (axila esquerda). O exame anatomopatológico mostrou micrometástases, no seio subcapsular de ambos. Seguindo a recomendação do American Joint Committee 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 Committee on Cancer 2009, sugerindo biópsia para esses pacientes.

Palavras-chave: Biópsia de linfonodo sentinela; Melanoma; Metástase linfática; Mitose; Neoplasias

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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/mm² 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/mm². In this study 588 cases were analyzed, of which 350 cases had a mitotic rate of ≥ 1/mm². 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/mm² (Figure 1). The anatopathological examination revealed moderate intratumoral and peritumoral lymphocytic infiltration, without angiolympathecic 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.

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 pre-operative 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.
DISCUSSION
The incidence of melanoma is increasing worldwide. 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 Committee on Cancer Melanoma Staging includes mitosis as an important prognostic risk factor for thin melanomas, suggesting sentinel node biopsy for patients in this condition. 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. Mitosis in primary melanoma identifies patients with a high risk of recurrence, as can be clearly observed in the case described above.

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