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ORIGINAL ARTICLE

Risk Factors for the Development of Locoregional Cutaneous Metastases as the Sole Form of Recurrence in Patients With Melanoma[☆]

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KEYWORDS

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Intralymphatic metastases;
Risk factors

Abstract

Background: While locoregional cutaneous metastases (in transit and satellite) in melanoma have received little attention from researchers to date, they have pathogenic and prognostic features that distinguish them from other forms of locoregional recurrence. Identifying predictors of these metastases would be of great value for their prevention, early diagnosis, and treatment. The aim of this study was to identify the risk factors associated with locoregional cutaneous metastases as the first form of recurrence in the metastatic progression of melanoma. **Material and methods:** Between 2000 and 2010, we prospectively collected the data of 1327 patients diagnosed with stage I and II melanoma. During follow up, 112 patients (8.4%) developed metastases. Of these, 36 had exclusively locoregional cutaneous metastases. The clinical and histological characteristics of this subgroup were evaluated.

Results: In the univariate analysis, significant predictors were patient age, primary tumor thickness, site, ulceration, mitotic index, and histological type. After multivariate analysis, the independent risk factors were tumor thickness (risk ratio [RR] 5.6; 95% CI: 2.7-11.5) and the location of the primary tumor on the lower limbs (RR 3.4; 95% CI: 1.0-11.5), on the head or neck (RR 4.8; 95% IC: 1.7-13.5), or in acral sites (RR 6.7; 95% IC: 2.2-20.8).

Conclusion: Patients who have melanomas with a Breslow thickness of more than 2 mm located on the lower limbs, head, neck, or acral sites have a higher risk of developing locoregional cutaneous metastases. These findings could be useful in the design of future guidelines for the monitoring and management of melanoma.

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PALABRAS CLAVE

Melanoma cutáneo;
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 Metástasis intralinfáticas;
 Factores de riesgo

Factores de riesgo para el desarrollo de metástasis cutáneas locorregionales como forma única de recaída en los pacientes con melanoma

Resumen

Introducción: Las metástasis cutáneas locorregionales (en tránsito y satelitosis) constituyen un evento poco estudiado en la progresión del melanoma, con diferencias patogénicas y pronósticas respecto a otras formas de recaída locorregional. Conocer las variables predictivas de este evento sería de gran utilidad en su prevención, diagnóstico precoz y tratamiento. El objetivo de este trabajo fue evaluar los posibles factores de riesgo asociados a la aparición de metástasis cutáneas locorregionales como primera forma de recaída en la progresión metastásica del melanoma.

Material y métodos: Entre 2000 y 2010, los datos de 1.327 pacientes diagnosticados de melanoma en estadios I y II fueron recogidos de forma prospectiva en nuestras consultas. Durante el seguimiento, un total de 112 (8,4%) pacientes sufrió progresión metastásica de su enfermedad. De ellos, 36 pacientes presentaron metástasis cutáneas locorregionales no concurrentes con otras formas de recurrencia. Las características clínicas e histológicas de este subgrupo fueron evaluadas.

Resultados: En el análisis univariante, los factores predictivos significativos fueron la edad del paciente, el espesor del tumor primario, la localización, la ulceración, el índice mitótico y el tipo histológico. Después del análisis multivariante, se mantuvieron como factores de riesgo independientes el espesor (razón de riesgo [RR] 5,6 e IC 95%: 2,7-11,5), la localización del tumor primario en miembros inferiores (RR 3,4 e IC 95%: 1,0-11,5), en cabeza/cuello (RR 4,8 e IC 95%: 1,7-13,5) y en zonas acrales (RR 6,7 e IC 95%: 2,2-20,8).

Conclusión: Los pacientes con melanomas de más de 2 mm de Breslow, localizados en miembros inferiores, cabeza/cuello y zonas acrales tienen un mayor riesgo de padecer metástasis cutáneas locorregionales. Estos datos podrían ser útiles en el diseño de futuras guías para el seguimiento y manejo del melanoma.

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Introduction

Cutaneous melanoma, a tumor with high metastatic potential, is considered to be among the cancers with the fastest growing incidence in white populations.¹

Twenty percent of patients who develop recurrent cutaneous melanoma have exclusively locoregional cutaneous involvement (local recurrence, satellite metastases, or in-transit metastases).^{2,3} In locally recurrent melanoma (in which tumor cells are present in the primary tumor excision scar), a distinction is made between recurrences that are assumed to be satellite metastases and recurrences that might be caused by the persistence of tumor cells from an incompletely excised primary tumor. Satellite metastases and/or in-transit metastases usually precede lymph node metastases, whereas the development of distant metastases appears to be an independent event in neoplastic spread.^{2,4} Few studies have evaluated the risk factors associated with exclusively locoregional cutaneous tumor progression in patients with melanoma⁵⁻¹³ but an association has been reported between risk of recurrence and the clinical and pathologic characteristics of the primary tumor (thickness, site, ulceration), extent of disease, and patient age and sex. Other factors, such as mitotic index, have been examined by very few studies.^{12,14} In the specific case of intralymphatic (in-transit and satellite) metastases, the location of the primary tumor on the lower limbs, intralymphatic invasion, and the presence of lymph node metastases have been identified as risk factors.^{5,6,15-20}

These last 2 characteristics are used to classify stage III patients according to the most recent staging criteria published by the American Joint Committee on Cancer (AJCC).⁸ However, no previous studies have evaluated in patients without previous lymphatic involvement (locoregional cutaneous or lymph node metastases) the risk factors associated with in-transit and satellite cutaneous metastases as an isolated event in the progression of melanoma, in the absence of other forms of recurrence (lymph node or distant metastases). It is of fundamental importance to understand and characterize the specific risk factors associated with locoregional cutaneous metastasis because it differs from other forms of tumor progression in terms of prognosis and management.⁸

The primary objective of this study was to evaluate the possible clinical and pathologic risk factors for the development of locoregional cutaneous metastases as the first and sole form of metastatic spread in patients with cutaneous melanoma.

Material and Methods

A total of 1327 consecutive patients diagnosed with primary localized cutaneous melanoma (pathologic stages I and II)⁸ between January 2000 and July 2010 were identified in the melanoma databases of the Instituto Valenciano de Oncología and the Consorcio Hospital General Universitario de Valencia in Valencia, Spain.²¹ Table 1 shows the

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