Cartilaginous melanoma: case report and review of the literature

Melanoma cartilagineo: caso clinico e revisao da literatura

Joana Devesa Parente¹  José Manuel Pereira da Silva Labareda²
Elvira Augusta Felgueira Leonardo Fernandes Bártolo³ Maria Fernanda Sachse Pinto Fonseca Santos⁴
Esmeralda Maria Seco do Vale⁵

DOI: http://dx.doi.org/10.1590/abd1806-4841.20131595

Abstract: Malignant melanoma can present a variety of histopathological patterns. Cartilaginous change in the absence of osteogenic differentiation is extremely rare in malignant melanoma, being among the least frequent of the wide range of melanoma histologic patterns. We report a case of a 47-year-old woman with a subungual nodule on her right great toe for many years. Histopathological examination of the lesion led to a diagnosis of malignant melanoma with cartilaginous differentiation devoid of concomitant osseous areas. It would appear that this unusual form of melanoma has a predilection for acral location, particularly the subungual region. Malignant melanoma with chondroid stroma should therefore be considered in the differential diagnosis of cartilaginous lesions of the toes and fingers. Careful examination of the overlying epidermis and identification of an in situ component of melanoma may be necessary in order to establish the correct diagnosis.

Keywords: Cartilage; Melanoma; Toes

Resumo: O melanoma maligno pode apresentar uma grande variedade de padrões histopatológicos. A presença de diferenciação cartilagínnea, na ausência de diferenciação osteogénica, é extremamente rara no melanoma maligno. O melanoma cartilagínneo está entre os padrões histológicos menos frequentes. Relatamos um caso de uma doente do sexo feminino de 47 anos de idade com um nódulo subungueal no 1º dedo do pé direito com muitos anos de evolução. O exame histopatológico da lesão revelou melanoma cartilagínneo, sem áreas de diferenciação osteogénica. Esta variante de melanoma parece ter predileção pela extremidades, sobretudo pela região subungueal. Assim, o melanoma maligno com diferenciação condroide, deve ser tido em consideração no diagnóstico diferencial de lesões acrais cartilaginosas. A observação cuidadosa da epiderme e a identificação de um componente do melanoma in situ podem ser necessários para estabelecer um diagnóstico correto.

Palavras-chave: Cartilagem; Dedos do pé; Melanoma

INTRODUCTION

Malignant melanoma can present a wide variety of histopathological patterns, mimicking other malignant tumors. A number of variants have been described in addition to the classic forms of melanoma, such as polypoid, verrucous, desmoplastic, myxoid, chondroid, ballooning cell, rhabdoid, animal type, amelanotic, spitzoid, and nevoid.¹

Divergent differentiation is a rare phenomenon and, when it occurs, can be missed by unwary pathologists and lead to diagnostic uncertainty.

The clinical significance of such aberrations is uncertain, as are their underlying mechanisms.

Cartilaginous change in the absence of osteogenic differentiation is extremely rare in malignant melanoma,² being among the least frequent of the wide range of melanoma histologic patterns.² To date only 12 reported cases have shown cartilaginous differentiation devoid of concomitant osseous areas.²-¹¹
CASE REPORT

A 47-year-old woman presented with a painful subungual lesion on the right big toe which appeared one year before as a hyperkeratotic lesion and treated with oral terbinafine, with no improvement. Twelve years ago she underwent laser therapy for a lesion at the same location. A histopathological examination was not performed.

Physical examination revealed a painful subungual nodule on her right big toe. There was no regional lymphadenopathy.

An excisional biopsy of the nodule was performed. Histopathological examination showed an ulcerated tumor extending in a diffuse pattern from the epidermis to the inferior limit of the specimen. Rounded cells with vesicular nucleus, scant cytoplasm, numerous mitotic figures, dyskeratotic and apoptotic cells were observed (Figure 1).

The presence of nests of large, bizarre chondrocytes embedded in a chondroid matrix was observed in around one third of the lesion, strongly suggesting positivity for Alcian Blue (Figure 2).

On the periphery of the specimen hyperplasia and acanthosis of epidermis were observed as well as intracytoplasmic melanin pigment in small aggregates (Figure 3). Nests of atypical melanocytes were observed at the dermoepidermal junction without evidence of pagetoid spread, and isolated atypical melanocytes were present in the upper dermis (Figure 4).

Immunohistochemistry showed positivity of the junctional component and of melanocytes in the upper dermis for S-100 protein and positivity of the tumor cells for HMB-45 (Figures 5, 6 and 7). The cartilaginous component showed positivity for S-100 protein and for neuron specific enolase (Figure 8). We diagnosed melanoma with cartilaginous differentiation. The tumor had a Breslow depth higher than 5 mm (Clark level V).

The patient subsequently underwent amputation of the distal phalanx of the big right toe. Histopathological examination of the lesion confirmed the biopsy findings of malignant melanoma with cartilaginous differentiation, with a Breslow depth of 5.5 mm (Clark level V).
thickness of 9.9 mm and a Clark level of V. Sentinel lymph node biopsy was also performed, which proved negative for tumor. According to the TNM staging this malignant melanoma was T4b N0 M0, stage II B.

Two years after surgery an ulcerated lesion at the same location appeared. This was excised and proved by histopathological examination to be a local recurrence. The big and second toes were amputated. This subsequent wider excision showed no residual melanoma.

Neither local recurrence nor metastasis were observed during the following three years of follow-up.

DISCUSSION

There have been some reports of melanomas with pure cartilaginous differentiation, including primary melanomas and metastatic melanoma.2-11 Eight cases of primary melanomas with cartilaginous differentiation have been reported.12-14 In two
of these cases the location was subungual on the toe, as in our patient. Other locations include nose, lip, shoulder, ankle and mucosa (vagina, nasal cavity). All were amelanotic melanomas, with a lentiginous component present in the majority of them, and ulceration in five cases. Although immunohistochemical studies were not documented in all the cases, those that were tested showed consistent positivity for S-100 protein, and HMB-45 staining was variable.

The four cases of metastatic melanomas with cartilaginous differentiation reported had more variable features. The mechanisms underlying these heterologous differentiations are not well understood. As in our case, previous trauma (laser therapy) was a common feature of the reported cases with cartilaginous differentiation. It may represent a form of host response to injury, i.e. alteration of benign stromal fibroblastic cells to differentiate along cartilaginous or osseous lines.

Although the exact mechanism of cartilaginous differentiation in melanoma devoid of concomitant osseous areas is not well understood either, there have been recently speculative explanations have been advanced related to melanoma-inhibiting activity (MIA) factor, a soluble autocrine growth factor, secreted by melanoma cell lines but not by normal melanocytes.

Over-expression of the MIA factor might contribute to the exceptional development of cartilaginous differentiation in melanoma, supporting the chondrogenic phenotype while inhibiting osteogenic differentiation.

The differential diagnosis of a cutaneous or soft tissue tumor exhibiting cartilaginous differentiation is mandatory with other benign and malignant cartilaginous tumors, including malignant mixed tumor, chondrosarcoma, osteosarcoma with extensive cartilaginous matrix, malignant chondroid syringoma, extraskeletal chondroma, chondroid syringoma, myoepithelioma, parachordoma and myositis ossificans.

When identifying a junctional melanocytic component or areas of conventional melanoma it is important to diagnose melanoma with cartilaginous differentiation (as in our case). The immunohistochemical stains for S-100 protein, which is virtually positive in all cases, and for HMB-45, which is positive in the majority of cases, are also important elements in the diagnosis of melanoma.

The application of immunoperoxidase stains, including microphthalmia transcription factor protein, will also assist in future in correctly identifying this rare melanoma variant.

It has been impossible to attribute prognostic implications to this rare melanoma variant due to the small number of cases. However, in the reported cases there were no deaths due to melanoma. Local recurrence occurred in our case and in another case reported.

In summary, our report focuses on one case of an extremely rare type of primary melanoma with cartilaginous differentiation, in the absence of osteogenic differentiation. It would appear that this unusual form of melanoma has a predilection for acral location, particularly the subungual region. Therefore, malignant melanoma with chondroid stroma should be given special attention in the differential diagnosis of cartilaginous lesions of the toes and fingers. Careful examination of the overlying epidermis, and identification of an in situ component of melanoma, may be necessary in order to establish the correct diagnosis.
REFERENCES

1. Rongioletti F, Smoller BR. Unusual histological variants of cutaneous malignant melanoma with some clinical and possible prognostic correlations. J Cutan Pathol. 2005;32:589-603.
2. Ackley CD, Prieto VG, Bentley RC, Horenstein MG, Seigler HF, Shea CR. Primary chondroid melanoma. J. Cutan Pathol. 2001;28:482-5.
3. Banerjee SS, Coyne JD, Menasce LP, Lobo CJ, Hirsch PJ. Diagnostic lessons of mucosal melanoma with osteocartilaginous differentiation. Histopathology. 1998;33:255-60.
4. Murali R, McCarthy SW, Bothman J, Cachia A, Janarthanan P, Sharma R et al. Melanoma exhibiting cartilaginous differentiation. Histopathology. 2010;56:815-21.
5. Mete O, Bilgic B, Buyukbabani N. A tumor with many faces: metastatic malignant melanoma with extensive cartilaginous differentiation. Int J Surg Pathol. 2010;18:217-8.
6. Cachia AR, Kedziora AM. Subungual malignant melanoma with cartilaginous differentiation. Am J Dermatopathol. 1999;21:165-9.
7. Rinaggio J, Hameed M, Baredes S. Melanoma with cartilaginous differentiation originating within the mucosa of the nasal cavity. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008;106:861-5.
8. Slavik T, Hannah M, Schroder RA. Primary chondroid melanoma of the nasal skin: a rare melanoma variant at a previously undocumented site. J Cutan Pathol. 2007;34:427-30.
9. Grunwald MH, Rothem A, Feuerman EJ. Metastatic malignant melanoma with cartilaginous metaplasia. Dermatologica. 1985;170:249-52.
10. Hanley KZ, Weiss SW, Logani S. Melanoma with cartilaginous differentiation: diagnostic challenge on fine-needle aspiration with emphasis on differential diagnosis. Diagn Cytopathol. 2009;37:51-5.
11. Piana S, Valli R, Ricci C. Epidermotropic chondroid metastasis of melanoma: report of a case of metastatic melanoma with previously unreported morphological features. Am J Dermatopathol. 2009;31:301-4.

MAILING ADDRESS:
Joana Devesa Parente
Avenida Bernardo Santareno
Apartado, 115
2000-153 - Santarém - Portugal
E-mail: parentejoana81@hotmail.com

How to cite this article: Parente JD, Labareda J MPS, Bártolo E AFLF, Santos MFSPF, Vale EMS. Cartilaginous melanoma: case report and review of the literature. An Bras Dermatol. 2013;88(3):403-7.