

Epidermotropic Chondroid Metastasis of Melanoma: Report of a Case of Metastatic Melanoma With Previously Unreported Morphological Features

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Abstract: A potential diagnostic pitfall in the management of patients with melanoma is the inability to recognize metastatic melanoma, especially if it shows unusual features. We describe a case of multiple epidermotropic metastatic melanoma, which finally recurred with an extensive chondroid differentiation. To our knowledge, this is the first description of a case of epidermotropic chondroid metastatic melanoma.

Key Words: melanoma, metastasis, epidermotropism, chondroid, cartilage, metaplasia

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INTRODUCTION

Recognition of epidermotropic metastatic melanoma (EMM) is crucial in the treatment of patients with melanoma. In the past few decades, the concept of metastatic melanoma has changed completely,^{1–10} and it has been accepted that metastatic melanoma could share some morphological features with primary melanoma, mainly epidermotropism. With time, the morphologic spectrum of EMM has broadened, and its distinguishing features have become faint.

We report a case of multiple EMM showing chondroid changes that were very subtle in the initial recurrences but appeared to be well developed in the last one.

CASE REPORT

In June 2006, a 66 year-old woman came in for the evaluation of a brownish nodule on the dorsal skin of the little finger of her right hand that had been progressively increasing in size in the last few months. A clinical diagnosis of melanoma was suggested, and the lesion was first biopsied. The histological diagnosis was superficial spreading malignant melanoma, incompletely excised. A subsequent finger amputation and a sentinel lymph node procedure were performed. Histopathologic examination revealed a conventional malignant melanoma, Breslow depth of 1 mm (Clark level IV). The sentinel lymph node was negative; staging according to TNM was T1B N0 M0.

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The patient's medical history consisted of chemotherapy and radiotherapy for lobular breast carcinoma with axillary lymph node metastases in 2004.

From January 2007 to October 2008, the patient underwent surgical excision of 7 papules that progressively appeared in the skin of the right axillary region, in the presternal area, and on the mastectomy scar. In all the cases, the lesions were brownish and well defined, and the clinical differential diagnosis was metastatic melanoma versus metastatic breast carcinoma. All the lesions were excised with clear surgical margins.

PATHOLOGIC FEATURES

On histological examination, the first 6 lesions showed morphological features that were almost superimposable; they were small, well defined, and all made up of a junctional and a dermal component. The junctional component consisted of large atypical pigmented melanocytes with focal pagetoid spread (Fig. 1, top). The dermal component showed a superficial zone of atypical melanocytes, similar to the junctional ones, surrounded by a deeper proliferation of cytologically bland, amelanotic spindle cells set in a basophilic myxoid stroma (Fig. 1, bottom and inset). Immunohistochemical studies showed strong positivity for S100-protein (DakoCytomation, Glostrup, Denmark), HMB-45 (DakoCytomation, Glostrup, Denmark) and MART-1 (Cell Marque, USA) in the superficial pigmented melanocytes, both junctional and dermal, whereas the deep spindle cell component reacted only to S100 protein (Figs. 2A, B). Cytokeratin AE1/AE3 (Thermo Scientific) was negative in both the components.

The last lesion, excised in October 2008 and localized on the mastectomy scar, was slightly different, as it was larger (12 mm in greatest axis) and almost completely restricted to subcutis. Microscopically, the lesion was highly cellular and consisted of a nodular proliferation of pleomorphic epithelioid cells, sometimes arranged in small aggregates and embedded in a chondroid matrix (Fig. 3), strongly positive for Alcian Blue (pH = 2.5) (Fig. 3, inset). The small neoplastic chondroid aggregates were sometimes bordered by a clear space, recalling the lacunae of the normal cartilage (Fig. 4). Mitotic activity was high and exceeded 10 mitotic figures per 10 high-power field. The nodule was surrounded by the same proliferation of cytologically bland, amelanotic spindle cells immersed in a basophilic myxoid stroma, seen in the prior recurrences.

Subcutaneous adipose tissue was widely infiltrated and Breslow thickness was 12 mm. At immunohistochemistry, the

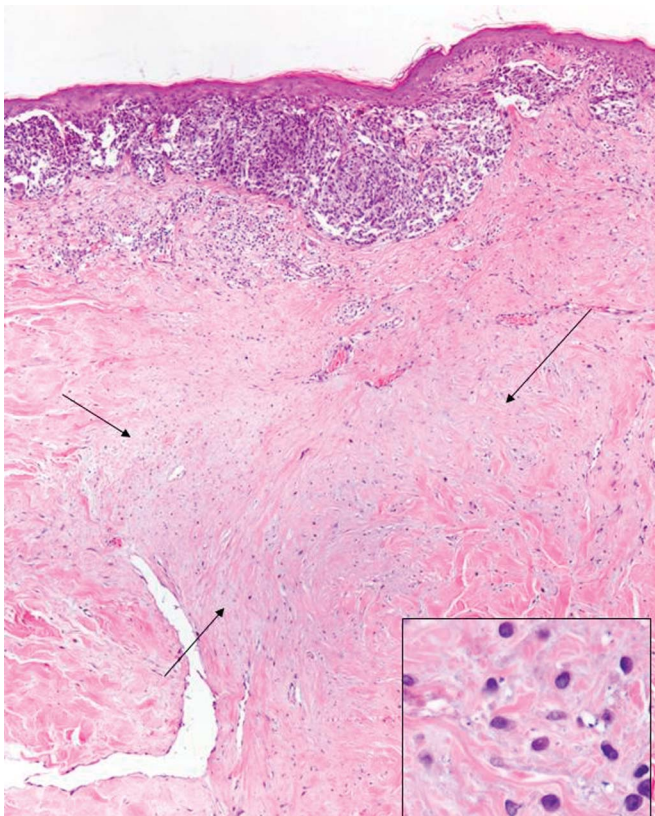


FIGURE 1. A conventional melanomatous proliferation is noted at the dermo-epidermal junction; amelanotic spindle cells occupy the whole dermis (arrows) and show bland cytological features (inset) (hematoxylin–eosin, $\times 40$).

pleomorphic epithelioid cells were positive with S100 protein and negative with HMB-45, MART-1, and cytokeratin AE1/AE3. A clear dermal zone separated the nodule from the epidermis; neither junctional nor dermal conventional neoplastic melanocytes were present.

DISCUSSION

Although the concept of EMM has been described since the 1970s, it remains especially challenging in the evaluation of a melanoma recurrence, and the differential diagnosis with another primary can be extremely difficult. Since the work of Kornberg et al,¹ who suggested some histological features to differentiate EMM from primary melanoma, morphological criteria have evolved, and more recent observations have confirmed that the distinction can be impossible.⁷ However, the distinction between an EMM and another primary melanoma is of paramount importance in the treatment of the patient.

All the classic criteria are now outdated, and the criteria according to which the EMMs are defined as usually symmetrical dermal nodules with a variable junctional component usually smaller than the dermal one is no longer acceptable. Likewise, the differential diagnosis cannot rely only on the dimension of the lesion or on the presence of atypical dermal melanocytes. A peer review of White and Hitchcock¹¹ emphasizes how the concept of metastatic melanoma has evolved.

A more critical updated approach would be to correlate histological features and clinical data, keeping in mind that if a melanoma shows unusual features, patient’s history must be investigated to exclude a melanoma metastasis. In the present

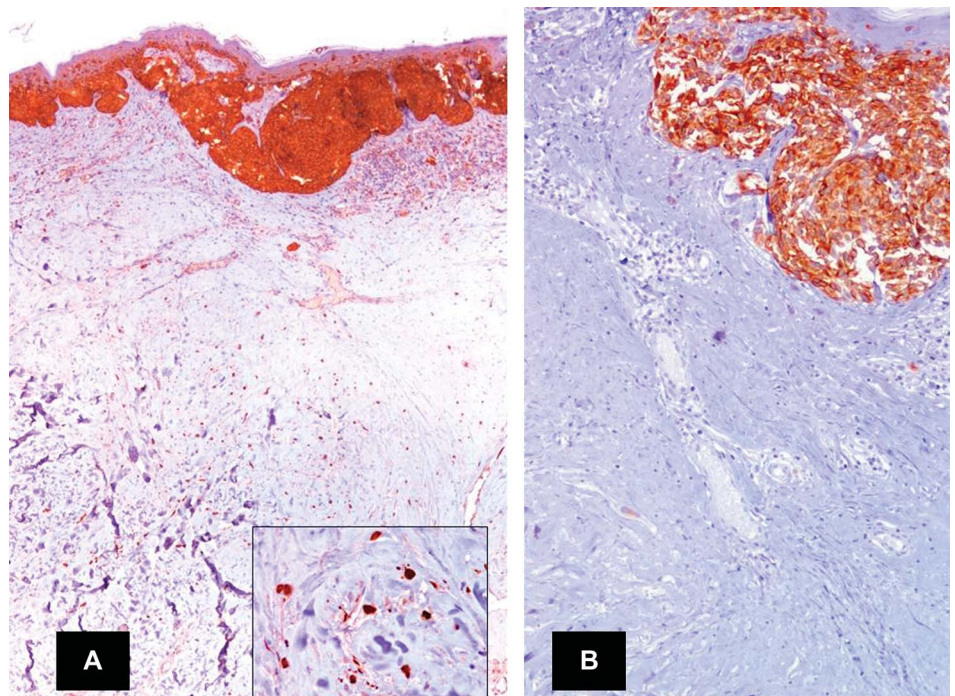


FIGURE 2. A, S100 protein is strongly positive either in the melanomatous junctional component or in the dermal spindle cell proliferation (inset) (immunoperoxidase technique, $\times 40$). B, MART-1 is expressed only in the conventional superficial melanomatous proliferation (immunoperoxidase technique, $\times 40$).

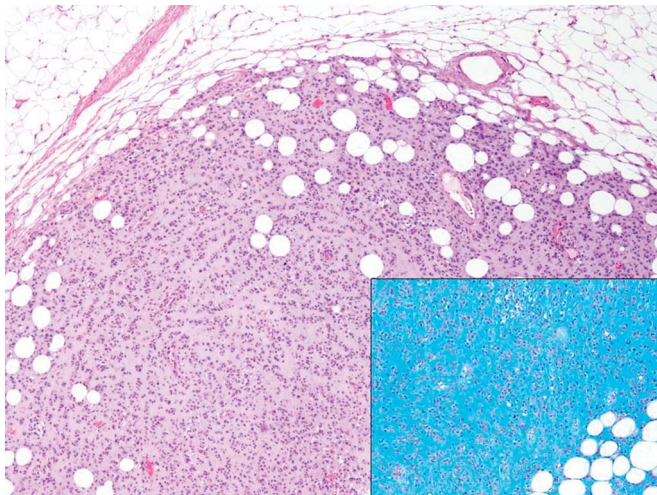


FIGURE 3. Dermal nodule consists of a proliferation of pleomorphic cells, arranged in small aggregates and embedded in a chondroid matrix, Alcian Blue positive (inset) (hematoxylin–eosin, $\times 100$).

case, the history of a melanoma few months before the first recurrence, together with the abnormal dermal component, helped in rendering a diagnosis of EMM. Last but not least, also a cutaneous metastasis of breast carcinoma was excluded morphologically and immunohistochemically.

Metaplastic changes are known to occur in melanomas,¹² and they are important because they can lead to diagnostic misinterpretation. Osteochondiliginous differentiation has been described both in cutaneous and mucosal melanomas,^{13–18} and in one case, bone formation was evident also in a subsequent lymph node metastasis.¹³ Pure cartilaginous metaplasia in melanoma is rarer, and few cases have been reported.^{19–21}

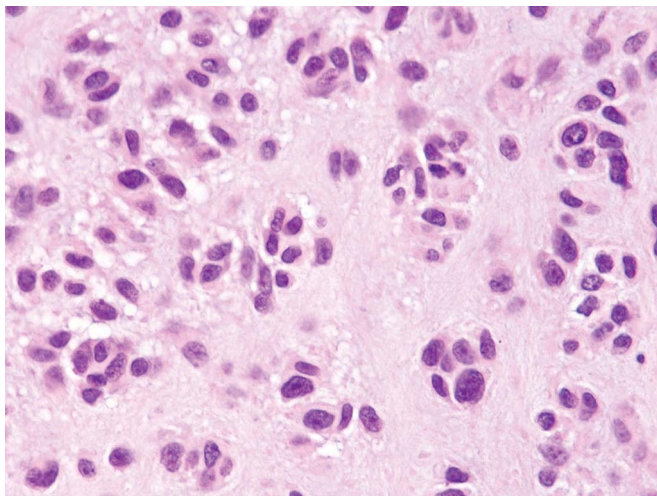


FIGURE 4. At high power, the small neoplastic chondroid aggregates recall the lacunae of the normal cartilage (hematoxylin–eosin, $\times 100$).

In our case, the first 6 recurrences invariably showed a peripheral collarette of bland spindle cells intermingled in a myxoid stroma, around a conventional melanocytic component; the last one consisted entirely of a dermal chondroid component, and the junctional melanocytic proliferation was lost. To our knowledge, this is the first case of pure cartilaginous differentiation in an EMM.

An interesting point is that both the spindle cells in the myxoid stroma and the chondroid component are S100 protein positive but do not react with melanocytic-specific antigens, such as HMB-45 and MART-1. It follows that the immunohistochemical panel, in case of a nodular chondroid subcutaneous malignancy, must be wide and that neither HMB-45 nor MART-1 negativity excludes the diagnosis of metastatic melanoma.

The clinical significance of the divergent differentiation seen in the last recurrence is yet to be characterized. There is increasing evidence that stem cell markers are expressed in melanomas^{12,22–24}; their self-renewal capacity, along with their high tumorigenicity, may explain the neoplastic progression and the differentiation into various mesenchymal and epithelial lineages. In the follow-up of a patient with melanoma, the pathologist is required to critically evaluate every cutaneous malignancy and to exclude a melanoma recurrence, even if this is morphologically unlikely.

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