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CLINICAL REPORT

A Variant of Junctional Naevus of Epithelioid and Spindle Cell Type Rich in Melanophages

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We describe a form of junctional melanocytic neoplasm with a massive production of melanin accumulated in the dermis. The pigment is stored in macrophages, which are by far the most numerous cellular component of the lesion. Another peculiar aspect is the occasional presence of a few melanocytes scattered in a pagetoid pattern above the dermo-epidermal junction in the spinous layer. The histological picture of this lesion is similar to a form of "tumoral melanosis" induced by a regressed malignant melanoma. The lesion had a worrisome clinical picture, its dark colour constituting a clinico-pathological diagnostic problem. The main clinical clues to the benign nature of this entity are the small lateral diameter, the uniform distribution of the pigment and the stability of the lesion over time; moreover, the patients are alive and well after a considerable length of time. Although a regressed dysplastic or malignant lesion cannot be totally excluded from a scientific point of view, we conclude that there is no sound morphological or clinical evidence that the lesion is other than biologically benign. The lesion is most likely another peculiar variant of epithelioid and spindle cell naevus. *Key words: melanoma simulator; tumoral melanosis.*

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Tumoral melanosis is a term that usually indicates a large amount of melanin contained in dermal macrophages (1). These macrophages, called melanophages, collect in a neoplasm-like mass or in roundish nodules. The cellular population seems quite heterogeneous, but in reality is almost entirely made up of melanophages; usually, no melanocytes are present.

The most classic form of tumoral melanosis is that resulting from a subtotal or total regression of malignant melanoma. In this case, melanophages can be extremely abundant with only a few atypical melanocytes recognizable at the junction or absent altogether. In metastatic epidermotrophic malignant melanoma, the deposition of melanin after complete regression of the melanocytes can be striking and melanophages occupy a large part of superficial dermis.

We report three cases of a melanocytic lesion in which the massive melanin synthesis caused an engulfment of pigment in the superficial dermis, where a large band of melanophages is present and can obscure the inconspicuous melanocytic proliferation sited at the junction. Being darkly pigmented, lesions had a worrisome clinical aspect and were histologically difficult to interpret: two of the cases were sent to us in consultation as suspected melanoma.

CASE REPORTS

Clinical features

Case 1: A 19-year-old male patient with the lesion on the left thigh. The patient referred to the lesion as having appeared a few years earlier but that it was stable; the clinician excised the naevus because of its dark colour. The lateral diameter was 4 mm and the lesion had a uniform pigmentation. The specimen was sent to us in consultation by a pathologist who suspected a regressed melanoma.

Case 2: A 24-year-old patient with a 6-mm lesion on the back. No other clinical data regarding the lesion were available.

Case 3: A 29-year-old woman noted a uniformly darkly pigmented 5 mm lesion on her leg 4 years prior to the excision. The lesion was sent to us in consultation by a colleague who suspected a regressed melanoma.

No similar lesions were found in any of the patients. No stories of melanoma or dysplastic naevus syndrome in the patients or their families were reported.

Follow-up has been performed for 5 years (patient 1), 2 years (patient 2) and 6 months (patient 3) without signs of recurrence.

Histological features

Case 1: Histologically, the lesion (Fig. 1A, B) shows an inconspicuous junctional component characterized by small nests of heavily pigmented melanocytes. These cells have well-developed cytoplasmatic dendritic processes. Pigmented dendrites are visible also among the keratinocytes of the squamous layer. Melanocytes are present along the epidermal basal layer lined in single

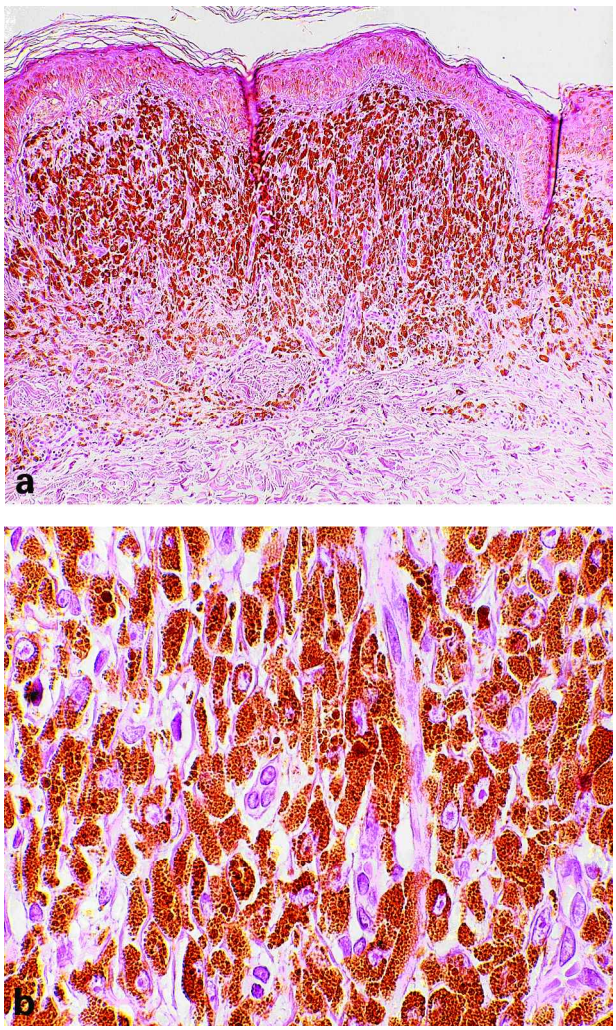

Fig. 1. A. Case 1. The lesion seems to be composed only of nodules of pigmented cells sited in an expanded papillary dermis and in the upper reticular dermis. The junctional component is readily overlooked and a diagnosis of regressed melanoma resulting in tumoral (nodular) melanosis can be made. (Haematoxylin and eosin; original magnification $\times$ 13.2). B. A closer view of the dermal infiltrate reveals that cells are macrophages filled with coarse granules of melanin. Besides these melanophages, only a few scattered lymphocytes are present. No melanocytes are clearly detectable. (Haematoxylin and eosin; original magnification $\times$ 198).

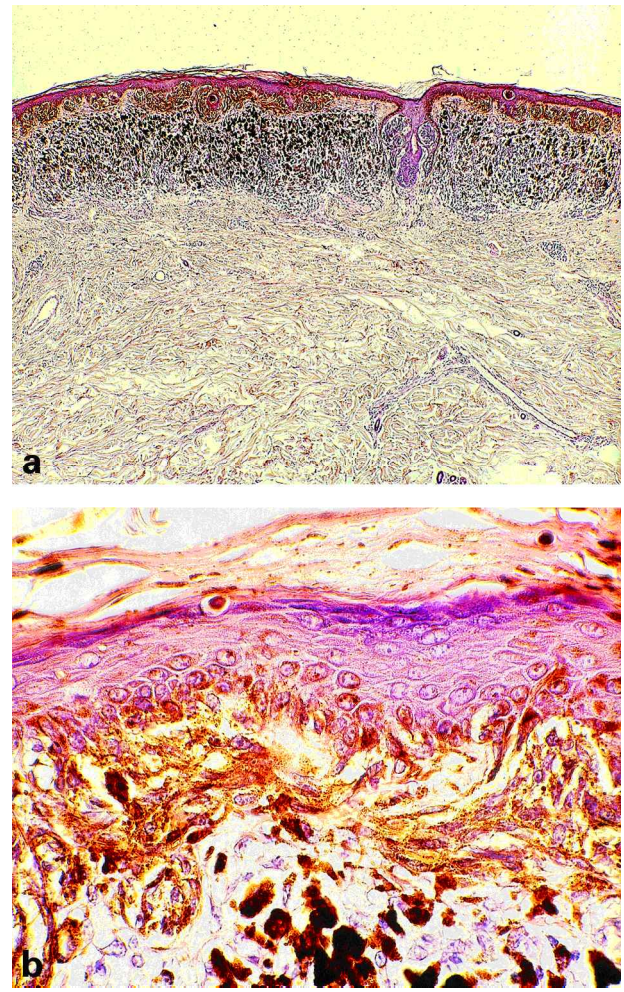

Fig. 2. A. Case 2. A large amount of melanin is present in the dermis. (Haematoxylin and eosin; original magnification $\times$ 13.2). B. A proliferation of spindle-shaped, dendritic and pigmented melanocytes is evident at the junction. They are gathered in elongated nests parallel to the epidermis. (Haematoxylin and eosin; original magnification $\times$ 198).

units in a lentiginous array; few of them are present above the dermo-epidermal junction in a pagetoid pattern. All the melanocytes in the nests, at the junction and above it, have an obvious monomorphic and benign-looking appearance; neither mitosis, nor cellular necrosis is detectable, nuclear membrane is thin and homogeneous, nucleoli are inconspicuous and uniform to each other. Melanin is present in abundance in the epidermis up to the corneus layer, where it is contained in small dots inside the corneocytes.

The lesion is sharply circumscribed in its lateral margins and ends at both lateral extremes with clear-cut nests.

The most impressive alteration in this lesion is in the dermis, where a large amount of melanin is accumulated, mostly, apparently, inside macrophages (2, 3).

No melanocytes are detectable by immunohistochemical survey with antibodies against S100 and Melan A. The melanophages are arranged in a vaguely nodular pattern and although the major part of the lesion is situated in the papillary dermis, also the reticular dermis seems to be involved. An inflammatory lymphocytic infiltrate is present but inconspicuous.

Case 2: The lesion has the basic architectural and cytological aspects of case 1 (Fig. 2A, B), but the junctional component is more obvious. The junctional nests at the junction are composed of elongated, heavily pigmented melanocytes characterized by thin branching dendrites. The nests are occasionally confluent and in the merging nests cells are spindle-shaped. A few, cytologically normal looking, melanocytes are found above the dermo-epidermal junction.

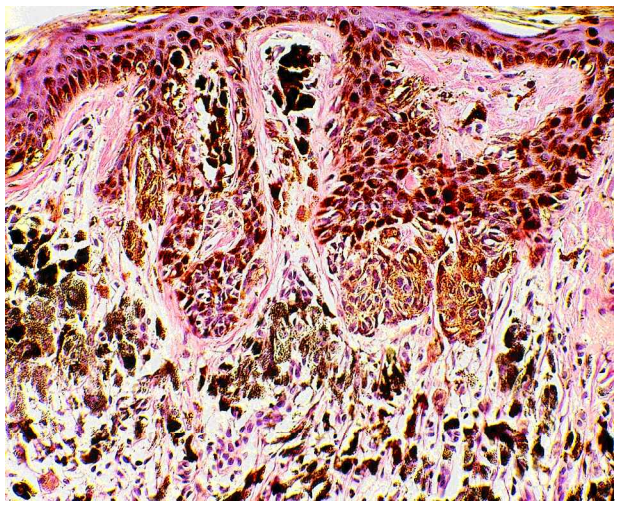

Fig. 3. Case 3. The melanophages engulfed with melanin are mingled with sparse lymphocytes. The junctional melanocytic component shows no atypia. Although a lymphocytic infiltrate is present junctional melanocytes show any sign of regression (Haematoxylin and eosin; original magnification $\times$ 13.2).

Case 3: This small lesion (Fig. 3) is characterized by an enlargement of the papillary dermis, where abundant pigment and lymphocytic infiltrate is present. The junctional component is organized in a nested pattern. Melanocytes are dendritic and pigmented, but cytologically inconspicuous. No signs of regression were noted.

The quantity of melanin in the dermis is clearly disproportionate to the cellular component of the lesion.

DISCUSSION

The large amount of melanin in the superficial dermis or in soft tissue is usually due to the regression of melanoma. Melanin is assumed to be released by the dying melanoma cells and quickly phagocyted. This peculiar storage of melanin has been called tumoral melanosis. The most frequent form of melanoma causing large nodules of tumoral melanosis is epidermotrophic metastasing melanoma, but other forms of melanoma can also be the source of tumoral melanosis (4).

Although metastatic melanoma and primitive cutaneous melanoma are the major culprits for tumoral melanosis, also other non-melanocytic epithelial neoplasms are known capable of inducing this phenomenon (5).

A form which resembles tumoral melanosis has not hitherto been reported in a benign melanocytic naevus. Also in the so-called Sutton naevus (halo naevus, naevus with regression) the melanin deposit in the dermis after the complete annulment of the naevus cells is never abundant enough to be called tumoral melanosis. Three peculiar naevi can indeed simulate tumoral melanosis; these are the hyperpigmented variant of Spitz naevus described by Choi et al. (6), the so-called compound blue naevus described by Kamino & Tam (7), and a few very rare forms of Reed naevus (8, 9). However, none of these lesions can be correctly labelled as tumoral melanosis, because in the dermal component of the naevus the presence of numerous melanocytes full of actively synthesized pigment is immediately evident. In tumoral melanosis, intradermal melanocytes are almost undetectable or absent altogether and cells are all (or almost all) melanophages and lymphocytes.

The finding of a large amount of melanophages in the dermis should always suggest a form of regressed melanoma, and this diagnosis should be sustained until the contrary is proved convincingly.

The type of lesion we report here closely simulates a form of tumoral melanosis (especially case 1) as seen in a regressed melanoma. In fact:

1) In the dermis there are vaguely nodular masses of densely pigmented cells. Pigment is melanin in coarse granules which obscure a vesicular nucleus centred by a prominent but homogeneous nucleolus. These cells are macrophages whose cytoplasm is engulfed with phagocytized melanin. A few lymphocytes are scattered among these cells.

2) Intradermal melanocytes are not detectable in convectional stain nor with immunostaining for S100 and Melan A proteins.

3) In cases 1 and 3 the junctional component of the lesion is readily overlooked, being composed of only a few melanocytes.

4) A pagetoid spread of melanocytes above the junction is appreciable in cases 1 and 2.

Thus a form of regressing melanoma leaving a tumoral melanosis seems a possible diagnosis. On the contrary, the lesion can be interpreted as a bizarre, but benign, form of naevus if the following details are taken into account:

5) At the junction, most of the cells are in discrete nests; these are similar to each other in size and shape and are equally distributed along the lesion.

6) The melanocytes distributed above the junction are scattered in a regular manner throughout the lesional epidermis; they are cytologically typical and monomorphous, and no mitosis nor cellular necrosis is present. Moreover, no pagetoid spread is present in perilesional epidermis.

7) All the visible epidermal melanocytes are obviously benign, despite their dendritic, spindle or epithelioid shape.

8) Lesions are small and well circumscribed.

9) With the exception of melanophages, no other clue indicating regression was present. No hint of regression is present in the junctional component of the neoplasms. In case 3, although the lymphocytic infiltrate should be referred to an ongoing process, no sign of melanocytic regression was present and the lesion had been stable for years.

In addition, clinical features point towards a benign nature of the lesion. Even if the follow-up periods are too short for primary melanoma to be ruled out, they seem long enough for a metastatic regressed melanoma to be excluded.

A form of regressed dysplastic naevus can be ruled out considering that this entity is never heavily pigmented like the lesion we present here; moreover, cells in our lesions are monomorphous and lamellar fibroplasia is absent in the dermis. Finally, dysplastic naevus is a large neoplasm, usually exceeding 6 mm in diameter.

All these considerations indicate that the melanocytic entity we present is a form of benign melanocytic lesion, i.e. a junctional naevus. We can interpret the large deposit of pigment in the dermis as the consequence of an exceedingly abundant production of pigment that is disproportionate to the number of melanocytes, but not representing the result of a regressed melanocytic neoplasm. The histological details of our lesions are in part similar to those attributed in the literature (8, 9) to the so-called Reed naevus (pigmented spindle cell naevus) reputed to be a variant of epithelioid and spindle cell naevus (Spitz Naevus).

We admit that absolute scientific proof of the benign nature of the lesion reported here is lacking and speculative. In fact, a regressed dysplastic naevus or melanoma has been excluded on morphological grounds only, using the criteria illustrated above. Morphology is always an unsatisfactory tool in biology, but only morphological criteria are available today for diagnosing a benign melanocytic lesion owing to the lack of reliability of special techniques (10). A cohort of benign lesions has recently been introduced in the medical literature with morphological and clinical support alone (11, 12).

In conclusion, we describe a rare form of "tumoral melanosis" without any morphological and clinical evidence that the lesion is other than biologically benign. Our interpretation is that the lesion we present here can be related to a variant of Reed naevus (8, 9) in which an unusual and overwhelming production of melanin occurs. The diagnosis of "melanophages rich junctional naevus" should be used with a warning regarding the possibility of a regressive melanoma.

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