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Case report

Pigmented epithelioid melanocytoma: report of a case with favourable outcome after a 4-year follow-up period

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Abstract. *Background:* Pigmented epitheliod melanocytoma (PEM) is a uncommon melanocytoma with unique histopathological features and possibly with a favourable prognosis, because, although sentinel lymph-node metastases may occur, in the great majority of cases described up to now there is no spread beyond regional lymph-nodes. The nature of PEM, its biologic behaviour and its relationships to naevi and melanoma, however, remain to be clearly established, and several Authors suggest that further cases of PEM with long follow-up should be published, in order to better assess the biologic/prognostic characteristics of PEM. *Methods and Results:* We report a new case of PEM, dealing with an oval, regularly marginated, darkly pigmented, asymptomatic nodule. The dermoscopic pattern showed a homogeneous blue-black pigmentation, without any other dermoscopic sign. The histopathologic analysis showed both isolated and nested oval melanocytes at the junctional level, and a mixture of epitheliod and spindle melanocytes, heavily pigmented, together with numerous melanophages in the dermis, with tendency to periadnexal distribution; cellular atypia was pronounced, but only occasional mitoses were identified in the superficial dermis. After a 4-year follow-up period after excision, no persistent lesion or metastases occurred. *Conclusions:* The present case suggests that PEM has a distinct histopathologic/diagnostic identity among melanocytic tumours. Although the up-to-now favourable outcome, however, our patient needs a large period of observation, and further studies with long follow-up are needed to better define the biologic/prognostic identity of PEM. (www.actabiomedica.it)

Key words: Naevus, Melanocytoma, Pigmented epitheliod melanocytoma, Borderline primary cutaneous melanocytic tumours, Melanocytic tumours of uncertain malignant potential

Introduction

The term "pigmented epithelioid melanocytoma" (PEM) was originally proposed (1) for tumours previously designated "animal-type melanoma" or "epithelioid blue naevus", which histologically were indistinguishable. Because of its unique characteristics, including clinical presentation, histological features, and malignant potential that was likely to be "intermediate" between a benign blue naevus and common melanoma, PEM was hypothesized to be allocated into a separate nosological category of "borderline" melanocytic tumours (2): in fact, although sentinel lymph-node metastases were sometimes found, PEM generally did not spread beyond regional lymph-nodes, and the great majority of patients had a favourable outcome (1). The prognostic characteristics of PEM, however, are still matter of debate, and stud-

ies of further cases of PEM with long-term follow-up are necessary to determine its definite biologic behaviour (3,4). The present article reports, indeed, a new case of PEM, with favourable outcome after a 4-year follow-up period after the excision.

Case report

A 7-year-old girl presented with a 5 mm diameter, oval, regularly marginated, darkly pigmented, asymptomatic nodule, started 2 years before, on her left upper arm (Fig. 1A). At the dermoscopic examination, a homogeneous blue-black pigmentation, without any other dermoscopic sign, was evident (Fig.1B). The lesion was excised October 22nd, 2009. At the histopathological analysis (Fig. 2), a dermal-domed, wedge-shaped, heavily pigmented lesion, with scarcely infiltrative margins, was observed (Fig. 2A). Epidermis was hyperplastic, with both isolated and nested oval melanocytes at the junction (Fig. 2B), whereas the dermis was filled with a mixture of epithelioid and spindle dendritic melanocytes with cytoplasmic pigmentation (Fig. 2C). Epithelioid cells were medium- to large-sized, showed moderate to abundant cytoplasm, presented nuclear atypia and eosinophilic nucleoli, and tendency to periadnexal distribution. After careful scrutiny, only a few mitoses were identified in the superficial dermis. No necrosis or ulceration or inflammatory reaction were observed, whereas melanophages were numerous. Immunohistochemical analysis showed a strong and diffuse positivity for both S-100 and HMB-45. Based on these histologic findings, a diagnosis of PEM (1-3,5) was established. After a follow-up of 4 years, no persistent lesion or metastases were observed.

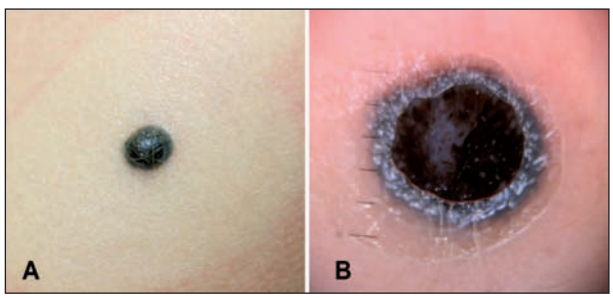

Figure 1. Clinical and dermoscopic appearance. (A) This 5 mm diameter, oval, regularly marginated, darkly pigmented papula was located at the upper left arm, and its surface was not eroded or crusted. (B) Dermoscopic pattern: a homogeneous, blue-black pigmentation, without any other dermoscopic sign, is evident.

Discussion

The present article reports a new case of PEM, recognizable by its morphologic/diagnostic characteristics. On the other hand, the ultimate identity of PEM in the controversial field of melanocytic lesions is, due to its biologic/prognostic characteristics, still matter of debate.

As far as the morphologic/diagnostic identity of PEM is concerned (Table 1), histological features of

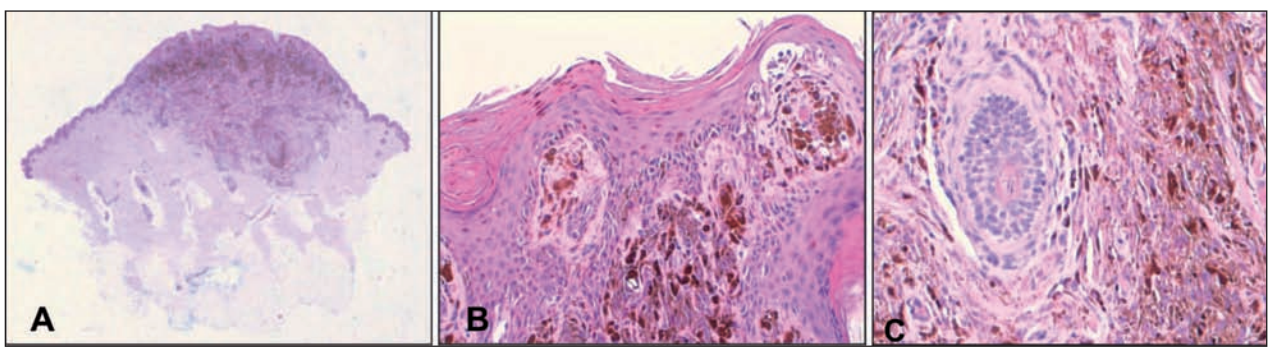

Figure 2. Histopathologic findings. (A) At low magnification, a dermal-domed, wedge-shaped lesion, heavily pigmented, with partially infiltrative margins, is observed (original magnification x2; haematoxylin and eosin). (B) At higher magnification, a hyperplastic epidermis is visible, with both isolated and nested oval melanocytes at the junctional level (original magnification x 20; haematoxylin and eosin). (C) The dermis is infiltrated by pigmented epithelioid/spindled melanocytes and melanophages, with tendency to periadnexal distribution (original magnification x20; haematoxylin and eosin).

Table 1. Clinical, dermoscopic and histological features of PEM, vs blue naevus, vs deep penetrating naevus.

	Diagnoses	Pigmented Epithelioid Melanocytoma	Common Blue Naevus	Deep Penetrating Naevus
	Clinical features	Darkly pigmented papule or nodule	Darkly pigmented papule or nodule	Blue, blue-gray or blue-black papule, nodule or plaque
	Dermoscopic patterns	Homogeneous blue-black pigmentation (present case)	Homogeneous blue-black pigmentation	Homogeneous structureless pigment pattern with variety of colours (blue, white-blue, black, brown and polychromatic)
Histological features	Location	From epidermis to deep reticular dermis	Superficial dermis	From superficial to deep reticular dermis and sometimes subcutis
	Silhouette	Wedge shaped, infiltrative margins	Poorly circumscribed	Relatively symmetric, well demarcated, wedge shaped
	Cell type	Heavily pigmented epitheliod and spindle cells (peripherally located)	Bipolar dendritic spindle cells (generally pigmented)	Oval epitheliod cells with dusty pigment, bipolar dendritic spindle cells
	Melanophages	Numerous	Scattered	Numerous in a chessboard pattern
	Cellular atypia	Pronounced	Minimal	Moderate
	Mitoses	Rare	Absent	Rare
	Immunohistochemistry	S-100+HMB-45+	S-100+HMB-45+	S-100+HMB-45+

PEM were recently summarized (6) to consist of a proliferation of spindle, epithelioid and large epitheliod melanocytes - abundant with melanin - arranged in sheets and/or nests localized in the dermis, from where they may infiltrate the subcutaneous fat or even the epidermis; cells show occasional atypia; positivity for immunohistochemical markers are the same as in melanoma (6). PEM, including the present case, shows, indeed, morphologic characters that may be considered "intermediate" if compared to those of either melanoma or naevi (2,4) (Table 1). Interestingly, even molecular evidence supports PEM as a distinct melanocytic tumour (7): in fact, loss of heterozygosity at locus 17q22 to 24 of the gene coding for the protein kinase A regulatory subunit type 1 (R1α) was found in PEM, other than in naevi and in melanoma (7); indeed, "Carney complex" or loss of R1α expression are tipically found in PEM and "Carney complex"- associated epithelioid blue naevus (8).

Over the last years, dermoscopy has remarkably enhanced the diagnostic accuracy of cutaneous melanocytic lesions. At the best of our knowledge, however, only two studies, apart from the present one, described up to date the dermoscopic appearance of PEM. In the first case, Vezzoni et al. (9) observed a homogeneous black-bluish pattern, irregular pseudopods in one quadrant, gray-blue areas arrayed at the periphery, and brownish perimetral hyperpigmentation (9). In the second case, Sadayasu et al. (10) reported a focal red-black area in the blue-whitish monotonous pattern of the tumour (10). In the present case we observed a homogeneous blue-black pigmentation, without any other dermoscopic sign (Fig. 1B). Since, therefore, three different dermoscopic patterns were described in three different cases of PEM, we are in agreement with Authors who propose that "comparative dermoscopy studies on a series of PEM are needed" (10).

Sentinel lymph-node investigation was not performed in the present case. As a matter of fact, Ito & Mihm (11) together with many other Authors recommended to perform it, whilst Mandal et al. (5) together with many other Authors claimed that it appears to provide, in patients with PEM, little, if any, evidence of the

lesion's biological potential and its risk of progression to metastatic disease. Indeed, in a most recent review-article dealing with sentinel lymph-node biopsy in non-melanoma skin cancer patients, Matthey-Giè et al. (12) stated that management of such patients is still a matter of debate in the absence of randomized trials (12).

As far as the biologic/prognostic identity of PEM is concerned, this is still controversial. In fact, PEM may be understood in the context of one of the following two categories: (i) a melanocytic lesion can only be identified either as a (benign) naevus or as a (malignant) melanoma (13); (ii) an intermediate (prognostic) category of melanocytic lesions may be envisioned between common naevus and melanoma, termed "melanocytoma" (5,11, 14). Clearly, long term follow-up is required (3,4) to discriminate whether PEM is a "metastasizing or recurring melanocytic tumour with a favourable clinical outcome" (1), or "simply an uncommon variant of melanoma" (15). In the cases of PEM reported in the literature, follow-up data are variable between a period of 16 months (11) and a period of seven years (6) after excision. In the initial paper (1) the mean follow-up period, regarding 26 patients, was 32 months, and only one patient experienced distant metastasis. Four years after the excision, our patient is well and displayed no metastasis or local recurrence: obviously she needs, however, continuous observation.

In conclusion, the present case can add evidence to the assumption that PEM shows unique morphologic features, and may, on the other hand, support, although within the limits of current follow-up period, the hypothesis that PEM might also have some biologic identity: this last possibility, however, needs observation of further cases with long follow-up.

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