

# Epidermolysis bullosa nevi: clinical, dermatoscopic and histological features in a case of recessive dystrophic form \*

Nevo da epidermólise bolhosa: aspectos clínicos, dermatoscópicos e histológicos em um caso de portador da forma distrófica recessiva

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**Abstract:** Acquired melanocytic lesions may present unusual clinical features in all forms of hereditary epidermolysis bullosa. These lesions are known as "EB nevi", and often pose a diagnostic challenge for dermatologists given their resemblance - clinically, dermoscopically and histologically - to melanoma. The lesions have been reported in all types of hereditary EB, most of them in childhood. We report the case of a 6-month-old boy suffering from recessive dystrophic epidermolysis bullosa (RDEB) that presented as a large pigmented lesion on his left thigh. We decided to monitor the lesion closely since we considered that the clinical and pathological aspects of the lesion were compatible with the description of other previously reported cases of EB nevi.

**Keywords:** Epidermolysis bullosa dystrophica; Nevi and melanomas; Melanoma

**Resumo:** As lesões melanocíticas adquiridas podem apresentar aspecto clínico não-usual em pacientes portadores de epidermólise bolhosa hereditária. Essas lesões são conhecidas como "nevus EB" e, muitas vezes, constituem um desafio diagnóstico ao dermatologista por apresentarem características clínicas, dermatoscópicas e histopatológicas semelhantes às encontradas no melanoma. Não são exclusivas de nenhuma forma de epidermólise bolhosa e têm sua frequência aumentada na infância. Relata-se o caso de um doente do sexo masculino, de 6 meses de idade, portador da forma distrófica recessiva da doença, com lesão pigmentada de rápido crescimento na coxa esquerda. Optou-se por seguimento clínico da lesão, considerando que os aspectos clínicos, dermatoscópicos e histológicos eram compatíveis com a descrição de outros casos de nevo EB previamente descritos.

**Palavras-chave:** Epidermólise bolhosa distrófica; Nevo; Melanoma

Received on 25.03.2010.

Approved by the Editorial Board and accepted for publication on 14.07.2010.

\* Trabalho realizado no Departamento de Dermatologia do Hospital das Clínicas da Universidade de São Paulo – Ambulatório de Dermatologia Pediátrica.

Conflict of interest: None / *Conflito de interesse: Nenhum*

Financial funding: None / *Suporte financeiro: Nenhum*

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## INTRODUCTION

Epidermolysis bullosa (EB) consist of a group of hereditary diseases characterized by fragile skin, and which can affect mucous membranes and other body organs. EB are transmitted genetically, with varying degrees of severity. Minor trauma can lead to blistering and exulcerations. Dystrophic EB is caused by mutations in the gene encoding collagen VII, and the mode of transmission can be autosomal dominant or recessive. Three main subtypes exist: (1) dominant dystrophic EB; (2) recessive dystrophic EB [Hallopeau-Siemens type]; and (3) non-recessive dystrophic EB [Hallopeau-Siemens type].

In 2001, Bauer *et al.* suggested the term *EB nevi* for melanocytic lesions in patients with epidermolysis bullosa.<sup>1</sup> These lesions, found in all types of EB, are clinically significant because their clinical, dermoscopic and histopathological characteristics often resemble cutaneous melanoma. However, no cases of melanoma were observed during the 20-year prospective study of 86 cases of epidermolysis bullosa.

## CASE REPORT

6-month-old white male patient with recessive dystrophic EB. The diagnosis of EB was based on family history, clinical features and immunomapping using monoclonal antibodies against the bullous pemphigoid antigen, laminin, collagen IV and collagen VII.

The patient had blisters all over his body from birth, including in the oral mucosa. At 4 months the mother noticed a rapidly-growing pigmented lesion on his left knee. The lesion was asymmetric, with irregular borders and with the color varying from shades of brown to black, measuring 14x7 cm. (Figures 1A and 1B).

At 5 months the lesion had extended to the left calf, increasing in size to 14x11 cm. On clinical examination we noted the asymmetry of the nevus, with irregular borders, a network similar to the pseudopodia observed during the dermatoscopic examination (Figure 2A), and the variegated brownish/ black color of the lesion.

Dermoscopic examination revealed a pigmented melanocytic lesion, with branched streaks, bluish-gray veil, black and brown globules and images resembling pseudopodia (Figure 2B). These features are found with variable frequency in cutaneous malignant melanoma.

Biopsies were performed on separate occasions on different areas of the lesion. The histopathological examinations showed subepidermal cleft and the presence of atypical melanocytes, either solitary or arranged in nests along the dermoepidermal junction, and sometimes in the epidermis. Melanocytes were not seen in the dermis (only melanophages). Due to



FIGURE 1: A. Nevus of epidermolysis bullosa in a patient with the recessive dystrophic form. B. Clinical aspect and evolution of the pigmented lesion on left leg

the intense pigmentation of some samples the slides were subjected to a preparation of hydrogen peroxide, as a result of which atypical melanocytes could be clearly observed (Figures 3 and 4).

Due to the large size of the nevus, the patient's parents refusal to allow surgery, and descriptions in the literature of the biological behavior of other EB nevi, we chose strict clinical and histopathological follow-up of the pigmented lesion. After one year we noted that the lesion had decreased significantly in size. After 4 years monitoring the case we observed no further changes, and the child remains in good general health.

## DISCUSSION

EB nevus was first described by Bauer *et al.* in 2001<sup>1</sup> as acquired melanocytic nevi affecting patients with all the forms of hereditary epidermolysis bullosa. While EB nevus show no predilection for either sex, its incidence is higher in children aged between 7 and 11 years, and in carriers of the recessive dystrophic and simple forms.<sup>2,3</sup> The lesions appear to be more common in skin sites subject to trauma, with frequent formation of blisters, scars and *milia*.

The lesions tend to appear suddenly and grow rapidly, often being diagnostically confused with cutaneous melanoma. The lesions are usually irregular in shape, of variegated color, and the primary EB nevi

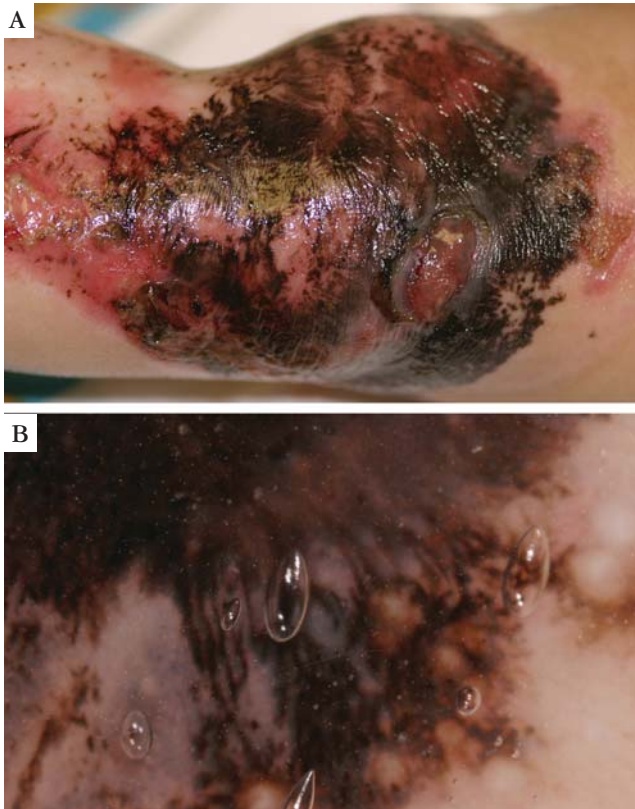


FIGURE 2: A. Detail of a pigmented lesion and dermatoscopic examination. B. The same aspect resembling pseudopodia can be seen on clinical examination and dermoscopy

occasionally spawn secondary satellite lesions. The dermatoscopic and histopathological aspects possess certain characteristics similar to melanoma, but it has been reliably established that when these are present in the EB nevi they are an exception to the diagnosis of malignancy.<sup>4</sup>

It has been postulated that the formation of globules in chronic epidermolysis bullosa causes inflammation and/or fibrosis which could cause changes in the melanocytes. We do not know for sure which mechanisms lead to this abnormal activation of melanocytes. A number of theories have been suggested, for example: (i) when globules are formed in the EB nevi, the interruption of the melanocytes in the cleft sites might act as a Köebner phenomenon, thus stimulating production of atypical melanocytes, or (ii) the formation of an EB blister could cause the spread of melanocytes that are already present in the skin and which, by the action of pro-inflammatory cytokines produced in the tissue repair process, could proliferate and lead to the emergence of the EB nevi.<sup>5,6</sup>

EB nevi could be explained as a collision between an inflammatory disease and a pigmented lesion, resulting in atypical nevi. Other situations can also trigger seemingly atypical nevi e.g. lichen sclero-

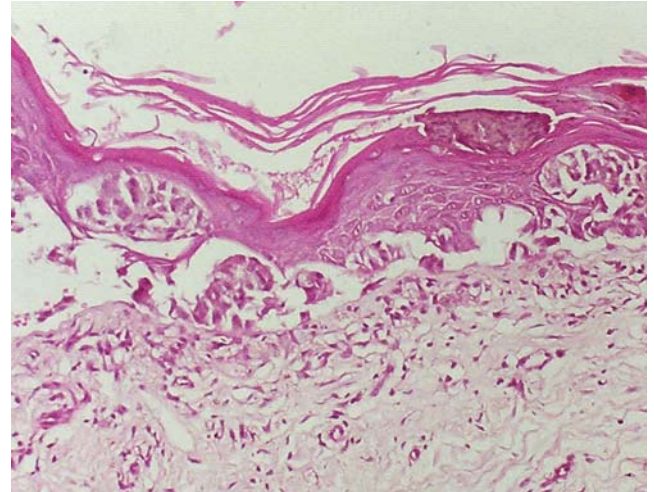


FIGURE 3: Nests of atypical melanocytes in the epidermis (low magnification)

sus et atrophicus coexisting with moles.<sup>7</sup> A parallel also exists with cases of erythema multiforme (EM) or Stevens-Johnson syndrome, in which nevi suddenly appear following improvement of the initial cutaneous inflammation.<sup>8</sup>

Some authors recommend 6-monthly follow-up of EB nevi, performing biopsies of the most heavily pigmented areas when dermatoscopic criteria are significant.<sup>9</sup> Prophylactic excision of the nevus is not recommended since these patients have skin fragility and poor healing resources.

It is well-established that chronic inflammatory diseases that evolve with scarring, such as epidermolysis bullosa, are at increased risk from squamous cell carcinoma.<sup>10</sup> Some reports suggest an even more substantial risk of developing melanoma in recessive dystrophic epidermolysis bullosa, but no well-documented cases have been published in the literature, in con-

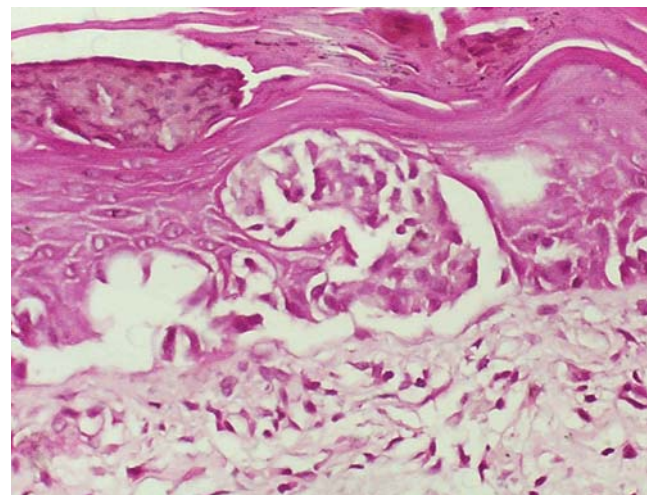


FIGURE 4: Presence of atypical melanocytes (high magnification)

trast to the link with squamous cell carcinoma.<sup>11</sup>

Dermatologists and pathologists should be aware of the phenomenon of EB nevi in order to avoid unnecessary and therapeutic measures that could lead to increased patient morbidity. When a diagnosis of melanoma is considered in a patient with epidermolysis bullosa, the possibility of it being an EB nevus should never be excluded.

Pigmented lesions classified as EB nevi require clinical, dermatoscopic and histopathological follow-up, given that these are often large nevi that rule out surgery. The possibility of benign behavior of the lesion, with spontaneous regression in many cases (as in the patient described above), should also be taken into account. □

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How to cite this article / *Como citar este artigo*: Melo JN, Teruya PY, Rivitti-Machado MC, Valente NS, Sotto MN, Oliveira ZNP. Epidermolysis bullosa nevi: clinical, dermatoscopical and histological characteristics in the case of a carrier of the recessive dystrophic form. *An Bras Dermatol.* 2011;86(4):743-6.