



# Epidermolysis bullosa nevus: case report and literature review \*

Nevo da epidermólise bolhosa: caso clínico e revisão da literatura

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**Abstract:** Acquired melanocytic lesions resembling malignant melanoma have been described in all major categories of Epidermolysis bullosa and referred to as "Epidermolysis bullosa nevi". They easily induce to diagnostic error, although no malignant transformation has been reported. We report the development of a large acquired melanocytic nevus at a site of recurrent blisters in a 5-year-old child with Epidermolysis bullosa simplex. The global dermoscopic pattern was suggestive of benignity, and the histopathological findings were compatible with a compound melanocytic nevus. This is the first published case of Epidermolysis bullosa nevi in Brazilian literature. Despite their benign behavior, we emphasize the importance of regular clinical and dermoscopic monitoring, since a malignant course still cannot be totally excluded.

**Keywords:** Biopsy; Dermoscopy; Epidermolysis bullosa; Melanoma; Nevus, pigmented

**Resumo:** Lesões melanocíticas adquiridas assemelhando-se à melanoma têm sido descritas nos principais grupos da Epidermólise bolhosa, e referidas como "Nevos da Epidermólise bolhosa". Induzem facilmente ao erro diagnóstico, apesar de nenhuma transformação maligna ter sido descrita.

Relatamos o desenvolvimento de um nevo melanocítico adquirido grande no local de bolhas recorrentes em uma criança de 5 anos portadora de Epidermólise bolhosa simples.

O padrão dermatoscópico global foi sugestivo de benignidade, e os achados histopatológicos foram compatíveis com um nevo melanocítico composto.

Este é o primeiro caso de um Nevo da Epidermólise bolhosa publicado na literatura brasileira.

**Palavras-chave:** Biópsia; Dermoscopia; Epidermólise bolhosa; Melanoma; Nevo pigmentado

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## INTRODUCTION

Epidermolysis bullosa (EB) nevus is the name given to the acquired melanocytic nevus that develops in Epidermolysis bullosa (EB).<sup>1</sup> Despite its benign course, this nevus is particularly important for being clinically indistinguishable from melanoma, according to the ABCD rule.<sup>1-6</sup> As it simulates melanoma, this may induce to unnecessary aggressive treatment.

Our review of the literature revealed that it occurs predominantly in dystrophic forms of EB. The case presented below will be the fourth case published in the international literature of EB nevus in an Epidermolysis bullosa simplex patient, and it is the first case published in Brazilian literature.

## CASE REPORT

A white, 5-year old female patient diagnosed with Epidermolysis bullosa simplex (EBS) was referred for evaluation of a pigmented lesion with progressive growth, for approximately three months, located on the fourth left toe, the site of recurrent bullous lesions. The daughter of non-consanguineous healthy parents, she had presented recurrent bullous lesions since the first days of life, mainly on the extremities.

Upon clinical examination, the patient presented flaccid blisters and eroded areas on the soles of feet and between the toes. On the fourth toe there was a pigmented macula affecting almost its whole extension, asymmetrical, with irregular margins and a few satellite lesions on its periphery (Figure 1). There was pigmentation variation with black, light brown and dark brown colors. The dermoscopic aspect of the macula included irregular dark brown dots on its surface and aggregated globules on its periphery (Figures 2 and 3). On the plantar surface were



FIGURE 2: Dermoscopy of the lesion center – multiple irregular brownish dots

observed fibrillar or parallel furrow patterns, with some isolated black dots on the periphery (Figure 4). No vascular structures were observed. The global dermoscopic pattern of the pigmented lesion suggested benignity and was compatible with the homogeneous globular pattern.

Histopathology of a dense pigmented area revealed the presence of nests of regular melanocytes located on the upper and middle dermis and on the dermoepidermal junction, without cellular or architectural atypical structures (Figure 5). No upper pagetoid migrations of melanocytes and mitotic figures were observed. Therefore, the histopathological findings were compatible with a compound melanocytic nevus.

The clinical and histopathological findings led to an EB nevus diagnosis.



FIGURE 1: Asymmetrical pigmented lesion with irregular borders, satellite lesions and various colors



FIGURE 3: Dermoscopy of the periphery of lesion – aggregated irregular globules between areas of healthy skin



FIGURE 4: Dermoscopy of the plantar surface – parallel furrow and fibrillar patterns

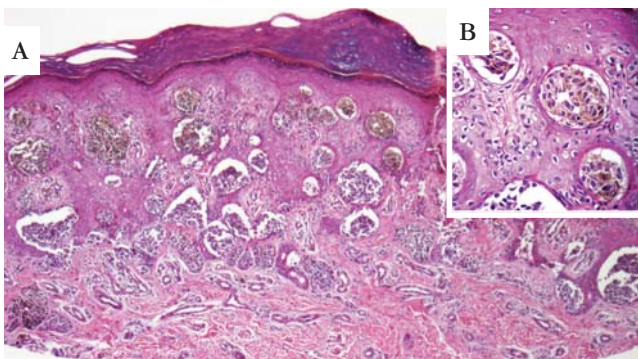


FIGURE 5: A. Nests of melanocytes restricted to dermoepidermal junction and papillary dermis (HE, 40X) B. Detail of regular nests, without atypical forms (HE, 100X)

Considering the benign behavior of these nevi described in the literature, we opted for periodical follow-up of this patient.

## DISCUSSION

Epidermolysis bullosa represents an heterogeneous group of mechanobullous diseases, genetically determined and secondary to an intrinsic defect in the structural component of the basement membrane zone (BMZ). It is characterized by cutaneous fragility and bullous lesions that appear as result of trivial traumas.<sup>15</sup>

Uncommon large and eruptive melanocytic nevi have been described in EB patients.<sup>16</sup> Their similarity with melanoma easily induces to diagnostic error.

The EB nevi term was proposed by Bauer and collaborators in 2001 to designate acquired melanocytic lesions that have a peculiar combination of clinical, histopathological and biologic criteria.<sup>1</sup> In

their case study with 86 EB patients, they found 12 patients affected in the three main EB groups, suggesting that EB nevi are not so rare among EB patients.

The onset of EB nevi usually occurs in childhood and appears as a large, eruptive and pigmented lesion on areas of recurrent bullous lesions. It has marked asymmetry, pigmentation variation, cicatricial areas and regression focuses.<sup>1,3-6</sup> Such characteristics suggest a false impression of malignancy, reinforced when the pigmented lesion shows continuous and sometimes sudden growth, with onset of satellite lesions, as occurred in our patient.<sup>2</sup>

The EB nevus has a dynamic evolution, with fast growth and possible changes on its surface.<sup>15</sup> Bauer and collaborators described two patients with generalized atrophic EB, in whom similar lesions lost their pigmentation and their surfaces became papillomatous in a period between seven and eight years.<sup>1</sup> Cash and collaborators described another patient who had dystrophic EB and an EB nevus that lost pigmentation after 18 months of follow-up.<sup>4</sup>

Considering that morphological alterations in pigmented lesions are described as significant predictors of malignancy, it was suggested that the EB nevus could be an exception to this rule, since continuous clinical modifications of these nevi have been documented for 25 years, and cutaneous melanoma was excluded through repeated histological evaluation.<sup>1,2,7</sup>

Lanschuetzer and collaborators analyzed the dermoscopic characteristics of 23 EB nevus lesions in 11 patients.<sup>2</sup> This study found a high frequency of dermoscopic criteria associated with melanoma as multicomponents (20 of 23), atypical pigmented network (17 of 23), globules and irregular dots (16 of 23), irregular pigmentation (22 of 23) and atypical vascular pattern (7 of 23). However, strong indicators for invasive cutaneous melanoma such as gray-blue areas, black dots and blue-white veil were not common characteristics of EB nevi. They observed a new vascular pattern similar to glomerular vessels, suggesting that it could be specific of EB nevi, representing an exaggerated neovascularization during the skin repair process. In the same study, most lesions presented false-positive results when the ABCD rules and Seven-Point method of dermoscopy were applied. Likewise, in our patient the EB nevus presented a false-positive result when dermoscopic algorithms were calculated, but the global dermoscopic pattern was compatible with the homogeneous globular pattern, which is suggestive of benignity. This means that the EB nevus represents an exception to diagnostic dermoscopic algorithms, although the global dermoscopic evaluation frequently permits an estimation of a benign nature.<sup>2</sup>

The histopathological pattern of the EB nevus

may be compatible with a compound/ junctional nevus, or a persistent nevus.<sup>1,6</sup> The first pattern was described in three EBS cases in the literature, and was also observed in the case here described.<sup>1,4,5</sup> The persistent nevus pattern is more frequent in recessive dystrophic EB patients.<sup>1,4,5</sup> A challenge related to the EB nevus histopathology is the difficulty in distinguishing a persistent melanocytic nevus pattern from a melanoma pattern.<sup>4</sup> Monomorphic melanocytes, absence of mitotic figures, normal proliferative rates and knowledge about the EB nevus phenomenon may help distinguish them.<sup>4</sup>

The EB nevus pathogenesis is not completely understood. The most accepted hypothesis is that repeated traumas to the basal layer where recurrent blisters appear could induce proliferation of melanocytes, according to inflammation and reepithelization processes.<sup>1,6</sup> The phenomenon of Koebner, represented as the expansion of an incipient nest of nevic cells, or of melanocytes present in the epidermis or in the follicular epithelium, could be involved.<sup>1,4,5,6,8</sup> In addition, in EBS the lysis of basal keratinocytes, which is associated with the complete destruction of melanocytes, could modify the normal relationship between these two cells, and residual melanocytes would proliferate freely.<sup>3</sup> The disordered arrangement of these melanocyte clones could explain the dermoscopic characteristics seen in EB nevi.<sup>2,3,4</sup>

Although large and eruptive melanocytic nevi have already been described in the main EB categories, there is predominance of dystrophic and junctional forms of the disease.<sup>1,5</sup> The complete loss of a specific protein of the basement membrane zone (BMZ) in the recessive forms of EB would favor development of these nevi.<sup>1,3,5</sup> Note that the EB nevus was reported in only three EBS patients; our case is the fourth one described in the international literature, and the first described in Brazilian literature.

Similar cases of eruptive melanocytic nevi were described following Stevens-Johnson syndrome episodes, erythema multiforme and associated with lichen sclerosus and atrophicus<sup>9-12</sup>. The proposed pathogenesis is similar to that related to EB nevus.<sup>3,9-12</sup>

There is only one report describing a child with bullous pemphigoid located on the vulva, where recurrent blisters developed, an atypical melanocytic nevus with clinical and dermoscopic characteristics of melanoma.<sup>13</sup> This was the first case where a melanocytic nevus developed on the site of bullous lesions, in bullous autoimmune and subepidermal disease in childhood.

Monitoring EB nevus patients for over 25 years did not make any malignant alteration evident.<sup>1,2</sup> Considering the benign course of these nevi, we adopted a conservative therapy, with periodical follow-up of our patient.

In conclusion, we emphasize the importance of clinical, dermoscopic and histopathological studies of these nevi to avoid diagnostic error and unnecessary interventions. Despite their benign course, we point out that it is very important to make a differential diagnosis in comparison with melanoma, as well as regular monitoring, since malignant evolution cannot be completely excluded. □

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