

International Journal of Clinical Pathology and Diagnosis

Kantarjiev V, et al. Int J Clin Pathol Diagn: IJCP-127.

DOI: 10.29011/2577-2139.000027

Case Report

Epidermolysis Bullosa Nevi -A Concept of Awareness

Vessel Kantarjiev¹, Todor Yordanov¹, Valentina Broshtilova^{1,2*}

¹Department of Dermatology and Venereology, Military Medical Academy, Sofia, Bulgaria

²Department of Infectious diseases, parasitology and dermatovenereology, Medical University, Bulgaria

***Corresponding author:** Valentina Broshtilova, Department of Dermatology and Venereology, Military Medical Academy, Sofia, Bulgaria. Tel: +359888257905; Email: broshitolova@mail.bg

Citation: Kantarjiev V, Yordanov T, Broshtilova V(2019) Epidermolysis Bullosa Nevi - A Concept of Awareness. Int J Clin Pathol Diagn: IJCP-127. DOI: 10.29011/2577-2139.000027

Received Date: 17 December, 2018; **Accepted Date:** 18 January, 2019; **Published Date:** 28 January, 2019

Abstract

Melanocytic nevi are benign hamartomatous proliferations of melanocytes. Large, irregular, asymmetric melanocytic lesions, frequently suggestive of melanoma, often evolve in patients with epidermolysis bullosa, hence, making the clinical and dermoscopic differentiation extremely unequivocal. Herein, we critically approach the concept of “epidermolysis bullosa nevi”, describing a 26-year-old Caucasian woman with epidermolysis bullosa simplex, multiple dysplastic nevi on sites of pre-existing vesiculo-bullous exanthema, and a rapidly growing melanocytic proliferation on her back, excised and verified as a malignant melanoma. A high index of suspicion is always needed despite the widely accepted hypothesis of more benign nature of melanocytic tumors in all patients with epidermolysis bullosa.

Keywords: Dermoscopy; Epidermolysis Bullosa Nevi; Malignant Melanoma

Introduction

Epidermolysis Bullosa (EB) represents a heterogeneous group of hereditary bullous dermatoses due to intrinsic defects of the basement membrane zone structural components [1]. Those patients often develop large, irregular, rapidly growing nevi with clinical features of atypical melanocytic proliferations on sites of pre-existing vesiculo-bullous eruption [2]. The pigmented lesions often show clinical and dermoscopic features of malignancy, such as asymmetry, irregular borders, and color variegation, however, a malignant transformation has been randomly described [3]. Thus, the hypothesis of “EB nevi” that recommends a more conservative management strategy of close clinical, dermoscopic and occasionally histologic examinations for EB patients, was introduced [4]. Herein, we present a case of malignant melanoma, arising in a patient with EB simplex, to highlight the importance of critically approach all patients, irrelevant to previous clinical entity labels and controversy.

Case Report

A 26-year-old Caucasian female with multiple dysplastic nevi referred to our Department for routine examination. The patient was clinically, histologically and immunofluorescently diagnosed with EB simplex since birth. She experienced multiple vesiculo-bullous eruptions on sites of mechanical trauma. Most of her melanocytic lesions appeared on such previously affected areas. In the last six months she noticed an enlarging and changing color mole on the right subscapular zone (Figure 1). Dermoscopy showed multicomponent pattern with irregular form and structure of the lesion, uneven net with sharply outlined borders and globules with different calibers. Multiple colours of red, light brown, dark brown, blue and white, were also presented-seen (Figure 2). Histological sample displayed a wide non-circumscribed melanocytic lesion presented by atypical fusiform melanocytes with vertical, upward, pagetoid spreading, and horizontal bridging with penetration into the papillary dermis (Figure 3). Nests of pre-existing dermal nevus were seen at the periphery of the specimen.



Figure 1: Irregular, asymmetrical lesion on the right subscapular area of the patient.

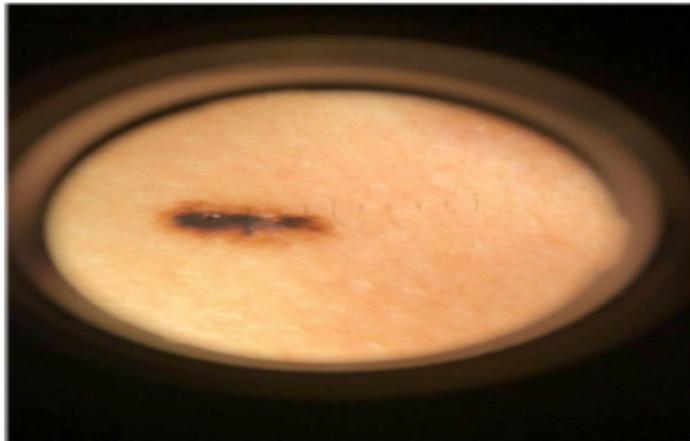


Figure 2: Dermoscopic features of the pigmented lesion.

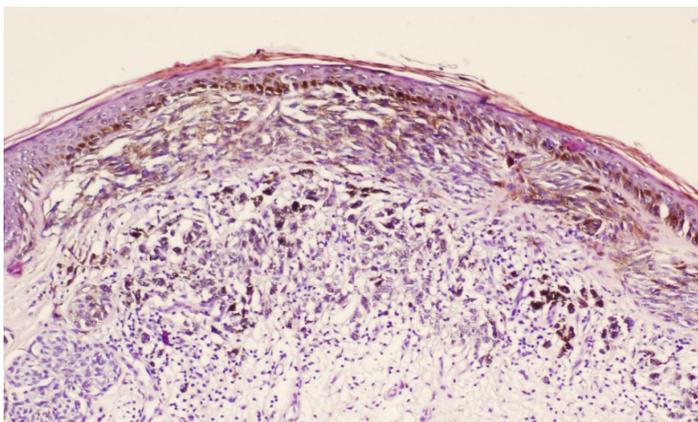


Figure 3: Histological findings of superficial spreading melanoma.

A superficial spreading melanoma (Clark II, Breslow 0,25mm), without ulceration and active stromal reaction, arising on the site of pre-existing dermal melanocytic nevus, was con-

cluded. Immunohistochemical markers confirmed the pigmented character of the lesion and showed medium to high proliferative index. On account of the localization, size, clinical and dermatoscopic features, the lesion was radically removed.

Discussion

EB is an inherited mechano-bullous disorder with multiple variations, characterized by chronic relapsing course and numerous complications such as infections, joint and gastro-intestinal damage, non-melanoma skin tumors, etc[5]. Large, eruptive, asymmetrical nevi have been described to appear on sites of vesicles and blisters in EB patients[6]. Initially reported in generalized atrophic benign EB, multiple nevi seem to be a frequent phenomenon in all EB patients, thus suggesting the hypothesis of “EB nevi” [7]. Two pathogenetic mechanisms seem to play crucial role in the development of the pigmented lesions. First, the higher proliferation index of the affected keratinocytes on the sites of repetitive disruption, promote local nevus cell nests or individual melanocytes to undergo simultaneous proliferation. Second, the free-floating melanocytes in the cavity of the EB blister migrate and settle at its periphery and proliferate in the micro-environment of the surrounding regenerating keratinocytes. A burst of cytokines and growth factors have been detected at the sites of such vesiculo-bullous defects – hepatocyte growth factor, interleukin 8, granulocyte-macrophage colony-stimulating factor, prostaglandin E2, and leukotriene 4, thus potentially enhancing melanocytic proliferation [8]. The eruption of various melanocytic lesions is of significant clinical importance, since they may act as simulators and precursors of malignant melanoma. Of note, some clinical and dermoscopic observations have shown more benign character of EB nevi [9]. A 24-month follow up of EB patients showed that suspected lesions undergo clinically and dermoscopic spontaneous involution [10].

In 2013 Hocker et al. published the most important differential features of EB nevi compared to melanoma malignum on terms of affected age group, localization on the pathological lesions, presence of near-by lesions and clinical behaviour in time [11]. Histological finding in EB nevi demonstrates well-defined nests with different calibers of mature nevus cells. Interestingly, EB nevi show analogy to recurrent nevi after incomplete nevus surgical excision or trauma. Such traumatized moles also frequently mimic melanoma, clinically, dermoscopically and histologically [12]. While dermoscopy and, more recently, Reflectance Confocal Microscopy (RCM) have proven to be valuable tools in the diagnosis of most pigmented lesions, little is currently known about their clinical value in the differential diagnosis of recurrent melanocytic proliferations [13]. Longo et al. investigated dermoscopic and RCM features of seven histopathologically diagnosed cases of recurrent melanocytic proliferations [13]. Repigmentation occurring within the scar through dermoscopy was a clue suggestive for nevi, while a lateral spreading of the pigmentation, extending from the border

of the scar towards the surrounding normal skin was observed in all cases of melanoma. Although scar pigmentation is a frequent phenomenon, there are few papers on this subject [14].

Yoshida et al. reported the case of a 47-year-old patient with a mole on her left arm since childhood, where a darker pigmentation had been observed. A starburst pattern was seen on dermoscopy [15]. Histopathology diagnosed a melanocytic nevus with partial recurrence after minor trauma. Similarly to what happens in EB nevi, it was speculated that stimulation of melanin production might have been induced in the wound healing process [16]. Lanschuetzer et al. used dermoscopy to test usefulness of this technique in distinguishing EB nevi from melanoma [17]. Twenty-three nevi of 11 patients were analyzed with a dermoscope. Twenty of the 23 lesions were classified as having a multicomponent pattern or showed a 3-structure type pattern, both highly suggestive of malignant melanoma. More than half of the lesions achieved a high score for the ABCD and 7-point checklist. Nevertheless, strong morphologic indicators for invasive cutaneous melanoma, or a blue-whitish veil to represent a melanoma-induced acanthotic epidermis, were not observed. The authors conclude that unequivocal discrimination of the benign nature of EB nevi is often not possible and a regular follow-up is mandatory.

Conclusions

Based on the clinical, dermoscopic and histologic features, EB nevi can be considered a peculiar group of melanocytic proliferations. An expertise dermatologist has to be aware of their specificity in order not to be tempted to establish a more aggressive diagnosis and treatment. A clinical and dermoscopic/semestral review is more secure and convenient therapeutic strategy for these fragile dermatological patients. On the other hand, misled by the benign prognosis of EB nevi, the clinician risks to underestimate some melanocytic lesions with malignant nature. This is highly relevant to EB cases with pre-existing history of benign nevi with spontaneous regression. Therefore, we recommend an attentive clinical and dermoscopic follow-up for each pigmented lesion arising in EB patient.

References

1. Bauer JW, Schaeppi H, Kaserer C, Hantich B, Hintner H (2001) Large melanocytic nevi in hereditary epidermolysis bullosa. *J Am Acad Dermatol* 44: 577-584.
2. Botella-Estrada R, Nagore E, Sopena J, Cremades A, Alfaro A, et al. (2006) Clinical, dermoscopy and histological correlation study of melanotic pigmentations in excision scars of melanocytic tumours. *Br J Dermatol* 154:478-484.
3. Gllardo F, Toll A, Malveyh J, Mascaró-Galy JM, Lloreta J, et al. (2005) Large atypical melanocytic nevi in recessive dystrophic epidermolysis bullosa: clinicopathological, ultrastructural and dermoscopic study. *Pediatr Dermatol* 22: 338-343.
4. Natsuga K, Akiyama M, Sato-Matsumura KC, Tsuchiya K, Shimizu H (2005) Two cases of atypical melanocytic lesions in recessive dystrophic epidermolysis bullosa infants. *Clin Exp Dermatol* 30: 636-639.
5. Hoss DM, McNutt NS, Carter DM, Rothaus KO, Kenet BJ, et al. (1994) Atypical melanocytic lesions in epidermolysis bullosa. *J Cutan Pathol* 21: 164-169.
6. Bauer JW, Schaeppi H, Kaserer C, Hantich B, Hintner H (2001) Large melanocytic nevi in hereditary epidermolysis bullosa. *J Am Acad Dermatol* 44: 577-584.
7. FineJD, JohnsonLB, TienH (1994) Risk of skin cancers and inherited epidermolysis bullosa (EB): determination of differences across major EB subtypes, as assessed by lifetable analysis techniques. *J Invest Dermatol* 103: 848.
8. Lanschuetzer CM, Emberger M, Hametner R, Klausegger A, Pohla-Gubo G, et al. (2003) Pathogenic mechanisms in epidermolysis bullosa naevi. *Acta Derm Venereol* 83: 332-337.
9. Stavrianeas NG, Katoulis AC, Moussatou V, Bozi E, Petropoulou Hax, et al. (2003) Eruptive large melanocytic nevus in a patient with hereditary epidermolysis bullosa simplex. *Dermatology* 207: 402-404.
10. Lanschuetzer CM, Laimer M, Nischler E, Hintner H (2010) Epidermolysis bullosa nevi. *Dermatol Clin* 28: 179-183.
11. Hocker TL, Fox MC, Kozlow JH, Gonzalez JV, Shwayder TA, et al. (2013) Malignant melanoma arising in the setting of epidermolysis bullosa simplex: an important distinction from epidermolysis bullosa nevus. *JAMA Dermatol* 149: 1195-1198.
12. Hoss DM, McNutt NS, Carter DM, Rothaus KO, Kenet BJ, et al. (1994) Atypical melanocytic lesions in epidermolysis bullosa. *J Cutan Pathol* 21: 164-169.
13. Longo C, Moscarella E, Pepe P, Cesinaro AM, Casari A, et al. (2011) Confocal microscopy of recurrent naevi and recurrent melanomas: a retrospective morphological study. *Br J Dermatol* 165: 61-68.
14. Fuscaldi L, Bucard A, Quiroz Alvarez C, Barcaui C (2011) Epidermolysis bullosa nevi: report of a case and review of the literature. *Case Rep Dermatol* 3: 235-239.
15. Yoshida Y, Yamada N, Adachi K, Tanaka M, Yamamoto O (2008) Traumatized recurrent melanocytic naevus with typical starburst pattern on dermoscopy. *Acta Derm Venereol* 88: 408-409.
16. Schiffner R, Schiffner-Rhoe J, Vogt T, Landthaler M, Wlotzke U, et al. (2000) Improvement of early recognition of lentigo maligna using dermoscopy. *J Am Acad Dermatol* 42: 25-28.
17. Lanschuetzer CM, Emberger M, Laimer M, Diem A, Bauer JW, et al. (2005) Epidermolysis bullosa naevi reveal a distinctive dermoscopic pattern. *Br J Dermatol* 153: 97-102.