DERMATOLOGY PRACTICAL & CONCEPTUAL
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Melanocytic nevi and melanoma: overlapping criteria—the degree is the key

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Citation: Hurwitz RM, Buckel LJ, Summerlin DJ. Melanocytic nevi and melanoma: overlapping criteria—the degree is the key. Dermatol Pract Concept. 2014;4(2):5. http://dx.doi.org/10.5826/dpc.0402a05

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Introduction

Gross and microscopic criteria are morphologic and thus subjectivity abounds for the pathologist in the diagnosis of benign and malignant melanocytic proliferations [1]. The state-of-the-art criteria, often touted to be definitive, delineates between benign and malignant conditions clinically and histopathologically. This issue becomes murky, however, when the same criteria, on occasion, are present in both benign and malignant entities. This twist of fate is commonly referred to as overlapping criteria. This is exemplified frequently in benign melanocytic proliferations, i.e., melanocytic nevus and its variants (so-called combined nevus, Spitz's nevus, juvenile melanoma, dysplastic nevus, atypical nevus, nevus with architectural disorder and sever/moderate cytologic atypia, deep penetrating nevus, Reed's nevus, spindle-cell tumor, pre-melanoma, borderline melanoma, and recurrent/persistent melanocytic nevus, all of which are nothing more than a benign melanocytic nevus with findings focal common to those of the infamous melanoma. Overlapping criteria in benign and malignant melanocytic proliferations are well known and expected findings [1-3]. Because of the confusion that overlapping criteria create, it is essential to separate those proliferations truly benign from those that are in fact malignant. Furthermore, it is important, if not imperative, to recognize the degree of criteria, i.e., mild, moderate or extensive. In other words, is the criterion or criteria, an occasional finding, focal, isolated, or diffuse? What is the degree of criteria? Is it just happenstance, and does it matter? This is the question. The assessment of the degree of criteria is of the essence in order to arrive at an accurate diagnosis and avoid a misdiagnosis.

Discussion

The spectrum of criteria to differentiate a melanocytic nevus from melanoma is variable. Clinically, the criteria are few in number and include asymmetry, border, color, and diameter. However, many of the acknowledged criteria for the clinical diagnosis for melanoma may be found in other benign or malignant proliferations, such as melanocytic nevus, seborrheic keratosis, hemangioma, adnexal proliferations, basal and squamous-cell carcinoma, and lymphoma, to mention but a few. However, microscopically the criteria for melanoma are diverse and at times perplexing. They include asymmetry, poor circumscription, cellular/nuclear jumbling or crowding, atypia, pleomorphism, nuclear hyperchromatic and heterochromasia, increased small and/or large nuclei, large nucleoli, mitoses (typical and atypical), lack of maturation of solitary melanocytes and aggregations of melanocytes with progressive descent into the dermis, single cells predominate over aggregates of melanocytes within the epidermis, scatter of melanocytes within the upper spinous layer, atypical and typical pagetoid cells, pagetoid cells in pagetoid pattern, aggregates of melanocytes with bizarre shapes and confluence with pseudoacantholysis. The above criteria alone are not definitive for a diagnosis of

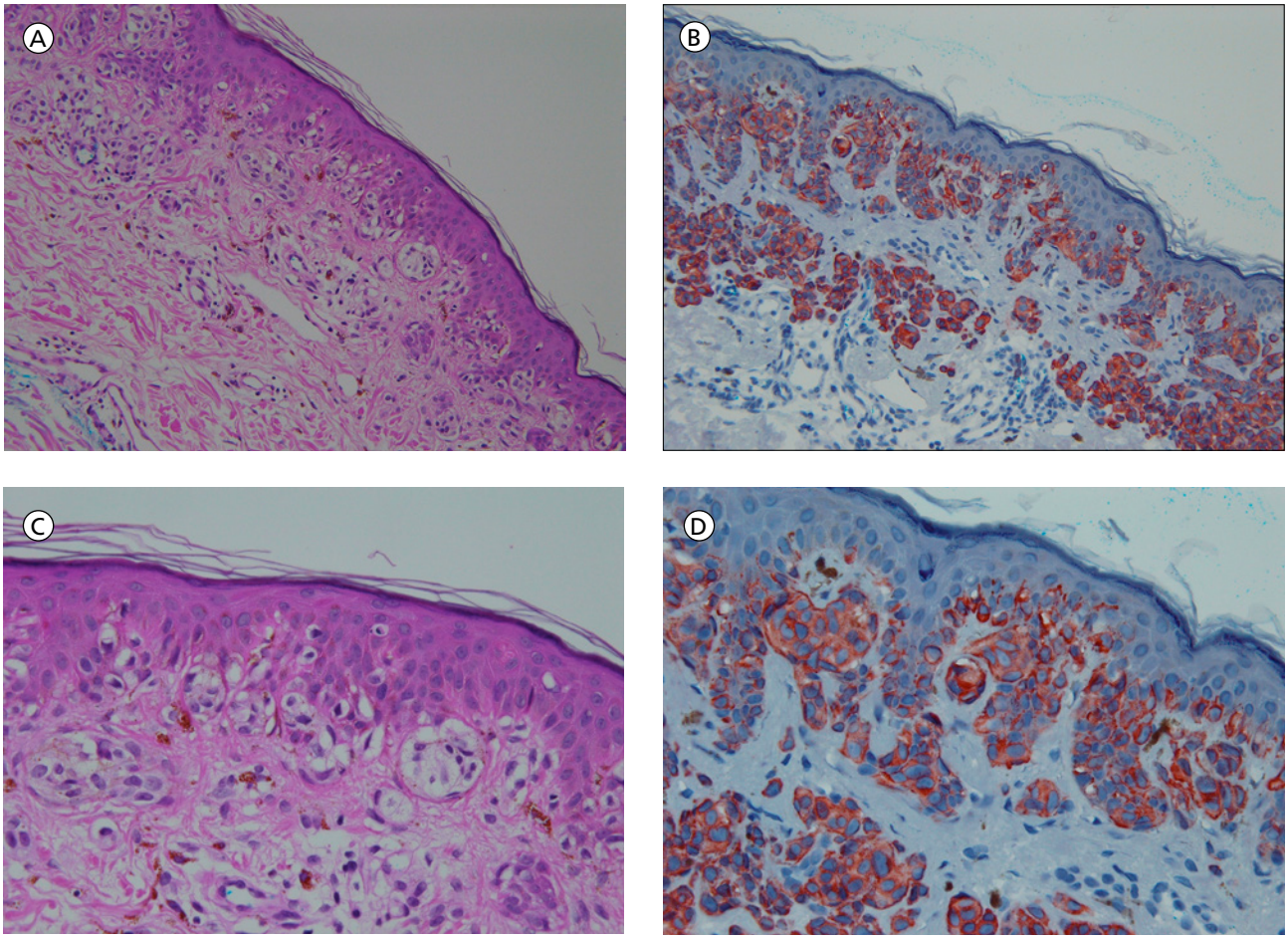

Figure 1. Melanocytic nevus on the back of a 22-year-old female. (A & B) (H&E) There are nests of melanocytes with relatively small round-oval nuclei, some with prominent pale staining cytoplasm, typical pagetoid cells, within the epidermis at the dermoepidermal junction and within the thickened papillary dermis. Focally, there is a scatter of solitary melanocytes within the upper spinous layer of the epidermis above the dermoepidermal junction, as well as maturation of melanocytes from the epidermis and dermis of typical pagetoid cells with loss of its prominent cytoplasm. (C & D) Melan A outlines the solitary and nested melanocytes. Focally there are scattered solitary melanocytes above the dermoepidermal junction within the upper spinous layer. [Copyright: ©2014 Hurwitz et al.]

melanoma because on occasion, if not repeatedly, they may be found in some benign melanocytic nevi. Therefore, it is crucial to consider the degree of the findings. In other words, the finding of a single, isolated criterion, which may occur in

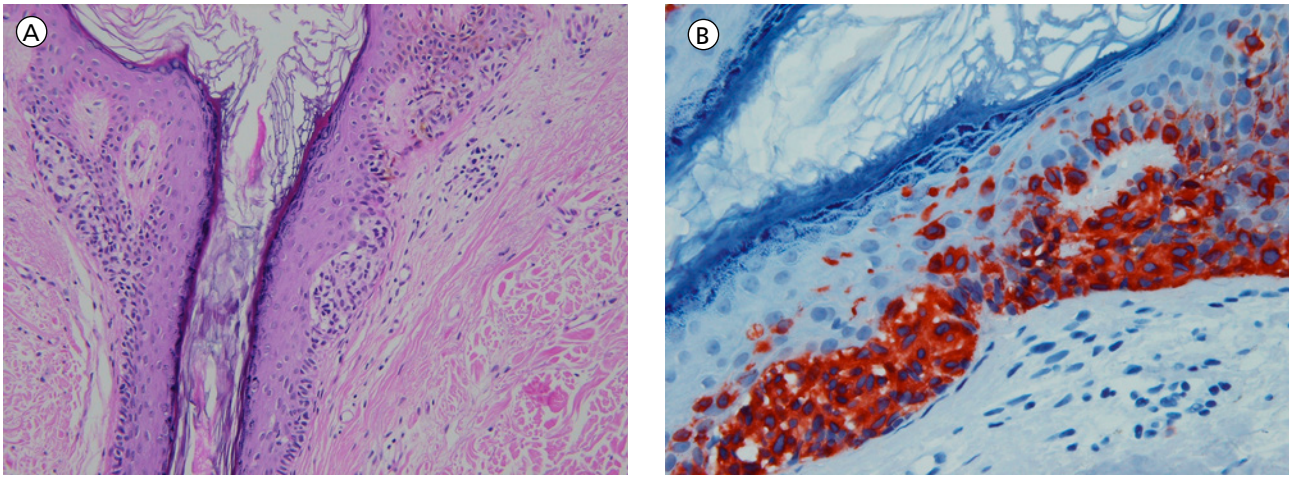

Figure 2. Melanocytic nevus on the back of a 60 year-old male. (A) (H&E) There are round and elongated confluent nests of melanocytes along with crowded solitary melanocytes with monomorphous small, round-oval nuclei with paltry cytoplasm, at the dermoepidermal junction and upper spinous layers of the infundibulum and surface epidermis. (B) Melan A outlines solitary, crowded and nested melanocytes, some confluent, as well as focally scattered solitary, monomorphous small round-oval melanocytes with paltry cytoplasm within the upper spinous layer of the epidermis and infundibulum. [Copyright: ©2014 Hurwitz et al.]

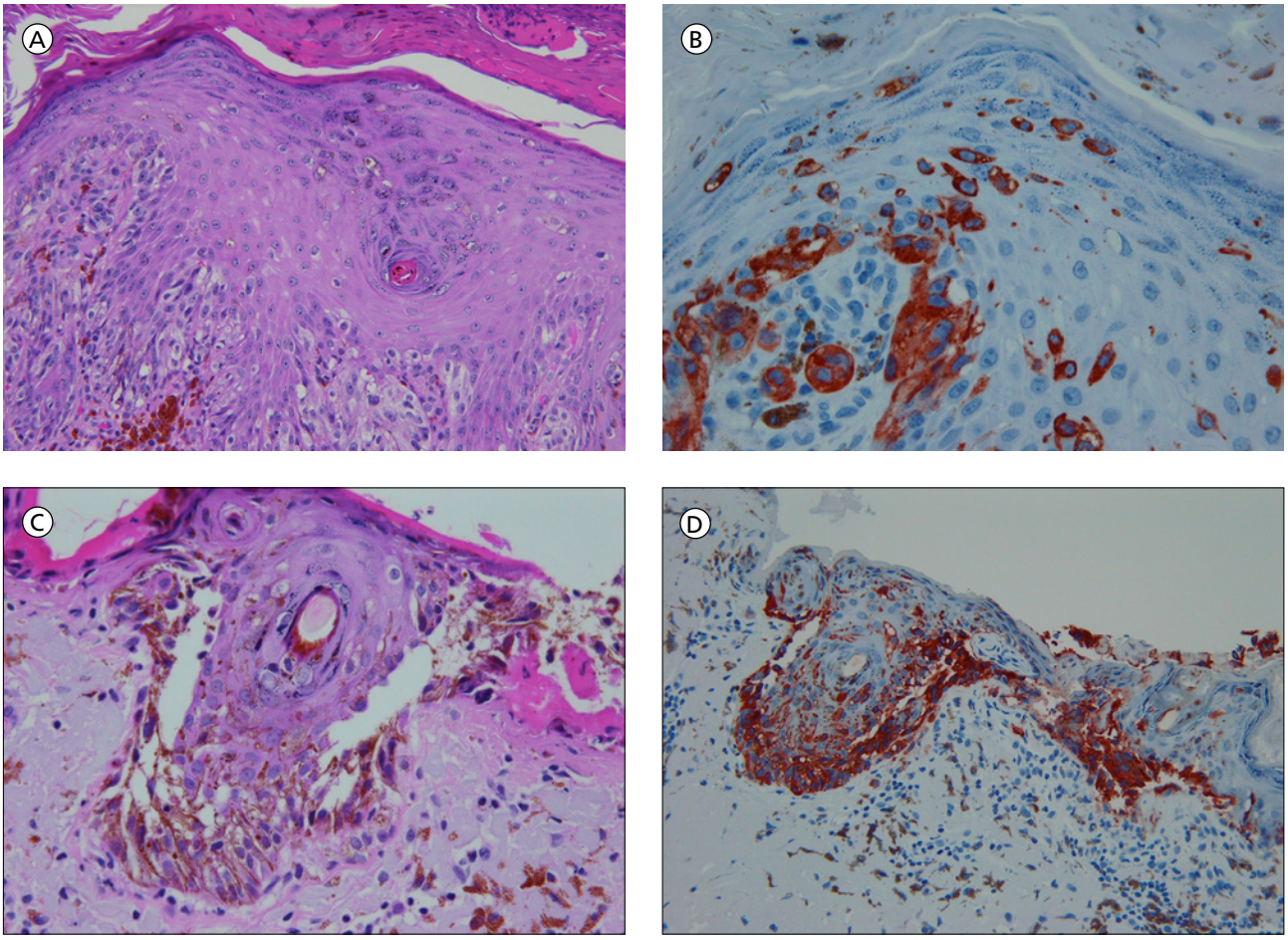

Figure 3. Melanoma on the cheek of a 94 year-old female. (A) (H&E) There are nested and solitary crowded atypical melanocytes with small and large round hyperchromatic nuclei, some with increased pale cytoplasm, scattered within the spinous layer at and above the dermoepidermal junction of the hyperplastic epidermis and infundibulum that houses scale-crust. (B) Melan A outlines solitary and nested, crowded, confluent, atypical melanocytes. (C) (H&E) Crowded solitary and nested confluent atypical melanocytes within the ulcerated and crusted surface epidermis and infundibulum overlying dermal severe solar elastosis, patchy lymphocytes and numerous melanophages. (D) Melan A outlines confluent nests of crowded solitary atypical melanocytes within infundibulum and epidermis. [Copyright: ©2014 Hurwitz et al.]

melanocytic nevus, or extensive criteria in multiple locations, which commonly occur in a melanoma, allows for the differentiation of melanocytic nevus from melanoma (Figures 1, 2, 3).

Nonetheless, a melanocytic nevus biopsied shortly after birth is well known to have criteria consonant with melanoma. In addition, a specific anatomic site of a melanocytic proliferation is referred to as a special site. Melanocytic nevi on special sites may have histopathologic finding similar to those of a melanoma. Special sites include areas such as the palm and sole, genitalia, perianal, buttocks, umbilicus, breast, ear, scalp, and regions intertrigenous. To boot, traumatized melanocytic nevi and persistent melanocytic nevi commonly and often regularly have comparable criteria to a melanoma. Oftentimes, the criteria on special sites, traumatized and persistent melanocytic nevi are present in a mild, moderate or widespread degree, e.g., focal and/or diffuse scatter of solitary and/or nested melanocytes above the dermoepidermal within the upper spinous layers, nuclear crowding with atypia in areas especially with excoriation, ulceration, scale-crust, or scarring. Accordingly, in view of the foregoing, it is essential to be knowledgeable of special sites, persistent melanocytic nevi, as well as the effects of trauma on a melanocytic nevus, to avoid a misdiagnosis.

Furthermore, it is worthy to acknowledge that, without a doubt, the relevance of subjectivity of the diagnosis by pathologists, especially in controversial melanocytic lesions, results in part in the totality of our attitudes and emotions. We are personally influenced, in addition to our degree of diagnostic threshold, by our indoctrination into the various aspects of controversial melanocytic neoplasia. The influence, of course, is predicated upon our enthusiasm and bias, as well as that of our mentors. During and after formal training, one's mentor may emphasize or diminish subjective morphologic findings, which influence and prejudice our acceptance or rejection of one criterion over another, especially over the degree of criteria. The result, at times, may be the over-diagnosis or the misdiagnosis of melanoma. This event is painfully evident in those thorny, demanding, controversial and problematical melanocytic lesions, which as a consequence of the foregoing, for sure, are expected to be logically and understandably

defensible, especially and regularly in medico-legal issues [5]. To be precise, overlapping criteria and the various range of degree of criteria, as a consequence, expose the practice of medicine and pathology for what they are: an ever changing, imperfect as well as a vexing science. Certainly, our individual concepts, views, beliefs and bias formed during and after our formal educational process (which by the way never ends) are significantly affected and powerfully influenced by our own and our mentor's interest and zeal, and how!

Summary

Summing up, the concept of the degree of criteria is the key to overlapping subjective criteria in melanocytic proliferations. This is the lesson to be learned. Although criteria that are used to come to a diagnosis of melanoma are well known and as a whole accepted, it is the degree or number or quantity of criteria, that is a few or many, that are vitally important, and at times crucial to arrive at the correct diagnosis of melanocytic nevus or melanoma. Until the time when there is a definitive litmus test to differentiate a melanocytic nevus from a melanoma with absolute certainty, the degree of overlapping criteria will remain essential, even though misdiagnoses will, from time to time, continue to occur. Fittingly, the words of the late A. Bernard Ackerman, M.D., who during his career was incredibly unrestrained and exceptionally passionate on the subject of melanocytic neoplasia, are to the point: "The effort here at characterization accurate of the changes is defensible, but not verifiable! It being subjective, as are all judgments predicated on observations morphologic" [6].

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