

Signature nevi: individuals with multiple melanocytic nevi commonly have similar clinical and histologic patterns

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Introduction

Individuals with multiple melanocytic nevi oftentimes have melanocytic nevi, usually two, with similar clinical and histopathologic patterns that may be typical or atypical. The melanocytic nevi are known in common parlance as signature nevi [1, 2]. In addition to being aware of these nevi, finding multiple unconventional melanocytic nevi with architectural pattern asymmetric and/or cellular pattern atypical helps to lend credence to the diagnosis of melanocytic nevus rather than melanoma. In order to evaluate the concept of the signature nevus we reviewed the histopathologic patterns of melanocytic nevi from patients having at least two nevi with similar histologic patterns.

Materials and methods

Melanocytic nevi from patients with multiple melanocytic nevi having at least two with similar histologic pattern were retrieved retrospectively from the files of Dermatopathol-

ogy Laboratory Inc., PC. Melanocytic nevi were classified according to their pattern as previously described (Figures 1-4) [3]. Two dermatopathologists (RMH & LJB) reviewed the nevi over an eight-month period.

Results

Two hundred and eight melanocytic nevi from 77 patients, 59 females and 18 males, were included in the analysis. Ages of the patients ranged from 13 to 82 years with a mean of 40 years and a median of 47 years. The signature melanocytic nevi were present on different anatomic sites (e.g., back, abdomen, face, scalp and extremity, etc.) in 51 of the patients, and on the same anatomic site in 26 patients. The 208 melanocytic nevi included 13 (17%) with three similar patterns and one (1.3%) with four similar patterns. The frequencies of melanocytic nevi according to histologic pattern are given in Table 1. There were 14 variable histologic patterns, which included the most common “melanocytic nevus, compound, keratotic, lichenoid, perivascular & interstitial

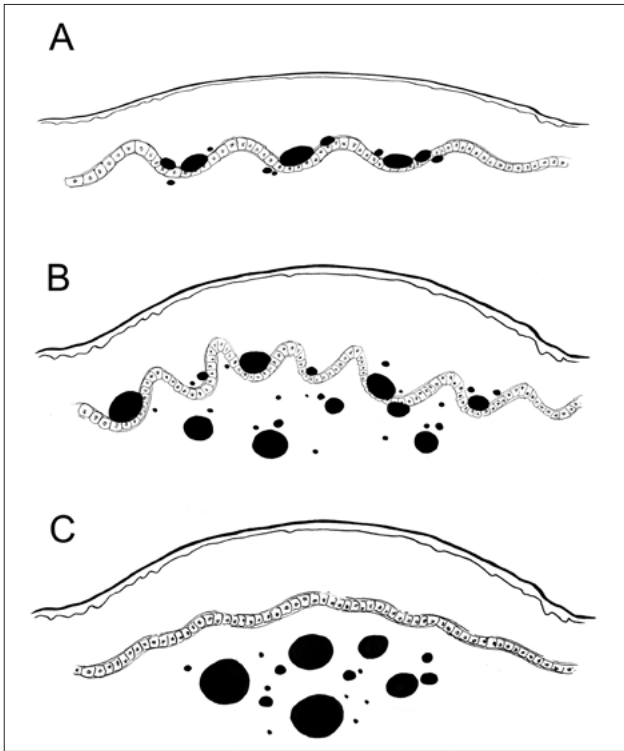


Figure 1. Anatomic patterns of melanocytic nevi. A, Junctional: Single, nested melanocytes at the dermoepidermal junction and lower spinous layer. B, Compound: Single and nested melanocytes at the dermoepidermal junction, papillary dermis and/or reticular dermis. C, Intradermal: Single and nested melanocytes confined to the reticular dermis.

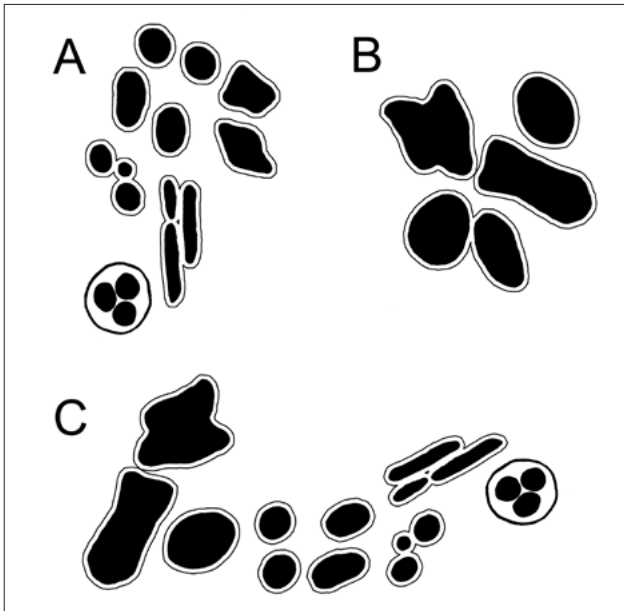


Figure 3. Cellular patterns of melanocytic nevi. A, Typical (small and monomorphous): Small, round, oval, polygonal, spindle or multinucleate melanocytes. B, Atypical (large and pleomorphic). C, Combined: Both typical and atypical melanocytes.

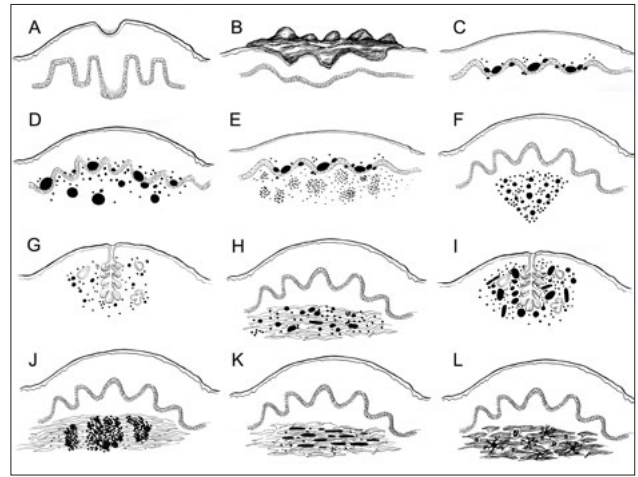


Figure 2. Architectural patterns of melanocytic nevi. A, Epidermal: Prominent epidermal rete and infundibula. B, Keratotic: Prominent surface and infundibular hyperkeratosis. C, Interface: Single and nested melanocytes at the dermoepidermal junction and lower spinous zone. D, Lichenoid melanocytic: Single and nested melanocytes at the dermoepidermal junction and lower spinous zone. E, Lichenoid lymphocytic: Single and nested melanocytes limited to the dermoepidermal junction and lower spinous zone associated with a patchy lymphocytic infiltration within a thickened papillary dermis. F, Wedge-shaped: Single and nested melanocytes in a “V” or wedge-shaped pattern in the reticular dermis. G, Perivascular, periadnexal: Single and small nested melanocytes around and associated with vascular and adnexal structures. H, Interstitial: Single and nested melanocytes splayed among collagen bundles in the reticular dermis. I, Nodular: Large round or oval collections of melanocytes in the dermis in the region of vascular and adnexal structures. J, Diffuse: Sheets of confluent melanocytes in the reticular dermis with little intervening stroma. K, Fascicular: Fascicles of melanocytes in the midst of collagen bundles in the reticular dermis. L, Pigmented dendritic: Melanin-laden, pigmented dendritic melanocytes and melanophages coupled with thickened collagen bundles.



Figure 4. Example of melanocytic nevus diagnosis based on anatomic, architectural and cellular patterns. A composite of single anatomic and cellular patterns with single or multiple architectural patterns. Example: Melanocytic nevus, compound, keratotic, lichenoid, perivascular and interstitial, typical cellular pattern.

Table 1. Common Histologic Patterns and Number of Signature Nevi in 77 Patients with Multiple Melanocytic Nevi

1. Melanocytic nevus, compound, keratotic, lichenoid, perivascular & interstitial pattern (52)
2. Melanocytic nevus, junctional, epidermal/interface pattern (34)
3. Melanocytic nevus, compound, patchy lichenoid pattern (26)
4. Melanocytic nevus, intradermal, nodular, perivascular & interstitial pattern (12)
5. Melanocytic nevus, compound, keratotic pattern (8)
6. Melanocytic nevus, intradermal, perivascular & interstitial pattern (7)
7. Melanocytic nevus, compound, keratotic, perivascular-periadnexal, diffuse pattern (7)
8. Melanocytic nevus, intradermal, wedge-shaped pattern (7)
9. Melanocytic nevus, compound, lichenoid, perivascular & interstitial pattern (6)
10. Melanocytic nevus, intradermal, keratotic, perivascular & interstitial pattern (6)
11. Melanocytic nevus, compound, perivascular-interstitial & keratotic pattern (2)
12. Melanocytic nevus, nodular pattern (2)
13. Melanocytic nevus, nodular-diffuse pattern (2)
14. Melanocytic nevus, compound, perivascular & interstitial pattern (2)

pattern” (n=52) and “melanocytic nevus, junctional, epidermal/interface pattern” (n=26), while “melanocytic nevus, nodular” was one of the least (n=2).

Discussion

The article Signature nevi [1] by Suh and Bologna emphasized 10 clinical types or patterns of melanocytic nevi. These signature nevi predominate in patients with multiple melanocytic nevi and share a similar clinical appearance. Ricotti presented the histopathologic phenomenon of “Signature Nevi” at the 12th Joint Meeting of The International Society of Dermatopathology [2]. Likewise, we reviewed the histopathologic changes from biopsies of 208 melanocytic nevi taken from 77 patients over a period of eight months. Biopsies were taken from two or more of their melanocytic nevi over four years that retrospectively had at least two similar histologic patterns, i.e., anatomic, architectural and cellular. Interestingly, included in this total number of melanocytic nevi, 13 (17%) of the patients had similar histologic patterns in three of their melanocytic nevi, and one patient had 4 similar histologic patterns. Thus, melanocytic nevi commonly have similar clinical as well as similar histologic patterns in patients with multiple melanocytic nevi, i.e., signature nevi. When one encounters a troublesome or atypical histologic pattern in one melanocytic nevus from an individual with many melanocytic nevi, e.g., architectural asymmetry and/or focal cellular atypia, it is common and expected to find other melanocytic nevi from that patient to have similar atypical histologic patterns.

Melanocytic nevi have been reported to have a variety of clinical phenotypic patterns [11], and a variety of histologic anatomic (Figure 1), architectural (Figure 2) and cellular patterns (Figure 3) [3], not unlike that situation commonly

found in apocrine neoplasia [4] and inflammatory skin diseases [5]. On occasion, an unusual melanocytic nevus will present with clinical and histologic changes that may be difficult to differentiate from a melanoma (Figure 5a–c) and (Figure 6a–c). A quandary often occurs when there are histologic changes in pattern architectural such as asymmetry or pattern combined cellular such as focal cellular atypia [6]. These variations may be found and are expected in melanomas as well as in some unusual melanocytic nevi, such as signature nevi [7], nevi with the “ugly duckling” sign [8, 9], acquired nevi [10], congenital nevi, Spitz’s nevi [11, 12], dysplastic nevi [13], traumatized nevi, or those found on a “special site” such as the genitalia, perineum, thigh, umbilicus, palm, sole, scalp and ear, etc. In addition, some atypical patterns of melanocytic nevi are classified by acronyms such as MIN [14], SAMPUS and MELTUMP [15], and eponyms such as Unna, Clark, Reed, Miescher, Zitelli, Mark, Seab and Ackerman [16, 17], or too often with hazy descriptive monikers such as atypical nevus, dysplastic nevus with architectural disorder with moderate to severe cytologic atypia. The latter are often used to announce uncertainty and indecision by the pathologist as to whether the melanocytic proliferation is benign or malignant. Those bewildering and evocative names unfortunately all too often bode ill for the patient and may lead to unwarranted surgical procedures, e.g. sentinel lymph node biopsy and lymphadenectomy [18]. Regrettably, to date, there is no unanimity or litmus test to distinguish between those unusual and tricky clinical and histologic melanocytic nevi, or melanocytic proliferations from subtle melanomas. Sorry to say, we must alas rely upon questionable subjective clinical and histologic morphologic criteria to arrive at a definitive diagnosis, nevus or melanoma [19, 20].

In summary, we agree that awareness and knowledge of the fact that an individual with multiple melanocytic nevi is prone to have several melanocytic nevi with similar and

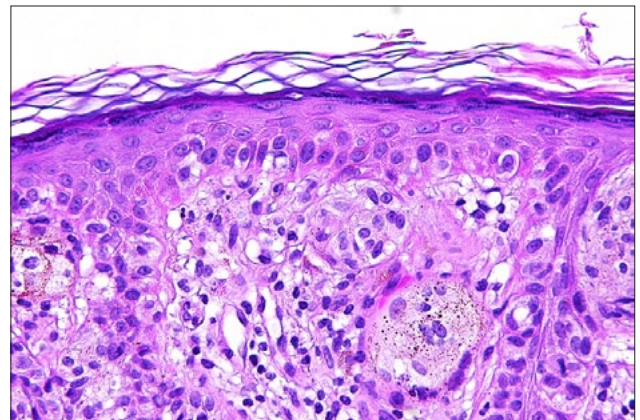
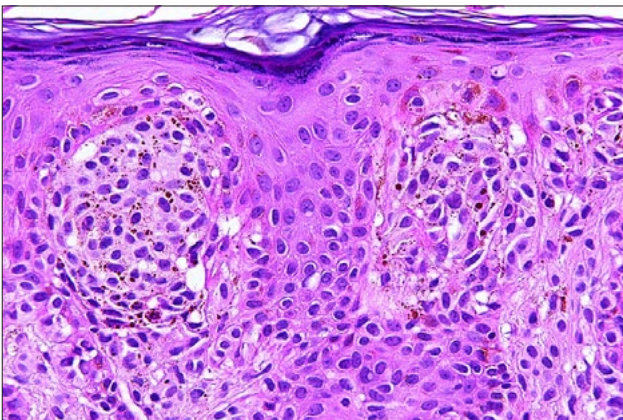
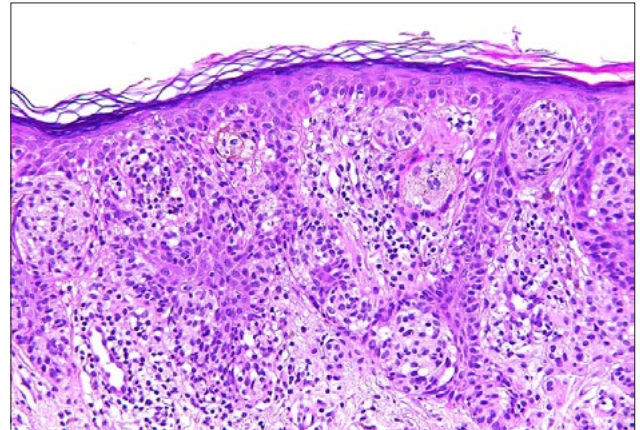
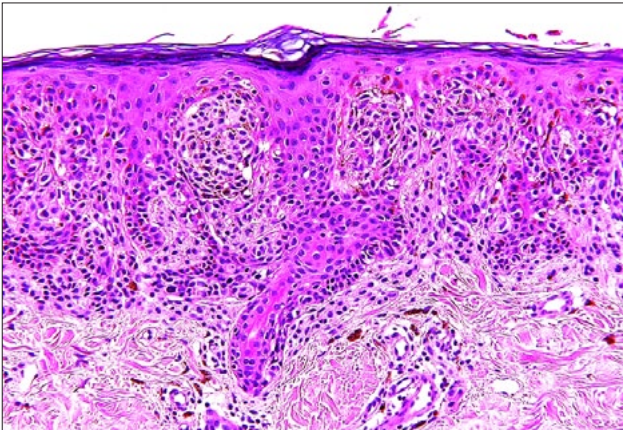
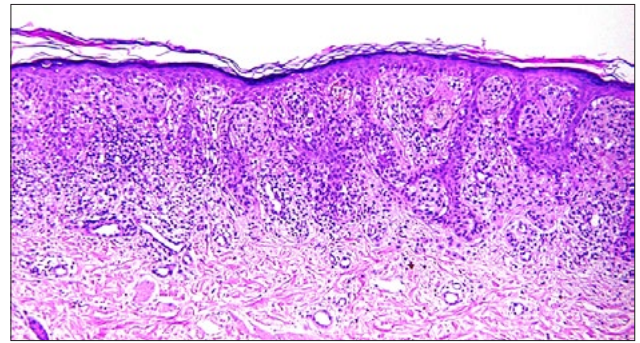
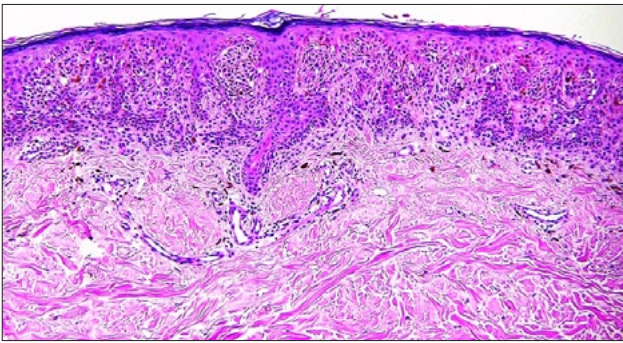


Figure 5. Melanocytic nevus, compound, lichenoid, combined cellular pattern from a 4x4 mm changing nevus on the back of a 29-year-old woman. Melanocytic nevus, compound, lichenoid, combined cellular pattern from a 4x4 mm changing nevus on the back of a 29-year-old woman. There are predominately small round and oval pigmented melanocytes singly and in nests within the lower epidermis, structure of adnexa, and thickened papillary dermis where there are prominent, elongated rete ridges. There are a few melanocytes present above the dermoepidermal junction, several melanocytes with atypical nuclei in the midst of those with increased cytoplasm and prominent pigmented melanin granules, plus a variety of irregularly shaped nests of melanocytes.

Figure 6. Melanocytic nevus, compound, lichenoid, combined cellular pattern from a 3x3 changing nevus on the abdomen of the same 29-year-old woman seen in Figure 5. Melanocytic nevus, compound, lichenoid, combined cellular pattern from a 3x3 mm changing nevus on the abdomen of the same 29-year-old woman seen in Figure 5. There are predominately small round and oval pigmented melanocytes within the lower epidermis and thickened papillary dermis where there are prominent, elongated rete ridges. There are a few melanocytes present above the dermoepidermal junction, several melanocytes with atypical nuclei, and a number of various melanocytes with abundant pale staining cytoplasm with melanin pigmented granules, in addition to several nests of melanocytes that vary in size and shape.

sometimes unusual clinical patterns (signature nevi) as well as common and/or unconventional histologic patterns (anatomic, architectural and cellular). As a result, this concept of signature nevi supports unusual findings, clinical and histologic, to be customary and expected in melanocytic nevi for a particular individual with many melanocytic nevi. When a melanoma is in the differential diagnosis of a lesion pigmented, this valuable lesson may help to eliminate mistakes [21], avoid over diagnosing melanoma, and eliminate unnecessary surgery. Thus, in the end, one will be more prone to arrive at an accurate, precise and definitive diagnosis of melanocytic nevus.

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