Benign Atypical Junctional Melanocytic Hyperplasia Associated with Intradermal Nevi: A Common Finding That May Be Confused with Melanoma *In Situ*

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Over the past few years, consultation cases thought to represent melanoma *in situ* have been received that consisted of otherwise normal intradermal nevi with an abnormal but benign junctional proliferation of melanocytes that we have termed benign atypical junctional melanocytic hyperplasia. In order to evaluate the incidence of this feature, 400 cases of intradermal nevi were reviewed. Of these, 25 (6.2%) qualified for inclusion, making this a rather common phenomenon. Clinically, patient ages ranged from 18 to 64 years (mean, 35 years), with a male to female ratio of 1:1. Face (40%) and back (32%) were the most common locations. Histologically, the lesions were predominantly dome-shaped with an intradermal component consisting of conventional nevus cells. Most importantly, each lesion exhibited prominent individual nevomelanocytic cells dispersed at uneven intervals along the dermoepidermal junction in insufficient numbers to be considered compound nevi. The cells exhibited abundant pale to clear cytoplasm, an increased nuclear:cytoplasmic ratio, and often exhibited prominent nucleoli. However, these lesions could be distinguished from melanoma *in situ* by the lack of several features including lateral spread, upward epidermal migration, marked cytologic atypia, finely granular "smoky" melanin pigment, mitotic figures, and a subjacent host inflammatory response. All cases behaved in a benign fashion. Although benign atypical junctional melanocytic hyperplasia is a relatively common histological curiosity, it is a potential pitfall in the diagnosis of pigmented lesions.

KEY WORDS: Melanocytic hyperplasia, Melanoma *in situ,* Nevus, Pagetoid.

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Over the past few years, our laboratory has received several consultation cases that consisted of otherwise normal intradermal nevi, but with a junctional proliferation of melanocytes thought to represent melanoma *in situ*. For want of a better term we have used benign atypical junctional melanocytic hyperplasia to describe these changes. Although a somewhat common histological curiosity (for pathologists faced with interpreting an increasing number of nevomelanocytic neoplasms, along with the increasing emphasis on diagnosing very early melanoma), these changes are a potential pitfall.

MATERIALS AND METHODS

Four hundred intradermal nevi from the files of the Dermatopathology Laboratory at the University of California, Irvine were reviewed. A single hematoxylin-eosin stained slide from each case was independently reviewed by two pathologists (JO, RB) for the presence of benign atypical junctional melanocytic hyperplasia. The criteria for inclusion were intradermal nevi that demonstrated prominent nevomelanocytic cells dispersed at random intervals along the dermoepidermal junction. The cells contained enlarged nuclei and abundant pale to clear cytoplasm. The proliferation was restricted to the area above the intradermal component and lacked a host inflammatory response (see Histological Findings for additional details). Clinical and follow-up information was obtained from the patients' referring physicians.

RESULTS

Clinical Findings

Twenty-five of the 400 cases reviewed (6.2%) exhibited benign atypical junctional melanocytic hyperplasia. Patient ages ranged from 18 to 64 years (mean, 35 years). The male to female ratio was 1:1. Lesions were predominantly located on the face (40%) and back (32%). Additional locations included the neck, chest, abdomen, thigh, and calf. The majority had the clinical appearance of a uni-

form nevus or papule (68%). Others demonstrated features of an atypical nevus (dysplastic nevus, Clark's nevus) (12%), inflamed nevus (12%), and "growing" nevus (8%).

Clinical follow-up ranged from 6 to 24 months. Because of the benign diagnosis, many of the lesions have not been completely removed. No patient has developed a subsequent melanoma or other aggressive nevomelanocytic lesion. One patient developed a small hyperpigmented focus at the biopsy site within two months. Under observation, the lesion has remained stable now for 20 months.

Histologic Findings

The lesions were typically dome-shaped, or occasionally papillated. The intradermal component consisted of conventional nevus cells (Fig. 1). Each displayed variable degrees of benign atypical junctional melanocytic hyperplasia. This change consisted of conspicuous individual nevomelanocytic cells dispersed at uneven intervals along the dermoepidermal junction. Continuous, lentiginous proliferations and nests were not present. The cells contained abundant pale to clear cytoplasm (Fig. 2). Some cells contained coarse melanin pigment, but no finely granular, "smoky", melanin was observed. The nuclei were moderately enlarged with an increased nuclear:cytoplasmic ratio and often exhibited prominent nucleoli (Fig. 3). Occasional multinucleated cells were identified, but marked cytologic atypia and mitotic figures were not present. The changes were restricted to the area above the intradermal component, and the subjacent dermis lacked a host inflammatory or fibrotic response.

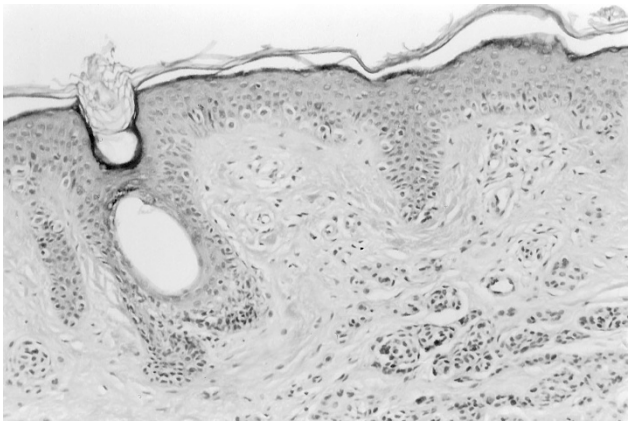

FIGURE 1. Benign atypical junctional melanocytic hyperplasia characterized by prominent scattered nevomelanocytic cells along dermoepidermal junction overlying an intradermal nevus. Subjacent dermis lacks inflammatory or fibrotic response (hematoxylin and eosin, 100×).

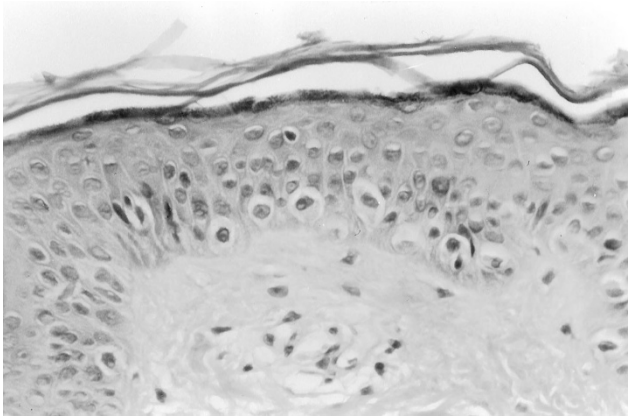

FIGURE 2. Atypical cells characterized by abundant pale to clear cytoplasm, moderately enlarged nuclei (hematoxylin and eosin, 200×).

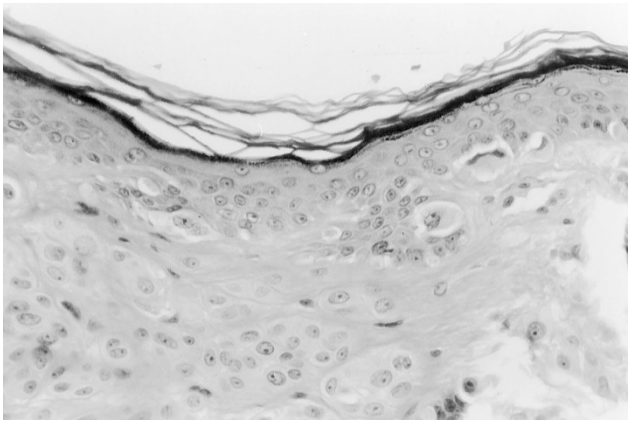

FIGURE 3. Multinucleated atypical cells with abundant pale to clear cytoplasm and prominent nucleoli overlying intradermal nevus (hematoxylin and eosin, 200×).

DISCUSSION

Benign atypical junctional melanocytic hyperplasia is a descriptive term for a relatively common microscopic alteration. This feature was found in 6.2% of otherwise normal intradermal nevi. Although it probably represents a benign histological curiosity, its significance lies in the occasional case in which presence of this change may be mistaken for malignant melanoma. This has become especially problematic due to the increasing emphasis on the diagnosis of very early melanoma. Over the past few years, our laboratory has received several consultation cases exhibiting this change that were initially interpreted as possible melanoma.

The expression "benign atypical junctional melanocytic hyperplasia" is used here to describe the cytologic features observed. The cells contain large round or plump oval nuclei and abundant pale-staining cytoplasm. It does not refer to the architectural pattern of upward extension, in which cells are scattered well above the basal layer of the epidermis (1). Benign atypical junctional melanocytic hyperplasia is characterized by a proliferation of these large

cells along the dermoepidermal junction. They are dispersed at uneven intervals and are too few in number to be considered compound nevi.

Several features distinguish this change from melanoma *in situ* (2) (Table 1, Figs. 4, 5). The cells are restricted to the area above the intradermal component. There is no lateral spread, and the lesion remains symmetric. The cells do not extend up into the epidermis. Although the cells are much larger than standard melanocytes, they lack the marked cytologic atypia and fine granular, "smoky" melanin pigment associated with melanoma cells. Mitotic activity is not a feature. The underlying dermis does not exhibit a host response. Inflammatory cells, melanophages, and dermal fibrosis are typically absent.

These lesions have all behaved in a benign fashion. Most do not demonstrate clinical atypia and present as a uniform nevus or papule. None of the 25 cases identified have progressed in an aggressive manner, including many that were incompletely excised. Maize *et al.* (3) and LeBoit (4) have described a similar change above nevi and have also concluded that it confers no prognostic implication.

In addition, benign atypical junctional melanocytic hyperplasia has been described in other lesions including PUVA lentigo (5) and fibrous papule (6). The changes described in those lesions were also felt to represent a benign alteration.

Two other terms that described similar cytology have been used in the literature for entirely different lesions. "Pagetoid melanocytosis" has been used to describe lesions that exhibit pagetoid architecture (7). Several nevomelanocytic lesions, malignant and benign, may display cells that extend upward into the epidermis. Pagetoid cytology was not necessarily a feature of those lesions and none of the ordinary acquired nevi studied contained this pattern. UV-irradiated melanocytic nevi (8, 9) as well as unusual nevus variants have also been shown to demonstrate this pattern (Table 2). "Pagetoid melanocytic proliferation" was coined by the 1991 Consensus Panel, "Melanoma Without Walls" (10). They defined this term as "atypical (usually larger and epithelioid) melanocytes singly or in nests dispersed through the full thickness of the epidermis including the granular layer with no atypical melanocytes in the dermis." However, many would still prefer to use the term melanoma *in situ* for these lesions.

TABLE 1. Features That Distinguish Benign Junctional Melanocytic Hyperplasia from Melanoma In Situ

No lateral spread
No upward extension into epidermis
No finely granular, "smoky" melanin
No marked cytologic atypia
No mitotic figures
No host inflammatory-fibrotic response

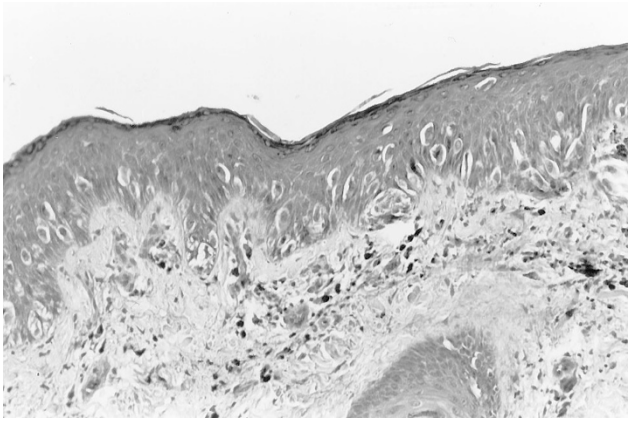

FIGURE 4. Melanoma *in situ* typified by a more florid proliferation of cells distributed continuously along the dermoepidermal junction, in nests, and extending up into epidermis . Subjacent dermis exhibits prominent inflammation and fibrosis (hematoxylin and eosin, 100×).

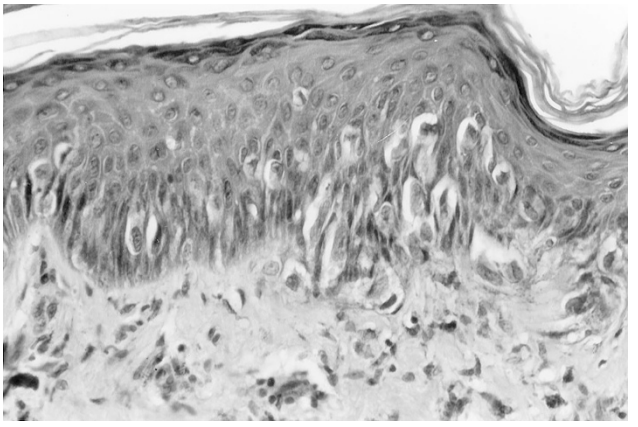

FIGURE 5. Melanoma *in situ* cells exhibit marked nuclear atypia, a higher N/C ratio, and finely granular melanin pigment (hematoxylin and eosin, 200×).

TABLE 2. Lesions That Frequently Exhibit Pagetoid Architecture

Melanoma
"Genital" nevi and related variants (nipple, axilla, umbilicus, groin)
Acral nevi (palmar, plantar, subungual)
Spitz nevi
Congenital nevi
UV-irradiated nevi
"Recurrent nevi"

In summary, benign atypical junctional melanocytic hyperplasia represents a relatively common finding above nevi and should not be mistaken as a sign of atypia or malignancy. Recognition of this change will aid in distinguishing between benign nevi and melanoma, avoiding a potential pitfall in the diagnosis of pigmented lesions.

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