
Quantification of melanocytes in sun-damaged skin

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Background: The density of melanocytes varies by anatomic site and degree of sun damage.

Objective: To determine the density of melanocytes and frequency of confluence in specimens adjacent to nonmelanoma skin cancers.

Methods: Two hundred final layer specimens from Mohs surgery for basal cell carcinomas were analyzed by using MART-1.

Results: Data for 162 skin specimens from the head demonstrated an average keratinocyte to melanocyte ratio of 7.12 and 8.19 for epidermis and adnexal structures, respectively. The 23 specimens from the trunk demonstrated respective ratios of 7.54 and 7.46, and 13 specimens from extremities demonstrated ratios of 8.69 and 12.38.

Limitations: Margins from Mohs micrographic surgery for nonmelanoma skin cancers were utilized as a proxy for chronically sun-damaged skin.

Conclusion: Our results suggest that chronically sun-exposed skin demonstrates increased melanocytic density, but confluence of melanocytes is rare. Occasionally intraepidermal pagetoid scatter and isolated melanocytic nests were rarely noted. These findings alone should not support an unequivocal diagnosis of melanoma in situ. (J Am Acad Dermatol 2011;64:548-52.)

Key words: lentigo maligna; MART-1; melanocyte density; melanoma in situ; Mohs micrographic surgery; sun damage.

INTRODUCTION

The background pattern of melanocytes in chronically sun-exposed skin must be differentiated from melanoma in situ in the interpretation of melanoma margins on the head, neck, upper trunk, and extremities. Recent studies with margins of nonmelanoma skin cancers and melanoma as a proxy for sun-exposed skin suggest that an increase in melanocyte density and areas of confluence can be expected^{1,2}. Hendi, Brodland, and Zitelli¹ found that the mean number of melanocytes in sun-damaged skin was

15.6 (range, 6-29), and melanocyte confluence was present in 89% of the specimens (severe 1%, moderate 34.0%, and mild 35%). Although they reported areas of confluence of more than 6 melanocytes, no image was shown to demonstrate this degree of confluence. An image of "near confluence" was presented, but we view these as very different and do not use increased density in the absence of true confluence as a criterion for the diagnosis of melanoma in situ (MIS). Overall density overlaps significantly between MIS and sun-damaged skin. Runs of confluence are used as a criterion for MIS. We undertook this study because Hendi, Brodland, and Zitelli¹ reported runs of confluence in sun-damaged skin. More recently, Barlow, Maize, and Lang² reported an average of 7.97 melanocytes per 1 mm of epidermis and contiguous melanocytes in 16.7% (30/180) of specimens.² These authors also noted melanocytic nesting and pagetoid spread and urged caution in the interpretation of melanoma margins in sun-damaged skin. The goal of our study was to document melanocyte density in heavily sun-damaged skin in sites where melanoma in situ is common. We assessed the ratio of melanocytes to

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Funding sources: None.

Conflicts of interest: None declared.

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0190-9622/\$36.00

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doi:10.1016/j.jaad.2010.05.021

keratinocytes in the epidermis and adnexal structures and noted episodes of melanocyte confluence as well as the degree of solar elastosis present.

METHODS

The study was approved by the Geisinger Medical Center Institutional Review Board.

Tissue blocks from the final stage of 200 consecutive patients undergoing Mohs micrographic surgery for non-melanoma skin cancers were sectioned and stained permanently with the MART-1 (melanoma antigen recognized by T cells) immunostain. The epidermis and hair follicles of each specimen were analyzed for the ratio of keratinocytes to melanocytes, episodes of confluent melanocytes, and the degree of solar elastosis. All specimens were compared with the applicable positive and negative controls. Specimens that failed to express MART-1 were excluded. MART-1 was selected as an immunostain for its superior sensitivity and specificity as a melanocyte marker for permanent sections.³⁻⁶

RESULTS

Results for the study by region are noted in Tables I, II, and III and Figs 1 to 4. The composite melanocytic density for the face was an average of 7.2 keratinocytes per melanocyte; the ratio in the adnexal structures was 8.19 keratinocytes per melanocyte. For the extremities, the ratio in the epidermis was 8.69 keratinocytes per melanocyte, and 10.07 keratinocytes per melanocyte for the adnexal structures. The trunk/back demonstrated a ratio of 7.87 keratinocytes per melanocyte, with a ratio for the adnexal structures in this region of 7.78 keratinocytes per melanocyte. Rarely, an isolated small melanocytic nest was noted.

Confluence

Seventy-three percent of specimens from the head (115/157), 70% of specimens (16/23) from the trunk, and 77% (10/13) of extremity specimens lacked any melanocytic confluence (two or more

melanocytic nuclei with no intervening keratinocyte nucleus). For the remaining specimens, almost all of the confluence identified was limited to doublets, with 8 triplets and one quadruplet found among all specimens. These data differ dramatically from that of Hendi et al,¹ which showed an 88% incidence of melanocyte confluence. Both their patients and ours

reside in Pennsylvania, but individual patterns of sun exposure were not studied in detail. In contrast to previous studies,^{1,2} we demonstrated an appearance of pagetoid spread confined to the lower half of the epidermis in 42% of all specimens. This is common in tangential sections and represents an artifact of sectioning. However, specimens taken from the face were found to have pagetoid melanocytes in the upper half of the epidermis. In addition, approximately 7% (13/193) of specimens were also found to have dermal MART-1-positive dendritic cells. Other authors have noted scattered dermal dendritic cells with MART-1 staining. Although their exact nature remains to be determined, they do not appear to correlate with the presence of melanoma and may not even represent melanocytes.⁴ Severe solar elastosis was present in 99% (191/193) of our specimens, confirm-

ing that they represented heavily sun-damaged skin.

DISCUSSION

Melanocytic density in the human epidermis is known to vary by region of the body.⁷ Although Whiteman and colleagues⁸ speculated that these differences could be predetermined, other authors attribute much of the difference to the effects of sun exposure.⁹⁻¹⁴ The precise magnitude of the effect is not certain, but one study reported up to a twofold increase in melanocyte density in sun-exposed skin compared with shielded skin.⁹ Unexpectedly, our study showed a relative diminutive melanocyte density for the eyebrow and eyelid (Q11.75 and Q11.0, respectively). This is probably due to sampling; these areas accounted for only 3.5% of all

CAPSULE SUMMARY

- The evaluation of melanoma margins in sun-damaged skin may be complicated by background melanocytic hyperplasia.
- We sought to define the density of melanocytes and frequency of confluence in sun-damaged skin to determine whether or not existing criteria for the diagnosis of melanoma in situ need to be modified in this setting.
- The melanocytic density in sun-damaged skin on the face averaged 7.2 keratinocytes per melanocyte. For the extremities, the ratio was 8.69 keratinocytes per melanocyte. The trunk/back demonstrated a ratio of 7.87 keratinocytes per melanocyte.
- Confluence (two or more melanocytic nuclei with no intervening keratinocyte nucleus) was largely limited to doublets, with 8 triplets and 1 quadruplet found among all specimens.
- Our results suggest that the degree of melanocytic hyperplasia and confluence present in sun-damaged skin differs from that seen in melanoma in situ.

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