Ultraviolet Radiation of Melanocytic Nevi

A Dermoscopic Study

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Background: UV radiation can lead to clinical, histological, and ultrastructural changes in melanocytic nevi. In this study, we investigated whether exposure to 2 minimal erythema doses of UV radiation induces changes in the dermoscopic image of acquired melanocytic nevi.

Observations: Fifteen melanocytic nevi were exposed to 2 minimal erythema doses of UV radiation. Differences in dermoscopic parameters (asymmetry, border, erythema, and telangiectasias in the nevus; pigmentation; hypopigmented areas; presence, regularity, and sharpness of pigment network; and brown-black globules) in digital dermoscopic images taken before and 3, 7, 14, and 28 days after UV irradiation were scored. Three days after UV irradiation, the borders of nevi were more faded ($P < .02$), the nevi were darker brown ($P < .02$), the hypopigmented areas were smaller ($P < .02$), and the pigment network structures were more faded ($P < .007$) and less prominent ($P < .02$) than before UV irradiation. Seven days after UV irradiation, pigmented globules have also grown ($P < .05$). After 28 days, all parameters, except hypopigmented areas, were essentially the same as before UV irradiation.

Conclusion: UV irradiation of melanocytic nevi with 2 minimal erythema doses induces transient changes in their dermoscopic appearance that are sometimes suggestive of malignant melanoma.

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Ultraviolet radiation is considered one of the most important agents of skin cancer, although its exact role in the development of benign and malignant melanocytic skin tumors remains unclear. Results of several epidemiological studies indicate that intermittent exposure to UV radiation is especially linked to the development of a higher number of nevi. Moreover, sunburns during childhood seem to be an independent risk factor for the development of malignant melanoma. In recent years, dermoscopy (ie, dermatoscopy, direct skin microscopy, epiluminescence microscopy, and surface microscopy) has become a routine clinical method for the more accurate diagnosis of melanocytic skin lesions. Therefore, in this study, we investigated whether a single exposure of acquired melanocytic nevi to 2 minimal erythema doses (MEDs) results in changes detectable by dermoscopy.

RESULTS

GENERAL OBSERVATIONS

Documentation of the nevi with the digital dermoscopic workstation guaranteed the optimal quality of dermoscopic images, the resolution of the digital images being equal to the resolution of conventional kodachrome images. Moreover, the images were viewed immediately after documentation on the screen of the workstation to prove the photographic quality. The interobserver correlation for the different dermoscopic parameters yielded the highest correlation coefficient for black-brown globules (0.93) and the lowest for telangiectasias in the nevus (0.55). In all cases, UV irradiation induced erythema of the adjacent skin. In the skin adjacent to a nevus located on the lower part of the abdomen, a blister developed 2 days after irradiation. In this nevus, the network structures changed markedly, and these changes were still evident after 28 days and even after 1 year (Figure 1). In general, dermoscopic images of reddish brown nevi with discrete network structures showed only slight changes after irradiation with 2 MEDs, whereas dermoscopic images of nevi with prominent network structures showed more obvious alterations. Two nevi (13.3%) showed almost identical dermoscopic images at days 0, 3, 7, 14, and 28. In 7 nevi (46.7%), at least 1 dermoscopic parameter differs slightly (≤4 points difference on the visual analog scale from...
SUBJECTS, MATERIALS, AND METHODS

VOLUNTEERS AND LESIONS

Fifteen acquired melanocytic nevi in 4 volunteers (all men) were chosen for study. The volunteers ranged in age from 29 to 41 years and had either skin type II (n = 2) or skin type III (n = 2). The nevi were situated on the trunk or on the upper arms and showed no clinical or dermoscopic signs of malignancy. None of these nevi had been exposed to UV radiation within 3 months of the investigation. The diameters of the nevi ranged from 0.7 to 1.6 cm.

UV IRRADIATION

For UV irradiation, a UV lamp (Sellasol 1200 lamp, Sellas GmbH, Gevelsberg, Germany) was used. The lamp generates UV-B at a mean intensity of 7.8 mW/cm² and UV-A at a mean intensity of 87.8 mW/cm² at a distance of 30 cm. For each volunteer, the individual MED was determined on the volar aspect of the forearm 24 hours after exposure to a test ladder of UV doses produced by the UV lamp. Each nevus and 2 cm of the adjacent skin were then irradiated with 2 doses of the individual MED. In each nevus larger than 1 cm (n = 8), half of the nevus was randomly chosen to be protected with opaque tape during UV irradiation.

DIGITAL DERMOSCOPIC DOCUMENTATION

The nevi were documented under standardized conditions using a Dermaphot apparatus (Heine, Optrotechnik, Herrsching, Germany) connected to a digital camera (Kodak DCS 460, Eastman Kodak Co, Rochester, NY). The digital images were stored at a digital dermoscopic workstation (Digital ELM Teledermatology Workstation, Vanguard Imaging Ltd, Cambridge, Mass). Each nevus was documented before and 3, 7, 14, and 28 days after irradiation.

MEASUREMENT OF ERYTHEMA AND PIGMENTATION OF ADJACENT SKIN

Erythema and pigmentation of the adjacent skin were measured with a reflectance photometer (DermaSpectometer, Cortex Technology, Hadsund, Denmark) on the days when the dermoscopic images were taken. Relative values for erythema and pigmentation range from 0 to 999. The mean value of 3 separate measurements was recorded.

EVALUATION OF DERMOSCOPIC IMAGES

Digitized dermoscopic images of each nevus taken before and 3, 7, 14, and 28 days after UV irradiation were viewed side by side on the screen of the dermoscopic workstation and on color prints (Kodak XLS 8600 Printer, Eastman Kodak Co) by 2 investigators (R.H.-W. and H.P.S.). The following 10 dermoscopic parameters were graded on a visual analog scale from 0 to 10 (0 indicates absent and 10 indicates prominent, unless otherwise noted): asymmetry, border (sharp, 0; faded, 10), erythema in the nevus, telangiectasias in the nevus, pigmentation, hypopigmented areas, pigmentation network, sharpness of pigment network (sharp, 0; faded, 10), regularity of pigment network (irregular, 0; regular, 10), and brown-black globules.

In the second step of analysis, the images of the protected and unprotected halves of large nevi taken at days 3, 7, 14, and 28 were compared with each other.

STATISTICAL EVALUATION

The matched-pairs signed-rank test was applied to compare the scores for the images taken before UV irradiation with the scores for the images taken 3, 7, 14, and 28 days after UV irradiation. In addition, the scores of the protected halves were compared with those of the unprotected halves of the large nevi. For statistical evaluation, the Statistical Package for the Social Sciences (SPSS Program for Windows, SPSS Inc, Chicago, Ill) was used. If the $P$ values of both investigators for a parameter were less than .05, the difference was considered significant. In the “Results” section, only the higher $P$ value of both investigators is given.

0 to 10) at any time, and in 6 nevi (40%), marked changes in the dermoscopic appearance could be observed (>4 points difference on the scale in at least 2 parameters) at any time.

ERYTHEMA AND PIGMENTATION OF THE ADJACENT SKIN

After UV irradiation, the adjacent skin of all nevi developed marked erythema, as measured by the reflectance photometer. The mean value for erythema of all volunteers increased from 8.6 before irradiation to 17.2 on day 3 (matched-pairs signed-rank test, $P < .001$) and then decreased to 12.7 on day 7 ($P < .003$), 11.9 on day 14 ($P < .003$), and 10.5 ($P < .07$) on day 28.

Before UV irradiation, the mean value for pigmentation of all volunteers was 23.6. After UV irradiation, the mean value for pigmentation increased to 29.4 on day 3 ($P < .003$) and 31.1 on day 7 ($P < .001$) but then decreased to 26.8 on day 14 ($P < .003$) and 28.4 on day 28 ($P < .003$).

DERMOSCOPIC PARAMETERS OF SMALL MELANOCYTIC NEVI AND THE UNPROTECTED HALVES OF LARGE MELANOCYTIC NEVI

The dermoscopic parameters of small melanocytic nevi and the unprotected halves of large melanocytic nevi before UV irradiation were compared with those after UV irradiation, and the results are shown in Figure 2 and the Table.

Day 3

The borders of the nevi were more faded ($P < .03$), the nevi were more darkly pigmented ($P < .02$), and, inversely, the hypopigmented areas were significantly less prominent ($P < .02$). In addition, the pigment net-
work structures were less prominent \((P<.01)\) and more faded \((P<.007)\). There were no significant changes in asymmetry, erythema in the nevus, telangiectasia, regularity of pigment network, or presence of brown-black globules.

Day 7

The changes in the dermoscopic images were most prominent. The borders of the nevi were more faded \((P<.05)\), the nevi were more darkly pigmented \((P<.001)\), and, inversely, the hypopigmented areas were significantly less prominent \((P<.01)\). The pigment network structures were less prominent \((P<.01)\) and more faded \((P<.007)\). In addition to the parameters that differed significantly at day 3, the number and intensity of brown-black globules increased \((P<.05)\).

Day 14

The nevi were still darker brown \((P<.01)\), and the hypopigmented areas were less prominent \((P<.02)\).
Only the hypopigmented areas were still less prominent than before UV irradiation (P<.05).

DERMOSCOPIC PARAMETERS OF PROTECTED HALVES OF LARGE MELANOCYTIC NEVI

Images of the protected halves of the nevi (n = 8) taken before and 3, 7, 14, and 28 days after UV irradiation did not differ in any dermoscopic parameter at any time.

DERMOSCOPIC PARAMETERS OF PROTECTED AND UNPROTECTED HALVES OF THE SAME MELANOCYTIC NEVUS

Dermoscopic parameters of protected and unprotected halves of the same melanocytic nevus are shown in Figure 3.

Day 3

The borders of unprotected halves were more faded and showed more pronounced erythema (P<.05 for both) than those of the protected halves.

Day 7

The borders of unprotected halves were more faded, and the unprotected halves were darker brown and less hypopigmented (P<.05 for all).

Day 14

The unprotected halves were darker brown and less hypopigmented (P<.05 for both).

The unprotected halves did not differ significantly in any parameter compared with the protected halves. There was no significant difference in the pigment network between unprotected and protected halves at any time.

COMMENT

The aim of this study was to investigate whether 2 MEDs of UV radiation can change the dermoscopic appearance of acquired melanocytic nevi. We found that the pigmentation of UV-irradiated nevi became significantly darker and that brown-black globules increased in number and intensity. Inversely, the hypopigmented areas decreased. The pigment networks became more faded and less prominent. In addition, the borders of the nevi became more faded. Most of the changes were already evident 3 days after UV irradiation and resolved within 28 days.

The dermoscopic changes seen in melanocytic nevi after exposure to 2 MEDs may reflect an activation of melanin synthesis by melanocytes and the induction of an inflammatory dermal infiltrate. The activation of melanin synthesis seems to be the most important factor for the dermoscopic changes found in this study. The increase of pigmentation and brown-black globules especially correlates with an induction of melanin synthesis. In this regard, Tronnier et al16 found that a single exposure of nevi to 2 MEDs of UV radiation can induce activation of melanocytes, resulting in histopathologic changes simulating melanoma in situ within a week of exposure. However, the proliferative activity of melanocytes assessed by antibody staining against the proliferating cell nuclear antigen was not increased in the melanocytic nevi.16 In a second study, Tronnier et al17 demonstrated an up-regulation of integrins of the keratinocytes in the overlaying
The authors hypothesized that this induction of integrins may lead to the observed emigration of single melanocytes into the suprabasal layers of the epidermis. Results of an ultrastructural investigation of UV-irradiated nevi by Pawlowski et al revealed prominent rough endoplasmic reticulum, Golgi complex, and mitochondria with tubular cristae, suggesting increased cellular metabolism. Also, centrioles indicating mitotic activity were frequently found. The delayed UV-induced erythema (ie, sunburn) may cause the fading of the border and of the pigment network structures because of an increase of blood flow and induction of an inflammatory infiltrate triggered mainly by prostaglandins and by the damage to DNA.

The dermoscopic changes of melanocytic nevi observed in the present study are also somehow in accordance with histopathologic findings of nevi excised in summer months, which showed significantly more mitoses and inflammatory infiltrate compared with nevi excised in winter months.

Three studies have already focused on the impact of UV irradiation on the dermoscopic appearance of melanocytic nevi. First, Stanganelli et al found an increase in pigmentation and an increased prevalence of black dots in dermoscopic images of melanocytic nevi taken in summer months vs winter months. In contrast to our study results, these authors reported a higher frequency of broad and prominent pigment network structures in the summer series. Second, Stanganelli et al documented that intense sun exposure influenced the dermoscopic image of melanocytic nevi. In this study, nevi showed more black dots, brown globules, and pigment network structures after 5 to 13 days of intense natural sun exposure. Three lesions also exhibited dermoscopic features often found in malignant melanoma. Third, Hofmann-Wellenhof et al recently conducted a study in pa-

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Figure 3. Ultraviolet irradiation of an acquired melanocytic nevus. Comparison of the protected and the unprotected halves of a large nevus. A, Dermoscopic image of a nevus before irradiation. The right half was protected and the left half was unprotected. The arrows indicate the border of the tape. B, The same nevus 3 days after UV irradiation. Note the faded border and the brown-black globules in the UV-irradiated half of the nevus. C, The same nevus 14 days after irradiation. In the UV-irradiated half, the brown-black globules are now more prominent and indistinguishable from black dots. The pigmentation of the irradiated half is more pronounced in contrast to the protected half. D, The same nevus 28 days after UV irradiation. No dermoscopic differences are evident compared with before UV irradiation.
patients undergoing UV-B therapy and observed effects on the dermoscopic appearance of melanocytic nevi similar to those noted by Stanganelli et al. All these studies underline that UV irradiation in the long and short term may induce various changes in the dermoscopic features of melanocytic nevi.

The most relevant dermoscopic changes seen in our study, ie, the increase in black-brown globules and the darkening of pigmentation, are referred to by several authors as dermoscopic signs of malignancy. Argenziano et al\(^\text{24}\) found brown globules in approximately 78% of superficial spreading melanomas with 0.30- to 0.75-mm maximal vertical tumor thickness. Multiple brown globules bore a specificity for melanoma greater than 85% in a study by Menzies et al.\(^\text{25}\) Moreover, using a \(\times 10\) magnification, black-brown globules are sometimes indistinguishable from black dots, one of the most specific dermoscopic criteria for melanoma.\(^\text{26-27}\)

Furthermore, electron microscopic images of stripped material of black dots as well as of brown globules showed the same ultrastructural substrate, namely, melanosomes in the corneocytes.\(^\text{28}\) Finally, Nilles et al\(^\text{29}\) found darker pigmentation in a significantly higher percentage in melanoma than in melanocytic nevi. In contrast, a faded border, discrete pigment network, low amount of hypopigmented areas, and regularity of the pigment network are considered to be dermoscopic criteria of benign melanocytic skin lesions.\(^\text{25,26,30}\)

In conclusion, we found that the exposure of melanocytic nevi to 2 MEDs of UV radiation can induce transient changes in their dermoscopic images. These changes are mainly caused by an induction of pigmentation. In most cases, the dermoscopic appearance of a UV-irradiated melanocytic nevus is still suggestive of a nevus. However, in some cases, the changes in the dermoscopic images are prominent and may lead to diagnosis of malignant melanoma. Therefore, the dermoscopic diagnosis of melanocytic skin lesions in patients who present shortly after a severe sunburn reaction should be handled with care. We recommend reexamination of these patients 1 month later to avoid unnecessary surgery.

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