Ultraviolet Radiation of Melanocytic Nevi

A Dermoscopic Study

Rainer Hofmann-Wellenhof, MD; H. Peter Soyer, MD; Ingrid H. Wolf, MD; Josef Smolle, MD; Sebastian Reischle, MD; Edgar Rieger, MD; Robert O. Kenet, MD, PhD; Peter Wolf, MD; Helmut Kerl, MD

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.

Arch Dermatol. 1998;134:845-850

From the Department of Dermatology, University of Graz, Graz, Austria (Drs Hofmann-Wellenhof, Soyer, I. H. Wolf, Smolle, Reischle, Rieger, P. Wolf, and Kerl); and the Department of Medicine, Cornell University Medical College, New York, NY (Dr Kenet).

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 ($\leq 4$ points difference on the visual analog scale from...
Erythema and pigmentation of the adjacent skin were measured with a reflectance photometer (Dermaspectrometer, 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, pigment 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 .005, the difference was considered significant. In the “Results” section, only the higher P value of both investigators is given.

**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 ($P<0.01$) and more faded ($P<0.007$). 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 ($P<0.05$), the nevi were more darkly pigmented ($P<0.001$), and, inversely, the hypopigmented areas were significantly less prominent ($P<0.01$). The pigment network structures were less prominent ($P<0.01$) and more faded ($P<0.007$). In addition to the parameters that differed significantly at day 3, the number and intensity of brown-black globules increased ($P<0.05$).

**Day 14**

The nevi were still darker brown ($P<0.01$), and the hypopigmented areas were less prominent ($P<0.02$).
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 al.16 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 al.17 demonstrated an up-regulation of integrins of the keratinocytes in the overlying.
The epidermis of UV-irradiated nevi. The authors hypothesized that this induction of integrins may lead to the observed emigration of single melanocytes into the suprabasal layers of the epidermis.17 Results of an ultrastructural investigation of UV-irradiated nevi by Pawlowski et al18 revealed prominent rough endoplasmic reticulum, Golgi complex, and mitochondria with tubular cristae, suggesting increased cellular metabolism. Also, centrioles indicating mitotic activity were frequently found.18 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.8

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.19,20

Three studies have already focused on the impact of UV irradiation on the dermoscopic appearance of melanocytic nevi. First, Stanganelli et al21 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.21 Second, Stanganelli et al22 documented that intense sun exposure influenced the dermoscopic image of melanocytic nevi. In this study,22 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.22 Third, Hofmann-Wellenhof et al23 recently conducted a study in pa...

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 al24 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.25 Moreover, using a ×10 magnification, black-brown globules are sometimes indistinguishable from black dots, one of the most specific dermoscopic criteria for melanoma.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.28 Finally, Nilles et al29 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.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.

Accepted for publication March 19, 1998.

This study was supported by a grant from the Österreichische Krebshilfe Steiermark, Graz, Austria.

Corresponding author: H. Peter Soyer, MD, Department of Dermatology, University of Graz, Auenbruggerplatz 8, A-8036, Graz, Austria (e-mail: peter.soyer@kfunigraz.ac.at).

REFERENCES

11. Holman CD, Armstrong BK, Heenan PJ. Relationship of cutaneous malignant melano