OBSERVATION

Malignant Melanoma in Marathon Runners

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Background: Marathon running has surged in popularity; it is generally believed to be healthy, but may be associated with medical risks. Over the past decade, we observed 8 ultramarathon runners with malignant melanoma. UV exposure, immunosuppression due to long-term intensive exercise, or both have been discussed as potential triggers in these patients. To further evaluate risk factors for malignant melanoma in marathon runners, we examined anamnestic, phenotypic, sun-related, and clinical variables in 210 athletes and compared them with those of an age- and sex-matched control group.

Observations: Although control subjects exhibited higher sun sensitivity and more common melanocytic nevi, marathon runners presented with more atypical melanocytic nevi, solar lentigines, and lesions suggestive of nonmelanoma skin cancer. These findings correlated with increasing training intensity. During exercising, most runners wore shorts (96.7%) and shirts (98.6%) that would not or would only partially cover their back and extremities. Regular use of sunscreen was reported in only 56.2% of runners.

Conclusions: Compared with a representative control group, marathon runners presented with an increased risk for malignant melanoma and nonmelanoma skin cancer. They should reduce UV exposure during exercising by choosing training and competition schedules with low sun exposure, wearing adequate clothing, and regularly using water-resistant sunscreens.

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RUNNING IN GENERAL AND marathon running in particular has surged in popularity over the past years. While regular low-impact exercise is considered to improve one's health, endurance exercise, such as marathon running, may be associated with severe illness.[1-3] Over the past decade, we observed 8 ultramarathon runners (7 men and 1 woman; median age, 50 years; age range, 35-56 years; mean weekly training intensity, 120 km) with malignant melanoma (MM). Their clinical and histopathological characteristics are shown in **Table 1**. With an average of 300 newly diagnosed melanoma cases each year at our department, one of Austria's melanoma referral centers, the findings in these 8 patients clearly did not reach any statistical significance. Yet, we were concerned by this observation because all of us are enthusiastic runners and 2 of us (H.P.S. and H.K.) regularly participate in marathons. The observation that all melanomas were located on parts of the body that were not or were only partially covered by cloth during exercising (upper back, 6 of 8 runners; and lower thigh and calf, 1 of 8 runners each) and that, histopathologically, all but 1 melanoma arose in association with an atypical or congenital melanocytic nevus led us to reflect on potential causative factors for the development of MM in marathon runners. Besides other risk factors, including genetics and immunity, UV radiation has been established as the most important environmental risk factor for melanoma and nonmelanoma skin cancer (NMSC).[4] During training and competition, marathon runners may be exposed to considerable UV radiation. In addition, it is possible that repeated immunosuppression due to endurance exercise,[5] such as a marathon and, even more, an ultramarathon (100- or 160-km marathon), may favor MM development in such athletes. This pilot case-control study obtains an impression of the distribution of risk factors for MM in marathon runners compared with those of a representative control group (CG).

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METHODS

STUDY AND CONTROL SUBJECTS

Approval from the Medical University of Graz Ethics Committee was obtained for this study. After giving their informed consent, 210 marathon runners (166 men and 44 women; median age, 37 years; age range, 19-71 years) were enrolled in this study. At the annual Graz marathon, subjects were recruited at random voluntarily on the day before the race, when they collected their starting numbers. The 210 study

Table 1. Clinical and Histopathological Characteristics of 8 Ultramarathon Runners With MM*

Patient No./ Sex/Age, y	MM Location	Clark Level/Breslow Tumor Thickness, mm	Histopathological Association	Skin Type	>50 Melanocytic Nevi	>1 Atypical Melanocytic Nevus
1/M/50	Upper back	II/<0.75	Atypical melanocytic nevus	III	–	+
2/F/50	Upper back	Total regression	NA	II	+	–
3/M/55	Calf	IV/1.60	Congenital compound nevus†	III	–	+
4/M/53	Upper back	II/<0.50	Congenital dermal nevus†	III	–	+
5/M/35	Upper back	IV/1.75	Atypical melanocytic nevus	II-III	+	–
6/M/56	Upper back	III/3.25	Congenital dermal nevus†	II	–	–
7/M/35	Thigh	III/1.25	Atypical melanocytic nevus	III	–	+
8/M/48	Upper back	III/1.60	Atypical melanocytic nevus	II	–	–

Abbreviations: MM, malignant melanoma; NA, data not available; +, present; –, absent.
*All patients had numerous solar lentigines.
†The associated congenital nevi were only evident on histopathological examination. Clinically, the overall diameters of the lesions ranged from 9 to 14 mm.

subjects represented 12.8% of 1646 marathon participants. Control subjects were recruited in the same way during a skin cancer screening campaign in 5 recreation centers in Graz and Styria, the surrounding state. A total of 1057 individuals participated in the screening campaign, of whom 210 age- and sex-matched control subjects were selected for this study. To be included in this study, all subjects, cases and controls, had to be white residents of Styria.

STUDY QUESTIONNAIRE AND TOTAL BODY SKIN EXAMINATION

Study and control subjects were asked to answer a comprehensive questionnaire that included questions on anamnestic, phenotypic, and sunlight-related risk factors for the development of MM. Information collected with regard to anamnestic factors included personal and/or family history of skin cancer and changes in skin lesions. Information collected with regard to phenotypic markers included hair color, eye color, number of ephelides, and sun sensitivity. Information collected with regard to sunlight-related factors included number of sunburns with and without blisters. All subjects had a total body skin examination performed by an experienced dermatologist and were screened for skin cancer. Skin type (according to Fitzpatrick[6]) and numbers of common melanocytic nevi, atypical melanocytic nevi, and solar lentigines were recorded for each individual. In addition, information regarding training habits was collected from marathon runners, and included weekly training intensity, type of sportswear, and use of sunscreen when training and/or competing.

STATISTICAL ANALYSIS

Descriptive analysis was undertaken using a commercially available software program (SPSS, version 11.0; SPSS Inc, Chicago, Ill) to examine frequency distributions of the various risk factors. Data were reported as frequencies and percentages. To compare risk factors between the marathon group (MG) and the CG, statistical testing was performed using the χ^2 test. $P \leq .05$ was considered to indicate statistical significance.

RESULTS

Table 2 shows the distribution of anamnestic, phenotypic, sunlight-related, and clinical risk factors for MM in the MG and the CG, and in 3 subgroups of the MG. Those resulted from stratification of MG according to the weekly training intensity of the marathon runners (ie, <40, 40-70, and >70 km/wk). All subjects, cases and controls, exhibited numerous risk factors for the development of MM. When we compared these between MG and CG, the following significant differences were observed. Although control subjects exhibited higher sun sensitivity, reflected by more individuals with blue, green, or gray eye color and skin type I or II, and more common melanocytic nevi, marathon runners presented with more atypical nevi and solar lentigines. These were particularly pronounced in the subgroup with the highest training intensity. On clinical examination, no skin lesions suggestive of MM were diagnosed in either group. Yet, 24 persons in the MG and 14 persons in the CG were referred to local dermatologists for surgical treatment of skin lesions suggestive of NMSC, including basal cell carcinomas, squamous cell carcinomas, and actinic keratoses. Within the MG subgroups, the highest referral rate was observed for the group with the highest training intensity. Follow-up data on these patients and their histopathological results are not available because information was collected anonymously because of Austrian laws on personal privacy. In addition, information regarding training habits was collected in marathon runners and included weekly training intensity, type of sportswear, and use of sunscreen when training and/or competing. Most marathon runners ran either up to 40 km/wk (78 [37.1%]) or 40 to 70 km/wk (101 [48.1%]); 31 subjects (14.8%) regularly ran more than 70 km/wk. When asked about the type of sportswear they usually used, most reported they wore running shorts (203 [96.7%]) and short-sleeved (184 [87.6%]) or sleeveless (23 [11.0%]) shirts, which would not or would only partially cover the shoulders and upper arms. Regular use of sunscreen during exercising was reported by 118 subjects (56.2%), and occasional use was reported by 88 subjects (41.9%); 4 persons (1.9%) reported no use of sunscreen.

COMMENT

In this study, compared with an age- and sex-matched control population of the same area and ethnicity, marathon runners presented with significantly more atypical

Table 2. Distribution of Risk Factors for Malignant Melanoma in MG Compared With the Age- and Sex-Matched CG in This Study*

Risk Factor	Total MG (N = 210)	Total CG (N = 210)	Training Intensity of the MG, km/wk		
			<40 (n = 78)	40-70 (n = 101)	>70 (n = 31)
Anamnestic					
Personal or family history of skin cancer	**3** (1.4)	6 (2.9)	0	2 (2.0)	1 (3.2)
Changes in skin lesions	**28** (13.3)	36 (17.1)	10 (12.8)	16 (15.8)	2 (6.5)
Phenotypic					
Blond or red hair	**58** (27.6)	50 (23.8)	23 (29.5)	26 (25.7)	9 (29.0)
Blue, gray, or green eyes	**117** (55.7)†	141 (67.1)	41 (52.6)‡	56 (55.4)	20 (64.5)
Numerous ephelides	**53** (25.2)	58 (27.6)	25 (32.1)	23 (22.8)	5 (16.1)
High sun sensitivity (skin type I or II)	**114** (54.3)§	156 (74.3)	42 (53.8)§	56 (55.4)§	16 (51.6)‖
Sun related					
>10 Sunburns	**82** (39.0)	82 (39.0)	28 (35.9)	42 (41.6)	12 (38.7)
At least 1 sunburn with blisters	**46** (21.9)	59 (28.1)	20 (25.6)	15 (14.9)‖	11 (35.5)
Clinical					
>50 Common melanocytic nevi	**29** (13.8)‡	47 (22.4)	9 (11.5)	18 (17.8)	2 (6.5)
>1 Atypical melanocytic nevus	**99** (47.1)§	66 (31.4)	32 (41.0)	51 (50.5)§	16 (51.6)¶
Numerous solar lentigines	**64** (30.5)‖	42 (20.0)	23 (29.5)	28 (27.7)	13 (41.9)‖
Referral for excision	**24** (11.4)	14 (6.7)	5 (6.4)	13 (12.9)	6 (19.4)¶

Abbreviations: CG, control group; MG, marathon group.
*Data are given as number (percentages) of subjects.
†P=.02 vs CG.
‡P=.03 vs CG.
§P=.001 vs CG.
‖P=.01 vs CG.
¶P=.04 vs CG.

melanocytic nevi and more solar lentigines. In addition, the referral rate for surgical removal of skin lesions suggestive of NMSC was higher in marathon runners than in control subjects. These findings were particularly pronounced in the subgroup of runners with the highest training intensity. Besides the number of common melanocytic nevi, the number of atypical melanocytic nevi and solar lentigines has been shown to be the strongest independent indicator of an increased risk for the development of MM.[7] There is broad evidence that besides genetic susceptibility and immunity, exposure to sunlight is the major environmental factor involved in the cause of MM. Recent epidemiological studies[8,9] indicate that, along with sunburn history, recreational intermittent sunlight exposure plays a major role in the formation of MM. Marathon runners are exposed during training and competition. As pointed out by Moehrle,[10] in most outdoor activities with exposed skin, even if performed for a short time in sunny conditions, the limit for UV exposure of 0.3 minimal erythema doses per 8-hour work shift, as issued by the International Commission on Non-Ionizing Radiation Protection[11] and the American Conference of Governmental Industrial Hygienists,[12] is likely to be exceeded. By using *Bacillus subtilis* spore film dosimeters to measure UV exposure in athletes, Moehrle and coworkers[10,13] demonstrated that in outdoor sports, such as professional cycling or a triathlon, these limits were exceeded up to more than 30 times during competition. They also showed that sweating because of physical exercise may significantly contribute to UV-related skin damage, because it increases the photosensitivity of the skin, facilitating the risk of sunburns.[14] These effects are presumably due to hydration of the horny layer, which leads to a shift in the stratum corneum UV absorption spectrum, to shorter wavelengths, and to a decrease in reflection and dispersion.[15] When asked about the type of sportswear most commonly used when exercising, most marathon runners in this study indicated that they wore gear that would not or would only partially cover especially UV-exposed body sites, such as the upper back, the arms, and legs. Only half of them (56.2%) reported regular use of sunscreen during training and/or competing, while 1.9% did not use sunscreen at all. Along with the undoubtedly important sun exposure, it may be speculated that exercise-induced immunosuppression in endurance sports may contribute to the risk of MM in marathon runners. Immunosuppressive therapy in patients who have undergone transplantation leads not only to an increase in the incidence of NMSC but also to an increase in melanocytic nevi and MM.[16] Although regular low-impact exercise is well established to improve one's health, overtraining, high-intensity training, and excessive exercise, such as cumulative training for a marathon, the marathon itself, and, in particular, an ultramarathon, may lead to suppressed immune function. This is thought to be the result of tissue trauma sustained during intense exercise, inducing cytokines that drive the development of a T helper 2 lymphocytic profile that results in simultaneous suppression of cell-mediated immunity, rendering the athlete susceptible to infection.[17]

In short, until further sport-physiologic studies elucidate in detail the potential association between exercise-induced immunosuppression and MM, runners should be alerted to the crucial role of UV radiation in the development of MM and NMSC. In particular, they should be advised to reduce UV exposure during exercising by

choosing training and competition schedules with low sun exposure, wearing adequate clothing, and regularly using water-resistant sunscreens.

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