ORIGINAL ARTICLE

Dermoscopic changes in melanocytic nevi in patients receiving immunosuppressive and biologic treatments: Results of a prospective case-control study

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Background: The immune system restrains benign melanocytic lesions, however the relationship between immunosuppression and changes in nevi is not known.

Objectives: We sought to investigate the development of new nevi in patients using immunosuppressive agents, to evaluate any size or dermoscopic changes in existent nevi, and to evaluate any risk of developing melanoma.

Methods: There were 266 melanocytic lesions in 103 patients undergoing immunosuppressive therapy and 180 melanocytic lesions matched for age, sex, race, and Fitzpatrick skin type in 60 healthy control subjects.

Results: Nevus counts increased from baseline in the treatment group ($P < .001$) as did nevus size ($P = .046$) but the increase compared with the control group only remained statistically significant for nevus numbers ($P = .001$). There was a statistically significant appearance of dermoscopic changes in the nevi of immunosuppressed patients compared with healthy control subjects ($P < .001$). Ten lesions were excised including 6 because of significant dermoscopic change during treatment and all were benign.

Limitations: Follow-up duration was short and the number of patients was small.

Conclusion: Immunosuppressive therapy was associated with increased nevus counts and changed dermoscopic appearance but as none of the changed and subsequently excised nevi were malignant, continued monitoring for invasive features is a reasonable alternative to excision. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2015.07.013.)

Key words: anti–tumor necrosis factor-alfa; azathioprine; cyclosporine; dermoscopy; immunosuppression; immunosuppressive treatment; melanocytic nevus; melanoma; methotrexate.

Melanoma is a malignant tumor that originates from melanocytes. Exposure to ultraviolet radiation and genetic predisposition are the major risk factors for developing melanoma.[1] The immune system is the main factor restraining melanocyte proliferation.[2] "Eruptive nevus syndrome" is defined as the eruption of multiple nevi over a short time period in immunosuppressed patients.[3] Although it has been shown that a healthy immune system restrains benign melanocytic lesions, the relationship between immunosuppression and melanoma genesis has not been fully elucidated.[2]

Abbreviations used:

ABCD:	asymmetry, border, color, dermoscopic structures
7PCLS:	7-point checklist score
TNF:	tumor necrosis factor

The primary end points of our study included changes in nevus count, nevus size, and dermoscopic scores in patients taking immunosuppressive agents and the secondary outcome of the study was the histopathological diagnosis of excised lesions.

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METHODS

The study protocol was designed as a prospective case-control trial. It included a total of 446 melanocytic lesions. There were 266 melanocytic lesions in 103 patients older than 18 years of age undergoing immunosuppressive therapy (including anti–tumor necrosis factor [TNF]-alfa, cyclosporine, methotrexate, and azathioprine) and 180 melanocytic lesions matched for age, sex, race, and Fitzpatrick skin type in 60 healthy control subjects.

CAPSULE SUMMARY

- The immune system restrains melanocytic proliferations.
- Although this study showed that immunosuppressive therapy influences nevus counts and morphology there was no evidence that this was linked to melanoma development.
- Monitoring may be a reasonable alternative to excision for many of these lesions.

Data were recorded for patients and healthy control subjects: Fitzpatrick skin type, history of sunburn, sunscreen use, place of residence, total sun-exposure score,[4] and immunosuppressant therapy protocols (initiation, total time, and dosage).

Melanocytic nevi on the trunk, arms, and legs were counted and photographed in standard poses.

Dermoscopic evaluations at each visit were carried out with the Dermlite II Pro (3GEN LLC, San Juan Capistrano, CA) hand dermoscope and with digital dermoscopy (Molemax II, Derma Medical Systems, Vienna, Austria).

The dermoscopic features of each lesion at the first visit were evaluated according to: (1) color and structural symmetry; (2) parameters in the rule of asymmetry, border, color, dermoscopic structures (ABCD)[5]; and (3) melanoma-specific criteria (atypical pigment network, atypical vascular pattern, blue-white veil, irregular streaks, irregular pigmented blotches, irregular dot/globules, and regression structures), which were included in the 7-point checklist score (7PCLS).[6] Dermoscopy scores were determined for each lesion according to the ABCD rule and the 7PCLS. Evaluations were repeated at follow-up visits, which were performed at 3-month intervals for 12 months. Dermoscopic changes in lesions were evaluated by the observation of 3 groups of changes, as follows, which determined their dermoscopy scores[7]: (1) changes in size; (2) symmetric or asymmetric changes in structure or color; and (3) melanoma-specific criteria (eccentric structureless area, reticular or branched thick lines, gray or blue structures, peripheral black dots or clods, radial lines or pseudopods, white lines, polymorphous vessels or parallel ridge pattern in acral lesions).[8] These 3 groups of changes were evaluated, and total change scores were determined as follows: (1) no change: none of the above changes are present; (2) minor change: symmetric structural/color changes without alteration in size or with maximum 2-mm growth; (3) moderate change: asymmetric structural/color changes without alteration in size or with maximum 2-mm growth, or symmetric structural/color changes with growth over 2 mm; and (4) major change: asymmetric structural/color changes with growth over 2 mm or demonstration of melanoma-specific criteria, regardless of changes in growth.

Lesions demonstrating melanoma-specific dermoscopic findings and high scoring lesions (according to the ABCD rule and the 7PCLS) were excised for histopathological examination.

Patients undergoing immunosuppressive therapy were evaluated for the effects of immunosuppression time and immunosuppressant dosage, on dermoscopic changes.

A computer program (SPSS Windows 18, IBM Corp, Armonk, NY) was used for statistical analysis. Mean ± SD or median (minimum, maximum) were used as descriptive statistics. Analysis of variance, Wilcoxon signed rank test, and Kruskal-Wallis test were used for comparisons between groups. Differences between the groups for categorical variables were analyzed using χ^2 test. Difference among 5 groups for continuous variables was evaluated by 1-way analysis of variance or Kruskal-Wallis analysis of variance, where applicable. When the P value from the Kruskal-Wallis test statistics was statistically significant, multiple comparison test was used to know which groups differed from which others.[9] Comparison of nonnormally distributed continuous variables was evaluated by the Wilcoxon signed ranks test. Nevi diameters, nevi numbers, total dermoscopic score according to the ABCD rule and 7PCLS, and dermoscopic evaluation at the initial examination and at the last visit were also compared. Values of P less than .05 were accepted as significant.

RESULTS

Demographic data and nevus numbers of the patients and control subjects are shown in Table I. There were no significant differences between the immunosuppressant therapy and healthy control groups with regard to age, sex, Fitzpatrick skin type, history of sunburn, total sun-exposure score, and use of sunscreen and hats.