Interferon Induces Some Involution of Atypical Nevi

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PARIS — Treatment of atypical nevi with high-dose interferon alfa-2b may induce at least partial involution, based on the results of a small study.

Six of eight atypical nevi demonstrated a decrease in their greatest diameter, perimeter, or surface area, suggesting partial involution following treatment with high-dose interferon alfa-2b, reported Dr. Mona Amini-Adle of the department of dermatology at Hôpital de l'Hôtel Dieu, Lyon, France.

Partial clinical involution of atypical nevi was associated with an upregulation of CD4/CD8 ratio in the intra-nevi compartment, Dr. Amini-Adle said at the annual congress of the European Academy of Dermatology and Venereology.

Clinical atypia and histologic dysplasia were correlated in half of the lesions, but the clinical changes were not accompanied by histologic signs of involution.

For the study, 10 patients with stage IIB-III melanoma, and at least four atypical nevi from each patient, were enrolled. The four nevi were identified as A-D at enrollment and photographed.

Two nevi were selected at random for removal prior to treatment; the remaining two were removed after 3 months of treatment. All nevi were evaluated clinically, pathologically, and with a double immunohistochemistry procedure (CD4-CD8; CD1a-CD83).

Patients were treated according to their melanoma status. Patients at high risk for melanoma were treated with a regimen of 20 million U/m^2 per day given intravenously five times a week for 4 weeks, followed by 10 million U/m^2 per day given subcutaneously three times a week until 1 year of treatment was reached. Lower-risk patients received 3 million U/day subcutaneously three times a week for 3 months.

Dr. Amini-Adle reported on eight patients with a mean age of 36 years, half of whom were women. Sixteen clinical photos (eight pre- and eight posttreatment) from five patients were informative. Biopsy samples from eight patients were informative for 27 lesions—14 pre- and 13 posttreatment nevi. "We did not observe any histologic regression," said Dr. Amini-Adle.

Clinical atypia and histologic dysplasia were correlated in half of the lesions. The clinical changes were not accompanied by histologic signs of involution. Immunohistochemistry analysis showed alterations in lymphocyte infiltrates in nevi that were focal, with histologic signs of dysplasia and a significant upregulation of the CD4/CD8 ratio in the intra-nevi compartment ($P = .0076$).

No changes in lymphocyte response were observed after treatment, nor were any changes seen in the degree of atypia of these lesions. With regard to lymphocytic infiltrates, there was a trend of upregulation of CD4 cells and downregulation of CD8 cells, Dr. Amini-Adle said.

This resulted in upregulation of the CD4/CD8 ratio. These changes, however, were observed only in dysplastic nevi, not normal melanocytic nevi.

Dissociated responses of lymphocytes in both normal and atypical nevi suggest differential immunologic response to these entities. The dendritic cell infiltrate was not found to be influenced either in atypical nevi or normal nevi following treatment.

Atypical nevi have been shown to be nonobligate precursors of, and risk markers for, melanoma. Interferon alfa-2b is the only agent that has been shown to have a consistent and durable impact on relapse-free survival in melanoma patients, but it has not been studied for atypical nevi.

Interferon is known to enhance the immunogenicity of tumors. It is also known to suppress immune tolerance and to increase the degree of lymphocytic infiltrate in lesions that progress under treatment. Interestingly, in spontaneous regressive melanoma, the CD4/CD8 ratio is upregulated.

The meaning of upregulation in dysplastic nevi is unclear.

Dr. Amini-Adle noted that CD4 cells appear to play an important role in this regression. ■