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Regression of nevi in a melanoma patient treated with interferon

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Background

High-risk melanoma patients are occasionally offered adjuvant treatment with interferon alpha 2b as a postsurgical treatment. This treatment is thought to improve disease-free survival by upgrading immunomodulatory functions, which cause an antitumor effect [1,2].

We describe a patient treated with adjuvant interferon therapy for stage III melanoma, who presented multiple regressing nevi after the treatment.

Case report

A 58-year-old male patient with a history of multiple basal cell carcinomas and a previous melanoma was diagnosed upon presentation with stage III melanoma, consisting of a primary melanoma of the lower back with inguinal lymph node metastases. After excision of the primary tumor, the patient was treated with high-dose interferon alpha 2b for six months. Four months after completing the interferon treatment, the patient sought treatment at the pigmented lesion clinic of Sheba Medical Center, Tel Hashomer, Israel. Full body skin examination revealed multiple pigmented nevi of the trunk and extremities. Of them, six nevi had a similar dermoscopic pattern, including a network and localized fine and coarse gray granularity which in general represent regression (Figures 1, 2). In order to further analyze the lesions, confocal microscopy was performed (VivaScope 1500, Lucid Inc, Rochester, New York). Instrumentation and acquisition procedures have been described previously [3,4]. Confocal mosaic image (5 mm X 5 mm, compatible with low magnification microscopy) showed a ringed pattern correlating with the reticular dermoscopic pattern (Figure 3). Individual confocal images (0.5 mm X 0.5 mm, equivalent to high magnification microscopy) showed that in certain areas the ringed pattern is not visible and instead there are elongated refractile structures compatible with dendritic cells (Figure 4). These dendritic cells could represent melanocytes, raising the possibility of pagetoid spread of a melanoma or

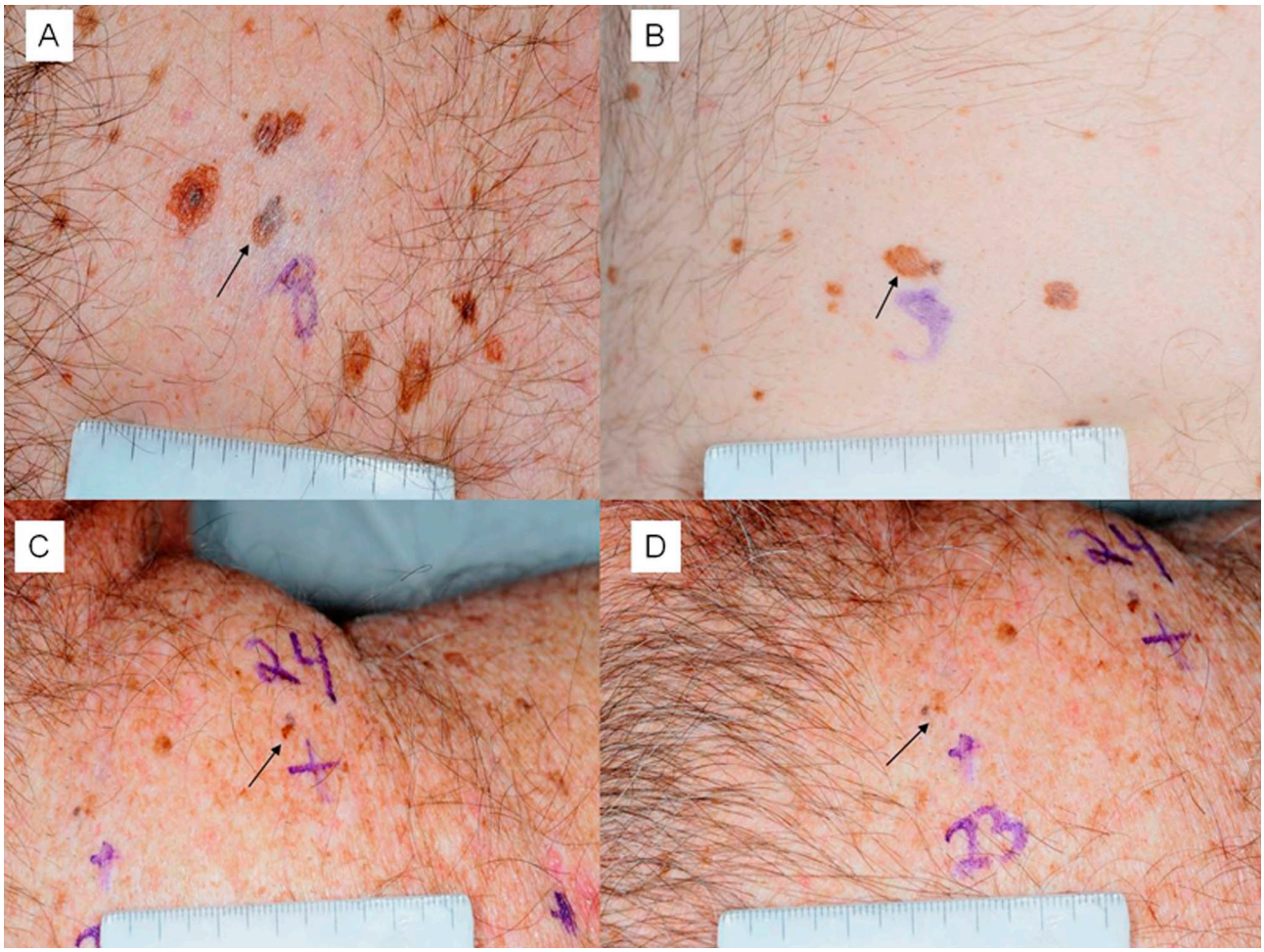

Figure 1. Close-up clinical images of four of the patient's nevi (arrows), showing pigmented maculae with a distinct gray focus. [Copyright: ©2012 Rishpon et al.]

Langerhans cell, as part of the inflammation. Histopathologic analysis of this lesion showed a dysplastic nevus with areas of melanosis, fibrosis and inflammation and no sign of pagetoid spread (Figure 5A). In order to further identify the dendritic cells, CD1a and Melan-A stains were performed. CD1a stain was positive throughout the epidermis (Figure 5B) and Melan-A stain was positive at the lower epidermis (Figure 5C), suggesting that the dendritic cells represent Langerhans cells as part of the inflammatory reaction.

The five other lesions were biopsied as well, all showing histopathologically a dysplastic nevus with focal areas of regression.

Discussion

Regression of nevi in the setting of melanoma and interferon treatment might be induced by the melanoma, the interferon treatment, or both. Examples of remote regression induced by melanoma include halo nevi and melanoma-associated leukoderma. These phenomena result from an immune reaction against shared antigens on benign and malignant melanocytes [5,6].

Hu and colleagues described primary melanomas presenting as inflamed pigmented lesions during adjuvant interferon treatment for melanoma [7]. They suggest that the immunomodulatory effects of interferon targeting melanoma unmasked or "lit up" these subsequent primary melanomas. We hypothesize that this same effect might be responsible for causing inflammation, not only in melanomas, but also in nevi.

It has been suggested that imiquimod, which stimulates interferon transcription, can cause regression or resolution of atypical nevi [8,9]. In a previous study, four of imiquimod treated nevi (compared to 0 non-treated nevi) showed partial regression on histopathology after 10 weeks of imiquimod treatment [8]. Another study examined three patients, each with one atypical nevus treated with imiquimod for 12 weeks [9]. Two lesions demonstrated inflammation on excisional biopsy.

Of note, since we saw the patient for the first time only after he had already completed the interferon treatment, the concept of the regression being caused by the interferon treatment is merely a hypothesis. As we do not have previous documentation of this patient's nevi, we cannot rule out that this was the patient's original nevi pattern. In fact there are

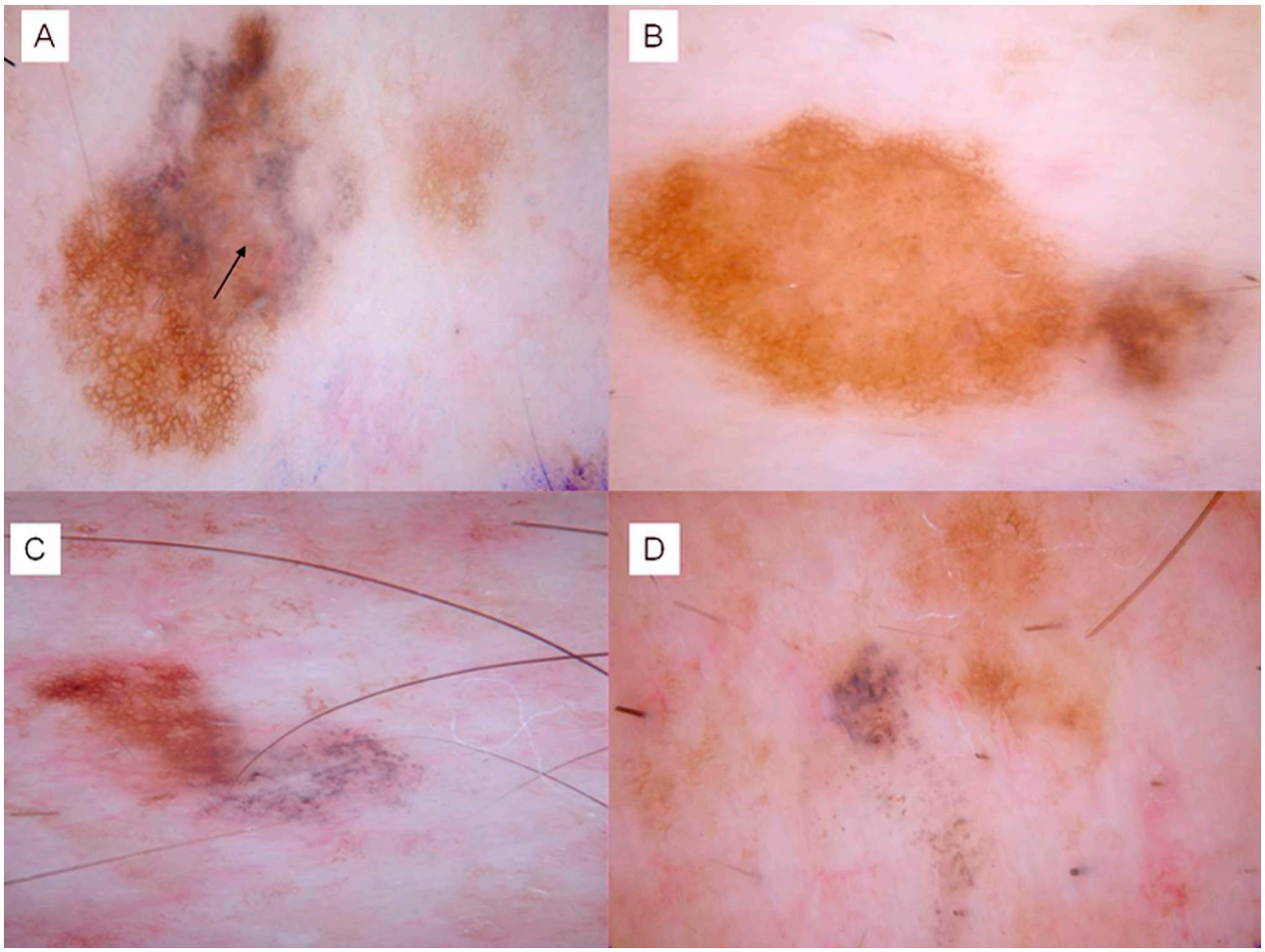

Figure 2. Dermoscopic images of the four nevi showing network and localized gray granularity. [Copyright: ©2012 Rishpon et al.]

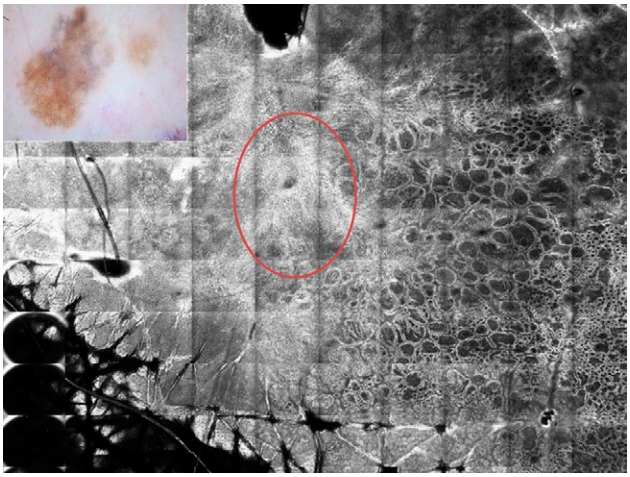

Figure 3. Confocal microscopy mosaic (5 x 5 mm) at the level of the dermo-epidermal junction showing a ringed pattern on the right, and a disorganized pattern with disappearance of the ringed pattern in the center (red circle). Inset: dermoscopic figure showing a network with localized gray granularity. [Copyright: ©2012 Rishpon et al.]

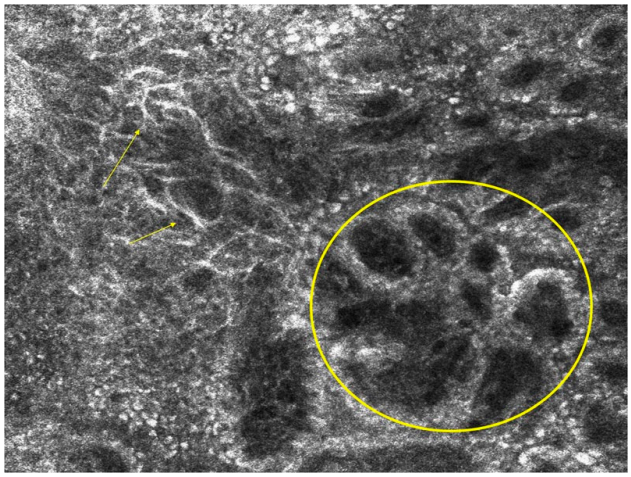

Figure 4. Individual confocal image (500 x 500 microns) showing a close-up view of the ringed pattern (circle) and dendritic structures (arrows). [Copyright: ©2012 Rishpon et al.]

three possible interpretations of this regression, its being, the original nevi pattern of this patient, caused by the melanoma, or caused by the adjuvant interferon treatment. Understanding the pathogenesis of the findings described could have a role in improved melanoma diagnosis and treatment. For example, regression in nevi could be a surrogate for identifying patients in whom interferon mediates an inflammatory response against melanocytes. Future studies regarding the pathogenesis of nevi regression in the setting of melanoma and interferon treatment are needed.

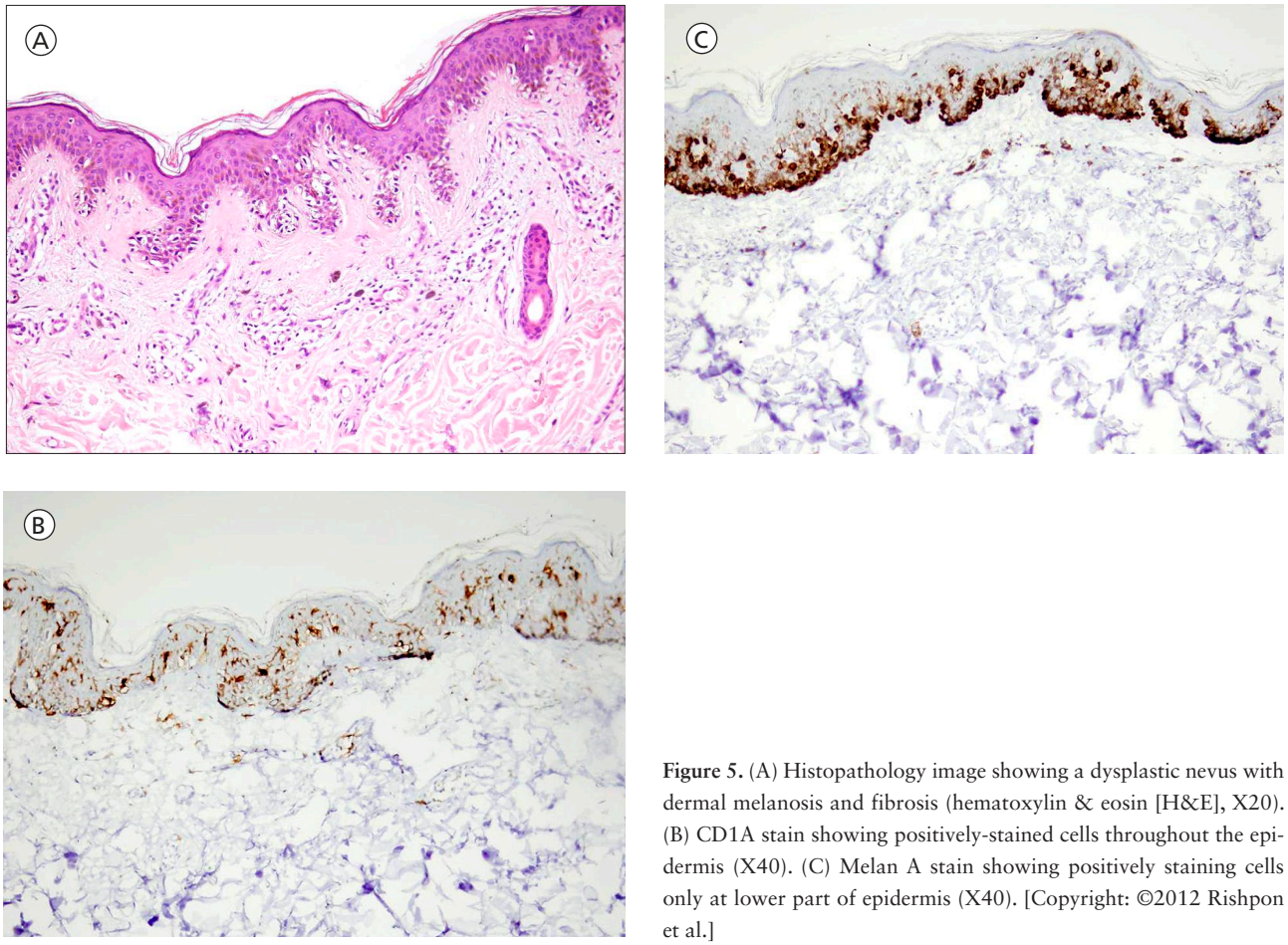

Figure 5. (A) Histopathology image showing a dysplastic nevus with dermal melanosis and fibrosis (hematoxylin & eosin [H&E], X20). (B) CD1A stain showing positively-stained cells throughout the epidermis (X40). (C) Melan A stain showing positively staining cells only at lower part of epidermis (X40). [Copyright: ©2012 Rishpon et al.]

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