RESEARCH LETTERS

Nodular melanomas associated with nevi

To the Editor: Nodular melanoma (NM) represents approximately 9% to 15% of invasive melanomas.[1,2] The histopathologic definition of NM is based on the absence of a radial growth phase. Most frequently, it manifests itself in midlife with a median age at presentation of 53 years, and it is more common in males than in females.[3] In 11% to 25% of the cases, NM is histologically associated with nevi.[4,5] We report the experience of the Melanoma Unit of University Hospital Spedali Civili of Brescia, Italy. Between January 1, 1982 and October 1, 2009, 95 patients with cutaneous NM were identified from a group of 1865 patients with histologically confirmed melanoma; the incidence was 5.1% (95/1865). Of the 95 patients evaluated, 49 (51.6%) were males and 46 (48.4%) were females. All patients were white. The average age was 54.5 years (range, 15-91). Primary melanomas were found in different body sites as follows: eight (8.4%) lesions were on the head and neck, 32 (33.7%) on the trunk, 22 (23.2%) on the upper extremities, and 33 (34.7%) on the lower extremities. The lesions appeared most frequently on the trunk in male patients and on the lower extremities, upper extremities, and trunk in female patients. None of our 95 cases had a documented family history of melanoma. With regard to invasive melanomas, Breslow thickness ranged from 0.5 mm to 11 mm, with a mean thickness of 3.9 mm. The mean Breslow thickness was 4.4 mm in male patients and 3.4 mm in female patients.

Ten out of 95 patients (10.5%) showed histologic evidence of an associated nevus; five patients were male and five were female. The average age of these 10 patients was 55.9 years. In seven patients, melanoma arose in association with an acquired nevus (2 dysplastic nevus and 5 other acquired nevi). In the remaining three patients, melanoma arose in association with a small congenital nevus. When examined by anatomic location, one lesion was on the head and neck, five were on the trunk, one was on the upper extremities, and three were on the lower extremities. The mean Breslow thickness for these 10 patients was 2.3 mm. When comparing the two groups (NM vs NM associated with nevi), the second group showed a thinner Breslow thickness (4.04 mm vs 2.3 mm).

Our findings support the belief that in most cases, NM arises in absence of a precursor lesion. NM often fails to exhibit the original ABCD diagnostic criteria, but we believe that the "E" (evolving) criterion may help in the clinical diagnosis.

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A noninvasive technique, reflectance confocal microscopy, for the characterization of melanocyte loss in untreated and treated vitiligo lesions

To the Editor: Vitiligo is a common depigmentation disorder that is characterized by the progressive loss of melanocytes. The etiopathogenesis of depigmentation is not fully known, and neither is the source of repigmentation. In vivo reflectance confocal microscopy (RCM) is a new technique that allows noninvasive skin imaging at a cellular resolution. Because melanin is the strongest endogenous contrast in the skin, RCM is particularly suitable to analyze pigmentary disorders.[1] We used RCM to characterize the

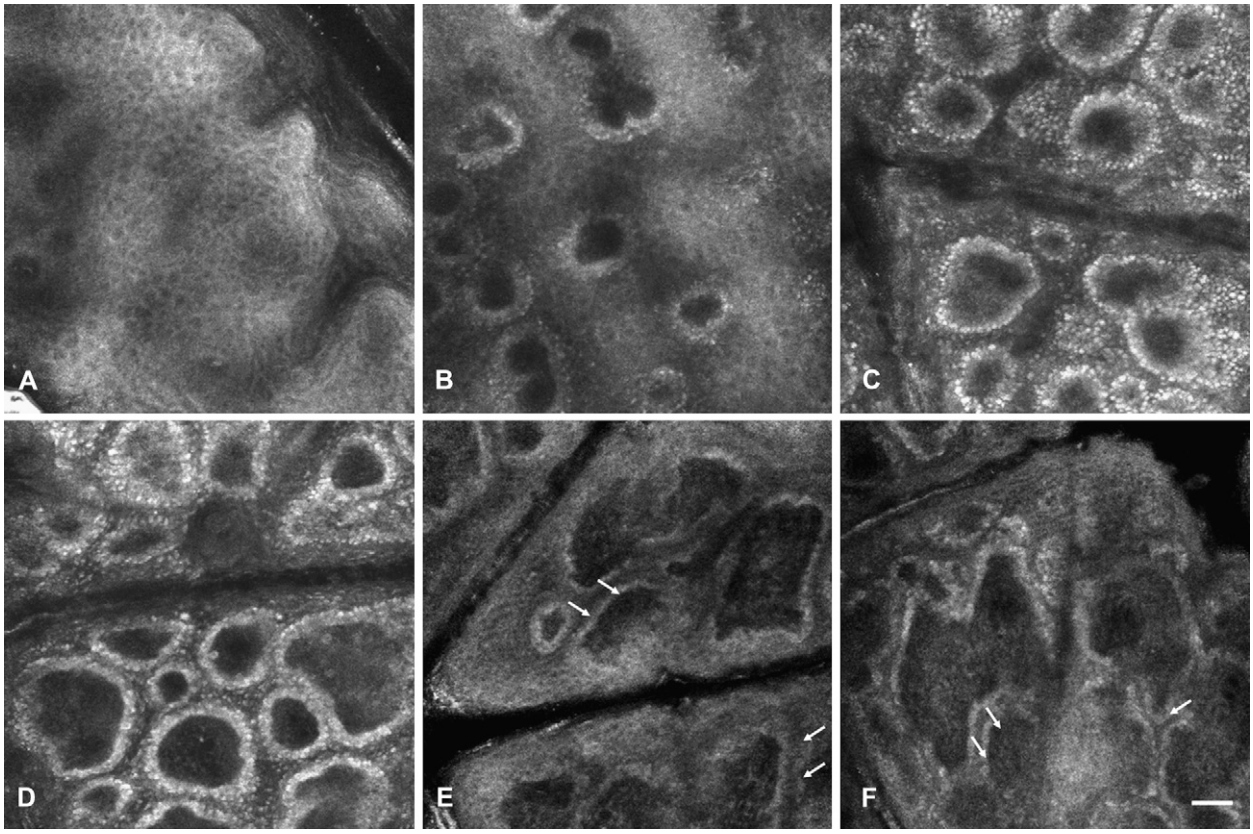

Fig 1. Reflectance confocal microscopy (RCM) imaging of vitiligo (patient 1). **A**, RCM images of lesional skin showed no bright cells and the disappearance of the normal papillary ring at the level of basal layer. The brightness of the basal cells in perilesional skin (**B**) is lighter than distant normal skin (**C**), but there is no difference between distant normal skin of a vitiligo patient (**C**) and normal skin of the healthy control (**D**). **E**, So-called "half rings" or "scalloped border-like rings" were observed in distant normal skin, but also normal skin of control (**F**). Scale bar: 50 μm.

depigmenting process and the response to ultraviolet B light (UVB) therapy in vitiligo.

Eleven patients with Fitzpatrick skin types II through VI presenting with nonsegmental vitiligo and who gave informed consent were enrolled in this study. Their ages ranged between 16 and 60 years; the study included five females and six males. They were required not to receive treatment for vitiligo for at least 3 months. RCM images were taken at 5-μm intervals from the corneal layer to the superficial dermis using a reflectance confocal laser scanning microscope (Vivascope 1500; Lucid, Rochester, NY). We compared vitiliginous skin, perilesional normal skin, and distant normal skin (abdomen) of patients, and abdomen skin of healthy controls matched for age and phototype. The brightness of basal cells was scored independently by two different observers as 0 (no pigmentation) to 6 (marked pigmentation). In three patients, a vitiligo lesion was examined weekly during the course of narrowband UVB therapy.

Normal pigmentation in the RCM images appears as bright cells grouped around dermal papilla defining characteristic ring structures. RCM examination of vitiligo lesions showed a disappearance of papillary rings at the basal layer level and no evidence of melanocytes (Fig 1). Perilesional normal skin showed intact papillary rings, but the brightness of cells was significantly reduced compared to distant normal skin (2.5 ± 1.1 vs 3.4 ± 1.7; $P < .05$; Mann–Whitney U test). Distant normal skin showed no difference with controls (3.4 ± 1.7 vs 3.6 ± 1.4; $P = .08$). RCM examination in the course of UVB therapy showed large dendritic melanocytes in hair follicles, in the epidermis of perilesional skin, and of repigmentation islands (Fig 2).

Vitiligo presents clinically as well circumscribed achromic patches, but the true extent of the depigmentation process is debated.[2,3] Taking advantage of the noninvasive process of RCM, we compared the microscopic structure of the skin in vitiligo at different body sites and at different times during UVB therapy.

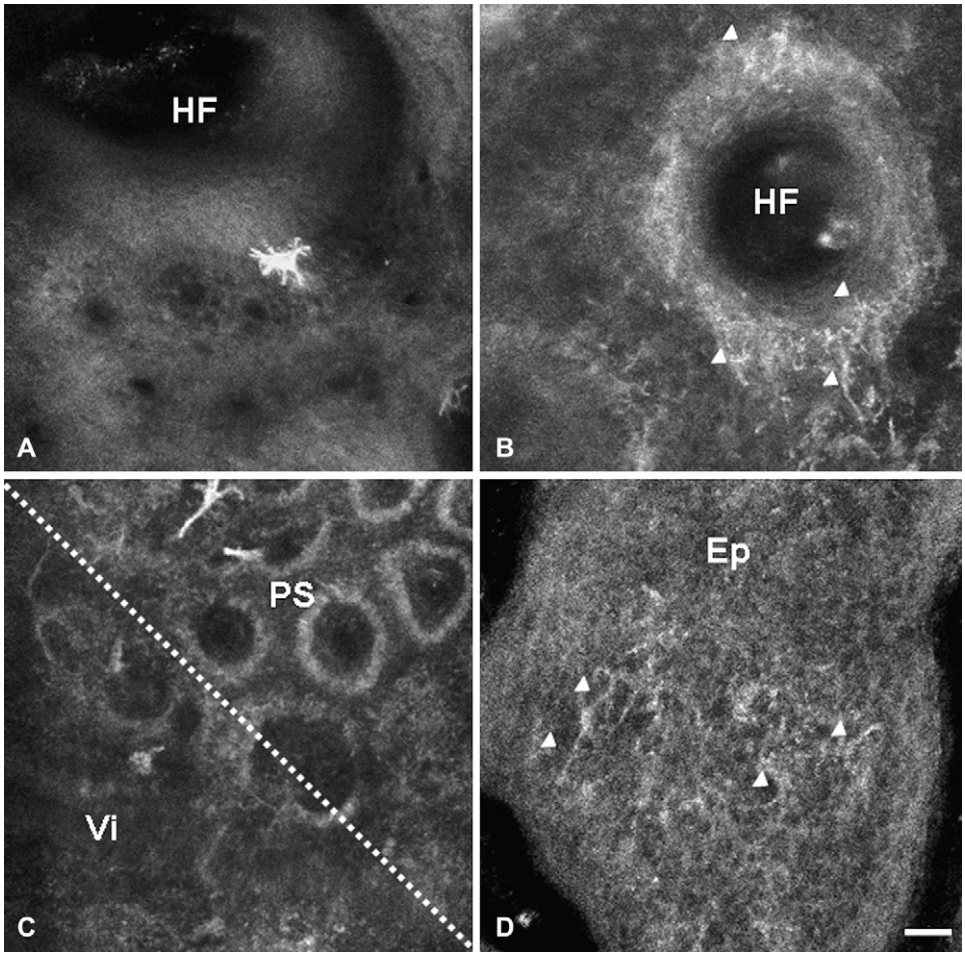

Fig 2. Reflectance confocal microscopy imaging of vitiligo during ultraviolet B light therapy showing bright dendritic melanocytes (*arrowheads*) in the (**A**) outer root sheath of a hair follicle, (**B**) around a hair follicle, (**C**) at the basal layer of perilesional skin, and (**D**) in a repigmenting epidermal island. *Ep*, Epidermis; *HF*, hair follicle; *PS*, perilesional skin; *Vi*, vitiliginous skin. Scale bar: 5 μm.

At baseline, we found no pigmented cells in vitiligo lesions, significantly fewer pigmented cells in perilesional skin, and normal features in skin distant from vitiligo lesions. RCM did not clarify the presence or absence of dormant melanocytes in vitiligo lesions, because RCM detects only melanized melanocytes. Incomplete papillary rings were previously reported as an abnormal RCM feature of normal skin in vitiligo.[4] However, we found the same feature in controls, suggesting a physiologic variation rather than a pathologic trait. It seems likely that whole skin of vitiligo patients is not susceptible to loss of pigmentation at one single point in time. During UVB therapy, RCM showed an appearance of bright dendritic melanocytes in vitiligo lesions. Melanocytes with such RCM features are likely to be active, because they express tyrosinase[5] and they are found in hyperpigmented lesions of melasma.[6] Interestingly, RCM detected some of these melanocytes in hair follicles, the previously described follicular "reservoir" of vitiligo.[7] The present study does not indicate the origin of melanocytes for repigmentation process in vitiligo, but it suggests that a time-course RCM study during phototherapy of vitiligo lesions could clarify this question.

In conclusion, the noninvasive technique of RCM is a promising tool for characterizing the nature of melanocytes loss in untreated and treated vitiligo lesions.

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A randomized, double-blind, active-controlled, parallel-group pilot study to compare the efficacy and sedative effects of desloratadine 5 mg with levocetirizine 5 mg in the treatment of chronic idiopathic urticaria

To the Editor: The new generation antihistamines, such as desloratadine and levocetirizine, have provided major advances in the treatment of chronic idiopathic urticaria (CIU).[1] There has been debate regarding the efficacy and sedative effects of desloratadine and levocetirizine, with findings from several studies indicating that levocetirizine is superior to desloratadine in terms of drug activity.[2,3] However, the comparative sedative effects of the two drugs have not been well studied.

We conducted a randomized, double-blind, active-controlled, parallel-group pilot trial of 64 patients (20 males, 44 females) with CIU who received once-daily desloratadine 5 mg (Denosin; Lotus Pharmaceutical, Taipei, Taiwan) and levocetirizine 5 mg (Xyzal; UCB Farchim SA, Switzerland) for 6 weeks (Fig 1). The therapeutic response to the study medication, jointly assessed by the investigator and the patients, was evaluated every 2 weeks using a 5-point scale (1 = complete relief, 2 = marked relief, 3 = moderate relief, 4 = slight relief, and 5 = treatment failure). Sedative effects were assessed using the Epworth Sleepiness Scale (ESS), visual analogue scale (VAS), and Stanford Sleepiness Scale (SSS). Data pertaining to efficacy and sleepiness were compared between treatment groups by fitting marginal linear regression models using the generalized estimating equations method for our repeated measures data, with treatment and baseline values included in the model.[4]

In the multivariate analysis, we found that conditioning on age, gender, body mass index, renal/liver function, health problems, interactions between visits and treatments, drug changes, comedication, and completeness of treatment, levocetirizine was independently associated with a better therapeutic response than desloratadine ($P = .0468$; Table I). Levocetirizine was associated with a significantly higher VAS sleepiness score than desloratadine in the first 2 weeks of treatment ($P = .0456$; Table I) but not beyond. For ESS and SSS scores, levocetirizine was also associated with more sedative effects than desloratadine but there was no significant between-group difference.

To date, no prospective randomized study has compared levels of sedation caused by these two drugs. In 2006, a retrospective comparison of selected events from previous prescription-event monitoring studies pertaining to desloratadine and levoceterizine was conducted.[5] It showed that levocetirizine was more likely to cause sedation than desloratadine during the first month of observation, although the overall incidence was low for both drugs. This finding is similar to that reported herein. In our study, the levocetirizine group had a higher VAS score, implying more sedation, than the desloratadine group. The between-group difference achieved statistical significance in the evaluation on day 14 but not beyond.

These results indicate that desloratadine was less sedative and levocetirizine was more efficacious. With continued treatment for more than 2 weeks, these differences in sedative effect may be somewhat minimized. The findings suggest that levocetirizine may facilitate better control than desloratadine for severe CIU. However, desloratadine should be considered if the patient has a strict contraindication to the sedative effects of levocetirizine and other antihistamines, especially in the early phase of treatment.