ORIGINAL ARTICLE

Clinical markers of vitiligo activity

Laila Benzekri, PhD,[a] and Yvon Gauthier, MD[b]
Rabat, Morocco, and Bordeaux, France

Background: Current modalities of understanding disease state (active/stable) are limited when considering treatment of vitiligo.

Objective: We sought to develop a rapid, accurate, and noninvasive assessment of vitiligo state.

Methods: In daylight and Wood's light examinations, 2 common clinical types of vitiligo were identified as amelanotic with sharply demarcated borders and hypomelanotic with poorly defined borders. Photographs were taken at the time of examination and a skin biopsy at the edge of a vitiligo lesion was performed. One year after the initial visit, the vitiligo was classified as stable if no new lesions had appeared, and as active if the number, size, or both of existing vitiligo lesions were increased. Skin biopsy specimens from 71 patients were stained and immunostained for melanocytes, $CD8^+$ T lymphocytes, and E-cadherin.

Results: The active lesions were associated with hypomelanotic appearance with poorly defined borders ($P < .001$), and histologically with an infiltration of $CD8^+$ T lymphocytes in the epidermis and dermis ($P = .017$), with a strong expression of E-cadherin ($P = .044$).

Limitation: The fact that this was a single-center study and that activity was sometimes site-dependent are limitations.

Conclusion: The hypomelanotic with poorly defined borders type could be a good indicator of the actual activity of a vitiligo lesion. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2016.12.040.)

Key words: activity; clinical aspect; histology; perilesional skin; vitiligo; Wood's light.

Vitiligo is a polymorphous, multifactorial, and polygenic disease characterized by the loss of melanocytes from the epidermis and hair follicle reservoirs.[1] Taking into account exclusively the clinical aspect of the lesions under daylight and Wood's light, 2 common clinical types of vitiligo lesions can be described: amelanotic with sharply demarcated borders (ASDB) and hypomelanotic with poorly defined borders (HPDB).[2,3] Trichrome, pentachrome, and inflammatory raised border types and more recently confetti-like depigmentation could be considered HPDB subtypes.[4-7] The evolution of vitiligo is not easy to predict. However, 2 states can be described: the active state and the stable state.[8]

Abbreviations used:

ASDB:	amelanotic with sharply demarcated borders
HPDB:	hypomelanotic with poorly defined borders
RCM:	reflectance confocal microscopy
VETF:	Vitiligo European Task Force

Clinical, histologic, and biological methods have been used in attempts to identify markers to allow prediction of the probable course in individual patients, with their own limitations. However, in the majority of cases, the evaluation of the stability status of vitiligo was the essential prerequisite. There

From Department of Dermatology, Mohammed V University in Rabat, Ibn Sina University Hospital,[a] and Pigmentary Disorders Outpatient Clinic, Hospital Saint-André, Bordeaux.[b]
Funding sources: None.
Conflicts of interest: None declared.
Accepted for publication December 23, 2016.
Reprints not available from the authors.
Correspondence to: Laila Benzekri, PhD, Department of Dermatology, Mohammed V University in Rabat, Ibn Sina University Hospital, Res. Nassim Riad, Av. Mehdi Ben Barka, Im.3, no. 6, Hay Riad, Sect. 8, 10100 Rabat, Morocco. E-mail: benzekrilaila@yahoo.fr.
Published online February 25, 2017.
0190-9622/$36.00

http://dx.doi.org/10.1016/j.jaad.2016.12.040

are several existing clinical approaches to determining the status of vitiligo, these approaches include: first history taking on the onset of new lesions and on the extension of pre-existing lesions from 1 to 2 years,[9,10] second at the time of examination on positivity of Koebner phenomenon,[11] third on high VIDASCORE (Vitiligo Disease Activity Score),[12] and fourth on negativity of minigrafting test without any repigmentation.[13] But these evaluations of the activity status of vitiligo are imprecise (patients often forgot the date of the onset of lesions), nonimmediate, and time-consuming. The assessment of some biochemical and ultrastructural parameters related to the autoimmune hypothesis,[14-16] melanocytorrhagy hypothesis,[17,18] neural hypothesis,[19] or oxidative stress[20,21] are not useful in daily practice. So far, the most reliable data were provided by histologic studies of the edge and more recently by in vivo reflectance confocal microscopy (RCM) of the perilesional skin.[22] In active compared with stable lesions, we can observe the following with the help of these methods: first, a progressive loss of pigment and melanocytes; second, a more prominent inflammatory reaction at the edge (including $CD3^+$, $CD4^+$, $CD8^+$ T-lymphocyte infiltration in the epidermis and dermis)[23-26]; and third, absence of melanocyte detachment.[2] In all these methods, the percentage chance of progression has never been evaluated. It was only reported that some changes are more prominent in the skin of active vitiligo than in stable vitiligo. If the histologic methods[27,28] can rapidly give the most reliable parameters, they are unfortunately invasive. RCM is a new imaging tool able to examine lesional skin noninvasively and determine immediately the activity levels of vitiligo lesions.[22] RCM is not, however, widely available before selecting a therapeutic approach. So a rapid clinical tool that does not require training or specialized equipment would be attractive. In the current study, we tried for the first time, to our knowledge. to find good association between clinical features and histologic and immunohistologic findings, which might allow with good reliability to clinically differentiate stable from active vitiligo.

CAPSULE SUMMARY

- The clinical course of vitiligo is difficult to predict.
- The hypomelanotic appearance of vitiligo lesions with poorly defined borders was found to be associated with active status.
- This clinical tool may be useful for assessing vitiligo activity.

METHODS

This cross-sectional prospective study was performed over 1 year with the approval of the Mohammed V University Ethics Committee, Rabat, Morocco. Informed consent was obtained from all patients before inclusion.

Clinical blind assessment and disease activity

All patients recruited for this study previously received various medical treatments without success and were seeking surgical treatment of 1 or 2 patches. Patients stopped treatments for at least 1 year to avoid a possible influence of such treatments on vitiligo state. We recruited patients with nonsegmental vitiligo without any treatment between the 2 visits. Subjects with segmental vitiligo and a history of immunosuppression were excluded. Patients were systematically examined both under daylight and under a Wood's lamp (Verre et Quartz, Bussy-Saint-Georges, France). Under Wood's light, analysis of the concentric zones of different colors was performed as follows: we determined for each lesion the type of color arrangement with 2 colors (pigmented and achromia areas or pigmented and hypochromia areas) or the arrangement with 3 colors (pigmented, hypochromia, and achromia). After careful examination of the center of the macule and the edges, each vitiligo lesion was classified as either ASDB or HPDB as previously described[3] (Fig 1). The Vitiligo European Task Force (VETF) scoring system of the total surface at baseline was used (rule of nine). Serial digital photographs of the full body and of each lesion were taken at the first visit and after 1 year in the same setting with respect to patient positioning, background, lighting, and camera setting. A single biopsy was performed at the junction of depigmented and pigmented areas of 1 nonsun-exposed lesion only at the first visit to assess the absence or presence of inflammatory infiltrate in the dermis and epidermis at the edge. To determine if vitiligo lesions were stable or progressing, all patients were examined and photographed 1 year after their first visit as recommended by the VETF and the Indian Association of Dermatologists and Venereologists Task Force. Serial photographs taken at the end of the study revealed the stability or the extent of the disease. The assessment of clinical appearance was blinded with respect to whether vitiligo was stable or active. With the VETF scoring system, 0 indicates stable disease and +1 indicates additional patches in a given area or demonstrated