Journal of the Turkish Academy of Dermatology
eISSN 1307-394X

Case Report DOI: 10.6003/jtad.16104c1

Development of Pigmented Macules During Vitiligo Treatment with Vitix® Gel

Esra Adışen, MD, Selda Ünal, MD, Murat Orhan Öztaş, MD, Mehmet Ali Gürer, MD

Address: Gazi University Faculty of Medicine, Department of Dermatology, Ankara, Turkey
E-mail: eozsoy@gazi.edu.tr
** Corresponding Author:* Dr. Esra Adışen, Gazi University Faculty of Medicine, Department of Dermatology, Ankara, Turkey

Published:
J Turk Acad Dermatol 2016; **10 (4)**: 16104c1
This article is available from: http://www.jtad.org/2016/4/jtad16104c1.pdf
Keywords: Antioxidants, hyperpigmentation, topical therapy, Vitix ®, vitiligo

Abstract

Observation: Topical application of preparations containing superoxide dismutase and catalase in the treatment of vitiligo has a recent onset. Till the present time no such adverse reaction has been reported. In this article we present a case who developed pigmented macules with distant localization to depigmented patches during therapy with a plant extract containing superoxide dismutase and catalase (Vitix®). This is the first report of an adverse effect of Vitix® in the English language literature. Patients with facial vitiligo should be warned of this possibility.

Introduction

Vitiligo is a relatively common pigmentation disorder that is characterized by well-circumscribed depigmented macules. The disease is estimated to affect 1-4% of the worldwide. Both sexes are equally affected and it has onset before the age of 20 years. The causes of the melanocyte death remain unclear. Mainly three hypothesis have been proposed about the pathogenesis of vitiligo: neural, self destruction and immune hypothesis [**1, 2, 3**]. However a uniform combined theory which explains the pathogenesis of the disease does not exist. It has been suggested that the changes in the antioxidant enzyme levels may have a part in the pathogenesis of vitiligo [**2, 3, 4, 5, 6, 7, 8**]. These studies resulted in use of antioxidant treatment modalities [**7, 9, 10, 11**]. Recently, a plant extract formulation from Cucumis melo (Vitix®, Assos Pharmaceuticals, İstanbul) has been introduced for the treatment of vitiligo. Herein we present a case who developed pigmented macules inside and out side of the depigmented patches during therapy with Vitix®.

Case Report

A 21 year old female with a four year history of vitiligo attended to our out patient department. She had used many topical corticosteroid preparation without any benefit. On dermatological examination, depigmented patches were distributed on left half of the face, mainly localized in periorbital, forehead and malar region. The patient was given Vitix®. Vitix® was applied directly to the lesions twice daily and expose to sunlight for 30 minutes. She was also instructed to use topical sunscreen SPF 30. After four weeks of therapy, she presented with numerous pigmented macules placed both inside and outside of depigmented area (**Figure 1**). The pigmented macules vary in size, up to 0.5 cm diameter and were non-follicular pigmented lesi-

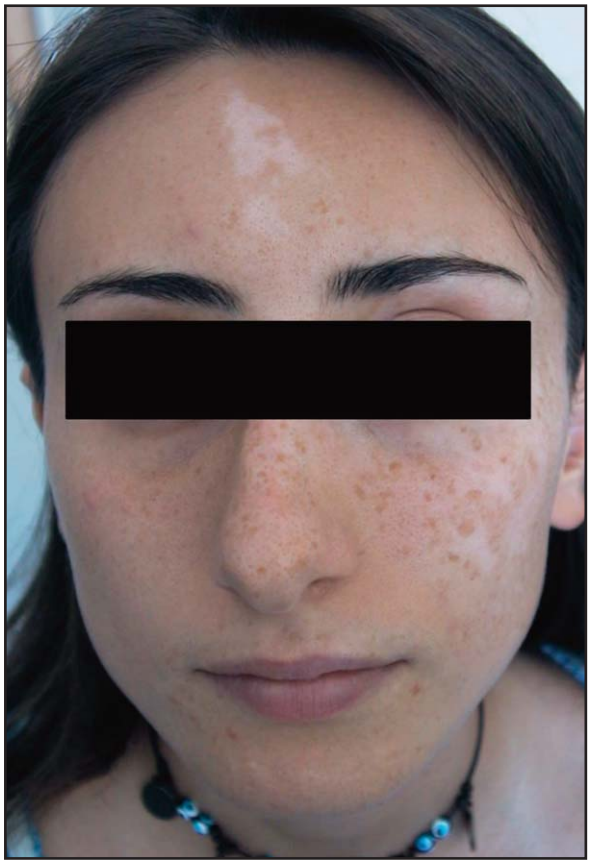

Figure 1. Hyperpigmented macules on face

ons with irregular borders and uniform pigment distribution. The patient gave a history that she had used Vitix® regularly and the macules had started to develop after two weeks of therapy. Their numbers had slowly increased since then. She denied any other topical agent use. Wood lamp examination revealed accentuation of the pigmentation. Dermoscopic examination showed a uniform homogenous pigmentation (**Figure 2**). After discontinuation of Vitix®, she was followed with sunscreen and the pigmentation spontaneously faded over two months.

Discussion

Free radicals occur during several physiological and pathological processes. Free radicals produced in excessive amounts may cause toxic effects described as oxidative damage on tissues. When oxidative stress took part in the organism, the antioxidant enzyme activity begins to increase and prevents the tissue injury. Thus the balance between oxidant and antioxidant systems has critical role in the maintenance of cell survival. Recently many studies have investigated the role of

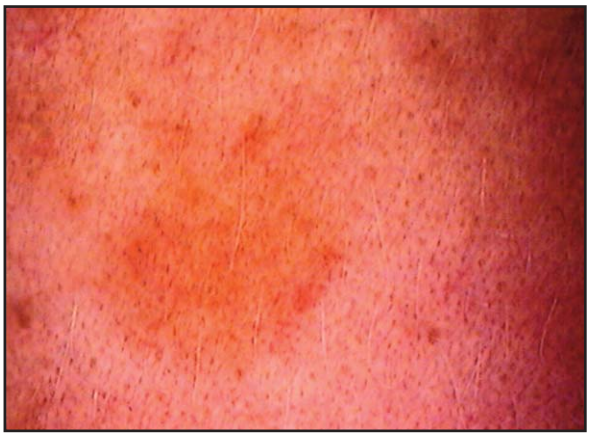

Figure 2. Dermoscopic view of the macules; nonspecific hyperpigmentation pattern

oxidative stress in the etiopathogenesis of vitiligo [**2, 3, 4, 5, 6, 7, 8**]. Lower levels of SOD, catalase and glutathione peroxidase were observed in patients with vitiligo when compared with controls [**2, 3, 4, 5, 6, 7, 8**]. Moreover, extensive amounts of hydrogen peroxide has been observed in vitiligo patients [**6, 7**]. These findings resulted in use of antioxidant therapies in vitiligo treatment. Vitix® gel contains the combination of superoxide dismutase and catalase. English literature lacks sufficient data about this medication but two studies one from France and the other from Russia revealed success with its use in the therapy of vitiligo [**10, 11**]. The effect of this preparation is based on melon's extract rich in antioxidants [**11**]. Though it was proposed that Vitix® had the ability to re-establish the free radicals physiological equilibrium in epidermal cells [**10**], *Schallreuter* et al [**9**] failed to show that Vitix® had the capacity to reduce hydrogen peroxide. In the Russian study, improvement of clinical condition was observed in 56% of patients after six months of therapy [**10**].

Our patient developed pigmented macules during Vitix® therapy for facial vitiligo. The hyperpigmented macules were different from lentigines on dermoscopic examination. They showed non-follicular, uniform, homogenous pigmentation with irregular borders. We evaluated the possible causes of these hyperpigmented macules in our patient. Firstly, we considered the possibility whether these macules could present a new repigmentation pattern of vitiligo. *Parsad* et al [**12**] investigated the types of repigmentation patterns

obtained with various treatment modalities such as topical and oral steroids, topical and systemic psoralen- UVA and calcipotriol in 353 vitiliginous patches of 125 patients. All vitiligo patches showed perifollicular, diffuse, marginal, combined repigmentation patterns in their study. In 55% of lesions, perifollicular pigmentation was the dominant pattern of repigmentation. Furthermore, a clinical trial with Vitix® achieved similar repigmentation patterns of which a majority showed diffuse pigmentation. The hyperpigmented macules distant to vitiliginous areas had not been observed in any study in the literature. Vitix® can cause erythema and mild itching but this kind of side effect was not reported before [**10, 11**]. The lesions were firmly restricted to left half of the face. This location clearly ruled out the impact of sun exposure in the occurrence of lesions. Though we don't know the exact mechanism of their occurrence, it is possible that Vitix® may induce pigmentation in normal skin similar to its effect on vitiliginous patches.

We believe that the lesion occurred as a consequence of Vitix® use, as lesions developed after the agent, they were restricted to the treated area and spontaneously faded with discontinuation of the agent.

In conclusion, we believe that pigmented macules occurring on the entire treated area resulted from the Vitix® use. This is the first report of an adverse effect of Vitix® in the English language literature. Vitix® is a new topical agent in the treatment of vitiligo and we will be able to learn its side effects when it is more commonly used.

References

1. Mosher DB, Fitzpatrick TB, Ortonne JP, Hori Y. Hypomelanosis and hypermelanosis. In: Freedberg IM, Eisen AZ, Wolff K, eds. Dermatolgy in General Medicine. 5th edn. New York: McGraw-Hill Inc, 1999; 945-1017.
2. Koca R, Armutcu F, Altınyazar HC, Gürel A. Oxidant-antioxidant enzymes and lipid peroxidation in generalized vitiligo. Clin Exp Dermatol 2004; 29: 406-409. PMID: 15245542
3. Yıldırım M, Baysal V, İnalöz S, Can M. The role of oxidants and antioxidants in generalized vitiligo at tissue level. J Eur Acad Dermatol 2004; 18: 683-686. PMID: 15482295
4. Passi S, Grandinetti M, Maggıo F, Stancato A, De Luca C. Epidermal Oxidative Stress in Vitiligo. Pigment Cell Res 1998; 11: 81-85. PMID: 9585244
5. Picardo M, Passi S, Morrone A, Grandinetti M, Carlo A, Ippolito F. Antioxidant Status in the Blood of Patients With Active Vitiligo. Pigment Cell Res 1994; 7: 110-115. PMID: 8066016
6. Maresca V, Roccella M, Roccella F, et al. Increased sensitivity to peroxidative agents as a possible pathogenic factor of melanocyte damage in vitiligo. J Invest Dermatol 1997; 109: 310-313. PMID: 9284096
7. Schallreuter KU, Moore J, Wood JM, et al. In vivo and in vitro evidence for hydrogen peroxide accumulation in the epidermis of patients with vitiligo and its successful removal by a UVB activated pseudocatalase. J Invest Dermatol Symp Proc 1999; 4: 91-96. PMID: 10537016
8. Schallreuter KU, Wood JM, Berger J. Low catalase levels in the epidermis of patients with vitiligo. J Invest Dermatol 1991; 97: 1081-1085. PMID:1748819
9. Schallreuter KU, Rokos H. Vitix ® - a new treatment for Vitiligo? Int J Dermatol 2005; 44: 969-970. PMID: 16336538
10. Tsiskarishvili N. Cuprum sulfate and vitix in the treatment of vitiligo in children. Georgian Med News 2005; 7: 48-51. PMID: 15908724
11. Khemis A, Ortonne JP. Study comparing a vegetal extract with superoxide dismutase and catalase activities plus selective UVB phototherapy versus an excipent plus selective UVB phototherapy in the treatment of vitiligo vulgaris. Nouv Dermatol 2004; 23: 45-46.
12. Parsad D, Pandhi R, Dogra S, Kumar B. Clinical study of repigmentation patterns with different treatment modalities and their correlation with speed and stability of repigmentation in 352 vitiliginous patches. J Am Acad Dermatol 2004; 50: 63-67. PMID: 14699367