

Case Report

Vitiligo-Like Hypopigmentation Induced by Imiquimod

Zekayi Kutlubay,* MD

Address: Lazerart Clinics, Division of Dermatology, İstanbul, Turkey.

E-mail: zekayikutlubay@hotmail.com

* Corresponding author: Zekayi Kutlubay, MD, Lazerart Clinics, Division of Dermatology, İstanbul, Turkey.

Published:

J Turk Acad Dermatol 2009; **3** (3): 93302c

This article is available from: <http://www.jtad.org/2009/3/jtad93302c.pdf>

Key Words: hypopigmentation, vitiligo, imiquimod

Abstract

Observations: Imiquimod 5% cream, an immune response modifier, licensed for the treatment of external anogenital warts and superficial basal cell carcinomas. Hypopigmentation associated with topical imiquimod use is an infrequent side effect that is attributed to the drug's Th1 stimulating activity. Herein we report two cases of hypopigmentation which appeared after topical application of imiquimod for genital warts. Dermatologists who are prescribing this drug should be aware of this infrequent side effect associated with topical imiquimod treatment.

Introduction

Imiquimod is an immune response modifier that has been approved for topical treatment of anogenital warts. It enhances both the innate and cellular immune response by acting on a number of cell types [1]. Although it is generally a well-tolerated drug, erythema, flaking, scabbing, edema and excoriation are frequently expected side effects [2]. There have been increasing reports of hypopigmentation associated with the use of imiquimod in the literature.

Here we report two cases of hypopigmentation induced by imiquimod after topical use for genital warts.

Case Report

CASE 1

A 26-year old male presented with warts on the penis and scrotum which existed for 4 months. The warts were cauterized without complications. After the lesions healed without any pigment changes, he started using imiquimod cream three times a week which resulted with

hypopigmented plaques after 4 months (**Figure 1**). He was then prescribed a herbal cream (superoxide dysmutase and catalase), but after 2 months there was no improvement of the hypopigmented plaques. History of vitiligo was lacking for the patient and his family.



Figure 1. Hypopigmented patches on penis and scrotum



Figure 2. Hypopigmented macules on scrotum

CASE 2

A 27-year old male presented with warts on the penile shaft and scrotum. After cauterization without any complications, imiquimod cream was prescribed three times a week. After 3 months he came back with hypopigmented macules at the areas where imiquimod was applied (**Figure 2**). A trial of an herbal cream (superoxide dysmutase and catalase) for 3 months yielded no benefits. He and his family did not have a history of vitiligo.

Discussion

Pigmentary changes associated with imiquimod treatment are listed as possible side effects on the package insert but have not been well described [3]. The *US Food and Drug Administration* records about adverse events of imiquimod in 1997 to November 2003 included 1257 reports of which 68 (5.4%) were pigmentary changes. Of these 68 reports, 43 were reports of depigmentation, 7 of vitiligo, 1 of hypopigmentation and 17 of hyperpigmentation [4].

The mode of action of imiquimod involves stimulation of the innate immune response and the cell-mediated adaptive immunity. Imiquimod binds to the Toll-like receptors (TLR) 7 and 8 which are cell-surface receptors recognizing ligands associated with pathogenic organisms. TLR7 activates the T-helper (Th) 1 response and increases production of pro-inflammatory cytokines mainly IFN- α , TNF- α and IL-12. The stimu-

lation of the Th1 pathway results in a predominantly perilesional CD4⁺ T cell infiltrate and many CD8⁺ T cells. The CD4⁺ cells are stimulated by IL-12 to produce IFN- α and IL-2 which are known to play a role in the pathogenesis of vitiligo [5]. In addition, imiquimod promotes secretion of IL-6, IL-8 and IL-10, which are pro-inflammatory and pro-apoptosis cytokines that can cause vitiligo [6].

In our patients despite discontinuation of imiquimod and utilization of a herbal cream, the hypopigmentation did not improve. Previous case reports also mentioned that the hypopigmented areas remained unchanged despite discontinuation of imiquimod and suggested that trial with macrolide immunomodulators could yield some benefits for the patients [4]. Our patients refused to get further therapy for the hypopigmented areas.

This valuable drug which has significant benefits in the treatment of various dermatological disorders such as warts, actinic keratoses and basal cell carcinomas has an expanding list of indications day by day. As dermatologists prescribing this drug frequently, we should be aware of this bothering side effect and inform the patient about the possibility of hypopigmentation before the treatment.

References

1. Stefanaki C, Nicolaidou E, Hadjivassiliou M, Antoniou C, Katsambas A. Imiquimod-induced vitiligo in a patient with genital warts. *J Eur Acad Dermatol Venereol* 2006; 20: 755-756. PMID: 16836520
2. Senel E, Seckin D. Imiquimod-induced vitiligo-like depigmentation. *Indian J Dermatol Venereol Leprol* 2007; 73: 423. PMID: 18032867
3. Brown T, Zirvi M, Cotsarelis G, Gelfand JM. Vitiligo-like hypopigmentation associated with imiquimod treatment of genital warts. *J Am Acad Dermatol* 2005; 52: 715-716. PMID: 15793538
4. Al-Dujaili Z, Hsu S. Imiquimod-induced vitiligo. *Dermatol Online J* 2007; 13: 10. PMID: 17498429
5. Mashiah J, Brenner S. Possible mechanisms in the induction of vitiligo-like hypopigmentation by topical imiquimod. *Clin Exp Dermatol* 2008; 33: 74-76. PMID: 17979992
6. Dahl MV. Imiquimod: a cytokine inducer. *J Am Acad Dermatol* 2002; 47: 205-208. PMID: 12271278