Dermatology Practical & Conceptual

Imiquimod-Induced Vitiligo: An HLA Case Investigated

Eleni Klimi[1]

1 Department of Dermatology, Thriassio General Hospital, Magula, Athens, Greece

Key words: Imiquimod, HLA, Vitiligo

Citation: Klimi E. Imiquimod-Induced Vitiligo: An HLA Case Investigated. *Dermatol Pract Concept*. 2025;15(4):5797. DOI: https://doi.org/10.5826/dpc.1504a5797

Accepted: April 22, 2025; **Published:** October 2025

Funding: None.

Competing Interests: None.

Authorship: All authors have contributed significantly to this publication.

Corresponding Author: Eleni Klimi MD, PhD Department of Dermatology, Thriassio General Hospital, Magula, Athens, Greece. ORCID: 0000-0001-5113-5640. E-mail: elenik2019@yahoo.com

Introduction

Vitiligo is an autoimmune disease of the skin that manifests with well-circumscribed white patches due to epidermal melanocyte loss [1]. It may appear de novo, but it may also be associated with either thyroid dysfunction or atopy. It may also be the side effect of cancer treatment with immune checkpoint inhibitors. Development of vitiligo is linked with genetic predisposition. Herein we present a case of imiquimod-induced vitiligo that was HLA investigated.

Case Presentation

A 57-year-old male with unremarkable past medical and family history was prescribed three times weekly for four months the application of imiquimod, an interferon inducer that provokes a CD8+ cytotoxic reaction against keratinocytes infected with HPV virus, for the treatment of genital warts. At the beginning of the third month of application, the patient noticed erythema, severe irritation, and ulceration at the site of application. Despite these side effects, the patient completed the treatment, which led to the resolution of the lesions. One and a half months after the end of the treatment, the patient noticed depigmentation of the penis and scrotum without involvement of other areas (Figure 1). The clinical diagnosis was imiquimod-induced vitiligo. The patient persisted in questioning about the nature and the cause of the disease; this motivated an HLA examination. The HLA typing was performed for the HLA-A, -B, and -C antigens using the sequence specific oligonucleotide- polymerase chain reaction (PCR), and for the HLA-DR, DQ the sequence specific primer PCR-based assay. The patient proved positive for the HLA Class I A31, 68, HLA B 49,51, HLA C:0,715. HLA Class II HLA DRB1*11:01, HLADQB1*03,05. HLA-A31 has been associated with vitiligo development in Indian patients [2] and HLA DQB1*03 and DQB1*05 alleles have been associated with vitiligo in Chinese patients as well [3]. In addition, DRB1*11:01 has been associated with the development of thrombocytopenic purpura in Turkey [4]. Several case reports of imiquimod-induced vitiligo have been found in the literature, one of which reporting vitiligo in an one patient the wife of the affected couple and lichen planus

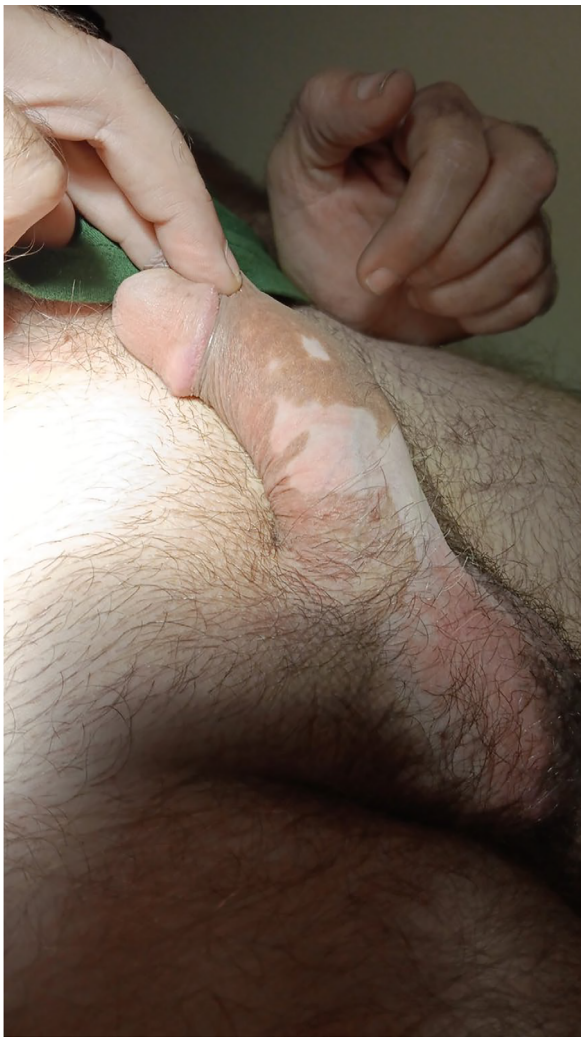

Figure 1. Vitiligo of the penis and scrotum.

in the husband, lichen planus being also a CD8* cytotoxic-mediated reaction suggesting a common immunopathogenic mechanism for both side effects [5]. An association between nivolumab-induced vitiligo, used for metastatic acral melanoma, and HLA Bw4, DRB107:01, and HLA A 02:179 was reported in a recent study in the literature [6].

Conclusion

Vitiligo is a rare side effect following treatment with imiquimod for genital warts. However, it provokes considerable discomfort and anxiety in the affected patients. Therefore, it should be included as a side effect of the medication in the leaflet of the drug. This case is reported to increase awareness about the possible occurrence of imiquimod-induced vitiligo in genetically predisposed individuals. HLA genetic test should be performed before initiation of treatment if suspicion of such genetic predisposition-stigmata of autoimmunity- already exists.

References

1. Wang Y, Li S, Li C. Clinical Features, Immunopathogenesis, and Therapeutic Strategies in Vitiligo. *Clin Rev Allergy Immunol*. 2021 Dec;61(3):299-323. DOI: 10.1007/s12016-021-08868-z. Epub 2021 Jul 20. Erratum in: Clin Rev Allergy Immunol. 2021 Dec;61(3):449. DOI: 10.1007/s12016-021-08884-z. PMID: 34283349.
2. Misri R, Khopkar U, Shankarkumar U, et al. Comparative case control study of clinical features and human leukocyte antigen susceptibility between familial and nonfamilial vitiligo. *Indian J Dermatol Venereol Leprol*. 2009 Nov-Dec;75(6):583-7. DOI: 10.4103/0378-6323.57719. PMID: 19915238
3. Yang S, Wang JY, Gao M, et al. Association of HLA-DQA1 and DQB1 genes with vitiligo in Chinese Hans. *Int J Dermatol*. 2005 Dec;44(12):1022-7. DOI: 10.1111/j.1365-4632.2004.02389.x. PMID: 16409268..
4. Kikili Cİ, Kivanç D, Ortaboz D, et al. Identification of HLA alleles involved in immune thrombotic thrombocytopenic purpura patients from Turkey. *Blood Coagul Fibrinolysis*. 2024 Sep 1;35(6):307-315. DOI: 10.1097/MBC.0000000000001318. Epub 2024 Jul 24. PMID: 39083057.
5. Wang HW, Miao F, Shi L et al. Imiquimod-induced localized vitiligo in wife and lichen planus in husband. *Chin Med J (Engl)*. 2013 Jul;126(13):2593. PMID: 23823845.
6. Gandarillas S, Newland ES, Toppmeyer D, Stephenson R, Denzin L, Dasgeb B. HLA inherence as a potential parameter in checkpoint inhibitor-associated autoimmune adverse event assessment. *Front Med (Lausanne)*. 2024;10:1288844. Published 2024 Jan 8. DOI:10.3389/fmed.2023.1288844. PMID: 38259857.