Topical ingenol mebutate is effective against plantar warts in immunocompromised patients

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Key words: human papillomavirus; immunocompromised patients; ingenol mebutate; plantar warts; renal transplant.

INTRODUCTION

Sustainability of transplanted organs requires lifetime immunosuppressive treatments. Resulting immune deficiency leads to an increased risk of viral infections and virus-induced tumors.[1] Human papillomavirus (HPV) skin infections are the most common in such cases. More than 80% of patients suffer from warts 5 years after the transplant.[2] Unlike lesions in immunocompetent hosts, these warts rarely respond to usual treatments.[3]

We report a case of plantar warts in an immunocompromised patient, resistant to multiple therapies, treated successfully with ingenol mebutate cream.

OBSERVATION

A 30-year-old man with a kidney transplant presented with multiple painful plantar lesions that had been resistant to multiple therapies including cryotherapy, topical 5-fluorouracil, topical imiquimod, topical podophyllin, laser CO_2 treatment, and electrocoagulation under general anesthesia. The patient was receiving daily immunosuppressive therapy including cyclosporine, 175 mg, azathioprine, 100 mg, and prednisone, 10 mg. The physical examination found large, multiple, hyperkeratotic, confluent plaques filled with punctuate black dots at the soles of the feet (Fig 1). The diagnosis of plantar warts in an immunocompromised patient was made on clinical grounds, and polymerase chain reaction performed on a punch biopsy specimen confirmed the presence of HPV types 1 and 2. Given the resistance to classic therapeutic options and the clinical worsening of his condition, a compassionate treatment with ingenol mebutate, 500 μg/g cream for 2 consecutive days was initiated. Significant improvement occurred after the first treatment, and a second and third course of 2 days of treatment at weeks 6 and 12 led to the healing of the lesions (Figs 2 and 3). No recurrence was observed at the 12-month follow-up (Fig 3).

Abbreviation used:

HPV: human papillomavirus

DISCUSSION

The treatment of immunosuppressed patients with plantar warts presents a therapeutic challenge as illustrated in our case in which multiple and various treatments were initiated.[4]

Ingenol mebutate is a diterpene ester, an active molecule derived from the plant *Euphorbia peplus*, known for its properties in cancers.[5] Topical application of ingenol mebutate results in chemoablation through a direct topical apoptotic effect coupled with cellular toxicity, a neutrophil-mediated eradication of lesions induced by the activation of protein-kinase C delta.[6] Localized skin irritation occurs and subsides within days to weeks, and the optimal therapeutic effect can be measured 8 weeks after treatment.

Actinic keratoses represent the current official indication for ingenol mebutate. Lesions of the face and scalp are treated with 150 μg/g ingenol mebutate applied daily for 3 consecutive days, whereas actinic keratoses of the trunk and extremities are treated with 500 μg/g applied for 2 days.[7]

From the Department of Dermatology, Holy Spirit University of Kaslik.

Funding sources: None.
Conflicts of interest: None declared.

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JAAD Case Reports 2018;4:53-4.
2352-5126

https://doi.org/10.1016/j.jdcr.2017.09.029

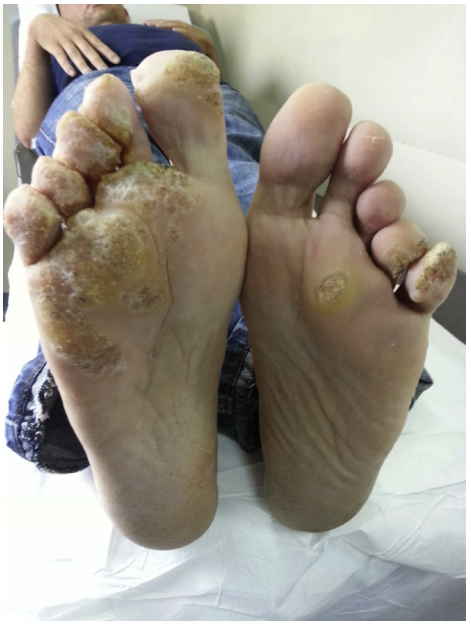

Fig 1. Plantar warts before treatment.

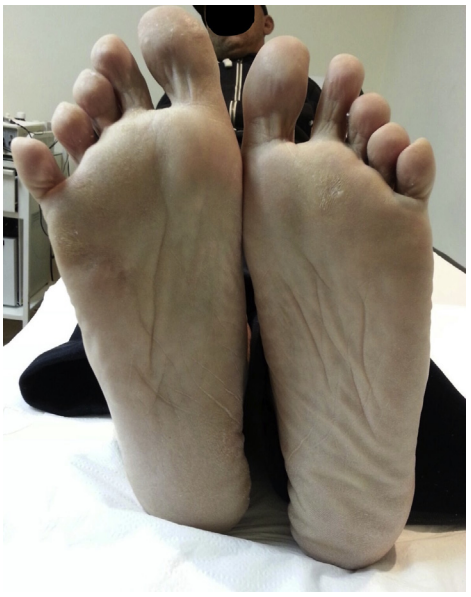

Fig 2. Plantar warts after the second course of topical treatment with ingenol mebutate.

Ongoing clinical trials are currently assessing the efficiency and tolerability of ingenol mebutate in genital warts, and reports are lately emerging about its usefulness in treating cutaneous warts.[8]

CONCLUSION

Our observation represents the first reported case, to our knowledge, of extensive plantar warts in an immunocompromised patient successfully treated with ingenol mebutate and suggests that this agent could be a valuable addition to the therapeutic armamentarium against difficult-to-treat HPV infections. Future observations and large-scale data are needed to further define the role of ingenol mebutate in the treatment of extensive HPV lesions in immunosuppressed subjects.

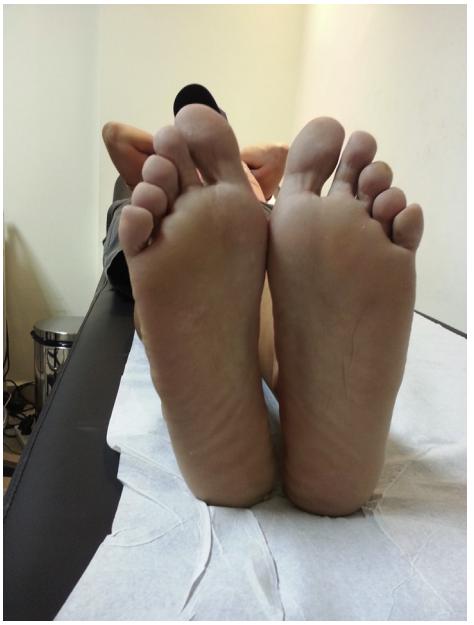

Fig 3. Complete remission at 12-month follow-up.

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