

# Topical Imiquimod for Recalcitrant Facial Flat Warts

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*Imiquimod is a unique topical therapeutic agent useful in the treatment of external genital and perianal warts (condyloma acuminata) in adults. The authors report a case of a 21-year-old woman who experienced complete clearance of recalcitrant facial flat warts after 3 weeks of therapy with topical imiquimod 5% cream.*

Topical imiquimod is a unique therapeutic agent useful in the treatment of cutaneous human papillomavirus infections. Imiquimod exerts its action by stimulating the release of cytokines from local peripheral blood mononuclear cells and keratinocytes. Specific cytokines released include interferon-alpha, tumor necrosis factor, and interleukins 1, 6, and 8. These cytokines stimulate local immune effects that are cytotoxic against the human papillomavirus.

Currently, topical imiquimod 5% cream is indicated for the treatment of external genital and perianal warts (condyloma acuminata) in adults. The authors report a case of a 21-year-old female who experienced complete clearance of recalcitrant facial flat warts after 3 weeks of therapy with topical imiquimod 5% cream.

## Case Report

A 21-year-old female was referred for the evaluation of persistent flat warts on her forehead, present for the preceding 2 years. Many prior attempts at treatment had failed, including topical tretinoin cream, gel, and solution formulations, adapalene gel, 5-fluorouracil cream, cryotherapy with liquid nitrogen, and systemic therapy with oral cimetidine. None of these treatments resulted in the complete resolution of her



FIGURE 1. Flat warts before treatment.

facial skin lesions. Her current method of treatment consisted of topical tretinoin gel, which produced unacceptable irritation. The patient had no underlying medical problems, no allergies to medication, and was not pregnant.

Examination of the skin revealed multiple, widespread, single, and confluent 1 to 2 mm flesh-colored to erythematous, flat-topped papules on the forehead (Figure 1). A clinical diagnosis of recalcitrant facial flat warts was made. The patient expressed emotional distress over the appearance of her face and frustration with the failure of prior therapies. Because this patient did not respond to treatment with multiple conventional agents, an alternative therapeutic approach was attempted.

Topical imiquimod 5% cream was prescribed to be applied to the forehead three times per week (Monday, Wednesday, and Friday) at bedtime. After 1 week of therapy, the patient experienced partial clearing of the flat warts (Figure 2). Immediately prior to clearing of the warts, crusting and scabbing of individual lesions occurred. The patient did not experience pain, burn-

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REPRINTS are not available.



**FIGURE 2.** Partial resolution after 1 week of therapy.



**FIGURE 3.** Complete clearing of warts after 3 weeks of therapy.

ing, stinging, redness, or edema at the treatment site. However, she did report soreness of the musculature of her upper back and posterior cervical region. Additionally, she developed tender submental lymphadenopathy after the first week of therapy. No new side effects were noted after the first week of therapy.

After 2 weeks of therapy, near complete clearing of the flat warts had occurred. The submental lymphadenopathy and myalgias had completely resolved. The patient remained free of any other cutaneous or systemic side effects throughout the remainder of treatment. Complete clearing of all flat warts occurred after 3 weeks of therapy with topical imiquimod 5% cream (Figure 3).

### Comments

Our patient did not respond to multiple conventional therapies. Due to the cosmetic significance of the area involved, we opted against potentially scarring therapies such as electrodesiccation and curettage, and laser vaporization. Pulsed dye laser treatment generally results in significant purpura and can be painful,<sup>1,3</sup> therefore, it

was also deemed a less desirable treatment option.

Topical imiquimod 5% cream is marketed and approved by the Food and Drug Administration (FDA) for the treatment of external genital and perianal warts (condyloma acuminata) in adults.<sup>4,5</sup> Imiquimod is not FDA-approved for the treatment of flat warts. Therefore, its use in this condition is considered “off-label” at this time. Chemically, imiquimod is an imidazoquinolin heterocyclic amine that functions as an immune response modifier.<sup>5,9</sup>

Both flat warts and anogenital warts represent cutaneous infections by various subtypes of the human papillomavirus (HPV). Flat warts are commonly caused by HPV types 3 and 10, while anogenital warts may be caused by a number of HPV types including 6, 11, 16, 18, 31, and 33.<sup>1,2,10</sup>

Imiquimod is not a true antiviral agent; rather, it enhances the body’s immune response to HPV infection. Specifically, imiquimod stimulates local peripheral blood mononuclear cells and keratinocytes to secrete cytokines, including interferon-alpha, tumor necrosis factor, and interleukins 1, 6, and 8.<sup>5,9</sup> These

cytokines stimulate local immune effects that are cytotoxic against HPV without causing the tissue destruction characteristic of other treatment methods.<sup>1-9</sup>

In a published study of topical imiquimod for the treatment of external anogenital warts, the most common adverse event experienced was erythema at the treatment site.<sup>9</sup> Other less commonly experienced adverse events included local erosions, flaking, scabbing, induration, and edema.<sup>9</sup> Although our patient experienced little irritation at the site of application, the agent should be used cautiously. The manufacturer lists systemic side effects including flu-like symptoms, headache, and myalgias to topically applied imiquimod 5% cream.<sup>5</sup> Our patient experienced self-limited myalgias of the upper back and posterior cervical region during the first week of therapy. An adverse effect not previously reported in the literature, but experienced by our patient, was tender submental lymphadenopathy. This effect was also self-limited despite continued topical therapy with imiquimod 5% cream.

Imiquimod represents a unique therapeutic agent in the armamentarium against cutaneous HPV infection. In our patient, the use of topical imiquimod resulted in the rapid clinical resolution of recalcitrant facial flat warts. Overall, the treatment was safe, nonirritating, easy to use, and resulted in an excellent cosmetic outcome. Topical imiquimod may prove to be an effective treatment for other cutaneous HPV infections.

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