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CASE REPORT

Treatment of Recalcitrant Viral Warts with Combination Therapy of Systemic Acitretin and Diphenylcyclopropenone Immunotherapy

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Viral warts are benign proliferations of the epithelium caused by human papilloma virus (HPV) infection. Diverse therapeutic options are available for viral warts, depending on extension and severity of the disease. We report a case of a 19-year-old man who presented with multiple viral warts on hands and feet for 5 years. He was treated at other clinics before visiting our hospital, but there was no improvement. We treated the lesions with a combination therapy of systemic acitretin and diphenylcyclopropenone (DPCP) immunotherapy for 6 months. A significant improvement was observed during the 12th week of therapy. Herein, we report a case of recalcitrant viral warts showing complete regression when a combination therapy of oral acitretin and immunotherapy was administered. **(Ann Dermatol 32(3) 243～246, 2020)**

-Keywords-
Acitretin, Diphenylcyclopropenone immunotherapy, Viral wart

INTRODUCTION

Viral warts are caused by several strains of human papilloma virus (HPV) and have a prevalence of approximately 10%[1]. Among the etiological strains, HPV types 1, 2, and 57 are common causes. HPV 4 and 7 are relatively rare and usually more difficult to treat[2]. Although various treatment modalities are available, treatment of viral warts can be laborious in some cases, and a combination therapy of different treatment modalities can be performed in such conditions. Even though cases have been reported in which systemic acitretin therapy produced satisfactory results for viral warts resistant to other treatment modalities[3], the use of oral acitretin therapy has been limited to date. Herein, we report a case of a 19-year-old man with multiple recalcitrant warts successfully treated with a combination of oral acitretin and diphenylcyclopropenone (DPCP) immunotherapy. We received the patient's consent form about publishing all photographic materials.

CASE REPORT

A 19-year-old man presented with multiple hyperkeratotic papules and plaques located on hands and feet for 5 years (Fig. 1). The lesions were clinically compatible with diagnosis of viral warts. There were nonspecific findings on baseline routine laboratory evaluations. He had no history of constitutional symptoms or immunosuppression and no family history of warts or immunodeficiencies. Previous treatments with cryotherapy and topical 5-fluorouracil and salicylic acid had resulted in minimal response.

The patient started immunotherapy with 0.2% DPCP. However, only mild improvement was observed after 3 months of treatment. Therefore, oral acitretin (20 mg/day) was added to the treatment regimen, and considerable re-

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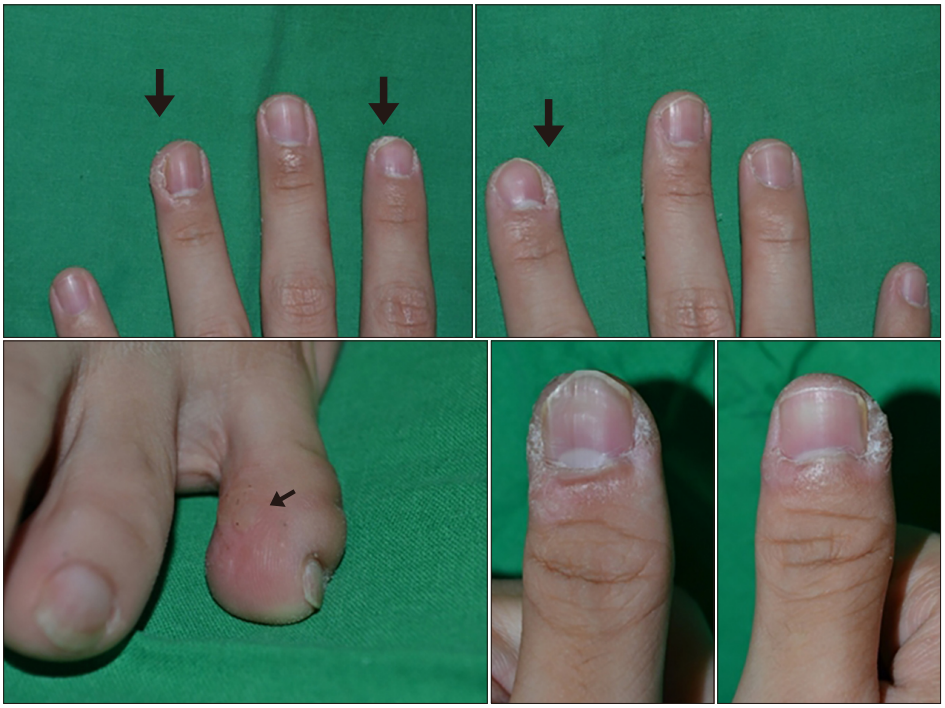

Fig. 1. Warts on hands and feet before therapy (arrows).

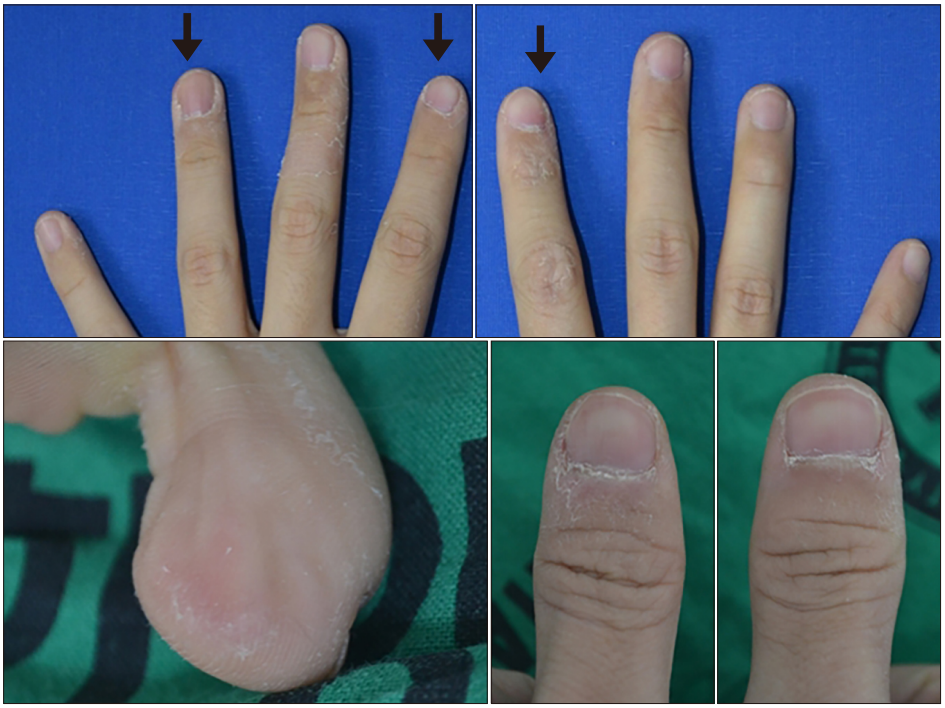

Fig. 2. Warts on hands and feet after therapy (arrows).

gression of the warts was observed after 3 months (Fig. 2). Acitretin was discontinued after 3 months of the additional treatment. Mild dryness was the only side effect that occurred after the start of oral acitretin therapy and was controlled with liberal moisturizing. No signs of recurrence after cessation of treatment have been reported for 3 months.

DISCUSSION

Viral warts are a common skin disease caused by HPV, and there are numerous treatment modalities including cryotherapy, lasers, topical keratolytic and antimitotic agents, and immunotherapy. Despite such diverse treatment options, no single treatment is completely effective

due to the lack of specific antiviral medications against HPV infection. Consequently, different treatment modalities may be combined to treat viral warts[2].

Treatment of viral warts can be especially difficult in patients with intractable lesions. Oral retinoids have produced successful results in some cases of recalcitrant viral warts[4]. In a previous case report, considerable improvement was observed after administration of 1 mg/kg/day of acitretin for 2 months in a 25-year-old man with multiple recalcitrant warts on both hands[5]. Although the lesions recurred after acitretin was discontinued, improvement was again observed after restarting the therapy. In another report, dramatic clearance of periungual warts, which had lasted for approximately 11 years, occurred in a 46-year-old woman[3]. The patient was treated with 25 mg/day of acitretin for 3 months, followed by treatment every other day. Clinical remission was maintained for approximately 6 months after discontinuing acitretin. In another case report by Monastirli et al.[6], the successful treatment of intractable and extensive viral warts was described in a patient with low-grade B-cell small lymphocytic lymphoma using oral isotretinoin therapy. There was no evidence of recurred lesions.

Acitretin belongs to second-generation retinoids. The retinoids have a wide range of various biological effects on cells by exerting influence on the regulation of cell growth and differentiation. They promote the differentiation of keratinocytes and inhibit epidermal hyperplasia. These mechanisms are considered to suppress viral replication and assembly within infected keratinocytes. In a previous study, an inverse relationship was found between retinoid concentration and HPV-DNA level in infected cells[7]. This result further supports the negative influence of retinoids on viral replication. Retinoids can also show potent immunomodulating effects and have apoptotic activity[8], regarded as a factor that can induce therapeutic results.

DPCP immunotherapy is another treatment option that can be considered for recalcitrant viral warts. A number of clinical trials have proved efficacy of this treatment modality. In a previous open-label study, immunotherapy with DPCP was proved to be an effective and well-tolerated option for the treatment of recalcitrant warts[9]. In a case report regarding disseminated facial warts, DPCP appeared to be a valuable and safe treatment for resistant and chronic facial warts[10].

It is assumed that DPCP immunotherapy works for the treatment of warts by inducing a type IV hypersensitivity reaction[11]. This cell-mediated response is believed to act against a complex of contact agent hapten bound to protein of viral or human origin. It leads to the regression of wart after application of contact agent, triggering spontaneous wart clearance.

Considering different mechanisms of acitretin and DPCP immunotherapy, we thought that combining two therapies could produce synergistic effects. Although no literature regarding acitretin and DPCP combination therapy has been reported so far, there was a performed study about the combined therapy of acitretin and Candida antigen immunotherapy[12]. The study revealed the superiority of the combination therapy over either agent alone in treating recalcitrant warts. Both Candida antigen and DPCP therapy belong to contact immunotherapy and their mechanisms of action are quite similar obviously. On this basis, we supposed that clinical improvement in our case could be attributed to the combined effects of both acitretin and DPCP.

The limitation of our case is that the patient had already received DPCP immunotherapy for 3 months before the combination therapy, which implies that the observed therapeutic effect could have been influenced by this prior treatment. However, considering that the duration of DPCP immunotherapy was sufficient to take effect, it is much more likely that clinical improvement was the result of a combination therapy.

In conclusion, the successful treatment of recalcitrant viral warts using a combination therapy of systemic acitretin and DPCP immunotherapy was described in our case. The patient showed significant clinical response to the combination therapy and no major side effects. A combination therapy of acitretin and DPCP should be considered a promising treatment modality for management of viral warts recalcitrant to other conventional therapies.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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