

THERAPEUTIC HOTLINE

Complete remission of recalcitrant genital warts with a combination approach of surgical debulking and oral isotretinoin in a patient with systemic lupus erythematosus

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ABSTRACT: Genital warts in immunocompromised patients can be extensive and recalcitrant to treatment. We report a case of recalcitrant genital warts in a female patient with systemic lupus erythematosus (SLE), who achieved complete remission with a combination approach of surgical debulking and oral isotretinoin at an initial dose of 20 mg/day with a gradual taper of dose over 8 months. She had previously been treated with a combination of topical imiquimod cream and regular fortnightly liquid nitrogen. Although there was partial response, there was no complete clearance. Her condition worsened after topical imiquimod cream was stopped because of her pregnancy. She underwent a combination approach of surgical debulking and oral isotretinoin after her delivery and achieved full clearance for more than 2 years duration. Oral isotretinoin, especially in the treatment of recalcitrant genital warts, is a valuable and feasible option when other more conventional treatment methods have failed or are not possible. It can be used alone or in combination with other local or physical treatment methods.

KEYWORDS: genital warts, isotretinoin, SLE

Introduction

Genital warts are common and are caused by human papillomavirus (HPV) infection. There is a greater prevalence of HPV infection among female patients with systemic lupus erythematosus (SLE) compared with controls (11.8% vs. 7.3%) (1). This is probably attributed to the immunosuppressed

state caused by immunosuppressants used in SLE and the disease itself (2). Viral warts in immunosuppressed or immunocompromised patients tend to have extensive involvement and be recalcitrant to treatment (3). We report a case of recalcitrant genital warts in a female patient with SLE, who achieved complete remission with a combination approach of surgical debulking and oral isotretinoin.

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Case report

A 27-year-old Chinese woman with a 4-year history of SLE with vasculitic rash, synovitis, and Class

IV/V lupus nephritis presented to our tertiary dermatology outpatient clinic with a 3-month history of perianal warts in July 2007. She was receiving oral prednisolone and hydroxychloroquine for her SLE treatment and had previously received eight doses of pulsed intravenous cyclophosphamide therapy for her lupus nephritis from August 2006 to April 2007. She had started to develop perianal warts since she began her monthly doses of intravenous cyclophosphamide. She was switched to oral azathioprine in April 2007 subsequently in view of her worsening perianal warts and decreasing total white cell counts.

Twice weekly topical imiquimod cream to the perianal warts was initiated as she initially could not come regularly for liquid nitrogen therapy. However, her condition did not improve after 2 months of topical therapy. She was subsequently started on weekly liquid nitrogen therapy for almost a year from August 2007 to July 2008. Her perianal warts were still recalcitrant and a combination approach of two weekly liquid nitrogen therapy and five times a week topical imiquimod therapy was adopted. There was good control with this combination approach but her perianal warts did not resolve completely. Topical imiquimod therapy had to be stopped when patient became pregnant. Throughout her pregnancy, she only had two weekly liquid nitrogen therapy. There was poor response and her genital warts were getting more extensive in terms of both size (measuring up to 7 cm) and area of involvement (FIG. 1).

Decision was made to start a combination approach of staged surgical debulking and oral isotretinoin after she had a successful cesarean delivery in May 2009. She underwent debulking surgical excision of her perianal warts over three sessions in May 2009, July 2009, and December

2009. She was also started on oral isotretinoin at a dose of 20 mg/day from June 2009 to December 2009 and reduced further to a dose of 20 mg every other day from December 2009 to February 2010, with the advice of its potential side effects and need to avoid being pregnant. She was not breastfeeding and had no plans for future pregnancies. She achieved good response with clearance of all genital warts and good healing of surgical excision site in March 2010 (FIG. 2). At the same time, the control of her SLE was satisfactory and she was only on oral prednisolone and hydroxyquinone with discontinuation of oral azathioprine in October 2009. She is currently still undergoing regular 6 monthly follow-up for the past 2 years and there has not been any recurrence of her genital warts.

Discussion

HPV infection is more common in SLE patients (1). They are often immunosuppressed secondary to the disease or the treatment. Immunosuppressed individuals may not be able to mount an adequate T cell-mediated immune response to the virus (4). This is observed in patients with HIV (5) and kidney transplant patients (6). In one study, it has been shown that cutaneous warts are more common among kidney transplant patients receiving oral azathioprine when compared to those receiving oral mycophenolate mofetil (6). Our patient started to have perianal warts after pulsed intravenous cyclophosphamide therapy and she received azathioprine subsequently for her SLE. This can potentially explain her extensive recalcitrant genital warts.

Treatment of genital warts in immunocompromised patients can be challenging because the



FIG. 1. Extensive genital wart at the perianal area.



FIG. 2. Clearance of the perianal warts.

genital warts are often extensive, recurrent, and recalcitrant to treatment. This can pose significant morbidity in such patients. Topical imiquimod cream has been reported to be useful in the treatment of recalcitrant warts in immunosuppressed individuals (4). Up to 36% of patients with recalcitrant warts were shown to benefit from topical imiquimod in a recent study. However, our patient in this case did not achieve a complete clearance of her warts despite a combination approach of topical imiquimod and liquid nitrogen therapy. Furthermore, topical imiquimod had to be discontinued because of her pregnancy. Other immunoadjuvant treatments such as photodynamic therapy, diphenylcyclopropenone, and intralesional Bacillus Calmette–Guérin were also not suitable in view of her pregnancy.

Most conventional treatments for genital warts are methods that act locally. Some believe that the use of an oral systemic agent may have a more effective control of the warts and provide a solution to unsatisfactory response rates and high recurrence rates in the treatment of genital warts (7). In our patient, a prior treatment course with an immunoadjuvant agent (topical imiquimod) and local treatment (liquid nitrogen therapy) was unsuccessful. In view of its size and involvement, decision was made to combine surgical debulking with an oral systemic agent after her delivery instead of topical treatments. Oral systemic agents such as cimetidine, retinoids, and zinc sulfate have been reported in the treatment of warts, but there has been limited evidence (8). Cimetidine is an H₂-receptor antagonist and its use as an oral immunomodulator agent in the treatment of warts has been reported. However, evidence for its effectiveness is still limited. A recent systematic review reported that pooled data from four placebo-controlled trials did not reveal any statistical difference in treatment cure rates between treatment and control arms (8).

Oral isotretinoin was started, although there has been conflicting evidence with the use of oral isotretinoin in the treatment of recalcitrant genital warts. Several studies have demonstrated benefit of oral isotretinoin in the treatment of recalcitrant or severe genital warts (7,9,10). One study had showed good treatment results with shorter treatment duration with the use of combination of interferon alpha-2a and oral isotretinoin (10). However, one study had reported no response with the use of oral isotretinoin when compared to the use of systemic interferon alpha-n1 (11). It is not clear how retinoids have a beneficial effect in the treatment of HPV infection. It is, however,

known that isotretinoin affects keratinocyte differentiation and proliferation, while HPV replication and assembly of the virus requires keratinocytes to be in an advanced rate of differentiation (7). By altering keratinization, isotretinoin is able to downregulate viral replication. Our patient responded very well to a combination treatment of oral isotretinoin with surgical debulking of the warts. Her response could possibly have been aided by the stopping of azathioprine during the latter half of the combination treatment. She has since remained free of recurrence of her genital warts during her follow-up for more than 2 years.

Oral isotretinoin, especially in the treatment of recalcitrant genital warts, is a valuable and feasible option when other more conventional treatment methods have failed or are not possible. It can be used alone or in combination with other local or physical treatment methods. However, it is important to be mindful of its possible side effects and precaution in its use among child-bearing age women.

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