



Photodynamic Therapy for Condyloma Acuminatum and Cervical Intraepithelial Neoplasia Grade I in a Young Female Patient with Systemic Lupus Erythematosus: A Case Report

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Abstract: Condyloma acuminatum (CA), commonly known as anogenital warts, is a prevalent sexually transmitted disease primarily caused by low risk human papillomavirus (HPV) types 6 and 11. This case report outlines the successful use of photodynamic therapy (PDT) to treat extensive condyloma acuminatum in a young female patient with systemic lupus erythematosus (SLE) undergoing immunosuppressive treatment. The patient also had cervical intraepithelial neoplasia grade I. Carbon dioxide laser treatment were initially used to remove some surface warts, followed by PDT, resulting in satisfactory outcomes. After seven sessions, the warty growths were successfully removed. Interdisciplinary collaboration, involving rheumatology, gynecology, and dermatology, facilitated comprehensive management. This case highlights the efficacy and safety of PDT in treating condyloma acuminatum and suggests its potential as an alternative treatment for young SLE patients with similar conditions.

Keywords: condyloma acuminatum, photodynamic therapy, systemic lupus erythematosus

Introduction

Condyloma acuminatum (CA), also known as anogenital warts, is a common sexually transmitted disease caused by low risk human papillomavirus (HPV) types 6 and 11.¹ Systemic lupus erythematosus (SLE) is recognized as a chronic autoimmune disorder that predominantly impacts young women. The activation of autoreactive T and B cells occurs, along with the release of pro-inflammatory cytokines, which may be associated with an elevated risk of certain cancers. Additionally, immunosuppressive therapies employed to treat SLE can lead to a diminished immune response against malignant tumors, resulting in increased susceptibility to infections among these patients.² Increased susceptibility to HPV infection has been reported in patients with systemic lupus erythematosus (SLE) compared to the general population. The heightened risk of HPV infection is also associated with the immunosuppressive therapy administered to SLE patients.³ Herein we report a young female with SLE undergoing immunosuppressive therapy in whom photodynamic therapy (PDT) successfully treated CA involving the cervix, external genitalia, anal canal, and perianal region, while improving the grade I cervical intraepithelial neoplasia (CIN I).

Case Report

An 18-year-old female presented with extensive warty growths around the anus and in the genital area of 4 months duration, without any associated itching or pain. The patient had a male partner with whom she engaged in sexual intercourse several times within the year prior to the onset of genital warts. There is no history of other adverse habits. The physical examination reveals multiple cauliflower-like growths in the vulvar and perianal regions, with a rough surface, some of

which are fused into plaque-like lesions. The patient reported fevers and butterfly erythema on the face 5 months prior to visit. She was diagnosed elsewhere with SLE based on laboratory testing. Initially, she was treated with rituximab at another hospital. The size and number of warty lesions subsequently increased. The patient was admitted to the Rheumatology Department at our hospital because of poor SLE control. Upon hospital admission, the following laboratory findings were recorded: anti-double-stranded DNA level, 294 IU/mL; anti-nuclear antibody titer, 1:1,280; anti-Smith (Sm) antibody, positive; anti-nRNP antibody, positive; anti-SSA antibody, positive; anti-histone antibody, positive; complement C3 level, 0.16 g/L; complement C4 level, 0.02 g/L; white blood cell count, $2.7 \times 10^9/L$; hemoglobin level, 113 g/L; erythrocyte sedimentation rate, 53 mm/h; alanine aminotransferase level, 111.9 U/L; aspartate aminotransferase level, 70.8 U/L; immunoglobulin G level, 28.40 g/L; immunoglobulin A level, 4.28 g/L; 24-hour urinary protein level, 0.56 g/24 h; and direct Coombs' test, positive. Despite receiving three cycles of glucocorticoids combined with belimumab and hydroxychloroquine, the CA lesions continued to grow. The belimumab therapy was therefore discontinued and glucocorticoids with hydroxychloroquine and iguratimod therapy was initiated. Notably, the extensive CA involving external genitalia was a treatment challenge. After consultation with the Dermatology Department, a physical examination revealed multiple wart-like growths in the external genitalia, cervix, and perianal region, with diameters ranging from 2–30 mm (Figure 1A, C). Cervical testing revealed HPV-DNA positivity for types 11, 31, and 59 with an HPV E6/E7 mRNA expression of 22.031

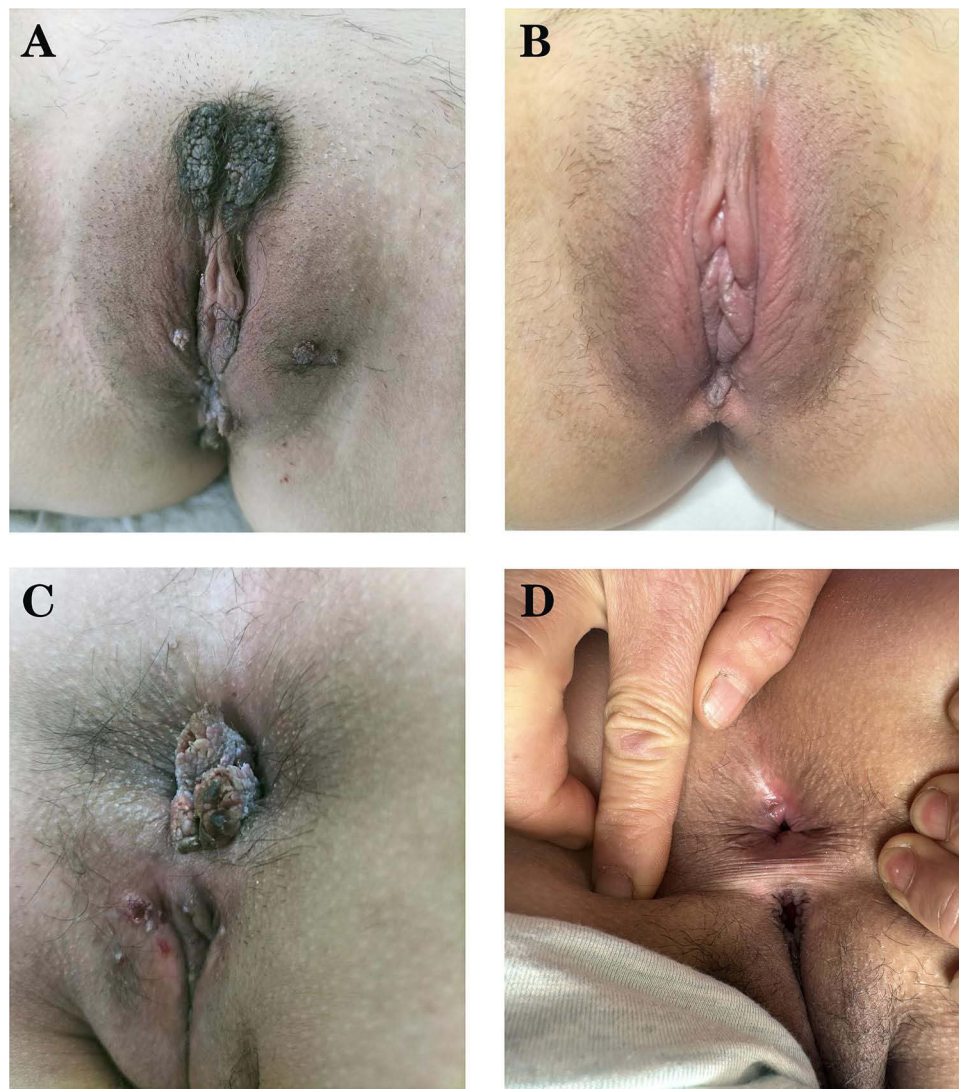


Figure 1 Images before and after photodynamic therapy for condyloma acuminatum. (A,C) Cauliflower-like condyloma acuminatum on the external genitalia and perianal area before photodynamic therapy. (B,D) Complete eradication of warty growths on the external genitalia and perianal area after 7 sessions of photodynamic therapy.

copies/mL. The cervical ThinPrep[®] test (TCT) suggested atypical squamous cells of undetermined significance. A gynecologic examination and cervical biopsy were performed, which showed positive acetic acid and negative iodine staining tests (Figure 2A, D). A histopathologic examination of the biopsy indicated grade I cervical intraepithelial neoplasia (Figure 2G). Furthermore, DNA triplex testing for urinary and genital tract infections yielded a positive result for *Ureaplasma urealyticum* DNA. Considering the desire for fertility preservation and an aesthetically pleasing outcome, PDT emerged as the primary approach. Carbon dioxide laser ablation was performed on the larger warts before PDT, which facilitated infiltration of the photosensitizer, 5-aminolevulinic acid (ALA), thereby enhancing the efficacy of PDT, potentially reducing the required medication dosage, and alleviating the economic burden on patients. After cleansing the treatment area, a 20% ALA gel (Shanghai Fudan Zhangjiang Bio-Pharmaceutical Co. Ltd., Shanghai, China) was applied to the lesion and the surrounding 1 cm, then covered with an opaque film. Following 3 h of light avoidance, the area was treated with red light irradiation (80–100 J/cm²; 633 nm for 20 min).⁴ The patient experienced a mild burning sensation during treatment, with a pain score of 5 on the Visual Analogue Scale. The patient had an increased vaginal discharge 1–3 days after each treatment. ALA-PDT was administered once weekly or every 2 weeks for a total of seven sessions with successful removal of anogenital warts confirmed by physical examination (Figure 1B, D). The *U. urealyticum* infection was treated with sustained-release clarithromycin tablets (0.5 g orally daily) and HPV-DNA testing was performed 3, 6, and 12 months post-treatment. The cutaneous lupus lesions gradually improved and she was regularly followed in the

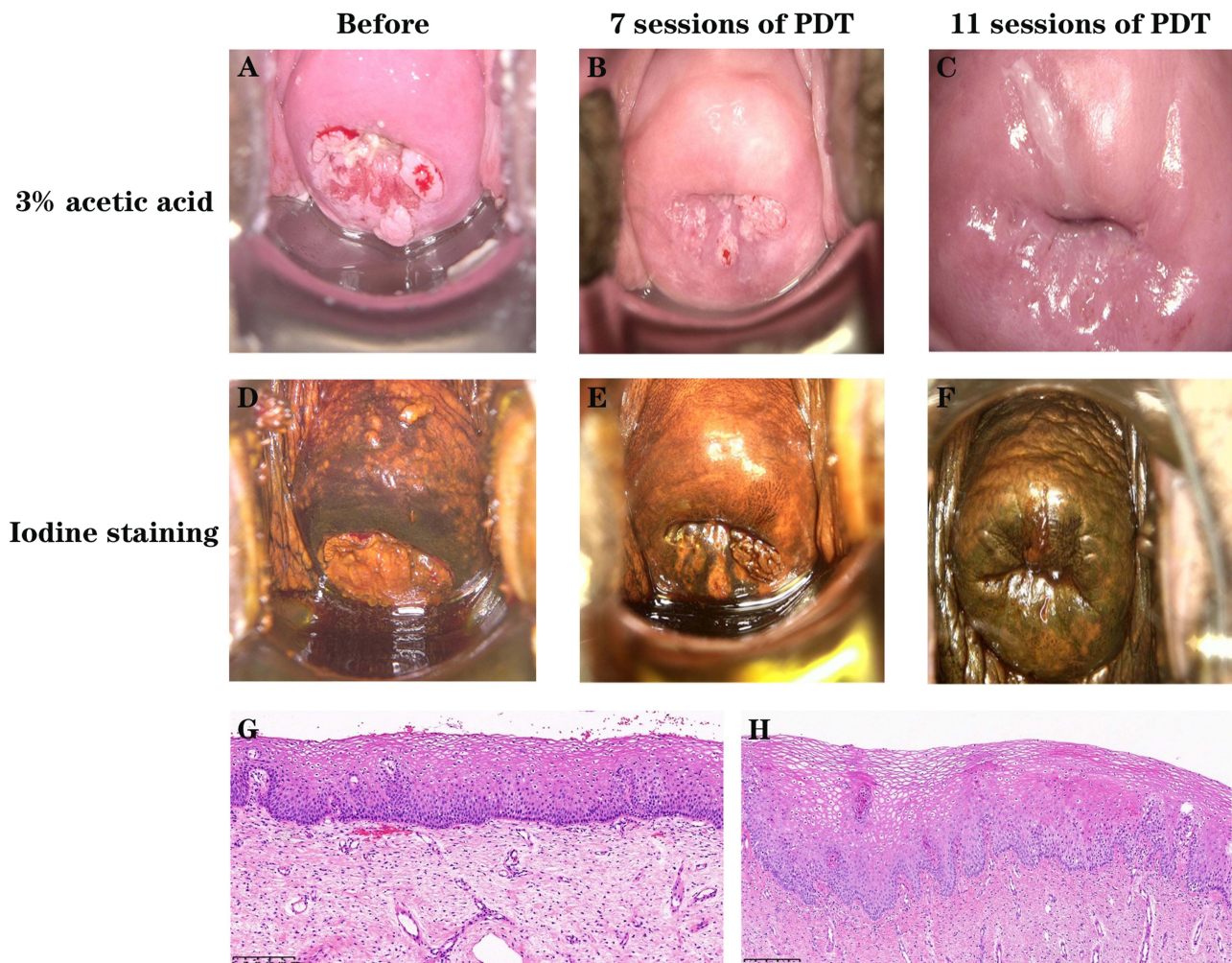


Figure 2 (A-F) Colposcopy images and of a patient with both CA and CIN before PDT treatment and at the 7th and 11th PDT. (A-C) Images of 3% acetic acid test. (D-F) Images of iodine staining test. (G-H) Before and after 7 sessions of PDT treatment in the patient, the Hematoxylin and Eosin (H&E) staining of cervical biopsy pathology indicates grade I cervical intraepithelial neoplasia.

Rheumatology and Dermatology Departments at our hospital. After 12 months, HPV-DNA typing was positive for type 6 and negative for other types. HPV E6/E7 mRNA was negative. TCT was negative for intraepithelial lesions or malignancy and Mycoplasma testing was negative. To better evaluate the patient's cervical condition and due to the remaining HPV type 6 positivity, colposcopy and biopsy were performed, which revealed a mostly smooth cervix with a cluster of acrocyanotic warts in the 3–5 o'clock position (Figure 2B, E). Biopsy of the deeper cervical canal area was performed, indicating persistent grade I cervical intraepithelial neoplasia (Figure 2H). A routine examination without colposcopy might have missed this lesion, then the warty lesions on the cervix were scraped. Given the ongoing need for long-term glucocorticoid and immunosuppressive or immunomodulatory drugs, such as iguratimod, an additional four sessions of PDT were recommended. Following completion of the initial treatment course, a repeat colposcopy was performed due to the patient's unique circumstances, which revealed complete clearance of the warts. (Figure 2C, F) The patient continued to be monitored with no recurrence of warts in the anogenital or vulvar areas for 14 months. The SLE treatment regimen currently includes prednisone acetate tablets (7.5 mg orally daily), iguratimod tablets (25 mg orally, twice a day), and hydroxychloroquine tablets (0.2 g orally, twice a day), ensuring stable control of SLE.

Discussion

PDT is an emerging treatment technique that utilizes the photodynamic properties of photosensitizers to selectively destroy localized pathologic tissues. PDT selectively induces cytotoxic effects on malignant cells through three key components: photosensitizer, oxygen, and a light source. The process involves applying the photosensitizer to the targeted area and irradiating it with light corresponding to the sensitizer's absorption spectrum. In the presence of oxygen, this triggers photochemical reactions that cause tumor cell death, damage to the microvascular system, and a localized inflammatory response.⁵ First-generation photosensitizers, such as Photofrin, are characterized by low chemical purity, poor tissue penetration, and excessive accumulation in the skin. The development of second-generation photosensitizers has addressed these issues to some extent, leading to a reduction in photosensitivity reactions. One notable example is 5-aminolevulinic acid (ALA). ALA is a prodrug that converts to the active photosensitizer protoporphyrin IX. It can be administered topically or orally for various clinical applications, making it a widely used second-generation photosensitizer.⁶ Compared to uninfected cells, HPV-infected cells undergo rapid proliferation and selectively accumulate protoporphyrin IX. Upon activation by light, protoporphyrin IX is converted into reactive oxygen species (ROS), which subsequently react with various biomolecules within the HPV-infected cells. This interaction triggers a series of cytotoxic responses, ultimately leading to cell death.⁷ Pain and discomfort during irradiation are the main adverse reactions, while erythema and edema typically resolve quickly within a few days. Long-term adverse effects, such as pigment changes, scarring, or contact dermatitis, are rare.⁸ PDT has received clinical approval for treating numerous diseases.⁵ The traditional treatments for CA include topical medications, such as podophyllin resin and imiquimod, and surgical and destructive therapies, such as cryotherapy and carbon dioxide laser. However, these methods can only remove surface warts and cannot eliminate a latent HPV infection, which may be a potential source of lesion recurrence. In contrast, ALA-PDT presents specific advantages in treating latent HPV infections.⁹ Wang et al¹⁰ achieved a pathologic regression rate of 90.01% in 55 patients 21–45 years of age with low grade intraepithelial lesions who were treated with PDT. The patient reported herein had SLE and presented with CA and CIN caused by an HPV infection. The warty lesions were difficult to control and recurred during immunotherapy. For such patients with autoimmune diseases prone to multiple warts and concurrent cervical lesions, traditional treatment methods are suboptimal and may cause significant damage, especially in young women. We used a combination approach involving carbon dioxide laser therapy and PDT. The current case demonstrated the efficacy and safety of PDT in treating CA in SLE patients. The 12-month follow-up evaluation revealed incomplete reversal of grade I CIN and persistence of HPV infection, suggesting potential hidden lesions, such as in the cervical canal in females, urethra in males, and anal canal. Therefore, a thorough examination and timely detection of lesions in these areas are crucial. For such unique case, PDT can be repeated and combined with other treatment modalities to achieve individualized therapy. Moreover, interdisciplinary collaboration is essential for comprehensive management. In this case, a multidisciplinary approach involving rheumatology, gynecology, and dermatology was adopted, benefiting the patient. In summary, for young women with recurrent CA and CIN, especially those of childbearing age, PDT may be the preferred alternative treatment,

particularly for patients with unique immunologic conditions, allowing for a tailored therapeutic approach with combination therapies.

Ethics Approval and Informed Consent

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

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Disclosure

All authors declare that there is no conflict of interest in this work.

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